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Body Composition in Childhood: Is the Window for Influencing Lung Function Still Open?

The impact of early-life factors on adult lung disease has been increasingly recognized since the pivotal work by Barker and colleagues in the 1990s (1). Early-life developmental factors have been systematically studied, and birth weight has been shown to be a consistent factor in determining the maximal lung function achieved (2). Catch-up growth and early growth also have shown small but significant influence on adult lung function (3). Childhood respiratory factors have been studied in longitudinal cohorts to hone and predict adult lung function and risk profile for adult chronic obstructive pulmonary disease (COPD) (4, 5). At least half of all cases of COPD can be attributed to childhood factors and not achieving peak lung function in early adulthood (6, 7).

The changing demographic of the growth pattern in children and adolescents has shown increasing obesity across the world (8). There is evidence to suggest that weight gain in late childhood is associated with reduced lung function (3), and a meta-analysis has shown obesity to be detrimental to lung function (9). In longitudinal studies where asthma was followed prospectively, the lung function trajectory appears to be set early in life and continues to track into adulthood (10).

Although there is unequivocal evidence that pediatric and developmental factors determine adult lung function and thereby influence adult morbidity, it is important that we look for signals in our birth and longitudinal cohorts to tease out factors and patterns that might be amenable to modification or intervention.

In this issue of the *Journal*, Peralta and colleagues (pp. 75–83), have examined growth patterns through childhood, specifically body composition trajectory, and studied the relationship to lung function at 15 years (11). Their premise was that the commonly used body mass index (BMI), which related height and weight, was not sensitive enough to examine relationships between growth and lung function. They used the data from the ALSPAC (Avon Longitudinal Study of Parents and Children) to determine the influence of body composition trends, collected through 9 to 15 years of age, on lung function measured at 8 and 15 years of age.

The unique feature of this study was looking at body composition in terms of lean BMI (LBMI) and fat mass index (FMI) and tracking each of these variables through childhood. A novel statistical tool has been used to derive the trajectories, and clear patterns and trends are observed across the ages in both LBMI and FMI (12). The impact on lung function shows significant differences between LBMI and FMI trajectory groups. Very clearly, in both sexes, a greater increase in LBMI confers higher lung function growth. This is present for all lung function values FVC, FEV_1, and forced expiratory flow, midexpiratory phase ($FEF_{25–75}$). In boys, it was 0.62 L increase in FVC in the highest trajectory group compared with the lowest trajectory, 0.53 L increase for FEV_1, and 0.53 L/s increase for $FEF_{25–75}$. In girls, it was 0.37 L increase for FVC, 0.30 L increase for FEV_1, and 0.35 L/s increase for $FEF_{25–75}$. The association is strong and persisting, even after correcting for a range of variables that have been shown to impact lung function. On the other hand, the FMI shows variable associations with significant negative association for FEV_1 (−0.14 L), $FEF_{25–75}$ (−0.20 L/s), and FEV_1/FVC (−1.44) in boys and FEV_1/FVC (−2.05) only for girls between the lowest trajectory group to the highest trajectory group.

This study gives us insight into inconsistencies that have been reported in the association between BMI and lung function in other longitudinal studies. An increase in both lean body mass and fat mass will increase BMI, yet the data reported by Peralta and colleagues show the very different influences that these have on lung function growth (11).

The method used by Peralta and colleagues for deriving trajectories is a useful addition in interpreting complex longitudinal datasets, and, as the authors rightly point out, there is potential risk for smoothening effect (11). In experienced statistical hands, these tools will help us in understanding growth trends and their effects.

In addition, they have also looked at the rate of growth of lung function from 8 to 15 years of age, and the linear association with LBMI is seen strongly across all lung function values. Looking further ahead, it would be reasonable to hypothesize and investigate further whether higher LBMI trends in childhood and adolescence lead to slower decline in lung function through adulthood.

Lung function trajectories appear to be set early (13), and this study raises the question of the appropriate window to intervene in terms of body composition to influence eventual peak lung function achieved.

Originally Published in Press as DOI: 10.1164/rccm.201812-2327ED on January 11, 2019

This study throws us a few more questions in addition to some of the answers it provided. As stated above, it would be interesting to explore whether higher LBMI in adolescence is a predictor for slow decline in lung function, thereby reducing the risk of adulthood respiratory disorders. Could lifestyle modifications that reduced fat mass and the FMI trajectory alter decline in lung function in later life? Does the variable strength of association of FMI to lower lung function between boys and girls demonstrate the preprogrammed risk of COPD in adult men to be higher than in women? Are there specific factors that influence lung function through the adolescent growth phase?

An individual might be endowed with high or low lung function, but it appears to be within his or her own ability to avoid losing lung function by maintaining a healthy FMI. The public health implications are clear: maintain a healthy body composition with lower FMI to preserve adult lung function and reduce the risk of chronic respiratory disease. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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*P.S. is Associate Editor of *AJRCCM*. His participation complies with American Thoracic Society requirements for recusal from review and decisions for authored works.

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Importance of Mcl-1 for Alveolar Macrophage Apoptosis–associated Bacterial Killing

Community-acquired pneumonia (CAP) is the most common type of pneumonia and remains a leading cause of morbidity and mortality worldwide (1–3). Although many different pathogens can contribute to pneumonia, *Streptococcus pneumoniae* is one of the common bacterial pathogens that underlie CAP (4). In healthy individuals, despite frequent colonization of the upper airways by pathogenic bacteria, multiple innate mechanisms help to protect the lower airways, and CAP is relatively uncommon.

Alveolar macrophages (AMs) are long-lived resident innate immune cells of the airways and key effectors of antibacterial host defense against microbes. Previous work has illustrated that effective bacterial elimination by AMs proceeds in two separate phases: an initial period of macrophage viability and intracellular bacterial killing followed by a later induction of apoptosis and clearance of bacteria (5). Although antimicrobicidal mechanisms contribute to early phagosomal killing of *S. pneumoniae*, AMs demonstrate a finite capacity for bacterial processing and must use a secondary mechanism to control infection.

Supported by National Institute on Aging grants R01AG052530 and R01AG056699 (H.W.S.-D.).

Originally Published in Press as DOI: 10.1164/rccm.201901-0159ED on February 20, 2019