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Normal Peripheral Blood B-cell Maturation Charts

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Rationale: Flow cytometry is a diagnostic tool frequently used in the evaluation of immunodeficiency disorders. Although the use of flow cytometry is increasing, few studies have been performed evaluating the reference ranges of different B cell subset populations, especially in the pediatric age group. Adult reference ranges are not applicable in children which makes both interpretation of flow cytometry reports and subsequent diagnosis in the pediatric population challenging.

The purpose of this study was to create charts that establish the age related 5th, 25th, 50th, 75th, and 95th percentiles for each B cell subset in a manner similar to standardized growth charts for height and weight. These charts can be used by an immunologist to determine the reference range of B cell subset at a particular age and follow the evolution of the B cell over time. The existence of reference ranges and the ability to trend the data could facilitate early detection of immune disorders.

Methods: A total of 460 subjects evaluated in an outpatient allergy and immunology clinic between 2010 -2013 were included in this study. Adults age 22 or older and all subjects with known primary or secondary immunodeficiency were excluded. All subjects had a normal immune evaluation including CBC and serum immunoglobulin. All subjects over the age of 2 had an appropriate antibody response to pneumococcal vaccine as determined by titers. Clinical and laboratory data including B-cell subset were obtained from the patients' records. Subjects were divided into nine groups based on their age, and the 5th, 25th, 50th, 75th, and 95th percentiles were calculated. Data was analyzed using SPSS, version 21.

The study was approved by Western IRB , and informed consent was given by patients or their parents.

Results: Absolute B cell count drops significantly in the first 5 years of life. In contrast, total B cell percentage and CD5+ B cells show sigmoid curves with two rapid declining phases and relatively flat line in between. The initial declining phase is from birth until 3 years of life, and the second phase is after the age of 11.

As expected, both IgD and IgM B cells decrease with age while IgG and IgA increase with age. Switched Memory B cells increase with age with a correlation coefficient of 0.36 and P value of < 0.001 while unswitched memory cells do not have any correlation with age.

Conclusion: The establishment of age related percentiles will help immunologists in the evaluation of B cell maturation in the pediatric age group and can possibly be used over time for early detection of immune disorders (specific antibody deficiency).

Many B cell subset values show a sigmoid pattern in relation to age suggesting a possible hormonal influence on the B cell maturation. Further research is needed to investigate this theory.

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