ORIGINAL ARTICLE

Relationship between blood-spot insulin-like growth factor 1 levels and hand-wrist assessment of skeletal maturity

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Introduction: Accurate prediction of the timing of the pubertal growth spurt and the amount of remaining growth are factors that affect treatment decisions in orthodontics, orthognathic surgery, and dental implantology. For many years, medical and dental professionals have considered hand-wrist radiographs the method of choice for the assessment of skeletal maturity. Insulin-like growth factor 1 (IGF-1) mirrors growth hormone levels and is used by endocrinologists to diagnose growth hormone disturbances. **Methods:** The objective of this study was to establish a relationship between IGF-1 levels collected from blood-spot samples and hand-wrist radiographs at various skeletal stages. Eighty-four subjects (45 female, 39 male) between the ages of 5 and 25 were included in the study. Each subject had personal information, a hand-wrist radiograph, and a blood-spot sample collected on the same day. **Results:** The IGF-1 levels were highest at the hand-wrist skeletal stages that were previously associated with the greatest amount of mandibular growth. These levels were significantly higher than at prepuburtal and postpubertal stages. In the postpubertal group, the IGF-1 levels were lower as the subjects' ages increased and they moved away from the onset of puberty. **Conclusions:** Longitudinal data are necessary to confirm the usefulness of this technique in predicting the timing, the intensity, and the end of the growth spurt. (Am J Orthod Dentofacial Orthop 2009;136:59-64)

Using hand-wrist radiographs to assess skeletal maturity was first described by Todd[1] in his 1937 publication, *Atlas of Skeletal Maturation*. In 1959, Greulich and Pyle[2] developed their atlas for determining skeletal age; to this day, it is the most widely used method for assessing skeletal maturity. The atlas consists of 2 series of standard plates obtained from hand-wrist radiographs of white, upper middle-class boys and girls taken at 6- to 12-month intervals. The standards are supposed to represent the central tendencies of the population from which they were collected, with the assigned skeletal age corresponding to the hand-wrist appearance most commonly found at that age. Several studies have correlated facial growth with this technique and consistently shown a significant but modest correlation between them.[3,4] This atlas, however, does not describe a specific method for reading the radiographs; this is a reason that Tanner et al[5] developed the TW2 method. This technique differs in that it uses a bone-specific approach in which biologically weighted scoring is used to assign the patient a skeletal age. However, the concept of skeletal age, the ultimate result of both techniques, has the drawback of applying only to the population from which the samples were collected. Therefore, it must be related to the skeletal ages of the population at hand. In addition to the questionable accuracy of this deduction, bone age is often not available.

Moore et al[6] related the TW2 method to facial growth and found that girls had significant growth deceleration between the bone ages of 11 to 12 and 13 to 14. In boys, there was significant acceleration in facial growth between the skeletal ages of 11 to 12 and 13 to 14, and significant deceleration between the ages of 13 to 14 and 15 to 16. However, correlation

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Harvard Medical School's technology transfer department is attempting to register a patent based on the findings of this study. At this time, the authors have no financial benefit from these results.

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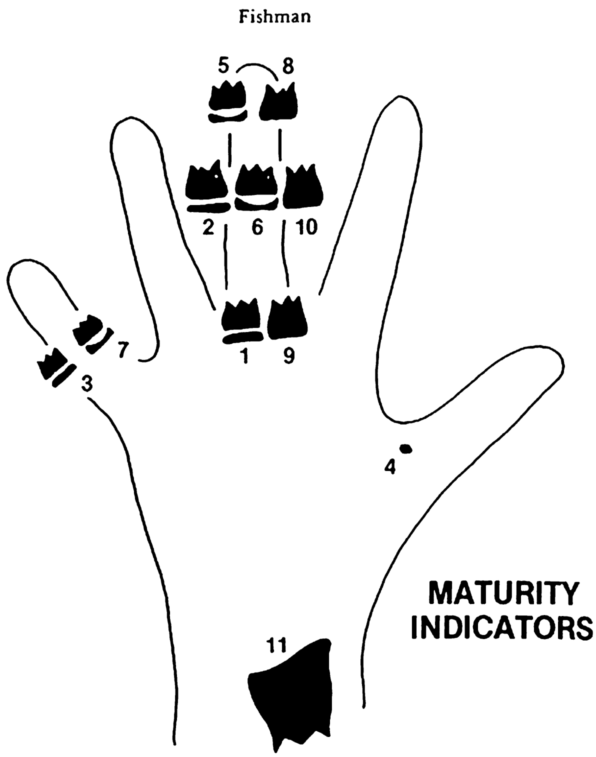

Fig 1. Fishman's skeletal maturity indicator stages (reprinted with permission of Angle Orthod 1982;52: 88-112).

coefficients between skeletal maturity intervals and the accelerations and decelerations in facial growth velocity were moderate at best. Fishman[7] later developed a technique of evaluating hand-wrist radiographs that involved looking at specific skeletal maturity indicators that were plotted against the pubertal growth curve. In that technique, 11 adolescent skeletal maturation indicators (SMIs) were described. The system has only 4 stages of bone maturation, all found at 6 anatomic sites, located on the thumb, third finger, fifth finger, and radius. The SMIs are shown in chronologic order (Fig 1). In the first 3 stages, the epiphyses becomes as wide as the diaphyses as shown in Figure 1. In stage 4, ossification occurs in the adductor sesamoid of the thumb. In stages 5 to 7, the epiphyses cap the diaphyses in the order shown, and, in stages 8 to 11, the growth plates fuse, with fusion of the radius marking the end of growth.

Fishman[7] related his method of assessing skeletal maturity to changes in statural height, as well as maxillary and mandibular growth rates. His findings showed that peak mandibular growth occurs at SMI 7, whereas peak statural growth occurs between SMIs 5 and 6. Chronologically, peak mandibular growth occurs on average about a year after the peak in statural growth. It was also demonstrated that boys and girls had similar percentages of completed growth at each stage.

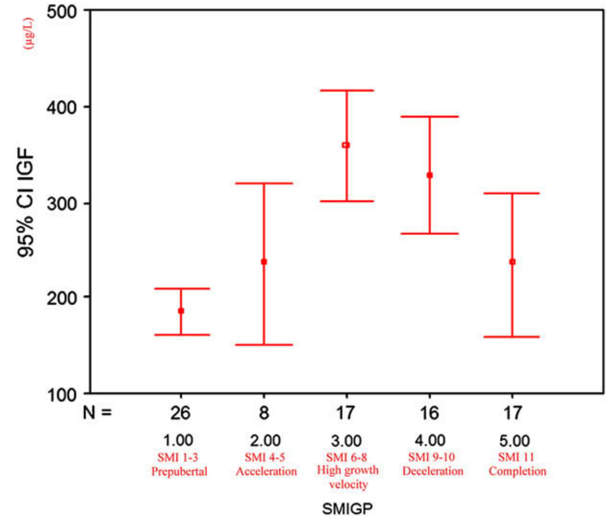

Fig 2. Mean IGF-1 levels and 95% confidence interval for each skeletal stage.

The advantage of SMIs rather than using an atlas is that it eliminates the concept of assigning a patient a skeletal age and deals with the more relevant issue of where the person is on a growth curve. The disadvantage is that it assumes that the chosen sites are actually more important than other sites that would be looked at if one used an atlas. Fishman also stated that not everyone follows the average growth curve and that adolescents can have their peak growth velocities at different SMIs.

Insulin-like growth factor 1 (IGF-1) is a mediator for growth hormone (GH) that plays an essential role in both local and systemic regulation of bone growth.[8-23] IGF-1 levels have been shown to depend on GH before puberty. However, during puberty, IGF-1 levels can also be independent of GH because IGF-1 production can be directly stimulated by androgens.[24] Recent studies have also shown that the condylar cartilage is highly sensitive to changes in IGF-1 concentrations.[25,26] Several growth studies demonstrated that serum IGF-1 levels reflect serum GH levels but without the fluctuation involved with the latter. Therefore, IGF-1 levels have been used by endocrinologists to diagnose GH disturbances.[27] Serum IGF-1 levels have also been related to chronologic age and sexual maturity stages, and have been shown to peak late in puberty.[28-31] This peak is mainly due to the stimulation of GH secretion by adrenal and gonadal steroids.[24] Blood-spot measurement of IGF-1 has recently been proposed as an alternative to conventional