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# CERTIFICATES OF GROWING UP AND GROWING OLD*

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Growing is a subject for comment and congratulation. No child but revels in growth so vigorous that clothes have missed their chance of wearing out. Even if growth is measured in terms of weight, it is dimension not tonnage which gives pride and satisfaction. So dear to our hearts are the thoughts of our childhood that this one never fades and growth remains increase in dimension in all our natural ambition. With some misgivings and a trace of regret we force ourselves to think of growing up and hotly resent the thought of growing old. Both seem to be symbols of fading or of loss, Time's stealthy step like some far minute bell tolling us to our doom. Experience does not mean decline nor age senility. Organs are geared to last our time: their functional reserve or regenerative power preserves their integrity throughout life. Acute injuries followed by processes of repair, MacNider has shown, cause fixed cells to change their configuration, to modify their receptivity to injurious agents (7). Thus tissue resistance is acquired. The process of growing old enhances adaptability. Infirmity is the outcome of another process, the weakening of the resistance of these same cells, with senility as its end result if intercurrent afflictions have not destroyed the metabolic power. The organs are the armies, the adventurers, but the somatic tissues are the terrain which bears the scars of battle and the evidence of progress. Some somatic tissues, like the skin and hair and nails, can undergo great changes apparently with little consequent effect on the organism itself. Perhaps the central nervous system falls into this category. The ectoderm may even be misleading. Ento-

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dermic integrity is far more vital. But in the mesodermic structures bone and muscle, circulatory and respiratory systems, is betrayed the progress of the aging process which the organs themselves conceal. Of these the skeleton is most readily investigated, thanks to roentgenography. And that is why I ask your attention in a study of the bones, not as zoologists or anatomists, but as biologists intent upon the fundamental principles of life and their expression.

It is in an investigation such as this that one realizes most clearly the futility of sideral time to express in any way the progress of aging. The waxing phase of aging lasts we say some twenty years, a short portion of our whole life span but one during which aging progresses with tremendous speed. The waning phase is said to last from thirty-five years till the close of life, a period long in time but marked by relatively little change, so slowly does the aging process affect the healthy body. Twice previously have efforts been made to measure progress in aging, neither however very simple in execution. Lecomte de Noüy measured the rate of healing in a wound at different ages and found that it follows an exponential curve (6). The tissues of the body and the blood plasma together complete a closed system, changes in the one being reflected in the other. Consequently it has been suggested that the characters of the blood plasma may be used to demonstrate the progress of aging, through its power of retarding the vigor of cellular subdivision in vitro. Young plasma has very little more effect than a nutritive saline solution. Aged plasma will completely inhibit the subdivision (1).

The method which I propose has the advantage of calling for very simple technique, of affording a simple assessment, and of being equally reliable with the other two methods to which allusion has just been made. It also is applicable to all mammals as well as Man and readily enables comparisons of aging to be made in very different forms of mammal. It has the further advantage of registering health as well as maturity. The technique required is the roentgeneography of the limbs to show the stage of development of epiphysial centers if the animal be young; the condition of articular ends and degree of mineralization of the bones if the animal be adult. In human beings and large animals we make roentgenograms of left side only, hand, foot, elbow, knee, shoulder and hip. At certain stages roentgenograms of the vertebral column and perhaps of the sternal

ends of the clavicles are essential. But the vertebral column roentgenogram is no longer helpful after the twentieth birthday for then epiphyses of centra are united (21). And the roentgenogram of the clavicle is useless for a similar reason after the age of twenty-eight (12). Symphysis pubis can, however, be helpful up to thirty-five years (13). If the animal is small it is simplest to make one roentgenographic film of the entire body.

The method merely accomplishes by a quickly and easily applied technique what otherwise can be readily carried out by actual examination of the skeleton (11, 19, 20). It is applicable equally to the living and the dead. It gives us a picture of life in the fourth dimension, namely duration.

One need scarcely remind a biological audience that there are, in the skeleton, primary and secondary centers of ossification, that these appear at certain stages of early life, enlarge, take on the adult contour of the bone and finally merge themselves as integral parts of the skeleton. I purposely speak of primary as well as secondary centers for I do not want to confine our attention to epiphyses but include such skeletal elements as carpals and tarsals, union of primary innominate elements and even sutures.

The initial appearance of these centers and the ultimate incorporation of the bony element into which they develop in the skeleton, or fusion with the shaft if they appear in epiphyses, has been very crudely and unsatisfactorily investigated, usually without any collateral inquiry into the health or living conditions of the children studied. Consequently statistical reductions of age relationships have labelled both ossification and union unreliable as age indicators because of the considerable age range covered by each of these stages. That there is a considerable range in age is perfectly true. The important point is that if unions are systematically studied, it is found that the sequence of union is invariable. This fact I pointed out to Stevenson in 1923 on the basis of researches already carried out while making the collections of human and mammalian skeletons for the Hamann Museum. It was utilized by Stevenson as the theme for his thesis (11). The invariable sequence, despite the range in age relationship of union in each item, throws a very different light on the problem. It means that the entire union pattern is speeded up or retarded in relation to sidereal time. The question naturally arises: Why the individual

variation? Plotting our results on a very large series of observations (18), we find the curve skewed. It has an abrupt forward boundary and a straggling tail. Hence, there is a very definite limit to acceleration but no practical limit at all to retardation. Clearly this is not a feature inherent in the organism but something induced by the environment. Further investigation shows that retardation may be experimentally induced (17) or result from adverse conditions of health, diet or housing (16). As the result of infliction on successive generations the retardation may develop the aspect at least of a hereditary character (2).

Another closely related question occurs to one at this stage, namely, how, if the entire union sequence can swing forward or backward in sidereal time, one can tell without the evidence of the years whether the sequence is retarded or not. When retardation has reached a clinically significant degree, there are definite evidences, pathological or quasi-pathological in nature, which testify to its irregularity (3, 17, 20).

Still another question arises, born this time of the conventional linkage of ossification with union of epiphyses in thought and discussion. The epiphyses which ossify first unite last, it is said. In a sense this is true, but it is one of the half-truths which prove most misleading. Both primary and secondary centers appear in sheaves from which one or more centers may be missing owing to defects in available mineral, Vitamin D or both (4, 23). If a center fails to ossify on time, it may be delayed for a long while and other centers ossify ahead of it. But that has no influence on the age of final union. These two morphological processes, being influenced quite separately by environmental conditions occurring at great intervals of time, could not, except by accident, present a unified relationship to a third phenomenon.

It is extraordinary also that investigators of epiphysial ossification or union rarely thought of studying the bony nodule in the interior (9) until I brought this forcibly to scientific notice (14, 15, 18). At first mineral is laid down as a finely granular dot in the nubbin of cartilage. The granular dot is approximately spherical. Then it begins to grow lopsided and next fashions for itself a contour, extending irregularly until it begins to resemble the periphery of the adult bone or bone-end. The later stages, if it be a separate bone such as a carpal or a tarsal, progress slowly but individuality and vigor of outline is the result with all the characteristic modelling of the finished

bone. If the ossification is that of an epiphysis, there are stages in the face abutting on the shaft, just as characteristic as those of the subarticular contour, but they are not so suited for assessment into a chronological sequence.

The orderly sequence of development in the epiphysial, carpal or tarsal contour can readily be recorded as we have done for the human skeleton (15) and are now describing in more complete detail (18). Thus initial ossification, sequence in fashioning of contour and ultimate union can all be used as indicators of progressive maturation in the skeleton.

But there are pitfalls. The sick child or unhealthy animal will not be easy to assess. Retardation of progress may result in delayed union, though the sequence of union in the approximately fifty skeletal areas of epiphyses to be studied will usually be retarded as a program, not in some haphazard fashion. Under certain conditions, it is true, one or two epiphyses are picked out and retarded while the progress of union in the skeleton as a whole passes them by. Retardation which is often erratic, irregular and asymmetrical in the epiphysis, though not bilaterally asymmetrical, may occur in the phase of expanding bony contour. Deficiency in necessary mineral or catalyst may cause delay in the initial ossification of one or more in a sheaf of centers. All these are special problems for the investigator who is making a tool of the phenomenon of ossification. They have been discussed in considerable detail elsewhere and need not delay us now. It is these features, however, which have given rise to the assumption of natural variation through lack of understanding of the cause of individual difference.

The first use to which we put this special knowledge of the sequence in skeletal maturation was archeological. It was the identification of the age of Akhenaten, the heretic pharaoh of the Eighteenth Dynasty. Our assignment of twenty-two years to this active and restless personality has never been accepted but no one cavilled at the eighteen years assigned to one of his successors, Tutankhamen. We are now at work on the age of the famous Princes in the Tower, Edward V of England and his brother, the Duke of York. There is no doubt that the bones are the bones of these princes but they show evidence of such poor health in the children that both are retarded in progress between one and two years. The story of our disentangling the

mystery of a skeleton in a famous oil litigation has been already described in full (8).

Not only the anthropologist or the medico-legal expert finds an effective tool in skeletal maturation. The zoologist is enabled thereby to judge the comparative age of young skeletons and to assess in terms of maturation the evidence in any skeleton set before him. It is true in other mammals as in children that vagaries may be induced by dietetic deficiencies or health defects. But barring these, the assessment of maturation in any mammalian skeleton is not a difficult task. The assessment provides a ready means of investigating the duration of the several phases of growing up.

The physiologist's problem is this one of differential maturation. Our investigation of living primates, for the sequence can be studied by roentgenography in the living just as well as by dissection of the dead, shows that the phase of infancy and that of the grade school period in the anthropoid are very short whereas the preschool and adolescent phases cover about as much time as those phases of a child's life. It is in the slowing down of progress in different phases of maturation that the primate differs from the non-primate, the anthropoid from the Old World ape and Man from the anthropoid.

There is definite usefulness for this tool in the nutritionist's work. Not only is the sequence of maturation significant in keeping a check upon experimental animals but fluctuations in its progress may be assessed against a standard table or against controls in the investigation of optimum conditions of life and health or the influence upon the animal of specific experimental procedures.

Then there is a clinician's problem which has already been lightly sketched. Disturbances in the maturation program, retardations that is in progress, are signs of handicap far more pronounced than those which result merely in failure of growth. The recovery of a child from one of these more severe handicaps is announced in the restoration of normal progress in the maturation schedule.

There is a farmer's problem to be touched upon here. And this is not by any means the least significant for it is bound up in the larger issue of early and late maturing of stock and the raising of animals for meat. It has been touched upon but not systematically studied by Sanson (10), von Tscherwinsky

(22) and Hammond (5). We have given it considerable attention in our laboratory (17) and find it a fascinating study of very great practical community importance.

Of all the several aspects of the maturation pattern to which I would refer in this brief discussion, however, there is none that equals in its import that of the educator and the parent. Our school system is based on age and it is in terms of age that we evaluate the responsibilities of a child. That is our convention: it may lead us right or it may lead us wrong. The child himself chooses his companions by size without regard to age and this is a surer guide. But he realizes himself in terms of his maturity which is betrayed in his skeletal pattern for the organism, to be in health, must function as a unit. His aspirations, his hopes, his cravings, his human relationships are postulated not on age or experience or stature or weight but on the level he has reached in maturity, which we lightly call, "growing up." It is of little moment that a boy be twelve years old or have the stature of a lad of fourteen. If the level of his maturity be but ten years his thoughts and feelings will be determined by that level. Experiences beyond that will pass ineffectively over his head. If the girl be twelve years old and her stature that of ten, these will have no bearing at all on her capacity for social adjustment should her level in maturity be fifteen. To treat her as a child will be but to outrage her whole being and to evoke in her a resentment and the sullen rebellion in which unremitted misunderstanding inevitably results. When we shall have realized and based our domestic and social relationships upon this more complete knowledge, life will have greater fulness both for our children and for ourselves.

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