

A CANCER HYPOTHESIS

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The Cancer Problem

DEATH is attributed to cancer today more frequently than to any other cause but one (heart disease) in the categories in which official mortality figures are compiled. It has risen rapidly towards this position during the twentieth century, in its advance displacing tuberculosis.

However the new standing of cancer among the recognized causes of death does not necessarily mean that cancer is on the increase absolutely. The result could be occasioned and is certainly affected by mankind's new control over tuberculosis which has reduced deaths from this cause. People who formerly would have been carried off by tuberculosis now survive long enough to develop cancer. The real significance of the statistical position of cancer is that cancer is a disease which has stubbornly resisted progressing public health methods and that cancer is now probably the most important public health problem. Rather than a new increasing menace, cancer is a residuary problem: it has remained while tuberculosis, typhus and others have been largely cleared away.

A vital difference between cancer and the diseases which have been yielding place to it,—yielding before medical science and public health measures—is revealed in methods of treatment applied. There is no specific like insulin for diabetes that will either cure or prevent cancer, nor is there for tuberculosis. Methods in active cases of both consist of efforts to isolate and reduce the affection. But the circumstances in which tuberculosis usually develops are known—bad housing, malnutrition, overwork, and hereditary susceptibility. These social conditions can be eliminated. Progress in the control of tuberculosis has been the result of preventive work, better public health standards generally maintained, although economic progress raising standards of living must take a share of the credit for this along with the medical profession and public health authorities.

Full understanding of tuberculosis has indicated these preventive measures, and proved deductively their efficacy. But only an actual cancer can be treated. People cannot be treated against cancer. They cannot be told that if they take more care

of their health their immunity will be increased. There are no known measures that public health authorities or society as a whole can take to increase immunity—except measures to promote study of the problem.

Treatment of cancer to-day is then, comparatively, unsatisfactory. Actual cancerous growths can be detected, although increased public co-operation and probably increased facilities for expert examination are necessary if adequately prompt detection in the population as a whole is to occur. Identified cancers can be eliminated in the individual either by surgical removal or by exposure to x-rays or radium rays which kill the cancer cells. This treatment is hardly a cure. The origin of the cancer is not known and not treated, so the same type of growth frequently recurs in the patient. Thus the treatment merely postpones death from this cause. There is nothing in the way of social treatment for what, by its statistical position as the second most important cause of death, is a social problem.

Thus the problem of cancer is lack of knowledge of how it comes about. Out of what circumstances does a cancer grow? The essential known fact is that growth, the dividing and multiplying of living cells, starts and continues in cancer in place of healthy growth of cells which maintain the structure and carry on the activities of the body as a whole. Cancer is a "wild" growth. No foreign bacterial cause has been found, nor has any lack like the lack of vitamins causing rickets been definitely discovered. Being a problem of growth, cancer brings science very close to the basic problems of life itself. This circumstance may explain the delay in solving it.

Hypothesis in Scientific Research

The research problem of cancer has been attacked from two different positions. Let nothing in what follows be taken as implying that making attacks has been neglected, or that either courage or pertinacity has been lacking. Bad luck is just as possible in science as in anything else. Neither of the research army's bases has been fortunate in results to date.

The positions of the attackers, referred to in the last paragraph of the previous section of this article, were, first, that there might be a cancer germ, and, second, that a failure of some substance or function of the body occasioned cancer. The former was the preferred position during most of the period of modern scientific research. This was partly because the germ hunt initiated by Pasteur had been so generally successful, producing so many germs

explaining disease problems. It was also partly because the conception of virulent bacteria is almost anthropomorphic—congenial to man who himself attacks enemies—while the conception of functional failure is abstract and difficult.

The attempt to find a cancer germ was the outcome of a hypothesis. The cases themselves did not suggest bacterial infection: the microscope did not show it, there was no evidence of contagion. The search for a germ was inspired by a speculation. But that is the method of science, unmethodical though it may seem phrased as "following a hunch". Hypothesis precedes the work of research as popularly conceived—the microscopes and test tubes. These prove the theory. But without the theory they are purposeless, their facts insignificant. And there has been laborious research work which has not been related to a guiding hypothesis, with the result that it has been only a semblance of science. The broad imaginative outlook which produces a hypothesis also catches the significance of particulars of information in scattered fields and brings them together in a structure of proof. Science to-day is departmentalized, and at the same time all departments of the material sciences have got down to profound, fundamental problems. This quality of the hypothesis—a magnetism drawing together bits of iron fact and arranging them on lines of force—this is the more difficult and rare, likewise the more important, in such circumstances of science.

Smoking and other supposed irritations of living matter until it became cancerous, represent crude explorations with another hypothesis. The hypothesis is the second of two, mentioned above, the one that is difficult and vague because it is an abstract conception—functional disorder. The analysis of what has been learned from the examination of cases of cancer, given below, will show that this theory actually fits the facts. The very amorphous quality of the theory however is the reason for this dubious success. It spreads out to cover the facts instead of drawing them tightly together. It says that a cancer is a part of the body that is not functioning properly, which is very like saying a man is sick because he is not well. Scientists reserve the term hypothesis for constructive ideas. It is necessary to know that the cells in a cancerous growth differ from cells that in the same part of the body would contribute to general health, in specific ways. And then the history of those differences must be obtained, to the last conclusive detail, so that ultimately preventive measures may be discovered.

It is not always applying your theory most closely to your problem that brings you most quickly to the solution. There are

practical difficulties in experiment, for instance. Experiment is often essentially negative, elimination of factors you are not interested in or of things you do not want to happen. The outcome must be a one-one relationship, an effect and a cause with no possible alternative. A crude example,—cancer of the uterus occurs most frequently in mothers. Motherhood might be regarded as contributory until it is recalled that most women are mothers.

True experiments to elaborate a hypothesis are very often difficult to obtain. Interference from uncontrolled circumstances is hard to eliminate. Before Lister surgical shock was regarded as very dangerous, but deaths attributed to it frequently were occasioned by lack of sterilization of instruments, need for which was not understood. People cannot be dissected before they get cancer with any certainty that they would have got cancer if they had lived—or animals kept for experimental purposes either. The technical problem in connection with experiment in general, therefore, has the effect that the only relative experiment for a special problem may be found or may have to be made in quite another field of study. The relevance may be accidental—the experiment made in following up an unrelated hypothesis. The relevance in such cases is entirely dependent on the hypothesis which transfers the observed fact to the new meaningful context. Hypothesis then is what enables use to be made of isolated observations to make progress in knowledge. It is the systematizing element in science.

A hypothesis involving much novelty is possible now in regard to cancer. There is justification for it in the fact that cancer is still a problem. Of course a hypothesis never by itself solved any problem. But the place of this scientific kind of conjecture has been shown. The new cancer hypothesis may be productive of significance in facts known but overlooked. It may lead to decisive new experiments. And thus it may contribute to reaching the ultimate explanation and cure of the disease. For, needless to add, cure or prevention usually quickly follows complete explanation.

The Symptoms of Cancer

A cancer is a growth of living matter, but neither conforming nor contributing to the organized life of the whole body, like a fungus in a tree except for the foreign origin of a fungus by its spores. The language of this description of cancer is not academic, but the purposes of this article would not be served by a technical presentation, and in any case scientific terminology is apt to become a jargon, about the meaning of which the users forget to think.

Living cells constitute the cancerous growth. All living things are composed of cells, which in turn are essentially protoplasm enclosed in a membrane. Cells from separate cancers may have minor differences among themselves, but they share a crucial difference from healthy cells. Healthy cells in a mature body are specialized. Every cell has a part to play in the life of the whole, and lives its own life through this co-operative arrangement. Cells begin to take on special characteristics immediately after a new organic life is conceived. They become the cells of nerves, of digestive organs, of muscle tissue, blood, skin. They remain, in health, subordinate to the general design of the body in which they participate.

This specialization of cells in the development of a living being, whereby the original fertilized cells divide into two then four and ultimately millions of cells which take different directions and forms arriving at just the destinations which enable the total to work as one, has long been the great mystery of life. Most evident during the period from conception to maturity, the mystery persists as long as there is life. Cells even in a body that has "stopped growing" apparently, are constantly wearing out, wearing out but being replaced. The new cells growing in at any part of the body grow (in health) in the place and form of the old cell, specialized so that the work of that nerve or muscle for the general good may be continued.

How can a cell "know" to prepare itself to be sensitive to light, when it starts out with its neighbours to form an eye? How is purpose given to growth? The human mind balks at the problem: teleology has perplexed science, and before that, philosophy. Scientists have attempted to ignore the mystery as philosophical and therefore either ridiculous or unreal. But cancer will not be solved by that attitude. A substance that controls and directs the growth activities of cells would be an explanation, however, that would be in keeping with science. Discovering such a substance would give an intelligible reason for growth, and might enable man to create purposeful growth, and then control other growths, even though posing another problem as to how the substance came to be present in organic life in the first place. Failing a substance, "co-operation" can be suggested as the explanation—cells specializing because the very fact of their being several enables them to "trade jobs". But this explanation would have to stop with the coining of the name. It contains no possibility of bringing cells into co-operation again if a "strike" is declared, and cancer is a sort of rebellion against the social rule of a body's cells made by

one group. The last resort for explanation of teleology is direct and continued intervention by God. Indeed Adam Smith felt that specialization among men based on co-operation or trade was not an explanation and required God to explain it. Teleology and God go together, the former being a favorite proof of the existence of the latter. The argument, besides being circular, makes cancer sufferers especial victims of God's wrath.

Growth frequently forgets the rules and limits of purpose in the whole body and produces tumors. As growths these are of course cellular. A part of the body swells—it exceeds the limits of health—by too many cells forming at some point. Although too numerous, the cells have no other fault. They are specialized, and they do not prevent their neighbours outside the tumor from specializing differently, and so they do not interfere with the co-operative life supported by the variety of the cells. A tumor has simply to be removed and that is the end of it. The lapse from obedience to the plan is forgotten.

Sinister denial of authority is that given by cancer. Besides failing to recognize the limits of proper healthy growth in the neighbourhood where it occurs, its cells also deny the co-operative purpose. Occurring on the lip, for instance, they grow not as skin and supporting flesh but as just selfish cancer cells, good for nothing to the body, indeed by replacing healthy specialized cells preventing the parts of the body from doing their particular jobs. Cancer cells are in the first place useless.

Cancer in the second place spreads. A worn-out normal cell next to a cancer cell is replaced by a cancer cell. How this comes to happen is a mystery, a strange case of the great mystery and miracle of life suddenly ceasing. Why a cell growing in a healthy body should happen to develop exactly the right form to help give man sight (or sense of touch or digestive powers) is quite unknown. It seems likely that knowledge of healthy growth would be very important, perhaps essential, to understanding why a cell becomes a cancer cell by not taking on the right form.

Thirdly cancers travel. Not waiting to capture territory by winning the positions of worn-out cells in juxtaposition with their cancerous cells, they loose into the blood stream colonies which lodge in other parts of the body and there continue the process of filling the places of specialized cells by cancer cells. This is the accepted explanation of the fact that in advanced cases cancers are discovered in many parts of the body. However if there is a condition of the body as a whole such as a lack of organizing power which is responsible for the uncontrolled, unspecialized

kind of growth of cancer being allowed to start in one place, then this condition would equally permit other cancers to occur, independently of each other.

The march of cancer cells sooner or later crosses and blocks some vital path in the body, causing immediate death of the whole body. The vital tissues of the brain or spinal cord are replaced by cancer, or the stomach walls or lungs are destroyed so that the body starves or suffocates. Presumably the cancer might survive the body if nourishment were supplied to its cells artificially to replace the stream of blood which of course ceases its feeding work with the body's death.

Definite areas of the human body show cancer occurrence with varying frequency. Cancer of the female sexual organs, breast and uterus, is most frequent, but cancer can and does occur in any cellular part. The digestive tract of both sexes is a frequent location—stomach, liver and rectum. Throat and tongue cancers are also recognized varieties.

Cancer occurrence according to age shows wide variations also. Occurrence in the sexes on the average of all ages does not vary tremendously, but men and women show variations in cancer occurrence at different periods of age. (Cancer occurrence can sadly be equated practically with deaths from cancer, so little difference in the figures have therapeutics made to date). The following figures are derived from the Metropolitan Life Insurance Company's compilations. They represent deaths from cancer per hundred thousand people of the ages shown living in the United States in 1934.

| Age | Male | Female |
|-------------|--------|--------|
| 0-1 | 2.8 | 1.8 |
| 1-4 | 4.3 | 3.3 |
| 5-9 | 2.7 | 2.0 |
| 10-14 | 2.8 | 2.2 |
| 15-19 | 4.2 | 2.9 |
| 20-24 | 5.5 | 6.1 |
| 25-34 | 11.4 | 21.4 |
| 35-44 | 36.6 | 84.0* |
| 45-54 | 125.2 | 209.8 |
| 55-64 | 320.6 | 400.0 |
| 65-74 | 714.9 | 692.1 |
| 75 and over | 1203.1 | 1071.7 |
| all ages | 96.2 | 115.5 |

Cancer deaths become numerous from thirty-five on, increasing much more rapidly in the first years after thirty-five in women. The figure for men begins to approach that for women only after

fifty-five. All of these figures are much higher for 1934 as compared with similar figures at the beginning of this century, with one extraordinary exception. 85.9 women per hundred thousand women of 35-44 died of cancer in the average for 1900-5, and only 84 in 1934. This is the only classification in which there is a decline. Reason? Nothing can be known until cancer is understood. Indeed statistics have only a very supplementary place in the handling of a problem like cancer, perhaps suggesting extensions of theories based on direct and detailed analysis or providing encouraging confirmatory information.

The Organizer

Possibly cancer as a disease of the human body and one of the most deadly afflictions of mankind is caused by deficiency of a substance which in healthy bodies organizes growth. This hypothesis as to the cause of cancer has been suggested at several points previously in the discussion. The hypothecated organizing substance—or rather its absence or inadequacy of amount or form—would explain important features of the occurrence and course of cancerous growth.

The existence of a substance, like a catalyst, in the presence of which individual cells undergo specialization so as to compose larger organisms with new powers and without which they can grow but only quantitatively, would appear to provide the material of distinction between cancer and healthy flesh. Cancer would be what happens to the normal and necessary continual new growth of cells to replace worn-out cells, when the directional purposive factor was not present in proper amount and form. The actual cancer would be the outcome of growth in the absence of this substance, as the malformations of rickets and cretinism are attributable to the absence of enough vitamin D and enough thyroid secretion respectively.

Cancer caused by deficiency of a "planning" substance would explain the tendencies of the disease to spread and "travel" in the body, also the discouraging recurrence of cancer after apparently successful treatment by current methods of removing or killing existing growths. The breakdown of healthy cell growth into unspecialized and socially useless, in effect parasitic, growth, if caused by a lack of this kind which affects the body as a whole, might commence almost indifferently in any part of the body. The condition (lack of the controlling substance) might cause several cancers simultaneously and independently. Arresting cancerous growth at one point, contemporary treatment, in these

circumstances would be obviously as useless for permanent cure as actual results show it to be. A body "disintegrating"—the growth tendency becoming cancerous instead of organized and integrated—would show the phenomena of new cancers starting in different parts which are now assumed to be the result of the original or parent cancer "sending out colonies" or transplanting itself."

The incidence of cancer pictured by the statistics of deaths by age groups shows the disease almost exclusively one of maturity and largely one of old age. Maturity brings, indeed is constituted by, a restriction and limitation of the growth processes which might logically be accompanied by a reduction in the quantity of the substance hypothecated in connection with growth. In a child the total of cells is increasing, in an adult merely being maintained. In adults capable of procreation, however, very rapid growth in the form of new organic life can be initiated, while in the aged this possibility has disappeared, suggesting a further reduction in the amount of an organizing substance that might be expected to be available in the body. The highest incidence of cancer for women is in the age groups after the menopause. The highest is later for men than for women, corresponding with the longer duration of procreative powers. That single absolute decline in cancer incidence, for women of thirty-five to forty-four, might as a speculation be correlated with the extension of "youth" or vitality achieved by women in the present century by diet, exercise and social emancipation.

The substance hypothecated would dissolve the great prime mystery of growth as well as the problem of cancer. It would shortly dispose of a great deal of philosophers' fiction. Theories of vitalism and transcendentalism generally in regard to biological phenomena would be proved irrelevant and unnecessary. The supremely useful scientific principle, materialism, would receive as triumphant a vindication as by any discovery in the history of science. But the implications for formal philosophy can be left to the Schools, where they will be recognized in a century or so. The valuable interest and encouragement of unprejudiced minds are concentrated on progressive work. Much should be achieved in the biological and medical sciences through the materialization of growth.

The fact of tremendous interest is then that a growth-directing substance has been located experimentally. The substance of our hypothesis has been discovered and has been named the Organizer. The record in brief is that in studies in embryology Hans Speman

found the substance in the fertilized ovum, before growth by cell division had commenced, found it in a region near the point where the fertilizing sperm entered. The substance was proved by Needham and Waddington (working in Cambridge, England, in 1935) to be a definite and distinct chemical compound, by the analysis as far as carried a member of the sterol family. A substance answering the description of this one has been found also in all the adult tissues of all animals tested. However it has been discovered frequently in more complex compounds. This circumstance has given rise to the suggestion that it is set free to guide growth only on the creation of a new embryo. Alternatively its activity may vary in accordance with the combinations in which it is found—directing rapid growth when free, growth contributing to reproduction when in one degree of combination and replacement growth when relatively deficient or neutralized by a further combination.

The sterol group to which the Organizer appears to belong has indicated a connection with cancer in other as yet uncorrelated experiments. Kennaway (London, Eng.) following up a clue with certain sterol-like substances, has found cancers in previously healthy subjects after treating them with these substances. The sterol family, or more specifically the phenanthrene ring, is known to include a substance called oestrin. Oestrin has been correlated with sexual excitability, for example the phenomenon of "rut" in animals. An apparent point of concentration for it is the breasts. As mentioned, cancer of the female sexual organs is the most frequent of all varieties. Reproduction which they serve creates the greatest need for organized cellular growth. Besides oestrin the biochemical family includes vitamin D, popularly known for its importance to quantitative growth.

The cancer hypothesis of an organizing substance should when fully developed explain all these at present isolated facts. It will then however be a comprehensive principle, not a hypothesis any longer. Principles are accepted truth, although most were once only hypotheses, hypotheses which were found susceptible of proof.

In the meantime it is sufficient that our cancer hypothesis is constructive, clearly indicating a programme of further experiment. Crucial will be the proof of the presence of the Organizer in the human embryo, and likewise the discovery of its exact and complete formula. The next step would be to prove deficiency of the Organizer in the presence of cancer. Then, develop a technique of compensating that deficiency. Therapy might take either of two directions, preferably both. If cancer is caused by the

lack of a certain chemical, it may be possible to inject the substance in some form which, correcting the chemical imbalance, will stop a cancer at least in the early stages and prevent others developing. This would be a cure for cancer. Perhaps better still, how to prevent cancer might be learned. This would probably be a regimen which would prevent deficiency of the Organizer from occurring. Prevention might be secured simply by individual action—improved diet, or other health habits—which, however, society would have to teach all its individuals to take, to lift the social burden of cancer. Or again the mode of life giving freedom from cancer might demand structural changes in society. Such a change is the universal free access to sanatoria, superseding private treatment, which has been so important in tuberculosis.

In summary it may already be said that the discovery of the Organizer is probably the longest forward step ever made in the study of cancer. It may well be the decisive discovery, because it is crucial to a hypothesis which covers the facts of cancer revealed by analysis and which contains a logical plan of action concluding, if it can be completed, with cure and prevention.

Corollary: Sexuality

A scientific hypothesis stops with the Organizer. Confirmation in experiment must be awaited before synthesizing imagination is allowed to throw another bridge of intelligent conjecture forward into the unknown. And only when a hypothesis becomes a demonstrated principle can it properly have a corollary. However, there are further possibilities suggested by our hypothetical solution of cancer which, in view of certain factors in public health regarded as a social problem, justify transgressing against the rules of scientific method.

The social factors in public health referred to are, on the one hand the false modesty of the public, on the other the crudely mechanical and callous attitude towards sex which the medical profession tends to acquire from its unceasing struggle with much less subtle problems. Doctors have made no organized protest against working conditions which are to-day having a widely felt effect on the sexual potency of the employees of American industry. Disinclination to the performance of marital obligations would seem to them of small concern compared with other afflictions, there being yet no evidence of physical complications resulting. Were more importance in a healthy sex life to be proved to doctors and were their attitude to change, public prudery would still be a difficulty. Treatment of cancer even now, within the limits of

present knowledge, is held back by women's reluctance to submit to examination of their breasts. Public health, so dependent on public knowledge, requires a frankness about the possible sexual aspects of cancer even in the present early stages of the research work, in case sexual aspects should be vital to the ultimate methods of prevention in society as a whole.

The incidence of cancer by sex and age groups suggests that it increases with the decline of sexual vitality. The discovery of the Organizer in the fertilized embryo, and of a similar substance, oestrin, in the mammary glands, suggest that the Organizer, which may be the factor on which we are dependent for protection against cancer, has a connection with sexual vitality. These circumstances in turn suggest that maintenance of sexual vitality may eventually be recognized as a condition helpful to the prevention of cancer. Healthy sex life is known to involve adequate conditions of sexual satisfaction, and this is a much larger matter than the sex act as such. It is dependent on favourable circumstances in both the spheres of private knowledge and public conditions of life. The former demands universal sex education of quite a new kind, while the latter may require changes in industrial organization to provide relief from present high speed, tension and nervous strain. For the elucidation of these possibilities new work is necessary to extend the unique and great contribution made by Havelock Ellis.