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Dr. Shanti Ghosh, Past President of IAP passed away to her heavenly abode on Saturday morning, August 16, 2014.

For many years Dr. Shanti Ghosh headed the pediatric department at Safdarjung Hospital, one of the largest tertiary level multi-disciplinary healthcare institutions in Asia. Dr. Ghosh had authored several books on health, nutrition and child care and published over 150 articles in national and international journals. Her numerous accolades include the Dr. Kamala Menon Award and Dr. M.K. Seshadri Award from the Indian Council of Medical Research, Outstanding Asian Pediatrician Award of the Association of Pediatric Societies of South Asia and International Pioneer of Newborn Medicine by the American Academy of Pediatrics. As her contributions in maternal and child health have led to major policy reforms, she is fondly referred to as the “the mother of neonatal care in India”.

Dr. Ghosh had been advising the Delhi Ministry of Health for several years. As a chairperson of the Child Survival Group and member of the Safe Motherhood Group, she was involved in the planning of India’s progress in maternal and child health for decades. Internationally, Dr. Ghosh had served as advisor for the WHO regional office, Food and Agriculture Organization, World Food Program, SIDA and other international agencies Bangladesh and Bhutan. From 1978 to 1983, she served as WHO’s advisor for family health in Afghanistan.

Dr. Ghosh worked with Mahatma Gandhi during India’s freedom struggle, and her late husband Sudhir Ghosh served as Gandhi’s official emissary on several missions.

Dr Shanti Ghosh was felicitated by “Lifetime achievement award” by Indian Academy of Pediatrics during Golden Jubilee Pedicon in Kolkata on 17 January 2013.
Editorial

About 4 million newborn babies die every year; these deaths constitute around 40% of all deaths in children younger than 5 years; this proportion is rising because of a slower decline in neonatal mortality than in mortality of children younger than 5 years; and, therefore, MDG 4 to reduce child mortality cannot be achieved without substantial reductions in neonatal mortality.

From the 1970s through the 1990s, many individuals worked on infant and child survival in low-income countries, but only a few focused on newborn survival. They had little interaction and faced an environment unsympathetic to the idea that very sick newborn babies in poor countries could be saved. Before 2000, few organisations paid much attention to neonatal mortality. Since that year, several organisations came up to address the problem, including foundations, UN agencies, bilateral development agencies, governments of low-income countries, and non-governmental organisations (NGOs).

Improving newborn survival is a national priority in child health today. A staggering 26 million babies are born in our country every year. Of these 1.2 million die in the first 28 days of life accounting for 20% of the global burden of newborn deaths. If these deaths have to be reduced, one must begin by improving health of mothers during pregnancy and upgrade services for delivery.

In 1999, a seminar at Johns Hopkins University, Baltimore, MD, USA, helped to form initial activities in this field. The most important development at the seminar was to introduce these individuals to the work of an Indian physician, Abhay Bang, who with colleagues had shown the effectiveness of home-based neonatal care delivered by village women. But the conditions and circumstances prevailing with urban poor are quite different and things may not be applicable to them.

Roughly 1.37 crore households, or 17.4% of urban Indian households lived in a slum in 2011, as per data released by the registrar general and census commissioner’s office.

The proportion of slum households (%) worked out to be in Greater Mumbai 41.3, Kolkata 29.6, Chennai 28.5, Delhi 14.6 and Bengaluru 8.5.

The pregnant mother and her neonate form the vulnerable sector of our society, more so in the rural areas and in the urban slums. In the past few decades a greater emphasis has been laid on rural health as 80% of our population lived in villages. Urbanization is rapidly spreading throughout the developing world resulting in changing proportion of urban to rural population. In 1988 for the first time the percentage of urban poor surpassed the rural poor. The urban poor are at the inter-face between under development and industrialization. Urban health in the slums presents serious public health concerns and challenges predominant among them are neonatal health and mortality. Although urban mortality statistics are comparatively better than the rural, there is a wide disparity between the urban rich and the urban poor and hence the existing urban statistics do not give a true representation of urban slums. Another major...
problem in urban slums is that unlike its rural counterpart there is no envisaged Primary Health Center with its planned network. In urban slum, multiple health authorities administer health services. Unfortunately, these services are not effectively organized, resulting in duplication of services in some areas and non-existence of health services in other areas.

The problems at urban slums are quite different and they need attention differently. Moreover a city can’t claim to improve its health statistics without paying attention to them. They tend to derail every good intervention done. The burden of health problems in these slums tend to stress out every government hospital. Certain facts are enumerated below.

Fewer births in urban slum (50%) were attended by a trained professional than were births in rural areas (65%). Gulati, et al. reported that 96% of deliveries were conducted at home in urban slums of Ludhiana conditions are no better in Kolkata though no statistics are available.

Macro and micro deficiencies, infections, addictions in urban slums predispose mothers to adverse pregnancy outcomes and low-birth weight. In a multi-centric study on urban slums, 68% of the expectant women had a pre-gravid weight of 45 kg or less. Nearly 51.7 % of the women had moderate anemia. Of these mothers 41.4% delivered low birth weight babies.

A large number of women in slums work outside the home. This results in inadequate rest during pregnancy and early return to work undermining exclusive breastfeeding practices and increase neglect of the newborn.

The health structure in slums vary from city to city and often depends on the stability i.e. the number of years the slum has been in existence. Well-established slums may have ICDS services in place. A few large cities like Mumbai, Calcutta, Chennai under the Indian Population Project have looked at health infrastructure establishment in urban slums. New slums, may have just private clinics and hospitals situated either in the slum or in the vicinity. Availability and accessibility as a rule is not a major problem in urban slums. Transport is comparatively easier in urban areas. Affordability could be an issue, since medical services are more expensive in a city. Despite the fact that free maternity services are available provided by the government or the municipal corporation the first preference for medical advice is the private practitioners.

Studies on a few urban slums have indicated that despite availability of public hospitals, up to 90% of deliveries in certain slums take place at home and antenatal care is minimal. Late recognition of neonatal illnesses and delay in seeking medical help were responsible for increased neonatal mortality. Private practitioners in the locality were the first preference. Only 19% of neonates were taken directly to the hospital. Care takers reported full compliance with prescribed oral therapy, 50% did not comply with advice for hospitalization reasons include lack of perception that the child was gravely ill, other siblings at home, economic reasons and unpleasant past experience

Urban slums have a heterogeneous population that migrate from different parts of the state and country. The sense of collective responsibility is low and voluntary efforts are less common. A multiplicity of agencies are involved including government and voluntary agencies which makes coordination difficult. Presence of a large number of unqualified but affordable health practitioners on one hand and poor image of the public sector result in delay and inappropriate care for the sick newborn.

All is not well even in cities just below our eyes. All said and done slums need a multi pronged approach to improve the facilities so that a newborn with his first cry yells out all is well.

Prof. Atul Kumar Gupta
Editor-in-Chief
Predictive Value of Umbilical Cord Serum Bilirubin For Postnatal Hyperbilirubinemia In Term Healthy Newborns

*Deepak Vaishnav, **Gautam Ghosh, ***Tarun Choudhuri, ****Debasish Bandyopadhyay
3rd yr DNB PGT, **Consultant, ***HOD, ****ACHD; Dept of Pediatrics, B.R.Singh Hospital & Centre for Medical Education & Research, Kolkata

Introduction
Neonatal jaundice refers to yellow discoloration of the skin and the sclera of newborn babies that result from accumulation of bilirubin in the skin and mucous membranes. It is one of the most common conditions requiring medical attention in newborn babies.

Any serum total bilirubin (STB) elevation exceeding 17 mg/dl (291µmol/l) is considered pathologic and warrants investigations for a cause and possible therapeutic interventions1.

Hyperbilirubinemia is a cause of concern for the parents as well as for the pediatricians. It occurs in 5-10% of healthy term newborns2-3. Neonatal hyperbilirubinemia is one of the common reasons for re-admission after early discharge4. Early discharge of healthy term new-borns after delivery has become a common practice, because of medical and social reasons and economic constraints5. Thus, the recognition, follow up and early treatment of jaundice has become more difficult as a result of early discharge from the hospital. Severe jaundice and even kernicterus can occur in some full term healthy new-borns who are discharged early with no apparent findings of haemolysis6.

The American Academy of Paediatrics recommends that new-borns discharged within 48 hours of birth should have a follow up visit after 2-3 days for any significant jaundice and other problems7. This recommendation is not feasible for our country due to limited follow up facilities in the community8.

In this context there is an obvious need to design and implement a follow up program. The present study was conducted to find out the critical value of serum bilirubin in the cord blood in predicting the subsequent development of hyper-bilirubinaemia in term healthy new-born.

Aims & objectives:
To estimate the critical cord blood bilirubin level as a predictor of significant hyperbilirubinemia in term healthy newborns.

Method:
A prospective study was conducted at B.R. Singh Hospital and Centre for Medical Education and Research, Kolkata. Two hundred term, exclusively breast fed, appropriate for gestational age new-borns, having birth weight 2500 grams to 4000 grams, and a gestational age 37 weeks to 42 weeks were selected for this study. Newborn showing evidences of haemolysis, Rh or blood group incompatibility, septicaemia, birth asphyxia, birth injuries, congenital anomalies, metabolic abnormalities (hypothyroidism, hypoglycemia, hypoproteinaemia, hypocalcemia or inborn error of metabolism) and those requiring admission and treatment in neonatal I.C.U. for causes other than jaundice were excluded from the study.

Informed consent was obtained from the parents of the newborns enrolled in the study. Relevant informations were collected in a predesigned and pretested proforma.

The cord blood bilirubin estimation was done at birth and serum bilirubin level on day 3 and 5 after birth. The cord and serum bilirubin estimation was done using - modified Jendrassik-Grof method, a photometric method for estimation of direct and total bilirubin.

Bilirubin level at which Babies required phototherapy or exchange transfusion was defined as hyperbilirubinemia. Collected data was analyzed by appropriate statistical methods.

Statistical methods used were the Student t test, Descriptive analysis and Chi square tests. The critical cord bilirubin level having the highest sensitivity was determined with receiver operating characteristics (ROC) curve analysis.
Results

Descriptive Statistics:

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOTHERS AGE (yrs)</td>
<td>19.0</td>
<td>41.0</td>
<td>26.28</td>
<td>5.19</td>
<td>0.467</td>
</tr>
<tr>
<td>BIRTH WT (Kg)</td>
<td>2.6</td>
<td>4.0</td>
<td>2.94</td>
<td>0.28</td>
<td>0.088</td>
</tr>
<tr>
<td>GESTATION AGE (wks)</td>
<td>37.0</td>
<td>42.0</td>
<td>38.74</td>
<td>1.18</td>
<td>0.397</td>
</tr>
<tr>
<td>CORD BLOOD HB (mg%)</td>
<td>12.0</td>
<td>20.0</td>
<td>15.98</td>
<td>1.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CORD BLOOD BILIRUBIN (mg%)</td>
<td>0.6</td>
<td>3.2</td>
<td>1.80</td>
<td>0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERUM BILIRUBIN ON DAY 3 (mg%)</td>
<td>4.0</td>
<td>22.0</td>
<td>10.83</td>
<td>3.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERUM BILIRUBIN ON DAY 5 (mg%)</td>
<td>5.0</td>
<td>21.0</td>
<td>11.78</td>
<td>2.93</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MODE OF DELIVERY</th>
<th>Number</th>
<th>Percent</th>
<th>Hyperbilirubinemia</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>72</td>
<td>36.0</td>
<td>8 (11%)</td>
<td>0.224</td>
</tr>
<tr>
<td>NVD</td>
<td>128</td>
<td>64.0</td>
<td>8 (6%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SEX</th>
<th>Number</th>
<th>Percent</th>
<th>Hyperbilirubinemia</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>94</td>
<td>47.0</td>
<td>7 (7%)</td>
<td>0.786</td>
</tr>
<tr>
<td>Male</td>
<td>106</td>
<td>53.0</td>
<td>9 (8%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hyperbilirubinemia</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>184</td>
<td>92.0</td>
</tr>
<tr>
<td>Absent</td>
<td>16</td>
<td>8.0</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Sensitivity & Specificity

Sensitivity and specificity of various cord blood bilirubin level for prediction of hyperbilirubinemia

<table>
<thead>
<tr>
<th>Cord blood bilirubin (mg/dl)</th>
<th>sensitivity</th>
<th>specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>1.00</td>
<td>0.38</td>
</tr>
<tr>
<td>2.0</td>
<td>1.00</td>
<td>0.70</td>
</tr>
<tr>
<td>2.5</td>
<td>0.88</td>
<td>0.95</td>
</tr>
<tr>
<td>3.0</td>
<td>0.19</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cord blood Bilirubin 2.5mg/dl</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>No. of newborns</th>
<th>Newborn with hyperbilirubinemia</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>88.00%</td>
<td>95.00%</td>
<td>176</td>
<td>2</td>
<td>1.13%</td>
</tr>
<tr>
<td>Specificity</td>
<td>88.00%</td>
<td>95.00%</td>
<td>24</td>
<td>14</td>
<td>58.33%</td>
</tr>
</tbody>
</table>
Figure-1: ROC CURVE

![ROC Curve](image)

<table>
<thead>
<tr>
<th>Area</th>
<th>Std. Error</th>
<th>Asymptotic Sig.</th>
<th>Asymptotic 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.985</td>
<td>0.009</td>
<td>&lt;0.001</td>
<td>0.965 - 0.998</td>
</tr>
</tbody>
</table>

The test result variable(s): CORD BLOOD BILIRUBIN has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption
b. Null hypothesis true area = 0.5

Discussion

The results of the study showed that no statistically significant difference noted in the development of hyperbilirubinemia among the various groups as far as the mode of delivery, sex of baby, mother’s age and birth weight of baby were concerned. There was a statistically significant difference noted between cord blood bilirubin levels and development of hyperbilirubinemia. Cord blood bilirubin level of 2.55mg/dl has had the highest sensitivity (88%) and specificity (95%), and this critical bilirubin level had a very high (98.56%) negative predictive value and fairly low (58.33%) positive predictive value. However, the cord bilirubin level of <2.55 mg/dL did not completely exclude the development of significant hyperbilirubinemia; only 2 babies (1.29%) with cord bilirubin levels of < 2.55mg/dL developed jaundice.

A 98.7% negative predictive value in the present study suggests that measurement of cord serum bilirubin can help to identify those newborns who are unlikely to require further evaluation and intervention.

So, we conclude that the use of the critical cord bilirubin level of = 2.55 mg/dL in healthy term newborns can predict likelihood of significant hyperbilirubinemia.

Limitation of study:

(a) This study was conducted at single center with a small no. of subjects. To generalize these results there is a need to conduct similar studies at multiple centers with a larger no. of subjects.

(b) Serum bilirubin was measured on day 3 and day 5 of life because physiological hyperbilirubinemia usually peaks at this time , but there remains some risk of missing the child who may develop hyperbilirubinemia before or after this period. Ideally we should measure serum bilirubin daily but because it is an invasive procedure, it is not practical in babies with normal clinical findings.

Conclusion:

Cord bilirubin level of =2.5 mg/dL in healthy term newborns can predict development of significant hyper-bilirubinemia.

References:


Introduction:
Perinatal asphyxia is still a major cause of mortality and morbidity in our country. Perinatal asphyxia accounts for a third of total death in first 24 hours of life in India¹. Several studies done worldwide consistently demonstrated, moderate hypothermia reduces cerebral injury and improves neurological outcome. Therapeutic hypothermia is now an established modality for treatment for babies with birth asphyxia with moderate to severe hypoxaemic ischaemic encephalopathy (HIE). In this article we present a brief overview of the therapy, with a special reference to its feasibility in Indian perspective.

Birth asphyxia and cerebral injury:
The mechanism of cerebral injury involves in three phases. Hypoxia leads to primary energy failure in the neurones. But after a short time following resuscitation and re-oxygenation aerobic metabolism and cell functions resume. However at this stage a number of electrochemical changes occur at the cellular level, leading to secondary energy failure that lasts for 24-48 hrs. This secondary event causes considerable damage to the brain tissue.

During acute reduction of cerebral oxygen delivery energy is depleted inside the cells and Na⁺K⁺ pump fails. As a result cells take up Na⁺, Ca+++, and Cl⁻ ions. This calcium overload activates various enzymes like lipase, proteases, and endonucleases which in turn destroys the cells. During this process, the uptake of glutamate (a major excitatory neurotransmitter) is also impaired. Furthermore, up gradation of EAA (Excitatory Amino acid) receptors occur at the cellular level, including NMDA (N-methyl-D-aspartate) receptor. Activation of NMDA receptor leads to intracellular Ca++ accumulation and further pathologic cascades ensue. This acute breakdown of energy metabolism also causes disturbances in protein synthesis, which is essential for tissue repair.

A few hours later during the reperfusion injury the energy status is diminished once again in the affected tissue. Simultaneously, a secondary cell edema develops, leading to epileptogenic activity. These events are likely to be caused or at least modulated by free oxygen radicals, nitric oxide (NO), inflammatory reactions and excitatory amino acids, particularly glutamate². Free oxygen radicals are produced through activation of a variety of pathways involving xanthine oxidase, superoxide dismutase and the Haber–Weiss reaction. The rise in intracellular calcium activates NO-synthetase, which produces NO, citrulline and water from arginine, NADPH and oxygen³. NO, like free ion, can raise the toxicity of superoxide radicals significantly by converting them into highly potent radicals which in turn cause neuronal cell damage.

Over the last few years more evidences are coming that demonstrates the apoptosis theory of cellular destruction. This has been argued that after cerebral ischemia neuronal cell damage occurs not only through necrotic but also through apoptotic processes. These processes have been shown to be significantly involved in secondary neuronal cell death after perinatal hypoxic ischemic insults⁴.

Neuro-protective measures
Evidences suggest that neuro-protective treatment targeting the latent phase before the secondary energy failure begins may limit the secondary neuronal damage due to perinatal asphyxia⁵.

Several modalities have been tried to tackle the neuronal damage at various stages. For example, allopurinol, a xanthine oxidase inhibitor engulf the free radicals, and thereby preventing further damage. A Cochrane review comprising three randomised trials showed reduction in combined morbidity and mortality but only in moderate HIE⁶. Trials with erythropoietin have shown to improve neurological...
outcome on mild to moderate HIE. Erythropoietin with its anti-inflammatory effect reduce production of NO and other free oxygen radicals. EPO also stimulates neuronal anti-apoptotic mechanism.

In a small randomized trial, high-dose phenobarbital (40 mg/kg) prophylactically was also shown to result in fewer seizures and improved neurological outcome in babies with severe HIE.

However so far, moderate hypothermia produced most consistent result in improving combined death and disability in long term follow ups in patients with moderate to severe HIE. Hypothermia reduces cellular energy utilisation, anaerobic metabolism and the formation of free radicals. Hypothermia also reduces the release of glutamate and pro-apoptotic factors.

Evidences for hypothermia

The pioneer study by Seetha Shankaran et al in 2005 in a randomised controlled trial involving 205 infants who presented with moderate to severe HIE, showed reduction in death and moderate to severe disability from 62 per cent in control group to 44 per cent in the hypothermia group, and the rate of cerebral palsy was down from 30 per cent to 19 per cent in the survivors respectively.

Cochrane review involving 11 randomised trials involving 1505 patients convincingly demonstrated therapeutic hypothermia is beneficial in term and late preterm newborns with HIE. Cooling reduces mortality without increasing major disability in survivors. The benefits of cooling on survival and neurodevelopment outweigh the short-term adverse effects.

Recently an updated metanalysis have been published on the long term follow up of babies receiving hypothermia for neonatal HIE. The study looked at 7 trials involving 1214 newborns. The study showed a reduction in the risk of death or major neurodisability (risk ratio [RR], 0.76; 95% CI, 0.69-0.84) and increase in the rate of survival with normal neurological function (1.63; 1.36-1.95) at age 18 months. Hypothermia reduced the risk of death or major neurodevelopmental disability at age 18 months in newborns with moderate HIE (RR, 0.67; 95% CI, 0.56-0.81) and in newborns with severe HIE (0.83; 0.74-0.92). Both total body cooling and selective head cooling resulted in reduction in the risk of death or major neurodevelopmental disability (RR, 0.75; 95% CI, 0.66-0.85 and 0.77; 0.65-0.93, respectively).

Cooling criteria:

Cooling must be initiated within 6 hours after birth for the best outcome, however in many centres accept babies up to first 12 hours of birth.

Infant must meet both physiologic and neurologic criteria.

A. Physiologic criteria (Blood gas is defined as cord gas or within 1 hr)
1. Blood gas pH <7 or base deficit of > 16
2. No blood gas or blood gas pH 7-7.15 or base deficit of 10-15.9 with an acute perinatal event plus either a or b
   a. A 10 minute APGAR less than 5
   b. A continued need for ventilation initiated at birth and continued for at least 10 minutes.

B. Neurologic Criteria
1. The presence of seizures is automatic inclusion
2. Physical exam consistent with moderate to severe encephalopathy in 3 of the 6 categories

<table>
<thead>
<tr>
<th>Neurological examination</th>
<th>Moderate encephalopathy</th>
<th>Severe encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Level of consciousness</td>
<td>Lethargic</td>
<td>Stupor or coma</td>
</tr>
<tr>
<td>2 Spontaneous movement</td>
<td>Decreased activity</td>
<td>No activity</td>
</tr>
<tr>
<td>3 Posture</td>
<td>Distal flexion</td>
<td>Decerebrate</td>
</tr>
<tr>
<td>4 Tone</td>
<td>Hypotonia focal or general</td>
<td>Flaccid</td>
</tr>
<tr>
<td>5 Primitive reflex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Suck</td>
<td>Weak</td>
<td>Absent</td>
</tr>
<tr>
<td>• Moro’s</td>
<td>Incomplete</td>
<td>Absent</td>
</tr>
<tr>
<td>6 Autonomic system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pupil</td>
<td>Constricted</td>
<td>Dilated, Nonreactive</td>
</tr>
<tr>
<td>• Heart rate</td>
<td>Bradycardia</td>
<td>Variable</td>
</tr>
<tr>
<td>• Respiration</td>
<td>Periodic breathing</td>
<td>Apnoea</td>
</tr>
</tbody>
</table>
The process involved:

Baby is put on a water-filled cooling mattress to reduce body temperature. Continuous oesophageal temperature is monitored to achieve a target of 33.5°C.

Brain activities including seizures are recorded on cerebro function monitor (CFM). The movement of CFM trace upwards from the base line suggests improvement. At the same time CFM captures seizure activity, if noted should be controlled using phenobarbitone. Intensive monitoring of vitals and laboratory parameters are required. Hypothermia tends to produce shivering and often baby requires complete paralysis or sedation. Continuous invasive blood pressure monitor is also necessary. Birth asphyxia usually affects several organs and systems. Hence monitoring of kidney heart and liver functions is also important. After completion of 72 hours the core body temperature is increased by 0.5°C per hour.

Our experience:

There have been a few researches published recently on how to deliver therapeutic hypothermia in low cost settings. Study from Switzerland showed hypothermia can be achieved by passive cooling technique using icepacks. This study compared the time required to achieve hypothermia target and any adverse effects with the National Institute of Child Health and Human Development (NICHD) trial. They concluded that passive cooling for asphyxiated newborns appears to be feasible for induction and maintenance of hypothermia with a lower risk of overshoot. Similar study done from Vellore India in showed similar efficacy.

Babies should be transferred without any heating on, and may be cooled in an intensive care unit with icepacks and using air-condition machine. In absence of CFM monitor a portable EEG can serve the purpose to show brain activity and seizure, however continuous monitoring may not be possible. In this situation the clinician and nurses should be more vigilant, and intense monitoring of vitals including blood pressure, temperature, and blood glucose and coagulation profile is required.

Conclusion:

In our country where antenatal care and foetal monitoring needing wide improvement, birth asphyxia will continue to be a major contributor to perinatal deaths. Therapeutic hypothermia is achievable at low cost setting and is the only way forward. However, caregivers should be more knowledgeable and vigilant as early referral to tertiary centres is extreme crucial for the best outcome of the baby.

Reference:

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India a country rich in diversity unfortunately suffers for its diverse and varied health care facility and its utilization. In order to improve the newborn care across the country we need to formulate some working guidelines that can maximize the use of resources with minimal confusion. Doctors, paramedics and nursing persons should try to adopt some simple easy and practical guideline as per their set up so as to optimize the care in emergency situation. In the last decade worldwide the use of CPAP and Surfactant have been widely recognized. India is no exception. Different national and state initiatives as well as private set up have started using CPAP. The cost effectiveness of surfactant is gradually making it more popular. This article aims to give an outline for managing babies with respiratory distress in different scenarios even in remote areas by giving some guidelines for using CPAP and Surfactant where ever they are indicated.

CPAP aims to prevent alveolar collapse at end expiration. It is used for infants with moderate respiratory distress and for recurrent apneas. It is also used for weaning from mechanical ventilation. The use of continuous positive airways pressure (CPAP) in preterm infants has a number of theoretical advantages. Different studies suggest that CPAP improves oxygenation, decrease periodic breathing, lowers arterial partial pressure of carbon dioxide, improves lung compliance and resistance, improves functional residual capacity so reducing post-extubation atelectasis and avoids airway damage associated with intermittent positive pressure ventilation. CPAP can be used clinically in a number of situations: as an alternative to intermittent positive pressure ventilation, to aid in extubation of preterm infants, for recurrent apnea, and as an alternative means of respiratory support to ventilation when a baby is requiring a high inspired oxygen concentration.

**Indications for CPAP:**

(i) Babies weighing less than 1000 gms with respiratory distress

(ii) Moderately poor gases showing respiratory acidosis.

(iii) Post extubation in VLBW babies

(iv) Ambient oxygen requirement increased to 40% for preterms and 60% for term babies

(v) Clinically increasing respiratory distress (please rule out pneumothorax either clinically or by radiology)

The following outlines the guidelines for the use of CPAP

1. As an alternative to intermittent positive pressure ventilation in respiratory distress syndrome

2. Institutions using CPAP as primary intervention have reported reduced rates of BPD without a coincident increase in mortality.

   All babies who require respiratory support other than oxygen as a result of respiratory disease in the immediate neonatal period should be intubated with an endotracheal tube on delivery suite, given surfactant when appropriate and receive intermittent positive pressure ventilation until they arrive on the neonatal unit. If gases are acceptable, rapid weaning should take place and baby should be transferred onto CPAP or head box oxygen depending on birth weight as below.

3. Use of CPAP as an aid to extubation

4. As an alternative means of ventilator support when a baby with chronic lung disease is receiving a high inspired oxygen concentration

5. Recurrent apnea:

   Non-randomized observations suggest that CPAP reduces the risk of apnea in preterm infants. Preterm babies who therefore are having episodes of recurrent apnea and require frequent stimulation by the nursing staff may be given a trial of CPAP. It is important to ensure that caffeine is prescribed at the appropriate dose in these babies

**Guidelines for setting up CPAP:**

(i) CPAP should preferentially be provided by Infant Flow Driver.
The most appropriate hat size should be selected. The most appropriate size of prongs and/or mask The fit should be “snug” but never tight The fixing ties should never be over tightened in order to maintain a seal as this may cause damage to the face. The flow of gases should be set between 8L and 11.5L depending on how much CPAP pressure is required. Humidity must be used when delivering CPAP; humidified oxygen must be delivered at a temperature of 37 oC at the baby’s nose Normal CPAP pressures are 5 to 6 cm of water.

**Practical considerations:**
Babies weighing less than one kilogram and not requiring IPPV ventilation should be nursed on nCPAP. If CPAP is commenced on the labour ward, the transport system of CPAP must be applied for the transfer to the N.I.C.U. On arrival, aim for the smooth transition to naso CPAP (nCPA P) without the loss of lung inflation. Normal CPAP pressures is 5 to 6 cm of water. As the condition of the baby improves so the pressures can be reduced to 4cm water. Some babies become agitated on CPAP. Appropriate “nesting” and removal of noxious stimuli such as light and noise can alleviate this. Occasionally sedation such as Chloral Hydrate (if available) or analgesic (paracetamol) may need to be considered if these strategies are not working.

For preterm infants with RDS on CPAP consider intubation and ventilation if the oxygen requirement increases above 40%.

**Weaning from CPAP:**
(i) Once respiratory distress is settling, weaning from CPAP may be commenced.
(ii) Babies weighing less than one kilogram, who are being nursed on nCPAP, should not be weaned from CPAP until the attending consultant and team decide that the baby is strong enough.
(iii) Pre term and / or Low Birth Weight babies should be weaned gradually by cycling off CPAP for increasing amounts of time. This should be planned incrementally to avoid increasing respiratory distress. Ideally the baby should be able to tolerate CPAP levels of 4cm first.
(iv) This may begin by a short time off CPAP during “all cares” The nursing staff are usually the best positioned to advise on when to try off CPAP.
(v) If the baby has to work excessively to maintain respiratory status then CPAP should be reinstated.

**Signs of excessive effort include –**
(i) Increasing respiratory rate
(ii) Increasing recession
(iii) Increase in oxygen by more than 10%
(iv) Increase in the number of desaturations /bradycardias

Removal from CPAP without Waning Term/Near term babies may require CPAP for only a short time and may not need to wean incrementally from CPAP but may cope well in ambient oxygen or air

**Use of Blood Gases in CPAP**
Any baby who is placed on CPAP for worsening respiratory distress should have gases taken as frequently as clinical condition dictates

**For Term / near term babies**
(i) Take gases 4 hrs after CPAP discontinued
(ii) If saturations are > 98% in air, gases do not need to be taken again
(iii) If in oxygen, do at least one blood gas daily

**Preterm/LBW Babies 1 to 14 days**
(i) Gases should be taken daily for babies who are on CPAP in oxygen.
(ii) Gases should be taken 2 times a week for babies on CPAP in air.

**Preterm/LBW Babies 14 days to 28 days**
(i) Gases should be taken daily for babies who are stable on CPAP with Oxygen

**Preterm/LBW Babies over 28 days**
Gases should be taken once weekly with routine bloods for babies who have Been on CPAP for more than 28 days

**For all Babies**
For any baby whose condition is thought to be worsening a gas should be taken urgently

**Complications of CPAP:**
(i) Pneumothorax
(ii) Gaseous distension of the stomach with or without feeding difficulties
(iii) Nasal trauma

**Consideration for Preterm infants, who were <32 weeks**
Take Care technique - Tracheal instillation of surfactant via 5-F catheter during spontaneous breathing under nCPAP.

In SurE technique- infants were intubated, received positive pressure ventilation for 30 seconds after surfactant instillation,
and placed on nCPAP immediately.

**InSurE technique and its application in Indian scenario:**
As we discussed at the beginning of this article we need a simple and practical approach to handle preterm babies with respiratory distress. Fortunately in the present scenario surfactant and CPAP facility are available even in rural areas. It has been proven repeatedly that only a handful of babies need ventilator if we can ensure the basic resuscitation steps systematically and bag mask ventilation effectively. Evidences have been suggestive of avoiding invasive ventilation as much as possible in order to avoid barotraumas and lung injury. In this context using InSurE method holds a definitive promise.

A simple approach for ensuring InSurE technique:

**Things needed- Surfactant**
(i) ET tube (2.00-2.50, 3.00cm)
(ii) Nasogastric tube (size 4, 5)
(iii) Syringes (2ml, 5ml)
(iv) Bag and mask
(v) Sterile gloves

**Steps:**
1. Bring the surfactant in room temperature
2. Calculate the volume to be given (usual dose 100-200mg/kg) but for InSurE usual dose recommended 100mg/kg.
3. Measure the length of NG tube as per the size of ET Tube but the tip of NG tube should not go beyond the tip of ET Tube.
4. Prime the NG tube with the surfactant after withdrawing the expected volume of the surfactant by a 2 ml syringe.
5. Stabiles the baby after delivery and bag mask adequately to make the baby pink.
6. Intubate and push half of the volume of surfactant and bag the baby for at least 30 second.
7. Re-insert the NG tube and push the rest half of the surfactant and continue IPPV for another 30 -60 second. No need to tilt the posture of the baby.
8. Withdraw the ET tube and put the baby on CPAP.

**Precautions:**
1. Avoid single lung intubation.
2. Do not use cold surfactant
3. Be prepared for ventilating the baby either in your own set up or keep a back up institute for transferring out the baby if needed.
4. Everyone in the unit should be regularly receiving training regarding IPPV, intubation etc.
5. Be vigilant with the CPAP and its complication( i.e. monitoring of the pressure, seal, etc)
6. Do not ignore the baby and ensure close monitoring.

**Suggested further reading:**
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Markers In Diagnosing Neonatal Sepsis

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Introduction:
Neonatal sepsis or septicaemia is a clinical syndrome characterized by systemic signs of circulatory compromise (e.g., poor peripheral perfusion, pallor, hypotonia, poor responsiveness) caused by invasion of the bloodstream by bacteria in the first month of life. In the pre-antibiotic era neonatal sepsis was usually fatal. Case fatality rates in antibiotic treated infants now range between 5% and 60% with the highest rates reported from the lowest-income countries. The World Health Organization (WHO) estimates that 1 million deaths per year (10% of all under-five mortality) are due to neonatal sepsis and that 42% of these deaths occur in the first week of life. Thus neonatal sepsis is one of the dreaded contributors to neonatal mortality and morbidity.

With higher survival rates of very low birth weight and extremely low birth weight babies both early and late onset neonatal sepsis are devastating complications. The subtle, and often minimal presentation and rapid deterioration when undetected makes sepsis a deadly disease entity. Rapid and appropriate treatment are required to combat neonatal sepsis. However, as microbiological culture results and antimicrobial susceptibility data are not usually available until at least 48 hours after the specimen reaches the laboratory, early identification of genuine sepsis is a major diagnostic problem. Diagnostic markers that are accurate, rapid, with high sensitivity and high negative predictive value are needed to start appropriate treatment and at the same time prevent over treatment. The characteristics of an ideal marker of neonatal sepsis in tabulated in Table 1.

With emergence of multidrug resistance, it is equally important to avoid unnecessary use of antibiotics to treat non-septic neonates. A long list of markers that have been used as bio markers for neonatal sepsis is enumerated in Table 2. While some markers have been tested and tried, some are relatively new with limited availability and requires further evidence before being widely used. This article reviews the markers both conventional and old that are available at present and their role in diagnosing neonatal sepsis.

Table 1. Characteristics of an ideal infection marker

Clinical characteristics:
1. A well defined optimal cut off that is comparable between different NICUs
2. Favourable diagnostic utilities:
   (a) sensitivity (approaching 100%)
   (b) specificity (85%)
   (c) positive predictive value (85%)
   (d) negative predictive value (approaching 100%)
3. Detects infection at an early stage
4. Differentiates between different types of pathogen (viral v bacterial)
5. Guides antibiotic use (type and duration)
6. Monitors progress of treatment
7. Prognostication

Laboratory characteristics:
1. Stable compound
2. Adequate time window for specimen sampling (sustained increase or decrease in level for at least 48 h after the onset of clinical manifestations)
3. Quantitative measurement
4. Small volume of specimen
5. Easy method of measurement
6. Quick laboratory turnover time
7. Results comparable between laboratories
8. Low cost

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Table 2. Diagnostic markers of infection for preterm and newborn infants

**Haematological tests:**
- Total white blood cell count
- Total neutrophil count
- Immature neutrophil count
- Immature to total neutrophil ratio
- Neutrophil morphology: vacuolisation, toxic granulations, Döhle bodies, intracellular bacteria
- Platelet count
- Granulocyte colony-stimulating factor (G-CSF)
- D-dimer
- Fibrinogen
- Thrombin-antithrombin III complex (TAT)
- Plasminogen activator inhibitor-1 (PAI-1)
- Plasminogen tissue activator (tPA)

**Acute phase proteins and other proteins:**
- Alpha-1 Antitrypsin
- C-reactive protein (CRP)
- Fibronectin
- Haptoglobin
- Lactoferrin
- Neopterin
- Orosomucoid
- Procalcitonin (PCT)

**Components of the complement system:**
- C3a-desArg
- C3bBbP
- sC5b-9

**Chemokines, cytokines and adhesion molecules:**
- Interleukin (IL) 1b, IL1ra, IL2, IL2R, IL4, IL5, IL6, IL8, IL10
- Tumour necrosis factor a (TNFa), 11sTNFR-p55, 12sTNFR-p75
- Interferon c (IFNc)
- E-selectin
- L-selectin
- Soluble intracellular adhesion molecule-1 (sICAM-1)
- Vascular cell adhesion molecule-1 (VCAM-1)

**Cell surface markers:**
- Neutrophil Lymphocyte Monocyte
- CD11b CD3 CD12
- CD11c CD19
- CD13 CD25
- CD15 CD26
- CD33 CD45RO
- CD64 CD69
- CD66b CD71

**Others:**
- Lactate
- Micro-erythrocyte sedimentation
- Superoxide anion (respiratory burst)

**Conventional markers**

*Hematological:* Hematological parameters have been conventionally used as an important markers for neonatal sepsis. Total leucocyte count, total neutrophil count, immature neutrophil count, immature to total neutrophil (I/T) ratio, immature to mature neutrophil ratio, morphological or degenerative changes in neutrophil such as vacuolisation, Döhle bodies, intracellular bacteria, toxic granulation, and platelet count have been studied either singly or in combination. Results of white cell counts and ratios varied widely across studies, with sensitivity and specificity ranging from 17% to 90% and 31% to 100% respectively. In general, the abnormal leucocyte ratios, including the I/T ratio > 0.2, tend to have high sensitivity, whereas abnormal leucocyte counts, such as leucopenia and neutropenia, tend to have high specificity. Advantages of hematological tests are that these specimens do not require sterility and a heel prick specimen can be used.

*Acute phase markers:* Acute phase reactants are the group of endogenous peptides produced by the liver as part of an immediate response to infection or tissue injury.

CRP has been extensively investigated as a marker for neonatal sepsis. It is synthesized within 6-8 hours of exposure to an infective process or tissue damage. Its half life is 19 hours and increases 1000 fold during an acute phase response. The ranges of sensitivity and specificity for diagnosis of early onset sepsis ranges are 43–90% and 70–78% respectively. The specific and positive predictive value of CRP ranges from 93% to 100% in late onset sepsis. Thus CRP is a “specific” but “late” marker of neonatal infection. CRP as a diagnostic marker in neonates has higher sensitivity and specificity than total neutrophil count and immature to total neutrophil ratio.

Procalcitonin is another important acute phase reactant produced by monocytes and hepatocytes which begins to rise four hours after exposure to bacterial endotoxin, peaking at six to eight hours, and remaining raised for at least 24 hours with a half life of 25–30 hours. Several studies have shown that serum procalcitonin concentrations increase...
appreciably in systemic bacterial infection, necrotising enterocolitis, and during both early and late onset neonatal sepsis. It may be superior to other acute phase proteins, with sensitivity and specificity ranging from 87% to 100%. It may be useful in assessing the severity of infection, following the progress of treatment, and predicting outcomes. However, it is not a readily available diagnostic assay in most institutions. The advantages of Procalcitonin lie in the fact that it helps in early detection and levels quickly reduce in response to appropriate therapy. Procalcitonin also has the additional advantage of being specifically responsive to bacterial infection and not viral.

Cytokines:
Cytokines have a central role in innate immunity. Neonates initially depend on innate immunity as antigen specific immunity develops later. Innate immunity involves phagocytosis (by monocytes, tissue macrophages, and neutrophils), natural killer cells, and humoral mediators (CRP, Complement, and transplacentally acquired maternal antibodies). Antigens such as bacterial endotoxin, activate tissue macrophages which produce TNF and IL1. They in turn initiate cytokine cascade towards increased production of IL 6, IL 8 and chemokines.

IL6 is an important cytokine of the early host response to infection. Its concentration increases sharply after exposure to bacterial products and precedes the increase in CRP. Umbilical cord blood IL6 has been consistently shown to be a sensitive marker for diagnosing neonatal infection within 72 hours of birth, the sensitivities and negative predictive values being 87–100% and 93–100% respectively. Less promising results from some studies are probably due to the use of less sensitive assay methods. IL6 is equally effective as a diagnostic marker for late onset nosocomial infection in preterm infants. At the onset of infection, IL6 has the highest sensitivity (89%) and negative predictive value (91%) compared with other biochemical markers, including CRP, IL1ß, TNFa, and E-selectin. However, it has a very short half life, and the concentrations fall precipitously with treatment and become undetectable in most infected patients within 24 hours.

The sensitivity is therefore reduced to a much lower concentration at 24 and 48 hours (67% and 58% respectively). IL6 can result in earlier initiation of antimicrobial treatment with correspondingly better clinical outcome.

Interleukin-8 is a cytokine that has a role in the release, activation and chemotaxis of neutrophils. Serum IL-8 level has been reported to increase both in early- and late onset neonatal sepsis and to have a sensitivity of about 80–91% and a specificity of about 76–100%. In both early and late onset sepsis, IL8 and IL8 mRNA concentrations are substantially higher in infected than non-infected newborns. The diagnostic accuracy is further enhanced by simultaneous measurement of either CRP or neutrophil cell surface marker CD11b. The combination of IL8 and CRP has also been suggested to be useful in restricting unnecessary antibiotic use.

Another group of proinflammatory cytokines often linked with sepsis is the IL1 family, including IL1a, IL1ß, and IL1 receptor antagonist (IL1ra), the last of which exists in substantial excess as bacterial endotoxin, activate tissue macrophages which produce TNF and IL1. They in turn initiate cytokine cascade towards increased production of IL 6, IL 8 and chemokines. IL6 is an important cytokine of the early host response to infection. Its concentration increases sharply after exposure to bacterial products and precedes the increase in CRP. Umbilical cord blood IL6 has been consistently shown to be a sensitive marker for diagnosing neonatal infection within 72 hours of birth, the sensitivities and negative predictive values being 87–100% and 93–100% respectively. Less promising results from some studies are probably due to the use of less sensitive assay methods.

In newborns, Neutrophil CD11b and CD64 have been found to show significant increase in neonates with sepsis. Other markers which show significant increase in neonates with sepsis include adhesion molecules (intercellular adhesion molecule 1, vascular cell adhesion molecule 1, E-selectin, L-selectin) and complement activation products (C3a-desArg, C3bBbP, sC5b-9) but require further evaluation for clinical application in the diagnosis of newborn infection.

Cell Surface Markers:
Once inflammatory cells get activated by bacteria or their cellular products specific leucocyte surface antigens are known to be expressed in substantial quantities. Flow cytometric analysis detects such cell surface antigen on blood cells and are able to localise the activated markers to a specific cell type. These tests require only a minimal volume of blood (0.05 ml whole blood). Besides assessing the cellular response to cytokines can be a better way of identifying an early immunological response to bacterial invasion as the circulating concentrations of cytokines may not necessarily reflect their biological activities.

In newborns, Neutrophil CD11b and CD64 have been found to be promising markers for diagnosis of early and late
infections respectively. CD11b is an a subunit of the β2 integrin adhesion molecule. It is normally expressed at a very low concentration on the surface of non-activated neutrophils. Once the inflammatory cells come into contact with bacteria and endotoxins, the expression of this cell surface marker increases dramatically within a few minutes. This acute rise from almost undetectable levels enables CD11b to be used as a potential early warning marker for prediction of bacterial infection. The sensitivity and specificity of CD11b for diagnosing early onset neonatal sepsis are very high, being 96–100% and 100% in two studies. However, its accuracy in diagnosing late onset nosocomial infection in preterm infants is more variable.

For the purpose of diagnosis late onset sepsis in neonates CD 64 has emerged to be an effective marker. Expression of CD64 with IL6 or CRP further enhances the ability to diagnose bacterial infections to the same extent as term infants, children and adults. In 2002, a study showed evidence that amongst neutrophils from preterm infants express CD64 during the first 24 hours later were equally impressive. Combining the use of CD64 with IL6 or CRP further enhances the ability to diagnose localised infections, and improves the sensitivity and negative predictive value to 100%. Of other cell surface markers there is some interest in CD45RO, which is a memory antigen for T lymphocytes. But it is probably more useful in detecting congenital viral infection. There is an increase in the number of lymphocyte (CD3, CD19, CD25, CD26, CD71 and CD69) and neutrophil (CD11b, CD11c, CD13, CD15, CD33 and CD66b) antigens in preterm newborns in response to infection, with increased expression of CD19, CD33, and CD66b. However, the diagnostic utilities and availabilities are issues to be considered.

Conclusion:
Markers such as PCT, CRP, IL1, IL6, CD11, CD 64 have proved to be accurate in diagnosing both early and late onset neonatal sepsis. Some markers like PCT, CD11b, IL1, IL6, are ‘early sensitive’ markers, while some like CRP are ‘late specific markers’. Overall, when used in timely fashion and in combination, these markers contribute greatly in early diagnosis of sepsis, will indeed guide clinicians in taking decisions regarding early antibiotic therapy as well as when to stop antibiotic therapy. However till date none of the diagnostic markers have provided enough evidence which shall justify withholding antibiotics in a suggested clinical scenario. Hence, the search for the ‘ideal marker’ still continues.

References:


Neonatal Hypothermia – A Dread

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Abstract:
Hypothermia in newborn is known to be a contributor for morbidity and mortality for centuries yet the prevalence both at hospital and at home is disturbingly high even in tropical environment. The premature and low birth weight babies because of physiological reasons are even more likely to suffer from hypothermia. The WHO has set up guidelines for the management of babies at risk with hypothermia but survival of this group of babies still remains a challenge in most of the developing countries including India. 

Key words: hypothermia, thermoneutral environment, non-shivering thermogenesis

Neonatal Hypothermia is considered an important contributor to neonatal morbidity and mortality in developing countries. Hypothermia is common in infants born at hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in tropical environments. It is a fact that more than 99% of neonatal deaths occur in developing countries and neonatal deaths account for more than 40% of under 5 mortalities, and thus to reach Millennium Development Goal (MDG) 4 will require substantial reduction in newborn mortality. It is needless to mention prevention of hypothermia would contribute to a large extent in reducing morbidity and mortality in newborns.

It is estimated that annually 18 million, or 14% of all babies, are born with low birth weight (LBW), half of them in South Asia. LBW infants account for 60% to 80% of neonatal deaths. The World Health Organization (WHO) has set up guidelines for the management of babies at risk with hypothermia but survival of this group of babies still remains a challenge in most of the developing countries including India.

Neonatal mortality globally the leading causes include Sepsis (36%), complications related to prematurity (29%) birth asphyxia (23%), other causes are responsible for 19% of the deaths. Neonatal hypothermia is associated with these conditions but whether a direct relation exists is unclear. The mortality rates for the neonatal period are 30-fold higher than later during infancy. Immediately after birth, an infant is at highest risk of dying, with 25% to 45% of neonatal mortality occurring during the first 24 h and 75% of neonatal mortality during the first week of life. This assumes importance as addressing hypothermia at this stage would result in significant reduction in neonatal mortality.

Definition – (WHO)
(i) Normal axillary temperature is 36.5-37.5°C.
(ii) Cold stress 36.0°C to 36.4°C
(iii) Moderate hypothermia 32.0°C to 35.9°C
(iv) Severe hypothermia <32°C

Neutral Thermal Environment
Human newborns are homeotherms. The temperature range during which the basal metabolic rate of the baby is at a minimum, oxygen utilization is least and baby thrives well is known as ‘Thermo-neutral range of temperature’ or ‘Neutral Thermal Environment’.

Risk factors for hypothermia
The importance of keeping newborn babies warm has been known for centuries. As early as 1950’s William Silverman and others showed link between temperature control and neonatal mortality. The baby exchange heat with the environment through radiation, convection, conduction and evaporation. A newborn is prone to develop hypothermia because of the...
large surface area per unit of body weight. The newborn is hypothermic but control of body temperature is achieved over narrower range of ambient conditions. The pre-term and low birth weight babies are even more difficult to maintain body temperature and at times behave like poikilothermic - their body temperature tending to change in response ambient temperature.

Pierre Budin, a French obstetrician known as the father of Perinatology focused on temperature and thermal regulation in his book The Nursling, published in 1907. He noted that the temperature of term infants at birth is higher than that of uterus and premature infants are at much greater risk for hypothermia. Indeed the temperature of the fetus is between 0.5°C and 1°C higher than that of mother.

The EPICure study of extremely LBW infants in the UK identified hypothermia as an independent risk factor for mortality.

In newborn, heat production depends largely on non-shivering thermogenesis or direct heat production through the metabolism of brown adipose tissue.

Contrary to earlier beliefs, brown adipose tissue is in fact present and well developed even in extremely premature infants as early as 25 weeks’ gestation, but in lesser amounts than at term. A naked newborn in a 23°C environment (warmer than many delivery rooms) suffers the same cold stress that a naked adult would experience at 0°C, and protective mechanisms are diminished or overwhelmed in the presence of hypoxia.

The most vulnerable times are immediately after birth when a wet newborn can lose heat at a rate of 200 kcal/kg per minute or greater.

The newborn has a higher skin surface area to weight (volume) ratio than the older child or adult, a ratio that increases dramatically in smaller infants. Heat loss is exacerbated by the relative thinness of the newborn skin, and the diminished amount of subcutaneous fat provides little help as an insulating barrier.

Normal newborn body temperature is defined by the World Health Organization as within the range of 36.5°C to 37.5°C, and hypothermia is defined as a body temperature below this range. Mild hypothermia (36°C–36.5°C) is caused by cold stress and should lead to evaluation and corrective action because it indicates that the infant is losing more heat than can be produced.

Heat loss occurs via a combination of four different phenomena: evaporation, conduction, radiation, and convection.

The most common cause at the time of birth is evaporation. Even after birth, baths may result in increased risk, but it must be recognized that evaporative heat loss continues even when the infant is dry, especially in low humidity environments something seen during peak winters in our country.

Conductive heat loss occurs when an unclothed infant is placed on a cold surface, such as a procedure table or a scale.

Radiational heat loss is more difficult to control because the heat is lost via the radiation of infrared energy from infant to nearby cold surfaces, such as a wall or a window. In term and larger premature infants, it is the major route of heat loss.

Convective loss occurs when the infant is in contact with moving air or water that is cooler than body temperature and is again proportional to the temperature differential between the fluid and the infant.

The neonate unlike other children and adults does not have well developed thermogenic mechanism; in addition preterm infants have unstable vasomotor responses and do not vasoconstrict adequately to slow down heat losses.

**Mechanism of heat loss (Fig 1)**

The heat loss in newborn is about four times that of the adult per unit body weight.

Heat production in the newborn is predominantly achieved by non-shivering thermogenesis, which starts when skin temperature falls below 36°C, unfortunately the premature babies fail to respond because of reduced brown fat and this is found principally around the scapular region, nape of neck and around the neck muscles, extending under the clavicles into the axilla.

Brown fat has rich capillary network, numerous mitochondria with respiratory chain enzymes and densely innervated by sympathetic nerve fibers. Cold stress stimulates the sympathetic nerve endings to release non-epinephrine which in turn initiates a cascade of reaction resulting in generation of heat in the brown fat. About 2.5 calories liberated per gram of brown fat.

After the birth of the baby, the body temperatures fall because of both environmental and neonatal factors, especially when preventive measures are inappropriate.

The delivery room temperature should be 25°C which is usually less and the wet infant with the large body surface which is about the three times that of an adult puts the newborn at increased risk of hypothermia.
Four ways a newborn may lose heat to the environment

Fig 1. Showing Mechanism of heat loss

Effects of Hypothermia (Fig 2)
The primary response to cold is an increase in oxygen consumption and metabolic rate, and the metabolism of brown adipose tissue, all of which may ultimately result in hypoxia and metabolic acidosis.

Hypothermia is associated with organ dysfunction, including acute renal failure and coagulopathy, as well as persistent pulmonary hypertension and intraventricular hemorrhage. Extended periods of cold stress can lead to harmful side effects, including delayed adaptation to extrauterine life, hypoglycemia, respiratory distress, hypoxia, metabolic acidosis, coagulation defects, acute renal failure, necrotizing enterocolitis, and failure to gain weight or weight loss and death.

Many factors are associated with an increased risk of hypothermia. These include prematurity, intrauterine growth restriction, central nervous system damage and congenital defects such as abdominal wall defects where bowel is exposed to the air.

(Adapted from Aylott 2006 – The Energy Triangle Thermoregulatory and Respiratory Adaptation, Pediatric Nursing, vol. 18 no.7)

Fig 2. The Energy Triangle Thermoregulatory and Respiratory Adaptation
Signs and symptoms of hypothermia (NNF teaching aids newborn care)

(a) Peripheral vasoconstriction
   Acrocyanosis
   Cool extremities
   Decreased peripheral perfusion

(b) CNS depression
   Lethargy
   Bradycardia
   Apnea
   Poor feeding

(c) Increased metabolism
   Hypoglycemia
   Hypoxia
   Metabolic acidosis

(d) Increase of pulmonary artery pressure
   Distress
   Tachypnea

(e) Chronic signs
   Weight loss, poor weight gain

The principles in the management of Neonatal Hypothermia:

Early recognition includes simple measures like touching the extremities or removing wet linens and drying the baby. It has been found by merely drying the infant reduces heat loss during the first 30 minutes of life by 19.1 calories/kg/min.

Prevention of further heat loss can be done by using caps, plastic bags and stockinet especially as a barrier to heat loss for low birth weight babies. Use of external heat source such as radiant warmer, light bulb heated cot are also commonly used means for prevention and maintenance of normothermia. The concept of WHO warm chain is a highly effective means for adequate thermal care at birth and thereafter.

The concept of "Warm Chain": (WHO)

The "warm chain" is a set of ten interlinked procedures carried out at birth and later, which will minimize the likelihood of hypothermia in all newborns.

1. Warm delivery room (> 25°C)
2. Warm resuscitation
3. Immediate drying
4. Skin-to-skin contact between baby and the mother
5. Breastfeeding
6. Bathing and weighing postponed
7. Appropriate clothing and bedding
8. Mother and baby together
9. Warm transportation
10. Training/awareness of healthcare providers

Mild Hypothermia or cold stress (36.0 to 36.4°C) – passive rewarming can be achieved by Kangaroo Mother Care or by using warm clothing in a warm room.

The Moderately hypothermic (32.0-35.9°C) baby will require slow active external rewarming aimed at raising the temperature at the rate of 0.5°C – 1.0°C per hour. The severely hypothermic (< 32°C) baby will require resuscitation and rewarming concurrently. Once baby's temperature reaches 34°C the rewarming process should be slowed down. Infection should be suspected if hypothermia persists despite above measures.

Conclusion

Although importance of keeping newborn babies normothermic are known for centuries, however it continues to be major area of concern even in 21st century especially in the developing countries. Increasing awareness amongst health workers on morbidity and mortality associated with the condition will improve the management. Use of simple measures like warm delivery room, kangaroo mother care, breast feeding, delaying bath may be lifesaving in resource restricted setting.

Members are generously requested to provide News, Views, Reviews, Case Reports, Articles to our esteemed journal.

Contact:
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Introduction
Hospital Acquired Infections (HAIs) are one of the leading causes of neonatal morbidity and mortality in sick neonatal care units. The preventive interventions for these health care related infections must include strategies to break the chain of transmission of organisms to the neonates. The infection control procedures should emphasize on the following interventions along with other management strategies and universal precautions–

(i) Compliance on hand hygiene by all neonatal care providers.
(ii) Maintenance of environmental hygiene and meticulous house-keeping practices.
(iii) Optimal spacing and staffing in neonatal care units, and
(iv) Disinfection and sterilization practices of neonatal equipments and care articles.

Every neonatal care units (NICU, SNCU, NBSU, and NBCC) should have written protocols for the infection control procedures and practices which must be available to all care providers. Continuous supervision for these procedures and practices are the most significant aspect for reduction of incidence of HAIs.

Disinfection and Sterilization methods of common Neonatal Care equipments and articles

Radiant Warmer (Open Care System) :

(a) When occupied by the baby, body of the radiant warmer and bassinet should be disinfected by mopping with 2 % bacillocid /Bacillol – 25 solutions daily in morning shift.

(b) It can be just clean with soap and water daily, according to the unit protocol, where the incidence of neonatal sepsis is less.

(c) After discharge or death or at the interval of every seven days, the bassinet should be cleaned thoroughly with cleansing solution/soap water. Then it should be allowed to dry and disinfected by mopping with 2 % bacillocid.

(d) Don’t allow a baby in a bassinet for more than seven days at a stretch.

(e) Control panel of the radiant warmer to be cleaned with wet mop only, no chemicals to be used as it may damage the micro-computer control system of the radiant warmer.

(f) Mattress should be cleaned with soap and water. It should be allowed to dry completely before spreading baby sheet on it to prepare the bed.

(g) Alcohol or other organic solvent must not be used to decontaminate the glass side panels of bassinet or display panel of radiant warmer.

Oxygen hood :
It should be cleaned with soap and water/cleansing solution daily and after each use and to be dried with sterile autoclaved linen.

Pulse oximeter :
It should be cleaned daily with wet mop using clean water only.

Skin Thermometer :
It should be decontaminated with 70 % alcohol after each use. Precautions to be taken to prevent alcohol to enter in digital display part. Use separate thermometer for each baby. Store the clean thermometer in a container with dry cotton or in the container supplied by the manufacturer.

Stethoscope, Measuring tape, BP Cuff, Probes (Radiant warmer, Incubator, Monitor, Pulse oximeter) and Laryngoscope :
These articles should be decontaminated with 70 % alcohol after each use. Ideally, each baby should have all these items separate, no sharing with other baby.
**Weighing scale:**
It should be disinfected by mopping with 2% bacillocid / Bacillol – 25 solutions each time before placing the baby on tray/pan of weighing machine.

**Syringe Pump / Infusion Pump:**
This should be cleaned with moist clean cloth daily in morning shift. If it is stained with blood then clean with soap and water and decontaminate with 2% bacillocid.

**Phototherapy Unit:**
It should be cleaned with wet mop using plain water daily. Special attention to be given to remove dust from the reflectors or plexi-glass covering.

**Resuscitation Bag and Mask, Oxygen tubes, Humidifiers, Suction tubes, Suction containers/bottles, ventilator tubings:**
(a) Clean with soap and water thoroughly after each use and allowed to dry, then
(b) Immerse fully in 2% gluteraldehyde for 10 minutes for disinfection and 10 hours for sterilization. (Manufacturer’s recommended time).
(c) Before use, take out from 2% gluteraldehyde, rinse thoroughly with sterile water, dry with sterile linen and reassemble with aseptic techniques.
(d) 2% gluteraldehyde is active for 14 days from the day of preparation i.e. mixing of supplied lotion and powder. Date of activation should be recorded and labeled.
(e) Ventilator tubings and monitors can be sterilized by EO (Ethylene Oxide) gas, if available.

**Ventilator body and Monitor:**
(a) It should be cleaned with wet mopping daily.
(b) Filters to be washed with running clean water in each shift.

**Incubators:**
(a) It should be cleaned with soap and water daily when occupied by the baby.
(b) But when un-occupied then it should be disinfected with 2% bacillocid after thorough cleaning with cleansing solution.
(c) Special attention to be taken for cleaning and disinfection of humidification chamber of the incubator.

**Procedures Set:**
(a) All the articles of the set should be cleaned with soap and water thoroughly after each use, then to be dried and arranged in steel drum before sending for sterilization by autoclaving.
(b) Special care to be taken for glass articles, gloves and rubber goods when packing for the procedure set.
(c) Re-autoclaving of the set or drum to be done after 72 hours, if not used.

**Baby linen, baby blanket, blanket cover, cotton, gauze, gloves:**
Wash thoroughly with soap and water, dry and autoclaved in steel drums.

**Cheatle Forceps:**
(a) It should be cleaned with soap and water and to be autoclaved daily.
(b) Put the sterile Cheatle forceps in sterile autoclave wide mouth container/bottle with dry sterile cotton or even in empty sterile container.
(c) Don’t add any lotion in the container/bottle.
(d) Don’t use sterile Cheatle forceps with the sterile container for more than 24 hours.

**Feeding Utensils (Bowls, Paladai, katories, Spoon):**
(a) Clean thoroughly with soap and water/cleansing solution after each use, then
(b) Boil for 15 – 20 minutes from the boiling point of water.

**Knife dish, Medicine tray, Steel swab containers:**
(a) Clean with soap and water/cleansing solution daily.
(b) Boil for 15 – 20 minutes or send for autoclaving.
(c) These articles should be kept separate for each baby.

**Refrigerator:**
Defrost and clean with soap/cleansing solution and water once a week.

**Disinfection of Rooms**
Room disinfection can be done by the following methods

**Decontamination of floor and walls:**
(a) Wet mopping of the floor should be done 3 – 4 times a day with 0.5% – 2% Bacillocid solution (as recommended by manufacturer).
(b) Walls must be cleaned with 2% Bacillocid at least once a day. Mopping of walls with disinfectant for two – three times per day can be more effective.
(c) Corners of the rooms should be cleaned with special
emphasis.
(d) Avoid dry sweeping and dry cleaning to prevent spreading of dust.

Fumigation:
(a) It is done by OT care machine (Vaporizer) using 30 ml of 40% formalin in 90 ml of water for 1000 cubic feet area.
(b) Calculated amount of formalin and water to be taken in OT care machine and it should be switched on for required time to produce fume of the total amount.
(c) The contact time after completion of fumigation should be at least 6 hours. The room to be kept closed for 6 hours.
(d) For earlier use, 180 ml Ammonium hydroxide is added in OT care machine after the removal of formalin.
(e) Before fumigation all A/C machine, central oxygen and suction should be shut off. Doors and windows should be tightly closed and sealed.
(f) On completion of fumigation and before using the room for neonate, the room must be thoroughly cleaned with soap – water and disinfected with 2% Bacillocid solution.

Fogging:
(a) It is done by Fogger machine using 200 ml Eco-shield with 800 ml of de-mineralized water for 1000 cubic feet area.
(b) Calculated amount of formalin and water to be taken in fogger machine and it should be switched on for required time to produce fog of the total amount.
(c) The contact time after complete fogging should be one hour.
(d) Other than Eco-shield, any commercially available room disinfectant can be used.
(e) Before fogging and on completion of fogging same precautions to be followed as fumigation.
(f) Routine fumigation and fogging is not recommended at present, if regular cleaning of floor and walls is done with disinfectant meticulously. But before starting a new neonatal unit or in presence of severely infected baby in the unit or an epidemic of infection or in low occupancy phase or after any construction or renovation inside the unit fogging or fumigation can be done to disinfect the room.

Sterilization, Disinfection, and antiseptic agents
(a) Sterilization is killing of microorganism including spore. It is best done by autoclaving i.e. steam under pressure. Chemical sterilization is usually done by 2% gluteraldehyde for various items. Ethylene oxide gas is used for sterilization of delicate and costly items like ventilator tubings.
(b) Disinfectants are the agent which is used to kill microorganisms and can be used for inanimate objects or on non-living substance. Commonly used disinfectant are - Bacillocid – 2%, Bacillol – 25, Phenol – 3%, Lysol – 5%, etc.
(c) Antiseptic agents are used to inhibit the growth of microorganisms and can be used on living tissue e.g. – Alcohol – 70%, Povidone-iodine-10%, Chlorhexidine, etc.

Conclusion
For the disinfection and sterilization of most of the electro-medical equipments the manufacturer’s instructions and recommendations should be followed for better control of infection and longevity of the costly items. Every piece of equipment and care article in neonatal units is a potential source infection, directly or indirectly. So, meticulous and obsessive practices of disinfection and sterilization should be considered as important preventive strategies of neonatal sepsis, which helps in better survival of the neonates.

Reference
2. Essential Newborn Nursing for Small Hospitals, WHO Collaborating Centre for Training and Research in Newborn Care, AIIMS, New Delhi, 2nd edition, 2009, page-7/10
Birth is a beautiful miraculous and very personal event for all of us but at the same time it is a potential medical emergency. All babies need assessment for resuscitation and the need for resuscitation at birth cannot always be anticipated.

It's remarkable that more than 90% of babies make the transition from intrauterine to extra uterine life perfectly smoothly, with little to no assistance required and approximately 10% of newborn require some resuscitation and 1% out of it require extensive resuscitation to survive, for them is the neonatal resuscitation programme is designed.

The importance of ‘First Golden Minute’ can be emphasized from the fact that failure to initiate breathing during this time may result in development of birth asphyxia which accounts for 23% of all neonatal deaths worldwide and those who survive may go on to suffer from cerebral palsy, learning difficulties and other disabilities.

The Apgar score which is used in day to day practice is not used to determine the need for resuscitation as it is generally performed at 1 and 5 minutes after birth and resuscitation if needed is to be started soon after birth. However being an objective method of evaluating the newborn condition it conveys about the newborn's overall status and response to resuscitation.

This article tries to highlight the recent advances made in the field of neonatal resuscitation (Based on NRP 6th edition by AAP/AHA and consultative meet by IAP&NNF in July 2012) and what the future beholds for it

**Anticipation for Need of Resuscitation**

In certain special cases the need of resuscitation is most likely. They are as follows

(a) Mother >35 yrs old
(b) Uterine tachysystole with fetal heart rate changes
(c) Category 2 or 3 fetal heart rate patterns

**Standard Precautions**

(a) Every birth should be attended by at least one person skilled in neonatal resuscitation.
(b) All resuscitation should be conducted under strict asepsis
(c) All equipments should be clean, sterile and disposable where indicated.

**Equipment Check Up**

All equipments which can be used in neonatal resuscitation should be checked prior to delivery to ascertain its proper functioning. The following equipments are now considered Desirable and not Optional in neonatal resuscitation. They are as follows

(a) Oxygen blender-It is used to mix oxygen and compressed air and is used to titrate oxygen concentration between 21% to 100%
(b) Pulse oximeter-It is to be used to measure oxygenation status wherever available. Pulse oximeters working on ‘Signal Extraction Technique (SET)’ which is designed to minimize movement artifact is preferable.
(c) CPAP delivery device
(d) Pressure manometer
(e) Polythene bags for premature neonates <29 wks

**Routine Care and Initial Steps**

All babies at the time of birth should be assessed for need of resuscitation. This is judged by asking only one question now unlike three previously which were a) is it term? b) breathing or crying? have good muscle tone?, and that question is “Is the baby breathing or crying?”. Breathing is adequate if a baby is vigorously crying or has good regular chest movements with no pauses or indrawing. Routine care is indicated for term vigorous babies with no risk factors. These babies need not be separated from the mother after birth for monitoring purpose.
Newborn Resuscitation

Birth

Breathing or crying?

Yes, stay with mother

No

Warm, clear airway if necessary, dry, stimulate

No

HR below 100, gasping, or apneas?

Yes, stay with mother

No

Labored breathing or persistent cyanosis?

Yes

Clear airway SpO₂, monitoring, Consider CPAP

No

PPV, SpO₂ monitoring

No

HR below 100?

Yes

Take ventilation corrective steps

No

HR below 60?

Yes

Consider intubation, Chest compressions, Coordinate with PPV

No

Take ventilation corrective steps Intubate if no chest rise!

Yes

HR below 60?

Yes

IV epinephrine

Postresuscitation care

Routine care
- Provide warmth
- Clear airway if necessary
- Dry
- Ongoing evaluation

Targeted Prenatal SpO₂

After Birth
1 min 60%-65%
2 min 65%-70%
3 min 70%-75%
4 min 75%-80%
5 min 80%-85%
10 min 85%-95%
Sequential assessment of baby after initial steps is primarily based on simultaneous assessment of respiration and heart rate. Response to resuscitation is best judged by increasing heart rate and good regular chest movements. Use of pulse oximeter for oxygenation status in addition if facilities exist. Both heart rate and breathing is assessed every 30 seconds.

**Positive Pressure Ventilation, Chest Compression, Endotracheal Intubation and Medications**

Positive pressure ventilation in all term babies should be started with room air (21%) and in preterm with somewhat higher concentration (40% to 60%). Other changes in neonatal resuscitation is the time for assessment after starting chest compression has been changed from 30 seconds to 45 to 60 seconds and the time given for endotracheal intubation has also been increased from 20 to 30 seconds. Laryngeal mask airway is a newer modality added in neonatal resuscitation where the facilities for it exist along with the use of CPAP delivery devices in case of laboured breathing and cyanosis. Regarding medications sodium bicarbonate 4.2% and naloxone is no longer required to be present for immediate resuscitation.

**Resuscitation In Some Special Conditions**

(a) Home delivery/outside hospital delivery: Resuscitation of babies should ideally be done in a hospital setup but in unavoidable circumstances if delivery occurs outside hospital or in home special attention should be paid to keep the baby warm by either using warm clothes to wrap the baby or encouraging skin to skin contact.

(b) Preterm babies: Temperature regulation is an important aspect of preterm babies not requiring resuscitation and can be achieved by measures stated above or by wrapping the baby in plastic polyethylene plastic wrap for babies <29 wks of gestation. Delayed cord clamping for more than 1 minute is a new safe procedure in preterm and LBW babies who do not require resuscitation. It appears to reduce the need of transfusion later.

**Novel Therapies**

Therapeutic Hypothermia: Currently therapeutic hypothermia is not standard of care in India. However if the expertise and facility for providing therapeutic hypothermia exist it can be considered on an experimental basis in the following conditions:

(a) Babies >36 wks gestation who meet previously defined criteria.

(b) Initiated before 6 hours after birth.

**Ethics And Care at The End of Life**

The decision of when to resuscitate and how much to resuscitate is a complex issue. Such decisions are best made with an understanding of the relevant neonatal data, ethical issues including the rights of newborn and parents. Some examples where noninitiation of resuscitation is appropriate are as follows:

(a) Confirmed gestational age of less than 23 weeks or a birth weight of less than 400 gms.

(b) Anencephaly

(c) Confirmed lethal genetic disorder or malformations such as Edward syndrome.

Resuscitation is to be discontinued after 10 minutes of absent heart rate. The ideal situation is one where the health care team and family come together and make the best possible decision for all involved.

**Corrigendum**

Designation of 2nd author of the article “Study on Birth Weight of Newborns Delivered in a District Hospital of West Bengal” published in Vol. 17, No. 4, September - December 2013 issue of this journal has been incorrectly written as District Programme Officer, NPCDCS & NPCHE, Jalpaiguri.

The correct designation of 2nd author (Dr. Rabindra Nath Sinha) of the article is Professor of Public Health, All India Institute of Hygiene & Public Health, Kolkata.
Currently India is going through a critical phase of establishing the health care priority among the paediatric population. The improved survival of the ‘at risk’ newborns at district level sick newborn care units has emphasized the need for structured neurodevelopment follow up. The risks of developing suboptimal neurosensory and behavioural function has been in the rising trend because of the highest number of late preterm birth in India. This may be the reason of apparently static rates of Cerebral palsy remained at 4.5-10% over the past two decades. Among high risk neonates. The incidence of severe disabilities like Cerebral palsy this is also associated with reports of increasingly high incidence of neuro-sensory impairment (blindness and deafness) and cognitive, learning disabilities, behavioural problems like ADHD and Autism. Timely and appropriate intervention can prevent or modify many of these disabilities.

This has got immense impact on planning of health care budget for paediatric population, the huge expenses of immediate and for long term management of various complications of surviving neonates creates tremendous pressure on country’s existing economic structure.

All these will collectively impair country’s economic and social development. The primary concern of decreasing neonatal and infant mortality rate has been shifted to sustain quality lives of the special cohort of high risk newborns. The recently launched Rashtriya Bal Swasthya Karyakram is the most recent endeavour of Govt of India to prevent the burden of medical and neurodevelopmental long-term morbidities throughout our country.

The planning for developing structured follow up for high risk newborns both in urban facility and district level is rapidly gaining importance. There is absolute lack of uniformity in the follow up protocol by which any deviation or delay in development and behavioural function can be detected early and can be ameliorated with appropriate and timely intervention. The components of comprehensive neurodevelopmental follow up will include

(a) Risk categorization of newborn and enrolment for follow up at discharge
(b) Selection of space and trained manpower at follow up clinic
(c) Selection of culturally appropriate assessment tools
(d) Formulation of structured follow up schedule

The enrolment of newborns at high risk follow up clinic should be done based on the risk categorization to utilize the maximum benefit with existing resources. Though until now there is no uniform categorization of ‘at risks’, the NNF, India has already addressed this issue based on antenatal and perinatal factors. The babies are enrolled before discharge from NICU or SNCUs, the moderate and high risk group will need comprehensive follow up and mild ‘at risk’ may be followed up in OPD or well baby clinic under close vigil.

The predischarge counselling:

The counselling session with the parents will include discussion of baby’s antenatal perinatal complications, relevant investigations and imaging, screening for retinopathy of prematurity, importance of neurodevelopment follow up and possible outcome, always keep the parents informed about potential risk for missed follow up for ROP.

The date for first follow up: 40 weeks corrected gestation for preterm if already over then 3 months corrected age.

For term baby: first follow up at 40 weeks then at 3 months onwards.

The treating physician and follow up team should have a close coordination to maintain the continuum care.
<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Mild risk</th>
<th>Moderate risk</th>
<th>Severe risk</th>
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<tr>
<td>Perinatal risk factors</td>
<td>Abnormal fetal growth</td>
<td>Fetal distress</td>
<td></td>
</tr>
<tr>
<td>Gestational wk</td>
<td>&gt;37 weeks</td>
<td>33-36 weeks</td>
<td>&lt;33 weeks</td>
</tr>
<tr>
<td>Birth weight</td>
<td>&gt;2500 gram</td>
<td>1500-2500 gram</td>
<td>&lt;1500 gram</td>
</tr>
<tr>
<td>Place of delivery</td>
<td>Booked pregnancy</td>
<td>Suboptimal prenatal care</td>
<td>Suboptimal transport, extramural</td>
</tr>
<tr>
<td>Intramural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANS</td>
<td>Complete course</td>
<td>Incomplete course</td>
<td>No ANS</td>
</tr>
<tr>
<td>Resuscitation need</td>
<td>No need for resuscitation</td>
<td>Need for resuscitation at birth</td>
<td>APGAR &lt; 3 at 5 min</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>Levene grade 1</td>
<td>Levene grade 2</td>
<td>Levene grade 3</td>
</tr>
<tr>
<td>Ventilation</td>
<td>No ventilation</td>
<td>Ventilation uncomplicated</td>
<td>Ventilation more than 7 days, Hypocarbia, Pneumothorax Apnoea requiring resuscitation</td>
</tr>
<tr>
<td>Shock</td>
<td>No shock</td>
<td>Shock</td>
<td>Refractory shock Hemodynamically significant PDA</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>Transient hypoglycaemia</td>
<td>Hypoglycaemia, blood sugar &lt; 25 mg / dL, &gt; 3 days</td>
<td>Symptomatic hypoglycaemia, seizure</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Suspect sepsis (screen negative)</td>
<td>Sepsis (culture +ve/ clinical and screen +ve)</td>
<td>Meningitis</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Neonatal jaundice needing phototherapy</td>
<td>Neonatal jaundice leading to Exchange transfusion</td>
<td>Kernicterus</td>
</tr>
<tr>
<td>NICU admission</td>
<td>NICU admission</td>
<td>(Complex course – NEC &amp; PDA (needing surgery))</td>
<td>CLD</td>
</tr>
<tr>
<td>Imaging</td>
<td>Preterm IVH grade 1 or 2, no abnormality at 40 wks</td>
<td>Intra-Ventricular Haemorrhage (IVH) &gt; grade 2 on Neurosonogram</td>
<td>Ventriculomegaly and / or cystic periventricular leukomalacia (at 40 weeks), hydrocephalus</td>
</tr>
<tr>
<td>Neuro exam</td>
<td>Normal neurologic exam at discharge</td>
<td>Severe / prolonged encephalopathy Any cause</td>
<td>Abnormal neurologic examination at discharge / Suspect development</td>
</tr>
<tr>
<td>Follow up</td>
<td>Good home environment + optimal follow up</td>
<td>Sub-optimal Home Environment (Parent coping poor/ low socio-economic)</td>
<td>Parent concern for NDD</td>
</tr>
</tbody>
</table>

The ideal space for follow up:
Preferably it should contain at least
(i) Registration, anthropometry room
(ii) Room for paediatrician/ neonatologist
(iii) Physiotherapy and early intervention room
(iv) Vision testing room
(v) Audiological screening and audiometry room preferably sound treated
(vi) Speech therapy room
(vii) Developmental assessment room
(viii) Drinking water, toilet, baby changing area.

Trained professionals for early intervention
(i) Paediatrician/ neonatologist: Should act as coordinator of the follow up team, clinical examination, neurological examination
(ii) Physiotherapist: Assessment of motor development, early detection of abnormal tone and posture and intervention
(iii) Developmental paediatrician: Developmental assessment by norm based standardized age appropriate tool
(iv) Optometrist: vision testing, management of abnormal visual behaviour and organization of ROP follow up
(v) Audiologist: Hearing screening, audiometry, speech therapy.
(vi) Psychologist: Developmental assessment, evaluation for ADHD, Autism, behavioural problems and intervention.
(vii) Early intervention/ special educators: Home based intervention for developmental delay.
(viii) Social worker/ public health nurse: Registration, immunisation, anthropometry and counselling.

The setting up multidisciplinary follow up services needs good amounts of funds. So the transdisciplinary model of early
intervention is newly gaining popularity in resource poor settings where the early interventionist or developmental paediatrician plays the key role as multiprofessional therapist and subsequently refer to higher facilities for specific management.

Flow diagram at neurodevelopment clinic
Proforma for neurodevelopment assessment

<table>
<thead>
<tr>
<th>Name ---------------------</th>
<th>Birth Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother’s name ------------</td>
<td>Gestational age (wk)</td>
</tr>
<tr>
<td>Identification no</td>
<td>Sex M F</td>
</tr>
</tbody>
</table>

Day of life  
Corrected age (wk)/(months)  
Weight (g)  
Length (cm)  
HC (cm)  

Physical Examination

<table>
<thead>
<tr>
<th>Age (corrected)</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head circumference</td>
<td>± 2S</td>
<td>&gt;2SD</td>
<td>&gt;2SD</td>
</tr>
<tr>
<td>Cranial sutures</td>
<td>Edge to edge</td>
<td>Overlapping</td>
<td>Separated</td>
</tr>
<tr>
<td>Anterior fontanel</td>
<td>Normal</td>
<td>Tense</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>Eyes including red reflex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest</td>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen</td>
<td>Spine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limbs</td>
<td>hip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitalia</td>
<td>Neurocutaneous marker</td>
<td></td>
<td></td>
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32
Neurological examination
Observation & interview

<table>
<thead>
<tr>
<th>Seizure</th>
<th>Alertness &amp; attention</th>
<th>Hyperexcitability</th>
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Cranial nerve

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<tr>
<th>Facial expression</th>
<th>Conjugate movement of eyes</th>
<th>Visual fix and following</th>
<th>Auditory response</th>
<th>Sucking swallowing</th>
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</table>

Muscle tone

<table>
<thead>
<tr>
<th>Scarf Sign</th>
<th>Adductor Angle</th>
<th>Popliteal Angle</th>
<th>Dorsiflexion of Foot</th>
<th>Pull to Sit</th>
<th>Horizontal Suspension</th>
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Motor Milestones

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<th>Head control</th>
<th>Head holding in prone</th>
<th>Roll over</th>
<th>Sitting</th>
<th>Bearing weight on both legs</th>
<th>Walking independently</th>
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Reflexes

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<th>Primitive reflexes</th>
<th>ATNR</th>
<th>Palmer and planter grasp</th>
<th>Emerging reaction</th>
<th>Parachute</th>
<th>Lateral propping</th>
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<tr>
<td></td>
<td></td>
<td>Deep tendon reflexes</td>
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Conclusion: The relative lack of long-term studies on outcome of high-risk neonates, the effect of various risk factors and quality of care on long-term outcome, lack of coordination and uniformity in follow-up protocol among health care facilities hinders the development of national database on long-term outcome of at-risk neonates. Currently, this should be the major area of research for planning and implementation of health care initiatives in India.

Reference

1. RashtriyaBalSwasthyaKaryakram (RBSK), Child Health Screening and Early Intervention Services under NRHM, Ministry of Health & Family Welfare, Govt. of India October 2013.
2. NNF Clinical Practice Guidelines, Follow up of high risk newborns
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<tr>
<th>Professionals</th>
<th>Medical Officer</th>
<th>Social worker/ Public health Nurse</th>
<th>Physiotherapist</th>
<th>Audiologist</th>
<th>Optometrist</th>
<th>Psychologist</th>
<th>Special educator</th>
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<td>Job responsibilities</td>
<td>History taking, physical exam, neuroexam screening for developmental delay, red reflex (OAE, automated ABER - optional)</td>
<td>Registration, feeding counselling, immunization, anthropometry</td>
<td>Assessment of motor development, Physiotherapy, Oromotor stimulation</td>
<td>Screening &amp; Diagnostic Audiological tests, assessment &amp; therapy of speech &amp; articulation disorder</td>
<td>Red reflex, ROP screening by retinal camera, squint, visual acuity testing, visual stimulation</td>
<td>Developmental assessment, screening for autism, ADHD, LD, Counselling</td>
<td>Home based intervention of dev. delay</td>
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### ANNEXURE – 02

Selection of culturally appropriate assessment tools and formulation of structured follow up schedule

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<th>40 weeks</th>
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<td>Filling up proforma, Detailed history, Immunisation</td>
<td>Filling up proforma, Detailed history, check immunisation (if first visit)</td>
<td>Advice for supplemental feeding, immunisation at 9 months</td>
<td>Feeding advice, immunisation at 15-16 months</td>
<td>Immunisation optional vaccine</td>
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<td>Weight, length, HC</td>
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<td>Neuro examination (Dubowitz)</td>
<td>Neuro examination (Dubowitz/ Amiel Tison)</td>
<td>Neurological examination (Dubowitz/ Amiel Tison)</td>
<td>Neurological examination (Amiel Tison)</td>
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<td>Eye &amp; vision</td>
<td>Examination of eyes and red reflex</td>
<td>Examination of eyes and red reflex</td>
<td>Examination of eyes, visual acuity, red reflex</td>
<td>Examination of eyes, visual acuity, red reflex</td>
<td>Examination of eyes, visual acuity, red reflex</td>
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<td>Hearing &amp; speech</td>
<td>OAE, screening ABER</td>
<td>Screening ABER (if not done before)*/ Diagnostic ABER in high risk</td>
<td>Screening ABER (if not done before)*/ Diagnostic ABER in high risk</td>
<td>Repeat ABER for Down syndrome, Meningitis,</td>
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<td>M CHAT for **suspected cases</td>
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OAE for universal screening, screening ABER of NICU / SNCU graduates

M CHAT (Modified checklist of Autism in toddlers)
A few practical points on neonatal jaundice

Jaundice is a common problem in neonatal population encountered by pediatrician. Almost 50% of term and higher percentage of preterm infants develop jaundice during the first week of life. Majority babies remain well (physiological jaundice), require only monitoring but a few of them needs intervention in the form of phototherapy or exchange transfusion. At physiologic levels bilirubin may exert some antioxidant effects. However, at certain concentrations higher than physiological levels unconjugated bilirubin is neurotoxic and severe unconjugated hyperbilirubinemia if left untreated may lead to irreversible chronic encephalopathy (kernicterus). Conjugated hyperbilirubinemia usually signifies a serious systemic disorder.

Where bilirubin pigments are deposited in jaundice?

Yellowness of skin in jaundice results from deposition of non-polar, lipid soluble bilirubin pigments in the dermis and subcutaneous tissue generated from break down of red blood cells in unconjugated hyperbilirubinemia. This is important to know because lights used for phototherapy to be effective for managing neonatal jaundice should penetrate epidermal layer. Lights having wavelength less than 350 nm usually do not pass through epidermis. Efficacy of phototherapy also depends on spectral quality of light used. Blue-green spectrum (450 – 475 nm) has the maximum interaction with bilirubin with good penetration to dermis that is why lights with most output in blue-green spectrum are most effective for lowering bilirubin levels in jaundice and recommended by AAP.

Why is there cephalocaudal progression of jaundice?

First we should understand the mechanism of yellowness of skin in jaundice. There are two mechanisms described in the literature. First of these two is deposition of bilirubin in the skin that results from presence of considerable amount of albumin in the extravascular space to which bilirubin demonstrates high affinity. The proposed second mechanism explains deposition of bilirubin acid in the skin. There is precipitation of bilirubin acid when this comes in contact with phospholipid membranes in the skin. Yellowness also depends on basic skin colour.

Once bilirubin reaches blood, it binds to albumin tightly. This process involves fast bimolecular combination between these two molecules within 10 milliseconds followed by slow conformational changes. The final change takes place 8 minutes after binding. Lower bilirubin binding affinity is expected during the process of change owing to disturbance in binding equilibrium between albumin and bilirubin. Therefore, increasing gradient of bilirubin affinity to albumin exists with the lowest just after blood leaves RE system. As circulation time from RE system to distal parts of body is longer than proximal parts, a cephalocaudal gradient of increasing bilirubin affinity to albumin is expected.

More bilirubin acid will be precipitated in the proximal parts of body. As bilirubin loading in these proximal parts is higher, bilirubin deposition is also higher. Bilirubin deposition is more in head and upper body parts than legs and feet. This is important to know because light used for phototherapy to be effective should penetrate skin of these parts.

### Practical Points

<table>
<thead>
<tr>
<th>Zone</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categories of zones</td>
<td>Head and Neck</td>
<td>Chest, upper abdomen</td>
<td>Lower abdomen, thigh (above knee)</td>
<td>Arms and lower legs</td>
<td>Palms &amp; soles</td>
</tr>
<tr>
<td>Bilirubin (mmol/ L)</td>
<td>100</td>
<td>150</td>
<td>200</td>
<td>250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Bilirubin (mg/ dl)</td>
<td>6</td>
<td>9</td>
<td>12</td>
<td>15</td>
<td>&gt;15</td>
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</tbody>
</table>

**Correspondance:** Tapas Kr Som, Associate professor, Department of Neonatology IPGMER, Email: tapassom@yahoo.com
the body as a result of lower bilirubin binding affinity to albumin due to conformational changes. Thus, cephalocaudal progression of jaundice is expected in presence of cephalocaudal increase in gradient of bilirubin affinity to albumin.  

**What is Kramer’s rule?**

Cephalocaudal progression of jaundice was first described by Rolleston and McNee in 1929 but correlation of this observation with actual serum bilirubin levels had not been established. Kramer established the positive relationship between concentration of serum bilirubin and cephalocaudal progression of dermal icterus. Jaundice is assessed clinically by blanching the skin with digital pressure in daylight at a window. Kramer's rule is based on cephalocaudal progression of jaundice as bilirubin rises. Baby's body is divided into following five zones. This is useful to decide whether or not baby's TSB needs to be measured. Kramer's rule is not applicable once baby has received phototherapy.  

**How good is the visual assessment of jaundice?**

Ability to evaluate jaundice varies widely amongst clinicians. Although neonatologist can effectively evaluate newborns for the presence and severity of jaundice, clinical errors might occur in the following instances: darkly pigmented skin, appearance of jaundice with 24 – 36 hours where a difference of 3 mg/ dl might lead to risk stratification from 40th percentile to 95th percentile. To prevent this potential error associated with visual diagnosis it is recommended to estimate TSB prior to discharge form health facility by laboratory measurement or to estimate TcB by transcutaneous bilirubinometer which can estimate bilirubin level reliably below 15 mg/ dl.  

**How reliable is the estimation of bilirubin by transcutaneous bilirubinometer?**

Study published by Bhutani et al concluded that transcutaneous bilirubin level (TcB) estimated using multiwavelength spectral analysis can accurately and reliably estimate predischARGE bilirubin (TcB) in term and late preterm infants of diverse races and ethnicities. This study also suggested for further studies to assess the efficacy of this technique in preterm infants, those receiving phototherapy and those with TSB value above 15 mg/ dl.  

Further studies suggested TcB measurements become less precise with decreasing gestation and its utility is questionable below 30 weeks of gestation.  

**What is the gold standard for estimation of bilirubin?**

High pressure liquid chromatography is the gold standard method for estimation of bilirubin. However, laboratory estimation of total serum bilirubin (TSB) has been accepted as standard method for measuring bilirubin in day to day clinical practice. Regarding samples, all studies published on relationship of TSB and kernicterus and neurodevelopmental outcomes are based on capillary samples, thus capillary samples are the gold standard for estimation of TSB. Because of effects of light, laboratory manuals recommend that serum should be protected from light before analysis. One study suggests that ambient light has got no effect on total serum bilirubin levels at least for 8 hours.  

**When TSB estimation is indicated?**

Following are some indications where TSB should be estimated:

1. Jaundice within first 24 hours of life  
2. Clinically jaundice appears excessive for infant's age  
3. Babies receiving phototherapy/ TSB rising rapidly (>0.5 mg/ dl/ hr)  
4. Jaundice approaching exchange level  
5. Conjugated hyperbilirubinemia  
6. Prolonged jaundice/ sick infants

**How jaundice is being managed in day to day clinical practice?**

From management perspective, newborn population may be categorized in the following groups.

1. **Group I** (Babies born in hospital but expected to be discharged within 48 hours): Routinely jaundice should be estimated using TcB meter as we follow before discharge, and the value is plotted against hour specific nomogram for categorization in risk group and parents should be advised to attend for follow up based on risk stratification (AAP 2004). As earlier mentioned, clinical estimation based on Kramer's rule may not be appropriate in this situation.  
2. **Group II** (Babies born in hospital and expected to be discharged 5 to 7 days after birth): Babies developing jaundice are monitored clinically or by measuring TcB and if baby's level of jaundice approaches to the range of phototherapy or above 75th percentile in the bilirubin nomogram TSB is estimated. If TSB is just below phototherapy range, TSB monitoring to be continued for another 24 hours keeping in mind the natural history of peaks and troughs of jaundice in term and preterm population.
3. **Group III** (Babies born outside, or discharged but readmitted): TSB is estimated on admission if baby appears to be jaundiced and managed accordingly as mentioned above.

4. **Group IV** (Babies receiving phototherapy):
   (a) Jaundice approaching exchange level, or jaundice appeared within 24 hours of life or jaundice associated with hemolytic etiology, TSB should be re-estimated within 4 – 6 hours after starting phototherapy.
   (b) Jaundice of non-hemolytic etiology is just above cut off for phototherapy level in term and late preterm infants, TSB should be re-estimated after 24 hours of starting phototherapy.
   (c) TSB should be re-estimated in any infants received phototherapy within 12 – 24 hours after discontinuation of phototherapy to check rebound increase in TSB level.

**How to evaluate for cause of jaundice?**

In some infants, cause of jaundice is apparent from history and physical examination. For example, babies having cephalhematoma, or having excessive bruises need no further laboratory testing unless course and severity is beyond reasonable expectation. Cause of jaundice should be sought in every infants receiving phototherapy, TSB rising rapidly, or is not explained by history and physical examination.

The following investigations must be done to identify/ specify the cause of jaundice when a baby is presenting within first two weeks.

1. TSB/ hematocrit
2. Blood group and type of both mother and baby
3. Direct coombs’ test (DCT)
4. Peripheral blood smear for RBC morphology
5. Reticulocyte count
6. G 6 PD assay

**Which part of history and physical examination is relevant to evaluate jaundice?**

**Important points in history:**

1. Family history of hemolytic anemia (G 6 PD and hereditary spherocytosis), liver disease (Galactosemia, alfa 1 antitrypsin deficiency, cystic fibrosis, Gilbert disease, Crigler-Najjar syndrome)
2. Sibling history (Rh/ABO incompatibility)
3. Maternal history (TORCH infections, Diabetes, drug intake in pregnancy)
4. Infant’s history (Infrequent stoolsing, intestinal obstruction, pyloric stenosis, sepsis, breast feeding history, perinatal asphyxia)

**Important points on examination:**

1. Prematurity/ Small for dates (polycythemia, congenital infections)
2. Anemia, polycythemia, petechiae (congenital infections)
3. Weight loss/ dehydration
4. Urine/ stool colour
5. Extravascular blood (cephalhematoma, bruising)
6. Microcephaly (congenital infections)
7. Hepatosplenomegaly (congenital infections, hemolysis, liver disease)
8. Chorioretinitis (congenital infections)
9. Features of hypothryoidism

**What is pathological jaundice?**

1. Jaundice appearing within 24 hours of age
2. Jaundice requiring phototherapy/ exchange transfusion
3. Jaundice involving palms and soles
4. A rise in TSB >0.5 mg/ dl/ hr
5. Persistent jaundice after 8 days in term and 14 days in preterm infants requiring interventions
6. Jaundice with signs of underlying illness (Lethargy, excessive weight loss, apnea)

**What is BIND?**

Severe unconjugated hyperbilirubinemia if left untreated might lead to bilirubin induced toxicity in basal ganglia and various brain stem nuclei. To avoid confusion and encourage consistency AAP recommends the term acute bilirubin encephalopathy to describe the acute clinical manifestations of bilirubin toxicity that is noted in first weeks after birth and the term kernicterus for chronic and resultant sequelae of acute bilirubin toxicity. Recently Johnson and associates\(^{10}\) suggested the term bilirubin induced neurologic dysfunctions (BIND) to describe both acute and chronic manifestations of bilirubin toxicity\(^{11}\).

**What are the clinical manifestations of BIND?**

In acute encephalopathy infant passes through three distinct phases. In the early phase, infant becomes lethargic, hypotonic and sucks poorly. The intermediate phase is characterized by moderate stupor, irritability and hypertonia (retrocollis, opisthotonus). The infant may develop fever and high pitched
cry. The advanced phase is characterized by deep stupor to coma, pronounced retrocollis-opisthotonus, shrill cry, fever, refusal to feed, apnea sometimes seizures and death. Infants develop hypertonia in the intermediate phase certainly develop chronic encephalopathy, although an emergent exchange transfusion might in some cases reverse the CNS changes.

Occurrence of clinical features in acute bilirubin encephalopathy

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Percent (%) of cases</th>
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</thead>
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<tr>
<td>No definite neurologic manifestations</td>
<td>15</td>
</tr>
<tr>
<td>Equivocal neurologic manifestations</td>
<td>20 - 30</td>
</tr>
<tr>
<td>Definite neurologic manifestations</td>
<td>55 - 65</td>
</tr>
</tbody>
</table>

Van Praagh found that consistently neurologically normal infants in first weeks of life never developed chronic encephalopathy. However, other investigators found later evidence of brain damage in some infants in whom no or equivocal neurologic manifestations of encephalopathy were apparent during newborn periods.

Chronic bilirubin encephalopathy is characterized by a tetrad which consisting of extrapyramidal manifestations, auditory disturbances, gaze palsies and dental dysplasia.

What is the role of neuro- imaging in bilirubin encephalopathy?

Acute as well as chronic encephalopathy can be diagnosed by MRI. The characteristic image is a bilateral, symmetric, high intensity signals noted on T1 and T2 weighted images in the globus pallidus in acute (first 3 weeks) and chronic encephalopathy respectively. Acute lesions may disappear. Presence of chronic abnormality consistently associated with classic features of chronic encephalopathy.

What is the role of BAER in the management of bilirubin encephalopathy?

Several studies have documented a relationship between BAER and TSB levels. Auditory neuropathy or dyssynchrony is functionally defined as abnormal BAER test with normal inner ear function as tested by OAE. This has been reported in literature in children diagnosed with kernicterus. Acute changes in BAER can be reversed by lowering TSB levels with phototherapy or exchange transfusion.

What are the diagnostic criteria for ABO incompatibility?

The following conditions should be fulfilled to diagnose ABO incompatibility, mere presence of group O mother and group A or B baby does not confirm the diagnosis.

- Mother group O and baby group A or B
- Direct coombs’ test (DCT) positive
- Jaundice appearing within 12 – 24 hours of life
- Reticulocytosis and presence of microspherocytes on smear
- DCT negative, but homozygous for Gilbert’s syndrome

Should blood type and DCT be performed on cord blood of all infants of group O mother?

AAP recommends routine cord blood screening for infants of group O positive mothers is an option and is not required routinely provided a system of appropriate surveillance and risk assessment exists before discharge and follow up so that significantly jaundiced infants are not missed.

How do we define conjugated hyperbilirubinemia?

Conjugated hyperbilirubinemia is defined as a clinical condition where direct reacting bilirubin is greater than 1 mg/dl if TSB is less than equal to 5 mg/dl and direct reacting bilirubin is more than 20% if TSB is greater than 5 mg/dl.

What is aggressive phototherapy?

NICHD Neonatal Research Network conducted a multicentre trial to evaluate the effects of aggressive phototherapy (beneficial vs. harmful) as compared with conservative phototherapy in ELBW infants.

Infants were enrolled in two treatment groups (aggressive and conservative). Infants were further stratified based on birth weight (501 to 750 and 751 to 1000 gm). For infants in the aggressive-phototherapy group, phototherapy was initiated when the TSB level was expected to be approximately 5 mg/dl. Conservative phototherapy was initiated, continued, or restarted whenever the TSB level was 8 mg/dl or higher for infants weighing 501 to 750 g at birth and 10 mg/dl or higher for infants weighing 751 to 1000 g at birth.

It was found that aggressive therapy resulted in significantly reduced mean peak TSB (7.0 vs. 9.8 mg%) level as compared with conservative therapy but not the rates of death or neurodevelopmental impairment at corrected age of 18 – 22 months (52% vs. 55%). Further, rates of death were higher in aggressive therapy group (24% vs 23%) as compared with conservative group, more so in infants with birth weight of 501 to 750 gm (39% vs. 34%), although rates of neurodevelopmental impairment were significantly reduced (26% vs. 30%).

Conclusion was aggressive therapy may be preferred in infants with birth weight of 751 to 1000 gm as it did reduce the rates
of neurodevelopmental impairment without increasing the rates of death or other adverse outcomes at 18 to 22 months corrected age. For infants with birth weight of 501 to 750 gm, this should be viewed with skepticism because of increased mortality.

What is intensive phototherapy?
AAP recommends Intensive phototherapy3 if any baby needs phototherapy for unconjugated hyperbilirubinemia that implies irradiance in the blue-green spectrum (wavelengths of approximately 430 to 490 nm) of at least 30 µW/cm² per nm where irradiance is measured at the infant’s skin directly below the center of the phototherapy unit and it should be delivered to as much of the infant’s surface area as possible. Measurements should be made with a fluxmeter specified by the manufacturer of the phototherapy unit.

References

Basic Health Indicators of India and adjoining countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Under 5 mortality rank</th>
<th>Under 5 mortality rate</th>
<th>Under 5 mortality rate by sex</th>
<th>Infant mortality rate (under 1)</th>
<th>Neonatal mortality rate 2012</th>
<th>Life expectancy at birth (years) 2012</th>
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<tr>
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</table>
Although neonates are very different from adults in their disposition of and response to drugs, information relevant to this group is almost always collected after the drug has been tested in adults. Ethical considerations hinder rigorous studies in neonates, and in many cases the lack of micro methods for drug analysis hampers detailed trials in neonates. But, when considering drug therapy one cannot merely think of a neonate as just a smaller version of an adult. Significant differences in thermoregulation, glucose regulation, and neurological, cardiopulmonary, immunologic development and responses have all been well documented in the neonatal age group. So when we consider drug therapy in neonates, it must be administered with forethought of the special circumstances these patients present.

A major challenge of neonatal drug therapy is that the physiologic, and hence pharmacokinetic properties are dynamic. As a neonate matures, how it handled a drug a week ago may be significantly different from today and these differences could be clinically significant depending on the condition treated and/or the therapeutic index of the drug. A given drug’s properties of absorption, distribution, biotransformation (metabolism) and elimination in a patient are the primary pharmacokinetic parameters studied.

**Drug Absorption**

Altered neonatal physiology has implications for drug administration via oral, Intramuscular, Subcutaneous, Percutaneous, Rectal, and Inhalation routes. Intramuscular injections of drugs may be sporadically absorbed due to reduced vascularity and the small size of muscles. Neonates have far less fat as percentage of body weight than adequately nourished adults and subcutaneous injections may be more rapidly absorbed in the neonate. Thermoregulation of neonates is very dependent on external factors and cold ambient temperatures or hypothermic conditions can impair subcutaneous absorption. When giving drugs or fluids to neonates the resulting osmolarity of the solution should not exceed 460 mOsm/kg. Hypertonic solutions have resulted in intracranial hemorrhage after parenteral administration and large volumes of hypertonic orally administered drugs or fluids can cause a necrotizing enterocolitis.

Oral absorption of drugs in neonates is altered by several factors. The two major determinants of gastrointestinal absorption, gastric acidity and gastric emptying time, differ between newborn infants and adults. Gastric acidity is poorly maintained in neonates. Only by age 3 years does the production of acidity reach adult capacity (H1 per hour, 0.15 mmol/10 kg body wt. in neonates vs 2 mmol/10 kg in adults after a stimulation test). These differences in gastric pH have been shown to affect the absorption of several drugs. For example, oral penicillin, ampicillin, and nafcillins (all acid labile) achieve higher concentrations in neonates than in children or adults. On the other hand, acidic drugs, such as nalidixic acid, are better absorbed in their nonionized form. In alkaline pH, a larger fraction of the drug is ionized and is therefore less well absorbed by the small infant. After birth, there is a gradual improvement of gastrointestinal absorption of drugs, and by age 3 months, absorption may be comparable with or even more complete than in adults.

During the first few days of life when colostrum is presented, intestinal permeability to large molecules is increased. During this phase, drugs not normally absorbed from the GI tract may be more readily absorbed due to increased absorption and increased absorption may occur with others, but this attribute is generally not useful clinically as it is difficult to predict the absorptive characteristics for a given drug, and may actually lead to toxicity when drugs are administered orally during this time.

Non-traditional drug administration routes may be indicated in some neonatal patients. On occasion when vascular access is not possible, intraosseous or intraperitoneal...
administration of drugs or fluids is performed. Endotracheal administration of diluted lipid-soluble drugs such as atropine, epinephrine, naloxone or lidocaine may be used. When oral or intravenous drug administration is not indicated or possible, rectal administration may be a viable alternative in the neonate.

Two major factors determine the rate and extent of percutaneous absorption and may cause excessive absorption of an agent applied to the skin in the neonate and small infants—skin thickness and the state of hydration of skin. The thickness of the epidermal stratum corneum is inversely related to absorption, whereas the state of skin hydration directly influences absorption. Several antiseptic agents have been implicated in cases of severe toxicity in neonates after percutaneous absorption.

**Drug Distribution**

When compared to adults, distribution of drugs can vary significantly in neonates. Neonates have a higher percentage of body weight as water than their adult counterparts. Conversely, total body fat is very low at birth and increases with time. Distribution of body water is also different in the neonate. At birth about 62% of body water is in the extracellular fluid. This ratio actually increases to 66% at day 42 and then slowly reverses until the percentages of extracellular and intracellular fluids are about equal at 6 months of age. The pharmacokinetic ramifications of these differences are that with highly water-soluble drugs, plasma drug concentrations can be reduced. Because total body fat is decreased, drugs with high lipid solubility may have increased plasma concentrations that could lead to toxicity.

Plasma protein concentrations are significantly lower in neonates versus adults. During the first four weeks of life, total protein averages about 4 g/dl (vs. 5.4 – 7.4 g/dl in adults). However, neonatal serum albumin levels are generally similar (albeit slightly lower) to adult values. While albumin levels are only slightly below those of adults, neonatal albumin does not exhibit as high degree of affinity for many drugs as in the adult. Neonates also have decreased levels of alpha1-acid glycoprotein, which is important for certain drugs such as lidocaine. The net result is that drugs that are normally very highly protein bound in the adult, may have increased “free” levels in the neonate thereby exhibiting greater therapeutic or toxic effects4,7.

The so-called blood-brain barrier is more permeable in neonates than adults. CNS permeability can be up to 6 times “normal” for drugs such as morphine or pentobarbital.

**Drug Biotransformation (Metabolism)**

Biotransformation for certain drugs can be altered significantly in the neonate. Hepatic enzyme systems responsible for metabolizing many drugs (e.g., cytochrome P-450, hydroxylation, demethylation, etc.) may not be equivalent to adult capacities until babies are 5 months old. Drugs that have a high first-pass effect (i.e., propranolol) after oral dosing or are extensively metabolized may need to have their dosages reduced. Certain pro-drugs (primidone, methylprednisolone, prednisone) may have their efficacy reduced as formation of the active metabolite may be delayed.

**Drug Elimination (Excretion)**

Elimination of drugs is primarily by renal routes and neonates
have reduced capabilities to excrete drugs via renal mechanisms. Glomerular filtration rate (GFR) and tubular secretion are reduced in neonates. At birth, GFR is approximately 20% of the adult value. Physical development of the kidneys is not complete until babies are three weeks old and renal excretion of drugs may be reduced when compared with adult values for the first few months of life. Drugs most clinically important are those that are highly water soluble and have significant toxic potential such as aminoglycoside antibiotics.

### Specific Problems Associated with Drug Administration in Neonates and Infants

It is generally assumed that the intravenous route of drug administration guarantees proper delivery of the intended dose. This assumption cannot be taken for granted in the neonate. Slow infusion rates, various injection sites, variable injection volumes, and different relative densities (specific gravities) of injected solutions are some of the factors that may influence the rate and extent of intravenous administration of antimicrobial drugs. In addition, medication errors are probably more common in this age group than is generally appreciated.

### Considerations for specific drugs

#### Resuscitative Drug Therapy:

**Atropine for bradycardia in newborns:** Atropine is generally not recommended because bradycardia in newborns is likely caused by direct myocardial depression and is not vagally mediated. Therefore atropine is unlikely to be effective and could actually increase cardiac oxygen demand.

**Doxapram for respiratory stimulation:** Although a time-honored treatment for neonatal apnea, doxapram’s use is not supported by the literature for this indication. It may increase ventilatory efforts of the newborn after they have started, but its duration of effect is very short.

**Epinephrine for cardiac arrest:** While still the drug of choice for neonatal cardiac asystole, there is debate about dosages and routes of administration. Adult dosages (0.2 mg/kg) may yield the best results, but increase the risk of significant hypertension. Some are proponents of endotracheal administration, but because of unpredictable absorption, intravenous or intraosseous administration, if available, are generally preferred.

**Naloxone for apnea or narcotic reversal:** The opiate reversal
Table III-Drugs that should be monitored in Neonates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Clinical condition</th>
<th>Assay availability*</th>
<th>Initial TAT*h</th>
<th>Peak sampling time post IV infusion</th>
<th>Drug concern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Sepsis, proven or suspected</td>
<td>Routine</td>
<td>&lt;2</td>
<td>0.5</td>
<td>peak 6-8 nL, trough &lt;2</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Sepsis, proven or suspected</td>
<td>Routine</td>
<td>&lt;2</td>
<td>0.5-1.0</td>
<td>peak 25-40 nL, trough &lt;2</td>
</tr>
<tr>
<td>Chloramphenicol, mg/L</td>
<td>Sepsis, proven or suspected</td>
<td>Routine</td>
<td>&lt;2</td>
<td>4</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Theophylline/caffeine, μmol/L</td>
<td>Neonatal apnea</td>
<td>Routine</td>
<td>&lt;2</td>
<td>7.5-15</td>
<td>&gt;25</td>
</tr>
<tr>
<td>Digoxin, μmol/L (μg/L)</td>
<td>Congestive heart failure, supraventricular arrhythmias</td>
<td>Stat &amp; routine</td>
<td>&lt;2</td>
<td>25-100</td>
<td>&gt;3.1</td>
</tr>
<tr>
<td>Phenytoin, μmol/L (mg/L)</td>
<td>Seizures, ischemic encephalopathy</td>
<td>Stat &amp; routine</td>
<td>&lt;2</td>
<td>(0.5-2.0)</td>
<td>(&gt;2.4)</td>
</tr>
<tr>
<td>Phenobarbital, μmol/L (mg/L)</td>
<td>Seizures, ischemic encephalopathy</td>
<td>Stat &amp; routine</td>
<td>&lt;2</td>
<td>(10-40)</td>
<td>(&gt;60)</td>
</tr>
</tbody>
</table>

TAT, turnaround time; IV, intravenous.
*All should be available 24 h/day.
‡Requires treatment with FAB.
§Two hours after the post IV loading dose trough on day 2.

agent, naloxone has not been demonstrated to be an effective therapy to reverse apnea of newborns and its routine use for this is not indicated. If the mother has received opiates during parturition, naloxone may still be effective to reverse opiate-induced respiratory depression in newborns.

**Antibiotic Drug Therapy in Neonates:**

There does not appear to be consensus on the safety and recommended dosage adjustments (if any) for antibiotic therapy in neonates. Most tend to agree that beta-lactam antibiotics (penicillins, cephalosporins) are most likely the least toxic choices in neonates and should be considered for use first. But as neonatal sepsis is an acute, life-threatening disease in neonates and the most commonly reported causative microorganisms are both Gram negative and Gram positive pathogens (beta-hemolytic streptococci, Staphylococcus intermedius, Escherichia coli, Klebsiella pneumoniae, and Enterococcus species) that may be relatively resistant to many antibiotics, adequate coverage may not be possible with many of the beta-lactams. Additionally, because of the acuity of the disease, broad-spectrum antibiotic treatment must begin before the pathogen and antibiotic susceptibilities are determined. For that reason, clinicians have an extra challenge in treating without doing harm. The following are my conclusions and recommendations:

(i) For serious systemic bacterial infections avoid oral antibiotics at least during initial treatment, because of the inherent unpredictability of oral absorption of drugs in neonates and patients with critical illnesses. Subcutaneous, intravenous or intraosseous administration of drugs are all preferred over PO or IM dosing in seriously ill neonates.

(ii) No antibiotic is absolutely contraindicated in these patients. If the only antibiotic that shows activity is one to “avoid”, be prepared to use it if the infection warrants treatment.

(iii) Every antibiotic (even beta-lactams) carries some risk in these patients.

**Choosing Other Drugs and Dosages for Neonates**

Despite the lack of detailed recommendations in the literature for dosage adjustment in neonates a clinician can make reasonable clinical judgments in choosing direct therapy by using the information known about neonates in general and the drug in particular. The clinician should answer the following “universal” therapeutic questions to guide their treatment choices:

1. Is treatment necessary or wise? What are the relative risks of treating versus not treating with this (or any) particular agent?
2. Is there a “safer” drug that will do?
3. How much do we truly know about the drug(s) in this patient population?
4. If we don’t know very much, can we extrapolate data from other species (especially human)?

5. Is the owner “on board” with treatment options and decisions?

6. What are our therapeutic endpoints? And how will we monitor efficacy and toxicity? What will determine when we can halt therapy?

7. Should we be treating litter mates (and/or the mother) prophylactically?

“Indirect” Drug Therapy: Drugs in Maternal Milk

Certain drugs can be found in maternal milk in quantities that may be clinically significant to a nursing neonate. Among these include antineoplastic agents and certain immunosuppressant drugs. While there is some debate about whether certain antibiotics (tetracyclines, metronidazole, chloramphenicol and aminoglycosides) should be used, they probably are safe. Practically speaking, any drug with a narrow therapeutic index given to a nursing mother should be investigated with regard to its safety to nursing babies. The following drugs are considered by the American Academy of Pediatrics during breast-feeding to be:

Contraindicated: Cyclosporine, doxorubicin and cyclophosphamide because they have the potential to be immunosuppressive in the neonate.

Unknown effects, but of concern: Fluoxetine, sertraline, metronidazole.

Penicillin and its derivatives (including cephalosporins) are considered to be safe to use in nursing mothers. Levels found in milk are very low and would unlikely to cause significant problems.

Chloramphenicol, tetracyclines, metronidazole and the aminoglycoside and quinolone antibiotics are often listed as contraindicated or to be avoided in breast feeding in humans these agents could be used if “safer” (e.g., beta-lactams) drugs are not indicated. Although gentamicin is found in breast milk and half of human infants tested have detectable levels in their serum, it is unlikely to cause clinical effects. While tetracyclines would be thought to be contraindicated, the drug’s high binding to calcium and protein in milk limits its absorption in the newborn and is unlikely to cause tooth staining or delayed bone growth.

Although not directly harmful to offspring, certain drugs may inhibit lactation and should be avoided if possible. These drugs include estrogens, thiazide diuretics, and bromocriptine.

Conclusions

Neonatal developmental physiology is a dynamic process which affects drug absorption, distribution, metabolism, and excretion. There is tremendous inter-individual and intra-individual variability in neonatal pharmacokinetics. Choice of drug and dosing regimen should be based on: Drug physical characteristics, pharmacokinetics, and pharmacodynamics, patient characteristics and clinical status.

References


Rituximab In Pediatric Immunological Disorders.

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Abstract: Rituximab is a genetically engineered chimeric murine/human monoclonal antibody directed against anti-CD-20 antigen. Though primarily approved for B-cell NHL, it is now used in multiple autoimmune diseases. Though most of the studies in pediatric age group regarding its use in autoimmune diseases are non-controlled trials and case-reports but results are very much encouraging.

Key words: Rituximab, anti CD-20 antibody, Autoimmune diseases.

Introduction
Modern treatments of autoimmune diseases are based on immunological therapies. Rituximab is a human / murine chimeric monoclonal antibody primarily used for treating non-Hodgkin’s B-cell lymphoma. But recently it has also been used in the treatment of several autoimmune diseases. Rituximab induces a targeted B-cell depletion in the aim of eradicating auto reactive clones in various autoimmune disorders. Studies are going on and preliminary reports are very encouraging. Rituximab is FDA approved in treatment of refractory rheumatoid arthritis. Other autoimmune diseases that have been treated successfully with rituximab include idiopathic thrombocytopenic purpura, auto-immune hemolytic anemia, pemphigus, multiple sclerosis, SLE, steroid-resistant nephrotic syndrome. Rituximab is now used off-label in anti-rejection treatment for organ transplant.

History
Rituximab was invented in 1986 by Ivor Royston and Howard Birndorf. It was approved by the FDA in 1997 for treatment of B-cell NHL.

Description
Rituximab is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD-20 antigen found on the surface of B-lymphocytes. The antibody is an IgG1 kappa immunoglobulin containing murine light and heavy-chain variable region sequences and human constant region sequences. It is composed of two heavy chains of 451 amino acids and two light chains of 213 amino acids.

Mechanism of action
Rituximab binds to CD-20. CD-20 is widely expressed on B-cells from early pre- B cells to later in differentiation, but it is absent on terminally differentiated plasma cells. The exact mode of action of Rituximab is unclear but some proposed mechanisms are following
(a) Rituximab induce B-cell killing by NK –cells through antibody dependent cellular cytotoxicity (ADCC).
(b) Direct cross linking induce apoptosis.
(c) It may induce complement dependent cytotoxicity through membrane attack complex.
(d) Opsonization of B cells by Rituximab may also induce clearance of B cells through phagocytosis by RE system cells like monocyte and macrophages.

Pharmacology: Rituximab binds to CD-20 antigen on B-cells with volume of distribution 3.1 L. Most likely removed by opsonization via the RE cells with clearance 0.34 L/day. Half life – 0.8 hr.

How to use
This medication is used intravenously with slow infusion rate. Vial available are 100 mg and 500 mg. Avoid antihypertensive drugs from 12 hrs. before the infusion. 1st give antihistaminic drug like diphenhydramine and paracetamol single dose each 30 – 45 min before infusion. Many people also use steroid single dose before start of infusion. Dissolve the freeze-dried form in water for injection or normal saline. Then from it required
amount charged in normal saline and start infusion slowly. For 1st 2hrs., rate is 12.5mg/hr then 25mg/hr rest of the dose or increase the rate gradually.

**Adverse event**
Some serious adverse events though rare can occur like severe infusion reaction, hypotension, cardiac arrest, cytokine release syndrome, tumor lysis syndrome causing acute renal failure, Hepatitis B reactivation, progressive multifocal leukoencephalopathy, pulmonary toxicity.

**Use of Rituximab in pediatric immunological disorder**

The efficacy and relative lack of toxicities of Rituximab in the treatment of B-cell NHL lead to its incorporation in most treatment protocols for B-cell lymphomas. Dose is 375mg/m² in each cycle.

1. Cohort studies have described the use of Rituximab in autoimmune hemolytic anemia, all of whom failed conventional treatments. The Rituximab was given weekly for 1-6 wks (medium 4 weeks) with 92% children had complete response.

2. Infusion of Rituximab has the potential to avoid splenectomy in children in chronic ITP but apparently in not more than 50% cases. Standard dose is 375mg/m² weekly for 4 weeks.

3. There are some case reports of using rituximab in treatment of hemophilia with antibody to factor VIII and IX.

4. Children with severe SLE treated with targeted B-cell depletion with rituximab showed a beneficial effect of the drug in over 90% of children. It is used weekly doses for 2-4 doses. Initial dose 188mg/m², subsequently 375mg/m².

5. A number of case-reports and non-controlled clinical trials suggested that Rituximab may be effective in childhood refractory nephrotic syndrome.

6. A controlled study in patients with relapsing remitting multiple sclerosis has shown that Rituximab significantly reduces the number of new MRI lesions and improves clinical outcome. The drug is also effective in a number of patients with Devic’s disease, myasthenia gravis, autoimmune neuropathy and inflammatory myopathies.

Rituximab was also used in a patient with multiphasic ADEM resistant to conventional treatment with good result.


**Points to remember**

1. Rituximab-anti CD-20 antibody is primarily used in B-cell NHL. But recently it has also been used in treatment of autoimmune diseases.

2. Studies are continuing but preliminary reports are very encouraging in treatment of autoimmune hemolytic anemia, chronic immune thrombocytopenic purpura, multiple sclerosis, SLE and steroid resistant nephrotic syndrome.

3. Serious adverse event though rare can occur like severe infusion reaction, hypotension, cardiac arrest, cytokine release syndrome, pulmonary toxicity.

**References**


Use of antenatal ultrasound for evaluation of congenital anomalies in early pregnancy has become a common practice. Hydronephrosis is the most common congenital urological anomaly observed with antenatal ultrasonography. Early detection of hydronephrosis helps in postnatal management. The identification of hydronephrosis antenatally permits early parental counseling and in some instances allows antenatal interventions to be considered.

Hydronephrosis is the most common urological anomaly detected during pregnancy, the incidence is as high as 1-5%. Transient physiological dilatation of renal pelvis antenatally with resolution occurring by third trimester or early postnatal period is a common occurrence accounting for about 60% of antenatal hydronephrosis. As the fetal kidney has less concentrating capacity, it produces large amount of diluted urine. The narrow ureter of fetal kidney is unable to transmit it and results in dilatation of pelvicalyceal system, causing transient hydronephrosis. Other cause is delayed disappearance of Chawla’s membrane. Antenatally diagnosed pathological dilatation of the urinary tract can result from either impairment of urine flow or retrograde reflux of urine. Urine flow impairment can occur at any level in the urinary tract, and may affect one or both sides. In 17% to 54% cases the condition is bilateral. Pathological causes of antenatal hydronephrosis are:

1. Ureteropelvic junction obstruction
2. Vesicoureteral reflux
3. Ureterovesical junction obstruction (megaureter)
4. Posterior urethral valve
5. Ureterocele
6. Dilatation of one moiety of a duplex kidney
7. Prune Belly Syndrome
8. Urethral Aplasia

Other conditions presenting as hydronephrosis are

1. Multicystic dysplastic kidney
2. Polycystic kidney disease

Vesicoureteral reflux constitutes 33%, ureteropelvic junction obstruction (UPJO) accounts for approximately 10%, ureterovesical junction obstruction constitutes 4%, and posterior urethral valves (PUV), multicystic dysplastic kidney and ureteroceles together constitute between 2% and 4% of the cases.

Dilatation of the renal pelvis and calyces is the first anatomical response to impairment of urine flow and may lead to histological damage of the renal parenchyma and changes in renal function. Histological damage is related to the degree and level of urine flow impairment and its duration. When urine flow impairment is present early in pregnancy, the renal parenchyma develops dysplasia, while when urine flow impairment becomes significant later in gestation or is partial, it generates dilatation of the excretory system without affecting the parenchymal structure. While fetal urine is not a major contributor to amniotic fluid volume in the first trimester, but oliguria or anuria thereafter leads to oligohydramnios.

Two most commonly used grading systems for assessing antenatal hydronephrosis are the Society of fetal urology grading system and grading system based on the anteroposterior diameter of renal pelvis.

Society of Fetal Urology grading system for Antenatal Hydronephrosis as follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No splitting of renal pelvis</td>
</tr>
<tr>
<td>I</td>
<td>Splitting of renal pelvis</td>
</tr>
<tr>
<td>II</td>
<td>Splitting confined to sinus; calyces not dilated</td>
</tr>
<tr>
<td>III</td>
<td>Renal pelvis dilated beyond sinus; calyces uniformly dilated</td>
</tr>
<tr>
<td>IV</td>
<td>Renal parenchyma thinned to &lt;50% the contralateral side</td>
</tr>
</tbody>
</table>

Only grades III and IV are thought to be clinically significant postnatally.
In the antenatal period, the anteroposterior (AP) diameter of the renal pelvis in a transverse renal image has also been used as a quantitative parameter for monitoring the degree of hydronephrosis. Grading of antenatal hydronephrosis according to the antero-posterior diameter of pelvis as follows:

<table>
<thead>
<tr>
<th>Classification</th>
<th>Second Trimester</th>
<th>Third Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>4-6 mm</td>
<td>7-9 mm</td>
</tr>
<tr>
<td>Moderate</td>
<td>7-10 mm</td>
<td>10-15 mm</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;10 mm</td>
<td>&gt;15 mm</td>
</tr>
</tbody>
</table>

AP diameter of renal pelvis varies with gestation, maternal hydration and bladder distension. In one study, AP diameter cutoff =7 mm at 18-weeks or later distinguishes fetuses with postnatal reflux or obstruction from those without significant pathology. One study found renal APD thresholds of 5 mm and 8-10 mm in the second and third trimester, respectively were 100% sensitive in predicting the need for postnatal surgery, compared with another study where third trimester threshold of 10 mm missed 25% cases of pelviureteric junction obstruction and 50% cases of VUR. Others also propose that fetal renal APD greater than 4-5 mm in the second trimester and 7 mm in third trimester is abnormal. While lower cut-offs for defining hydronephrosis increase the sensitivity for detecting anomalies, it reduces specificity3.

Degree of renal pelvis dilatation, unilateral or bilateral involvement, ureteric dilatation, renal size and parenchymal appearance, visualization and size of the fetal bladder, status of posterior urethra as well as the amniotic fluid volume in relation to gestational age are the key facts to obtain from antenatal ultrasound in cases of antenatal hydronephrosis. Above factors can assess the differential diagnosis and prognosis. Apart from the renal pelvic parameters discussed above, bilateral disease, ureteric dilatation or bladder distension in antenatal USG warrants postnatal evaluation.

When antenatal hydronephrosis is discovered, it is imperative to confirm the diagnosis postnatally. Knowledge of the prenatal evaluations during the progression of pregnancy forms the starting point of the assessment of the newborn. The likelihood of significant postnatal pathology correlates to the severity of antenatal hydronephrosis. Lee et al in their meta analysis on the outcome of antenatal hydronephrosis, have concluded that children with any degree of antenatal hydronephrosis are at a greater risk of postnatal pathology compared to normal population.

The goal of postnatal management of infants with antenatal hydronephrosis is to identify patients with significant renal and urinary tract abnormalities while avoiding unnecessary testing in patients with physiologic or clinically insignificant hydronephrosis. Evaluation includes clinical assessment, observation of urinary flow and the use of radiologic studies to detect renal and urinary tract abnormalities. A palpable abdominal mass may be detected in an infant with a multicystic dysplastic kidney, UPJ obstruction, or autosomal recessive polycystic kidney disease. Absent abdominal wall musculature with bilateral undescended testicles suggests a diagnosis of prune belly syndrome. Infants with a palpable bladder may have posterior urethral valves (PUV) or urethral atresia or stricture. Features of Potter sequence secondary to low amniotic fluid volume may be present. Infants with abdominal mass, severe bilateral hydronephrosis or severe unilateral hydronephrosis in a single functioning kidney and patients with urosepsis warrant immediate postnatal evaluation with a USG, blood count, serum urea, creatinin. Micturating cystourethrogram (MCU) is mandatory in all these patients barring those with urosepsis. In asymptomatic infants, USG is done between 2-3 days age in male patients with antenatally detected bilateral hydronephrosis with hydroureter and distended bladder and in all other asymptomatic patients between 3-7days age.

Indication of surgery in isolated UPJ obstruction is based on renal scan showing obstructive pattern with initial function less than 40%. In patients with initial function > 40%, further follow up is required. Surgery is indicated if there is increase in AP diameter of pelvis or deterioration of function on renal scan. In bilateral UPJ obstruction in USG, obstructive pattern in renal scan indicates the need for surgery.

VUR is graded between Grade I to Grade V. Grading of VUR according to International Reflux Study Committee:

Grade I- Reflux upto ureter only
Grade II- Reflux up the ureter, pelvis and calyces with no dilation and normal calyceal fornices
Grade III- Grade II VUR with mild to moderate dilatation and tortuosity of the ureter, no blunting of calyces
Grade IV- Moderate dilatation of ureter, calyces and pelvis with complete blunting of fornices
Grade V- Gross dilatation of ureter, pelvis and calyces with absent papillary impression in the calyces.

Grade I and II usually are likely to resolve spontaneously with increasing age but as continuing VUR has the potential to cause long-term renal damage. Early diagnosis and prevention of pyelonephritis by prophylactic antibiotic treatment are very important. However, in higher grades of VUR (III, IV,
Algorithm for postnatal evaluation in the asymptomatic infant as follow:

**Postnatal ultrasound**

- No Hydronephrosis (AP dia ≤ 10mm)
- Hydronephrosis (AP dia ≥ 10mm)

**Ureter dilated**
- Repeat USG at 4-6 weeks

**AP dia ≤ 10 mm**
- AP dia ≥ 10 mm

- No further follow up

**AP dia ≥ 10 mm**
- MCU
- VUR present
- VUR absent
- Lower urinary tract obstruction

**VUR present**
- Manage according to grade
- VUJ obstruction
- Surgery

**VUR absent**
- Renal scan

- Differential func < 40%
- Differential func > 40%

- Surgery
- Serial USG 3-6 monthly

- Resolving Hydronephrosis
- Conservative approach with serial USG
- Renal Scan
- Reduction of renal func by 5-10%
- Surgery

- Persistent/progressive hydronephrosis

and V), there is no definite advantage of medical management over surgery.

Urterovesical junction obstruction (megaureter), Posterior urethral valve, Ureterocele, duplex kidney mandates surgical management.

Parental information, explanation, and counseling has a significant impact on management of disorder, as highlighted by Watson et al. There is a danger of causing unnecessary anxiety by covering in detail all possible outcomes, particularly since there are likely to be a significant number of false positive results. However, this is not an argument against counseling, nor should it act as deterrent.

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Communicating Hydrocephalus in Neurocysticercosis

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Abstract:
An 8 year old male presented with left sided incomplete hemiparesis. He was on valproate due to seizures caused by neurocysticercosis (NCC), detected 1 year back. MRI brain in this episode revealed a communicating hydrocephalus. No extra-parenchymal or intra-parenchymal cysts were visible. CSF study and serology for anti-neurocysticercal antibodies confirmed it to be a case of NCC. It was a rare case of communicating hydrocephalus due chronic basal arachnoiditis caused by racemose variety of NCC.

Key words: Neurocysticercosis, racemose variety, communicating hydrocephalus.

Introduction:
NCC is the most common parasite infesting the CNS in endemic countries like India. Seizure is the most common manifestation. Signs of increased intracranial pressure are often evident. Ring enhancing lesion on brain imaging makes the diagnosis. Initial management is symptom-based followed by antiparasitic drugs. Prevention of intestinal T.solium infection is the key measure for prevention of neurocysticercosis.

Case report:
An 8 year old Hindu male was admitted with history of weakness of the left upper and lower limbs for last 1 month. The weakness was gradually increasing in severity and at admission he was unable to walk without support. He was born out of a non-consanguinous marriage, term, appropriate for gestation. At 7 years of age he started having recurrent complex partial seizures. MRI brain revealed multiple ring-enhancing lesions suggestive of neurocysticercosis,(fig 1).

Since then he was on oral valproate and the seizures were under control. One year post detection was uneventful whereafter gradually the weakness and headache started. The headache was associated with nausea and vomiting but had no diurnal variation. There was no history of fever, loss of consciousness, any difficulty in vision or any head trauma.

History of contact with tuberculosis was absent. Clinical examination showed power 4/5 in both left upper and lower limb with exaggerated deep tendon reflexes and planter extensor on the left side. The younger brother was also a diagnosed case of NCC who was on regular anti-convulsant therapy. MRI of the brain was done for his weakness. It showed to be a case of communicating hydrocephalus (dilated lateral, 3rd, 4th ventricles and also basal cisterns) probably due to diffuse subarachnoid racemose variety of NCC. No intraparenchymal or extra-parenchymal cysts were visible in the MRI (fig -2). Patient was put on oral acetazolamide and was referred for ventriculo-peritoneal shunt. The patient had a normal chest x-ray, a negative mantoux and sputum examination negative for AFB. The IgG cysticercosis antibody was positive in both the CSF and serum by enzyme-linked immunosorbent assay. It was confirmed by enzyme-linked immunoelectrotransfer blot assay for both CSF and serum. The CSF study showed a total cell count of 65/cumm(77%
lymphocytes, 23% neutrophils) with a mild elevation of protein (60mg/d le) and a normal sugar (51mg/dl). The CSF T.B. PCR and adenosine deaminase level was normal. CSF culture, gram stain and Indian ink preparation were negative.

Discussion:

Neurocysticercosis is the most common parasitic infection of the central nervous system. In endemic countries like India it forms a major public health problem. A recent study reported an overall frequency of subarachnoid cysts in 2%, ventricular cysts in 6%, and hydrocephalus in 16% of NCC cases. Intraventricular NCC, the presence of Taenia solium cysts in the cerebral ventricular system, occurs in 7-30% of patients with NCC. According to recent studies, extraparenchymal NCC is probably more frequent than was previously thought. In our report it was a case of both intraparenchymal and extraparenchymal NCC with communicating hydrocephalus probably due to extra-parenchymal (subarachnoid cysts) or inflammatory exudation induced by diffuse, racemose variety of NCC. No intraventricular cyst was visible on imaging. It was only intra-parenchymal to start with 1 year ago. The disease course remained gradually progressive to become diffuse and devastating which is very rarely reported in literature. Extra-parenchymal NCC is associated with a local inflammatory response with high protein concentration and cell counts in the CSF. Clinical manifestations and CSF findings are similar to the more common tuberculous and fungal meningitis, since the CSF findings consist of pleocytosis (usually lymphocytic but frequently polymorphonuclear), reduced glucose with an elevated protein. In our case there was a lymphocytic pleocytosis with mild elevation of protein and normal sugar. An important clue may be the presence of eosinophils in the CSF in cysticercous meningitis which was seen in the initial phase of illness and usually occurs in 15% of the cases. CSF picture with lymphocytic pleocytosis, raised protein, decreased sugar, absence of typical eosinophilia with evidence of chronic meningitis, hydrocephalus on imaging and endemicity of the area all may bias a clinician towards a mis-diagnosis of tuberculosis. It is therefore a high level of clinical suspicion with supporting serological markers that are necessary for the diagnosis of cysticercal hydrocephalus for an effective management.

References:


Answer to Photo Quiz

1. Prune belly Syndrome (alternately it is also known as abdominal muscle deficiency syndrome, congenital absence of the abdominal muscles, Eagle-Barrett syndrome, Obrinsky syndrome, Fröhlich syndrome, Triad syndrome)

2. Prune belly syndrome is a group of birth defects that involve three main problems:
   (i) Poor development of the abdominal muscles, causing the skin of the belly area to wrinkle like a prune
   (ii) Undescended testicles (cryptorchidism)
   (iii) Urinary tract problems

3. Ventricular Septal defect, Malrotation of the gut, club foot.
E. Coli sepsis causing secondary HLH
(Hemophagocytic Lymphohistiocytosis)

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Abstract
HLH is an important haematological manifestation of various diseases. Reactive HLH secondary to infections occurs most commonly due to viruses. Other than EBV (Ebstein Barr Virus), HLH secondary to infections is associated with recovery in 60-70% cases. Here we report HLH occurring secondary to E.coli sepsis in an one year male child who presented with fever and hepatosplenomegaly.

Introduction
HLH also known as hemophagocyticlymphohistiocytosis is of two types-primary and secondary. Primary HLH may be familial or may be associated with immune deficiencies. It is usually triggered by an infection or may also occur de novo. Acquired HLH usually occurs secondary to malignancies like leukemia, Hodgkin or Non Hodgkin lymphoma, immunosuppressive therapy, autoimmune diseases, and infection. Common pathogens known to cause HLH include viruses eg EBV, Cytomegalo virus(CMV), HIV, Hepatitis A virus, bacteria eg, brucella, mycobacteriumtuberculi and fungi. HLH if not treated early is associated with high mortality.

Case Report
A one year male infant born out of non-consanguinous marriage with normal growth and development presented with high grade fever (with occasional chills) for 3 weeks and swelling of feet two days prior to admission. He was apparently healthy and did not have any history of joint pain, rash, chronic ailment in the family. There was no history of contact with tuberculosis.

On examination the child was pale, febrile and irritable. He had pedal edema with significant hepatosplenomegaly. Examination of other systems did not reveal any abnormality.

Routine complete hemogram showed-Hb 9gm/dl, total White blood cell(WBC) count-10,700/cumm(P20,L68,M6,E6,B0), Platelet count 70,000/cumm. ESR (mean) was 47mm, CRP [C reactive protein] 24mg/dl (normal 6 mg/dl). Peripheral blood smear did not reveal any malarial parasite and dual antigen for malarial parasite was negative. Serum urea, creatinine, sodium and potassium were within normal limits. Liver function test showed -total protein 6.1mg/dl(albumin 2mg/dl, globulin 4.1 mg/dl) SGOT 500IU/ml, SGPT 50IU/ml, alkaline phosphatise 234 IU/ml, total bilirubin 0.7mg/dl (conjugated 0.5mg/dl, unconjugated 0.2mg/dl). PT, APTT were within normal limits, INR 1.2.

HAV IgM, HCV antibody, HbsAg, HIV serology and Widal test were negative.

Routine examination of urine revealed 12-15 pus cells per high power field.

Mantoux test was negative and gastric aspirate on two consecutive days did not show acid fast bacilli. Chest Xray was normal. Ultrasonography of abdomen revealed hepatosplenomegaly with mild ascitis.

The child was put on broad spectrum antibiotic-intravenous ceftrioxone. But even after 48 hours fever continued with a further dip in haemoglobin(7mg/dl) and platelet count(30,000/cumm).

By this time urine and blood culture reports came in. Both grew E.coli which was resistant to all drugs except meropenem.

In the background of fever, splenomegaly, hepatitis (elevated transaminases SGOT>>SGPT), cytopenias, and hypo-albumenemia, serum ferritin and triglyceride were sent. Serum ferritin turned out 2500IU/ml and triglyceride 536 mg/dl.

Intravenous meropenem was started along with supportive therapy. The child responded within 48 hours, and became afebrile.

Discussion
HLH is characterised by fever, pancytopenia, splenomegaly and hemophagocytosis in bone marrow, liver or lymphnode. This entity was first described by Scott and Rob-Smith in 1993 and was then referred to as histioyctic medullary reticulosis. It includes common features of hemophagocytosis, hyperferritenemia, hypercytokinemia, variable cytopenia,
hypofibrinogenemia, multiorgan failure and even death. It is pathologically characterised by a defect in NK (natural killer) cells and cytolytic T cells leading to an overactivation of macrophages which causes engulfment of red blood cells, platelets, leucocytes and other precursor cells. These activated macrophages can be demonstrated in bone marrow, lymphnodes or spleen. The activated macrophages liberate a host of cytokines like IL-1, IL-6, TNFalpha that lead to a cytokine storm in the body.

**Criteria for the diagnosis of HLH** as proposed by the Histiocytic Society include molecular diagnosis, clinical, laboratory and histopathological features.

**HLH criteria 2009** include:

A) Molecular Diagnosis consistent with HLH.

B) Atleast 3 of 4:
- Fever
- Splenomegaly
- Hepatitis
- Cytopenias

C) Atleast 1 of 4:
- Hyperferritinemia
- Hemophagocytosis
- Decreased or absent NK cell activity
- Increased IL-2 R alpha

D) Other supportive criteria:
- Hypofibrinogenemia
- Hyponatraemia
- Hypertriglyceridemia

Of the central nervous system manifestations, encephalopathy, meningism and seizures are most common.

The clinical diagnostic criteria in the index case included fever, splenomegaly, hepatitis, hyperferritinaemia, hypertriglyceridemia and cytopenia. Bone marrow examination to demonstrate hemophagocytosis could not be done as the parents did not give consent for an invasive procedure.

For patients with reactive HLH associated with infection, supportive therapy along with treatment of the underlying infection is associated with recovery in 60-70% cases. EBV infection leading to secondary HLH however necessitates aggressive immune and chemotherapy.

It is important to differentiate secondary HLH due to infection from familial HLH triggered by an infection because contrary to previous beliefs familial HLH, first episode can occur at any age. The distinction is important because allogenic bone marrow transplantation is the treatment of choice in familial HLH.

HLH also needs to be distinguished from other conditions like sepsis, SIRS (Systemic Inflammatory Response Syndrome) and MODS (Multiple Organ Dysfunction Syndrome) which closely mimic HLH, as the management strategies and outcome of each other differ according to etiology. Most of the patients with secondary HLH have features like fever, hypotension, cytopenias, hypofibrinogenemia, hyperferritinaemia and hypertriglyceridemia which are also commonly found in severe sepsis. In such clinical scenario NK cell activity, soluble CD4 are two tests which will help us to differentiate these conditions from HLH as their sensitivity is 100%. Secondary HLH due to E.coli sepsis in the background of rheumatological diseases have been cited.

So far E.coli sepsis leading to secondary HLH in immunocompetent children have rarely been reported. The index case was an immunocompetent child secondary HLH due to E.coli sepsis. He responded to intravenous meropenem along with supportive therapy. At present the child regularly comes for follow up and is doing well.

**References**


Cooling for newborns with hypoxic ischaemic encephalopathy
Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG
Published Online: 28 March 2013
There is evidence that induced hypothermia (cooling) of newborn babies who may have suffered from a lack of oxygen at birth reduces death or disability, without increasing disability in survivors. This means that parents should expect that cooling will decrease their baby's chance of dying, and that if their baby survives, cooling will decrease his/her chance of major disability. A lack of oxygen before and during birth can destroy cells in a newborn baby's brain. The damage caused by the lack of oxygen continues for some time afterwards. One way to try to stop this damage is to induce hypothermia - cooling the baby or just the baby's head for hours to days. This treatment may reduce the amount of damage to brain cells. This review found that there is evidence from trials to show that induced hypothermia helps to improve survival and development at 18 to 24 months for term and late preterm newborn babies at risk of brain damage. More research is needed to understand which infants need cooling and the best way of cooling, including duration of treatment and method of cooling.

Early erythropoietin for preventing red blood cell transfusion in preterm, low birth weight infants, or preterm infants with low birth weight
Ohlsson A, Aher SM
Published Online: 26 April 2014
In newborn infants, the number of red blood cells in the circulation decreases after birth. In infants born before term this decrease is exaggerated by frequent withdrawal of blood, which may be necessary to monitor the infant's clinical condition. Therefore, infants born before term are likely to require transfusions of red blood cells. Low levels of erythropoietin (EPO), a substance in the blood that stimulates red blood cell production, in preterm infants provide a rationale for the use of EPO to prevent or treat anaemia. EPO can be given 'early' (before the infant reaches eight days of age) in order to prevent or decrease the use of red blood cell transfusions. A total of 2209 infants born before term have been enrolled in 27 studies that used this approach. Early EPO treatment reduced the number of red blood cell transfusions and donor exposures following its use. However, the overall benefit of EPO may not be clinically important as many of these infants had been exposed to red blood cell transfusions prior to entry into the trials. Treatment with early EPO did not have any important effects on mortality or common complications of preterm birth with the exception that EPO may increase the risk for retinopathy of prematurity, a serious complication that can cause blindness in babies born before term. Based on our findings EPO is not recommended for routine use in preterm infants.

Home- versus hospital-based treatment for uncomplicated newborn jaundice in term infants New Malwade US, Jardine LA
Published Online: 10 June 2014
Newborn infants commonly develop a condition called jaundice. Jaundice occurs as the result of accumulation of a yellowish-orange pigment called bilirubin in the skin and eyes. Bilirubin in increased concentrations can be damaging to the brain and can have profound long-term detrimental effects. Phototherapy is a form of treatment used in newborns to reduce levels of bilirubin. "Home-based phototherapy" can be used in the home setting with appropriate supervision. Home phototherapy is used only in cases of uncomplicated newborn
jaundice. Home-based phototherapy can offer certain advantages such as reduced hospital costs and improved bonding between an infant and mother. On the other hand, home-based phototherapy could be associated with problems such as increased risk of the damaging effects of bilirubin on the brain and increased risk of readmission to hospital. In this Cochrane review, home-based phototherapy was compared with hospital-based phototherapy for uncomplicated jaundice in full-term newborns. The review authors found no studies that met the eligibility criteria. The authors of this Cochrane review conclude that no high-quality evidence is currently available to support or refute the use of home phototherapy for uncomplicated newborn jaundice.

**Higher versus lower protein intake in formula-fed low birth weight infants**

*Fenton TR, Premji SS, Al-Wassia H, Sauve RS*

**Published Online:** 21 April 2014

Dietary protein is needed for normal growth and development. The protein intake required for growth of the low birth weight infant has been estimated by the growth rate of the fetus to be 3.5 to 4.0 g/kg/d. Controlling the amount of protein given to low birth weight babies (less than 2.5 kg) fed with formula is important. Too much protein can raise blood urea and amino acid (phenylalanine) levels, and this may harm neurodevelopment. Too low protein intake may limit the growth of these infants. The review authors searched the medical literature to identify studies that compared protein intake as follows: between 3 and 4 g of protein per kg of infant body weight each day versus less than 3.0 g/kg/d or greater than 4.0 g/kg/d by low birth weight infants fed formula during their initial hospital stay. Increased protein intake resulted in greater weight gain of around 2.0 g/kg/d. Based on increased body incorporation of nitrogen, this was associated with increased lean body mass. The present conclusion was based on six studies that changed only the protein content of the formula and was supported by three additional studies that made changes in other nutrients as well. No significant difference in the concentration of plasma phenylalanine was noted between infants fed high or low protein content formula. The review was limited in the conclusions made because differences in protein content among comparison groups in some of the individual trials were small and formulas differed substantially across studies; some studies included healthier and more mature premature infants. Study periods varied from eight days to two years, so information on long-term outcomes was limited. Existing research is not adequate to allow specific recommendations regarding formula with protein content that provides more than 4.0 g/kg/d.

**Probiotics for prevention of necrotizing enterocolitis in preterm infants**

*AlFaleh K, Anabrees J*

**Published Online:** 10 April 2014

Necrotizing enterocolitis (NEC) is a serious disease that affects the bowel of premature infants in the first few weeks of life. Although the cause of NEC is not entirely known, milk feeding and bacterial growth play a role. Probiotics (dietary supplements containing potentially beneficial bacteria or yeast) have been used to prevent NEC. Our review of studies found that the use of probiotics reduces the occurrence of NEC and death in premature infants born weighing less than 1500 grams. There is insufficient data with regard to the benefits and potential adverse effects in the most at risk infants weighing less than 1000 grams at birth.

**Dilute versus full strength formula in exclusively formula-fed preterm or low birth weight infants**

*Basuki F, Hadiati DR, Turner T, McDonald S, Hakimi M*

**Published Online:** 6 November 2013

Babies born prematurely (at less than 37 weeks gestation) or with a low birth weight (less than 2500 grams) have special feeding requirements. Preterm babies are often fed with formula milk because breast milk is not always available. The provision of artificial feeds varies considerably in preterm babies and there is concern that introducing full strength formulas too early may lead to the retention of feed in the stomach which is associated with feeding intolerance and the severe bowel disorder, necrotisingenterocolitis. This review looked at whether dilute formula milk is more effective than full strength formula milk in the initial feeding of preterm babies. The evidence for this review is current up to February 2013. Three studies were included in the review, one small, low-quality trial in 50 preterm infants; a second small, moderate quality trial in 38 preterm infants and a third very small trial of unclear quality in 14 preterm infants. The trials found that infants receiving dilute formula achieved full energy intake earlier than infants receiving full strength formula (20 kcal/oz) and experienced fewer episodes of feeding intolerance. A lack of data on other important outcomes, such as the incidence of necrotisingenterocolitis and weight gain, limits the usefulness of the studies and highlights areas that need to be addressed in future trials.
Day 1 : 13 December 2014 (Saturday)

08.30-09.30 : Award paper Session
   Oral Presentation
   Judges : Swapna Chakraborty, Prabhabati Banerjee, Dilip Pal
   Poster presentation
   Judges : Asha Mukherjee, B C Mondal, P K Das

09.30-10.20 : Panel Discussion : Approach to Bleeding Disorder in Children
   Moderator : Prantar Chakraborty
   Panelists : Anupam Sachdev, Gauri Kapoor, Madhusmita Sengupta, Arpita Bhattacharya, Maitreyee Bhattacharya

10.20-11.10 : Panel Discussion : Common ENT and Upper Respiratory Infection
   Moderator : Santanu Bhakta
   Panelists : Tapan Sinha Mahapatra, Kamal Halder, Abhijit Dutta, Sumantra Sarkar

11.10-12.10 : Plenary Session (20 mins each)
   Chairperson : Dilip Mukherjee, Nabendu Chaudhuri
   (i) Bleeding disorder in childhood – Anupam Sachdev
   (ii) Shared care in oncology : Gauri Kapoor
   (iii) Acute Encephalitis Syndrome: Apurba Ghosh

12.10-01.00 : Panel Discussion Management of Preterm, LBW Neonates
   Moderator : Arun Manglik
   Panelists : Atanu Jana, Kheya Ghosh Uttam, Kaustav Chaudhury, Suchandra Mukherjee

01.00-01.40 : Dr S P Ghosal Memorial Oration
   Chairperson : Madhusmita Sengupta, Santanu Bhakta
   Topic: Medical Education – Is its standard in decline ?
   Orator : Sukanta Chatterjee

01.40-02.30 : LUNCH

02.30-03.30 : Vaccine in Office Practice I (15+5 mins each)
   (a) JE, (b) DTP, (c) Rotavirus

03.30-04.20 : Panel Discussion : Child with Wheeze
   Moderator : Subhasis Roy
   Panelists : Atul Gupta, Pallab Chatterjee, Goutam Ghosh, Mousumi Mukherjee

04.30 : AGM of WBAP

05.30 : INAUGURATION OF WB PEDICON 2014

07.00 : Cultural Program and Banquet
Day 2 : 14 December 2014 (Sunday)

09.00-09.50 : Panel Discussion : Growth, Monitoring and Developmental Delay
  Moderator : Monidipa Banerjee
  Panelists : Ranjana Chatterjee, Jaydeb Ray, Nandita Chatterjee, Amiya Ghatak

09.50-10.40 : Panel Discussion : Joint Pain in children
  Moderator : Priyankar Pal
  Panelists : Raju Khubchandani, Tapas Sabui, Rakesh Mondal, Suparna Guha

10.40-11.20 : Plenary Session II
  Chairperson: Bhaskarmani Chatterjee, Amaresh De
  (i) Probiotic–how useful it is in children? Sutapa Ganguly
  (ii) Medical Management of Constipation in Children: Bhaswati Acharya

11.20-12.10 : Panel Discussion : Resistant Infection
  Moderator : Ritabrata Kundu
  Panelists : Nitin K Shah, Subhasis Bhattacharya, Nupur Ganguly, Madhumita Nandi

12.10-12.50 : Dr Tapan Kr Ghosh Memorial Oration :
  Chairperson : Sunil Kr Nag, Arup Roy
  Topic: Pediatric Rheumatology in India
  Orator : Raju Khubchandani

12.50-01.50 : Vaccine in Office Practice II
  (i) Typhoid Conjugate Vaccine – Monjori Mitra
  (ii) Pneumococcal - Jaydeep Choudhury
  (iii) Pertussis – Nitin K Shah

01.50-02.30 : LUNCH

02.30-03.20 : Panel Discussion : Interesting case Scenarios in Nephrology
  Moderator : Jayati Sengupta
  Panelists : Sushmita Banerjee, Amitava Pahari, Rajib Sinha, Mousumi Nandi

03.20-04.10 : Panel Discussion : Critical Case Scenarios in Intensive Care
  Moderator : Debjani Gupta
  Panelists : Agnisekhar Saha, Subhodeep Das, Soumen Meur, Brojogopal Ray

04.10 : Valedictory
Day 1 (8th Nov 2014)

08.30-09.00 am : Panel Discussion: 1 (NEONATOLOGY)
Topic: Neonatal Sepsis & Shock
Moderator : Dr. Nigam Prakash Narayan
Participant : Dr. Bijan Saha / Dr. Rajesh Kumar / Dr. Rita Bora / Dr. Sohit Gupta
Moderator : Dr. Nigam Prakash Narayan
Participant : Dr. Bijan Saha / Dr. Rajesh Kumar / Dr. Rita Bora / Dr. Sohit Gupta

09.00-10.00 am : PLENARY SESSION
Chairpersons: Dr. Bikash Roy & Dr. Krishna Chourajit Singh
Topic: 1. Health Status of Children of Bangladesh
Speaker: Dr. M. S. Akbar (Bangladesh)
Topic: 2. ORS: Yesterday, Today & Tomorrow
Speaker: Dr. Gadadhar Sarangi
Topic: 3. Empyema Thoracis: Dilemma in Treatment
Speaker: Dr. Apurba Ghosh

10.00-10.45 am : CRITICAL CARE SESSION
Chairpersons: Dr. Swapna Chakraborty / Dr. Ibochouba Singh
1. Oxygen Therapy in PICU
Speaker: Dr. Rashna Dass
2. Management of Pediatric Septic Shock
Speaker: Dr. Mrityunjoy Pao
3. Ventilator Associated Pneumonia
Speaker: Dr. Shyam Sundar Singh

10.45-11.00 am : BREAK

11.00-11.30 am : DR. TAPAN GHOSH MEMORIAL ORATION
Speaker: Dr. Bikash Roy
Chairpersons: Dr. Shahidullah (President, BPA) & Dr. Krishna Kumar

11.30-12.15 Noon : Panel Discussion: 2
Topic: Acute Encephalitis Syndrome
Moderator: Dr. Apurba Ghosh
Participant: Dr. Tapan Majumder / Dr. Manab Narayan Bora / Dr. L. Manglem Singh

12.15-12.45 pm : CARDIOLOGY SESSION
Chairpersons: Dr. Sunil Kr. Nag & Dr. Radha Tripathy
1. Benign Epilepsies of Childhood
Speaker: Dr. Jayanti Chakraborty
2. Autism Spectrum Disorder
Speaker: Dr. Anjan Bhatchharya
3. Headache in Children
Speaker: Dr. Santanu Deb

12.45-01.15 pm : NEPHROLOGY SESSION
Chairpersons: Dr. Bhaskarmani Chatterjee & Dr. Aswini Mohanty
1. Renal Tubular Diseases
Speaker: Dr. Arakhita Swain
2. Steroid Resistant Nephrotic Syndrome
Speaker: Dr. Himesh Burman

01.15-02.00 pm : LUNCH

02.00-03.00 pm : MIXED BAG Hall-1: Concurrent Session -1
Chairman: Dr. Keshab Debnath & Dr. Arup Roy
1. Sleep Disorder in Children
Speaker: Dr. Shantanu Bhakta
2. Chronic Diarrhoea & Malabsorption in Pediatric Practice
Speaker: Dr. Amitabha Bandopadhyay

3. Obesity
Speaker: Dr. D.P. Banerjee
4. Short Stature
Speaker: Dr. Amitabha Chakraborty

Mixed Bag: Hall-2
Chairpersons: Dr. B.R. Master / Dr. B.P. Jaiswal
1. Rickets: A Growing Concern
Speaker: Dr. N.R. Majumder
2. Organizational Overview of NRP-FGM with reference to Manipur
Speaker: Dr. L. Basanta Singh
3. Screening at Birth
Speaker: Dr. Tapash Ghosh
4. Know Your the "Dust of Blood"
Speaker: Dr. N Kameshore Singh

Day 2 (9th Nov 2014)

08.00-10.00 am : AWARD PAPER SESSION (Oral Presentation)
Judges: Dr. / Dr. R.B. Thakur / Dr. Ashutosh Datta
Presentation x 8 Nos. by PGTs
Poster Presentation Judges: Dr. D.P. Banerjee / Dr. Dipal Debbarma / Dr. Shyama Saikia

10.00 -10.45 am : RESPIRATORY CHAPTER
Chairpersons: Dr. Kalyamoy Bose & Dr. Radhapyari L
 Bronchoscopy in Children
Speaker: Dr. Pallab Chatterjee
Pulmonary Function Test
Speaker: Dr. Sudip Datta (Sikim)
Asthma Management: Recent Guidelines
Speaker: Dr. Rajkumar Koyal

10.45-11.15 am : VACCINOLOGY SESSION: 1
Chairpersons: Dr. Rahul Amin / Dr. Aswini Kr. Mohanty
Eradication of Polio: End Game -- What Next?
Speaker: Dr. A.K. Datta
Prevention of Hepatitis A
Speaker: Dr. Manjari Mitra

11.15-11.45 am : VACCINOLOGY SESSION: 2
MEET THE EXPERT ON VACCINOLOGY
Experts: Dr. A.K. Datta / Dr. Manjari Mitra / Dr. Sudhir Mishra

11.45-12.45 pm : MIXED BAG
Chairpersons: Dr. Satyabrata Banerjee & Dr. N.L. Bhaukim
1. Anemia in Adolescent Girls: Issues & Challenges
Speaker: Dr. Sudha Reddy
2. Menstrual disorder in Adolescents
Speaker: Dr. Garima Saikia
3. Needs of Probiotic in Pediatric Practice
Speaker: Dr. Jayanta Poddar
4. Hemoglobin estimation in Children 0-14 years in JNIMS
Speaker: Dr. RK Rupabati Devi

12.45-01.00 pm : ANNOUNCEMENT & DISTRIBUTION OF PRIZES
Award Paper + Poster

01.00-01.30 pm : LUNCH

01.30-02.15 pm : VALEDICTORY SESSION

For details:
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