

unrelated donor was performed at age 7.6 years, after preparation with busulfan, cyclophosphamide, and antithymocyte globulin. At 4.5 years after HSCT, the child has had no significant infections and is healthy, with a normal WBC count ($5.3 \times 10^9/L$) and lymphocyte distribution (CD3+, 58%; CD4+, 32%; CD8+, 22%; CD19+, 29%; CD16+, 11%). In vitro response to mitogens and NK cytotoxic activity also are normal. Antibody responses are positive to both protein and polysaccharide antigens and to attenuated viral vaccines.

These data confirm that NK-cell deficiency predisposes to severe varicella infection, and indicates the existence of a novel form of immune deficiency with NK- and B-lymphocyte deficiency that can be cured by HSCT.

Luigi D. Notarangelo, MD
Evelina Mazzolari, MD
Department of Pediatrics
University of Brescia
25123 Brescia, Italy
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Reply

To the Editor:

We thank Dr Zimmer and colleagues for their comments. As for their first comment, it should be noted that the case that they described as selective NK deficiency, which we did not include in our article, in fact was not a pure case of NK deficiency, because an expansion of a subset of lymphocytes that does not express the α/β heterodimer of the T-cell receptor was observed.¹ Indeed, an NK defect can be seen in TAP-deficient patients, but it is not a major feature in this rare form of primary immunodeficiency. Although there are some functional similarities between NK and NKT lymphocytes, we agree that NKT cell should be distinguished from NK cells. The case reported by Notarangelo and Mazzolari is a rare instance but again emphasizes the important role of NK cells in the immune response to varicella infection. Although their case is not a selective NK deficiency, but rather a combined immunodeficiency of unknown etiology, it seems logical to assume that severe disseminated varicella was indeed due to the total absence of NK cells. We believe that NK cell number and function should be evaluated in every case of severe varicella infection.

Amos Etzioni, MD
Meyer Children Hospital
Rapaport Medical School
Technion, Haifa Israel 31096
10.1016/j.jpeds.2006.01.018

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Oxygen and oxygenation in the delivery room

To the Editor:

We read with great pleasure the elegant editorial of N Paneth¹ in the July issue about the dangers and the hazards of the use of 100% oxygen in the delivery room. We would like to contribute a few questions and comments regarding the concept entered twice by Dr Paneth: "good reasons to resuscitate most babies with room air." There seems to be fairly clear information that 100% inspired oxygen (one extreme) is unnecessary for many infants, risky, and should not be routinely used for all cases. However, this is unfortunately still being received by many infants. The questions we would like to pose are: If this is truly bad, why recommend the other extreme (ie, 21% or room air) in all cases?

The history of "swinging the pendulum between extremes" has been frequent in neonatal care, sometimes with unfortunate consequences. Why must we choose between 21% (room air) versus 100% (pure oxygen) when there are "78 other options in between"? Would this be an acceptable, sound practice in the developed world and in any place where fairly expensive neonatal units and equipment do exist? Would it be a sound practice in areas with no or very limited resources?

As we learn about the physiology of oxygenation, 100% inspired oxygen could lead to significant hyperoxemia in all infants with a transient problem but with "healthy" cardiac anatomy and pulmonary function. Unfortunately, the published studies of administration of 100% oxygen²⁻⁴ do not report the levels of oxygenation in the infants treated. However, in all infants with otherwise normal cardiac anatomy and pulmonary function, as soon as circulation is restored, the PaO₂ is likely to be as high as 300 to 500 mm Hg with FiO₂ of 1.0. This will happen to the vast majority of infants who need transient resuscitation in the delivery room or elsewhere. However, during resuscitation and critical intensive care the issue is not only to avoid unnecessary exposure (FiO₂ 1.0) and hyperoxemia (PaO₂ > 80-90 mm Hg), but also to avoid hypoxemia in the few cases that cannot sustain normoxemia independently. We do not know the values as of which there is hyperoxemia or hypoxemia in the developing human after birth, and we do not know the best and ideal values for neonatal oxygenation.

In spite of this, we do have a pretty clear idea of the oxygen values that should be avoided to avoid both hyperoxemia and hypoxemia.^{5,6} It seems that a sound way to approach the problem of unnecessary oxygen exposure and hyperoxemia would be a practice in the delivery rooms similar to current oxygen use in

neonatal units all over the world. We have described this practice in a protocol⁷ for the use of pulse oximetry to provide, from the time of delivery, the “necessary” FiO_2 to maintain saturation levels that avoid hyperoxia (saturation levels around <95%-96%) and at the same time to avoid hypoxia (saturation level >85%).

Even if we discount the carcinogenic potential of 100% oxygen,² there are very good physiological reasons to resuscitate babies with the necessary amount of FiO_2 required for their clinical condition. Most infants will do just fine with room air (21% oxygen), many others will need supplemental oxygen adjusted rapidly according to their needs (FiO_2 between 22% and 99%), and a very, very few may need 100%.

To adjust oxygen exposure, oxygen blended with air must be available in the delivery room. In addition, the gas should be warm and humid for all infants who require intubation. This “extra” equipment (blenders, pulse oximetry, heater humidifier) is already available in every institution where babies are born in the industrialized world and in every institution in the world with neonatal specialized care. The cost cannot be an excuse for not having the equipment, because it is truly insignificant compared to the neonatal medical equipment expenditures in the same institutions.

Based on best available evidence, health care providers who regulate oxygen exposure when oxygen is delivered to a newborn will reduce unnecessary risks. In relation to resuscitation in the delivery room, it is now clear that it is not only important to do the “right thing” (ie, rapid recovery of affected infants), but to ask ourselves: Are we doing “things right” (ie, avoiding hyperoxia and hypoxia)?

Augusto Sola, MD
Richard Deulofeut, MD, MPH
Marta Rogido
Emory University
Atlanta, GA
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Clonidine exposures, not toxicity

To the Editor:

We read with interest the recent article by Spiller et al entitled “Toxic Clonidine Ingestions in Children.”¹ The title of the article is misleading on several levels. The condition of most of the patients was not “toxic,” and hardly any of them had confirmed “ingestions.” We define “ingestions” as those events that are either witnessed or can be confirmed by laboratory analysis. All other cases are considered “exposures,” which represent most pediatric cases reported to poison control centers. By including many children with “exposures,” the perceived severity of “ingestions” is diluted. Perhaps a more appropriate title would be “Clonidine Exposures in Children.” Although we understand that it is often difficult to obtain prospective cases of witnessed ingestions, we urge the authors to perform a more thorough investigation.

We are also concerned about the far-reaching conclusions of this article. Although most children will do well, we are in the practice of protecting them from what we consider lethal complications of hypotension, bradycardia, and bradypnea from clonidine. This case series reports development of coma, hypotension, and respiratory depression in several patients, one of whom had an unknown dose. This event alone should be enough to recommend transport to the emergency department for evaluation, monitoring, and, if necessary, therapy for all children with unintentional clonidine ingestions greater than their weight-appropriate therapeutic dose.

Melissa Langhan, MD
GarMing Chan, MD
New York City Poison Control Center
New York, NY
Department of Emergency Medicine
North Shore University Hospital
Manhasset, NY
10.1016/j.jpeds.2005.04.022

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Validity of HOMA-IR as index of insulin resistance in obesity

To the Editor:

We read with great interest the article of Balagopal et al,¹ where, in a small cohort of adolescents with obesity, a significant correlation between inflammatory state and insulin resistance was shown. This improved after a brief lifestyle-only intervention.

Insulin resistance was evaluated by using the surrogate index HOMA-IR (homeostasis model assessment of insulin resistance), and this needs to be considered when interpreting the results. HOMA-IR has only been validated in comparison to the euglycemic clamp technique in nondiabetic children. The validity of HOMA-IR remains to be determined in the