People change. Children change. They change and they change again. They change in height, they change in weight, and they change in shape. They change in function. Continuous centile curves to describe these changes are very familiar to our clinical colleagues. They have been using graphs such as the Centers for Disease Control and Prevention (CDC) growth curve displayed as Figure 1 to describe changes in height, weight, head circumference, and many other parameters of growth for years [1].

This change is seen in the distribution of the concentration of many of the analytes we measure in routine clinical chemistry laboratories. In the last decade we as clinical chemists have improved our ability to describe this change. Much of the marked improvement of our

Figure 1: Continuous centile growth curves for height and weight for girls of 2–20 years.
understanding in children’s chemistry has come about due to the gap analysis done by the CALIPER group of Canadian chemists. This was published as an editorial entitled “Pediatric reference intervals: Critical gap analysis and establishment of a national initiative” in 2006 [2]. We are all too familiar with the ethical and practical difficulties of generating reference intervals for children in a direct fashion. The CALIPER group took the bull by the horns and started. The publication of age and gender-related reference intervals across childhood by the CALIPER group has been a boon to patient care. Since then there continue to be reference interval studies published [3–5]. One of the challenges of children’s reference intervals is determining partitions. How does one determine where to partition is a particularly vexing question [6]. Once one has determined partitions one needs adequate numbers within each partition.

In this issue of Clinical Chemistry and Laboratory Medicine (CCLM), Zierk et al. publish very good distribution curves for alkaline phosphatase (ALP) derived in an indirect fashion [7]. They have done this using data mined from several different laboratories using a smoothing algorithm to describe the distribution of ALP by age in a continuous fashion. This distribution, by describing the 2.5 and 97.5 percentiles, can be used as traditional reference intervals. One of the strengths of this paper is that by data mining they have obtained more than 300,000 samples. It is particularly difficult to describe the distribution of analyte concentrations in infancy for obvious reasons. This group has obtained 10,000 samples for neonates and 30,000 samples for infants beyond the neonatal age group. As a result of these large numbers and the smoothing algorithm, these authors note a low level of ALP activity in the first fortnight of life. This observation has not been so clearly presented before now but with this publication it is clear.

A benefit of studies like this is the improvement in our understanding of the distribution of analytes in childhood group. Certainly this method of mapping our analytes improves our understanding. We have a long way to go in mapping the common chemistry analytes. The distribution of hormones and less common analytes such as α1-antitrypsin and caeruloplasmin need to be better determined. And of course once we have good maps of growth for our analytes we will need to learn how to represent these in our routine daily laboratory results. The smoothed distribution curves described in this and other papers, by describing the 2.5 and 97.5 percentiles can be used as traditional reference intervals. Yet another challenge will be finding a way to communicate this knowledge to our clinical colleagues on each and every report from the laboratory.

As we better map our analytes we will better understand the distribution of our analytes. This will help us to better understand children, both their normal growth and their pathologic disorders. Finding effective ways of communicating this knowledge in our reports will help us to better assist our clinical colleagues in the care of children.

References


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