Algorithmic Models to Predict Allergic Disease Using Multiple Neonatal Markers

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As more effective interventions towards the prevention of allergic disease are developed, accurate ways of identifying children who will develop disease will become more crucial. At present, a positive "family history" (i.e any first degree relatives with allergic disease) remains the only commonly used predictor of allergic disease. This is crude at best with a variable specificity (48-67%) and sensitivity (22-72%) and a positive predictive value generally less than 40%(1-3). There have been a number of attempts to find early biological markers of disease predisposition, but none of these has any established predictive value for future allergic disease(4). The level of IgE in cord blood was one of the first measures to be investigated in this context in the 1980's, however this has been disappointing. Although the specificity of the IgE tests ranges between 60-70% in several studies, the sensitivity (26-47%) and positive predictive value (22-42%) are generally very poor in predicting allergic disease(1-3,5,6). Ongoing research into the early immune function of newborns with allergic predisposition have revealed a number of functional differences compared with low risk infants, particularly in cytokine responses such as interferon gamma (IFNg). Despite the consistent relationships between lower neonatal IFNg responses and allergy risk(7-12), methods to assess this are not standardized and high variability in this and other functional responses have limited their value as predictive markers.

The paper presented by Shah and Bapat(13) in this edition of *Indian Pediatrics* shows a novel "algorithmic" approach using multiple measures to more accurately predict allergic disease with the use of cord serum. This study assessed the development of allergic symptoms at the age of 1 year in relation to a combination of potential neonatal markers measured in cord blood, including IgE and IFNg together with levels of ubiquitous perennial house dust mite (HDM) allergens (Der p1 and Blo t5), also measured in cord blood. The infants who were diagnosed with allergic diseases by 1 year of age had higher IgE, Der p1, Blo t5, and lower IFNg levels in cord serum than those infants who had not been diagnosed with allergy by 1 year of age. The authors have shown that individually these parameters cannot accurately predict whether a child is at risk for allergy. However, when two out of three of the tests were used in combination, the specificity and sensitivity increased to over 90%. Of these measures the levels of HDM allergens was of the least value, but it is curious that the sensitivity and specificity of this marker was better than any previously reported predictor including family history(1-4). It is important to note that at this stage the role and significance of *in utero* exposure to allergens in the development of allergic disease (or tolerance) remains controversial(14).

In summary, the results of this study illustrate that there is a potential role for exploring predictive algorithms that use multiple measure, rather than relying on inaccurate individual predictors of allergic disease. The significance of this particular model is as yet unclear as this is based on a small population of only 100 infants and allergic outcomes have only been determined at 1 year of age when the allergic phenotype may still be unclear. Thus, it

would be ideal to assess the effectiveness of this algorithmic model in a larger and more diverse cohort with a longer follow up period to ascertain whether this method is useful in predicting allergic disease beyond the first year of life.

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