Spread the word, children are still not "small adults"

From developmental and metabolic standpoints, the disease processes in children and their responses to therapies are unique from those in adults. Pediatricians must be constantly cognizant that therapies for adults should not be extrapolated to children without a thorough understanding of the developmental aspects of drug metabolism and, in ideal worlds, pharmacokinetic studies and randomized trials in the relevant patient population (Figure 1). These concerns are particularly pertinent for pulmonary vascular diseases of infancy and childhood. Fortunately, attention has finally been given to the need to develop different classification systems specifically for pediatric pulmonary hypertensive vascular diseases.[1,2] The efforts taken to outline relevant clinical and functional classification systems for children with pulmonary hypertension are highly commendable and should lead to significant advancements in the care of this patient population.

With these classification systems as guideposts, greater attention must now be given to the therapeutic needs of pediatric patients with pulmonary vascular disease. This is not to say that no progress has been made in the treatment of pulmonary hypertension for pediatric patients in the past few decades. Results of clinical and animal studies have led to the effective and safe use of inhaled nitric oxide (iNO) therapy for some infants with persistent pulmonary hypertension of the newborn (PPHN), a condition that reflects the failure to successfully transit from the high pulmonary vascular resistance of the in utero environment to the low pulmonary vascular resistance required for postnatal gas exchange and survival ex utero.[3] What is not widely recognized or acknowledged is that up to 40% of infants with PPHN fail to respond to iNO.[4] The need for therapeutic advancements for these infants is vastly underappreciated. Mechanistic studies that evaluate novel strategies for effective pulmonary vasodilation in neonatal animal models and human patients are needed to achieve this goal.

The need for new therapies for pediatric patients with pulmonary vascular disease is certainly not limited to neonates with PPHN. Inadequate investigation and funding have been devoted to improve outcomes and develop therapies for infants and children with progressive forms of pulmonary hypertension that occur with chronic cardiopulmonary disorders, such as bronchopulmonary dysplasia. Pediatric care givers are well aware that the mortality for these patients has not improved in the past 30 years.[5] One limitation to advancement in this field is the paucity of studies using animal models that are relevant to this pediatric patient population and their unique pathophysiological and developmental processes. Additional mechanistic understanding is needed to devise therapies specifically for pediatric patients, especially for those with non-inheritable forms of pulmonary arterial hypertension (PAH). It seems certain that unique therapeutic targets for pediatric pulmonary vascular diseases will be forthcoming if concerted efforts are made to find them.

Both the pediatric and adult scientific community must acknowledge the differences in therapeutic goals for children and adults, even if the mechanistic underpinnings of some therapies should prove to be similar. The need to develop therapies to reverse pulmonary vascular remodeling for adults with pulmonary vascular diseases is receiving a great deal of attention in the contemporary literature.[6,7] Unfortunately, the intended effect of many of these therapies, which is to impair growth of a variety of lung cells, could be devastating to the developing lungs of infants and young children. Treatment goals for pediatric patients must incorporate the need to enhance, not impede, pulmonary vascular growth and development.

We must strongly countermand all the commonly held beliefs that research in children and relevant animal models is not needed because therapies that work for adults with

Figure 1: Therapies for adults should not be applied to children without careful consideration of developmental and age-related differences in disease pathobiology and drug safety and metabolism.

pulmonary hypertension will also work for children, and the corrollary that therapies that do not improve outcomes for adults will be equally ineffective in children. As acknowledged by the group that worked to develop them, the pediatric classification systems are not meant to be therapeutic guides, but to provide a spring board for addressing the multitude of critically needed efforts to improve the outcome of pediatric pulmonary vascular diseases. This journal is doing its part to disseminate awareness of these needs. Funding agencies must design requests for applications (RFAs) and target funding for this understudied patient population. It is up to scientists and clinicians interested in improving outcomes for pediatric pulmonary vascular diseases to inform others, serve on study sections, and perform research to ensure that children with pulmonary hypertension are not treated as "small adults."

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