ON THE NATURE OF OLD AGE AND OF CANCER.

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AMONG the many facts which have been gathered together about cancer, I suppose that none is more striking than its close association with the degenerative periods of life. But, though particular attention has been given to this peculiarity, its bearing on the pathology of cancer is apparently not yet understood. The most obvious interpretation is that the cancer itself is nothing more than a manifestation of old age. But to all appearances so inconsistent are the cancer characters with those which distinguish the old age change, that such an explanation is too improbable to be entertained. Nothing, indeed, seems more unlikely than that the vigorously growing cancer cells, pushing the tissues before them or threading their way along the lymph spaces, should be smitten with the same blight as that which accounts for the ever-increasing decay and incapacity of normal senescence. But a little consideration may serve to show that the comparison between the cancer process and the senile process is not quite so remote as appears on the surface.

Though much of the work that is being done upon cancer does not explain cancer, it tends to clear the way for an explanation. Thus it seems positive that, though cancer may be started by the operation of external agencies, its real origin is not extrinsic but must be looked for in the perversion of some intrinsic condition. This narrows the scope of inquiry considerably, for the intrinsic processes of the body capable of such perversion are few in number. Indeed, it apparently confines the search to one of the five basic properties of growth, development, reproduction, nutrition, and immunity.

In seeking for the clue to the pathology of cancer, probably each of these five processes has now been well scrutinized, and none more thoroughly than development, for there is much in development to suggest that it contains the explanation of which we are in search.

CANCER A DEVELOPMENTAL CHANGE.

One feature of cancer suggestive of a developmental origin is the variability in its rate of growth. Such variability seems to be spontaneous or innate and reminiscent of the changes which characterize development, some being diurnal, others seasonal, others marking an epoch of evolution, and yet others arising from more recondite causes. Hence when we see a mass of cells sprouting from one of the organs or surfaces of the body, and notice that for no apparent reason its growth is at one time quickened, at another retarded or even arrested, we are reminded of the rhythmical or cyclical changes of normal development.

Another suggestive circumstance is the way in which the rapidity or malignance of cancer is influenced by the development of its host. Generally speaking, the earlier in life the cancer begins, the more rapid is its course, the greater its malignance. In other words, its malignance is as a rule in inverse ratio to the age of the individual affected.

But nothing, perhaps, points more definitely to cancer having its foundation in some perversion of normal development than its origin in cells whose developmental career has been prematurely stopped.

When Durante and Cohnheim formulated the theory based upon this important fact we seemed on the verge of discovering the nature of cancer. But as a matter of fact we have failed to explain the pathology of cancer by any theory founded upon the phenomena of embryonic life. Yet, at the same time, we need not conclude that it is hopeless to seek for the origin of cancer in some perversion of development. Development is not a process which terminates at birth or at adolescence, or even at middle age. On the contrary, the declining periods of life are just as truly developmental as are the rising periods. Development is coterminous with life, and takes the form of a curve which first ascends to its summit in middle age and then falls to its cessation in death. If, therefore, we are thoroughly to explore the different phases of development in our search for the pathology of cancer, we can

hardly regard their possibilities as exhausted until we examine the nature of the changes which mark the decline of development and usher in old age and death.

Let us, therefore, for a time ignore cancer *quâ* cancer and turn our attention to normal old age. Indeed, it is only because it is possible to approach our subject from this aspect that this article is written, for the writer has a profound conviction of the hopelessness of attempting to storm the cancer position by a direct frontal attack. For if an army of investigators, led by men of supreme ability, able to devote much of their time to the task, have not as yet been able to conquer the position, it is not likely that any one without special knowledge or equipment will do so. But it is a different matter when an attempt is to be made to overcome the difficulty by a movement on the flank—by dealing with it as an incident or side-issue arising in the course of a study of normal old age.

NATURE OF THE SENILE CHANGE.

The usual conception of the senile change as mere disorganization and decay with no orderly sequence is essentially false. Indeed, one may safely commit oneself to the general statement that wherever among biological processes we see nothing but muddle or disorganization, we may be assured that the confusion is not in what we observe, but in our own minds. However mad the phenomena may appear, it is certain that there is method in them. Hence it must be our object to get behind the more obvious revelations of senile decay, to study its mechanism and to seek for the principle or motive by which it is directed.

The degeneration of old age is by no means equable, but, on the contrary, is very partial in its distribution. Thus, a man of 70 may die of senile decay, and yet many of his organs may to the naked eye, and even to the microscope, be as sound and as free from evidence of degeneration as the normal organs of a youth. Indeed, it is conceivable that the senescence which is responsible for his death may be confined to one organ or even to part of one organ.

Such inequality of distribution is comparable with the similar partiality displayed by ascending development when the maturation of one organ, such as that of sex, may lag far behind that of another organ, such as the stomach, or liver. Indeed, as we well know, the thymus may even complete its curve of development while the sex organs are still in their infantile stage. But, as a rule, the manifestations of old age are fairly widespread, though invariably certain organs are in advance of the others.

It must be obvious that if descending development be a reversal of ascending development, old age need not necessarily be expressed by protoplasmic shrinkage or disintegration. It might also be manifested by a tendency for the lower class cells, such as connective tissue cells, to assert themselves and to proliferate at the expense of those of higher degree. Moreover, it is highly probable that as the more advanced cells deteriorate they may resume old habits and once again begin actively to divide. As a matter of fact, old age is shown in each of these three ways—that is, in (a) decay, in (b) fibrosis, and in (c) proliferation.

(a) Decay.

The method which underlies and informs the process of normal senile decay appears to be briefly as follows:

In ascending development there is a procession of changes all tending towards increasing complexity both of form and of function. The man recapitulates his development, beginning with the unicellular existence and rising through successive stages of evolutionary progress, until at middle age he arrives near the summit of his own particular standard of progress. The machine is then working at its best, and though certain organs are still capable of further improvement and further complexity, the body as a whole begins its developmental decline. Life becomes once again more simple, and this retrograde change is to a large extent reversible, making for second childhood and second infancy on the one hand, and for a more simian structure on the other. But so partial is the distribution of this reversion, that in some parts it may reach a point corresponding with the embryonic stage, or the beginning of rising development, though in most respects the individual may still be in his prime. The grosser manifestations of second infancy are the outcome of finer changes in the tissues, whereby the cell at the end of

life tends to resume that simplicity which characterized its appearance and its functions at the beginning of life. In the beginning the cell constituents, no matter what the tissue or organ may be, are of an indifferent rounded pattern, and their low organization is indicated by their rapid multiplication. But as development proceeds the cells of each organ tend to assume a character of their own, while the initial proliferative impulse gradually slackens and ultimately stops. The development of the cell is apparently more or less of an accretion, the parts about the nucleus representing the earlier structure and being the seat of the more elemental properties, whereas the periphery of the cell inside the lining protoplasm represents later acquirements. It is the angles of the liver cell and the processes of the nerve cell which are distinctive, and in molecular degeneration it is these angles and processes which seem to be most vulnerable, the parts about the nucleus being most stable. Or, as it is sometimes said, "the nucleus exerts a trophic influence upon the cytoplasm" of the cell, so that, apart from the surface layer, the farther the cytoplasm is from the nucleus the less resistant is it and the more prone to degenerate. The nature of the changes which mark the senile regression of a cell are perhaps best demonstrated in cells of highest development. Thus the brain cell, in which development has reached its acme, is a giant with a complicated network of processes. But when the degeneration of old age begins this complexity of structure at first ceases to continue, then definite regression takes place, and as the advancement of the cell is an addition and a centrifugal process, so its recession is a subtraction and a centripetal process. There is a tendency for the cell projections to decay first, the central parts about the nucleus being unaffected until molecular changes have obscured the remaining cytoplasm.

As it is with the cell, so is it in principle with the different tissues and organs of which the body is composed. It is the higher types of cells which are the first to be stricken with senility, those of lower types escaping. This is true in respect to each organ, though it may not be true of the body as a whole. Each organ seems to have its own standard of longevity irrespective of the state of development of its distinctive cells, and the more highly developed, or more differentiated the cells of which it is composed the sooner and the more completely do they decay. Thus, in the brain of old age, while the cells of Betz are obviously deteriorating, the glial cells show renewed activity. So also in the case of the liver, of muscle, or of any organ in which the cells are highly specialized, the degeneration is a degeneration of the more advanced constituents, and does not apparently extend to the more humble elements.

(b) *Fibrosis.*

We have just seen that the cells of lower type under the influence of senile decay do not undergo molecular degeneration, but simply multiply. Hence, in a liver or a brain advanced in senility we expect to find decided increase in connective tissue cells. It might be said that this in itself is evidence of degeneration, seeing that it means a return of connective tissue to its embryonic state. But apparently this change is not reversible, inasmuch as these fibroblasts are capable of returning to their resting stage and becoming fully developed fibrous tissue. But if this multiplication of cells be not degenerative, what is its purpose? The most likely explanation is that it is a sanitary or scavenging change. The molecular decay of higher cells loads their protoplasm with degenerative products. But the presence of any effete substance in an organ whose lower elements are still vigorous stimulates into action the mechanism of phagocytosis. Dead or half-dead material cannot be permitted to encumber the tissues. The fixed connective tissue cells of the part, which are phagocytic, and therefore proliferate, combine with cells derived from the endothelium, with plasma cells and with lymphocytes from the blood and lymph vessels to clear away the debris. Hence in an organ advanced in senility we see all stages of simplification of higher cells on the one hand, and of phagocytosis on the other. The disorganization of the special cells rarely goes to such an extreme that they become mere shells filled with granular or otherwise disintegrated protoplasm, but as a rule they shrink into a much smaller compass and become

less angular or, it may be, even rounded in shape. And mingled among them are so-called "inflammatory" cells, which have sprung into being from adjacent indifferent tissues. These are the phagocytes, some of which are of connective tissue origin. These latter, when they have accomplished their task, apparently settle down once again into fibrous tissue, and, as they have already undergone proliferation, there is more fibrous tissue at the end than there was at the beginning.

The phagocytosis of old age was first demonstrated by Metchnikoff, and his observations have been confirmed and extended by his co-workers at the Pasteur Institute. Although this phagocytosis has been denied by some other investigators, it is claimed that the findings of Metchnikoff and of his school can be verified by any one who is scrupulous in the preparation of his sections.

It must not be supposed that such changes are invariably to be observed in the organs of those who die from senile decay. Nor is it necessary that the individual should be very aged. Indeed, there is reason to believe that the man who dies in a state of senile decrepitude at 70 will be more likely to show typical senile changes than the man who dies a centenarian. At whatever age death takes place no organ need be examined which does not show by its toughness and by its appearance that it is definitely senile. Moreover, on examining such organs under the microscope, though plenty of new fibrous tissue may be seen, it must not be expected that the phagocytes will necessarily be engaged in the task of phagocytosis. It is conceivable that the presence of protoplasmic rubbish, which acts as the stimulus or incentive to call them into being, is usually dealt with, in the first place, by the more versatile, more available, lymphocytes, and that it is only under conditions of stress or of chronicity that the connective tissue cells come into action. Neither must it be supposed that we shall often witness decayed cells surrounded by clusters of phagocytes actually engaged in the work of absorption, such as Metchnikoff pictures. The evidence is, as a rule, more circumstantial than substantial or direct, and consists in the presence of cells whose function is known to be scavenging and reparative in the vicinity of other cells laden with protoplasmic litter, or whose size and shape are consistent with the view that they have undergone circumferential reduction. On quite insufficient evidence such adventitious cells have been termed inflammatory cells. As a fact they are not the cells whose office is to cope with the organisms which give rise to inflammation. They are not polymorphs, but are the cells which usually gather about non-toxic dead material, and whose object is known to be sanitary and constructive. They not only clear away litter, but themselves form scar tissue, filling up vacant spaces, and being afterwards reinforced or replaced by the more permanent tissue of fibroblastic origin.

In short, if we put on one side the direct evidence of phagocytosis, there is a chain of presumptive evidence which is in itself pretty convincing. The links of this chain are the tough, stringy organs of old age; the signs of activity among cells known to be phagocytic; the fact that these phagocytes are such as are ordinarily called forth for scavenging purposes and for purposes of repair; the presence of other cells laden with just such material as it is the office of these phagocytes to clear away; the presence of cells of the same type in an atrophic or shrunken state; and, lastly, new fibrous tissue resembling scar tissue such as is usually laid down in any part of the body in which phagocytes are engaged in the work of absorption and repair.

Until Metchnikoff showed the true meaning of the round-celled infiltration in senile tissues the fibrosis was itself regarded as the dominant change, whereas in reality it is but an incident in senility. The fundamental change is neither decay, nor phagocytosis, nor fibrosis, but is regression. As age creeps on acquirements are lost in the order of their acquisition. The longer established the habit the greater its stability, so that towards the end of life the old man in his dotage lives in the memory of the events of his youth or boyhood, and recalls to his mind incidents which in his middle age had been forgotten. Simplification of form and of function keep pace one with the other, the latter being the inevitable outcome of the former. Regression, therefore, is the dominating factor in the old age change. The cytoplasm of the periphery of the cell, which represents the acquirements of the distinctive cell experiences, is the first to undergo disintegration. Molecular alteration, phagocytosis, proliferation, and the formation of new fibrous tissue are all secondary to the regression, and constitute its expression.

(c) *Proliferation.*

We have observed that the reversion of old age in the higher order of cells is accomplished by means of molecular decay; and that apparently this manner of degeneration does not reach down to the meaner cells, such as serve a mechanical purpose or act in the lowly

capacity of phagocytes. Between cells of highest degree, such as nerve, muscle, reproductive, thyroid cells, and those of lowest degree, such as connective tissue cells and leucocytes, is a group in which senility is revealed, partly by molecular changes and partly by proliferation. To this group belong the epithelia. Metchnikoff has pointed out that the epithelium covering the surface of the body does not cease to grow in old age. On the contrary, growth may even become more active as age advances, as is evidenced by the crop of hair which springs, like an aftermath, from the general surface of the body, by the redundancy of epithelium sometimes manifested in the shape of corns and of callosities on parts exposed to pressure, and by the appearance of other cutaneous outgrowths. Renewed proliferative activity may also be observed in the secreting cells of organs. Thus, the breast tissue of the female at the menopause does not solely shrink, but the onset of mammary old age and the cessation of function are indicated by renewed activity. This activity, as a rule, is mainly of the connective tissue; but now and then the epithelium is extensively affected, so that the whole gland may enlarge. Moreover, it is not a functional but a degenerative phenomenon, for it marks an accession in quantity and a recession in quality.

We see the same kind of change in the epithelium of the kidney. As a rule here, too, it is the connective tissue elements which chiefly increase, but sometimes senile decay is shown by epithelial overgrowth, the redundant, more or less altered, epithelium being exuded from the tubules in the form of casts. Any one who takes the trouble minutely to examine the organs of those who die in a state of senile decrepitude will not uncommonly observe these changes. Degeneration of this kind may even become so advanced as to cause enlargement of the kidney.¹

Similar multiplication occurs in the liver, for in the senile liver, while some of the cells show molecular decay and fibrosis, others are often to be detected in the act of dividing. This growth, as a rule, is slight or moderate in degree, but occasionally it becomes more pronounced, giving rise almost to adenomatosis and merging gradually into the proliferation of cirrhosis. Senility may be manifested in a similar way in bone. Thus Rindfleisch² has shown that there is renewed periosteal activity in old age, leading to thickening of the lower-class elements of the periosteum on the one hand, and to absorption of the more differentiated bone tissue on the other. The bone, in fact, reverses its development. Reversion, moreover, is the keynote of the proliferation of old age wherever it occurs. There is renewed activity among cells of low caste, and the higher-caste cells retrace the stages of their civilization, making up in growth what they lose in development. The cells go back to a period when both function and structure were simpler and when cell division was more active.

CANCER AS A SENILE CHANGE.

We are now in a position to deal with the cancer process. If the foregoing account of the anatomy and biology of old age be correct we can explain everything that happens in cancer in terms of senility. Superficially the cancer process seems very different from the old age process; but if we ignore these superficial distinctions and fix our attention upon the more fundamental changes, we see that in reality both are formed on the same plan and are actuated by the same motive. Thus, the typical cancer is made up of a collection of cells native to the part but of more embryonic type, and these cells are surrounded by collections of round indifferent cells derived from fibrous tissue and from other low-class structures, such as endothelium and leucocytes. The fibrous tissue, moreover, is often increased, as it is in the senile organ. These changes may be interpreted as follows. Certain somatic cells become aged while the tissues around them are still in a state of comparative youth. They express their senility by returning to a more embryonic form, and as they do so they increase in number, the faculty of multiplication being one of the manifestations of regression. But as this qualitative change takes place they become alien to their surroundings, and, as foreigners or rebels, stimulate into action the mechanism of phagocytosis. Not only is there an incursion of lymphocytes into the parts, but the connective tissue and endothelial cells in their vicinity revert to their embryonic state and begin the work of phagocytosis. But as a fact they have

to deal neither with the effete products of molecular degeneration nor with an inert foreign body, for though virtually strangers, cancer cells are by no means inactive. Hence the attack is abortive, except in so far as the phagocytes, by forming new fibrous tissue, tend mechanically to limit the proliferation of the cancer cells. For in the meantime the fixed connective tissue cells are themselves rapidly proliferating, with the result that when they cease their activity and return to their resting stage groups of cancer cells are cut off by intersecting bundles of fibrous tissue, while the whole mass is surrounded by an incomplete capsule of the same structure. This tends to limit the encroachment of the growing cancer, and were it not for the lymph spaces or capillaries, which are the gaps through which the growing cells escape, no doubt the limitation and strangulation of cancers would occur far more often than they do. It will be noticed that the more nearly the cells of a cancer approach the embryonic state the more rapid will be the growth, the less opportunity for fibrosis the more malignant the cancer.

We have seen that in senile decay the cells of highest type, or the more specialized cells, do not proliferate but undergo molecular decay, whereas those of lowest type express their degeneration not in decay, but in proliferation. So, also, cancer elements are never derived from these same higher kinds of cells, but invariably from the lower kinds. Moreover, as we have just seen, the lower type of cells to become the basis of the cancer process the greater is its malignancy. We may apply to the cancer process a similar phrase to that we made use of in summing-up the fundamental change of the old age process, and say that it is neither the appearance of phagocytes, nor the increase of fibrous tissue, nor indeed the proliferation of the cancer cells, which constitutes the cancer process. The root of the matter lies in the fact that the cancer cells have receded from a state of comparatively high development to a state of comparatively low development. Regression is the motive which prompts and animates the whole series of changes.

Cancer a Modification of Senility.

The question now arises, If both old age and cancer be manifestations of a similar act of degeneration, why is the cancer cell and cancer tissue so different from the old age cell and old age tissue? Thus, for example, though in the sarcoma the connective tissue cell is seen to be approaching its embryonic form, it never goes so far as to reproduce the primitive form. Moreover, so wide is the gulf which sometimes exists between the carcinoma cell and its undifferentiated ancestor, that cancers of the breast may even retain the property of secreting milk.

The explanation seems to be as follows. It is not contended that cancer is a genuine old age change, but that it is based upon the old age change. Cancer does not represent senile decay, but an extension or perversion of senile decay. The two processes are essentially similar, though they may differ widely in detail.

Thus, there is reason to suppose that cancer seldom or never springs directly from normal cells, but from cells which already have been thwarted in their development. The morbid process is therefore developmental from beginning to end, although the old age is grafted upon a prior abnormality. Thus, as Durante and Cohnheim showed, the pre-cancerous stage of cancer often consists in an arrest of development. A cell or a group of cells left behind by the advance of ascending development is shut in among uncongenial surroundings, with no inducement to progress. It therefore remains in a state of suspended development or infantilism. But so far from this infantilism conducing to longevity, it greatly favours the onset of premature old age. Apparently some of the stages which ordinarily constitute the summit of the developmental arch are left out, so that the curve of development is shortened. At any rate, it is certain that organs, such as the kidney or the testicle, which never properly develop, are peculiarly liable to undergo fibrous, pre-senile degeneration. Human beings whose development is conspicuously retarded, or are in a state of infantilism, are similarly prone to fall into premature senile decay. And in these cases it is to be observed that the result of the senile degeneration is never quite the same as that which takes place under normal circumstances. It is fundamentally similar but superficially different. One difference lies in the fact that the senescence seldom

or never takes place in its normal sequence, but is engrafted upon a state of infantilism which was itself abnormal. Of still more importance is it that the cell becomes senile less as a constituent of the body than in its individual capacity. In ordinary old age the regression of any particular cell element is only one detail of a widely extended design, and adjacent structures are in sympathy because they themselves are approaching their decline. But in cancer the degenerative regression is confined to a few cells, which are probably already abnormal and incongruous with their surroundings. These cells in their development, therefore, take a line of their own. It is true that they follow the ordinary routine of senile degeneration, but not closely. They are heterodox, and take an abrupt departure into cancer formation instead of keeping to the beaten paths of normal senile decay.

Degeneration, though it tends to obliterate distinctions by reducing everything to the same level, seldom goes so far as to destroy individuality. Hence, though old men in general exhibit certain common characters which seem to group them together and to differentiate them from the middle-aged, yet the senility of each old man is dominated by his own personality, the result of long years of acquirement and of heredity. So also is it with cancer. All cancers have certain features in common whereby we know they are cancers, but these common features do but little to obscure that individuality which distinguishes the tissue from which they spring. Hence, though all are cancers, we recognize cancers of connective tissue, cancers of epithelial tissue, and so forth, each tissue imposing its own peculiar features, which may in truth be so firmly fixed as indelibly to persist through generation after generation of engrafted cancers.

We are now in a position to make a general statement on the origin and pathology of cancer.

CONCLUSIONS.

Each species of living plant or animal is characterized by its uniformity of construction, which is displayed both in gross and in detail. This evenness of design is the outcome of heredity, and is not absolute, but is saved from monotony by occasional changes, and from these changes or variations no detail of organic life is exempt. Among other attributes of life liable to diversity is development. Ordinarily development is an ascent from the simple to the complex, followed by a descent from the complex to the simple. Hence the last stages of development are in some ways reminiscent of the first stages, the characters of the reversed childhood and infancy being added to those of middle age. As a rule the variations of this arch or trajectory of development are no more than "modifications," each modification being of little consequence. But sometimes they are more pronounced so as to come under the definition of specific "variations." Of these variations there are two kinds: the one termed "fluctuation," amenable to the influence of environment, which either awakens it from a dormant or latent state or accentuates it when already patent; the other, as a rule far more decisive, is a "mutation," and is uninfluenced by environment and often hereditary.

Let us suppose that the development of certain individual cells is either unduly retarded or unduly hastened. Among the countless millions of cells which constitute the human body such fluctuations of development must often occur and escape notice. But let there be some congenial (that is, pernicious) environment, such as the persistent friction of a rough surface, over-exposure to heat or x rays, or to some other local irritation, and the fluctuation, otherwise latent or normal, is liable to be exaggerated, until as a pre-senile degeneration it enters upon a state of disease. The cell or cells so affected return to a state of development approximating to that which characterized their embryonic life. They become simpler in form and in function, and multiply, assuming an aggressive attitude quite out of keeping with that of the cells by which they are surrounded. Indeed, an island of proliferating quasi-embryonic cells embedded among tissues still in their prime is as much out of place as the engrafted cells of a different species of animal. The machinery of phagocytosis is therefore stirred into action, and the fibrous tissue of the part proliferates. But cells which spring from embryonic residues and become senile

or quasi-embryonic in their individual capacity do not behave like normal cells undergoing the changes of normal old age. Nor is the fibrous reaction nor phagocytosis exactly the same as the phagocytosis or fibrosis of common senescence. It is more localized, more irregular, and is ineffectual or futile, not fulfilling the purpose for which it is ordinarily called forth.

As a rare event, the premature cell senility manifested in cancer appears without contemporary cause in two or more members of the same family. It may then exemplify the laws of familial heredity, showing itself early in life and in a virulent state of malignancy. Of such cancers the retinal gliomata are well-known examples. They answer to the description of discontinuous variations or mutations.

It is perhaps advisable to add by way of postscript that in the foregoing account of old age and of cancer none of the statements is based solely upon mere assertion. At the same time, not much in the way of evidence can be gathered from books. The crux of the subject is the nature of the alterations which take place in old age. But the scientific study of old age has been sadly neglected, so that any one who wishes to consult articles or books upon the anatomy of senility will find very little of value. There is a striking contrast in this respect between the two extremes of life, for, whereas a whole library of books has been written upon the early stages of development, it would be difficult to fill a single shelf with those which deal in a scientific spirit with the last stages of development. Yet there is no reason to suppose that old age is less worthy of study than embryology. On the contrary, having given some attention to this subject, I do not hesitate to affirm that the errors of development which arise during the declining periods of life are of more consequence from a pathological point of view than are the errors of antenatal development. Moreover, it is impossible thoroughly to understand the nature of cancer without inquiring particularly into the way in which premature old age affects entire organs, and, indeed, accounts for a host of diseases not yet identified with the senile change. But this is a wide subject, and therefore no attempt has been made in the above article to furnish evidence for many of the statements advanced. Direct and collateral evidence of this sort is very expansive, so that to compress it within the desired limits would either spoil the perspective or so crowd the picture as to cause confusion. It is hoped, therefore, that there is justification in giving a bare outline sketch, and in referring elsewhere for further particulars. Speaking generally, the subject is based upon the work of Metchnikoff and of other authorities, verified by actual examination of cancers and of senile tissues.

We hear much of the cancer problem, but cancer in reality provides not one but a whole series of problems, each of which may be solved without necessarily bringing about the solution of the remainder. Not only is the old age incidence of cancer still a mystery, but the occurrence of heredity, however rare, has not yet been explained; nor why cancer appears in one individual and not in another, though the conditions may seem to be as nearly as possible alike; nor why cancers can be grafted successfully into young and not into old animals. All these enigmas can readily be accounted for by the theory of premature local senescence or cell senilism, and so, also, can we account for the special tendency of cancers to spring from tissues in a state of local infantilism, from organs undergoing premature (pre-senile) fibrosis, from adenomata, or from other structures in a state of developmental instability.

It is claimed that this theory, though dull and commonplace, is satisfactory, seeing that it is based upon facts reasonably interpreted, and that it covers all the ground.

REFERENCES.

- ¹ Samuel West, Lettsomian Lectures, *Lancet*, 1899, vol. i, p. 352.
- ² *Pathological Histology*, vol. ii, New Sydenham Society's translation, p. 275. ³ *The Diseases of Post-natal Growth and Development*.

ACCORDING to the *Medical Record* the Equitable Life Assurance Society of New York has recently issued a review of its statistics showing that during the past ten years the indicated death-rate from cancer has increased by 30 per cent. among males and 22 per cent. among females in the United States registration area. The increase has occurred in every age group, but is considered largely due to more exact diagnosis.