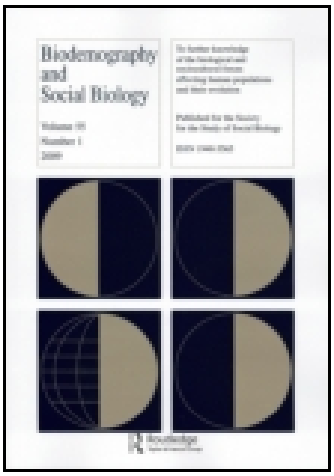

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The potential contribution of longitudinal twin studies: An appraisal

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THE POTENTIAL CONTRIBUTION OF LONGITUDINAL TWIN STUDIES

An Appraisal*

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Introduction

IN GENERAL DISCUSSIONS INVOLVING representatives of the varying disciplines of human biology, it is apparent that most authorities agree in considerable measure superficially, but there are certain basic fundamentals they do not agree upon. This leads to the proposition that more information is needed in the basic sciences in the disciplines connected with problems of growth and development.

In studying some of the many problems there is a need for cooperation of many different investigators and a strong plea for the interdisciplinary approach must be lodged at the outset. To give an example, in studying the genetic effect on growth and development, there is no sharp dividing line between, for instance, psychological and physical investigation. It is vital to record this view.

Clearly in the study of this complex subject we must accept the fundamental hypothesis that the overall gene "stream" of an individual runs through and under many influences which may be summarized as environmental, and, of course, hereditary. These two basic influences on growth and development with ultimate formation of a "type" of individual are irrevocably inseparable. What is wanted in the many branches of the fields of investigation under discussion is to know the weighting of the influences, and then how the results may become set or altered; and how the genetic stream may be affected by cultural, educational, physiological, and physical influences, which are quoted as clear-cut examples.

The human biologist eagerly seeks knowledge on the structural and behavioral patterns and their variations. It is a constant stimulation that in spite of the great amount of work carried out in the field in the past we still know surprisingly little about patterns of development, and especially correlations between them.

There are a great many facets of an individual, and his changing curve of development is indeed complex. D'Arcy Wentworth Thompson (1917) wrote: "A curve of growth to run all life long is only simple in the simplest of organisms, and is usually a very complex affair." What is confusing is that the differing characteristics are inter-related and influence each other. Some of these facets appear to change little in life—and it may be upon these that we rely to determine an individual's character, or "make-up," in the widest sense. Knowledge on such problems is fundamental for investigation in the basic sciences.

It is apparent that the final characteristics just discussed may be laid down in childhood and influenced sharply by environmental influences in this period. Mind-

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ful constantly of genetic influence, it is therefore important to study the child from these aspects on an inter-disciplinary and longitudinal basis.

It is perhaps important to say what is meant by longitudinal basis. Clearly it is easy, or easier, to obtain cross-sectional figures upon growth and development in any population. This consists of measuring for some factor a large number of individuals at the same time, at a certain age in childhood, or in adulthood. According to the worthiness or representation of the sample we gain information on the state of that measurement at certain points on a developmental curve.

With a changing organism, and certainly from the research point of view, it is more profitable and often necessary to study the organism as it changes to find out, for example, its speed of growth. If something is moving, you need to know at what speed it is moving. This can only be done by the longitudinal approach.

A child investigated more than once provides two measurements; the first measurement is subtracted from the second and the result is data vital to the researcher in the field—the incremental figure. It is not permissible, as one often sees in the literature, to deduce incremental figures from cross-sectional data. It is fully realized that the longitudinal approach to developmental problems is expensive and fraught with every kind of difficulty, but in the investigation of a changing organism it is difficult to see an alternative approach.

"Is maximum growth optimum growth," and such other stimulating questions cannot be answered unless you follow the growing organisms over a long period of time, and, indeed, there are some problems which cannot be investigated unless the organism is followed from birth to maturity. In fact, it is pertinent to note that environmental influences do not start to operate at birth but theoretically at the moment of conception. The fact that one can come from a good home or a bad home *in utero* is important and all too often neglected. Means of studying this prenatal environment are difficult but by no means impossible, as will be suggested.

A possible suitable method of study, based upon investigations of twins ideally from before birth, will be proposed.

It may be asked why it is necessary to center such a study on childhood. The crux is that as differentiations appear they presumably become fixed at some time in childhood. The varied influences can be seen acting, and their effect assessed. Clearly many problems, as has been mentioned, can only be solved by following children until they actually become adults, for in some children differentiations in childhood may be temporary and may not always persist to adulthood. The main aim, then, would be to study the inter-relation and identification of the many factors which lead to a differentiation of the character and "type" of the child or adult. "Type" is used here in the very widest sense. The diverse influences acting on the development of the child may be summarized from the investigation point of view under the headings psychological, physical, and physiological.

Mindful of these introductory remarks, it is obvious that investigators in the growth field and geneticists might turn to studies of identical twins. Such studies have been done before, and this is an idea, of course, which is by no means new.

Historical

Francis Galton founded the science that might be termed "Gemellology" in 1875 and 1883. First, his paper on "The History of Twins as a Criterion of the Relative Powers of Nature and Nurture," and then his book "Inquiries into Human Faculty and Its Development," showed that the proposed investigations were to throw light on the weight on "just scales of the effects of Nature and Nurture, and to ascertain their respective shares in framing the disposition and intellectual ability of men."

Thorndike in 1905, and Poll in 1914, published results of the measuration of twins, and in 1923 Apert and Siemens separately provided more comprehensive publications dealing with biological and pathological considerations. These scientists may be said to have been the pioneers. Dahlberg (1926) gave the first detailed work on the inheritance of physical characteristics which is a milestone in this history. Similar work was carried out by Stocks in 1930. It does not seem to be widely known that important publications were being produced from the Maxim Gorky Medical-Genetical Research Institute in Moscow up to 1936.

Professor S. G. Levit, its director, disappeared some short time after this, and little more has been heard from this important center. A large number of carefully documented twins were followed and investigations covered a wide range. Sobolera and Ignatier (1936) on the role of heredity and environment in variability of height and weight; Lichtenstein and Bassina (1936) on the mouth cavity in twins; and Lunia and Mirennova (1936) on the stability of the effect of training, serve as examples of the important work using twins as subjects which was carried out by members of this Institute. The production of appreciable differences in monozygous twins after the action of "exogenous" postnatal influences was shown by Komai and Fukuoka (1934). The classical work of Newman, Freeman and Holzinger was published in 1931 and described the investigations into identical twins who had been separated at birth or early in life and had been brought up in different environments. A general account of twins under study has been described by Gedda (1951). Penrose in 1937 reported a pair of monovular twins in which only one had congenital syphilis. This stimulated the very necessary interest in pre-natal influences upon identical twins, and these recognized pre-natal factors have been given in review form by Bass (1952). It was Price (1950) who pointed out our need to consider these biases of pre-natal onset which he maintains influence the development of twins. He divides them into natal factors, lateral inversion, and the effects of mutual circulation. These biases may affect both types of twins, but to a varying degree. Neel (1956) has suggested that "evidence on the magnitude of the biases must be obtained if we are to determine whether the twin method can be properly implemented as a tool for the appraisal of a nature-nurture interaction."

Despite the past excellent work done upon twins and briefly reviewed here, there is a need for a longtitudinal interdisciplinary study, in the widest sense, carried out over a number of years.

In summary, unusual opportunities are afforded in the study of monozygous and dizygous twins and their siblings on a longitudinal basis to elucidate the weightings of genetic and environmental influences. For a long time the dramatic concordance of the monozygous twin in psychological, physical, physiological, and pathological considerations has been an attractive and noticeable feature, but it should be brought to mind that it will be *discordant* features that will lead to greater knowledge concerning our problems.

International Cooperation

At this point it is necessary to digress and to describe some international growth studies which are at present in progress in Europe and Africa. Very briefly, the historical beginning of these growth studies started with an interdisciplinary longitudinal growth study in the widest sense in London approximately six years ago. This was not concerned with twins in any way. It was a study on so-called "healthy," randomly-selected children from an urban population, and the principle was to study them on a birth-to-maturity basis.

It was the desire of French colleagues that they start in Paris a similar growth study, the plan being to run on exactly parallel lines to the London study. It then

became apparent that other centers were interested in cooperating in this way and the writer foresaw the possibility of spending a life going around the capitals of Europe starting growth studies. This was alarming. The bringing of order, into what promised to be a possibly chaotic house, was effected by sponsorship of the International Children's Center in Paris. In short, there are now running five European longitudinal growth studies. They are all interdisciplinary. The principle behind them is that all have agreed to follow a very simple—and simple is emphasized—"base line" of investigations in all the disciplines (Falkner, 1957i). It is essential to note that no central "authority" is directing these growth studies. They all have very special interests and in some branches are doing very detailed work. That, in a way, is not the concern of the international group. What all have undertaken to do is to follow this agreed international base line.

Clearly, the base line must be improved, criticized and altered continually, especially on the psychological side, as the children are growing older. It is, therefore, necessary to meet regularly to do battle, criticize each other, compare data, plan work for the following year, and to standardize methods and techniques.

This international cooperative work is presented here, for its potential advantages are obvious—the production of comparative international data. There are two studies in Africa which are clearly on groups of very differently constituted samples of children, malnutrition being one of the big factors of difference. Their participation will lead to comparisons of great interest. These centers are in West Africa and East Africa, and the base line is used as far as possible. Already, although some of the growth studies are comparatively new, it is apparent that the African child, certainly in the first year of life, has a different pattern of mental and physical development compared to the European child. Allbrook (1956) has recently shown that there is a reduction in the adrenal cortical mass in the East African compared to the European. Such work stimulates one to speculate on the basis for such differing patterns of development and enhances the plea for more of such basic comparative data. The importance of studying the Negro comparatively in the United States is also clear.

Quite apart from the advantages of using truly comparative international data, the solution of such problems as the influence of racial factors upon human variability may be further investigated following such original observations as those of Muller (1954).

The Longitudinal Approach

To gain approval for such a proposed type of project is not easy. The reason is clear. Experience has shown that this type of study has not always been satisfactory from every point of view.

It is fully recognized that some problems can only be studied by following children from birth to maturity. The objections to this method are that it has been thought necessary to wait a great time before analyzing the data. Such growth studies have been attempted in the past and, with others, have collected large quantities of data which, excellent as they are, have been insufficiently analyzed because of difficulties to which all are fully sympathetic. There is a further danger in interdisciplinary long-term studies of this kind in that the various disciplines become bogged down with data which is sequestered and not coordinated.

Mindful of these disastrous pitfalls, and with these uppermost in thought, a solution is to follow children routinely on a "mixed longitudinal basis." The basic principle behind this is to recruit children in groups at all ages. This method enables investigation to be carried out on a whole age range of development by means of several overlapping longitudinal runs. Con-

veniently, these would be in five-year periods, and the important adolescent group would be included in the last two. The adult will be mentioned later. This method produces results much more quickly, and the investigators will clearly at the same time gain a much larger overall experience with the growing child in his entirety and in all the disciplines.

Although the work would be planned basically in runs of five years, it will be to everyone's advantage to follow some of the children for as long as possible, and to hope to follow the majority to maturity. It would be very desirable to recruit as many identical twins as possible before birth, and the expressed interest, for example, of obstetrical and radiological colleagues would ensure this. After recruitment of groups of monozygous and dizygous twins, the siblings ideally should be studied. An energetic attempt should also be made to find the greatest possible number of monozygous twins who had been separated in childhood. It is recognized that these are very rare.

In view of past experiences with growth studies in general the following is stated with considerable trepidation, but honesty requires that it be stated: It must be recognized that many basic problems of growth and behavior are unsolved. In any longitudinal multi-disciplinary project data is collected in quantity. In addition to clear-cut hypotheses to be tested—and these are essential—it is always probable that profitable lines of research and possible correlations, and so forth, will develop as the research does. It is best to clearly state this, and this concept is strongly claimed to justify *some* part of such a study's usefulness. The great pitfalls apparent when using this perhaps comforting hypothesis must be, and are, recognized.

A further aim is to provide information for other workers in the field. It is obvious that possible correlations would be very large. If the data is in a workable form, it is invaluable from time to time for specialized researchers who may require information from one part of the work. This has occurred successfully five times within the last three years in the cooperative European studies.

There is always the problem of keeping contact with a "longitudinal sample" and in large countries the geographical considerations of the moving members of the samples can be a source of worrying loss. It is, therefore, important to prophesy such a loss in order to minimize a final result of finishing with a sample too depleted to sustain reliable results.

One aspect of such growth studies in general is neglected: Their value as a teaching tool is not always appreciated. They can contribute much to post-graduate and graduate education during their actual routine and progressive existence while the educational value to the investigators themselves is large. In making a plea for this kind of work it is necessary to produce every possible advantage.

The great pitfalls, then, apparent when following the methodology of this type of research, are: (1) Over-collection and storage of large quantities of data. This may be largely overcome by the use of mechanically recorded data, and using modern statistical techniques and computation (Heumann, 1956). It is fully realized that by placing data on IBM cards, for instance, the problems of actual analysis of data are by no means solved. It does, however, place the data in a workable condition. (2) Lack of constant review of data. Such review should be stimulated by: (a) An Advisory Board, and (b) the availability of data for use of other research workers.

A word on "an Advisory Board": Entering the field of investigation into problems of growth and development is not unlike taking off across the high wire. Falling off is easy but staying on is not, and to undertake investigation into this sphere without the constant supervision and skilled help of a geneticist and biometrist is asking to fall very early in the precarious journey.

The advice and planning of a social science expert is also essential in order to be sure to investigate skillfully the all-important "socio-environmental" background of the subjects. Thus, the interdisciplinary approach must be carefully planned and the investigations themselves supervised by such a regularly meeting advisory body.

The Twin Study

Before carrying out any investigations, it is clearly essential to classify the twins studied and designate accurately the monozygous from the dizygous. Study of the placenta is important, and microscopic examination may be necessary but not conclusive. It is common that monozygous twins may exist *in utero* in separate fetal membrances for example (Von Vershner, 1939), and indeed may have separate placentas (Lassen, 1931). Other such diagnostic factors as concordance of sex, physical features, skin, hair and eye color, taste perception for phenylthiocarbamide, tongue curling, and fingerprints and palm prints are all of help in determining monozygosity. But at best their conclusiveness is never of complete certainty. It is of interest that authorities now make clear that fingerprints of identical twins are not necessarily identical (Federal Bureau of Investigation, 1953).

Happily the basic work of Race and Sanger (1950); Fisher (1951); Weiner (1935, 1940, 1952); Bryce, *et al.* (1951); and Walsh (1955) on the concordance of blood factors has made it possible to determine the truly monozygous pair with great accuracy. For theoretical considerations, use of the previously mentioned concordance factors together with determination of the ABO, MNS, and RH blood groups will ensure correct diagnosis.

Basic Hypotheses

There are three hypotheses to be tested which are vital and basic to interpretation of twin study data. In the past these influences may have been recognized as possibilities, but their effect has not been assessed. Hence, all work in this field is based upon assumptions which have not been and must be tested. These are: (1) that differing pre-natal and natal influences upon each twin of a monozygous pair cause discordant patterns of development. (For example, abnormal positioning *in utero* of one twin.) (2) That concordance in patterns of development of dizygous twins may be due to, or influenced by, a common circulation while *in utero*. Concordance held to be due to similar environment may be, in effect, due to this factor. (3) That certain definite maternal influences pre-natally produce discordance in monozygous twins. For example, one pair of monozygous twins had congenital syphilis and not the other. (Penrose, 1937)

To test these hypotheses, a group of prenatally recruited twins are needed and the cooperation of skilled obstetric colleagues required. After the thirty-second week of pregnancy positioning of each twin is rarely altered and careful observation at the birth should label each twin. Routine radiographic examinations are normally carried out after the thirty-second week and this further gives information as to the positioning. (Extra radiography for this study is not justified with the current consciousness of the effect of radiation on the fetus.) Regular plotting of the position of each fetal heart will be an added indicator of position, since the differing fetal heart rates commonly remain so. Labeling and accurate microscopic and macroscopic examinations of the placentas are necessary and practical, while an accurate maternal history during pregnancy is mandatory.

The subsequent groups of monozygous and dizygous twins form control groups.

Research on human twins has often had to be retrospective and obviously has involved twins who have both lived a certain time and usually a comparatively long time. The method of ante-natal study allows of the possibility of studying twins with the *prospects* of a long-term follow-

up; and perhaps more important of studying twins where one or both die before birth; and aborted twin pregnancies. Investigation of such aborted or still-born twins, coupled with histo-chemical and biochemical studies on healthy and diseased placentas in monozygous and dizygous pregnancies should reveal valuable information.

Further Investigations

In general, the lines of investigation of the proposed interdisciplinary study would proceed along the main lines already discussed and hypotheses other than the above basic three would be tested in the different disciplines of the research. It would be undesirable to carry out a great mass of highly detailed investigations on *all* the twins, for example. Sub-groups would be formed where suitable.

It may be profitable to discuss at this point some examples of problems from the various disciplines which should be investigated in such a study. Along the *physical line of approach,* Palmer (1934) has suggested that genetic determination of the *rate* of growth is likely to be independent of genes influencing *size* achieved. Further general work on this subject would clearly emerge. A most profitable feature would be to break down the growth in the twins to the unit involved: as an example, the whole concept of skeletal maturity is under discussion, for its accurate measurement is advantageous in many spheres. (Falkner, 1957ii). More information is needed on the genetic influence on the *pattern* of the individual variations in skeletal maturation before such improved assessment is possible. (Reynolds, 1943; Garn, 1956; Acheson, 1956). Patterns of development are always of interest to the growth investigator and these would, clearly, merge. A particular current interest is centered on the patterning of fat growth in the human, and the investigation of true genetic influence on obesity and the "normal" large variation of fat distribution in the child and adult would be profitable.

Physiologically certain problems present themselves for disentanglement. Two important examples are given: Are enzyme levels in the child genetically determined? And possibly more important, is the pattern of antibody formation in the human genetically determined? It is more correct to say in place of "genetically determined," is the weighting very heavy on the side of the genetic influence? Basic information on antibody formation is vital to us in the field of preventive medicine in the future—our synthesization of antibiotics may not for long outstrip the rate of sensitization of organisms.

Dobzhansky (1957) has pointed out to us that growth does not stop at the age of 20 years in the human but is represented by a trajectory which falls off at senescence. This is true, but it is continually fascinating in examining the incremental curves of size of many parts of the body to see how dramatically these incremental figures drop to zero at approximately the age of 20 years. Why does growth of size stop at this point and stay at the same point for often 40 years? Growth, to make a generalization, occurs by cell division rather than increase in cell size. (Neural tissue is a clear exception.) In some organs or tissues there are, then, two processes occurring during the active growing phase—cell division, and repair or replacement for regenerative processes. Clearly calories are needed for both; but a highly speculative suggestion is made that a constant supply and amount of a substance (say *M,* signifying mythical) is available which is quantitatively genetically determined, and which activates the division and regeneration process. When a certain size of that tissue mass is obtained, the regeneration now necessary for its constancy will use all the substance *M* available, and hence further calories above a basic amount will not result in any cell division and thus no in-

crease in size. Investigation at a basic level along this avenue might have a wide application.

In the area of *pathological processes,* it will be particularly helpful to establish the weighting of conditioning of disease by inheritance. Twin studies are a profitable field for such investigation. Warkany, *et al.* (1955) have described discordance in monozygous twins resulting in diabetes mellitus in one twin and obesity in the other. They point out the importance of this and similar observations for the study of the etiology of diabetes mellitus and of obesity.

Work on the inheritance of susceptibility to infection by tuberculosis was stimulated by Diehl (1933, 1936) and recently by workers in France. These are important indications of the part twin investigations can play in elucidating such important information of this type.

It must have been evident by now that this discussion has been centered very largely on fields of investigation other than the *psychological* one. It must be emphasized very strongly that this is not because of a reluctance to admit of its great importance, but it is simply due to an unwillingness to discuss something in which the writer has no special knowledge. With this reservation, however, some of his colleagues' observations and general ideas are put forward. Thompson (1957 has shown us that with modern mathematical, statistical and experimental psychological methods we are able to be far more objective today than we ever were before. On a very simple level, the psychological investigation methods as used in the international base line are summarized. This will show the basis of proposed work in this field for use in a twin study.

1. The interrelation of psychological influences with others affecting the behavior and development of the personality of the child is studied. In avoiding detailed description, the principles of investigation may be divided into (a) interview techniques. Here data obtained from interviewing the mother and close relatives of the child, and older child himself, is collected. (b) Standardized testing techniques for the assessment of the child's mental ability. These vary naturally according to the age of the child. It is pertinent to note that work has already been carried out by the international teams on attempting to assess present tests and devising new ones, particularly for the very young child and the infant. In respect to both of the above basic methods it should be pointed out that both are constantly subject to review and attempt at improvement. (c) Assessment of the temperament of the child by standard and experimental methods.

2. Assessment of the changing socio-environmental background of the child. This part of the investigation can be said to be vitally important to all sides of the research, but for the sake of convenience it is included under the psychological heading.

This sketchy account is merely the presentation of a non-expert in the field who realizes its paramount importance.

Constitution

Finally it is necessary to traverse the most slippery part of the high wire. In discussing the child and adults in growth and development studies, we are constantly coming across the concept of "types," "somatotypes," "body-types," "personality-types," and so on. It is clear that each of us has an individual subjective method of typing our fellow humans. This is not a new idea.

> "Let me have men about me that are fat, sleek-headed men and such as sleep of nights! Yon Cassius has a lean and hungry look, he thinks too much; such men are dangerous."
>
> . . . *Julius Caesar*
> Act 1, Scene 2.

Hippocrates (450 B.C.) described two types of people, apoplectic and phthisic, and the great clinicians in the past commonly gave us excellent constitutional descriptions of individuals with certain dis-

ease entities. Beneke (1878), the German pathologist, perhaps may be said to have founded the interest in constitutional disease. Two Frenchmen, Rostan in the middle of the nineteenth century and Sigaud at the beginning of the twentieth, started and continued the French "school" of constitutional classification of the human, and they divided man into "digestive," "muscular," "respiratory," and "cerebral" types. (Some individuals were not able to be fitted into these divisions and presumably were just unfortunate misfits.) There are still some French workers who adhere to this classification, and the school certainly stimulated work in the field. It was Kretschmer in 1921 who achieved considerable notice through his furtherance of this principle and he divided individuals into three groups: pyknic, athletic, and asthenic. Although Kretschmer was in fact working basically with mentally abnormal persons, and his notations have since been widely and very incorrectly used, his was the first real attempt to correlate character with body-type. His method was highly subjective, but he did at one time try to be more objective by physical measurements.

Since 1919, Viola, an Italian physician, has worked with the problem of constitution and its correlation with disease, and by physical measurements he devised an index of "morphological type." Here was a truly objective attempt, but he, too, placed the individual in three separate categories. It might repay us to study Viola's principles anew especially in relation to disease.

Up to this point the "constitutionalists" divided us into clear-cut categories. A newer development was that of factor analysis (examples: Burt, 1938; McCloy, C. H., 1940) which, reducing description to a very basic level, is a method of describing any physique conveniently as factors after statistical analysis of a series of correlated measurements. These measurements are anthropometric ones and what is actually measured is clearly important. (As far as is known no follower of this method takes into consideration the distribution of fat in the body.) Certainly this index moved us a step forward and did not place us in a pigeonhole.

Sheldon since 1940 (1940, 1942, 1949, 1954), has steadily put forward his important concept of constitutional factors. He, too, used a number of divisions of physical types, three—but with this vital difference —they became components and each individual type was assessed by means of the quantity present of each component. Sheldon's original work was highly objective and based on measurements carried out on standardized photographs of over 4000 young adult males. Since this time it has been realized that this method was too "static," and the present method now is to label the individual by division of subjects into age groups, the use of a height-to-weight ratio, and anthroscopy (or inspection of standardized photographs). This method, perhaps surprisingly to some, is satisfactorily objective (Tanner, 1954i.) I have carefully refrained from describing in words any of the physical types used over the centuries. Sheldon's nomenclature for the three basic components has caused some criticism, but I submit the actual names have really little importance. As a basis for research into the difficult problems of biological constitution it is clear a great amount of work has to be done, and it is timely to state that Sheldon himself has never stopped pointing out that his work and the work of others in the field (examples: Dupertuis and Michael, 1953; Tanner, 1954ii) is *provocative of new research.* The relationship of physique to temperament, that most fascinating of problems in this field, is the most controversial part of Sheldon's work, and it is here lies the stimulation for the beginning of a great amount of needed research. Do we not, all of us, have our individual methods of "rating" temperament as well as physique? Is there a true relationship between the two? Can temperament be altered? Is physique largely a static phe-

nomenon? Clearly not—but to what degree not? An ex-chief and friend, who was very much *not* of muscular athletic build (heavily endowed with "mesomorphy") and was very round, once asked me: "We should all like to be mesomorphs—how can I change; could I have done so whilst a baby?"

It is clear to me—and I am impressed by the number of colleagues who agree with me—that babies and children can be individually "typed" using the word very broadly. With the babies this is highly subjective. What is wanted is information on the type, not necessarily a static type reached at "maturity," but its continual trend or pattern of development. The work of animal physiologists (Hammond, 1954, 1955), stimulates us to investigate the changes of body build in the human basically genetically determined, for they have shown that differing nutritional status may produce great changes in configuration and actual body composition.

In the realm of environment, we are back into the concepts of the founders of constitutional medicine. I quote an example: Colleagues (Dowling *et al.*, 1956) are investigating the disease of infantile eczema (Prurigo Besnier) in a group of children. It is considered probable that this condition is a good example of "psychosomatic disease." It is becoming apparent to us that these children of all ages have a very large component of muscularity in their build. If this is proved and accepted at a scientific level, it is only one small step forward. The next and vital question is, what was, and is, the weighting of genetic and environmental factors which produced or altered the behavior, physique, and physiological state of a child so that he was more susceptible to this condition than if he were the child next door with a different make-up?

Newer objective provocative work on these fundamentals is being produced with the adult, examples of which are Gertler *et al.* (1951) on coronary occlusion, and Sutter and Tabah (1953) in France on the relation of consanguinity to the general structure of mortality.

In assessing the weighting of the genetic influence, it appears that a valuable contribution to this whole difficult field might be made by a long-term study of the human twin. It cannot be emphasized enough that great harm has been done in the past by some unscientific approaches to these problems and any future work from whatever angle must be made from an interdisciplinary standpoint and with rigid scientific standards. A collective approach to these problems should yield valuable results with simultaneous assessment of shape and constitution using psychological, anthropometric, biochemical, photogrammetric, radiological measurement, and volumetric estimations. But is an unraveling of the place of the genetic, physiological, and psychological biases as influences on human constitution likely to contribute to biological knowledge of the human? Surely, for ". . . morbidity and mortality constitute the long range criteria of the importance of differences in human physique" (Brozek, 1956).

Some varying components of temperament, behavior and body composition are influenced greatly by the human variables which we have discussed. All these variable aspects present a problem for further rethinking and research. Valid information on this subject gained by impeccable scientific attempt is needed and may be evaluated in degrees of future human health and happiness. It is a challenge of high endeavor to human biologists—a challenge full, I am sure, of heartbreaks but it must be taken up for the rewards will be very great.

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