The Operational Meaning of Maturity Criteria

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ABSTRACT The fact that specific radiographic criteria represent different proportions of attained maturity in males and females, in individuals of different geographical origin, in undernourished as opposed to over-nourished subjects and in genetic or chromosomal extremes together indicates the operational complexity of "skeletal maturity" and indicates the need to separate those aspects of skeletal development that are not sex-hormone dependent from those whose timing is directly dependent upon gonadal status.

The concept of skeletal maturity long antedates Roentgen's discovery. It is a Nineteenth Century concept, the creation of anatomists who came to appreciate the order of events in postnatal skeletal development. With relatively few skeletons to work with (most of questionable age at death), those anatomists laid down the basic concept, but without our doubts as to what "skeletal maturity" actually means.

Translated into silver images on glass plates, early skeletal radiographs presented a wealth of practical problems. Patients and volunteer subjects of known age proved remarkably advanced in skeletal development over the cadavers of the century just passed. Sex differences proved large, indicating the need for separate standards for males and females of all ages. Individual variations in the order of events were discovered, and family-line differences in maturational sequences were extensively documented between 1909 and 1914.

Some methodological problems were resolved by attention to both sample source and sample size. By 1920, workers such as T. W. Todd appreciated the need for adequate samples, drawn from well-nourished, non-hospitalized volunteers (cf. Todd, '37; Flory, '36). The importance of sex has been appreciated by most workers, and the need for separate sex-standards — or at least separate age-assignments — for the hand, knee and foot (Greulich and Pyle, '59; Pyle and Hoerr, '69; Hoerr, Pyle and Francis, '62). Innumerable writers have suggested that some ossification centers may have more utilitarian value than others, advocating less reliance on (1) epiphyses of small bones, (2) the round bones of the hand and foot, (3) the more variable nuclei of ossification, (4) bones that appear in atypical sequences, (5) early-appearing epiphyses and (6) those centers that have less predictive value as shown by lower statistical communalities (cf. Garn and Rohmann, '59; Garn and Rohmann, '66; Garn, Rohmann, Blumenthal and Kaplan, '66; Garn, Rohmann, Blumenthal and Silverman, '67; Garn, Rohmann and Silverman, '67).

Given 73–80 separate ossification centers in the "hemiskeleton," as Wilkins ('50) termed it, and far more than one thousand details of appearance, modeling, epiphyseal union and obliteration of epiphyseal lines, some simplification of endless possible detail is clearly necessary. Not every bony nucleus can have equal value in skeletal assessment when the timing of some nuclei scarcely relates to the timing of others. Not every facet, radiographically visible, can have equal contribution to maturational assessment. Even assuming comparable ease of viewing and reliability, it is inconceivable that union in the metatarsals and metacarpals, the medial epicondyle of the humerus and the iliac crest, the appearance of the tibial tubercle and the pisiform, the patella and the sesamoids, and the development of the spinous process of the tibia have equal numerical value in assessing skeletal maturity in males and females, Blacks and Whites, the penta-XY (i.e., XXXXXY), the XO, and 48 trisomy G XXX. Subjects with Morquio's syndrome and the Holt-Oram syndrome surely do not have the same basis of skeletal maturation as the well-nourished XX or XY of prototypical Scotch-English-Irish ancestral origin.

What appeared simple in 1880, when knowledge of skeletal development was new and limited is far from simple today. Now we have complete birth-to-maturity series of radiographs, in at least three centers of longitudinal growth research in the U.S.A. We now have in our files at the Center for Human Growth and Development over 45,000 radiographs from nine countries, and including subjects of African origin, Japanese and Chinese origin, from Central and South America, American "Indians" from the Southwest and the Northwest, and Puerto-Ricans, as well as numerous cases of 47-trisomy G, and variants of X and Y chromosomal number.

The order of maturational events is not exactly the same in both sexes, and in all populations. The degree of skeletal maturity suggested by different centers or by different regional assessments is not the same in both sexes. In all individuals and in all populations studied, the per cent of maturity suggested by a given criterion is not the same in the well-nourished or advanced child and in the poorly-nourished and skeletally delayed child, or in the XO or the XYY. The question is just how elastic the concept of skeletal maturity must truly be. The need for elasticity of definition rather than the answer is the subject of this paper.

THE PROBLEM OF SEX DIFFERENCES

Operational problems with the concept of skeletal maturity appear as soon as we consider the two sexes. The female is skeletally advanced over the male from before birth on, and by amounts that attain considerable proportions. The knee of the 10.25 year old girl corresponds to that of the 12.75 year old boy, following Pyle and Hoerr ('69), a difference of some 23%. The foot of the ten year old girl corresponds to that of a boy three years older, following Hoerr, Pyle and Francis ('62), a difference here of 28%. Taking individual centers of ossification from our own data (Garn, Rohmann and Silverman, '67), sexual dimorphism may exceed 50–60%, especially for the medial epicondyle of the humerus. Such sex differences in timing neither fit the $y = x$ hypothesis of no difference, nor the $y = Kx$ hypothesis of constant difference, but rather some sort of polynomial, with different sets of values for those early maturational criteria that relate to the appearance of centers, their apparent enlargement and modeling, and for later phenomena related to union of tubular bones and their epiphyses (cf. table 1).

If we discard age-equivalents, and think only of per cent maturity attained, sex differences provide yet another set of problems. Taking the appearance of the ischial tuberosity as the last center to appear (out of 73), and expressing each earlier center as per cent of maturity attained (20%, 40%, etc.), there are very large discrepancies between the sexes. Not only does the appearance of most ossification centers indicate a higher relative maturity in boys than in girls, but for many centers *per cent of maturity attained* may be greatly different, as for the epiphysis of the calcaneus, the medial epicondyle of the humerus, the patella, and so on (cf. table 2). Apparently, the same discrete events do not have identical maturational meanings in boys and in girls, and apparently, far less so for abnormal karyotypes involving the sex chromosomes or chromosomes number 18 and 21.

Methodologically, there are some paths around the problem, the very least of which is separate sex-standards. Moreover, with the details of the maturational scheme far from identical in males and females, it does not seem appropriate to use the same pictorial standards with separate sex-equivalents, at least for more systematic scientific comparisons. Since the same radiographically-visible phenomenon may not have identical maturity meaning in the two sexes, as shown in table 2, one may argue for selection of those criteria which more nearly agree, when seeking sex-comparability.

TABLE 1

Comparative sexual dimorphism by averaging methods and by individual ossification centers

Knee			Foot			Body			
Corresponding ages [1]		Per cent sexual dimorphism	Corresponding ages [2]		Per cent sexual dimorphism	Center numbers	Corresponding ages [3]		Per cent sexual dimorphism
Boys	Girls		Boys	Girls			Boys	Girls	
0.25	0.18	8	0.25	0.21	4	5	0.25	0.15	11
0.50	0.42	7	0.50	0.42	7	9	0.46	0.23	23
0.75	0.63	9	0.58	0.50	6	10	0.83	0.51	25
1.50	1.25	13	1.50	1.17	17	16–20	1.48	0.97	30
2.00	1.58	18	2.00	1.50	22	26–29	2.02	1.25	39
2.50	2.00	18	2.50	1.92	22	35–39	2.46	1.60	37
3.00	2.33	22	3.00	2.33	22	42–44	2.99	1.83	45
3.50	2.67	24	3.70	2.90	22	47–49	3.45	2.35	37
4.00	3.17	21	4.20	3.20	25	50–53	4.01	2.56	44
5.00	3.83	26	4.90	3.70	27	58	5.21	3.87	29
6.00	4.67	25	6.00	4.50	29	60–62	6.11	3.88	49
7.00	5.33	27	6.75	5.17	27	63	7.10	5.37	28
8.00	6.25	25	8.00	6.25	25	—	—	—	—
9.00	7.00	26	8.75	6.83	25	—	—	—	—
10.00	7.75	26	9.75	7.50	27	—	—	—	—
12.00	9.33	26	12.00	9.17	29	67	11.81	10.25	14
12.75	10.25	23	13.00	10.00	28	68	12.76	10.72	18
13.75	11.00	23	14.00	11.00	26	69–70	13.64	11.70	16
15.00	12.00	24	15.00	12.00	24	73	15.26	13.89	9

[1] From Pyle and Hoerr ('69).
[2] From Hoerr, Pyle and Francis ('62).
[3] From Garn, Rohmann and Silverman ('67). Centers grouped within 0.05 to 0.25 years. Per cent sexual dimorphism values conception-corrected.

TABLE 2

Centers having markedly different maturity values in boys and girls

Center	Median age at appearance [1]		Per cent ossification maturity indicated	
	Boys	Girls	Boys	Girls
Patella	4.00	2.48	26	18
Lunate	4.07	2.62	27	19
Epiphysis. distal 4th toe	4.38	2.58	29	19
Epiphysis. distal 2nd toe	4.64	2.93	30	21
Scaphoid	5.63	4.12	37	30
Trapezium	5.87	4.08	38	29
Trapezoid	6.22	4.17	41	30
Medial epicondyle, humerus	6.25	3.40	41	24
Distal epiphysis, ulna	7.10	5.37	47	39
Epiphysis of calcaneus	7.59	5.37	50	39
Acromion	13.74	11.92	90	86
Coracoid process	14.35	12.21	94	88

[1] From Garn, Rohmann and Silverman ('67, table 3), related to the timing of the ischial tuberosity.

INDIVIDUAL DIFFERENCES IN MATURITY INDICATORS

As has been long known, from Pryor's time on, the sequence of maturational events visible in skeletal radiographs is far from fixed. One ossification center may precede another in some children, yet follow it in other children. Centers such as the triquetral are remarkably variable, being as early as third (or possibly earlier still) among the hand centers, or twenty-fourth (or possibly even later). As the number of radiographs reviewed in our multi-state and multi-national surveys approaches 50,000, we see sequences that we would have regarded as utterly improbable earlier. We see phalangeal and metacarpal centers without visible carpals, and as many as six carpals with few metacarpal and phalangeal centers. We even see the distal epiphysis of the ulna first of all in the wrist-hand complex (cf. Garn, Sandusky, Miller and Nagy ('72)).

Faced with such sequential variability, some workers have suggested giving less emphasis to the carpus, or even eliminating the round bones from consideration completely. The oddly-shaped round bones of the wrist and the homologous centers of the tarsus are not necessarily at fault, however. We see situations where the phalangeal and metacarpal centers are uniquely delayed, as separately confirmed by examining the dimensions of the tubular bones of the hand. Strictly interpreted, the exclusional approach could lead to exclusion of all of the postnatal ossification centers of the hand and foot, since none is without fault.

The fact is that different postnatal ossification centers vary in the degree of skeletal maturity they suggest, not only between the sexes, but also between individuals. Even though it is possible to identify those postnatal centers that have maximum statistical communality, as we have done (Garn and Rohmann, '59, '66; Garn, Rohmann, Blumenthal and Kaplan, '66; Garn, Rohmann, Blumenthal and Silverman, '67), the problem of individuals still remains. For the details of modeling and of epiphyseal union and final closure, we do not yet know which of thousands of features has major meaning, and which features — however consistent — are of limited operational utility.

Because of individual differences, many of them clearly genetically-determined, we cannot yet be sure of the maturational meaning of most of the radiographic criteria we can reliably report and usefully assess. It is possible to select, from intercorrelation matrices, those phenomena that have the most to do with other radiographic phenomena, validating their selection against other growth phenomena, such as body size and body mass. But when the carpus is late as a whole, or early as a whole, when the order of union is not proximal-to-distal, we have operational problems as yet unsolved, except by the grossest of averaging procedures.

The knee can be ahead of the hand, meaningfully so, and since stature growth involves the knee far more than the hand, the knee may be preferred for stature prediction. In regional maturational divergences (as with those within an anatomical region or joint), the holistic concept of skeletal maturity is threatened. When two individuals are equally "mature," by an averaging system, but differently mature, which individual child truly has the greater "skeletal maturity"? Do we give greater credence to the hand or the foot, to the round bones or to the epiphyses, to advanced centers or retarded centers? Or are we asking nature to be more tightly consistent than a realistic concept of skeletal maturity truly allows?

RACE AND NUTRITIONAL STATUS

As we investigate subjects of different geographical origins, we frequently encounter sequences of ossification rarely encountered before. Some of them are minor, involving sequence reversals of centers having similar median ages of appearance. If the capitate/hamate hamate/capitate orders are of different frequency from group to group, this does not greatly disturb our useful approaches to skeletal maturation. Some sequence diversions are of greater magnitude, repeating what we have said about individual and family-line differences, and ultimately the meaning of skeletal maturity when the details differ (table 3).

In malnourished populations, where childhood growth is slowed by 20–30%, and in less well-nourished children in our own North American population, we encounter a different maturational problem. The earlier details of skeletal maturation, having to do with appearance of ossification centers may be equally delayed, 20–30% (cf. table 4). Later details, from adductor sesamoid appearance through union of epiphyses may be less delayed, often no more than 10–15%, as we also find in 47 trisomy G, and 48 trisomy G, XXX. Apparently sexual maturity is subject to less relative delay than earlier aspects of skeletal development, and so delay is by no means uniform for all skeletal criteria. From the hyperphagic Pickwickian and the iso-sexual precocities, to the malnourished, extremely-late maturing and in many chromosomal abnormalities the same anatomical maturity

TABLE 3

Relative timing of seven wrist centers in Whites, Negroes and Mexican-Americans [1]

Ossification center	Boys			Girls		
	White	Negro	Mexican-American	White	Negro	Mexican-American
Distal radius	17	12	—	15	14	—
Triquetral	38	35	21	30	25	38
Lunate	56	55	72	51	44	67
Scaphoid	84	82	88	75	69	80
Trapezoid	85	85	89	76	75	75
Trapezium	87	84	94	73	75	76
Distal ulna	100	100	100	100	100	100

[1] All data from the Ten-State Nutrition Survey of 1968–1970 expressed in relation to the distal epiphysis of the ulna.

TABLE 4

Effects of developmental delay on ossification timing in the hand and wrist

Center		Age at appearance				Per cent delay in Guatemala[1]		Relative timing of center			
		USA		Guatemala				USA		Guatemala	
		Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Capitate		0.25	0.15	0.26	0.15	1	0	2	1	2	1
Hamate		0.31	0.18	0.60	0.42	27	26	2	2	4	4
Distal radius		1.10	0.82	2.01	1.29	49	30	9	8	14	11
Proximal	3	1.37	0.85	1.92	1.10	26	16	11	8	14	9
Proximal	2	1.41	0.87	2.10	1.50	32	39	11	8	15	13
Proximal	4	1.49	0.90	2.12	1.20	28	18	12	8	15	10
Distal	1	1.51	0.99	2.11	1.65	27	38	12	9	15	14
Metacarpal	2	1.61	1.09	2.67	1,76	45	36	13	10	19	15
Metacarpal	3	1.79	1.13	3.14	1.99	53	46	14	11	22	17
Proximal	5	1.85	1.19	3.13	1.83	49	33	15	11	22	16
Middle	3	1.97	1.28	3.06	2.05	40	38	15	12	22	17
Metacarpal	4	2.03	1.29	3.35	2.07	47	38	16	12	24	18
Middle	4	2.05	1.24	3.08	2.08	37	42	16	12	22	18
Metacarpal	5	2.17	1.37	3.44	2.17	43	38	17	13	25	18
Middle	2	2.19	1.36	3.38	2.36	40	47	17	13	24	20
Distal	3	2.41	1.46	3.43	2.19	32	33	19	14	25	19
Triquetral		2.43	1.70	4.42	3.44	63	71	19	16	32	29
Distal	4	2.44	1.52	3.50	2.57	33	46	19	14	25	22
Metacarpal	1	2.59	1.60	4.12	2.82	46	52	20	15	29	24
Proximal	1	3.00	1.71	3.81	2.82	22	45	24	16	27	24
Distal	2	3.17	2.50	3.84	2.96	17	14	25	23	27	25
Distal	5	3.29	1.96	3.89	2.83	15	32	26	18	28	24
Middle	5	3.40	1.97	4.15	3.01	18	38	27	18	30	26
Lunate		4.07	2.62	5.66	4.79	33	64	32	24	40	41
Scaphoid		5.63	4.12	6.87	5.19	19	22	44	38	49	44
Trapezium (GM)		5.87	4.08	6.96	5.07	16	21	46	38	50	43
Trapezoid (LM)		6.22	4.17	7.21	5.27	14	22	49	39	52	45
Distal ulna		7.10	5.37	7.74	6.52	8	19	56	50	55	55
Adductor sesamoid		12.76	10.72	13.98	11.75	9	9	100	100	100	100

[1] Conception-corrected per cent delay.
[2] Expressed in relation to the adductor sesamoid.

criterion does not have the same maturity meaning. It may indicate 30, 40, or 50% of final skeletal maturity, with different implications to final size, or growth-to-come.

As a result, earlier details of skeletal development paradoxically represent a higher proportion or percentage of final maturity in those who are developmentally delayed. Arm and later hand centers may come close to adductor sesamoid appearance, to the late centers of the hip and shoulder, and to the phenomena of epiphyseal union. Stated somewhat differently, the maturity value of ossification centers may be relatively higher, in malnutrition, as it is ordinarily in the male, compared with the female. A chronically-malnourished child may be closer to skeletal maturity for a given set of "maturational" details than one who is better nourished or even over-nourished.

Given these disconcerting observations, the meaning of skeletal maturity must be even more elastic than our sex-comparisons and individual comparisons earlier suggested. To cite one example, the medial epicondyle of the humerus may represent 41% of ossification maturity in well-nourished boys, 24% in well-nourished girls, yet well over 50% in poorly-nourished boys and closer to 30% in chronically-malnourished girls. The very same "facts," so reliably determined on standardized 36-inch tube-to-film radiographs, may have different maturational meanings according to (1) sex, (2) race, (3) nutritional status, and (4) hormonal level.

DISCUSSION

As originally conceived, the early unitary concept of skeletal maturity had both appealing simplicity, and unquestioned utilitarian value. It is partially simple, still. Whether for early growth-appraisal or later stature-prediction, a child who is more advanced has less growth distance to go than one who is less advanced, and no one can argue the contrary.

From what we know now about chromosomal sex, males and females are both qualitatively and quantitatively different. Separate standards are unquestionably necessary, especially when the sexes are as much as three years apart, as much as 50–70% different for some ossification centers. Because the sexes differ in patterned details, a single set of standards with separate age-equivalents may not be most appropriate for careful scientific comparison. We may doubt that in any representation skeletal development of growing males and females is exactly comparable, or that abnormal karyotypes can exactly be compared to those of the normal XX and XY chromosomal complements.

What with individual variations, and some of the more remarkable sequences that we see in otherwise-normal individuals, a single concept of skeletal maturity cannot be given indefinitely elastic limits. We may question whether less-than-a-year differences between grossly disparate populations have major meaning, and whether fractional-year differences within populations are individually valid. That qualified workers can rate skeletal radiographs to ± 0.25 year need not be doubted, but except in longitudinal analysis of individual changes it is possible to challenge the meaning of such close age-assessments for different children, individually different genetically and in the rate of growth.

The elasticity of skeletal maturation in growth retardation and maturation, and the fact that one phase of skeletal development can be retarded far more than another, illuminates the fact that we conventionally collect different target-organ effects under a single label. As shown also by the XO, we have at least two clusters of maturational phenomena, and they can be quite independent. Even in normal children, ossification "onsets" and epiphyseal "completions" are quite unrelated, and in eunuchs or sexual precocities we may find the two impossibly intermixed in conventional approaches to assessment. It may be that a single concept of skeletal maturity is too broad, too comprehensive for all the end-uses we presently contrive.

This is not to reject the well-used Greulich-Pyle, Hoerr-Pyle and Pyle, Hoerr and Francis approaches, nor yet those derived from the Oxford Method (Acheson, '54, '57) and as elaborated by Tanner, Whitehouse and Healy ('59, '62). It is simply to say that the simplistic unitary concept of skeletal maturity born in pre-radiographic anatomy of the last century is simpler than the facts now allow today. For some purposes we may have achieved a close to final working solution, in terms of available methods and approaches, yet for other purposes we may be beginning to comprehend the complexities that earlier workers had no knowledge of.

Our present methods of skeletal assessment may be sufficiently elaborate now, with the complexities of sex, race, nutrition, family-line differences and endocrine normality necessitating an honest statement of uncertainty. It is possible that current methods of skeletal assessment can be made more precise by deleting those rating criteria of little predictive value, so that the whole is better represented by less than the sum of the parts (Garn, Silverman and Rohmann, '64). It is possible that the concept of skeletal maturity must be broadened, to encompass the fact that those who are less advanced (for their age) are more advanced, relative to final maturity and that those who are more advanced are paradoxically less advanced, by the very same definition.

Skeletal maturity is more than one phenomenon. It is at least two, and probably more. The different aspects of skeletal maturity are imperfectly related, and they may expand or telescope as development is hastened or retarded. We may gain precision of meaning and operational improvement by abandoning the single concept of skeletal maturity in favor of two or more clusters of maturational phenomena, just as we may gain operational utility by using less than the totality of discrete phenomena we can recognize and rate.

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