The Pediatric discussion group considered definitions, concepts, measures, and indices of wasting from the pediatric perspective, particularly with regard to the development of clinical trials involving children. Several overriding concepts emerged, most notably that study designs and analyses require development and interpretation in the context of a growing and constantly changing human organism. Whereas the group reiterated the necessity that children must be protected from unnecessary or premature clinical trials involving dangerous or untried agents, the group also affirmed its belief that children must not be categorically excluded, merely because such research including children presents additional challenges to investigators.

Growth and development are powerful markers of treatment efficacy, and investigators should be encouraged to take full advantage of these simple luxuries, unique to children. However, data from clinical trials involving children must be interpreted in the context of adequate normative data, which may include data standardized for chronologic age, bone age, gender, and stage of sexual development. Although extensive normative growth data exist, normative data pertaining to specific measures of body composition, biochemical markers of wasting or undernutrition, protein turnover, quality of life, and neuropsychologic development are scarce or lacking.

WHAT IS WASTING?

A definition of wasting in children should be considered in the context of normal growth and development. Whereas in adults, wasting and cachexia imply a loss of weight or body mass, in children a mere inability to increase either height or weight may result in wasting or a cachexic state. Thus, wasting is defined as a failure to thrive, including a failure to grow in stature or to gain weight. Severe wasting in children may involve actual loss of body weight and cell mass, and wasting often is associated with a failure of physical, sexual, emotional, and/or neuropsychologic development.

ENDPOINTS TO DEFINE EFFICACY OF TREATMENT

The principal endpoint in clinical trials examining therapeutic agents in the treatment of wasting is a normalization of height velocity and rate of weight gain. Many but not all therapeutic agents which might ameliorate wasting in children also would result in an improved quality of life and improved neuropsychologic development. However, improved quality of life and neuropsychologic development, while desirable, need not be considered requisite surrogate endpoints in therapeutic trials for treatment of wasting in children.

BEST METHODS TO DETERMINE AND TRACK EFFICACY IN LARGE CLINICAL TRIALS INVOLVING CHILDREN

The working group suggested that several simple outcome measures, including accurate height, weight, and head circumference measurements were of particular value in studies involving children. In addition, assessment of pubertal status, analysis of weight for height, and functional assessments of changes in body composition were felt to be of great value. Although numerous methods of assessing body composition have been studied extensively in children, including several newer methods such as DEXA scanning and bioelectrical impedance analysis, normative data for children are scarce or lacking. With specific regard to body composition assessments in children, the group consensus was that simple anthropometric measurements, such as skinfold thicknesses and waist and limb circumferences, particularly if combined with measures to assess muscle mass (such as urinary creatinine excretion), were of value in studies involving children. In addition, single growth measurements were only of limited value, whereas serial data utilizing multiple measurements for changes in height, weight, or other growth parameters over time were highly valuable.

With regard to specific methods for assessing body composition or nutritional state, it was felt that techniques and biochemical markers used in adults generally are valid in children. However, determinations and sample collections, which might be quite simple in adults, can be difficult or
impossible to obtain in children. Furthermore, interpretation of data is complicated by intrinsic error of measurements in children and, as noted above, lack of normative data. Although the use of newer methods of assessing body composition, nutritional state, and wasting can and should be applied to children, the complicating factors noted support greater reliance on simple, well-validated and readily available measures in children.

CONCLUSION

In conclusion, children are not simply small or scaled-down adults. Clinical trials of therapeutic agents for wasting in children require special appreciation for, and interpretation of data in the context of normal growth and development. Although recent advances in technology for assessing body composition and nutritional state appear to be applicable to children, several obstacles to application remain, including difficulty in obtaining samples, radiation exposure, and paucity of normative data. The principal endpoints for therapeutic efficacy for wasting in trials involving children are amelioration or normalization in height velocity and rate of weight gain, with the ultimate goal of development of the child into a normally grown, fully functional and healthy adult.