The Individual Man and Medicine*

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It is incumbent upon me first to express my deep appreciation of the honor of presenting to this distinguished body, the American College of Chest Physicians, the third Louis Mark lecture. It had not been my good fortune to know Dr. Mark, but in reading something of his life and works I have been impressed by his great versatility, his humanity and his understanding and, above all, by an inquiring mind intensely interested in the complexities of human nature which requires a fine appreciation of the individual. For this reason it has seemed appropriate to discuss in a memorial to such a man certain aspects of individuality, not in an environmental, behavioristic or psychological sense, but as to man’s physical constitution and variation. In doing so I do not overlook the cognate subject of biochemical individuality, which I touch upon only casually because of the limitations which must necessarily be set in an address such as this. In examining some of the origins and factors concerned in matters of human physical constitution, I shall have occasion to illustrate some of the principles by reference to the genesis of cardio-vascular anomalies in the hope that the subject matter may not seem to be too remote from the field of immediate concern and interest to the chest physician. If I should falter by lack of clarity or over-simplify in order to be clear, I would crave your indulgence.

Not quite 200 years ago, Giovanni Battista Morgagni (1682-1771), the great physician of Forli, entered his 80th year and, as though to celebrate the full ripening of his years and wisdom, published one of the most significant books in medical literature. This book, *De sedibus, et causis morborum per anatomen indagatis* (Venice, 1761), or in English entitled “On the seats and causes of diseases investigated by anatomy,” introduced, as Rudolf Virchow (1821-1902) put it, the “anatomical idea” into medical practice, but even more importantly, it so profoundly influenced medicine that we have scarcely recovered from the revolution which his ideas engendered. Although Morgagni, in giving credit to his predecessors Antonio Benivieni (c. 1440-1502), Andreas Vesalius (1514-1564), and Theophilus Bonetus (1620-1689), modestly disclaimed any great originality, he had in fact initiated the destruction of the individual as the object of scientific medical pursuit and investigation. Prior to Morgagni, the physician had thought in the Hippocratic tradition, in terms of the patient as a sick individual; after Morgagni, disease came to be regarded as the effect of a pathological process affecting an organ. Henceforth we would speak of diseases of the stomach, of the liver, of the lungs, and, if we failed to determine the “seat” of the disease, we could always avoid the patient by considering his syndrome. The further transition was gradual, for within a generation Morgagni’s concept of the diseased organ had been carried by the Frenchmen Marie-François-Xavier Bichat (1771-1802) and

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Jean Cruveilhier (1791-1873), into the tissues. Thence, the extension of the cellular theory of Matthias Schleiden (1804-1881) and Theodor Schwann (1810-1882) into a cellular pathology at the hands of John Goodsir (1814-1867) and Virchow, passed disease to the cells and, finally, to their ultimate physico-chemical constitution. If during this transition we have lost the individual, we have gained immeasurably in scientific precision to a point where some 20 years ago there was great optimism that man and all his biologically relevant processes could be interpreted by sufficiently accurate physical laws so that medicine and human biology would be fully scientific. But this optimism has been sorely misplaced so that physicians have shifted instinctively back to the concept of the whole man, as did their forefathers, with uncertain leanings on a psychosomatic prop which would not destroy their ideal of a fully scientific and materialist medicine.

Edwin Schrödinger, the distinguished physicist and Nobel laureate, points out that these optimistic expectations that biological processes are interpretable in terms of physical and chemical law would be regarded today not only as naive, but definitely wrong. These opinions were based upon the *a priori* view that because of the "cosmical" number of atoms involved in biological processes, "all the revelant laws of physics and physical chemistry would be safeguarded even under the very exacting demands of statistical physics in respect of large numbers." However, it has now been demonstrated that incredibly small numbers of atoms may play a dominating rôle in orderly biological processes. Such small numbers control observable developmental features of the organism and important characteristics of its physiological functions. Thus C. D. Darlington estimates that the volume of a gene is approximately that of a cube whose edge is 300 Å. This dimension is roughly only 100 to 150 atomic distances in a liquid or solid so that if a gene were a homogeneous liquid it would contain only a million or so atoms. But the gene is almost certainly a large protein molecule in which every atom and every radicle plays an *individual* rôle. Ignoring the unwarrantable neo-vitalistic implications of Schrödinger's discussion, there is much substance in his remark that the number of atoms is "much too small (from √n point of view) to entail an orderly and lawful behavior according to statistical physics—and that means according to physics." The recent brilliant work of Heinz Fraenkel-Conrat in Berkeley on viruses indicating that the nucleic acid fraction comprising but 4 per cent of the protein molecule is the operative factor, further emphasizes these facts.

The growth of Mendelianism into the modern science of genetics is very recent and has served somewhat to redress the balance in our thinking between the individual and the category by emphasizing inherited traits and characteristics, overt or recessive. In the sphere of teratology and malformation genetic concepts and mutation theory have played a most significant rôle in shaping our understanding, but by the same token, concepts of a predetermined individual and, by transference, interpretations of anomalies such as those which are so frequent in the cardio-vascular system, have brought about a nihilistic attitude as to possibilities of prevention except through mechanical means as exemplified by surgical procedures.
An archaic memory in the collective mind of medicine of the existence of the individual would obtrude itself from time to time. It sought to emphasize the individual by classification of man into several sub-types, each of which possessed a characteristic morphology reflecting an individualized physiology and temperament. This movement was carried to absurdity by Cesare Lombroso (1836-1909) who, in attempting to establish the constitutional basis of criminality, insanity and genius, thought he could determine whether the subject was destined to be hanged by the degree of adherence of the lobule of the ear. Nevertheless, Lombroso's imaginings had their useful effects in the development of techniques for the recognition of the individual by Bertillon (1886) and Francis Galton's method (1892) of identification by fingerprints. Heirs to the conception of constitutional types have long been with us. In our own time, Bryant\(^1\) and Goldthwaite\(^2\) were influential, if not very successful, in individualizing lesions of the back and locomotor system to herbivorous, carnivorous and omnivorous types of mankind as a substitute for the shetic and asthetic classification of an earlier generation. And now among the latest recruits are W. H. Sheldon (1940, 1954)\(^3\) with his great refinements of somatotype into endomorphic, mesomorphic and ectomorphic varieties in agreement with the germinal layers and thus possessing viscerotonic, somatotonic and cerebrotonic temperaments supposedly either to enjoy, or to act, or to think in consonance with their physical constitution.

Then we have the attempt of Behnke\(^4\) and associates (1942) to establish criteria of individual constitution in terms of the active tissues of the body by calculating "lean body mass," which is body mass minus the fat, as obtained by densiometric methods or derived (Miller and Blyth 1952)\(^5\) from studies of basal oxygen consumption. To these must be added the index of Tanner (1951)\(^6\) in which the degree of masculinity or femininity of the individual is rated by means of a formula reflecting the relationship between shoulder width, pelvic dimensions and leg length, so as to reveal the andric or masculine and the gynic or feminine components admixed in the individual.

It will be observed that in all these attempts to analyze constitution, there is the implication that the morphology of the individual is related to individual physiological function. Sheldon's classification stresses not only the organ derivatives of viscera, muscle and brain from the tripartite germinal layers but inherently the physiological action of these systems, and Tanner evidently is concerned with body form as an expression of endocrine balance. Doubtless the implication has justification on empirical grounds for we are all familiar with the effects of metabolic, endocrine and other factors on body form. Nevertheless, the conception is in many respects too crude in view of the enormous number of variables and one cannot escape the thought that dimension is not necessarily related to function, as evidenced by the well known example that the size of the brain is in no way correlated with the quality of the mind. Although generalizations on individual constitution may have some degree of validity, we must proceed with the very greatest caution since knowing so little of the mechanisms responsible for human variation we may be greatly misled. In order to test some of the assumptions, Milton DeLucchi,\(^7\) working in my department, investigated constitutional variation in rela-
tionship to the circulatory responses caused by orthostatic stress. The circulatory system was selected because it readily manifests by the quantitative changes in pulse rate, pulse pressure and in the ratio of pulse product to mean pressure, the ability of the individual to withstand gravitational forces in adjusting to the erect posture. Failure to adjust rapidly to the experimental conditions brings on the classical “effort syndrome” described by Lewis. In the eighty subjects examined and classified by such constitutional measurements as somatotype, index of lean body mass and index of androgyny, statistical correlations to the physiological response of the cardio-vascular system either did not exist or, where they did exist, could be explained as due to other purely physical factors inherent in the system of constitutional classification such as total height and relative size. Of great importance, and contrary to expectation, no relationship could be established between mesomorphy and lean body mass, and the correlation between cardio-vascular response and both mesomorphy and lean body mass was negative. In view of the fact that mesomorphy and the index of lean body mass are ostensibly a measure of muscularity, the failure to find any correlation with the preeminent mesodermal cardio-vascular system is disturbing. I quote this work not only because of my personal relationship to it but as the most complete investigation carried out in this connection. It should remind us of the great difficulties associated with any analysis of individual constitution.

Although we are unable to relate differences in constitutional morphology to physiological action with any great degree of success, there is very good evidence for a biochemical and metabolic individuality. Ever since the discoveries of Maraglino (1892), Landsteiner (1901) and Eisenberg (1901) on haemolysis and agglutination leading to blood-grouping, blood as such has ceased to exist, to be replaced by blood-type now refined to individual varieties of very great complexity, but it was Sir Archibald Garrod (1902) who, in announcing the existence of inborn errors of metabolism, suggested that “just as no two individuals of a species are absolutely identical in bodily structure, neither are their chemical processes carried out on exactly the same lines,” thus restoring concepts of diathesis and idiosyncrasy which a generation earlier Sir Jonathan Hutchinson (1881) in his essay on the “Pedigree of Disease” had sought to destroy. Since the beginning of the century the amount of circumstantial evidence which has accumulated is impressive. It has been shown that the range of values for blood sugar, uric acid, serum amylase, alkaline phosphatase, cholinesterase, β-glucuronidase, among many others, is relatively constant for the individual and these values may be well above or below accepted levels. Variations are often in excess of 30-fold, which would seem to indicate that the failure to individualize many of our common biochemical tests has left us with parameters which are entirely too coarse. Transplantation experiments (Loeb 1945), the response to drugs (Williams 1956), the allergies and numerous other investigations establish the view that every individual possesses his own metabolic pattern. From such considerations Leo Loeb (1945) in discussing the biological basis of individuality emphasizes that organisms which are highest on the evolutionary scale possess the greatest degree of biochemical individuality, and Roger Williams (1958) has recently proposed that the
individual metabolic pattern can lead the way to a chemical, as distinct from a physical, anthropology.

All, I think, will agree that the individual is an aggregation, genetically determined, representing the sum of morphological, physiological and biochemical characteristics. These characteristics in combination are peculiar to the individual. In morphological characteristics variation is very great and perhaps the major error which we make is the attempt to relate too closely this variation with physiological and biochemical characteristics. This error is understandable in view of the psychological difficulty of dissociating the morphological appearance of the individual from his total personality. However, if we enquire into the factors guiding the achievement of body form from genetic determinants we shall gain great insight into the meaning of individual variation and important understanding of congenital defects. These factors are the growth differentials and their interaction, timing and the action of the endocrine system and nutrition.

Some years ago in studying the growth of the fetal skeleton, Inman\textsuperscript{16} and I were able to establish the fact that the dimensions and angles of various structures increase throughout the fetal period by constant increments in relationship to sitting height. In other words, the curves fitted to the data follow straight lines and can be represented by the empirical equation of the general form $D = aL + b$ where $a$ is a constant representing the slope of the curve and hence the rate of growth of that part. These rates of change are characteristic for each dimension and their interaction is responsible for the changing bodily proportions of the individual as he passes from fetal to adult life. It is possible to project by extrapolation these rates of change obtained from the fetus forwards into adult life, thus revealing the mechanism whereby the well known differences in facial design and proportions come about. Consequently it is not difficult to appreciate how individual family resemblances as well as body proportions are achieved. These resemblances essentially depend upon the ratio of facial and other dimensions and these ratios, although they are without doubt genetically determined, are achieved by the interaction of the individualized rates of growth of the various dimensions. These rates of growth are, however, only potential and the potentiality may fail to express itself due to nutritional, endocrine, toxic or other disorders. Thus we observe that the human dwarf is round-headed or brachycephalic; the bridge of the nose is flat and the palatal region shortened, causing the upper jaw to be undershot; and the face is characteristically wide and flat, giving the appearance commonly called "dish-faced."	extsuperscript{17} In such a description we should recognize that all we are saying is that the fetal features have been retained due to a failure, whether the ultimate cause be endocrine, nutritional, or something else, to achieve the full growth potential of the various skull and facial dimensions.

The specific rate of change affects not only linear dimensions but also processes which interact with dimensional growth. A striking example of this is seen in the relationship of the rate of membranous ossification occurring in the bones of the calvarium in association with dimensional changes. Measurement shows that in the case of all membranous bone of the skull, there is a constant inflection in the growth rate when the individual achieves a sitting height of from 140 to 160 mm. The explanation
of this is seen when the rate of membranous ossification is plotted against the rate of growth of the skull in its circumference. The slowing down of the ossific process is due to the inhibition of the spread of ossification by the formation of the sutures. Obviously, without the inhibition of ossification by the sutures, the bones comprising the vault of the skull would soon fuse into a solid mass of bone permanently limiting further growth of its dimensions, as sometimes is seen in skull anomalies with premature fusion of the sutures. However, it should be observed that the rate of ossification of membranous bone is always greater than the rate of growth in dimension. This is of enormous importance and demonstrates one of the mechanisms of inner consonance which exist in bodily processes; in this instance insuring an adequate bony covering to the calvarium even though there be great variations in the size of the skull. Thus in a microcephalic skull, the membranous bones are soon ossified, having less area to cover, but they do not fuse at the sutures, which permits of some further growth of the skull. While in the case of a hydrocephalic skull of moderate degree the fontanelles are not enlarged nor the sutures widened since the rate of ossification is such that it can cover an area a third greater than that of a normal skull at birth.

The effects of differential rates of growth upon the structure and organization of the individual are profound. It serves to explain such paradoxes of development as why the parathyroid derived from the third or more cephalic of the pharyngeal pouches is inferior or caudal to that derived from the fourth or more caudal pouch. The transposition of the parathyroids is inevitable because the parathyroid III makes its appearance and differentiates earlier than the parathyroid IV in relationship to the growth of the rest of the neck. Minor changes in growth differentials and the timing of the appearance of organ “anlagen” or primordia are undoubtedly responsible for individual differences and variations in bodily structure and, if of slightly greater degree, may produce profound errors of development. This may be illustrated by the congenital anomalies either naturally caused or experimentally induced.

A fantastic and bizarre example of malformation from interference with timing of anlagen is seen in a rare case of penoscrotal transposition where the scrotum has come to lie anterior to the penis. As I showed some years ago (Saunders, et al., 1942) the scrotal elements arise bilaterally, independent of the phallus. Normally the phallus arises first from the genital tubercle and as it enlarges it carries forward a portion of the urogenital sinus to form a part of the future urethra. The scrotal elements appear later and at 15 mm. are seen as bilateral swellings cranial to the phallus. With further growth these swellings, due to differential growth, pass caudally relative to the phallus to occupy the traditional position for the scrotum. Delay in the development of the urogenital sinus leaves the scrotal elements in an anterior position to form a scrotum lying in front of the underdeveloped penis.

Modifications of, or a failure to express, the full potential of growth in proper relationship to other regions may not only affect the bodily proportions primarily concerned but may exercise in a purely secondary manner more distant regions of the body not basically related. This may be illustrated by examination of the genesis of cleft palate. It is usually thought
that cleft palate is due to a primary failure in the development and fusion of the palatal rudiments derived on either side from the maxilla. But this obvious explanation is far from the truth. Cleft palate is the result, not of defective formation of the palatal rudiments, but to a failure of the lower jaw to grow soon enough. This is revealed in studies in our laboratories by Monie and Nelson of anomalies produced experimentally in rat fetuses by transitory deficiencies of folic acid. Normally in both the rat and man, the tongue, which arises from the lower jaw, develops initially within a common naso-buccal cavity. In the interim the palatal rudiments appear and elongate downwards, pressed against the lateral walls, being unable to meet because of the presence of the tongue. The ensuing rapid growth and expansion of the arch of the lower jaw provides accommodation for the further growth of the tongue which now leaves the nasal cavity, releasing the palatal rudiments which, through their innate elasticity and turgor, spring upwards into relationship with one another and eventually, by fusing along their borders, roof the buccal cavity. Failure of the lower jaw to grow rapidly enough leaves the tongue in the nasal cavity, preventing the approximation of the palatal elements. When at length the jaw grows sufficiently to accommodate the tongue, the palatal rudiments on return find that the all-over growth of the rest of the face prevents the rudiments from coming into contact. The palatal elements, no longer subject to the stimulus of growth tension, remain stunted and short, and we have the characteristic and familiar deformity of cleft palate. Minor delays or slight decreases in the rate of growth of the mandible doubtless would lead to the formation of a highly vaulted arch. I am reminded that earlier students of the body constitution regarded a high palatal arch as a serious stigma of mental, moral and physical degeneration, which is illustrative of the weakness of the constitutional bridge over which many have attempted to pass in reaching for understanding of the individual.

Experimental teratogenesis is most revealing of the sort of factors responsible for individual variation and the failure of the individual to reach his full potential of physical development. The grosser degrees of this failure result in congenital anomalies; minor degrees, in the structural variation of the individual. Congenital defects may, of course, cause profound secondary upsets in body physiology which in turn may modify secondarily other parts. However, the distance between congenital defect and individual variation would seem to be only one of degree, and in any one organ the defects and variations, although elaborately and separately classified, are in fact connected to form a continuum of change or spectrum from the normal to variation, to the grossest of abnormal conditions.

The experimental embryologist has long been aware that certain toxic agents, especially those, such as the cyanides, radiation and Trypan blue, which interfere with the oxygen reduction potential of the tissues, will produce a variety of congenital malformations; the incidence of any particular anomaly being related to the period at which the agent is administered. To these we must add the remarkable clinical observations of Gregg in Australia, connecting cataract and congenital heart disease with maternal infection by the virus of rubella. Since then, observers have shown that injury to the fetus may be produced by the withdrawal of a
number of metabolites; vitamin A₁⁹ pantothenic acid,²⁰ riboflavin,²¹ folic acid,²² vitamin E,²¹ and vitamin B₁₂.²¹ It is important to recognize that teratogenic agents are non-specific. Almost all the varieties of malformation observed in man have been reproduced by these experimental means. Further, the maternal metabolic deficiency may be entirely transitory, of but two or three days, with little discernible effect on the mother, yet it will result in severe fetal anomalies which cannot be repaired by the restoration of the metabolite. The critical period for the embryo is short, probably between the second and the eighth week in the human subject, and between the eighth and fifteenth day in rats.

The cardio-vascular anomalies produced in the offspring of rats fed a diet deficient in folic acid (pteroylglutamic acid), studied in our laboratories by Baird et al. (1954)²² and Monie et al. (1957),²⁹ even though the deficiency was transient, ran the gamut of virtually all known types of abnormality. Among them have been observed defects of the ventricular and atrial septa, persistence of the truncus arteriosus, double or right-aortic arch, absence of the ductus arteriosus, aberrant subclavian arteries, variations in the arterial arch system, abnormalities of the pulmonary arteries and veins, persistence of the right-umbilical vein, and numerous others. As would be anticipated, deficiencies during the seventh to ninth day while the heart itself is undergoing rapid changes, showed a higher incidence of cardiac defects, whereas deficiencies during the ninth to tenth day were associated chiefly with anomalies of the vascular system.

We should not forget that in the physical development of the individual there is a dynamic relationship forming an endless circle between structure and function. This may again be illustrated by reference to the development of the heart and the genesis of such familiar cardio-vascular anomalies as over-riding of the aorta, transposition of the aorta, persistence of the truncus arteriosus, and the like. In discussing such anomalies, the evolutionist such as Spitzer²⁷ contends that they constitute a phylogenetic throwback to the heart of reptilia or the fishes, little mindful of the fantastic size of the camel which he asks us to swallow in striving for a gnat of explanation. Spitzer's view is so dominated by the outmoded doctrine of recapitulation that analogies are made which are often unwarrantable. J. E. Frazer²⁸ pointed this out many years ago in connection with the assumption that the pharyngeal pouches of man were the homologues of the gill clefts of fishes. In the case of the heart, Sir Arthur Keith introduced the conception of the bulbus cordis which, for reasons too lengthy to give here, probably has no equivalent in the human heart. By so doing he introduced much confusion in the understanding of cardiac development and the genesis of these common anomalies.

All who have examined the living fetus are aware that the heart in the earliest stages of formation commences its rythmical contraction to establish a primitive circulation. The first sign of its inner division into a right and left heart is the appearance of the ventral and dorsal endocardial cushions in the walls of the atrioventricular canal. Even prior to their fusion to separate the right from the left atrio-ventricular orifice, the cushions serve functionally to divide the blood stream into two. De Vries and I²⁹ have studied the fluid dynamics of such streams and have been able to show that, depending upon the angle of approach, the streams
will pass in spiral relationship with one another in a clockwise or counterclockwise direction. The period of the spiral will depend upon the force of the stream. There is little or no admixture of the two streams. Furthermore, in a restudy of the formation of the right ventricle we have been able to show that the development of the right heart is largely dependent upon the rapid elongation of that region hitherto called the bulbus cordis. In the normal heart the approach of the two streams is such as to result in the formation of a moving column of fluid which spirals counterclockwise as it enters the truncus arteriosus. In this way the right or pulmonary stream is directed into the sixth arch and the left or aortic stream into the fourth arch with little admixture of the two streams. The soft jelly-like endocardium can only extend into the neutral zone between the spiraling streams and by its condensation provide the spiral aortico-pulmonary septum which divides the future pulmonary artery from the aorta. Any failure of the right heart to elongate sufficiently rapidly will distort the angle of approach of the two streams, thus producing a clockwise spiral which leads to transposition. Other changes in the angle of approach of the streams will cause the column of blood to fuse, resulting in persistence of the truncus arteriosus or, depending on its degree, to various types of over-riding of the aorta. Dynamic factors associated with slight retardation in the development of the heart itself are capable of modifying the arrangement of the vessels themselves.

This is evidenced by a case of twins suffering from congenital cardiac lesions, both of whom came under the care of Dr. Ann Purdy of this city, to whom I am indebted for details. The first twin died at three months, exhibiting at autopsy (1) an interventricular septal defect of the pars membranacea; (2) a closed ductus arteriosus; (3) complete transposition of the great vessels; (4) normal atria and veins. The second of the twins succumbed at eighteen months and at autopsy the heart showed (1) an interventricular septal defect of the pars membranacea; (2) a huge patent ductus arteriosus; (3) a normal arrangement of the great vessels; (4) normal atria and veins. The importance of this case rests upon the fact that the twins were "identical," uniovular and homozygous, with but a single placenta, and therefore were of identical genetic constitution. Yet the vascular anomalies differed markedly and the only finding in common was an interventricular septal defect.

It is by no means presumptuous to assume that the identical twins were subjected in utero to the identical noxious factor acting at the identical chronological time and in the identical amount, which has resulted in greatly different anomalies from subtle differences in degree of embryonic injury and of timing. The vascular lesions themselves reflect slight differences in the dynamic factors which are not difficult to envisage. Among the subtle factors at work in creating these differences are those which determine the biological age of the individual as distinct from his chronological age. Anyone who has engaged in the mensuration of uniovular homozygous twins in the embryonic, fetal or post-fetal stage is aware of the differences between them. One member of the pair may exhibit features the equivalent of an eight-week embryo, whereas the other member, as judged by linear dimension and other criteria, may be only the
equivalent of a six- or seven-week embryo. These differences are due not only to the amount of placenta, and therefore of nutrition, which each member appropriates to itself, but also to the ratio of change occurring in various metabolic processes within the embryo or fetus itself and which may be designated generally as maturation. Sidereal or chronological time has reference to the movement of the sun, the moon and other astral bodies; biological time to internal metabolic processes. This is a concept of great practical importance for the understanding of developmental and growth processes. The principles have been employed with great effectiveness by Abbott and myself\textsuperscript{10} for such matters as the accurate prediction of the growth of the femur and tibia in lengthening or lengthening operations.

In its earlier history, the pursuit of the individual to obtain understanding of his nature and his being has written one of the most curious chapters in medicine and biology. It gave us the raft of pseudo-sciences, such as physiognomy, chiromancy, neomancy (divination by observation of the moles and warts on the body), phrenology and many others, which float in a sea of superstition, supernaturalism and charlatanism. William Lessa\textsuperscript{11} points out that these precursors of the science of human constitution, which he calls “somatomancy,” contained a germ of truth leading to the legitimate modern science of human constitution, or “biotypology,” as it is sometimes called. Unhappily, attempts to determine the morphogenotype of an individual, as by Sheldon's methods, are highly subjective, with few operational referents so that Washburn\textsuperscript{12} could caustically conclude that the “system has its roots in characterology, not science, and is ‘the new Phrenology in which the bumps of the buttocks take the place of the bumps of the skull’.” Be these critics as they may, the error would seem to rest with the too ready assumption that individual morphological variation necessarily reflects physiological and functional differences in the individual.

A study of development, individual variation and developmental defects, whether experimentally or naturally caused, makes us doubt that much insight into the physiological processes of the individual is to be gained by study of outward physical constitution. Nevertheless a study of the individual clearly differentiates between genetic factors determining individual characteristics, as distinct from factors of metabolism which enable the individual to achieve his individual physical potentiality. It may be said that the genes sketch the plan of the future individual in a light pencil drawing; the organizers, regulation and other factors of embryonic development ink in the blueprint; and nutritional and metabolic agents complete the building to a greater or less extent, depending upon external interruptions. Consequently we recognize that the overwhelming majority of congenital deformities are not genetically determined. The assumption that such deformities and variations seen in man are mutants is unproved and unwarranted: a fact which should be borne in mind in this period of hysteria over radioactive fallout. The extrapolation made in regard to the somatic effects of radiation depending upon statistics of congenital defect are most unreliable for the reason that the mechanisms are largely unknown and the almost universal failure to appreciate that most defects and
malformations in children are not mutations. Furthermore, with respect to congenital deformities, we should not adopt a position of therapeutic nihilism but recognize that preventive measures are a distinct possibility.

We are on the threshold of understanding biochemical and enzymatic factors. The existing evidence suggests a rich reward to those who would pursue this field as already shown by Beadle in his study on the biochemistry of the gene. Certain it is that we need to refine our parameters in applying chemical tests to the individual.

A more vigorous study of human individuality extending beyond the behavioristic and the psychological, to man's physiological and biochemical constitution is greatly needed and may lead, perhaps, to a newer, richer, Hippocratic medicine of the individual in the forthcoming age.

References will appear in author's reprints.