



# GROWTH AND MATURATION IN HUMAN BIOLOGY AND SPORTS

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BY FELLOWS AND COLLEAGUES*

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# THE FELS METHOD OF SKELETAL MATURITY

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## INTRODUCTION

Skeletal maturation, quantified as skeletal age, is the level of maturity expressed in years and months assigned to a bone or skeletal area irrespective of a child's chronological age (Roche *et al.*, 1988). Skeletal age helps to account for maturational variance among children in clinical and epidemiological studies of growth, body composition, physical status and performance (Beunen *et al.*, 1992; Malina *et al.*, 1999; Claessens *et al.*, 2006). The assessment of skeletal maturation is based upon the appearance, recognition and grading of maturity indicators. These are three dimensional features of a bone that appear two-dimensionally on a radiograph. For example, an indicator can be the initial ossification of a bone or an epiphysis, the shape of a bone, a radio-opaque line or zone that represents the edge of a bone or increased ossification in the metaphysis and/or epiphysis with fusion. A maturity indicator must occur during the maturation of every child in order to be useful in determining skeletal age (Pyle & Hoerr, 1969), and its progression of radiographic changes must appear in a regular sequential order as the bone matures to adult status (Roche, 1980). Skeletal age reflects the combined skeletal mechanisms occurring at different stages of growth and development based on the assumption of a universal progression of changes in the ossification, shape, joint formation, and epiphyseal fusion of bone(s) in the selected area of the skeleton in normal healthy children. During early childhood, skeletal age is primarily a measure of ossification onset; in mid-childhood it is a measure of changes in bone shape, individually and with respect to joint formation; and near the end of growth it measures the rate of epiphyseal fusion. Skeletal maturity is a system-wide phenomenon, but the assessment of skeletal maturation is typically done via hand-wrist radiographs. The hand-wrist is the most accepted site for skeletal maturity assessment due to its easy accessibility, the large number of bones in a very small area exposed to a small amount of radiation, and its history of numerous assessment methods (Roche, 1980; Cox, 1997).

## THE FELS METHOD

The FELS method for assessing skeletal maturity independently grades sex- and age-specific maturity indicators for the twenty bones in the hand-wrist, the distal radius and ulna, the carpals and the first, third and fifth metacarpals and their corresponding phalanges. It was developed using 13,823 serial radiographs of the left hand-wrist from 355 boys and 322 girls in the Fels Longitudinal Study that were taken between 1932 and

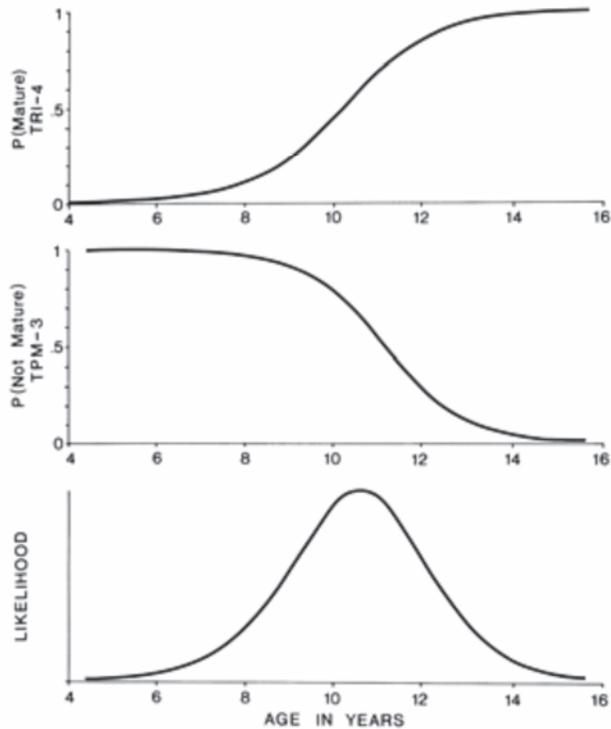
1977 (Chumlea, *et al.*, 1989; Roche *et al.*, 1988, 1992). Five criteria were used to select the maturity indicators: 1) discrimination, the ability of an indicator to distinguish between children at the same chronological age, 2) universality, the grades for an indicator occur during the maturation of each child, 3) high reliability, with both inter- and intra-observer differences in the prevalence of grades of an indicator of 8% or less, 4) validity, the prevalence of grades change systematically with age until the most mature grade for an indicator is universal, and 5) completeness, the extent an indicator clarifies and restricts the age ranges at which the final indicator grades are applicable. The FELS method provides a detailed description of indicators and the morphological differences between grades and presents radiographic pictures for the indicator grades of the bones to be scored. Some examples are the ossification and shape of the triquetral, the development of the hook of the hamate, the appearance of the styloid process of the radius, and epiphyseal fusion.

There are ninety-eight maturity indicators in the FELS method, but only subsets of indicators are used for assessment at any given chronological age. The non-selected indicators are those that do not vary between children at that selected age, and thus do not provide any maturational information. The number of indicators assessed ranges from a minimum of 21 for boys and 9 for girls at age 18 years (when adult status has occurred) to a maximum of 61 for boys and 64 for girls at 10 years of age which is a time of rapid skeletal maturation involving a number of ossification and epiphyseal changes. The assessed indicator grades are entered into a computer where the FELS software (Roche *et al.*, 1988), a maximum likelihood based analysis of the maturity indicators, calculates a skeletal age and standard error. The FELS Method is the only skeletal age assessment method that provides a standard error or confidence limit for the calculated skeletal age. The median standard error for the FELS method is about 0.3 years from chronological age 6 months to 14 years in both boys and girls, and then increases to about 0.6 years in boys and 0.5 years in girls by age 18 years.

#### Statistical Basis of the FELS Method

The FELS Method utilizes a maximum likelihood technique to estimate a child's skeletal age using three classes of skeletal maturity indicators: binary indicators such as ossification, multiple grade indicators such as fusion and continuous indicators such as the ratio of epiphyseal to metaphyseal widths. The probabilistic behavior as a function of chronological age is modeled for each of these types of indicators. For example, the prevalence of children in the calibration sample who are immature for a given binary indicator is modeled as a logistic function of age, allowing estimation of the probability of maturity for that indicator at any given age. The calibration sample was used to estimate the parameters of each indicator's probability distribution as a function of age. The FELS method skeletal age for a child is the chronological age at which that child's indicator values are most likely in the calibration sample; that is, in the calibration sample, the chronological age at which one is most likely to find a child with similar values of the assessed indicators. This age, along with its standard error, is estimated using maximum likelihood.

This technique can be demonstrated with a two-indicator example in Figure 1. In this example, both indicators are binary with grade 1 indicating immature and grade 2 indicating mature. As seen in Figure 1 for the first indicator, the probability of a mature score (grade 2) up to age 4 is zero. The probability of being scored as mature (grade 2) begins (becomes positive) at approximately five years of age, and increases with age so that by age 10 years the probability of a mature score is 0.5. By age 14, the probability of a mature score for this indicator is 1.0. For the second indicator, the probability of an immature score (grade 1) at age 4 is 1.0, at age 10, it is 0.8, and by age 15 years the probability of an immature score is zero (i.e., no one at age 15 should be immature for this indicator). The joint likelihood for both these indicators is shown at the bottom of Figure 1 as the product of the two probability curves, where the likelihood of observing both a grade 2 for the first indicator and a grade 1 for the second indicator at less than age 7 or greater than age 13 years is minimal. The likelihood of the score {2,1} is greatest at age 10.6 years. In this simple example, the skeletal age of a child with a score {2,1} for just these two indicators would be 10.6 years (Roche *et al.*, 1988).



**Figure 1.** Probability curves for two indicators and their joint likelihood in the FELS Method.

Incorporating additional maturity indicators into the model follows the same pattern as described above with probability curves initially identified for each indicator followed by the construction of the joint likelihood model from those curves. When all indicators required at a chronological age are considered together, an estimate of skeletal age is determined. This skeletal age is based on multiple maturity indicators of various types from different bones, and the estimated skeletal age maximizes the information from the maturity indicators.

## COMPARISONS AMONG THE HAND-WRIST METHODS

The Greulich-Pyle atlas method (Greulich & Pyle, 1950) is generally used as a set of flash cards to locate subjectively the single atlas radiograph that most closely resembles the whole hand-wrist radiograph in question. This incorrect, overly simplified use of this assessment technique has resulted in limited reliability (Greulich & Pyle, 1950; Tanner *et al., et al.*, 1975; Roche *et al., et al.*, 1988). In the early 1970's, it was recognized that this method did not reflect the skeletal age of normal healthy U.S. children accurately, and this was especially true for black children (Garn *et al., et al.*, 1967; Anderson, 1968). These findings have been reinforced repeatedly over the past several decades both in the U.S. for white, black, Hispanic- and Asian-American children (Loder *et al.*, 1993; Ontell *et al.*, 1996; Russell *et al.*, 2001; Mora *et al.*, 2001; Stanitski, 2006) and around the world (Shaikh *et al.*, 1998; Bull *et al.*, 1999; Koc *et al.*, 2001; Haiter-Neto *et al.*, 2006). The Tanner-Whitehouse method (now in its third edition, TW3) (Tanner and Whitehouse, 1959, Tanner *et al.*, 1962, 1997, 1975, 2001) is a more sophisticated assessment method than the Greulich-Pyle method that is based on scoring 20 bones in the hand-wrist to produce a skeletal maturity score (SMS) that measures skeletal maturity on an absolute (population invariant) scale. The SMS score can then be calibrated to any population of interest to produce a bone age. The TW3 bone age is calibrated to European and European-American populations. The population invariant nature of the SMS score, however, depends on the assumption that there are no population differences in the relative tempo of maturation among the bones of the hand-wrist. There is, in fact, some evidence that such differences exist, namely that there are secular trends of differing direction and magnitude in the timing of maturation of the bones of the hand-wrist (Duren *et al.*, 2010). Such secular differences within a single population imply that there are very likely to be between-population differences in the relative tempo of maturation of the bones of the hand-wrist. Thus, despite the calibration of TW3 to European-American children, it is not clear whether the underlying SMS scores are applicable to other than the European population used to derive them.

The FELS method provides accurate and reliable estimates of the skeletal ages of U.S. children (Roche *et al.*, 1988). As part of the validity testing for this method, a sample of 500 radiographs from white and black children in the first National Health and Nutrition Examination Survey were assessed. The mean skeletal ages for these US children were similar to their mean chronological ages at the assessed ages of the radiographs. There

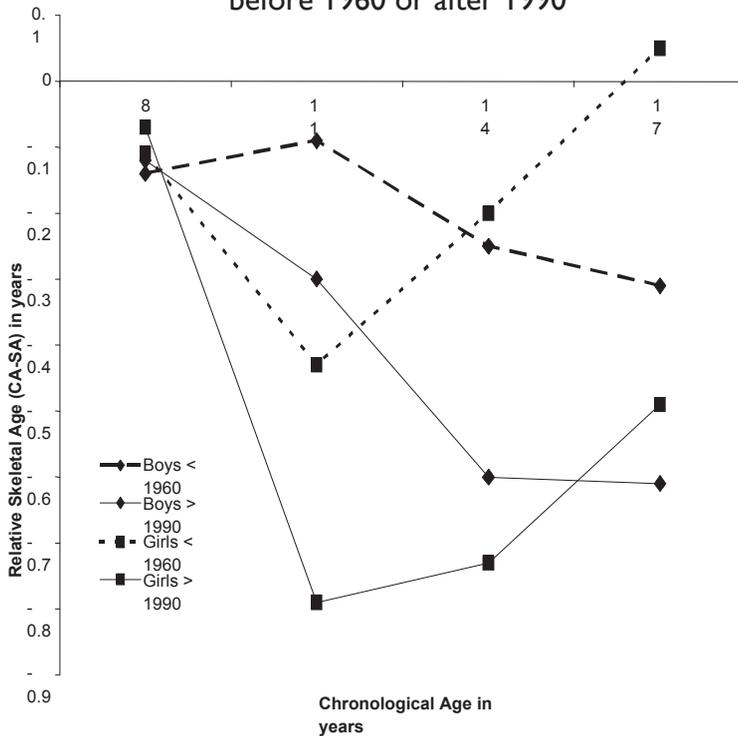
was no systematic trend in the differences between the chronological and FELS skeletal ages for each sex. These findings indicated that the FELS method was appropriate for the U.S. pediatric population of white and black children at that time (Chumlea *et al.*, 1989). The Greulich-Pyle and Tanner-Whitehouse methods lack accuracy, and have limited validity, and/or their levels of skeletal maturity do not reflect the skeletal age and maturity of normal U.S. children today. It is not possible to calculate confidence intervals for the estimated skeletal ages when using the Greulich-Pyle or Tanner-Whitehouse methods which are important in the proper interpretation of a skeletal age (Roche *et al.*, 1988). These differences reflect both the underlying samples from which the methods were developed and the statistical methodology used to derive a skeletal age.

## SECULAR TREND IN SKELETAL MATURITY AS A RELEVANT HYPOTHESIS FOR ADDITIONAL RESEARCH

Recent reports signal a world-wide secular trend in maturation (Karlberj, 2002) including skeletal maturity. Children today are more advanced in their skeletal maturity at least by age 10 years as compared to the children of just a few decades ago (Ranjitkar *et al.*, 2006; Lin *et al.*, 2006; Savaridas *et al.*, 2007). Data from our own study sample, the Fels Longitudinal Study, indicate a trend for accelerated skeletal maturity in children born since 1960, compared to those born in the 30 years prior. We conducted a small pilot analysis to determine if a shift in the relative skeletal ages (chronological age less skeletal age) of Fels Longitudinal Study children has occurred. We randomly selected a small group of children (N = 39 to 69 depending on the age group) who had a hand-wrist radiograph at ages 8, 11, 14 and 17 years before 1960 (one visit per child) and a random selection of unrelated Fels children (N = 24 to 46 depending on the age group) with corresponding age radiographs after 1990. Relative skeletal ages at the corresponding chronological ages are plotted in Figure 2.

The skeletal ages of the children with a radiograph before 1960 were used in the development of the FELS Method which explains the small values of their relative skeletal ages (in absolute value), which are similar to those reported in the details of the method (Roche *et al.*, 1988). In comparison, contemporary Fels children have relative skeletal ages that are considerably larger (in absolute value), approaching a -0.8 year difference. These preliminary findings indicate that the FELS method is potentially underestimating the skeletal ages of these healthy children during the critical period of pubescence by half a year or more. Moreover, an investigation of the various types of maturity indicators contained in the FELS method has revealed differences in the tempo (and, in some cases, direction) of the secular trend in skeletal maturity, with indicators such as fusion of the epiphyses exhibiting the most extreme trends towards earlier maturation (Duren *et al.*, 2010).

**Figure 2. Relative Skeletal Ages of Fels Children with Visits before 1960 or after 1990**



The accelerated maturation has implications for a variety of aspects of child growth, development, obesity and physical performance. This includes the potential age alterations in the timing of the magnitude of peak height velocity, bone mineral accrual, predicted adult stature, menarche and secondary sex characteristics and physical performance. Accelerated skeletal maturation as reflected in skeletal age can alter established uses of skeletal age in the interpretation of attained maturity at a chronological age affecting participation in youth sports (Malina *et al.*, 2010). In order to assess reliably the associations, timings and onset among these maturational processes with skeletal age, it is imperative that skeletal age methods reflect the maturity status of contemporary children. To this end, the FELS Method is undergoing a revision that should be available shortly.

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