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OXFORD CHILD HEALTH SURVEY

EFFECT OF CHILDISH AILMENTS ON SKELETAL DEVELOPMENT*

BY

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One of the main objectives of the Oxford Child Health Survey was to study the effects of environment on physical development (Ryle, 1948), and of the two dozen papers which have so far appeared six have dealt with this topic (Hewitt and Stewart, 1952; Acheson, 1952; Stewart and Westropp, 1953; Westropp, 1953; Acheson and Hewitt, 1954a, b; Acheson and Jefferson, 1954). The form that these studies have taken has varied considerably, since methods which are able to detect continuous influences cannot always be applied to the study of influences which operate for short periods or intermittently. In one of the earlier studies measurements of standing height and skeletal maturity at various ages were correlated with economic conditions (Acheson and Hewitt, 1954a). This relatively simple treatment of the data was justified because the number of children whose social background (as judged by the father's occupation) changed during the survey was negligible. Therefore the total measurements, which represented life increments of growth (*i.e.* height) and development (*i.e.* skeletal maturity) were appropriate to the analysis. That is to say, the study was focussed on a continuous influence which it was reasonable to suppose would be reflected in increases of certain types of body measurement.

On this occasion height and skeletal maturity are again used as indices of growth and maturation, but the influence which we propose to study, namely childhood illness, operated intermittently. The analyses are therefore conducted in terms, not of life increments, but of annual increments. It follows that the units of study will not be individual children —of whom there were 650—but *child-years*. The total child-years in the survey was 5 × 650 (3,250), but only 2,296 could be used in this study (Table I). The reason for this reduction is that annual increments could be obtained only for children who had been examined both at the beginning and end of a year. Since none of the relevant observations were made at birth the whole of the first year of life is automatically excluded.

TABLE I

NUMBER OF CHILDREN EXAMINED AT THE BEGINNING AND END OF EACH YEAR OF LIFE

Year	Boys	Girls	Total
Second	327	322	649
Third	301	295	596
Fourth	273	271	644
Fifth	254	253	507
Total No. of Child-years	1,155	1,141	2,296
No. of Individual Children	327	323	650

MATERIAL

A general account of the organization of the survey and the information collected has been given by Stewart and Russell (1952). The following data were assembled for the second, third, fourth, and fifth years of life:

(1) STANDING HEIGHT INCREMENTS.—For the third, fourth, and fifth years of life the difference was determined, in half-inch units, between the standing height at the beginning and end of each 12-month period. Since few of the children could stand at the age of 1 year the increment for the second year of life was taken as the difference between the leg length plus crown-rump length at 1 year and the standing height at 2 years (see footnote to Table II). There is, in fact, an appreciable difference between these two assessments of body length, but the error thus introduced should not bias the results since it is randomly distributed with respect to other variables studied.

(2) ILLNESSES (other than head colds).—Recruits to the Oxford Child Health Survey were all supposedly normal, healthy children, and though there were plentiful examples of acute illness the debilitating, chronic illnesses were not represented. On the basis of their annual sickness records, the children representing each year of life

* Material on which this paper is based was presented in part to the Association of Physicians of Great Britain and Ireland in Manchester on May 28, 1955 (Stewart and Acheson, 1955).

were allocated to one or more of eleven diagnostic groups, of which five were sufficiently large to justify separate analysis:

A. *Exanthemata* (mainly measles and chicken pox, also mumps, rubella, and scarlet fever).
B. *Lower Respiratory Infections* (only bronchitis, pertussis, and pneumonia).
C. *Upper Respiratory Infections* (mainly tonsillitis and otitis media, also mastoiditis and laryngitis).
D. *Skin Diseases* (mainly eczema and urticaria, also impetigo, scabies, etc.).
E. *Other Infections* (mainly intestinal, but also all other infections except head colds not included above).

If, in a given year, a child experienced several dissimilar illnesses, it appeared in each of the relevant diagnostic groups, but was never counted more than once in any individual calculation. In addition to the diagnostic grouping an arbitrary classification was made of the year's illness experience as a whole to distinguish children who had one or more "severe" illnesses from those whose illnesses were all "slight", or who had no illness at all (apart from head colds) during the year.

(3) RADIOLOGICAL STRIATION OF LONG BONES (HARRIS'S LINES).—The x-ray material included films of right and left hands and knees, and records were kept of films revealing—either in the distal end of the femur, radius, and ulna, or in the proximal end of the tibia—the transverse striations originally associated arrest of growth by Stettner (1921a, b) but known in Great Britain as Harris's lines* (Harris, 1926, 1933). The cases in which Harris's lines had been recorded in both knee films were then reviewed; if the lines traversed the whole width of the bones they were classified as "complete", if not as "partial". (Complete lines in knee films were almost always accompanied by similar lines in radius films, Figure, opposite). An examination of successive knee films made it possible to identify the child-years during which new Harris's lines had appeared. Sometimes more than one new line appeared in the course of the same child-year, but such years were still classified in the "partial" group unless at least one line was "complete".

*Harris (1926) suggested that the lines were caused by a temporary arrest of the growth of the epiphyseal cartilage; this view has been borne out by the researches of Follis and Park (Park, 1954).

(4) SKELETAL MATURITY INCREMENTS.—A method recently described (Acheson, 1954) for assessing skeletal maturity in "Oxford Units" was applied to the x-ray films of the hands and knees. By keeping separate scores for the carpus, the epiphyses of the long bones of the hand and wrist, and the knee, three assessments of skeletal maturity were made at half-yearly intervals from 6 months to 5 years.* From these assessments, three sets of annual increments were obtained by calculating differences in the scores at the beginning and end of each year.

METHODS OF ANALYSIS

From the assembled data, the following basic figures were calculated for boys and girls separately and for each successive year:

(*i*) Means and standard deviations of height increments (Table II);

(*ii*) Means and standard deviations of skeletal maturity increments for three sets of bones (Table III);

(*iii*) Children (with corresponding standard deviations) exhibiting new Harris's lines (Table IV).

TABLE II
AVERAGE HEIGHT INCREMENTS (INCHES) BY SEX AND YEAR OF LIFE

Year	Boys		Girls	
	Mean	S.D.	Mean	S.D.
Second*	3·25	1·27	3·26	1·15
Third	3·42	·80	3·65	·80
Fourth	2·85	·61	2·93	·60
Fifth	2·58	·53	2·63	·51

*Mean increment artificially low and standard deviation artificially high because leg length plus crown-rump length was used in place of standing height at 12 months (see text).

TABLE IV
INCIDENCE OF "COMPLETE" HARRIS'S LINES BY SEX AND YEAR OF LIFE

Year	Boys		Girls	
	Proportion	S.D.	Proportion	S.D.
Second	·1103	·3135	·1718	·3772
Third	·1833	·3869	·2519	·4340
Fourth	·3360	·4723	·3305	·4704
Fifth	·3377	·4730	·2895	·4525

*When this method was first described it was suggested that the units awarded to epiphyses of the long bones of the hand should be scaled down in such a way that the total scores for the three areas bore a linear relationship to age. No such scaling has been adopted here. See Discussion below.

TABLE III
AVERAGE SKELETAL MATURITY INCREMENT (IN OXFORD UNITS) BY SEX AND YEAR OF LIFE

Year	Carpus				Epiphyses: Hand and Wrist				Epiphyses: Knees			
	Boys		Girls		Boys		Girls		Boys		Girls	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Second	2·41	1·67	2·85	2·17	7·73	2·46	9·45	2·53	2·35	1·62	2·92	1·58
Third	2·58	2·32	4·20	3·78	5·72	2·22	3·48	2·52	2·63	1·71	3·88	1·85
Fourth	4·32	2·66	7·51	3·59	2·21	1·90	·87	1·10	2·59	1·62	4·11	2·20
Fifth	4·98	2·64	7·70	2·37	·63	1·33	·67	1·08	2·97	1·71	3·05	1·97

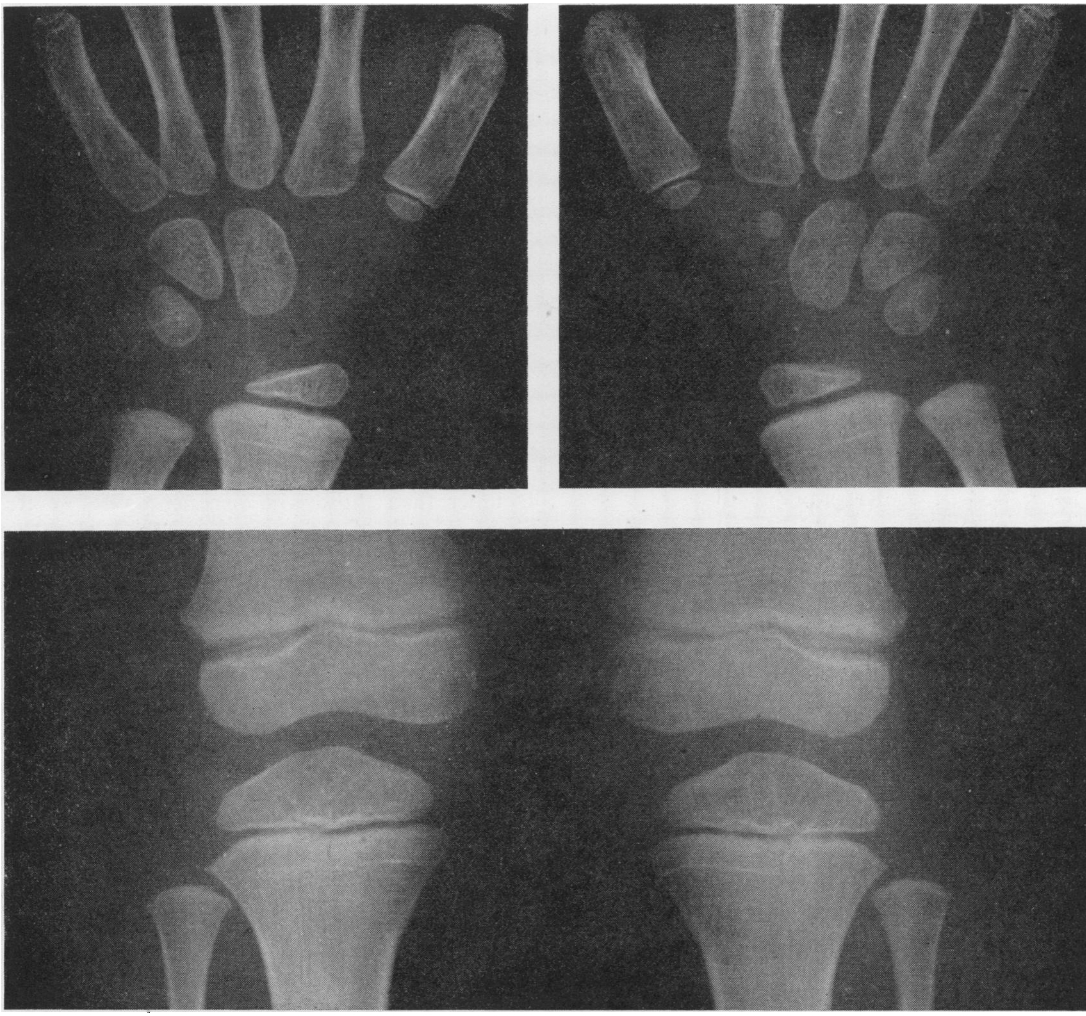

Figure.—Wrists and knees of a boy aged 5 years, showing transverse marking on each radius, femur, and tibia, and also on the right fibula. This child had suffered a severe attack of measles with bronchitis 9 months previously. The distance of the lines from the epiphyseal cartilage shows the amount of growth which has occurred since his illness.

Tables were then prepared to correlate six pairs of four variables, *viz.*:

(1) Illness with height increments,

(2) Illness with skeletal maturity increments,

(3) Illness with Harris's lines,

(4) Harris's lines with height increments,

(5) Harris's lines with skeletal maturity increments,

(6) Height increments with skeletal maturity increments (see final section of this paper).

For Pairs (1) to (5) of the above list the statistical analysis followed this pattern:

The group of child-years belonging to a given sex and year of life (*e.g.* boys aged between 12 and 24 months) was divided into sub-groups defined in terms of the first member of the pair (*e.g.* nil, slight, and severe illness experience) and mean values were calculated for each sub-group of the second member of the pair (*e.g.* mean height increments). In order that a direct comparison could be made between the effect of illness on skeletal maturation, on growth and on bone striation in any year, it was essential that these three processes were measured in comparable units. Therefore the mean of each sub-group was then compared with the mean for the whole group, and departures from the general mean were expressed in units of the appropriate standard deviation. This process was repeated seven times for the remaining sex and year of life groups. Finally all eight sets of differences were combined in a weighted average.

For example, the numbers of boys whose illness experience during the second year of life were rated as nil, slight, and severe, were 69, 135, and 51 respectively. Mean height increments of these sub-groups were:

nil 3·41″;
slight 3·25″;
severe 3·04″.

These means differed from the general mean of 3·25″ (see Table II) by +·16″, ·00″, and −·21″; expressed in standard deviation units these differences become +·13, ·00, and −·16.

When the same process had been followed eight times the weighted average differences were found to be:

nil +·12 (549 child-years)
slight −·02 (1,205 child-years)
severe −·20 (223 child-years).

In the calculations three-figure accuracy was preserved, but only the first two figures are shown in the Tables where it has also been found convenient to multiply each figure by one hundred (*i.e.* each standard unit (S.U.) equals 1 per cent. of a standard deviation).

Results

The results obtained from the first three tabulations listed above, which incorporate observations from the years of one to five, are summarized in Table V. In the first three lines of Table V the illnesses for approximately 2,000 child-years are classified on a severity basis in order to compare development during years with no illness other than head colds (28 per cent. of the total) with that achieved during years when there was slight illness (61 per cent.) or severe illness (11 per cent.). The lower part of Table V distinguishes five diagnostic groups in order to compare the effect on development of different types of illness.

Table V

DEVIATION (IN S.U.s) FROM AVERAGE HEIGHT INCREMENT, AVERAGE SKELETAL MATURITY INCREMENT, AND AVERAGE INCIDENCE OF COMPLETE HARRIS'S LINES, ASSOCIATED WITH HISTORY OF ILLNESS DURING THE YEAR
SEXES COMBINED, AGES ONE TO FIVE YEARS

Illness Group		Body Length Increment	Skeletal Maturity Increment	Complete Harris's Lines
Severity	Nil ..	+12	+2	−21
	Slight ..	−2	−0	+1
	Severe ..	−20	−3	+43
Diagnosis	A* ..	−6	+1	+25
	B ..	−3	−5	+28
	C ..	−7	+1	+1
	D ..	−10	+2	+8
	E ..	−2	−4	+13

*See text.

No one of the diagnostic groups seemed to affect growth much more or less than any other, but the severity groups were found to have significantly different height increments (from analysis of variance, $P < \cdot 001$). The effect of slight illnesses was to reduce contemporary height increment by 14 S.U.s (= 12 + 2), while severe illnesses brought about a reduction of 32 S.U.s (= 12 + 20). Similar findings were established for the two sexes separately, though the growth of boys appeared to be affected slightly more than that of girls. Thus the difference between the nil illness group and the combined slight and severe illness groups was + 19 S.U.s for boys ($P < \cdot 02$) and + 15 S.U.s for girls ($P < \cdot 05$). Corresponding differences for the sexes combined were:

Year	*S.U.s*
Second	+17
Third	+18
Fourth	+17
Fifth	+16

These findings imply that any children who escaped all illness between the ages of 1 and 5 would at the end of that period have been, on average, 1″ taller than those who experienced a "severe" illness in each of these years, and 0·4″ taller than those who had the average amount of illness. In fact, relatively short periods of sickness alternated with relatively long periods of good health, and it may be that the latter gave most children an opportunity to retrieve the ground that had been lost through illness. The present study, however, provides no positive evidence that such periods of compensation did occur. Thus the mean deviation from average height increment for 186 child-years immediately following years with severe illnesses was only + 8 S.U.s, which is less than half the negative deviation for years in which a severe illness occurred and does not differ significantly from zero. (Any compensatory spurt which occurred during the same 12-month period as an illness is, of course, already allowed for in the estimates shown in Table V.)

According to the second column of Table V differences between skeletal maturity increments for various illness groups were much smaller than corresponding differences in body length increments, and were not statistically significant. Thus the nil illness group gained only 5 S.U.s more, on average, than the severe illness group. As in the case of body length, boys appeared to be affected slightly more than girls, the mean difference between nil and other illness groups being + 3 S.U.s for boys and + 1 S.U. for girls. Even these trivial differences may exaggerate the effect of illness on skeletal maturation as a whole. For, although Table VI shows that there was a suggestive relationship between health and maturation of the *carpal bones*, the development of the *epiphyses of long bones* evidently bore no relation to the illness histories. According to Todd (1932, 1933), development of the carpal bones tends to be retarded by minor stresses, which makes these bones, in his view, less reliable as maturity indicators than the long bones of the hand and forearm. Neither Todd nor his associates have published evidence in support of this statement, but the present findings suggest that he may have been right.

TABLE VI

DEVIATION (IN S.U.s) FROM AVERAGE SKELETAL MATURITY INCREMENT ASSOCIATED WITH HISTORY OF ILLNESS

History	Carpus	Hand and Wrist	Knee
Nil	+ 4	+1	+1
Slight	+ 0	−1	−1
Severe	−12	+2	+2

The observation that illness failed to cause a delay in skeletal maturation commensurate with the interruption of longitudinal growth probably means that it will have an effect on final adult height. For it implies that during periods of ill-health the children advanced almost, if not quite, as far towards the stage at which their epiphyses would close and growth will cease as if they had always remained well and had grown in stature at their usual, healthy, rate.

The last column of Table V relates to the incidence of new, complete Harris's lines. Measured in S.U.s, variations associated with illness were much greater than variations in growth and maturation, the frequency of new lines being raised by 22 S.U.s (= 21 + 1) in the slight illness group and 64 S.U.s (= 21 + 43) in the severe illness group. These differences, which are highly significant ($P < \cdot 001$), confirm the views expressed by Stettner (1921a, b), Harris (1926), and Todd (1932) that illnesses which occur during the period of growth tend to produce these lines. In the present survey lower respiratory infections and exanthemata (particularly measles) stood out as diseases particularly likely to produce bony striation. Though the absolute frequency of Harris's lines was greater among boys than girls, their association with recorded illnesses was more clearly seen in girls. Thus the difference between the nil and the other illness groups was + 21 S.U.s for boys and + 36 S.U.s for girls, a difference which approaches statistical significance.

Though the association between Harris's lines and illness was strong, it was far from being a one-to-one correspondence. Several apparently severe illnesses had left no trace on the bones, and in several films heavy lines were seen when no illness had been recorded. Since Harris's lines cannot be distinguished until healthy bone has developed between them and the epiphyseal cartilage, it was possible that a number of the illnesses recorded occurred towards the end of a child-year and produced bony changes which did not appear until after the next *x*-ray had been taken. However, even when such cases were taken into account, there remained a substantial residue of "unexplained" lines.

This finding led us to compare the height and skeletal maturity increments achieved during years when Harris's lines had or had not appeared (regardless of whether they were associated with illness). This required an analysis of the fourth and fifth tabulations listed above, the results of which are summarized in Table VII. As in Table V there was a highly significant variation in height increment ($P < \cdot 001$ for both sexes combined and for boys alone; $P < \cdot 20$ for girls alone) and a much smaller, non-significant variation in skeletal maturity increments (only the result relating to *carpal* maturation in boys reached the conventional 5 per cent. level of significance).

TABLE VII

DEVIATION (IN S.U.s) FROM AVERAGE HEIGHT AND SKELETAL MATURITY INCREMENTS ASSOCIATED WITH APPEARANCE OF HARRIS'S LINES

Harris's Lines	Body Length Increment			Skeletal Maturity Increment (Average of 3 Areas)		
	Both Sexes	Boys	Girls	Both Sexes	Boys	Girls
Nil ..	+ 9	+17	+3	+3	+2	+3
Partial	+ 1	−1	+3	−1	+1	−4
Complete	−15	−21	−8	−2	−4	+0

To carry the analysis one stage further the material was so arranged that for each year of life the following combinations were identified:*

(*i*) severe illness and complete Harris's line,
(*ii*) severe illness but no Harris's line,
(*iii*) no illness but complete Harris's line,
(*iv*) no illness and no Harris's line.

This arrangement showed that the height increments had been more seriously affected when severe illness was associated with a complete Harris's line than when an illness or line was recorded alone (Table VIII, overleaf).

Once again, there was more disturbance of height increments than of skeletal maturity increments, the range of variation in the former (44 S.U.s) being nearly four times as great as in the latter (12 S.U.s).

*The arbitrary division of the material into 12-month periods may also have affected estimates of the effect of illness on growth and skeletal maturation, but in these cases there is no reason to expect either an upward or a downward bias in the apparent correlations, and in particular the relative magnitude of the correlations should not be affected.

TABLE VIII

DEVIATION (IN S.U.s) FROM AVERAGE HEIGHT AND SKELETAL MATURITY INCREMENTS IN CERTAIN SELECTED GROUPS OF CHILD-YEARS

Increment	Illness Experience			
	Nil		Severe	
	Harris's Lines		Harris's Lines	
	Nil	Complete	Nil	Complete
Height	+18	+9	−3	−26
Skeletal Maturity*	+ 4	−3	−4	−8

*Average for carpus and epiphyses of hand and knees

One pair of variables remains to be considered, height increment and skeletal maturity increment. One attempt has already been made (Acheson and Hewitt, 1954a) to measure the relationship between rate of growth and rate of skeletal maturation as assessed by the standards of Todd (1937). From this we concluded that children who are precocious in skeletal maturation tend to be tall for their age, but are appreciably shorter than older children of equal skeletal maturity. The present assessments of skeletal maturity, together with annual increments in place of life increments, provides an opportunity to study the normal relationship between growth and maturation in slightly greater detail. The results are summarized in Table IX, in which findings for the sexes and years of life are kept separate. Where possible the analysis was conducted in terms of product-moment correlation, but when the distribution of maturity increments made this impossible the children were divided into groups on the basis of maturity increment, and mean height increments calculated for each group. For the sake of conciseness Table IX shows only the sign of the association found for each sex and year of life, together with an indication of statistical significance.

TABLE IX

ASSOCIATION BETWEEN HEIGHT AND SKELETAL MATURITY INCREMENTS

Year of Life	Carpus		Epiphyses			
			Hand and Wrist		Knee	
	Boys	Girls	Boys	Girls	Boys	Girls
Second	+	−	+	+*	+***	+
Third ..	+	+	+	+	+	+
Fourth	+	+	−***	−*	−	+
Fifth ..	+	+	−	+	−	−

*$P < \cdot 05$ ***$P < \cdot 01$

Once again results for the carpus differed from results for the epiphyses. In the second and third years of life correlations between height increment and carpal maturity increment, and between height increment and epiphyseal maturity increment, were usually of the same order (positive) but the latter tended to be larger than the former. In the fourth and fifth years a positive relationship between height and carpal development was maintained, whereas for height and epiphyseal development an inverse relationship became the rule rather than the exception. In the knee the reversal of the growth-maturation relationship is of questionable significance, but as regards the epiphyses of hand and wrist there can be no doubt that children whose x rays recorded an increase in maturity units grew *less* than the average amount during the fourth year.

This negative correlation may be explained as follows:

The epiphyses of long bones of the hand appear in a rush during the second and third years of life. They also appear earliest in children whose general rate of skeletal development, including linear growth, is rapid. By the time these children are three years old they have gained all the epiphyseal maturity units that the present method of assessment allows for (Acheson, 1954), yet they continue to increase relatively rapidly in stature. The slow maturers, who are also slow growers, are still ossifying some of their hand epiphyses during the fourth year. Therefore during this year children who are growing rapidly show no maturity gain, while those who are growing slowly still show such a gain and a significant negative correlation is found.

DISCUSSION

The range of variation of height in a group of pre-school children of the same age and sex is of the order of 4–5½″ (Acheson, Kemp, and Parfit, 1955). In the present study we have shown that illness has a stunting effect on growth which is highly significant when the measurements of a large group of children who have been ill in a given year are compared with those of a large group who have remained healthy. However, in absolute terms, this stunting effect is rather less than ¼″, and is, in fact, tiny when compared with the *natural* variation in height of the children. Therefore it is hardly surprising that Hardy (1938), and others who have used similar methods, have failed to find any difference between the mean height of a group of children who had experienced much sickness, and that of another group of the same age and sex who had enjoyed good health. Nevertheless this small effect is important, because in the absence of an equivalent delay in skeletal maturation, it seems likely to influence final adult stature.

In respect both of growth and of maturation boys appear to have been more affected by their illnesses than girls. This seems to be in accord with previous studies of skeletal development in contrasted environments (Acheson and Hewitt, 1954a, b). The differing vulnerability of the sexes is also reflected in the mortality rates of early childhood when boys, though subject to similar environmental stresses, have a risk of death some 20 to 30 per cent. greater than girls (Registrar-General, 1954). The fact that the relationship between illness and the incidence of Harris's lines was more clearly demonstrated in girls may merely mean that some minor disturbance, not recognizable as "illness", which leave no trace on girls' bones, are sufficient to cause Harris's lines in boys, who also have a greater number of lines.

Since children with a rapid rate of skeletal maturation generally grow rapidly in height the apparent exceptions to this rule (see Table IX) call for a careful consideration of the method which we have used to measure skeletal maturity. Serial x rays of any part of the skeleton show that there are periods in a child's life when conspicuous changes occur in a short space of time and periods when very little change is detectable. For instance between Male Standards 7 and 10 of Todd's "Atlas" (1937) there is a considerable change in 18 months, and between Standards 22 and 26 there is very little change in 24 months. That is to say, there may be phases in the process of skeletal maturation analogous to the "shooting-up" phases of growth described by Harris (1947). Nevertheless, it is convenient to represent the skeletal maturation process by a variable which bears a linear relationship with chonological age. Though unsatisfactory in other respects, Todd's concept of "skeletal age" does fulfil this criterion. Our own method (which has the advantage of measuring skeletal maturation in terms not of age but of independent units of maturity) can be made to achieve the same object in two ways.

The easier method, which we have used hitherto, is to "weight" the maturity units awarded to separate parts of the skeleton so that the maturation assessment of the skeleton as a whole bears a linear relationship to age. In practice the overall assessments were based on three parts of the skeleton (hand, wrist, and knee) and carpal development has, of necessity, been given relatively great weight. This has two important disadvantages. In the first place carpal ossification may be more disturbed by adventitious factors than epiphyseal ossification. Secondly, carpal ossification does not necessarily have a direct bearing on the date of epiphyseal closure, and is therefore of questionable assistance in the prediction of final height.

A more difficult, but possibly more accurate method of assessing skeletal maturity would require detailed examination of all the epiphyses of the body throughout the growing period. In this way hitherto unidentified changes might be detected and maturity units scored during what now appear to be lulls in skeletal maturation.

Summary

An attempt has been made to measure the effect on growth and skeletal maturation of the illnesses recorded during approximately 2,000 child-years of the Oxford Child Health Survey. There was a small but definite diminution in the rate of growth during years in which an illness had been recorded. The amount of this loss was related to the severity of the illness and appeared to be slightly greater for boys than for girls. Since there is no commensurate reduction in the rate of skeletal maturation, it seems likely that adult height will be affected to some extent by even the minor illnesses of childhood. These effects of illness parallel those of adverse environment reported in earlier papers. Interruptions of growth but not of maturation were also found in years when transverse lines had appeared in the growing ends of the long bones. Such lines were frequently developed in conjunction with an episode of illness, particularly with bronchitis and the exanthemata. When this occurred, the effect was found to be greater than when an illness had left no mark on the bones, or when lines occurred without a recognized illness.

There were some slight indications that the maturation of the carpal bones was more susceptible to interruption by illness than that of the epiphyses of hand, wrist, and knee. But maturation of the epiphyses, as here measured, bore a much less stable relation to increase in height. The implications of this finding are discussed.

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