Heliox Use in Ventilation of Preterms

The recent randomized controlled trial by Xue, *et al*. [1] aims at reducing the length of ventilation as primary aim. The authors have also looked into lung inflammatory markers like Interleukin-6, which was positively correlated with the length of ventilation but was not proved significant.

Heliox gas flows in laminar fashion creating less resistance because of its property of low density and lower Reynolds number which thereby helps in gas exchange and reduced work of breathing, particularly in disease states where there is evidence of airway obstruction [2,3]. It is still unclear how heliox helps in improving outcome in respiratory distress syndrome; the possible explanation other than reducing lung inflammation is improving oxygenation and carbon dioxide elimination and thereby improving the blood pH and reducing pulmonary hypertension.

The participants in this study were mid-late premature infants (mean gestation 34 weeks); many ongoing/ completed trials aim to assess interventions for reducing morbidity, particularly chronic lung disease, in preterm cohorts born earlier than 34 weeks. Reduction in length of ventilation in this study cohort may not be too great as these babies generally require short term ventilation. Moreover, heliox is likely to be a costly intervention; the reported cost is 750• for 12 hours of treatment [4].

The authors have concluded that nasal intermittent positive pressure ventilation might have increased the efficacy of delivering heliox, as an earlier study [4] failed to show reduction in length of ventilation when CPAP was used. The population in the earlier trial was more premature (30 weeks) and the reduction in the length of ventilation was not the primary objective. Practically, heliox reduces the increasing oxygen requirement by effective delivery of gas thereby decreasing the threshold for surfactant/ ventilation and is unlikely to affect the length of ventilation. We suggest that the utility of heliox should be tested in more immature infants with the objective to reduce chronic lung disease and other morbidity.

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Heliox Use in Ventilaion of Newborns: Authors' Reply

Even though the distinct mechanisms of helium-induced organ protection have not been completely unraveled, several signaling pathways have been identified [1]. It has been shown that heliox could decrease neutrophil infiltration, intra-alveolar edema, perivacular hemorrhage and hyaline membrane formation of acute respiratory distress syndrome in rats [2]. Nawab, *et al*. [3] reported that heliox attenuated lung inflammation and structural alterations of piglets in acute lung injury. In our study, serum IL-6 at baseline was found be positively and significantly correlated with the length of ventilation (LoV) [4], which supported the speculation that helium might have anti-inflammatory effect in humans in *vivo*. Thus, we speculated that there might be other mechanisms of action of heliox, besides its physical effects in respiratory diseases.

Heliox has been demonstrated to decrease the threshold for surfactant and ventilation by reducing the increasing oxygen requirement in Colnaghi's study [5], which has important practical application. It is very important that the utility of heliox in reducing chronic lung disease should be expanded in more immature infants. However, one purpose of our study was to assess the effectiveness of heliox on lung inflammation cytokines. We tried to explain the reason why heliox could improve the outcome of RDS from another perspective.

Infants born before 32 weeks contribute to high occurrence of complications of prematurity such as

retinopathy of prematurity, intraventricular hemorrhage and periventricular leukomalacia. Nevertheless, premature infants born between 32-36 weeks form a large proportion in NICU, and some need assisted ventilation. Longtime ventilation will increase the risk of lung injury. Length of ventilation should be the primary outcome as it plays an important role leading to ventilator- associated lung injury. Further researchon the mechanisms of heliox in respiratory diseases are still needed.

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Immunization Recommendations Should not be Ambiguous

This refers to the Guidelines regarding immunization schedule for children upto the age of 18 years recommended by IAP [1]. There are some contradictory or confusing statements which need clarification:

Rotavirus vaccine: There is no change in the existing schedule of RV1 vaccine that includes the first dose at 10 weeks of age instead of 6 weeks in order to achieve better immune response, and the second dose at 14 weeks to fit with existing National immunization schedule [2]. It is further stated RV1 (Rotarix) should preferably be employed in 10 and 14 week schedule, instead of 6 and 10 weeks, which suggests that for RV5 (Rota Teq) 1st dose is to be administered at 6 weeks.

Hepatitis B vaccine: Under footnotes it is stated that ideally, the final (3rd or 4th) dose in the Hepatitis B vaccine series should be administered no earlier than age 24 weeks, and at least 16 weeks after the first dose, whichever is later. On the contrary, it also states "Hepatitis B vaccine may also be given in any of the following schedules: birth, 1 and 6 mo; birth, 6 and 14 weeks; 6, 10 and 14 weeks; birth, 6, 10 and 14 weeks."

HPV vaccine: It is stated that "two doses of HPV vaccine are advised for adolescent/pre-adolescent girls aged 9-14 years; for girls 15 years and older, current 3 dose schedule will continue." In the figure 1, range of recommended ages for all children in yellow shade is for 11 and 12 years, which would suggest that it is not recommended for 9 and 10 year old girls, and also that two doses are required till the age of 12 years, and not till age of 14 years.

Changing the needle: Under General instructions in the footnotes, authors state that changing needles between drawing vaccine into the syringe and injecting it into the child is not necessary. Currently used syringes and needles are meant for single use. When the needle pierces skin or rubber stopper, it loses its sharpness. To reduce pain, after refilling the syringe, it would be advisable that the needle be changed. There is no need to change the needle if vaccine or other liquid has been withdrawn from an ampule, and injected. In case liquid from one container is withdrawn and pushed in another containing vaccine and withdrawn, then needle should be changed.

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IAP Immunization Guildelines: Author's Reply

1. *Rotravirus vaccine*: It is true that the figure with range does not show the range of administration of rotavirus vaccines [1]. We have deliberately avoided providing a range since it is of paramount importance to complete the series with RV1 or RV5 within the stipulated time limit owing to higher incidence of intussusception if the prescribed age-limit is exceeded. It is not always possible to display all the information in a single figure or chart. The detailed information on administration of each of the vaccines shown in the figure is provided in the footnotes. One should also make note of the footnote immediately below the figure which reads, "These recommendations must be read with the footnotes that follow".
2. *Hepatitis B vaccine*: It is customary to provide ideal minimum and maximum intervals between different doses of a vaccine that is employed in more than one dose schedule. This is of significant importance for those who fall behind or start late, *i.e*. for catch-up vaccination. The schedule and duration provided in the IAP immunization schedule are ideal for immunizing an individual child in office practice. However, Hepatitis B vaccine is also provided through mass immunization in Universal Immunization Program (UIP) in a shorter schedule (*i.e.* at birth, 6, 10 and 14 weeks) mainly due to logistic and programmatic reasons. These schedules are also found to be protective and permitted for use in large scale immunization programs, particularly in developing countries [2].
3. *HPV vaccine*: The most appropriate time slot recommended for HPV vaccine is indicated in yellow shade in the figure [1]. As elaborated above, it is not possible to display all the information in a single figure and the figure must be read with the footnotes that follow.
4. *Changing the needle*: The current recommendation, *i.e.* "changing needles between drawing vaccine into the syringe and injecting it into the child is not necessary" is based on overall general vaccination practice all over the world. In most instances it is not necessary. The recommendation is also in concurrence with the guidelines issued by international agencies like CDC and WHO. However, on certain exceptional occasions when the clinician thinks the needle may have got blunted due to multiple punctures/pricks, it can be changed.

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Listen to Mother First

My daughter in law delivered a 3.5 kg baby with caesarean section. On third day, the baby was taken for immunization to a private pediatric nursing home where two pediatricians combine have a practice; each one attends the outpatient department on alternate days. The baby was given BCG, oral polio and hepatitis B vaccinations. The parents were advised to bring the baby on fifth day for re-examination. On 5th day, attending pediatrician did not read the immunization notes of his colleague. Inspite of telling that primary immunization was over on first visit, he turned deaf ears to mother's remarks and repeated all three vaccines. He tried to satisfy to worried mother by sham confidence that nothing will happen. He further remarked that all children who received initial vaccinations at government hospital are re-vaccinated within one week interval at their nursing home.

What will be the antibody response in such children due to immune insult caused by repeat vaccination within one week? What should be the advice to mother regarding immunization schedule in this situation?

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Listen to Mother First : Reply

It was indeed a serious lapse on the part of the consulting pediatrician. Mother's views/concerns should never be taken lightly more so in case of vaccination. Proper communication with parents becomes much more important considering that vaccines are given to healthy children and no vaccine is either 100% safe or 100% effective.

In the above instance, three vaccines were inadvertently re-administered within a week, which is against the established principles of vaccination in most instances. While only a single dose of BCG is indicated as per the vaccination schedule, more than one dose is required for OPV and Hepatitis-B. The birth dose of OPV and hepatitis-B serve only as 'priming' dose for the subsequent doses. For multi-dose vaccines, the minimum interval between 2 doses of the same vaccine is usually 4 weeks. This minimal interval of 4 weeks between primary doses allows development of successive waves of antigen-specific primary responses without interference [1].

While no untoward reaction should have occurred with the administered doses of OPV and Hepatitis-B, there may be some interference theoretically with the induction of 'priming' with previous doses. However, the clinical significance is extremely difficult to judge. These extra doses should not be counted and subsequent doses of both the vaccines should be administered on the scheduled dates as indicated by the vaccination timetable.

In case of BCG, which acts mainly through induction of T-cell mediated immunity, any interference with primary induction of immune responses may or may not occur. Also, some heightened local reactions like ulceration at vaccination site or marked regional adenitis may be anticipated few weeks/months later in few instances. There is no need of administration of extra dose of BCG to this child also.

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The Peshawar Peril

Hardly few weeks past the award ceremony of Nobel peace prize for a child in Pakistan and peace is in pieces by the Peshawar peril. The horrifying incidents involving school children in Peshawar, Pakistan and Beslan, Russia are quite disturbing and shaking the entire core of humanity. Children form a vulnerable population at any given point of time and during these man-made disasters, they are the worst affected [1,2]. Why should these innocent children lose their lives for no fault of theirs? Waging war against bacteria and viruses has no meaning when massacres are the order of the day. Exploring mars is pointless when these barbaric acts turn your backyards into graveyards. Terrorism is nothing but a novel way to relive the Stone Age or even darker ages earlier. Terrorism in any form against children is not acceptable and there should be a global awakening in this context.

The story of an act of terror does not end on the same day. The ripples of these events in the community and world as a whole are long-lasting and may generate untoward side effects. Post-traumatic stress disorders (PTSD) and disrupted family lives are usually severe and difficult for management. Just like basic life support, disaster preparedness should be made universal and should not be the headache of the affected nation alone [3]. The terrorists, and the culprits who sold them the weapons should be brought to book and penalized. Media also has a moral responsibility towards the mental wellbeing of children, and hence pictures and videos which may affect their normal milieu should not be broadcast. According to a recent meta-analysis, PTSD outcomes among children and adolescent survivors of natural and man-made disasters receiving psychological interventions were better when compared to those who did not receive any intervention [4]. Strong social support from families, teachers, and community coupled with economic resources to facilitate the family's adaptation should be part of the psychosocial rehabilitation [5]. A social change or revolution is the need of the hour for providing children a safe environment, irrespective of nationality and religion. All children have the right to live and this should not remain in paper alone, but ensured in

day to day practice. Roses should neither be nipped as buds nor soaked in blood.

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Treatment Guidelines for Seasonal Influenza: Need for a Rethink

This year again, H1N1 influenza has arrived in several States of India, and public is likely to get panicky if the number of cases or mortality due to the virus rises. For appropriate disease management, H1N1 wards have been activated in various hospitals in Delhi and a document titled 'National Treatment Guidelines for Treatment of Seasonal Influenza" has been circulated among the hospitals by Directorate of Health Services, Delhi [1]. The new guidelines are not yet available on the website of Delhi Government which still displays the 2012 recommendations [2]. Salient features of the new guidelines are as follows:

H1N1 mostly presents like other seasonal influenza cases but may have severe manifestations in certain situations. Children mostly have influenza like illness (ILI), and are to be managed with home isolation and cough hygiene, along with immediate reporting to health facility if they present with of warning signs (persistent high fever beyond 3-4 days, hemoptysis, breathing difficulty, chest pain, altered sensorium, worsening of associated comorbidity, inability to feed, vomiting, tachypnea, seizure in a young child). Mild or moderate complications include otitis media, bronchiolitis, croup, or reactive airway disease. Severe complications include diarrhea, dehydration, sepsis, exacerbation of chronic illness, or febrile seizure. Complications are more in 'high-risk group' that includes all children <5 y age, and those with chronic underlying pulmonary (e.g. asthma), cardiovascular (e.g. congenital heart disease), neurological (e.g. cerebral palsy), metabolic (e.g. diabetes), renal, hematologic (e.g. thalassemia), or immunological (e.g. primary or secondary immunodeficiency) conditions. Severe cases include those with clinical and radiological signs of lower respiratory tract disease, shock and multi-organ failure, exacerbation of underlying illness, progressive disease with respiratory compromise, central nervous system complications, or invasive bacterial infection. Nasopharyngeal swabs for real-time polymerase-chain-reaction for influenza should be sent if the patient has severe, complicated, or progressive disease; cluster of cases; and in high risk cases with ILIs. Antivirals are indicated only in confirmed cases of H1N1. Need of hospitalization is determined on individual basis. There is no role of chemoprophylaxis for the contacts.

These guidelines appear evasive on certain issues. Previous guidelines [3] included categories A, B and C, but in present guidelines the categorization has been done away with. According to the present guidelines, nasopharyngeal sampling is advised for all under-five children with ILIs. In a typical Governmental set-up, under-five children comprise almost two-thirds of the total daily pediatric outpatient attendance in this season. Approximately half of these children have symptoms of ILIs which amounts to approximate case load of 150 per day in our hospital. As per the new guidelines, these children constitute the high-risk group, and need to be sampled, which is neither practical nor feasible. Lack of clear-cut categories may amount to delayed treatment of cases and continuation of the virus in circulation by ignoring the contacts for treatment. Children with suspected H1N1 infection need to be classified in four distinct categories *viz.* A: where no intervention is required; B: where we test, but do not treat; C: where we test and treat, but hospitalization is not required; and D: where testing is followed by in-hospital treatment. The new guidelines have also done away with chemoprophylaxis of con-

tacts, in keeping with the current international recommendations; however it does not specify whether contacts are to be sampled or not. WHO guidelines recommend giving presumptive treatment to high risk cases [4] but the Delhi Government guidelines forbid antiviral treatment, except in proven cases. In a suspected case, by the time results of PCR are available, the patient is either cured or it may be too late for the antivirals to have a meaningful effect on the course of the disease; though the guidelines recommend treatment whenever the positive H1N1 report is available, irrespective of the duration of illness. Finally, the role of vaccination is not clearly spelt out.

Government guidelines on management and control of a public health issue need to be a benchmark backed by bull-eye accuracy and evidence-base, since these are followed by a large group of care-providers, including those from private sector. With the expertise available, the guidelines could have been focused and practical. It is time for the Indian Academy of Pediatrics to lead and advise its members on the correct approach to management and diagnosis of H1N1 cases.

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Editor's Note: After acceptance of this letter, Delhi Government has released another set of guidelines in the national newspapers which categorize patients as Category 1 (Low risk; no testing or treatment recommended), Category 2 (High risk; antiviral treatment without testing), and Category 3 (Severe disease; hospitalization, testing and treatment recommended).