OLD AGE

ALDRED SCOTT WARTHIN

OLD AGE
THE MAJOR INVOLUTION

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OLD AGE
THE MAJOR INVOLUTION
THE PHYSIOLOGY & PATHOLOGY OF THE AGING PROCESS

BY

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WITH 29 ILLUSTRATIONS

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TO

DR. FRANCIS PEYTON ROUS

ONE-TIME ASSISTANT OF MINE AND EVER SINCE
A DEARLY BELOVED FRIEND

FOREWORD

ON October 1, 1928, the Wesley M. Carpenter Lecture of The New York Academy of Medicine was delivered by me under the title of "The Pathology of the Aging Process." This address was fortunate enough to arouse a good deal of discussion among those who heard it, and numerous requests for published copies were received. It was printed in *The Bulletin of The New York Academy of Medicine.*[1] A second printing followed in the *New York State Journal of Medicine*, November 15, 1928.[2] Since these printings an increasing number of requests has been received, asking that the author enlarge upon the subject matter of that lecture and publish it in the form of a monograph. The majority of these requests have centered about the author's conception of the unity of the involution-processes as essentially physiologic in nature, and that old age is to be considered as a normal major involution and not as a pathologic process.

[1] S. 2, 4: 1006–1046, 1928.
[2] 28: 1349–1361, 1928.

To his surprise a certain minority of his correspondents, while accepting the view put forward as rational and based upon scientific facts, expressed themselves as "having been depressed" by the philosophical conclusions inevitably deducible from such a viewpoint. Just the opposite result was in the writer's mind—the presentation of a rational workable philosophy of Old Age as an antidote to the modern futilities of life-extension of the individual to extreme limits and of possible rejuvenation. The human race has advanced several points in both knowledge and philosophy since the time of Ponce de Leon. Today the scientific mind may obtain satisfaction and happiness in the contemplation of the potentialities of the mortal individual in carrying-on and advancing the immortal potentiality of the germplasm. On such a foundation there may be built a satisfying working philosophy of life. The *Wesley M. Carpenter Lecture* forms the nucleus of this monograph. To this nucleus much new matter has been added, particularly in the discussion of Involution as a Physiologic Process and Function. The essential viewpoint of the lecture remains unchanged; all additions and alterations have been made for the purpose of clarifying or enhancing that concept and the inevitable philosophy to be drawn from it.

To the New York Academy of Medicine I express here my grateful thanks for its kind courtesy and permission to use in whole or in part my Carpenter Lecture in the preparation of this little monograph.

ALDRED SCOTT WARTHIN

ANN ARBOR, MICHIGAN
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INTRODUCTION—THE TRAGICOMEDY OF HUMAN LIFE

IN the very heyday of man's powers, in the full summer of his creative possibilities, and of his desires and ambitions, the life drama played by each human actor discloses, quite suddenly and unexpectedly, its true tragicomic motive. It is as if the player, himself, had been acting a part in a drama, the course and the end of which he did not fully comprehend. It had begun as a pleasant play of exciting incident, joyous adventure, vital desire and satisfaction, ambition and achievement. The actor has wantoned with his rôle to his own pleasure, and now, well past the middle of the second act, he is startled by a sharp hint from the prompter's box that his interpretation of his rôle must be changed into another key—one less pleasant, more difficult and unsatisfying. From now on to the end of the third act he must portray the picture of gradually flagging desire and failing powers, of disillusionment, fading pleasures and progressive fatigue, in other words the portrayal of senescence, until his rôle ends in ultimate death.

The title of this tragicomedy is "The Life of Man;" its three acts are: I, Evolution; II, Maturity; III, Involution. It is the story of a living, multicellular organism, a chemicophysical machine transforming, storing and releasing energy, capable of building-up and restoring its own substance, and repairing its wear-and-tear damage within certain bounds. But only for a limited period of time! As is the case with all energy-producing machines, the life of the individual human machine is not immortal, but has, perforce, from the very nature of its substance and construction, the complexity and intricate relationships of its manifold parts, and the peculiar

Fig. 1. The Beginning of the Play. The First Day of Life.

nature of the work it has to do, a limited period of active and useful existence. The individual machine wears out; but before wearing out it has the power of producing out of its own substance and energy store the materials for the creation of other machines of the same type. Although mortal as an individual organism, it secures a potential immortality for its own kind. It does this, however, at the price of its own self-destruction, for under normal conditions its ultimate duration of existence is determined by factors inherent within the machine itself.

It is a curious fact that the human mind has always shown a definite aversion to the acceptance of old age and death as natural physiologic processes. In the years of evolution and maturity the possibilities of the inevitable hour for each and every human being are suppressed, almost wholly, by the average human individual. Youth, and the mature before the peak of life is reached, live as if they were immortal, as if the span of life had no relatively short fixed limit, to which they, themselves, must inevitably yield. To the young, age and the aged appear foreign, almost as representing another race of beings of a lower value, to be pitied, tolerated, or ridiculed, as occasion offers. This is undoubtedly a normal psychologic state for the immature mind of the species at this stage of its evolution. We feel this so strongly that we look upon the serious contemplation of age and death by a young person as unnatural and psychopathic. Serious thoughts on age and death do not usually appear in the human consciousness until the peak of life is reached, and their appearance then may actually be an indication that the downhill path has been entered. Only in those who have progressed some distance along this path do we regard the discussion of age and its problems as natural and normal. But even in these, the middle-aged, in particular, we consider it bad taste to recognize the signs and phenomena of age. Serious discussions upon this phase of life are usually discouraged; they are not in good form. Instead of recognizing and treating old age as a normal process we set ourselves to its concealment and denial. Surely this is an abnormal defence reaction of the common brain, intrinsic and inherited from the psychologic experiences of our human ancestors. We fear both age and death; we do not like to talk sensibly and scientifically about them; we are depressed by the scientific view that they are physiologic processes, necessary and inevitable. We have no normal philosophy of life in which they are rationally considered and evaluated.

There is no positive knowledge available of the psychology of animals as far as age and death are concerned; but it is generally assumed that the animal mind lacks concepts of both facts. The minds of the earliest human ancestors must have been quite similar in this respect. What anthropologic knowledge we possess in regard to the status of old age among primitive tribes yields abundant evidence of a predominance of customs disposing prematurely of the aged as useless economic encumbrances. Only in a minority of primitive tribes has age in defence been able to maintain itself and survive on the ground of superior wisdom in the tribal council. Throughout biblical and classical times scattered voices were raised in defense of old age as a normal phase of the individual life, although the general spirit of those civilizations regarded it with disfavor. Aristotle wrote bitterly of old age;

Xenophon, Plato and Cicero spoke in its defence. The status of old age was undoubtedly better in the Roman civilization than in the Hellenistic. But during the Christian centuries the position of the aged individual in the population at large must have been an unhappy one, if we judge by the numerous preserved literary references of ridicule and caricature of the old. The concept of Death, kept constantly before the popular mind, not only by the Church, but through the almost continuous experiences of wars and plagues, served to develop in the human consciousness an abnormal psychology towards age and death, as shown by the great popularity of the innumerable "Dances of Death" created in art and literature from the fourteenth century on—even to the present day, under the stimulus of the War.

From the records of the development of human culture we can glean no satisfactory philosophy of life giving to old age its true position as a normal physiologic process. The average mind is still fettered by the racial inheritance of its prehistoric ancestors and the religious fears of the Middle Ages. The individual minds forging ahead in release from these fetters find themselves only imperfectly adjusting their philosophy of life to the scientific facts which reason has forced them to accept. With the passing of any positive conviction as to the immortality of the individual after this bodily existence, few minds have been able to emerge from the soul struggle created by the conflict between reason and inherited so-called religious instincts to a new philosophical contemplation of the Universe that gives them complete peace and happiness. If age and death are normal and inevitable, life so sweet, the day so short, then why not seize it for all of the physical gratification possible? And, strange to say, even science comes to the aid of this modern epicureanism. In place of the old legend of a fountain of perpetual youth-giving waters, there is now offered the conception of age and death as diseases, *pathologic* and not *physiologic*, that can be inhibited or even, perhaps, prevented. A physiologic and morphologic rejuvenescence of the individual in this life, the pushing ahead of the life limit to ages much advanced, or the abrogation of the unpleasant features of age are among the biologic conjectures and promises of the day.

These lie so close to man's heart's desire, that his judgment may be confused, and his perception of the basic facts of biology so clouded that he is made unhappy by any biologic philosophy of life which insists that age and death are evolutionary functions, necessary to the species, physiologic and inevitable, capable of alteration only through vast evolutionary periods. But why not a philosophy of life based upon the species and not wholly upon the individual!

THE NATURE OF THE HUMAN MACHINE

AS far as our knowledge of energy and matter leads us to conclusions, more or less hypothetical rather than demonstrable, life is a chemicophysical energy quantum, differing from inanimate matter in some specific atomic or intra-atomic arrangement or relationship; and manifesting itself in the material form of individual energy machines —the living, protoplasmic animal organism. For these machines there are two states or conditions possible, the *living* and the *dead*. By the *living machine* we mean the active animal organism transforming, storing and releasing energy. Inasmuch as this engine requires fuel, we have come to call it a combustion-machine which burns and transmutes inert materials into living protoplasm with the production of heat and vital energy. The manifestations of its work we style the vital functions—nutrition and metabolism, irritability, motility and reproduction. As long as these functions are maintained we say the machine is *alive*. Their cessation is *death*. The vital machines have also the power of self-repair and self-restoration within certain degrees. They possess further the ability of reproducing themselves from minute portions of their own bodies, but only through the cooperation of two separate types of the vital machine, the male and the female, through the union of sperm and ovum. Through this mechanism of sexual reproduction the continued existence of the human organisms upon the earth is maintained, for the individual machines are doomed to wear out and to disappear. It is as if only a certain amount of the energy quantum, life, were given to each machine, or as if each machine were charged with an energy potentiality sufficient to carry it along for a definitely limited period of time. The union of the sperm and ovum marks the *charge* of the individual energy machine; that energy charge is expended at a constantly diminishing rate through the period of growth and development until maturity is reached, and after this it declines still more rapidly until the machine finally comes to a standstill. This termination of the activities of the protoplasmic energy machine due to the loss of its intrinsic energy, independent of the action of extrinsic forces, is *normal* or *biologic death*, and the period of its activity, the *biologic life limit.*

What determines this energy limit? The essential goal of the individual life appears to our understanding to be only the perpetuation and evolution of the life of the species through the successive renewal of the energy charge by the union of sperm and ovum, in other words the preservation, maturation, transmission and modification of the germ plasm. When this is assured or accomplished the individual life machine has served its purpose. Its duration of existence is determined, therefore, by the conditions and factors necessary to accomplish racial preservation and progress. Important among the factors are the length of the period preceding puberty, the duration of the reproductive period, and the length of time required for the postnatal care of the progeny. All of these factors are inherent within the germ plasm of the race; and the duration of life for the individual of any given species is dependent upon such intrinsic factors. The normal duration of life is, therefore, intrinsic and inherited.

As to the ultimate chemicophysical nature of life we, of course, know nothing, and it is not necessarily probable that we ever shall. It is generally accepted in science that the explanation of the life quantum and its energy phenomena can be only a chemico-physical or a physical one, but all theorizing in this direction at the present time is but pure surmise. We do not know the time or manner of the origin of life, whether all the life of the present epoch came from one common unicellular ancestor or whether there have been multiple independent origins of life in different periods. The demonstration of the planetary electron theory of the atom has not brought us any nearer to an understanding of the nature of life than the conviction that the explanation must be sought in the pursuit of still deeper and more obscure physical laws. We have not even a theory beyond the bald chromosome one that throws any light upon the nature of the chemicophysical processes of heredity and the modification of the germ plasm. The chromosome facts are purely morphologic. Nevertheless, the facts of heredity are accepted, as are also the facts of the mortality of the individual life machine and the potential immortality of the germ plasm through its successive energy renewals in the fertilization process. No recharging of the somatic body is possible. The continuity of the life of the species is maintained only through the production of new energy machines with new energy charges, which will in their turn run down and leave the machines useless and to be discarded. In all of this succession of energy cycles the mind of man can see a broad purpose running, the mechanism of species evolution and adaptation to the changing environment of the earth. The individual machine is but a temporary, albeit necessary, incident in the life of the species, and the latter in its turn is also only an incident in the grand march of collective life through the eons. Whither that march is tending we do not know. This present river of life flowing through us may come to extinction in the cycles of still greater evolutionary processes requiring re-creations of entirely different energy-machines, or its progress may be constant and infinite. What difference does either alternative make to us? If we can see law, order and purpose in that infinitesimally small section of the life stream in which we find ourselves, there need be no concern as to a future we cannot understand. All that we need to worry about is the efficiency of our own energy machine—to see that it performs its work in the best way possible and to provide new machines with unimpaired energy charges to carry on.

THE BIOLOGIC PERIODS OF HUMAN LIFE

THE life of the human individual created by the union of the sperm and ovum represents a continuous progression from its beginning to its end, but passes through a number of well-defined periods. The first work of the energy machine is its full development, then follows its maintenance at its height of maturity until the energy loss brings about its decline and finally its end. The curve of life will show an ascending portion, the period of growth (*evolution*), its apex a relatively short plateau (*maturity*), and the descending curve the period of retrogression (*involution*). These three main divisions of the individual life fall into two periods, the relatively short *intrauterine* period of ten lunar months, and the much longer *extrauterine* period that may be extended through nine or ten decades, but usually only seven or less. The intrauterine period divides itself naturally into two sections, the *embryonic* and the *fetal*, the line of demarcation between the two being fixed by the completion of sex differentiation in the third month. The fetal period covers the remainder of the ten lunar months to birth. The three main divisions of extrauterine life, evolution, maturity and involution, fall naturally into nine subdivisions, as shown in the chart in Figure 2. The period of childhood, one to seven years inclusive, shows two very distinct divisions, that of the nursling and that of neutral infancy. The first of these represents the first year of life, the second the age period from two to seven years inclusive. The period of neutral infancy, however, consists in itself of two well-marked divisions in the normally developing child, the period two to four known as Turgor I and that from five to seven known as Proceritas I. The nursling period is the toothless age, that of neutral infancy is coincident with the milk teeth. The period of youth extends from eight to twenty-one years, and it also subdivides into two main periods, that of the preadolescent or bisexual stage, eight to fifteen years, and that of puberty sixteen to twenty-one years. In the preadolescent period there occur also two distinct phases, Turgor II, eight to ten years, and Proceritas II, eleven to fifteen years. The period of youth

	I	II	III	IV	V	VI	VII	VIII	IX
	1. Evolution							2 Involution	
Intra-uterine Life	1. Ascent					2. Peak		3. Descent	
	1. Childhood			2. Youth			3. Maturity		4. Age
	1. Child			2. Boy Girl		3. Youth Maiden	4. Adult Male Adult Female		5. Old Man Old Woman
	1. Infancy ♂ ♀			2. Boyhood Girlhood		3. Adolescence Virginity	4. Virility Maternity	5. Maturity Climacteric	6. Senescence
	1. Nursling	2. Neutral Infancy		3. Bisexual Infancy		4. Puberty	5. Full Sexual Power	6. Ripe Age	7. Retrogression
		Turgor I	Proceritas I	Turgor II	Proceritas II				
	Year 0–1	2–4	5–7	8–10	11–15	16–21	21–40	41–60	61–100
	Toothless	Milk Teeth		Permanent Teeth					Loss of Teeth
	1 Play Age			2 School Age			3. Work Age Sexual Age		4. Resting Age
	I	II	III	IV	V	VI	VII	VIII	IX

THE STAGES OF LIFE

FIG. 2. THE STAGES OF HUMAN LIFE. (*After Stratz.*)

is the period of development of the permanent teeth. The period of maturity, that of reproductive activity, extends from twenty-one to sixty years, and may also be subdivided into two divisions, that of full sexual power, twenty-one to forty years, and ripe age, forty-one to sixty years. The final period, that of senescence, extends from sixty-one to one hundred, or to the end of life. During this period the teeth are lost. The different periods of extrauterine life may also be characterized as the play age (one to seven), the school age (eight to twenty-one), the sexual and working age (twenty-one to sixty) and the age of chronic fatigue, the resting age (sixty-one to one hundred).

The nine periods of the extrauterine life, as given above, are clearly defined in the normal individual, but usually only seven, "*the seven ages of man*," according to Shakespeare, receive general recognition. Some writers, however, recognize as many as fifteen periods of life, but these classifications are somewhat artificial, in that they include evolution and involution subdivisions for each major division. Especially important as to recognition are the four subdivisions of childhood, Turgor I, Proceritas I, Turgor II, and Proceritas II. We have followed the German terminology for these subperiods of development in early life, inasmuch as they have no satisfactory equivalents in medical English. They have not been sufficiently recognized by American writers on pediatrics or on child development. Yet they constitute very distinct developmental phases, characterized by two periods of weight increase and retardation of height increase, alternating with two periods of relative inhibition of weight increase with acceleration of increase in height, in other words two plump and two slender periods. Height-weight curves constructed mathematically on averages do not indicate these four normal variation stages. Further, they vary in both time limits and degree, according to the hereditary constitution of the individual.

Nothing is more striking than the variations in the individual's "constitution" in the earlier biologic periods of life, and even up to the peak of maturity. The changes in all that constitutes the *personality*, the composite of morphological, humoral and psychical factors or qualities, may be so marked that the individual in successive periods may be so unlike his former states as to make recognition difficult. He may appear as if transformed into quite "another person." It is almost as if he *moulted* or shed his previous personality in the transition from one period to another. Particularly is this marked change likely to occur in the transition from the preadolescent period to that of puberty, and in that from puberty to maturity. The child apparent is not always the father of the resultant man. It is well to remember this possibility in the prediction of constitutional traits and qualities in the case of children and youths in these periods.

THE ascending curve of growth begins in intrauterine life from the moment of the first division of the fertilized ovum, and rises rapidly through two distinct periods, the embryonic and fetal. The energy of growth of the fertilized egg during the first month is greater than that of any other period in the life of the given individual. According to the developmental charts of Stratz (Figures 3 and 4), the growth of the embryo during the second month is relatively greater than that from the period of birth to maturity; in the third month its growth equals relatively that of the first six years of extrauterine life; in the fourth month growth is relatively as great as in the first three years after birth; and in the fifth month as great as in the first year of life. This extraordinary release of energy in the growth following fertilization results chiefly in the production of cell masses and their differentiation into the three germ layers. By the end of the first month the embryo has passed through the most essential stages of its prehuman development, by the end of the second month it has attained well-defined human form, and in its third month its sex can be clearly recognized. This closes the germinal or embryonic period, and fetal growth and differentiation now proceed with a remarkable slowing-up of growth energy. Not all organs and tissues grow at the same rate, and these differences determine bodily form and proportions.

After approximately two hundred and eighty days the period of intrauterine life is completed, and with birth the individual enters upon his extrauterine period of growth and development which leads essentially to increase in height and weight. During this time also the differences in rate of growth bring about still further changes in conformation and bodily proportions. Within the period of extrauterine evolution, which extends from birth to that of maturity or completed sexual ripeness, there occur also the development of the teeth, the conformation of the head and face, the ossification of the bones, primary and secondary sex development, and various changes in the viscera and soft tissues. As has been stated above, this period normally shows six well-defined subdivisions (Fig. 2) in which growth proceeds at varying rates and for different purposes of evolution: The period of the nursling's development, followed by the period of neutral infancy with its two cycles of stationary and accelerated growth, the first periods of turgor and proceritas; then the bisexual period of childhood with also two distinct phases of growth, the second periods of turgor and proceritas in the preadolescent age; and finally the period of adolescence. After birth the growth energy is strongest during the first year; during this time height is increased about 50 per cent, and weight about 200 per cent, as shown in Figure 3. This preponderance of weight increase over height increase gives to the first year of life the greatest fullness and rotundity of the body seen at any stage of life. In Figure 4 the normal height and weight curves for both sexes, according to Stratz, are shown up to the period of full development, twenty-eight years for the male, and twenty-four years for the female. It will be seen that boys attain half of their total height by the end of their third year, while girls attain the same at the end of their second year. Half of the total weight for boys is attained in the thirteenth year, by girls the same is attained

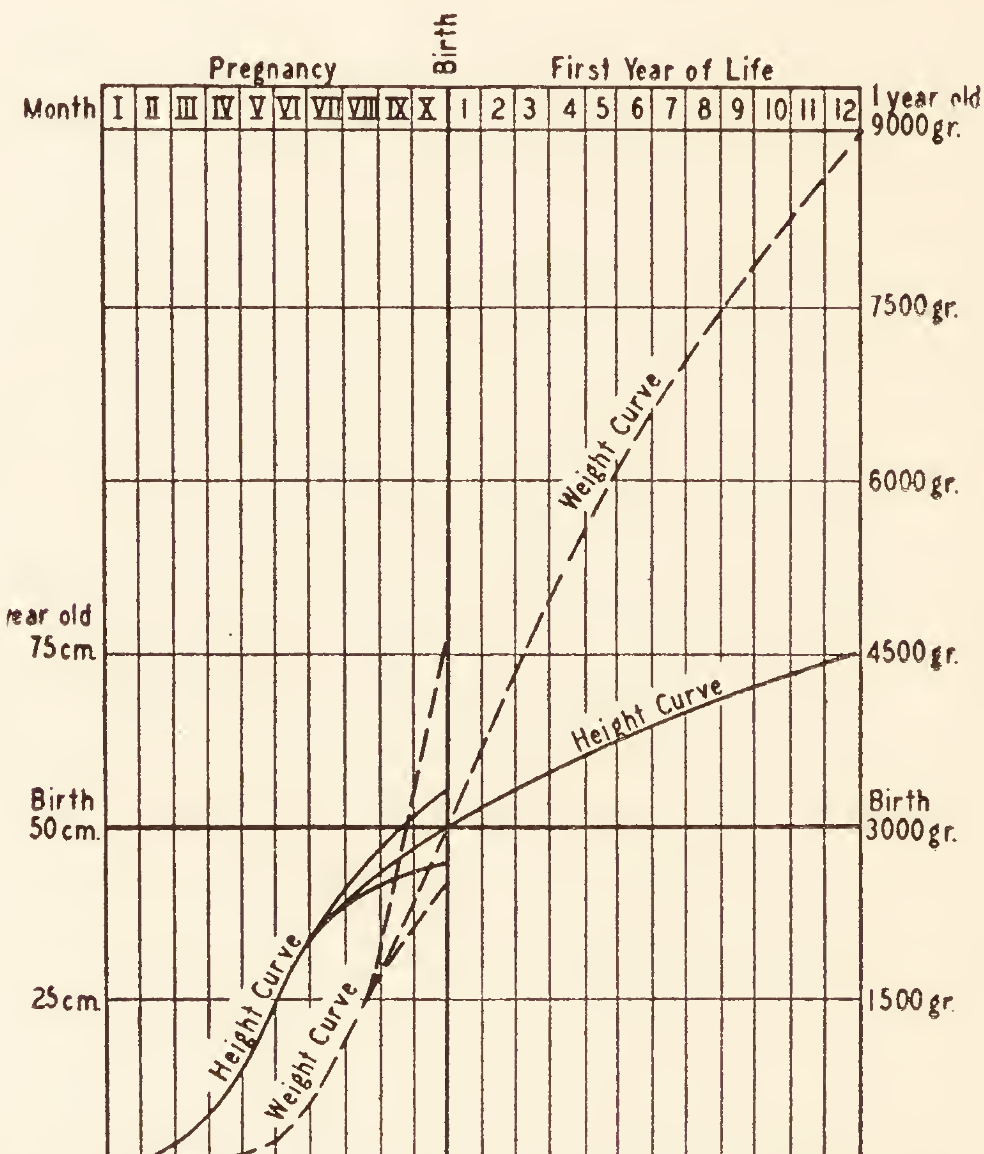


Fig. 3. Curves for Height and Weight in Fetal Life and the First Year of Extrauterine Life. (*After Stratz.*)

in the eleventh year. It is important to note that the extrauterine expenditure of growth energy does not progress uniformly, but in wave-like movements of retardation and

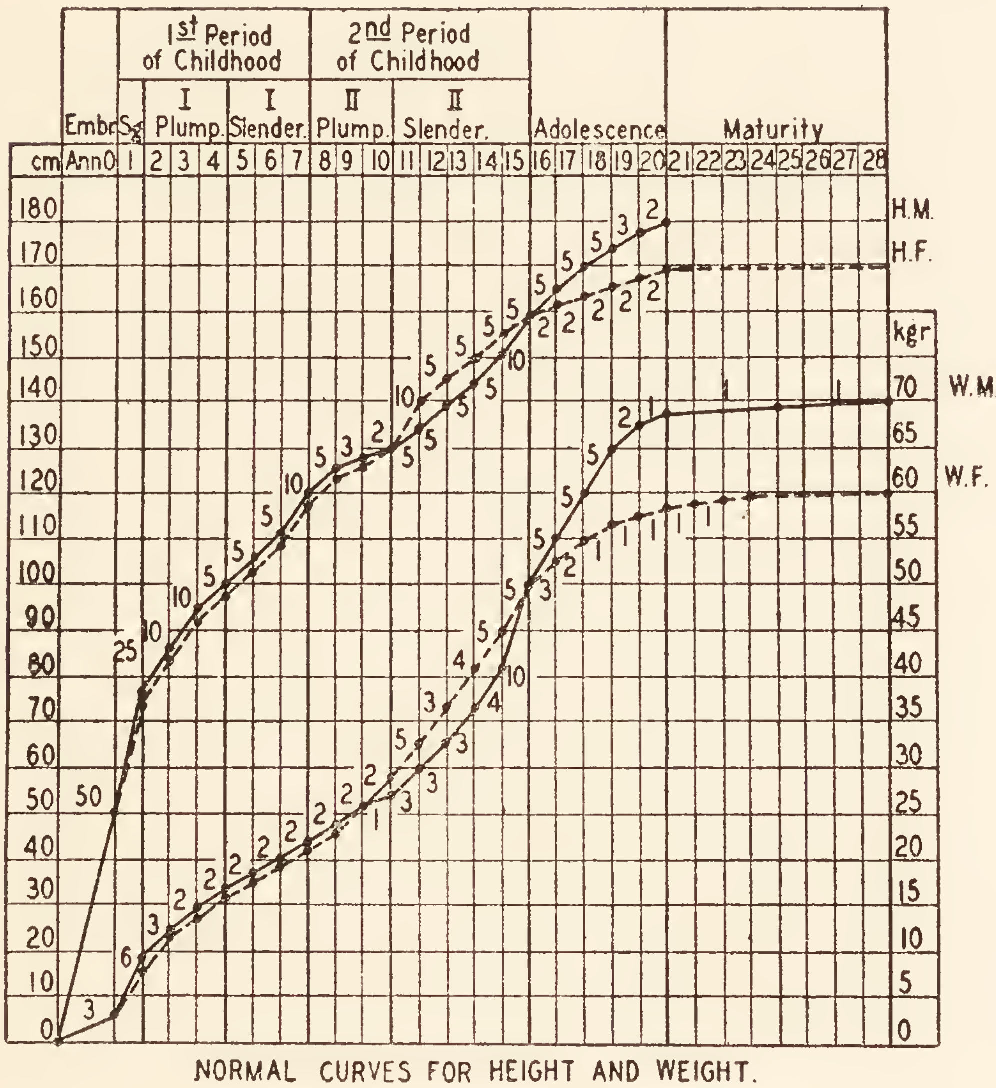


FIG. 4. NORMAL CURVES FOR HEIGHT AND WEIGHT.
(*After Stratz.*)

acceleration that may be roughly indicated as the two to four, five to seven, eight to ten and eleven to fifteen year periods, constituting the first and second cycles of turgor and proceritas. From the sixteenth to the twentieth year the curves of growth for the boy become steeper, those for the girl gradually flatter. Both sexes become larger, fuller, and more powerful as the sexual development approaches its completion. The general character of the personality approaches that of the fully developed male and female, and the psychology of both sexes centers about sex mating. Complete maturity of growth as evidenced by the flattening of the height-weight curves is usually attained by the male at twenty-eight years of age, and by the female at twenty-four years; at these ages the *plateau of maturity* or *ripeness* is reached, and the vital energies of the organism are directed toward the business of *reproduction.* All of the energy production and expenditure from the fertilization of the ovum, through embryonic and fetal life, birth and the six periods of extrauterine life have been apparently chiefly, or solely, for the attainment of one end, that the species shall not perish from the earth, but shall be renewed —with evolutionary modifications, we must surmise, or the whole process would seem to be without reason.

We have taken the height-weight curves as the most striking and important indices of the period of evolution. Similar curves could be plotted for the growth of the individual organs and tissues. In each of the eight periods of growth that we recognize as constituting the whole period of evolution, there are constant changes in body and organ proportions taking place due to the unequal growth of the different organs and tissues. As a general rule the organs that show the greatest degree of growth in extra-uterine life are those that were the least developed at birth. During the period of evolution the vital energy for growth is so strong that it exceeds that of the functional. This is the period in which regenerative and reparative processes proceed with greatest vigor. Compensatory hypertrophic and hyperplastic growths likewise show their greatest capacity during the period of development up to maturity, and plastic surgery and transplantation of tissues are most successful in this stage. At maturity growth energy and functional energy gradually become so balanced that cell destruction and cell growth are so equalized that repair is possible without loss of tissue elements and consequent atrophy. The curves of the different vital functions show

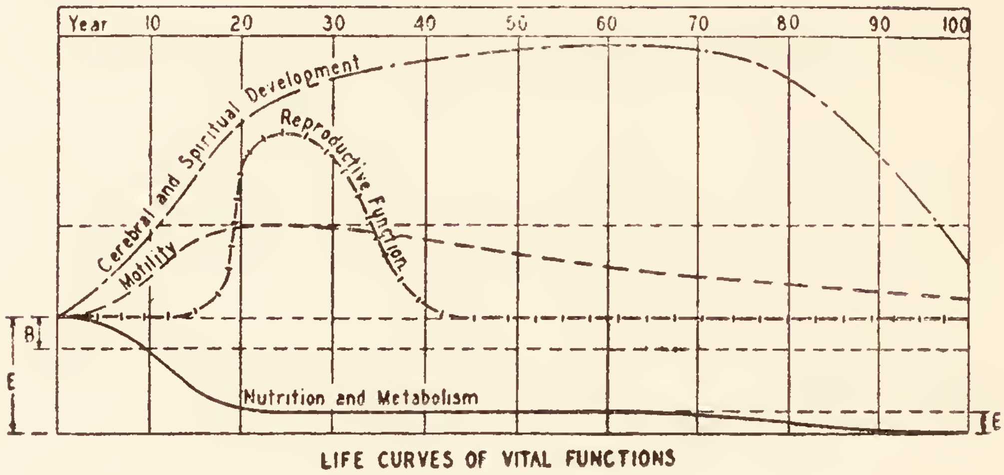


FIG. 5. LIFE CURVES OF VITAL FUNCTIONS.
(*Based in part upon Stratz. Author's modification.*)

great variations in their ascent during the period of evolution. In Figure 5 the curves of functional development are shown for the different decades of life. From birth the curve of *nutrition and metabolism* falls relatively as the organism attains its development, until about the twentieth year when it reaches a plateau which is continued until old age (involution) is established, when it falls again to the end of life. The curve of *motility* ascends proportionately to that of growth until the period of maturity, reaching its height in the third decade, and falling gradually after this to the end of life. The curve of *reproduction* (as measured by fertility) remains neutral until the sharp rise at puberty and begins to fall at about thirty, declining more rapidly during the following decades than the functions of motility and nutrition. On the other hand, the curve of the *cerebral and psychical function* ascends sharply, closely paralleling the curve of growth, but continues to ascend after the period of maturity is reached, even into old age, beginning to fall at about the middle of the seventh decade. It is the only vital function that shows persistent evolution after the peak of maturity has been reached.

There are, of course, great individual variations, within the limits of normal, throughout the entire period of evolution. The energy of growth and function is not maintained or expended in the same degree, or in the same time periods, in any two individuals. Differences may exist between individuals as great as between the two sexes. Consequently there are retardations and accelerations of the growth processes, and in consequence, of the functions also, which lead to great variations in the human individual by the time he has completed his period of growth. These variations are in part, if not largely, due to the fact that the energy machine of the human multicellular organism is really a complex of a number of smaller energy machines, each one of which may show variations in morphological and functional development. Inasmuch as some of these individual or specialized machine parts play an especial function in stimulating or inhibiting developmental processes at different stages, it can be readily understood how acceleration or retardation, excess or deficiency, or lack of correlation in growth processes may result from the hyperfunction, hypofunction or dysfunction of these minor specialized parts. Particularly is this true of those glands, the endocrine, that are especially concerned with the growth and development of the organism. These variations of growth and of function constitute one of the chief causes of the normal variations in *individuality*, or the *constitution.* In excessive degree, outside of the limits of normal individual variation, they produce *pathologic variations in the constitution.*

During the period of growth, as has already been indicated, variations in the character or constitution of the individual may occur during or after any one of the minor subdivisions of the evolutionary period. The *collective individuality* cannot be fixed during the period of growth; indeed, in its earliest stages the final outcome of any given developing human organism cannot even be predicted. Inherited variations or defects in the machine, or the action of the environment, may bring the process of development to an untimely end (*pathologic death*) or the natural course of development may be so altered as to result in extreme or pathologic aberrations.

In the earliest stages of embryonic development the individual human being passes through significant and revealing prehuman phases of morphologic evolution. Relatively quickly the mass of increasing cells becomes stamped with the human form, and shortly after this the individual's sex is fixed. After birth the human infant passes its first months of life in a more or less vegetative state, then through a purely animal period, followed by successive stages of mentality imitating in many ways the cerebral phenomena of primitive races. Then follows the rapid ascending curve of mental development, through the play and primary school period of childhood and the preadolescent stage, to the more serious preparatory and early working period of the age of puberty. Although each transition from one period of growth to another has been marked with certain difficulties or even dangers, the puberty period is the most difficult of all and presents the greatest dangers to the successful development of the individual personality of any of life's different stages. Of the greatest importance at this period is the psychical development and adjustment necessary to meet successfully the growing importunities of the rapidly developing sexual function. The difficult situation is aided, however, and not made worse, as some believe, by the coincident need of a successful establishment of the maturing youth in the practical business of creating a position for himself and the making of a living. This practical necessity is, however, only a necessary correlating factor in the fulfillment of the reproductive function in its broader significance—the founding of the home and the creation of the family.

THE PERIOD OF MATURITY

WITH the attainment of sexual maturity the peak of life is reached somewhere in the level plateau of the curve of life between the thirtieth and fiftieth years. These boundaries are far from being fixed; the individual variations are great, and it is no more possible to say in what year the peak is reached than to determine the exact boundary between evolution and maturity, or between maturity and regression. There is too much complicated interlocking of the vital processes, and the body machine is made up of other smaller machines that vary in their periods of evolution and maturity, so that full maturity is dependent upon the normal coordination of their functions. There is, therefore, a very wide degree of variation possible for the development of any one given individual, and to no two human beings does maturity come just in the same manner and in the same quality, or even in the same quantity, we may well believe. We may say that the peak is that point in the life curve at which the vital energies make use of the fuel taken in to run and repair the machine without adding to its substance. Growth is reduced to the minimum of necessary tissue restoration while tissue increase slows gradually until it ceases. Nevertheless, for a limited period after the attainment of reproductive maturity some growth does take place exceeding the repair of loss of substance. According to some authorities the limit of height may not be reached until the thirty-fifth to fortieth year, and there is usually an increase in weight for both sexes during this period, largely due to an increase in the storage of fat, and resulting chiefly from the disproportion between the fuel intake and fuel consumption. To what extent this increase in adipose tissue is physiologic or due to the environment of modern civilization cannot be positively determined. There is also a very definite relationship between the establishment of fixed sexual habits in the male and an increase in the amount of his panniculi. Likewise, in the female, oscillations in the panniculus amount occur with certain phases of the reproductive cycle, as in the latter months of pregnancy, and during lactation. The transformation from the slender figures of early adult life to the fuller and more rounded forms of maturity in both male and female, particularly in the case of the latter, has always been recognized in human art and literature as constituting normal and beautiful phases of the body. Human taste and feeling, however, make certain distinctions in the two sexes as far as these changes in human size and conformation during the period of maturity are concerned. The increase in size and weight of the virile male should be in the direction of muscular development, that of the young matron in more rounded forms of body conformations.

During the first half of the period of maturity (twenty-eight to forty-five) there is a very definite increase in the size of some of the internal organs, the heart, lungs, liver, kidneys, spleen, etc., although in varying degrees. These are quantitative enlargements rather than numerical. The individual cells of these organs are larger than in the period of evolution; the manifold activities of the body during the active reproductive period make full functional demands upon every organ and tissue, and this height of functional activity is coincident with the height of morphological development. If the heart muscle of the normal active male of thirty-five to forty years be compared with that of the young adult approaching thirty years of age, the individual fibers of the former appear to be almost hypertrophic. Indeed, in apparently normal males it becomes difficult often to decide between normal development and overdevelopment bordering upon the pathologic. According to some authorities the brain increases in weight until after the fortieth year, due to the increasing myelinization of the nerve fibers. Progressive ossification also goes on throughout this period; its significance may be that of involution rather than of growth. Practically, therefore, maturity has been fully attained when an equilibrium is established between the intake and the replacement of tissue loss through wear and tear processes without the formation of additional tissue. This stage is not a sharp peak in the life curve; it is a softly rounded, almost unrecognizable, elevation on the plateau of maturity, falling usually somewhere in the period from the thirty-fifth to the fiftieth year, occurring somewhat earlier for the female than for the male. On the side of the ascending curve of growth the period of maturity is interlocked insensibly with progressive growth curves of individual organs and with normal involutionary processes of the developmental period; on the descent side of the curve there is a similar interlocking of mature processes with those of a retrogressive involutionary nature. Growth, maturity and involution are coincident processes, bound together into a coordinated whole.

The period of maturity is preeminently the period of reproductive activity. Both sexes have completed their primary and secondary sexual development, and are now prepared for the consummation of their greatest function, the propagation of their race. In their completed development the individuals of the two sexes show marked biologic differences, almost as great as those existing between different animal species. Aside from the essential differences in the morphology and function of the sex organs the human male and female organisms present differences in development, morphology and function involving practically all of the tissues and organs of the body. The male, "the stronger sex," is characterized by the greater, stronger and heavier development of the height, weight, muscles, bones, lungs and heart, the development of beard and the "Adam's apple," the deeper voice, the heavier growth of body hair, and the greater development of the functions of cerebral activity and motility. The male's consumption of oxygen is greater, although his respiratory rate is less than that of the female; his heart is larger and his blood mass greater, but his cardiac rate nearly ten strokes per minute slower than in the female, and his average body temperature is slightly lower than hers. His movements are slower but with a longer excursion than those of the female; his actions are expressive of a greater degree of power, hers of a more marked degree of quickness, lightness and grace. The sexual life of the mature female is marked by its periodicity; in the male the cycles of sexual activity are so short that in the first half of the period of maturity they occur almost daily in the normal active individual, and hence give little or no impression of periodicity. In the riper latter half of the period of maturity the sexual

Fig. 8. Young Adult of Twenty-eight Years.
Full Maturity.

cycles of the male manifest themselves more distinctly in two to four day periods. There is a great individual variation in this respect; in many men these short sexual cycles are well-defined; other men claim that their sexual life shows no periodic phenomena.

All of the morphologic and functional differences between the fully developed male and female are purely the expression of the different rôles each one must play in the all-important business of reproduction. All of the vital energies of this period of bodily maturity urge them relentlessly to this consummation—the male to his activities of securing a mate, her impregnation and the protection of his sex partner and of their progeny; the female to her more strenuous sexual functions of ovulation and menstruation, pregnancy, birth, lactation, and the maternal care of the offspring. She exercises a twofold function in the fullest development of her sexual life, that of complementary sex partner and that of mother. The sex function of the normal male is also much broader than the single chemicophysical rôle he plays in the mechanism of reproduction. He can only impregnate; the female only can become impregnated, develop and bear the child, and nurse it. The more important aspects of his part in the function of reproduction are in the providing for and protecting of the mother and her children. From the fighting hunter of the cave-man period there has evolved the laborer, business and professional man of today who still must fight for his own place in the sun and for his mate and their children. The exigencies of this evolution have brought about a greater development of the cerebral functions in the case of the male than in the female. He fights now for the existence of his family chiefly with his brains. The period of sexual activity is, therefore, for the male the creative and productive age. The success of his life, his career in business or profession and his fullest mental and spiritual development are more closely related to and dependent upon his conduct and management of his reproductive period than upon any other period of his life. And upon the collective sex life of the individuals of the species rests the future of its existence—evolution or retrogression, in the latter case eventually extinction.

For the production of progeny undoubtedly the fourth decade of life brings the best

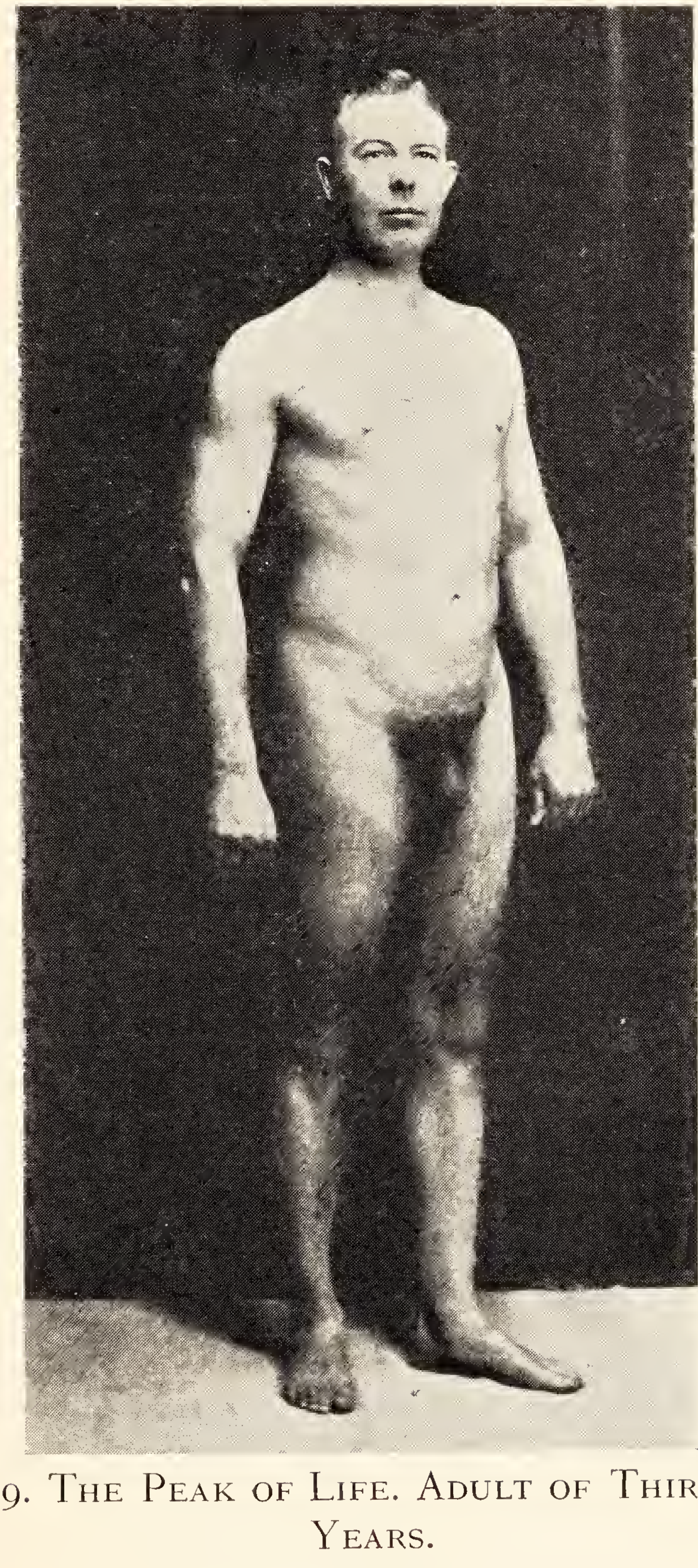


Fig. 9. The Peak of Life. Adult of Thirty-five Years.

results. Ideal ages for marriage are twenty-eight to thirty in the male, and twenty-six to twenty-eight in the female. In these years physical development is completed, the energy processes are in a stage of normal equilibrium, and the cerebral functions are sufficiently evolved as to secure a high degree of intelligence and moral character and ideals in the prospective parents of the next generation. Further, children born between thirty and forty years of parent age have a better chance of receiving the sufficient amount of paternal care before the parents themselves pass out of the active creative years of their maturity. If measured by fertility alone, the high point of life in America falls somewhere between the twenty-fifth and thirty-seventh years. The production of progeny alone, however, cannot be taken as the index of the highest point of life efficiency and achievement, because of the fact that the long postnatal period of care necessary in the present epoch for the preservation, education and evolution of human progeny not only has determined a later marriage age, but has led to the concentration of births in the early part of the fourth decade and the latter part of the third. As far as the human individual himself is concerned it seems more reasonable to assume that normally the peak of life extends into the fifth decade. With the birth and growth of children the mental and spiritual development of the parents rises progressively to a higher level. The parents renew themselves in the contact with their children, and constantly receive fresh stimuli from them. The educational period of the progeny should be a period of re-education and revivification for the parents; and as their children pass through the critical periods of adolescence and early adult life, the close social relationship between parents and children in the family life of the ideal home constitutes the chief factor in the safeguarding of the destinies of the race. The efficient sex partners and parents are those who actually "live for their children" in the best sense of that somewhat abused phrase.

PHYSIOLOGIC INVOLUTION AND THE MINOR INVOLUTIONS OF THE DEVELOPMENTAL PERIOD

DURING the developmental period, which has already been sketched, broadly rather than in full detail, the human organism passes through well-defined stages of a unicellular animal, a metazoan invertebrate, and a vertebrate animal, and finally reaches the height of its evolutionary progression as a mammal, in morphology and function similar to other mammalian animals. Various portions of man's organic structure pass through temporary stages typical of fully completed development in other vertebrates, in order to achieve at last the so-called human form divine. In general, his development parallels that of the other mammals, particularly that of the anthropoid apes; and, indeed, at birth he presents certain ape-like characters which disappear in the early postnatal evolution. His close blood relationship to the apes persists, however, throughout the whole period of his individual existence, as shown by the common susceptibility possessed by the apes and man to certain diseases and their common specific blood reactions. These similarities in the energy machines of man and the higher apes can mean only a common ancestral development, and the scientific human mind has so interpreted them. Geologic and paleontologic evidence supports this philosophy of the ascent of man, through untold ages of time, from the "inorganic world," up through the most primitive forms of life, through protozoan, invertebrate, and fish forms, then amphibian or reptilian forms, to the higher ape forms and finally culminating in man as he exists today, an animal superior in his energy quantum both quantitatively and qualitatively, but from the same common ancestral tree of all life, a descent and relationship in which he should feel only pride—the pride of the victor who has fought a glorious battle, and won, against great odds.

The development of the human individual is, therefore, not a simple process of cell increase and cell differentiation. *Progressive growth* is not the only mechanism of development by which each human individual achieves its ultimate creation. The organism rises on tiers and stages of its own substance and of its own formation; temporary scaffoldings and supporting structures, temporary energy machines and energy distribution contrivances, etc., are created at certain stages of development, play their rôles of temporary functional use, and then are transformed by rebuilding, or are cast aside as useless, having served their purpose. *Involution* is as necessary as *growth* in the complete building plan of the animal organism. But is the mystery of protoplasmic involution any more astounding than that of progressive growth and differentiation? Indeed, in the economy of the human energy machine the two processes have been coexistent from the time of the fertilization of the ovum and the beginning of its cell division. Throughout the whole period of development, both intrauterine and postnatal, the retrogression or involution of certain temporary organs and structures has been taking place; these serve their purpose of usefulness for a given period, and when no longer needed they are gotten out of the way. *Service* is, after all, the economic keynote of the organic development of the individual body, as it is of the broader progressive development of the species as a whole. In the former case any structure or organ of temporary function disappears when that function is no longer necessary; in the latter the individual himself comes to a similar end when he has lost his functional capacity. Throughout the whole period of growth up to maturity the progress of the individual life consists of an interlocking of *growth processes* and *involution processes*, all of which are necessary to complete development.

The most important of the *minor involutions* of the developmental period are shown in Figure 10. In the maturation of the ovum three potential ova, the three polar bodies, are non-functional and degenerate; they are sacrificed in order that the fourth one, the functional ovum with half the number of chromosomes characteristic of the species may have the requisite amount of nutritive material and cytoplasm for successful development, should fertilization occur. In the process of spermatogenesis the same reduction of the chromosomes results ultimately in the production of four potentially functional spermatozoa. The human mind is impressed by what seems to its judgment the wasteful extravagance of sperm-cell production and output by the mature human male. Out of the countless millions of spermatozoa produced during the period of maturity only a very few can possibly attain a functional realization in the fertilizing of an ovum. Of the many sperm cells reaching the ovum, only one penetrates it and becomes imbedded in its cytoplasm. There follows thereupon the involution and disappearance of its specialized locomotive organ, its tail. Having fulfilled its function of getting or assisting the spermatozoon to arrive at its destination, the tail is now functionless and useless, and passes out of existence absorbed by the cytoplasm of the ovum. In the completion of the mechanism of fertilization the female pronucleus loses its archoplasm sphere and centrosome after the completion of maturation, these structures disappearing into the cytoplasm to be replaced by a new archoplasm sphere and centrosome derived from the midpiece of the spermatozoon. When the two pronuclei, male and female, come into contact, the archoplasm sphere and centrosome derived from the sperm cell divide, and with the migration of the two so formed to opposite

THE MINOR INVOLUTIONS OF DEVELOPMENT.

Germinal	Loss of half of chromatin content.
Conceptional	Tail of Spermatozoon. Polar bodies of ovum.
Embryonic	Gill slits. Thyreoglossal duct. Postbranchial bodies. Branchial vessels. Craniopharyngeal duct. Notochord. Wolffian body and duct. Pronephros. Müllerian duct. Omphalomesenteric duct. Postanal duct. Tail. Supernumerary mammary anlage.
Fetal	Organ of Jacobson. Zuckerkandl organs. Tunica vasculosa lentis. Plica semilunaris. Chorionic vessels. Chorionic villi. Lanugo.
At Birth	Amnion and Placenta. Umbilical cord. Foramen ovale.
Following Birth	Umbilical vessels. Urachus. Ductus arteriosus. Lanugo.
Childhood	Sucking disk. Milk teeth. Absorbent organ. Interscapular hemolymph nodes.
Puberty and Early Adult Life	Thymus. Tonsils.
Functional	Involutions of Uterus, Breasts, etc.

FIG. 10. THE MINOR INVOLUTIONS OF DEVELOPMENT.

poles, the phases of mitotic cell division are begun, terminating ultimately in the formation of two cells with chromosomes restored to the normal number—the *new human individual* with its *new energy charge.* Thus the very beginnings of the individual life are dependent upon both progressive and retrogressive processes—*evolution and involution.* It would be perfectly reasonable to say that the three polar bodies, the female centrosome and the sperm tail fulfill their lives and *die. Death and life are inseparably connected from the very beginnings of the multicellular organism.*

In the great explosion of growth energy which now follows the first division of the compound male-female nucleus, in the development of the cell masses constituting the embryo and their differentiation into embryonic organs and tissues, the developmental rôle played by involution is more strikingly shown. Among these developmental involutions may be mentioned in the first place that of the *branchial clefts,* or gill slits, which are of great morphologic importance in the development of the human embryo, inasmuch as they determine largely the conformation and arrangement of various organs and structures of the head region. In the human embryo there are developed four branchial grooves and five branchial arches on each side of the body; they represent the respiratory gill arches and clefts of fishes. Under normal conditions in man these branchial grooves are closed by a thin membrane and are not open. They appear at an early stage of development, persist for a time, and then either disappear, or are transformed to serve some entirely different function than the respiratory rôle they play in fishes. Certain structures associated with the development of the branchial arches and grooves, as the branchial vessels and the postbranchial bodies, likewise are transitory in their existence. The transition from the invertebrate stage of the embryo to that of the vertebrate is marked by the development of the primitive longitudinal axis, the notochord. This likewise is but a temporary structure, only rudiments of which persist in the adult human body, being almost completely replaced by the vertebral column. Early in its development the human embryo presents a pointed projection of the vertebral column in the form of a tail; but later this is gradually incorporated within the body to become the coccyx. In early embryonic life two rows of mammary glands begin to develop, but of these rudimentary structures only two mammae persist, the others disappearing in the majority of individuals. It is outside of the field of our discussion to consider in detail the numerous examples of developmental involution occurring in the intrauterine life of human beings as this would mean a survey of practically the whole field of embryology. We may mention further only such temporary structures as the yolk sac and stalk, the thyreoglossal duct, the craniopharyngeal duct, the Wolffian body and duct, the Müllerian duct, the pronephros, the omphalomesenteric duct, the postanal duct, the organ of Jacobson, the Zuckerkandl organ, the tunica vasculosa lentis, plica semilunaris, the greater part of the lanugo, and others, all of which appear at certain stages of development, persist for a while, and then disappear, either wholly or in part, during normal developmental progress. Largely through the medium of these involutionary processes the human embryo recapitulates the evolutionary history of the species in its passage through lower invertebrate and vertebrate forms.

Especially remarkable is the life history of the placenta, the intermediate permeable nutrient organ interposed between the maternal and fetal circulations. At the time of birth it is a senile structure repeating in detail the essential pathologic tissue changes that later are to appear in the major involution of the mature organism: sclerosis of arteries with obliteration, fibrosis of stroma, atrophy and degeneration of the chorionic epithelium, thrombosis, infarction of villi, calcification, etc. All of the involutionary tissue changes of old age appear in this important vascular organ at the completion of the period of intrauterine life. In the fulfillment of its function the placenta passes through well-defined stages of evolution, maturity and senescence, and when its work is over it is discarded as useless and disappears from the scene of the individual life. Prophetic of the future fate of the organism as a whole!

Birth, with its change from the fetal type of circulation, is responsible for another group of involutionary changes in addition to the immediate discarding of placenta, amnion and umbilical cord. Portions of the old mechanism of the fetal circulation are now useless and must be disposed of. Coincidently with the first expansion of the lungs at birth the foramen ovale normally closes, later the ductus arteriosus, and the umbilical vessels in part become obliterated. During the development of the vascular system there were many venous and arterial branches which had a temporary function; these later degenerated, or were obliterated, or transformed into some other vessel. It is in the manner of obliteration or disappearance of these temporary blood vessels that we are especially interested, inasmuch as these vascular involutions are prophetic of the later arteriosclerotic changes that have been regarded as peculiarly characteristic of old age and have been considered of great etiologic importance in some of the theories of senescence. In the majority, or in all of the vascular involutions of the developmental period, the exciting cause of these premature senescent changes appears to be a *loss of usefulness*—a *reduced function* and not *overwork*. With the collapse of the vessel lumen, there occurs a thickening of the intima, a slight productive process with fibrosis, myxomatous or hyaline change, obliteration of the lumen, contraction of the vessel into a fibrous cord, with eventually atrophy of the muscle cells of the vessel wall. Lipoidosis (atheroma) also occurs in the involutionary obliteration of these primitive vessels. By the time puberty has been reached many of them have wholly disappeared, or persist only as fibrous cords. Particularly instructive are those vascular changes in the case of the ductus arteriosus and the hypogastric arteries. The point we wish to emphasize is that these early vascular changes are identical in kind with those of the arteriosclerosis of later life, but that they are associated with *disuse* and not with *overuse*. They cannot be explained on the basis of a *wear-and-tear* or *toxic* etiology. Their etiology is to be sought rather in the fulfillment of function. The obliteration and disappearance of the urachus is brought about by essentially the same factors of collapse, proliferation, fibrosis and contraction shown in the vascular involutions.

While the developmental involutions occur in greatest number in embryonic and fetal life, and immediately after birth, they continue to take place throughout the entire period of extrauterine development. We may mention the remaining portion of the lanugo, the "sucking disc" of the nursling's cheek, the interscapular hemolymph nodes (the so-called hibernating gland), the thymus, tonsils, milk-teeth, absorbent organ, etc.—all of these organs and structures for which the reason for disappearance can be seen only in a fulfillment of temporary function. Especially striking is the involution of the thymus which shows its maximum development at birth, or within the first two years of life, then gradually diminishes in size in the normal individual up to the age of puberty or early adult life, when it becomes reduced to small islets of lymphoid tissue still containing characteristic Hassall's corpuscles. The involution process here is essentially that of atrophy of the thymic parenchyma, obliteration and sclerosis of the blood vessels, fibrosis and eventually fatty infiltration of the stroma. We do not know the function of this organ, but its height of functional activity most probably coincides with its period of maximum development, and as the need for its function declines its involution proceeds.

Throughout the whole period of prepuberty development of the human female there occurs a cystic degeneration of Graafian follicles in the ovary. Whether this is functional or periodic we do not know, but such cystic follicles are practically always present in the ovaries of female infants and children, even in the case of the newborn. With the disappearance of the follicle involutionary changes take place in the vessels supplying that follicle. When puberty is established and periodic ovulation begun, the functional involution that follows the ripening and rupture of each follicle constitutes one of the most remarkable of the physiologic retrogressive cycles seen in the body. Following the discharge of the ovum the blood clot filling the follicle is replaced by the *corpus luteum;* this in turn undergoes involution after a definite period, and is replaced by a characteristic mass of hyaline connective tissue, the *corpus fibrosum,* which gradually contracts into a smaller and denser hyaline mass. In the rich vascular supply of the individual follicles there occurs a striking involution change in the form of collapse, productive thickening of the vessel walls, eventually marked sclerosis, with complete, or nearly so, obliteration. These involution changes in the ovary continue throughout the period of reproductive maturity until the functional activity of the organ ceases at the menopause. At that time the ovary is as distinctly a senile organ as was the placenta at full term. It is much reduced in size, except for cyst formation, irregularly scarred on its surface, and fibroid in consistency. Microscopically it consists chiefly of sclerotic blood vessels and the remains of corpora fibrosa, with here and there a cystic follicle. The cicatricial contraction produced by the hyaline corpora fibrosa developing after each ovulation must undoubtedly affect the vitality of undeveloped follicles, and thus secondarily lead to their degeneration. In these involutionary processes occurring in the human ovary before the middle of the individual life limit has been attained we see again the *essential processes of organ senescence.*

During the period of active reproductive life there occur also the remarkable functional involutions in the breast and uterus following lactation and pregnancy respectively. That in the breast consists essentially in an atrophy of the markedly hyperplastic acini that have been developed in the functional activity of the gland. With the cessation of function the great mass of glandular tissue becomes gradually smaller, chiefly through numerical atrophy and fatty degenerative changes of the epithelium with desquamation; the stroma condenses again, and the gland approaches but does not quite return to its resting condition. The acini and ducts remain more or less hyperplastic and dilated for some time. The process is more of a *reversal* from a markedly hyperplastic and hypertrophic state to the resting one. In the involuting uterus after delivery the involutionary process is both of a reversal and of a degenerative nature. The greatly hypertrophic unstriped muscle cells revert to their normal resting type; but the involution of the enormously enlarged blood vessels and sinuses of the placental site region is brought about by the same processes of collapse, productive thickening of the vessel wall, obliteration of lumen, eventually hyaline sclerosis and even calcification. These vascular involutionary changes following pregnancy are so characteristic that they become of diagnostic value as far as the question of the occurrence of pregnancy in any given case is concerned.

Without going more extensively into the occurrence and nature of developmental and functional involutionary processes, we have offered sufficient evidence to show that *growth* and *retrogression* go hand in hand in the broad economy of the organism, and are inseparably associated in all developmental processes, particularly in the most active stages of the release of growth energy in the embryo and fetus. We see that they occur at definitely fixed stages, that they are predetermined in the cells of the given tissue or organ; they are, therefore, intrinsic and inherited. The essential tissue changes of all of these developmental involutions are parenchymatous atrophy and degeneration with vascular obliteration and sclerosis, and, as we shall see later on, they are identical in kind with the tissue changes of the *major involution* which we call *old age.* In each and every instance they represent the passing of parts of the organism that have accomplished their purpose and become useless. Involution means fulfillment of purpose, and takes place only when this end has been accomplished.

The disturbance of any of these minor involutions of development leads necessarily to pathologic conditions of the body. The causes of such disturbances may be either intrinsic or extrinsic. A very large part of the abnormal morphologic and functional states of the organism included under anomalies, malformations and monstrosities is due to disturbances of normal evolutionary processes. For example, imperfect involution of the branchial clefts may present in the adult in the form of branchial cysts and fistulas; in the case of the thyreoglossal duct there may likewise result cysts and fistulas from imperfect resolution. Failure of mammary anlage to involute may be shown by the development of supernumerary breasts; the rudimentary tail may persist; the lanugo may not disappear; portions of the omphalomesenteric duct may persist in the form of umbilical fistulas, tumors of the umbilicus, or as intestinal diverticula; the urachus may continue to be patent; persistence of portions of the Wolffian body or duct, or of the Müllerian duct may present in the form of a great variety of so-called teratoid tumors; the foramen ovale and the ductus arteriosus may not close; the thymus may be persistent; and so on, through a great variety of pathologic conditions due to disturbances of normal involutionary processes. Since so many of the developmental involutions have a distinct evolutionary character, it follows that some of the pathologic conditions arising from their disturbance or inhibition hark back to prehuman forms of life, and are, therefore, regarded as *reversionary* or *vestigial* in nature. The latter term includes also certain structures present in all, or in a certain proportion of human beings, that show a much less complete development than is the case in other mammalian organisms. They are, therefore, regarded as structures destined to ultimate disappearance in man through a more complete involution yet to be attained. Among vestigial structures of this type are classed the appendix, the muscles of the ear, the Darwinian tubercle of the ear lobe, the plica semilunaris, etc. The occurrence of hypertrophic lanugo, supernumerary breasts and vertebrae are classed as *reversionary* in the sense of a phylogenetic inheritance. On the other hand, other functions and structures of the body, as the teeth, and the olfactory organ and function appear to be retrogressing. No two human individuals are exactly alike in morphology and function; these differences are the result of individual variations in the processes of growth and involution. When these individual variations exceed certain more or less arbitrary, vaguely defined limits, we regard the resultant condition as pathologic. It is possible, however, that some of these variations may represent certain progressive tendencies in the evolution of the species which we are unable to evaluate with our present knowledge.

OLD AGE—THE MAJOR INVOLUTION

THE mind accepts the localized organ involutions and tissue involutions of the developmental period as reasonable and normal processes in the evolution of the human body; they excite no apprehension, no fears, no regrets; to the average uneducated individual they are wholly unknown. The ordinary layman has little or no conception of the mechanism of his bodily development. Quite different is the case with respect to the signs and manifestations of that major involution involving the organism as a whole. We regard the appearance of the first signs of senescence as a tragic joke played upon us, which we resent more or less with a bitterness that is hopeless. We may attempt to blind ourselves to the fact that the peak of life has been passed and that the down-hill march has begun, and that from that first moment of recognition the descent is progressive and inevitable to the final moment of extinction. But we cannot; and the severest test of human character is at hand, whether we shall accept the situation with equanimity, or in sorrow vainly regretting.

Just when the tide begins to turn in any given individual from the high water mark of maturity down hill cannot be determined with any degree of accuracy. The individual variations are great, five to twenty years in apparently normal individuals. It becomes very difficult, therefore, to differentiate a normal first climacteric from a premature or a deferred one. As we have stated, the transition from the stage of growth equilibrium to that of regression shows no sharp line of demarcation. Age comes at first with a slow and insidious approach, unheralded and unperceived, until all at once the unwelcome guest is established with us. The functions of the various organs and tissues do not begin to diminish uniformly; there is an interlocking of mature function and retrogression, just as there is in the case of incompletely evolved and mature function on the ascending curve of life. Senescence is, therefore, a gradually developing complex, or syndrome, of organ involutions and tissue involutions. When these become sufficiently advanced as to be clinically apparent, then we say: "Age is upon us."

The aging process consists, therefore, of a combination of organ involutions and tissue involutions, shown histologically by well-defined tissue lesions and manifested clinically by descending function curves. While these individual tissue involutions and organ involutions begin at different times, and are more or less independent of one another, each single line of involution, once well initiated, may through the weakening or loss of the given function initiate or strengthen retrogressive changes in other organs. The various lines of involution are not wholly independent, but in the general economy of the organism aid and supplement one another until various vicious circles and correlations of retrogression are produced. *Senescence* is the gradual development of these lines of retrogression; the resulting complex is *Old Age.* Beginning very gradually and insidiously in the fifth and sixth decades of life for the two sexes respectively, the age complex rises rapidly above the clinical horizon in the seventh decade, and in the average individual is usually well developed in the period from sixty-five to seventy years of age. By this time the energy charge of the organism has fallen so low that senility is usually established in all organs and tissues and manifests itself in a change in all functions. There are, of course, great individual variations in this descent of the energy curve; not only as regards the involution of the organism as a whole but also in the case of individual tissues. Too great variations are not common as physiologic phenomena and must be regarded as having a pathologic significance.

We are defending the thesis that *senescence* is a *normal involutionary process*, and its underlying laws and phenomena are essentially identical with those of the minor involutions of the growth period of the organism. The main differences between the minor and the major involutions are those of degree, purpose and the organ or tissue involved. The minor involutions affect single specialized structures that are more or less temporary in function, and as soon as this temporary function is fulfilled, are unnecessary to the general economy of the organism and are disposed of without affecting the more permanent vital functions. The major involution, senescence, affects all of the vital organs and functions, not for any purpose of further growth and evolution, but for the purpose of getting rid of the organism, itself, as a whole. This can mean but one thing: the individual human machine has fulfilled its function, and, now useless, stands in the way of the progressive evolution of the species. In other words, the minor involutions take place for the good of the single individual, the major involution for the good of the species. Inasmuch as the reproductive function is the chief one of the individual life and from the biologic point of view the one logical reason for the ascent and maturity of the animal energy machine, it is but logical to conclude that when the carrier of the immortal germ plasm has arrived at maturity and continued at that stage sufficiently long to have secured its survival in his progeny, he, himself, is then in the way of evolution. Biologically useless he has become and he disappears from the scene by the gradual fading-away process of senescence. The old folk-saying, expressed here less vulgarly than in the original form, that "When the reproductive capacity has ceased, then the man is as good as dead!" is based upon an absolute foundation fact. All of the evolutionary processes of life with their minor involutions were but to prepare the individual organism for the performance of this function, and as soon as it has been accomplished the tide of the major involution begins to turn. We *live* but to *create* a new machine of a little later model than our own, a new life-machine that in some ineffable way can help along the great process of evolution of the species somehow more efficiently than we could do were we immortal. The Universe, by its very nature, demands mortality for the individual if the life of the species is to attain immortality through the ability to cope with the changing environment of the successive ages.

It is evident, therefore, that the major involution is dependent upon the fulfillment of function by the individual, the minor involution upon the fulfillment of function by the given organ or tissue. One is as necessary, as physiologic and as inevitable as the other. But it is very difficult for the average intelligent individual to adjust himself to the situation produced by the first indications that the high point of life has been reached and that he must now face the inevitable descent. Up to that painful moment he has lived under the stimulus of hopes and plans reaching far ahead into an apparently limitless future without any care or consideration of the fact that there is an inevitable definite limit to his life. It is not that he has blinded himself to this fact or purposely ignored it, but he simply has been unable to realize the significance of senescence until he, himself, has entered its pathway. It is *physiologic* for the human individual in the stages of development and reproductive maturity to live and plan as if one were immortal. Hence the shock of realization in the very height and fullness of such consciousness that the culminating stage of life's glorious adventure has been reached, and that hopes and plans have a mortal limit to their possibilities. The trouble is, that we have not been prepared by our education or philosophy of life for this physiologic moment, and its realization is a painful psychical shock. From this a biologic philosophy of life acquired in our growing period may perhaps have saved us. As it is, our unpreparedness for the entrance of senescence makes this a *critical period* for many human individuals, for some, even more critical than the age of puberty, for the latter period, whatever may happen, is still physiologically the age of optimism and ambitious hopes, while that of the climacteric is physiologically that of a psychical *let-down.* Hence the dangers of disillusionment, depression and discouragement as one faces the approach of senescence.

Fortunately, the cerebral functions have not yet completed their possibilities of development at the beginning of senescence, and these may continue an ascending curve for perhaps twenty or more years after the first signs of senescence, until senility is well established. Mental and spiritual evolution is thus assured to the senescent individual while other functions are weakening, if extrinsic accidents of life do not interfere with the normal course of the vital curve. Surely this should be a great compensation! Further, under normal conditions the lowering of the energy quantum is so gradual that the early part of senescence seems but a continuation of the period of maturity. Normally, it should be the period of full *ripeness.* Certain functions, particularly the sexual, assert themselves with less urgency, more comfortably. It is normally the *settled* age. The normal man should before this point is reached have accomplished successfully his sexual life, through a successful mating and parenthood, and achieved a sufficient degree of business or professional prosperity to keep the future safe. His progeny should now be in the adolescent period, and his close contact with them during this stage and that of their entrance into the period of early maturity should renew for him something of the spirit of the "joyous adventure," and counterbalance the physiologic descent in his own life. Any philosophy of life or education should at least prepare the human being for this achievement, if such philosophy or education has any practical value at all.

THE FUNCTIONAL CHANGES OF SENESCENCE

THE energy curves of the four chief vital functions of sensibility, motility, nutrition and reproduction are shown for a life of one hundred years in the chart of Figure 11. It will be seen that these cardinal vital functions develop closely together and supplement one another, although showing very different values at different periods of their evolution. The curve of nutrition rate drops from birth, being most active in the first and second decades, and is thence maintained at a level until about the sixtieth year, when the curve descends progressively to the end. The functional curve for the central nervous system rises continuously from birth until about the seventieth year when it begins a rapid descent. The motility curve rises during the first two decades of life, reaches a plateau for a decade or more, and falls gradually from about the thirty-fifth year. The curve for the reproductive function is stationary from birth until about the middle of the second decade, then rising steeply to reach its apex in the third or fourth decade, and falling to a neutral level in the fifth or sixth. Each decade of life has, therefore, its corresponding functional activity, and prepares for the vital processes of the succeeding ones.

There is then no *common* peak of energy expenditure for the cardinal vital activities, and this explains the vaguely defined demarcation between maturity and senescence. At the time that the first manifestations of the beginning of senescence are perceived the only function curve that shows any decided decline is that of the *reproductive function*. This has either reached, or is approaching, its period of fulfillment. This is in accord with the biologic conception of the meaning of the individual life. If we judge the course of this function by its results in progeny, that is, by the fertility of the human race, we should find that its peak is reached in the third decade of life. There are, however, so many other factors determining the production of children during this period, that fertility and reproductive capacity do not necessarily produce parallel curves; and it is much more probable that the peak of the functional capacity for reproduction falls rather in the latter part of the fourth decade or early in the fifth. After this is reached there takes place a very rapid decline in reproductive capacity for both sexes, earlier and more rapidly in the female, so that between forty-five and fifty years of age she usually loses completely her function of reproduction. The same climacteric for the male is usually placed about ten years later, from about fifty-five to sixty years. Manifestations of the sexual function may, however, still be active in the male after all possibilities of fertilization have ceased on his part. We do not know the approximate time when all spermatogenesis ceases in the human male. It has been generally assumed that active spermatogenesis in man persists usually into the sixties, and in some men until a much later time. There are, of course, in the literature numerous tales of very old men achieving fatherhood. It is possible that the individual variations as to spermatogenesis are as great as these tales would indicate, but there is also good reason for doubt as to the truth of many of the tales of senile fatherhood. Few male bodies over fifty-five years of age coming to the autopsy table show on microscopical examination any evidence of normal active spermatogenesis in their testes. While it is possible that in many such cases of aspermatogenesis this condition is the result of the disease causing the death of the individual, the same condition is also found in the testes of apparently healthy individuals of the same age killed accidentally. The great number of automobile deaths has added greatly to the evidence on this point. The writer is inclined to believe that for the majority of men active sperm formation ceases in the sixth decade. Nevertheless, in a very few instances we have had evidence that some sperm production does occur in men in the late sixties or early seventies. These old men may owe their long-continued virility either to a family inheritance, or to endocrinal disturbances in early life leading to prolongation of the preadolescent period and delayed puberty. It would seem probable that virility prolonged into the period of established senility has something of the pathologic about it.

The absence of sperm in the semen has apparently no absolute relationship to the persistence of sexual desire and potency for sexual intercourse, as these features of the reproductive function may persist, and even increase in intensity long after all sperm cells have disappeared from the semen. After spermatogenesis has normally ceased it would appear that the continuation of virility constitutes a certain social function in holding parents together until the future of their progeny is fully assured. This period also tends to bring out the highest qualities of sex companionship, and the most perfect sex satisfaction, if the psychology of the senescent male is adjusted to what is a normal and physiologic situation. Experience has taught the writer that many men over fifty years of age, priding themselves on the preservation of their virility, but finding that they are unable to produce children in marriage with younger women, show on microscopic examination total absence of spermatozoa in the seminal discharges, and without a history of previous venereal disease. This is not a question that has received any adequate investigative study; such is badly needed to throw additional light on the senescent period. From what knowledge we possess we can say reasonably that the peak of life coincides with the peak of the reproductive capacity (spermatogenesis), and the down-hill retrogression of senescence runs a fairly close parallel with the decline of the spermatogenic function. It should be emphasized in this connection that this view of senescence has nothing in common with the interstitial-cell theory. Coincident with the retrogression of sperm-cell production go other evidences of a progressive loss of energy. Chronic and progressive fatigue, lack of aggressiveness, disillusionment, mental and spiritual depression, and a gradual lowering of all activities mark this decline in varying degrees. It is probable that some of these psychologic reactions are only secondary to the man's realization that sexually he is not what he was in his third decade, and he is overconscious and secretly troubled by slight alterations in his sexual reactions. A certain degree of sexual neurasthenia is found in many, if not in the majority, of men about the age of fifty.

The chart in Figure 11 shows the comparative physiology of the stages of growth, maturity and involution for the body as a whole and the most important organs and tissues:

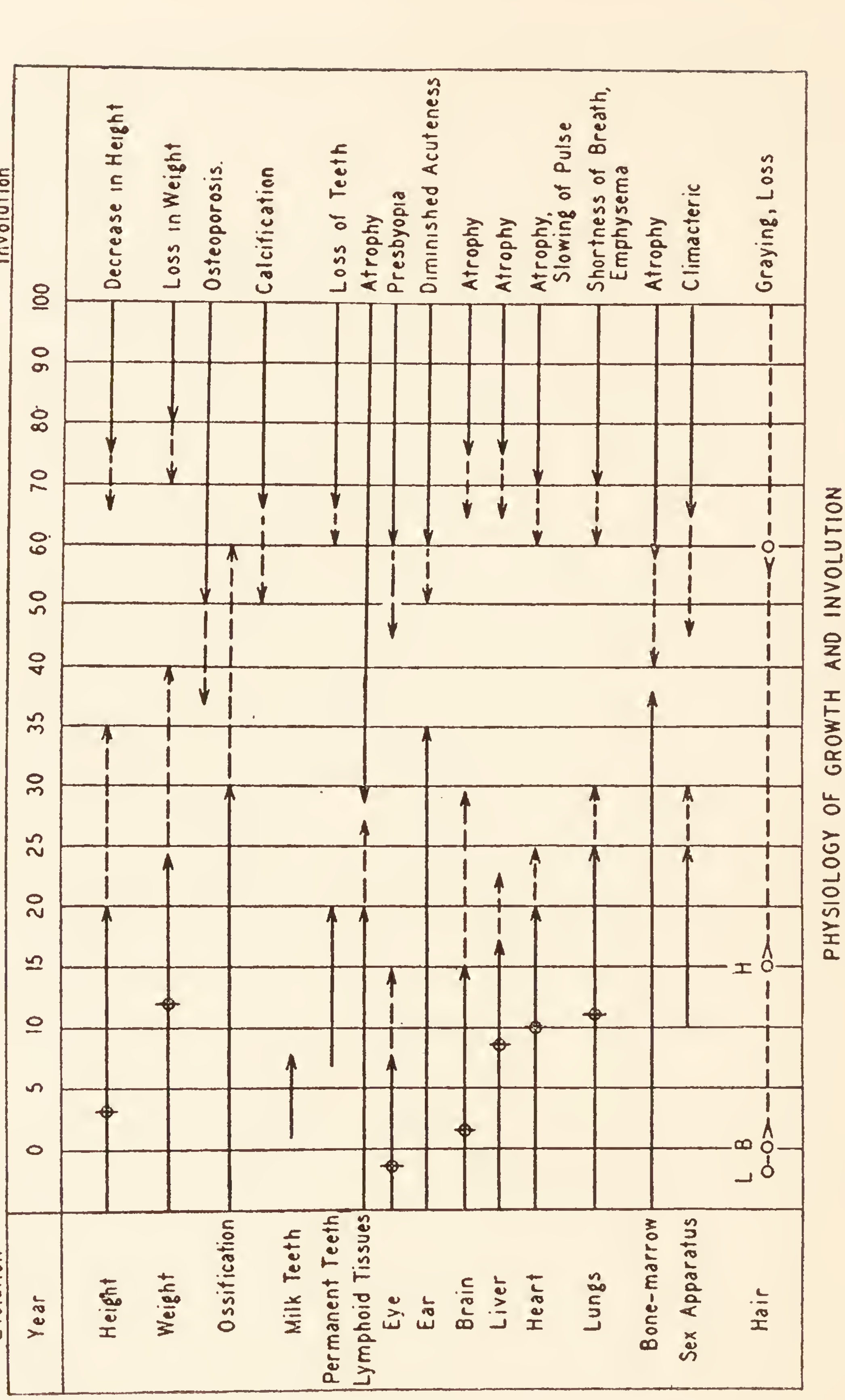


FIG. 11. PHYSIOLOGY OF GROWTH AND INVOLUTION.

Height. Full height is usually not attained until about the thirty-fifth to fortieth year, although the increase after the twentieth year is relatively slight. After the sixty-fifth year there is a gradual decrease in height, which is more marked after the seventy-fifth year, the total loss varying from 1 to 5 cm.

Weight. Very difficult is the determination of average normal weight curves. The individual constitutional variations are very great, and the influences of environment, personal habits, sexual activity, reduction in vital energy, etc., produce still greater variations. While many people attain their greatest weight in the years twenty-five to thirty, others reach it only in their fourth or fifth decades. In the early stages of his sexual life the male is more muscular than fat, but the female during pregnancy and lactation often shows a marked gain in fat. As the reproductive function declines the majority of both sexes show an increase in adipose tissue, and this increase may persist or the weight be maintained at this higher level until the middle or latter part of the seventh decade. How much of the climacteric tendency to obesity is physiologic, how much of it pathologic, due to disproportion between intake and combustion remains to be determined. In a certain degree the tendency to obesity of this period must be regarded as one of the signs of senescence, associated with the decline of the reproductive function (spermatogenesis) and the general decline in energy production. After the seventieth year there is a very definite loss of 2 to 5 kg., which is due chiefly to the loss of the water content and other changes in the connective tissues.

Skeleton. Processes of ossification may go on in the body even up to the seventieth year, but the normal extent is usually reached by the thirtieth year. Through the loss of water content the old bone becomes firmer, and this process of desiccation continues progressively during the period of involution. Sometimes earlier than, but usually after fifty years, the long bones and the larger flat ones gradually become osteoporotic, with larger marrow spaces and more delicate bony trabeculae, and corresponding increased fragility. They may retain, however, their normal conformation. The spinal column becomes shorter and more sharply curved; the intervertebral discs become contracted and thinner. With loss of the teeth atrophy of the alveolar process occurs, and there is developed the characteristic facies of senility which cannot be wholly concealed by artificial teeth. Changes in the conformation of skull and face occur, and the cranial sutures become indistinct or may wholly disappear. The cartilages of the joints become atrophic and frequently show erosions and roughened areas on the synovial surfaces. The joint capsules and ligaments are firmer, drier and less elastic. Articular movements in the aged are more restricted and become difficult and stiff. There is no hard and fast boundary between the physiologic joint changes of age and the very common pathologic affections of the joints of this period.

Calcification and Secondary Ossification. Coincident with the beginnings of osteoporosis deposits of lime salts begin to appear in the cartilages, sclerotic blood vessels and elsewhere. This is always to be regarded as a retrogressive change, secondary to some previous degenerative process. The demarcation between the purely physiologic involutionary change and pathologic processes of calcification is very difficult of determination, and we possess no criterion but that of degree. Following the deposit of lime salts there frequently takes place a transformation or metaplasia of the calcified area into true bone, even with marrow spaces and marrow tissue.

Teeth. The permanent teeth are usually fully developed by the twenty-fifth year, in some cases not until the thirtieth, and under physiologic conditions should persist until about the sixty-fifth year. Under modern conditions scarcely an individual of fifty years of age is in full possession of sound teeth, and the majority may be lost by the sixtieth year. As has already been mentioned there is reason to believe that in man an evolutionary retrogression of the teeth is taking place.

Lymphoid Tissues. The early retrogression of the thymus has already been considered as one of the minor involutions of the developmental period. The other lymphoid organs of the body reach their maximum development at about the twentieth year, and then diminish in size slowly throughout life. The tonsils are usually much reduced in size by the thirtieth year and in some individuals are markedly atrophic by the fortieth year. The spleen, larger in the female than in the male, reaches its maximum size at the peak of maturity, and then slowly diminishes, until fully developed senility when its atrophy increases in rate. The lymph nodes in general parallel the spleen in their development and retrogression. The functions of the lymphoid tissues being largely those of protection against infection there is less need for them, as the body in the course of life acquires active immunity against such a large proportion of the human infections.

Eyesight. From the time of birth the field of accommodation is progressively narrowed, from 14 diopters in the nursling, to 12 diopters at twenty years, 7 at thirty years, 4 at forty years, 2 at fifty-one years, and less than 1 diopter at sixty years of age. These changes constitute perhaps the best index of physiologic age recognizable clinically. The narrowing of the visual function leads gradually to presbyopia between forty-five and fifty, increasing much after the fiftieth year. In many individuals the advent of farsightedness is the *first* evident sign of senescence and recourse to eyeglasses marks the period for the individual. Between its appearance and the beginning of the decline of the sexual function there is apparently a very close relationship.

Hearing. A decided loss in acuteness of hearing begins usually at about sixty-five years, and may increase progressively to the end of life. In the very old there is usually a very marked degree of deafness.

Intellectual and Spiritual Life. While there are great individual variations, the functions of the central nervous system are usually preserved in physiologic senescence, and may increase in value until about the sixty-fifth year when some impairment of memory and mental reactions may begin to show; after seventy the retrogression of cerebral function proceeds rapidly, so that in those who reach or pass the eightieth year a characteristic picture of so-called "second childhood" develops. Here again we are confronted with the very great difficulty of distinguishing between purely physiologic involution and pathologic conditions because of the great range of individual variations dependent upon heredity or constitution.

Digestive Function. A lowering of this function begins shortly after the sixtieth year, in some individuals much earlier, and is shown chiefly in a lessened appetite, "heavy" and unpleasant digestion, gas production and constipation. With the loss of zest for food the senescent individual becomes capricious as to his choice of his daily food, and frequently completely changes his old dietary habits. These evidences of lowered functions in the alimentary tract increase progressively to the end of life. An inadequacy of pancreatic function is frequently shown in the so-called "benign glycosuria" of the aged. The bilirubin content of the blood serum is usually increased in old age.

Circulation. The pulse rate falls from 120 at birth to 70 to 80 at maturity, and after the sixtieth year to 60 per minute. In the majority of individuals there is usually some increase in tension from the fiftieth year on to about the seventieth when many old people show a decided lowering of blood pressure. More or less irregularity is common after the sixty-fifth year. Particularly with respect to this function are the boundaries between physiologic involution and pathologic conditions very poorly defined, and the individual variations are very large.

Respiration. The respiratory rate sinks from 28 in the newborn to 18 per minute at maturity and to 16 in the old man. Expiration is prolonged. Bronchial secretion is usually increased. Shortness of breath, in severe degrees asthmatic in character, constitutes one of the common and unpleasant symptoms of old age.

Bone Marrow. Blood cell formation is reduced; the senile individual presents always a certain degree of secondary anemia. Although immune to a large number of the infectious diseases through which he has passed in the course of his life, the senile individual loses resistance to the respiratory infections, the pyogenic cocci, to mould infections of the skin and to thrush. Various forms of pruritus due to tinea infections are very common in the aged, and the incidence of erysipelas is much increased in the period of senility.

Urinary Function. Disturbances of this function are very common after the sixtieth year. Polyuria, nycturia, pollakiuria, retention, incontinence, stasis of urine due to cystic glandular hyperplasia of the prostate, fermentation of urine in bladder, cystitis, calculus formation, etc., are among the most unpleasant and almost universal symptoms of the senile period. We are even at a greater handicap here in differentiating normal involutions and pathologic processes, and the individual equation plays a very large rôle as to the extent and degree of the urinary disturbances of old age.

Genital Functions. In the female, menstruation ceases at the beginning of, or early in, the senescent period, but cervical leucorrhea is common and troublesome. Prolapse is of frequent occurrence. The male gradually loses his erectile power as senility becomes established; he may have occasional discharges of seminal fluid containing no sperm, but showing numerous large phagocytic cells. Accumulation of prostatic fluid often becomes so unpleasant that prostatic massage is resorted to for relief. Psychologic sexual desire may outlive the physical potency; and this situation may lead to unpleasant or perverted behavior on the part of the uncontrolled old man.

Hair and Skin. Graying of the hair is regarded as a physiologic involutionary change, and usually has occurred by the sixtieth year. Coincident with this is the appearance of the coarse "senile bristles" in the nose, ears and eyebrows. The body hair becomes more abundant and usually coarser. It is still a mooted question whether baldness is a physiologic involution, or an inherited pathologic condition, or an acquired pathologic state resulting from the habits or conditions of life. Some individuals achieve the extreme limits of age without becoming bald; the majority, however, show varying degrees of baldness after maturity has passed, the daily loss of hair exceeding the new growth. Changes in the elasticity of the skin usually accompany those taking place in the body and head hair. "Wrinkles," "crow's feet," dryness, roughness, discoloration and a tendency to hyperkeratosis gradually develop after the fifty-fifth year; but here again the individual differences are so great, and the influence of the environment so potent, that no positive statements can be made as to the time and degree of the skin changes due purely to age. The same thing may be said as to the dependency of the female breasts as an index of age; it occurs in some women even shortly after puberty. All soft parts of

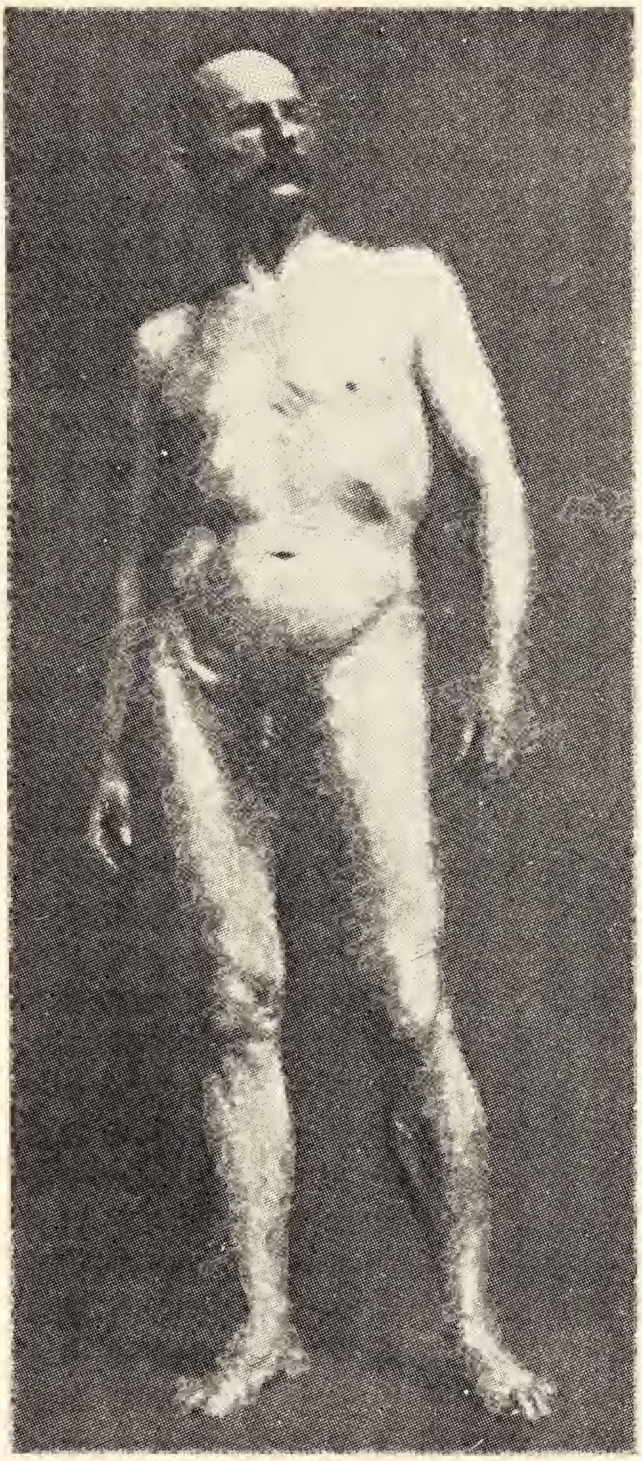


FIG. 12. THE CLIMAX OF THE PLAY. MAN OF SIXTY-THREE YEARS. JUST AT THE BEGINNING OF SENESCENCE. (*After Stratz.*)

the body undergo a very appreciable shrinking after the age of seventy due to the loss in water content. As the result of the loss of orbital fat the eyeballs appear sunken, and for the same reason of the disappearance of the subcutaneous fat in the cheeks, the latter fall in. All bony prominences become more marked.

Blood Vessels. Because of arteriosclerotic changes arteries that are visible beneath the skin, as the temporals, stand out prominently and show a marked tortuosity. Palpation of the arteries of the extremities reveal hard and thickened vessels, and frequently the "goose trachea" ribbing of Mönckeberg's calcification. The veins usually become more or less varicose, and hemorrhoids are almost universal in the aged.

Healing Power. Reparative and regenerative capacity on the part of different tissues diminishes progressively throughout senescence, and in the very aged may be almost wholly lost. Because of the marked drop in growth energy the transplantation of tissues in this period shows a marked decrease in the percentage of successful operations.

While this condensed abstract of the cardinal functional changes of senescence and senility presents the chief physiologic features of the major involution it does not pretend to give a complete detailed description of these. For example, a finished picture of the psychical functional changes of the senile individual would in itself require a volume. The psychology of the senescent period has never received an adequate study. The morphologic and objective features of fully developed senility will be pictured in detail in the next section. If we sum up all of the functional evidences of the major involution, and group them as to their order of appearance and importance, it is interesting to note that the first signs of age presented by the average male are: *presbyopia, sexual neurasthenia* and *chronic fatigue.* This triad of symptoms may be taken as *marking the advent of senescence,* and usually appears five to ten years in advance of the other functional changes of senescence. The average male recognizes their appearance in his life grudgingly and somewhat shamefacedly in such expressions as to the effect that he is "not quite what he used to be" or that he is "not so much interested" as he once was, with special reference to the sexual function. Because of the drop in energy production he is likely to change his habits as far as sport, exercise and recreation are concerned. The "taking to golf" is a definite characteristic of this period, and might almost be counted among the early signs of senescence.

THE PICTURE OF FULLY DEVELOPED SENILITY

BETWEEN the sixty-fifth and the seventy-sixth year the processes of the major involution have usually become so evident that the fully developed picture of Old Age is presented. The main features of this picture may be summed up briefly, as follows: a stooping or bent posture, reduction in height, general shrunken or withered appearance, increased bony prominences, stiffness of joints, loss of stretching power, a shuffling gait, uncertain movements, tremors, general weakness, loss of coördination, general emaciation, loss of panniculi, sunken eyes and cheeks, soft and flabby musculature, dependent breast, hang-belly, flabby and shrunken genitalia, low-hanging scrotum, frequent hydrocele, hernias, prolapse, atrophic vulva, barrel-shaped thorax with widening of the epigastric angle, obliterated interspaces, loss of teeth and atrophy of the alveolar processes, shortening of head and trunk length, inelastic, wrinkled, rough and discolored skin with frequent occurrence of patchy pigmentations and hyperkeratoses.

There is graying and loss of the head hair, while senile bristles develop in the eyebrows, nostrils and ears; the body hair is usually increased, particularly in the male, coarser, and grayish or white, becoming scanty in some individuals in extreme old age. Vision is dim and uncertain, the conjunctivae are reddened and watery, the cornea dull, the limbus thickened and opaque, in many cases a well-marked arcus senilis; hearing is dulled, often to the degree of total deafness in the very old; the voice is husky or cracked, speech slowed and uncertain; the mouth is dry, the tongue coated and fissured, and frequently there is a slight dry husky cough; respiration is slowed, shallow with prolonged expiration, shortness of breath and asthmatic tendency. The peripheral arteries are hard, roughened and tortuous, the pulse slow, irregular, and frequently altered in tension, either high or low; there is a marked tendency to varicose veins and hemorrhoids, and the ankles are edematous, particularly at night. The metabolic rate is lowered; the secretions of all organs diminished; digestion is slow, heavy and difficult, with excessive gas production, eructations and frequently constipation; benign glycosuria is not uncommon. Bladder control is often lost to some extent, and retention, pollakiuria, polyuria and incontinence are frequent symptoms. The body temperature is frequently subnormal, and the senile individual complains of cold and is easily chilled. The sensory nerve endings, tactile, sexual, etc., are dulled; and finally the involution processes in the central nervous system show themselves in loss of memory, failing powers of observation, attention and concentration, slowness of all mental reactions, lessened ability to initiate ideas, increasing errors of judgment, loss of effectivity, irritability, retrograde amnesia, pseudo-reminiscence, automatism, aphasias, psychical fatigue and weakness, daytime sleeping and nocturnal insomnia, melancholia, changes and perversions in personal habits, illusions and delusions, loss of orientation, and ultimately the fully developed stage of "second childhood" and senile dementia.

The physiology and the psychology of the senescent life in both of its stages, the early period of senescent ripeness, up to sixty-five years of age, and the degenerative period from sixty-five to the end of life, have been accorded few really scientific studies in

FIG. 13. THREESCORE AND TEN. ACTIVE MENTALITY. EMPHYSEMA THE ONLY SIGN OF OLD AGE.

recent years. Psychologists and sociologists have just begun to see that the senescent period of life is as distinct and individual as that of adolescence, and that in the fully rounded life of the human being it is of equal importance. The period from the peak of maturity to the end of life measured in years may constitute one-third or even one-half the total span of life. In many ways it is a more difficult life period than the ascending curve, because of its let-down in energy and the progressive decline of the sexual function. In the male the latter factor is by far the one most potent in determining whether the last period of life shall draw to a happy, normal, successful end, or whether, through the failure of the individual to adapt himself to the altered conditions of the sexual life, it will pass in unsatisfied physical or psychical longings and efforts, natural and unnatural, ending ultimately in physical and psychical wreckage. The tremendous importance of the declining sexual function and the way in which this is met by the senescent male who has had an active sexual life during the period of his maturity cannot be over emphasized. Much of the abnormal psychologic manifestations attending senescence and senility have their well-spring in the failure or maladjustment of the individual to his declining virility. On the other hand, the average senescent female meets the loss of sexual function on her part with equanimity, even with relief, and turns to new activities with zest and pleasure, so that the early years of senescence are often for her a period of revivification.

The chief characteristics of fully developed senility are well illustrated in Figures 14 and 15, the old man of seventy-six and the woman of seventy years of age, reproduced from the valuable work of Stratz, "Lebensalter und Geschlechter.[1] In both of these figures the impression of body energy and power at its lowest ebb is strikingly given in the drooping, lifeless attitude of body, the general atrophy of the muscles and panniculi, the body prominences, and the dependent abdomens and breasts. In Figure 17 there is presented the picture of a man of fourscore years. His body changes are similar to those of the man of seventy-six, but his mentality is better preserved, his eyes are bright and alive, and his general outlook upon life

[1]Stuttgart, 1926.

Fig. 14.

Fig. 15.

Fig. 14. Old Woman of Seventy Years. Well developed Senility. (*After Stratz.*)

Fig. 15. Old Man of Seventy-six Years. Well-developed Senility. (*After Stratz.*)

cheerful, in spite of the fact that he had a well-developed scirrhous carcinoma of the right breast, from which he died within the year. As cancer of the breast in senile males is of relatively very rare occurrence it is of interest to note that this man had a marked history of the multiple incidence of cancer in both paternal and maternal lines. His fate was predetermined by his inheritance. In Figure 16 the contrast between an old father of eighty years and his son of thirty-seven years emphasizes the differences existing between the period of full maturity and that of advanced senility. The weary, worn-out machine of the old man contrasted with the insolent aggressiveness of the son in the height of his maturity tells the story of the meaning of involution and old age more effectively than any detailed scientific description can do.

The individual variations in the symptom complex of fully developed senility are very great, and are determined chiefly by primary constitutional or organic susceptibilities that may be intrinsic and inherited, or acquired through the action of extrinsic factors. Much of the variations in the advent, type and degree of the clinical manifestations of the age complex are, therefore, due to the secondary pathology and not to the essential age process itself, although dependent primarily upon pathologic conditions in other organs that in themselves represent the normal involution process for that organ. The interdependence of function is, therefore, as important a factor in determining the age variations in time, place and degree as it is in the disease states of the organism before the period of involution has begun. Especially in the case of the vascular system does its primary involution become a factor of prime importance in determining the course of the involutionary processes in such important organs as the heart, kidneys and brain. Sclerosis of the arteries, with its resultant effects upon the circulation and nutrition of the organ concerned, becomes, then, a chief collaborative factor in hastening or exaggerating the parenchymatous involutions of senescence, clinically recognized as *premature age*, *senile dementia*, etc., or the converse condition of *deferred age* in the absence of a marked degree of arteriosclerosis. There is, of course, no line of demarcation possible between the purely physiologic and the pathologic process,

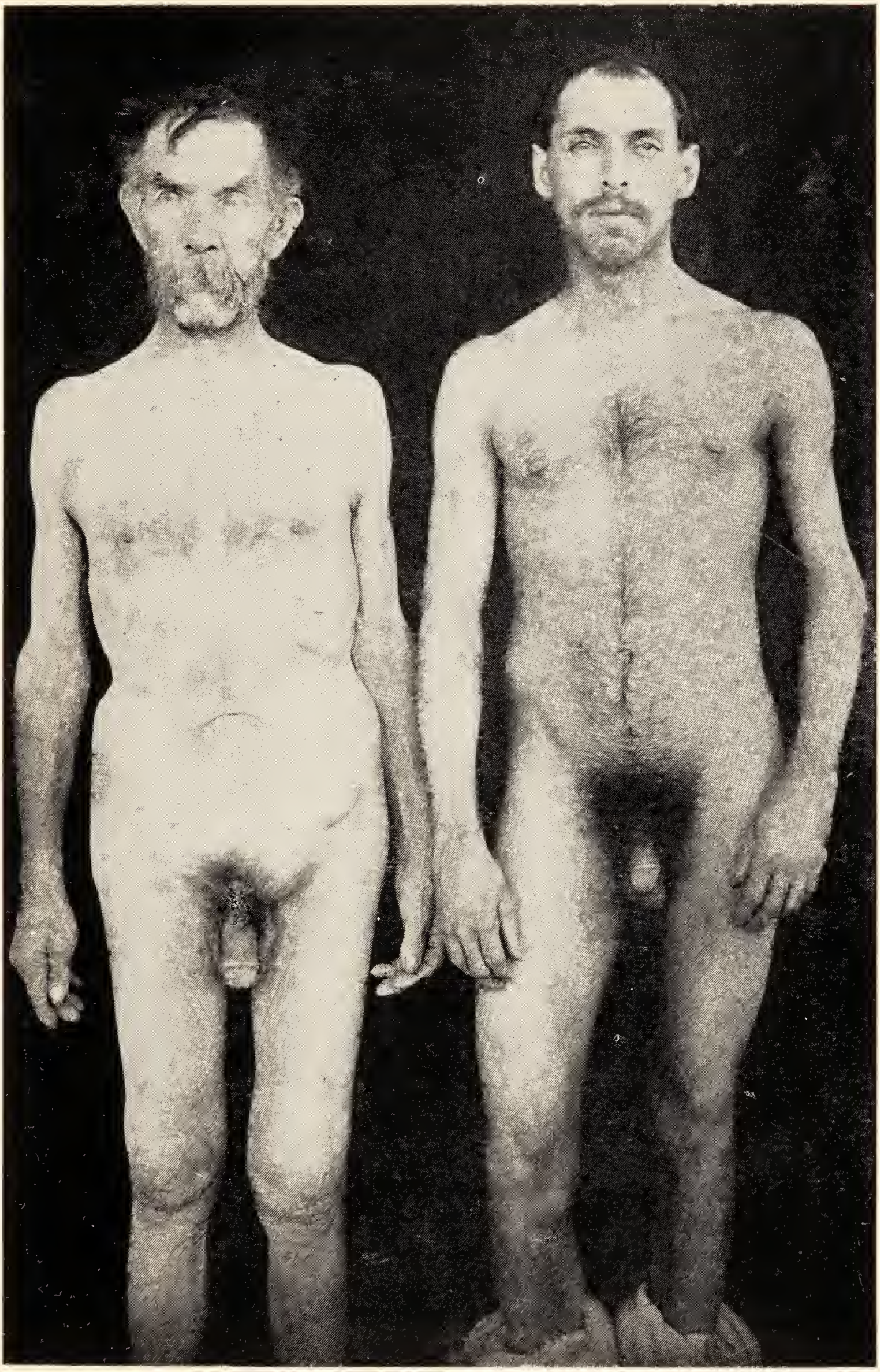


Fig. 16. Father of Eighty Years of Age and Son of Thirty-seven Years. Contrast between Fully Developed Senility and the Period of the Height of Maturity.

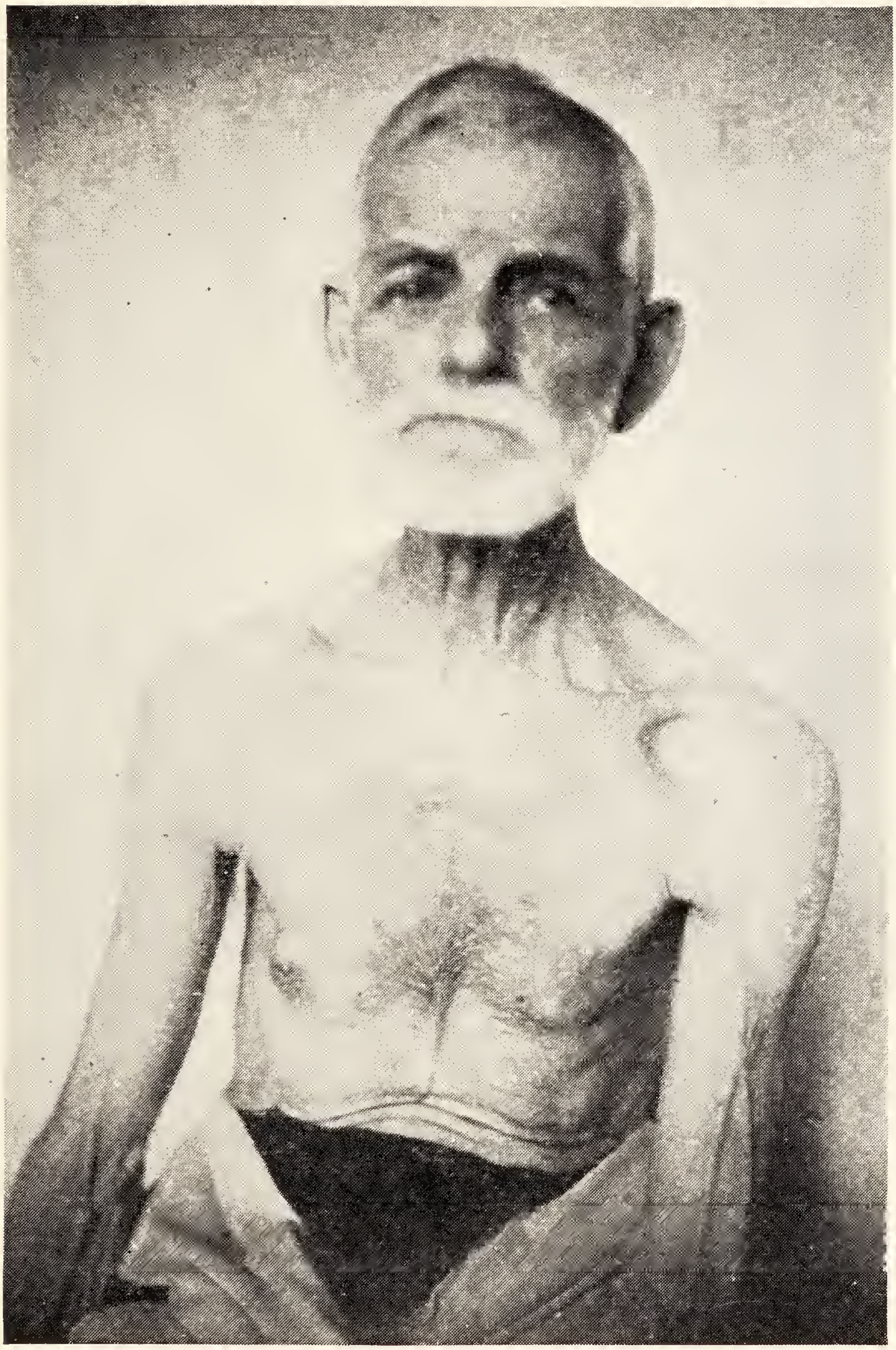


Fig. 17. Fourscore Years. Scirrhous Carcinoma of Right Mamma. Family History of Carcinoma on Both Paternal and Maternal Sides.

and our judgments are based wholly upon time and degree of intensity of the resultant effects. The *earlier* the appearance of senile dementia the greater the probability of its being a *secondary pathologic* condition of the brain due to *primary vascular lesions*. There are no essential differences in the psychical manifestations or in the lesions of nerve tissue of *senile dementia* and the *normal cerebral involution* of extreme age except those of *degree*. To a more or less marked degree of senile imbecility or exaggerated "second childhood" all who live sufficiently long must inevitably come. The earlier appearance of this final stage of the old-age process than the seventy-fifth to the eightieth year must be regarded as *pathologic*. In the normal human being the brain function is the latest to succumb to the involution process, and fortunately for the individual and his survivors the sad picture of the final period of "*second infancy*" or "*senile dementia*" is averted through some form of pathologic death secondary to the involution process.

In the world's literature there are many poetic descriptions of old age, as well as philosophic and hygienic discussions of its nature and treatment. Cornaro (1464–1566), the "apostle of senescence" as he has been called, wrote four essays after the age of eighty-three, the last one at ninety-five, in the praise of old age and how to attain it. Regimen and hygiene constituted his philosophy of life; and his treatment of life's problems is of great significance in that it made a lasting impression upon the thought of the next two centuries; he inspired or influenced Lord Bacon, Addison and others. Of the poems on old age not one can be said to have been written from the viewpoint of the normal physiologic conception of age and death. They deal chiefly with the generic aspects of death, the farewell to youth and life, pessimistic expressions of the physical and psychical states of the aged, or with the philosophy engendered by autobiographic reminiscences. Those of the last-named variety should be of the greatest value to the common mind of the race, if they had been inspired by normal living and normal senescence on the part of the writer, but unfortunately they too often represent the melancholy pessimism arising out of a life that has not been successfully lived from the standpoint of the reproductive function in its complete significance. To the human male who has failed in this, the one apparent real purpose of the individual life, there can come with senescence only a philosophy of failure and pessimism, or, perhaps even worse, a hopeless resignation or anticipation based upon surviving superstition and accepted religious conventionalities. There are very few exceptions in poetic literature to this pessimistic treatment of the last period of human life, and even these are tinged with regret that human aspirations of the period of youth are still far from possibility of consummation, when the end of life is presenting the closing door to all activities.

Only in Solomon's figurative description of old age, in the last chapter of Ecclesiastes, is there to be found, out of all of the world's literature, an adequate word-picture of the closing days of human life:

> In the day when the keepers of the house shall tremble, and the strong men shall bow themselves, and the grinders cease because they are few, and those that look out of the windows be darkened,
>
> And the doors shall be shut in the streets, when the sound of the grinding is low, and he

shall rise up at the voice of the bird, and all of the daughters of music shall be brought low;

Also when they shall be afraid of that which is high, and fears shall be in the way, and the almond tree shall flourish, and the grasshopper shall be a burden, and desire shall fail: because man goeth to his long home, and the mourners go about the streets.

THE PRIMARY TISSUE CHANGES OF SENESCENCE

THE primary tissue changes of the involutionary process are identically the same for the period of senescence as for the involution processes of temporary structures during the developmental periods of intrauterine and extrauterine life. The changes in the senile placenta may be taken as an example of their nature. There is a progressive thickening and condensation of the chorionic stroma; from a loose semimyxomatous structure it becomes increasingly fibroid, its stroma cells fewer in number, and the intercellular substance more hyaline in character; the arterioles and larger arteries of the chorionic stems of the cotyledons show a productive thickening of the vessel walls, ultimately a hyaline fibrosis or sclerosis, while the lumina gradually become narrowed. The veins and terminal capillaries in the villi become dilated, so that in the senile stage the smaller villi appear to be chiefly blood vessels with a scanty fibroid stroma. The cell-layer of Langhans of the chorionic ectoderm disappears by the middle or end of the third month of pregnancy by a process of simple numerical atrophy; the syncytium undergoes a gradual loss of proliferative power, the syncytial buds become fewer, and on the older and more fibroid portions of the chorion localized necrosis of the syncytial layer takes place, preceded by marked nuclear pyknosis and vacuolation. Intervillous thrombi are formed on the dead and degenerating syncytium, and deposits of lime salts take place in these fibrin masses when the vascular sclerosis and obliteration reaches a certain stage. A slow anemic infarction of a cotyledon or portion of such may take place—the physiologic anemic infarct of the placenta. The mature placenta at birth is, therefore, a senile organ presenting the picture of extensive primary and secondary involutionary changes that are wholly physiologic in nature, predetermined in the germ-cell union, intrinsic within the organ itself, and wholly independent of extrinsic factors.

Without going further into detail of the changes occurring in the various organ and tissue involutions, we may say that essentially they present identical tissue lesions, and that these are the same as those occurring in the involutionary processes of old age. These involutionary tissue changes are:

PRIMARY TISSUE CHANGES IN INVOLUTION.

1. Numerical Atrophy. Loss of Power of Cell Division. Fewer Mitoses. Diminished Growth. Slowness or Failure of Regeneration and Repair. Replacement of Parenchymatous Cells by Connective-tissue, Adipose-tissue or a Myxedematous Connective-tissue.

2. Quantitative Atrophy. Parenchymatous Cells Reduced in Size as Well as in Number. Reduction in Nucleus and Cytoplasm. Condensation of Chromatin, Pyknosis, Eventually Vacuolation and Karyolysis. Frequent Appearance of Lipoid Droplets in Cell Cytoplasm and Nucleus. Appearance of Lipoid Pigments ("Wear and Tear") Pigments in Many Cells. Loss of Glycogen and Water Content. Accumulation of Secretory or Excretory Products in Cells.

3. Shrinking and Condensation of Intercellular Substance; Loss of Water; Desiccation; Changes in Colloid States. Eventually a Hyaline Fibrosis. In the Panniculi the Fat Cells Replaced by a Mucin-Containing Stroma, Resembling that in Myxedema. Deposits of Lime Salts.

4. Vascular Changes. Collapse of Vessels. Obliteration of Lumen. Hyaline Fibrosis. Loss of Muscle Cells and Elastic Tissue. Lipoidosis. Calcification.

FIG. 18. THE PRIMARY TISSUE CHANGES IN INVOLUTION.

1. Loss of power of cell division. Fewer mitoses. Fewer regenerative and reparative proliferations. Numerical atrophy.

2. Quantitative atrophy. Parenchymatous cells fewer and smaller in size. Reduction in cytoplasm and in nucleus. Condensation of chromatin, pyknosis, eventually vacuolation and karyolysis. Fre-

quent appearance of lipoid droplets in cell protoplasm; in many cells lipoid pigments appear.

3. Shrinking and condensation of intercellular substance, most frequently a hyaline fibrosis; loss of water, with changes in the colloid state; in the panniculi the fat cells are frequently replaced by a mucin-containing stroma resembling that seen in myxedema.

4. Vascular changes. These are characteristic of the involutionary process at all periods in all organs and tissues that undergo such involution, and must be inherent within the vessels themselves, inasmuch as wear-and-tear forces can hardly explain the sclerotic changes occurring in the ductus arteriosus, umbilical vessels, involuting thymus, and later in the ovary after the first follicle has ripened and discharged. In all periods of developmental involution the vascular changes are histologically identical with those occurring during senescence. Without going into a detailed description of the well-known features of the arteriosclerosis of age, the essential lesions are an atherofibrosis of the vessel wall, with or without proliferative changes,

ultimate loss of elastic tissue and muscle cells, occlusion or dilatation of the lumen, and incidental lime-salt deposits in the altered portions of the vessel wall. Aside from the processes of thrombosis, embolism, aneurysmal dilatation, rupture, etc., which may be secondary to the vascular changes, the resulting disturbances of circulation and nutrition in the parts supplied by such sclerotic vessels are extremely important in the secondary pathology of senescence. In addition to the primary course of the arteriosclerosis occurring in the general arterial system in old age, the part played by extrinsic factors, such as overwork, intoxication, infection, etc., in the production of such sclerosis must be evaluated by the pathologist in any given case. Herein lies one of the most difficult problems of pathology, as the only criteria available are those of time, location and degree.

As seen in the autopsy, the main features of the gross pathology of the viscera of the senile body are: (1) Atrophy; reduction in size of all organs and tissues except the emphysematous lung and the hyperplastic prostate; (2) increase in consistency of the solid organs, due to the relative increase of stroma; (3) changes in color, grayer or browner; (4) changes in translucency, usually increased; (5) serous atrophy of the adipose tissue; (6) increased dryness and toughness of the muscles, fasciae and connective tissues throughout the entire body. Special senile features of the autopsy are the increased adherence of the dura mater to the inner table of the skull cap, the erosion of the latter by the meningeal vessels, the Pacchionian erosions and perforations, the thickened and more opaque meninges, the more sharply pointed cerebral convolutions, the thickened and frequently cystic chorioid plexus, the discoloration and calcification of the cartilages, osteoporosis of bones, the low diaphragm, barrel thorax, droplet heart, emphysematous lungs, ptoses of the gastrointestinal organs, the generalized atrophy and passive congestion. The senile atrophy of the viscera shows most markedly in the spleen, liver, testes, heart, lungs, pancreas and kidneys, differing in this order from the atrophy of starvation. The lymphoid tissues throughout the body are likewise markedly atrophic. The adrenals always show an excessive degree of lipoidosis. The atrophic testicles are browner in color from the lipoid pigment increase in the interstitial cells.

Before leaving the subject of the primary histologic lesions of age, the changes in the testis deserve additional attention. So much has been said and written about the potential immortality of the germ plasm that many people assume that its existence in the sex glands, at least in the testis, continues until the end of the life of the individual. We have made it clear above that the germinal epithelium of the spermatic tubules undergoes retrogression very early in senescence, and that its progressive atrophy is practically coincident with the advent of senescence. In the very old individual the testis may be fibroid, or nearly so, the tubules being represented by the hyaline basement membranes of the old tubules. If any tubules still persist the epithelium is reduced to a single layer of low vacuolated cells, or the epithelium may be gone entirely. No evidence of spermatogenesis may be found at all, and the testes while preserving their normal form and consistency are made up wholly of connective tissue showing the outlines of the vanished tubules, and containing here and there islets of brownish lipoid cells—the persistent interstitial cells. In other old men the testicles show large dilated tubules lined with a single row of vacuolated cells; the stroma may be increased more or less between the functionless tubules. These conditions appear to be associated with the lymphatic type of constitution. In men between seventy and eighty years, atypical spermatid formation is not infrequently found in the tubules, but the oldest case of active and apparently normal spermatogenesis in my material was that of a man of sixty-eight years. It is possible that constitutional and inheritable factors may underlie the occurrence of senile spermatogenesis. According to the writer's experience its occurrence is very rare. The routine microscopic examination of testes of men dying in their sixth and seventh decades has yielded results tending to show that there is a progressive atrophy of spermatogenic tissue developing in the early period of senescence, and increasing more rapidly toward the age of sixty-five. Between the ages of forty-five and sixty-five few testes obtained at autopsy show throughout the normal picture seen at the age of thirty. Since we know today that the testes are peculiarly susceptible to the action of various extrinsic agents, such as alcohol, lead, mercury, roentgen-ray irradiation and various infections, we have no criteria for the differentiation of changes due to these influences or those due wholly to age. As the tubular atrophy progresses throughout the period of senescence, the so-called interstitial cells become larger, and more prominent, brownish in color and filled with lipoid droplets. In the cases of complete atrophy with hyaline fibrosis of the stroma, they often form such striking masses of cells scattered through the atrophic tubules that an increase in their number and size seems probable. This prominence of these cells may persist, and apparently does so, until the end of life. Such changes are wholly in contradiction to any theory of a rejuvenating internal secretion ascribed to these cells. On the other hand the testicular lesions of old age support the view that their function is a metabolic, nutritional one, concerned in the process of spermatogenesis, and that when this process comes to an end, these cells become overburdened with a lipoid pigment similar to the *disuse* lipoid pigmentation occurring in other atrophic tissues.

In the material studied it is certain that the prominence of the interstitial cells is in direct proportion to the loss of spermatogenic function, and in so far as the clinical histories would indicate, also to the loss of sexual potency.

THE SECONDARY PATHOLOGIC CHANGES OF OLD AGE

THE secondary pathologic conditions that are made possible and favored by the primary involution process are many and of great clinical importance, because it is usually through some one of these that the senile individual is kept from achieving his full life limit and a biologic death. They include nearly all of the causes of the deaths which occur during the last third of life. They fall into several well-defined groups:

1. *Secondary to the Vascular Changes.* Thrombosis, embolism, infarction, atrophy, apoplexy, cerebral softening, paralysis, psychical degeneration, dementia, various psychoses, etc., due to cerebral arteriosclerosis; coronary thrombosis, embolism, myocardial infarction and fibrosis, angina pectoris, cardiac insufficiency, due to atrophy and myocardial degeneration, etc., resultant to sclerosis of the coronary arteries; atrophic kidneys, contracted kidneys, nephrosis, "chronic interstitial nephritis," compensatory hypertension, aortic sclerosis and cardiac hypertrophy, eventually dilata-

tion of the left ventricle, due to renal arteriosclerosis; aortalgia and angina pectoris, aortic aneurysm, rupture of aorta, thrombosis and embolism, caused by aortic atherosclerosis; Ayerza's syndrome of polycythemia, cyanosis and asthmatic attacks, due to sclerosis of the pulmonary arteries; pancreatic insufficiency due to atrophy and fibrosis of islands caused by sclerosis of pancreatic arterioles; atrophy and fibrosis of testis due to sclerotic changes in localized arterial branches; atrophy and gangrene of extremities, with thrombosis and embolism, intermittent claudication, myasthenia angiosclerotica, angina cruris, etc., resulting from arteriosclerosis of the peripheral arteries.

2. *Secondary to the General Atrophy.* Reduced function of all organs including the endocrinal, with a great variety of symptoms resulting from localized variations in the degree of atrophy. Among these functional inadequacies may be mentioned the frequent occurrence of hypothyroidism and glycosuria. In the case of the central nervous system there follows the primary atrophy of the nerve cells, even in the absence of sclerotic changes in the blood

vessels, the chain of psychic degenerations leading ultimately to the clinical picture of senile dementia. The primary atrophy of the heart muscle leads to myocardial insufficiency, arterial anemia, pulmonary congestion and generalized passive congestion. Atrophy of the lung tissue is followed by dilatation of the acini, emphysema, and this in turn by bronchitis, hypertrophy and dilatation of the right ventricle, and ultimately a generalized passive congestion; atrophy of the lymphoid tissues leads to a general lowering of resistance to infection. There is a greatly increased susceptibility in the majority of old people to respiratory infections, bronchitis and bronchopneumonia, and also to erysipelas. Atrophy of the bone marrow is responsible for the secondary anemia of age. Because of the increase in fatty marrow and the progressive osteoporosis of the long bones injuries to these are especially likely to be followed by the clinical manifestations of pulmonary fatty embolism. Atrophy of the cells of the organs of nutrition, as the gastrointestinal tract, liver, etc., may lead to a vicious circle of malnutrition or starvation atrophy of all the body tissues, the resultant tissue lesion being a combination of quantitative and numerical atrophy.

3. *Stasis Conditions.* Owing to the atrophy of the muscle in the duct walls and consequent dilatation of the duct, stasis conditions are of frequent occurrence in the aged, and lead to death in many instances because of the resulting infections and their subsequent spread. This is particularly true of the urinary and genital tract of the male senescent, and of the urinary tract alone in the female. Bladder intolerance is one of the most common and unpleasant conditions of age in both sexes. In the male it does not necessarily indicate an enlargement of the prostate. However, it does frequently lead to incontinence, which in itself favors the entrance of infection into the weakened bladder; there may follow then the chain of cystitis, ascending ureteritis, pyelitis and pyelonephritis, all of which conditions are very frequently terminal infections for the senile individual. In the male such infections may extend directly into the prostatic ducts, increasing the stasis of secretions already present in the gland due to the lack of ejaculatory emptying following the decline of the sexual

SECONDARY PATHOLOGICAL CONDITIONS ASSOCIATED WITH THE AGING PROCESS

Central Nervous System	[Cerebral arteriosclerosis.] Thrombosis. Embolism. Infarction. Hemorrhage. Atrophy. Sclerosis. [Loss of memory. Loss of self-control. Perversion. Senile dementia. Senile psychoses. Vertigo. Senile epilepsy. Senile chorea. Apoplexy.] Hemiplegia. Paraplegia. Aphasias. Apraxia. Brown-Sequard's Syndrome. Presbyophrenia. Hysteria. Autosuggestion. Insomnia. Melancholia. Exaggerated ego. Hallucinations.
Eye	Loss of Accommodation Power. Arcus Senilis. Senile Cataract.
Ear	Atrophy of Nerve. Sclerosis. Progressive Deafness.
Thyroid	Atrophy. Reduced metabolism. Skin changes.
Heart	Myocardial Degeneration. Cardiac Inadequacy. Coronary Thrombosis. Infarction. Cardiac Thrombosis. Angina. Numerous Functional Disturbances.
Aorta	Aortalgia. Angina. High or Low Pressure. Thrombosis. Embolism.
Lungs	Chronic Bronchitis. Bronchopneumonia.
Arteries	Thrombosis. Embolism. Infarction. Gangrene. Atrophy. Diminished Blood Supply.
Kidneys	Arteriosclerotic Atrophy. Pyelonephritis. Stasis-Kidney. Pollakiuria. Nycturia.
Bladder	Stasis. Cystitis. Calculus.
Prostate	Cystic Glandular Hyperplasia. Stasis. Secondary Infection.
Liver	Atrophy. Reduced Function.
Gall-bladder	Stasis. Calculi.
Pancreas	Atrophy. Lowered Function.
Gastrointestinal Tract	Atrophic Catarrh. Stasis. Disturbances of Digestion.
Lymphoid Structures and Bone Marrow	Lowered Resistance, Anemia.
Bones	Osteoporosis. Fragility. Fatty Embolism. Deficient Healing.

FIG. 19. SECONDARY PATHOLOGIC CONDITIONS ASSOCIATED WITH THE AGING PROCESS.

function. A vicious circle is set up here, which ultimately produces an enlarged prostate due to the cystic glandular dilatation and hyperplasia of the organ. In the gastrointestinal tract the diminished intestinal motility leads to constipation, stasis catarrhs, putrefactive fermentations, gas production, etc. Stasis in the biliary and pancreatic tracts may also lead to inflammation of these ducts, with the production of icterus, hepatitis or pancreatitis. A second important sequela of stasis in any of the body passages is the production of calculi (biliary, pancreatic, urinary, salivary, etc.).

Omitting the traumatic causes of death, mechanical violence, thermal, toxic, etc., it will be seen from the chart in Figure 19 that the secondary pathology of old age is responsible for the great majority of deaths occurring in the senescent period. It will be noted, however, that neoplasm, cancer in particular, has not been included among either the primary or the secondary pathological lesions due to old age. This omission is in harmony with our view as to the etiology of cancer, which is that the development of carcinoma in old age is only a coincidental manifestation of an intrinsic, inherited susceptibility which may appear at any age. Its relation to old age is analogous to that of gout, which is also an intrinsic, inherited susceptibility that requires time for its manifestation. While dependent upon the time element for the consummation of their respective susceptibilities, they cannot be regarded as a part of the old age process, inasmuch as not every old person develops either cancer or gout. The age relationship existing only in certain individuals between age and cancer, or age and gout, is, therefore, incidental in nature. Neither can be properly regarded as an intrinsic senile process.

THE CONCENTRATION OF DISEASE IN DIFFERENT LIFE PERIODS

ANOTHER striking relationship between disease and the time of life is shown in Figure 20 which represents the predominance of certain diseases in different age periods: rachitis in the first five years, rheumatic fever in childhood, tuberculosis in the late childhood and adolescent periods, venereal diseases at puberty and in early adult life, with the carrying-on of syphilis through middle life with the production of many varied pathologic conditions then, neoplasms other than carcinoma in the early part of adult life, carcinoma in the senescent period, likewise in this period various metabolic conditions associated with the progressive loss of energy, cardiovascular diseases in senility, and two periods for diseases of the central nervous system, that of early sexual life and that of early senescence. Numerous factors concerned with the environment, the stage of development, somatic differences at different ages, exposure to infection, and with psychologic, emotional and social states dependent upon the age, etc., are responsible for this concentration of diseases in certain periods of life. While this list applies to both sexes, there are decided sex differences in the concentration of diseases at different life periods that have to do with the differences in the function of the two sexes. The appearance of the menopause in women about ten years earlier than the climacteric of the male produces the same difference in the time periods at which the nervous and psychical disturbances common to the period of loss of sexual potency appear. The period of sexual activity has its own sex differences in the psychological life, and these differences again are very marked at the beginning and the end of the sexual life in the two sexes. The female is throughout her life much more influenced by her sex than is the male by his. Puberty, pregnancy, lactation and the menopause in themselves create conditions favorable to the concentration of various diseases in these periods. While some of the apparent sex predisposition to certain diseases is due undoubtedly to intrinsic biologic differences in the soma of the two sexes, some of it is undoubtedly dependent upon differences in occupation, habits of life, clothing, etc. Thus girls are more frequently born with congenital dislocation of the hips, boys with Hirschsprung's disease and a tendency to pyloric spasm. Women more frequently suffer from gallstones and carcinoma of the breasts, while men more frequently show hepatic cirrhosis, gout and cancer of the lip, tongue, larynx, esophagus and stomach. The most striking example of somatic sex differences is that shown in sex-limited inheritance, as in hemophilia and night-blindness, conditions which appear only in the male members of the affected family although transmitted by the females.

The higher morbidity of children for certain of the acute infectious diseases must depend upon the physiologic disposition of the youthful organism; but the resistance on the part of the adult to these diseases may rest only upon an acquired immunity. The more frequent occurrence of pemphigus, pyuria and middle-ear disease in the infant rest probably upon the defective development of the defensive apparatus. The somatic difference between children and adults is also well shown in the case of tuberculosis. In children tuberculosis is more frequently found in the lymph nodes, bones and joints than is the case with adults.

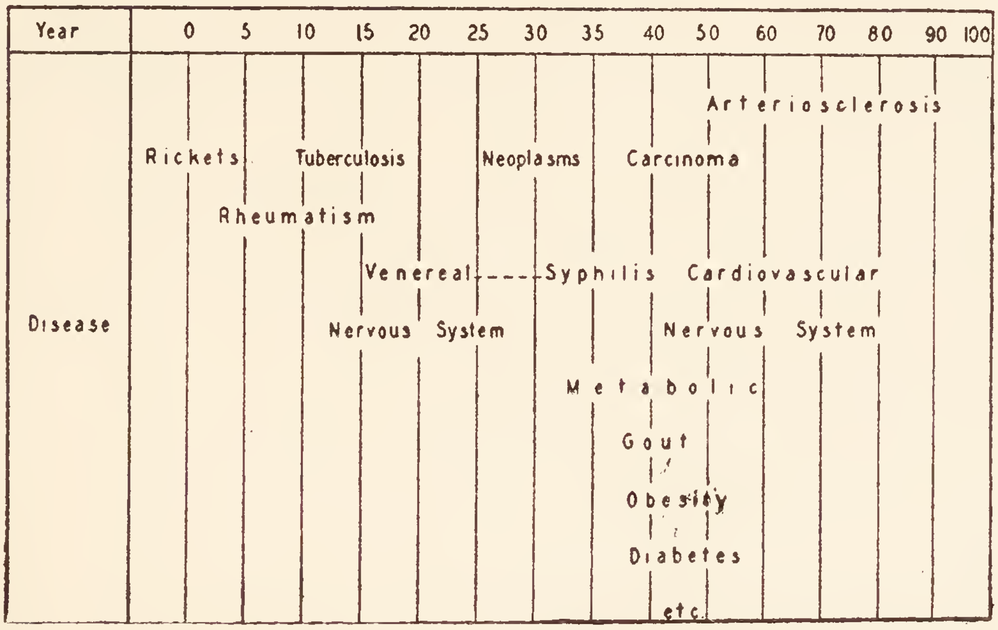


FIG. 20. CONCENTRATION OF PATHOLOGIC CONDITIONS IN VARIOUS AGE PERIODS.

The great frequency of infection with the tubercle bacillus in early life is, however, not to be regarded as due to any increased predisposition of the child's body to this infection but rather to the greater exposure to infection because of the child's habits in crawling, putting objects into its mouth, etc. That the physiologic predisposition changes with the build and physiologic processes of growth is shown by the fact that rickets beginning in the first half-year of life affects the cranium, then the ribs and the long bones; while "pigeon breast" and bowed limbs characterize the rickets of the second and third years. Spasmophilia is another condition that asserts itself in different forms in different stages of the developmental period.

The association of carcinoma with the senescent period is so striking that cancer is regarded by many as a disease of senescence. It does not, however, occur in all old people, as does arteriosclerosis; it is not a primary involution process, and not a biologic retrogression; it, therefore, is not an essential feature of old age, but, as has already been pointed out, it is dependent upon an inherited pathologic anomaly of constitution, that like gout and other metabolic anomalies, asserts its development coincidentally with senescence, hence its concentration in this period.

TERMINATION OF THE INVOLUTION PROCESS IN NORMAL DEATH

WHEN the involution of the organism has reached such a degree of functional lowering that any one of the vital functions cannot carry on, then *normal* or *biologic death* takes place, and the career of the individual human organism is closed. As we said earlier in this discussion such a biologic or normal death is rarely achieved by man; he usually succumbs to influences of the environment or dies prematurely because of inherent pathologic defects in his organism. Assuming, however, a case in which an individual achieves a natural biologic death, two leading questions arise: When will such a biologic death take place and how is it brought about? What is the natural limit of human life? By many biologists it is theoretically placed at about one-hundred years, but some old people reach natural death ten to twenty years earlier, while a small number exceed this limit by a number of years. It has been estimated that an animal should live from five to seven times the period of growth; applying this law to man he should have a life limit of one hundred to one hundred and forty years. Observations made on different animals, however, do not support this view. Observations on man himself have led some biologists to accept the general principle that for man the period of development lasts thirty years, that of maturity thirty years also, while that of involution requires the same time; therefore, the full life span for man should normally be ninety years. This is probably close to the actual facts; but the individual variations are so great and the differentiation of a natural intrinsic death from a pathologic extrinsic one so difficult that we possess no large amount of pathologic knowledge in regard to this point. Nevertheless, deaths do occur in the aged that we must ascribe to the primary lesions of senility alone, as all evidence of extrinsic disease is absent. It is a well-known fact that sudden death in old people is not uncommon during the enforced rest following a cataract operation. When allowed to get up or move about, the atrophic heart, which has lost tone through the period of inactivity, cannot recover its oxygenation power, and there then ensues an acute inadequacy of the myocardium which results in dilatation and sudden death. The only lesions of any significance found in some of these cases are those of old age: more or less coronary sclerosis, atrophy and fatty degenerative infiltration of the heart muscle. Precisely the same conditions will be found in the hearts of old people who have died quietly in bed. It is fair, I think, to ascribe these deaths to senility, although such a term is not an accepted designation as a cause of death. In my pathological experience of thirty-eight years I have seen not more than twenty-five autopsies in which I felt that the pathological diagnosis of pure intrinsic senile death could be justified, and all of these were due to myocardial atrophy and inadequacy. In these cases the degree of coronary sclerosis was not so marked as to give it the value of the exciting cause of the changes in the myocardium. In one case examined, that of an old man in the late nineties, who showed practically no sclerotic changes in any of his arteries, the only *pathologic change* found in any of his organs was that of a *marked simple atrophy* in the heart leading to cardiac insufficiency, arterial anemia and marked passive congestion. Personally, I would regard *myocardial atrophy and inade-*

Of every 100 human beings born	According to Hufeland (1800)	According to Silbergleit (1900)
Living to the 10th year	50	65
" " " 20 "	30	60
" " " 30 "	20	58
" " " 40 "	14	55
" " " 50 "	9	40
" " " 60 "	6	12
" " " 70 "	4	8
" " " 80 "	2	4

Fig. 21. Expectancy of the Duration of Life in Different Decades in 1800 and 1900, According to Hufeland and Silbergleit.

quacy as the most probable natural terminal lesion. The purely senile death should be, therefore, a *cardiac death.* The vital function of the circulation is more likely to cease before that of respiration or of the central nervous system.

The cause of intrinsic biologic death is intrinsic within the cell, and is an inherited character, *fixed* for the given species in the given period of evolutionary development. Few individuals will attain it because of the varying environment and the individual varying intrinsic reactions to the environment. The average equation resulting between these two factors brings about a life limit shorter by fifteen to twenty-five years than the theoretical biologic limit of one hundred years. This fact has tended to fix in the popular mind the Psalmist's *threescore and ten* as the ideal term of human life. But only a small per cent of human beings born alive can hope to attain even this. Out of every one hundred human beings born alive, only about 4 to 8 per cent pass the sixtieth year. Twenty per cent die in the first year of life; by the age of twenty years 40 per cent have died, and only 2 to 4 per cent attain the age of eighty years (see Fig. 21). The lowered resistance of the body during the period of senescence, and the pathologic conditions secondary to and dependent upon the tissue lesions of involution are the causes responsible for the rapid increase in the death rate after the peak of maturity has passed.

If atrophy of the individual cells of the organism be the tissue lesion invariably associated with intrinsic death, and, as far as we know, the immediate cause of the functional failure of the vital organs, which is death, we may well ask as to the nature of this atrophy. We can only say that it is the *morphologic expression of the reduced energy processes* of the cell. Age is a phenomenon common to all the metazoan animals; in all the same morphologic expression of atrophy is a constant factor; atrophy and reduced energy go constantly hand in hand; hence the atrophic cell is the worn-out energy unit; atrophy is the visible result of the exhausted cell, it is not the cause of the loss of energy. The energy charge initiated at fertilization is gradually dissipated during the period of development, at first rapidly, then more slowly during maturity, still more slowly during senescence, until it is finally exhausted and the organism dies of old age. It has been estimated that the human organism requires about four times as many food calories for its energy processes, after the time of full development has been reached, as do other mammals. Human cells have, therefore, a much greater capacity for obtaining energy from food than the cells of other mammals. The number of chemical transformations possible to a cell are limited; after the expenditure of this number physiologic death ensues. The greater the number of such chemical transformations possible to the cells of any animal, the longer the life limit of that animal. Man's longer limit of life is probably due to the fact that his cells can make a greater number of chemical transformations than those of other mammals.

PATHOLOGIC DEATH

WE have already remarked that by far the great majority of human beings die a *pathologic death,* that is, death resulting from an unfavorable action on the part of the environment (*extrinsic pathologic death*) or as the result of inheritable defects in the germ plasm (*intrinsic pathologic death*). The causes of extrinsic pathologic death are to be found in disturbances of nutrition and oxygen supply, overwork and underwork, the pathologic action of heat, cold, light, radiant energy, electricity, changes in atmospheric pressure, effects of mechanical force, chemical action or poisoning, infection, meteorologic influences, sociologic and psychologic influences. Extrinsic pathologic death may occur at any time in the life history of the individual, in embryonic or fetal life, during the extrauterine developmental periods, during maturity or in the senescent stage. Theoretically, the various forms of pathologic extrinsic death are preventable; and it is the prevention of such deaths due to extrinsic causes that has almost doubled the average longevity rate since 1800. Against all of the unfavorable factors of the environment modern sanitary science and hygiene are conducting a fight that eventually will bring the average life limit up to somewhere between fifty-five and sixty years.

Intrinsic pathologic death is inherent in the germ plasm and manifests itself in the form of *inherited disease,* or as a *mutation,* or as the result of *blastophthoria.* The prevention of pathologic intrinsic death becomes, therefore, wholly a genetic problem; it can be prevented only by a breeding-out process. As an example the inheritance of early arteriosclerosis may be taken. It is a well-known fact that in certain families the individual members have a limited period of existence, they die of a premature or early old age, dependent upon a premature sclerosis of their blood vessels. Among the intrinsic pathologic causes of death is to be reckoned also cancer, which is dependent for its development in any given individual upon the presence of an inheritable cancer susceptibility. While the total number of deaths due to intrinsic pathologic causes is much less than those produced by extrinsic causes yet the fact that cancer is included in this category makes the number very high in the senescent period of life. In general, we may say that pathologic intrinsic death embraces all deaths that are due to intrinsic pathologic conditions of the constitution, to intrinsic susceptibilities of the organism, and to intrinsic anomalies of the individual organs and tissues. All of these represent a lowered value of the germ plasm, some of them possessing indeed a *lethal* value. They constitute abnormalities of the germ plasm acquired by it through the action of the environment long ago in the developmental history of the particular line of germ plasm involved. Only through practical eugenics has preventive medicine any power of lessening or preventing the results of these intrinsic changes in the germ plasm, once they have been established.

THEORIES OF SENESCENCE

CURIOUSLY enough many medical men of the last century, lacking the wisdom of David and Solomon in recognizing that the life of man has a definite normal limit, have regarded the aging process as a progressive disease; according to Brown-Séquard caused by sclerotic changes in the vessels, according to Metchnikoff by intestinal putrefaction, according to Victor Horsley by degeneration of the thyroid gland; while Lorand and numerous followers of his believe that it is caused by the degeneration of all the ductless glands, particularly the thyroid, adrenals and gonads. The modern scientifically trained biologist, however, cannot look upon senescence and old age as disease processes but regards them as a physiologic entity, the result of involution processes inherent in the organism. The exact mechanism of this involution is, of course, the great problem, and concerning this there are various opinions. Weismann was the first biologist to recognize the intrinsic nature of biologic death and to interpret senility and natural death as having been acquired through natural selection as characters of advantage to the species as a whole. Minot extended the view of senescence and death as natural processes inherent within the cell, explaining them as due to the gradual loss of the energy stimulus which is supplied to the developing organism at fertilization, through its expenditure in cell growth and differentiation, until finally none is left, and the organism dies of old age. The individual is old at the age of twenty-five; in Minot's view the mature young man and the very old one are living but a very little above the dead line. Maturity is senescence according to this view. Minot failed utterly to grasp the fact that in maturity the cerebral function curve steadily rises; he had no conception of maturity. His mental attitude toward life is wholly that of the embryologist, life to him is measured only by the energy of growth and differentiation, never by the higher expenditure in function. Surely function is as much a measure of vital energy as is cell growth. According to Childs senescence and rejuvenescence are both going on in all cells all the time, and are not special processes. Death of cells from old age takes place at every stage of development, and at the death of the organism many cells are in a young state and possess the potentiality of continued growth. Life is not always a continuous progression, but regeneration or rejuvenescence of cells is constantly taking place, such regeneration retarding the aging of the tissue or organ as a whole. In the higher animals the progressive features are predominant and death ultimately results. Senescence in man is more continuous than in the lower forms. Death in man results from the death of the central nervous system which always dies first as it is the least capable of rejuvenescence through regeneration. Loeb's contribution to the discussion of the problems of life and death is essentially chemical. Death may not be inherent in the individual cell but may be only the fate of a complex organism in which the different parts are interdependent. Certain cells are able to produce substances that have a toxic action upon some vital organ, or some substance necessary to life is destroyed or reduced. Death is the result of the cessation of respiration. Pearl, on the basis of transplantation experiments and the culture of tissue cells, holds that death is not an inherent consequence of life, even in somatic cells, but that potential longevity inheres in most of the different kinds of cells for the metazoan body except those that are extremely differentiated for peculiar function. Cells in culture *in vitro* do not grow old. Characteristic senescent changes, he thinks, are not found in them. The reason that all the essential tissues are not actually immortal in multicellular animals is that the individual parts do not find in the body the conditions necessary for their continued existence, each part being dependent upon other parts. Pearl's view is directly contradictory to that of Minot that there is a specific inherent lethal process within the cells themselves that causes senescence. According to Carrel senility and death result because in normal conditions the blood does not succeed in washing away waste products, and after growth has been attained the blood undergoes progressive changes whereby it comes to lack the dynamic power of youth, and becomes senescent in character, inhibiting growth. The result is a gradual slowing of cell growth, which is progressive aging and death.

Summing up all of the modern views as to the nature of the mechanism of the aging process we find that they agree, in the main, that age is due to a loss of growth energy, so that the cell loss exceeds the regenerative powers, and numerical and quantitative atrophies ensue. This loss of cell energy of growth is due, according to different workers to:

1. Increase of specific growth-inhibiting factors.

2. Decrease of specific growth-stimulating factors.

3. A combination of the two preceding causes, both acting conjointly.

As to the source of these hypothetical specific substances there are wide variations of opinion, as follows:

a. Physicochemical changes in the blood serum (senescent serum).

b. Changes in the physicochemical equilibrium of the organism (changes in the colloid states, in the water content, in the P_H, acidosis, alkalosis, etc.).

c. Accumulation of toxic waste products of metabolism (chronic fatigue, autointoxication).

d. Endocrinal disturbances, either a hypoactivity, hyperactivity, or dysfunctional production of abnormal growth-inhibiting substances, disharmony in the pluriglandular endocrinal complex, loss of energy power due to the loss of specific rejuvenating substances produced by the interstitial cells of ovary and testis.

e. Disturbances of the intrinsic conditions of the metazoan organism associated with differentiation of cell function. Loss of differentiation power, reversal of growth processes due to nutritional factors, change in cell environment, etc.

A detailed critical review of these theories is not possible within the limits of this book. In general they are all built upon insecure foundations, hypothetical substances and hypothetical changes that may be due to the processes of senescence and not its cause. Not a single one of all the theories of senescence so far offered has a leg to stand upon; for the greater part they are pure hypotheses constructed about some single fact, such as the increased growth-inhibiting power of the senescent's blood, the cultivation of somatic cells in vitro, changes in the P_H, loss of water content or some other uncorrelated observation. Much has recently been made of the cultivation outside of the animal body of tissue and organ cells. A potential immortality has been claimed for the somatic cell as well as for the germ cell; because of this, biologic hints of the possible immortality of the soma are thrown out by overenthusiastic biologists and journalists. It is a great temptation to enlarge upon this subject, but it is perhaps futile to pursue arguments aggressively for which there is so little, or no, biologic foundation. The cultivation of tissue cells *in vitro* has precisely the same broad biologic significance as the cultivation of neoplasm cells. It is a pathologic situation, and not a biologic one. Further, all of the theories of senescence just mentioned are fundamentally wrong in that they look upon the phenomena of involution shown in senescence as in any way different from that of the involution of the temporary organs and tissues shown in early embryonic development, throughout the period of fetal life, the early periods of extrauterine development, and in fact throughout the whole period of existence of the organism. There is no difference in *kind* in any of these localized involutions, they take place to get rid of *parts that have fulfilled their use;* the *very same factors* come into play when the organism has completed its function and must be removed from the scene; it is only a question of *time* and *degree* of involution. Senescence cannot be considered as a physiologic entity belonging to the latter period of the metazoan organism, for it is operative in all periods of development. *Evolution* and *involution* are inseparable processes and go hand in hand from the time of the union of sperm cell and ovum. The discarding of the polar bodies, the loss of the tail of the sperm, the very act of fertilization, are prophetic of future involutionary processes in the life of the organism. The senescent processs is potent, therefore, from the very beginning, and grows in volume and extent in proportion to just one thing, the *fulfillment of function.* None of the theories of senescence just detailed is applicable to these *earlier and localized senescences;* if they cannot be fitted to the explanation of these, they cannot be applied to the explanation of the *major senescence.* It is evident then that *involution* is a biologic entity equally important with *evolution* in the broad scheme of the immortal procession of life. Its processes are as *physiologic* as those of growth. It is, therefore, inherent in the cell itself, an intrinsic, inherited quality of the germ plasm, and no slur or stigma of *pathologic* should be cast upon this process. What its exact chemicophysical mechanism is will be known only when we know the nature of the *energy-charge* and the *energy release* of the cell. We may say, therefore, that *age, the major involution, is due primarily to the gradually weakening energy charge set in action by the moment of fertilization, and is dependent upon the potential fulfillment of function by the organism. The immortality of the germ plasm rests upon the renewal of this energy charge from generation to generation.*

EXTENSION OF THE LIFE LIMIT

EXTENSION of the life limit of man is so strongly desired by the average individual that he is easily carried away by the overenthusiastic proponents of the new movement for periodic health examinations into very mistaken conceptions of the actual possibilities of the case. It is true that the average longevity of human beings in America has been raised from thirty-five years in 1880 to forty-two years for the male and forty-seven years for the female in 1910, and to fifty-four plus years for the male and fifty-six plus years for the female in 1920; but this fact does not warrant the prophecies that have been broadcast that the average longevity will be raised to sixty-five years in 1930, and to seventy-five, eighty and still higher life averages in future decades. One enthusiastic medical lecturer upon this subject has been so wrought upon by the spirit of euphoric prophecy, as to declare that life averages of one hundred twenty-five or even one hundred forty years are not beyond the reach of the human race in the next century or so. Such statements

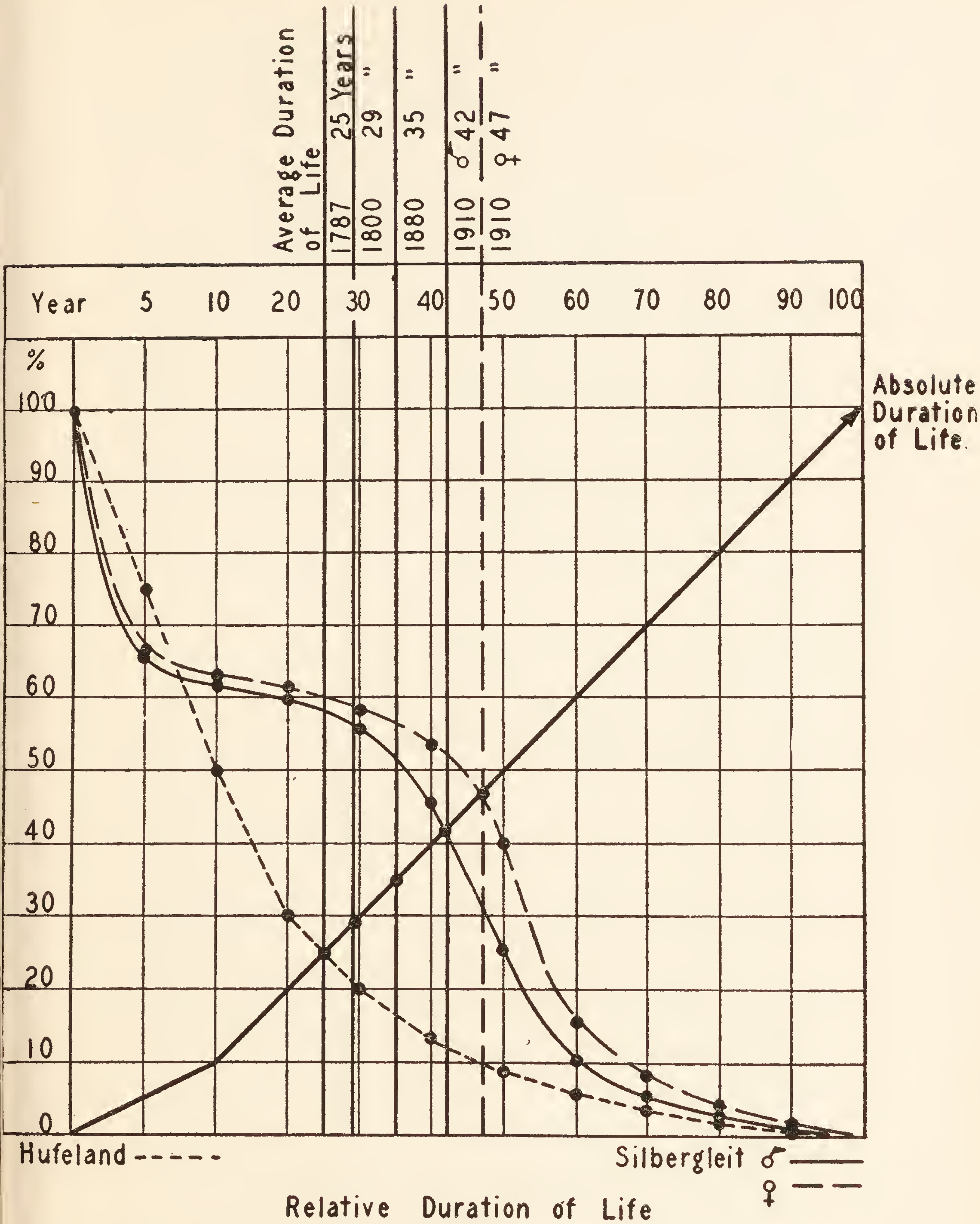


FIG. 22. RELATIVE DURATION OF LIFE, ACCORDING TO SILBERGLEIT.

as these are unscientific and absurd. It will be seen from the charts in Figures 23 and

Senile Survivors, Both Sexes in America According to Census Reports of 1880, 1890, 1900, 1910, and 1920.
(Census Report, 1920, Vol. II page 154.)

	1880	1890	1900	1910	1920
80–84	146,362	203,851	251,512	321,754	402,779
85–89	49,835	75,240	88,600	122,818	156,539
90–94	16,100	23,645	23,992	33,473	39,980
95–99	4,763	5,648	6,266	7,391	9,579
100 and over	4,016	3,981	3,504	3,555	4,267

Fig. 23. Senile Survivors in America, According to Census Reports of 1880, 1890, 1900, 1910 and 1920.

Total Survivors at Ages 80-89 and 90–100 According to Census Reports.

Age Decades	1880	1890	1900	1910	1920
80-89	196,197	279,091	340,119	444,572	559,318
90-100+	24,879	33,274	33,762	44,419	53,826
Ratio of Survivors at Ages 80–89 and 90–100+ to Total Population for Same Periods.					
80-89	.0039	.0044	.0045	.0048	.0053
90-100+	.0005–	.0005+	.0004+	.0005+	.0005+

Fig. 24. Ratio of Senile Survivors to Total Population in Decade Ninety to One Hundred Showing that Modern Life Has Not Increased the Biologic Span of Life.

24, that the increase in the average longevity is due to the saving of life through the prevention of extrinsic pathologic death in the earlier decades of life, but that there has been no extension of the normal or biologic life limit. The last five United States Census Reports show that while there is an increase in the number of senile survivors in the eighty to eighty-nine decade in 1920 over that of 1880, there is practically no increase in the ratio of senile survivors to the total population in the ninety to ninety-nine decade during the same period of time. The improved hygienic conditions of modern life have not increased the number of senile survivors after the age of ninety. This is in harmony with our view; modern preventive medicine and hygiene have not extended the biologic life limit, and cannot do so. All that has been accomplished in the direction of life extension is to raise the average longevity through the numbers of lives saved in the earlier decades of life. This has increased the *expectancy of life at birth*, and ensures an *average* longer duration of life. The expectation of life at birth in the original registration states was for white males in 1901, 48.23; in 1910, 50.23; and in 1919–1920, 54.05 years, representing a gain of 5.82 years; for white females it was in 1901, 51.08; in 1910, 53.62; and in 1919–1920, 56.41 years, a gain of 5.33 years (see Fig. 25).

Expectation of Life at Birth.

O. R. S.	1901	1910	1919-20	Gain
White Males	48.23	50.23	54.05	5.82
White Females	51.08	53.62	56.41	5.33

Average Longevity for White Males and Females in the Original Registration States, United States Census Reports for 1901, 1910, 1919-20, Showing a Gain of 5.82 Years for White Males and 5.33 Years for White Females.

Expectation of Life at 50 Years.

1840 —	19.00
1901 —	19.94
1920 —	20.35

A Negligible Gain in 80 Years.

Fig. 25. Expectancy of Life at Birth and at Fifty Years.

On the other hand the expectancy of life for age periods over fifty years for white males and females in the original registration states, as shown by the United States Census Reports of 1901, 1910 and 1919–1920 shows a definite *loss* of expectancy of life in the males over eighty years and in females over eighty-seven years (see Fig. 26). Calculations based upon the aggregate show

	1901		1910		1919–20		Loss or Gain	
Age	Male	Female	Male	Female	Male	Female	Male	Female
52	19.40	20.48	19.02	20.29	19.91	20.79	+0.51	+0.31
57	16.16	17.12	15.77	16.84	16.51	17.27	+0.35	+0.15
62	13.17	13.99	12.85	13.70	13.38	14.01	+0.21	+0.02
67	10.48	11.13	10.25	10.89	10.56	11.11	+0.08	−0.02
72	8.11	8.64	7.95	8.46	8.17	8.66	+0.06	+0.02
77	6.09	6.54	6.04	6.41	6.17	6.61	+0.08	+0.07
82	4.54	4.89	4.56	4.78	4.53	4.98	−0.01	+0.09
87	3.39	3.63	3.49	3.61	3.21	3.70	−0.18	+0.07
92	2.54	2.67	2.70	2.67	2.10	2.63	−0.44	−0.04

FIG. 26. EXPECTANCY OF LIFE FOR AGE-PERIODS OVER FIFTY YEARS, SHOWING LOSS OF EXPECTANCY OF LIFE IN MALES OVER EIGHTY YEARS OF AGE AND IN FEMALES OVER EIGHTY-SEVEN YEARS.

a gain in the expectancy of life at fifty years of only 1.35 during the last eighty years, a practically negligible gain (see Fig. 25). In spite of the gain in average longevity, there can be no doubt that the expectancy of life at the higher decades is actually falling. Thus in Figure 27 it will be seen that the expectancy of life in Massachusetts males in 1920 showed a loss of nearly half a year under that in 1910. If the average age of longevity be raised to sixty years this will probably be as high as the rate can be raised. That it can be raised to sixty-five or seventy-five years is impossible on the face of it, inasmuch as such an average rate would mean that the whole of the population living would have to reach sixty-five or seventy-five years. It is, therefore, neither possible nor probable that the average longevity can be raised to the heights prophesied by the over-zealous and very inaccurate advocates of life extension. The biologic limits of life will remain as before, fixed for this period of racial evolution, and what is more likely to take place in the next evolutionary phase is a *shortening of the biologic limit of life* rather than its lengthening. It may be that this shortening of the span of life has already begun. If the dangers of the environment be so reduced by the

Age Period	Change in Expectancy of Life 1890-1920
0-21	+ 2.77
22-52	+ 1.57
52-72	+ 0.44
72-Death	- 0.40

FIG. 27. LOSS OF NEARLY ONE-HALF YEAR IN EXPECTANCY OF LIFE IN MASSACHUSETTS MALES AT AGE OF SEVENTY-TWO, IN 1920, AS COMPARED TO 1890.

conditions of modern life that we save increasing numbers of the unfit as well as the fit, to fill up the middle decades of life, so as to increase the number of dependents in their senescence there may be brought about through the action of evolutionary factors an actual shortening of the biologic life limit instead of its prolongation. If the struggle for existence of the species is made easier, if more individuals reach the reproductive age, if fewer children are born, but if more children are born to *survive*, if the period of caring for the progeny is shortened, theoretically the next evolutionary period should see a shortening of man's normal life limit. Thus from two points of view the principle of life extension may ultimately defeat its own purpose.

MORE than thirty years after Brown-Séquard's first experiments, made in 1889, in the direction of establishing a relationship between senility and the production of sex hormones by the sex glands, this subject has again come to the fore in the active controversy that has centered about the so-called "rejuvenation" produced by testicular transplantation (Voronoff) and ligature of the vas deferens of the testis (Steinach). An immense mass of literature has accumulated, with results so contradictory that positive statements one way or the other cannot be made at this time as to the real status of the questions of the regeneration of sexual activities by these methods of transplantation and ligation. If anything does result from these procedures it is quite evident that it is nothing more than a re-erotization, associated with certain evidences of increased energy of the general metabolism. There is no evidence that the transplanted testis produces any secretion by living cells; what effects are produced are the results of resorption processes.

The most recent workers agree that the Voronoff operation, aside from the psychical influence on the patient, is without any specific effect, either on the sexual life or on the process of senescence. That there could possibly be any arrest of senility, or a rejuvenescence in the broad sense of restoration to youth, by the Voronoff operation is in the very nature of things an absurdity. Age is a quality characteristic of all cells and tissues in the human body; the cell changes of age are irreversible. There has been no evidence offered to show that either the Steinach or the Voronoff operation has abrogated the cell changes of senility, or has done anything more than to accelerate in some cases a dying sexual function and certain features of the general metabolism connected therewith. The only functions affected are those which depend upon sex hormones. In other words the so-called rejuvenation produced by the sex hormones of the transplanted testis or by ligation of the vas is no rejuvenation in any sense of the word but is a re-erotization wholly.

It is a sad commentary upon the mentality and character of the senile human male that he should seek such a re-erotization of his failing function. Such a process is not without its hazards; it is another example of the dangers of putting new wine into old bottles as has been shown by the sudden deaths of a number of re-eroticized old men. The question of the effect of ligating the vas deferens, whether due to increased hormone production by the interstitial cells, as Steinach supposes, or to the resorption of the products of decomposition of the seminal epithelium, as claimed by other observers, cannot be said to be fully settled, although evidence is accumulating to the effect that the interstitial cells are not glands of internal secretion, but represent specialized reticulo-endothelial cells concerned in lipoid metabolism, and bearing in their size and prominence an inverse relationship to the function of spermatogenesis. We may, therefore, be assured that there is *no rejuvenescence possible for the senile individual;* and that the idea of physical rejuvenation is but a myth of ancient lineage disguised in quasi-scientific garments.

WHAT philosophy then may we draw from this! Is old age inevitable? Yes, escape from it is possible only for those who meet a premature pathologic death. For those who live to their biologic life limit age cannot be escaped. *Nor can it be deferred. Nor is rejuvenescence possible.* The deferring of old age, the rejuvenating of the senescent individual is but idle and foolish talk, and we have had much of this in the last decade. What modern medicine has accomplished along the lines of hygiene and the prevention of disease has been only to increase the number of human individuals, both the fit and the unfit (unfortunately too many of the latter kind) who come to maturity and to the period of senescence. More individuals will achieve their biologic life limit; and this means what? Ultimately a much greater increase in the number of senile, more or less useless, human beings in the age decades of the eighties and the nineties. There will be some increase in the number who will reach the age of one hundred years or even pass it, due to their own family inheritance, but this number will not be greatly increased in the present period of evolution. But what advantage is gained for the individual or for the race by increasing the number of human dependents in the period of their second childhood! Does this thought never occur to the enthusiastic propagandists for the extension of life? I have never seen it mentioned in the literature of such propaganda.

But if age is inevitable, what shall be done about it? Meet it, of course, with courage and common sense, as something in the day's work, not pleasant wholly, but as the final turn of the screw, to be endured with that fortitude that in enduring acquires a quality of satisfaction. Moreover, the possibilities of a normal old age are great; it is the period of ripeness of experiences and observation, of the contemplation and philosophical evaluation of the world about us, of quiet brooding and the creative possibilities engendered by such. The compensations of the seventh and eighth decades are many because of the longer preservation of the spiritual and mental functions over that of the other functions. There is an old folk-word: "The first joys of life are those of the

FIG. 28. ADVANCED SENILITY. WOMAN OF NINETY-FIVE YEARS OF AGE, SECOND CHILDHOOD, SENILE DEMENTIA, FACIAL PARALYSIS, CATARACT IN LEFT EYE, ACNE ROSACEA, AND MALIGNANT HYPERKERATOSES.

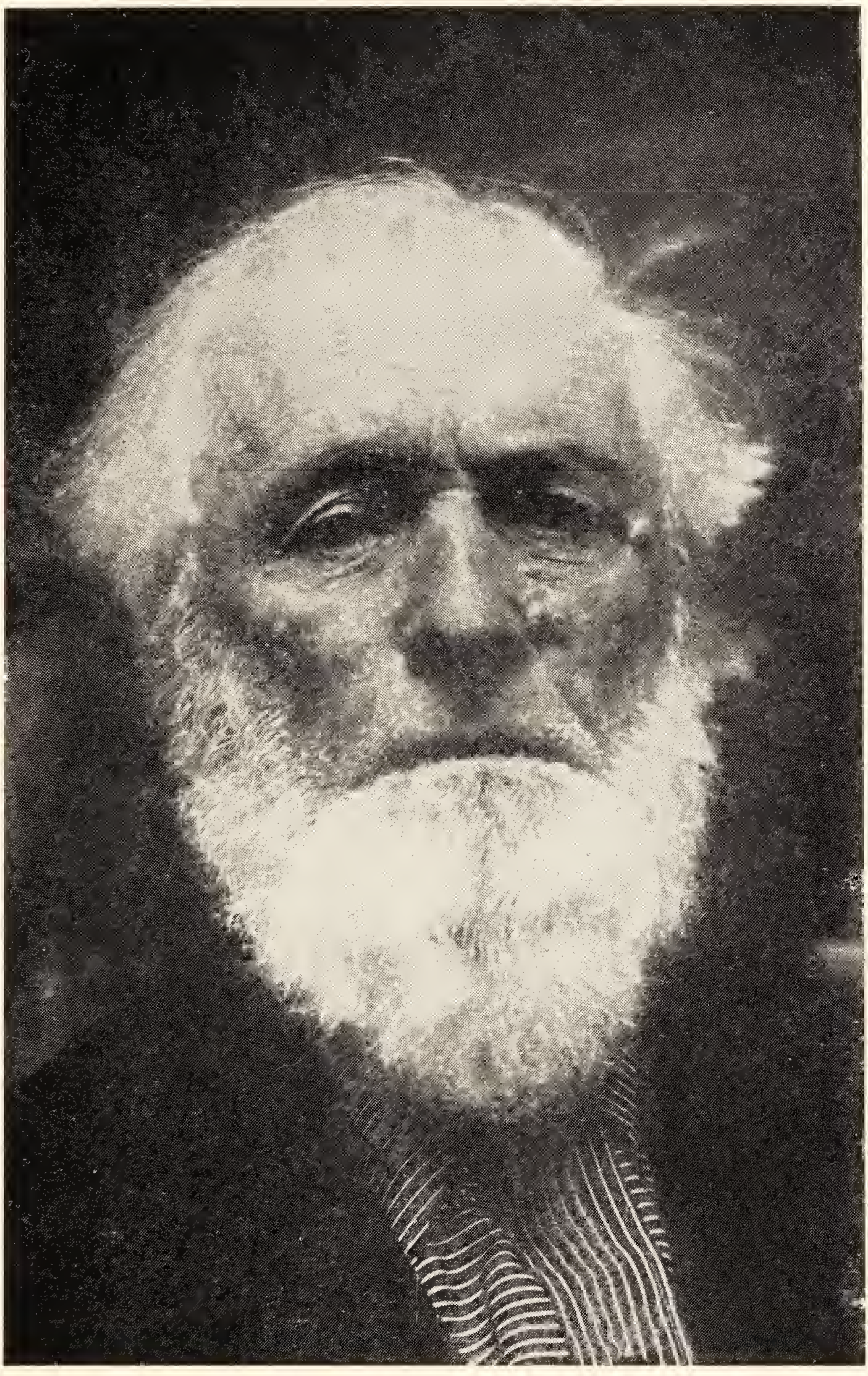


Fig. 29. The End of the Play. Man of Ninety-eight Years of Age, in Complete Second Childhood, with Multiple Malignant Senile Hyperkeratoses over Face and Body.

belly, the last ones those of the mind, but the fool knows none but those of the belly." Since the mental powers are preserved longer than any other function in senescence, happy is that man who comes into his old age with the capacity for intellectual pleasures fully developed, not in one line alone, but in many, in literature, art, music and science. If he has developed hobbies in any direction so much the better, and much better still if he has a number of hobbies and not merely one. Diversity of interests keeps the mind young; the passing from one interest to another freshens, rests and revivifies the mental processes. Creative mechanical work of some kind offers one of the best outlets to the old man's restlessness; and of all the occupations that may offer, that of gardening, of growing and planting and tending growing things, is the very best form of exercise and avocation adapted to the needs of the aged individual. There is also a very definite psychologic relationship shown in this return of the old man to the soil.

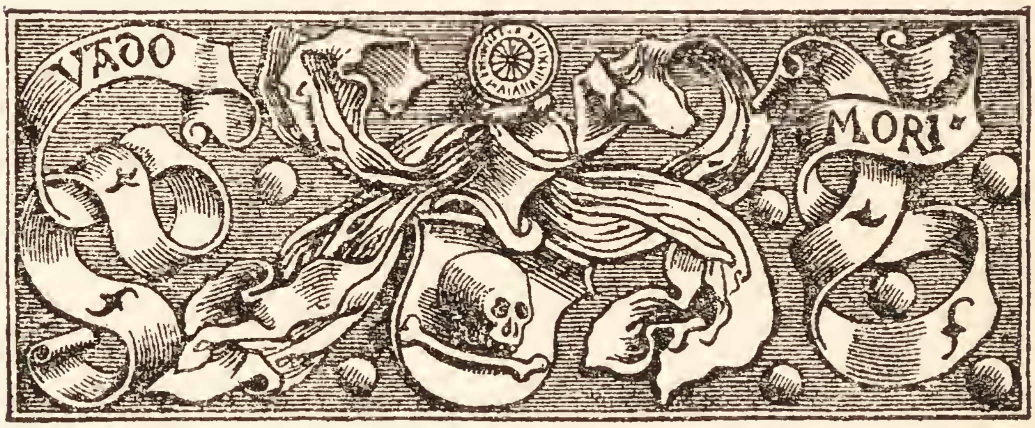
As to the hygiene of the period of senescence little need be said here. The question of food should settle itself for any intelligent person; one should eat sufficiently, but not too much, of whatever he desires; the bad psychologic effects of dieting should be avoided. One quickly learns how much and what one should eat, if one is to be comfortable, and it is best to follow that criterion. Important is the conservation of energy by resting regularly and frequently. Fatigue should be avoided above all things. On the other hand, the tonus of the heart muscle can be kept up only by daily exercise. Enforced rest is dangerous for the senescent, particularly if he has any degree of coronary sclerosis. After the sixty-fifth year the exercise of the sexual function is best relinquished; at any rate it should never be forced. The closing of this chapter is the most difficult period of the senescent's changing life, and great restraint and self-control are needed by many men at this time. Particularly unfortunate is he who retains and nourishes a psychical desire when physical potency is gone. The borderland between normal and pathological may become poorly demarcated in such cases, and old age may terminate in psychical wreckage.

There may be individuals who wish to live to the very limit of their biologic allotment, to pass the last decade or two of their descent to the grave in uselessness, nonproductive existence, dependency, in personal discomfort, and a burden to others. I personally am not of that sort. Rather the limit set by the Psalmist:

> The days of our years are three-score years and ten; and if by reason of strength they be four-score years, yet is their strength, labor and sorrow; for it is soon cut off, and we fly away. [Psalm 90, verse 10.]

In a life well ordered and well spent, of varied mental and physical activities, the break in cerebral function comes in the average case somewhere around the seventieth year, and the rapid down-hill descent is usually not apparent until after the seventy-fifth year. From this, of course, there are wide individual variations. But with mental powers still preserved this period from sixty-five to seventy-five may be one of satisfaction and happiness, even of cerebral productiveness. Happy then is the senescent who can approach his inevitable end with a normal rate of involution, still capable of intellectual pleasures, and the mature contemplation thereof, to meet a speedy release before the unhappy days of second childhood are upon him.

"Whatever is natural must be accounted good. When death comes to youth, Nature is up in arms and revolts. Yet to old men, what is more natural than dying?"—"CICERO, De Senectute."



"The eternity of things is connected with the reciprocal interchange of generation and decay; and as the sun, now in the east and then in the west, completes the measure of time by his ceaseless revolutions, so are the fleeting things of mortal existence made eternal through incessant change, and kinds and species are perpetuated though individuals die."
—William Harvey, "De Generatione."

"Keine Kunst ist's, alt zu werden, Es ist Kunst, es zu ertragen."—Goethe

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