It is well to note some characteristics of cooperative arrangements as safeguarding the value of the research to the public and upholding the independence and disinterestedness of the investigation and its findings, as required by some of the cooperating institutions. An advisory consulting committee considers the problem and the method of investigation, and may advise in the interpretation of results. The laboratory directs the investigation and controls the work and finally interprets the results and prepares the report. The results of the investigation are the property of the laboratory, and the institution will make publication if the value warrants. The product of the research is intended to be fully available to the public except that a patent may be applied for if this step is thought necessary to protect the interests of the public. It is seen that the purpose of the provisions is to conduct the research as a public activity, and that the advantages accruing to those who have financially supported it may be shared by others.

At another time I have said that pioneer American engineering depended almost wholly on ingenuity, experience, precedent, vision and judgment, and engineering science played a minor rôle. The increasing magnitude and difficulties of engineering projects, the need for greater permanency, economy and safety, and the greatly diversified nature of engineering work have emphasized the importance of basing engineering art more fully on engineering science. It will not be overlooked by any one that engineering will continue to need ingenuity, experience and judgment, and rules, precedent and vision, but more and more, as time goes on, will it be dependent on science and that accumulation of applied science that may be grouped under the term, "engineering science." And engineering science must be fed upon research, and thus research is essential to its advancement, to its fuller growth.

No attempt has been made here to name problems or projects that need the light of research thrown on them. The belief may be expressed, however, that the members of Section M recognize the great value and need of research in engineering lines and appreciate the importance of adequate provision of funds for the purpose. It is the hope of the retiring vice-president that Section M in some way may give effective aid in bringing this need to the attention of those who may be able and willing to contribute liberally to the support of engineering research.

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CELLULAR DIVISION IN RELATION TO CANCER[1]

CANCER is a disease characterized by division and multiplication of cells. In the unrestrained condition the tendency of cells is to grow and multiply. In tissue or cell culture each cell divides twice and the colony doubles in volume. A colony, originally one cubic millimeter, will form approximately one cubic centimeter in twenty days. After sixty days the volume of tissue would be more than one cubic meter, and in less than one hundred days, one million cubic meters. Indeed, Carrel has estimated that, if the tissue cultures which he has kept growing for sixteen years had not been restrained, the mass would be not only larger than the planet, but even greater than the universe.

Cells are endowed with far greater potentialities than they display within the human body. There the immense capacity for growth possessed by the cells of the human tissue must be kept under restraint while these cells live as part of the organism within the body. The resting condition of adult tissue depends upon the composition of the fluids or humors in which they are immersed, or, to put it in other words, the environment of the cell determines the rate of its growth and division.

In the light of this, cancer is characterized by more or less suppression of normal balanced cell activities with accentuation of that of cellular multiplication. Suppression of multiplication is removed and there is a release from normal growth gradients which determine body structure. Inhibition is replaced by the embryonic qualities of multiplication.

In cancer we have to do with a state, not a thing—with a state of cell wherein the cell is allowed to grow and multiply without the usual restraint common to adult body tissue. A most important study, therefore, is the mechanism whereby restraint of cell growth may be obtained.

In the consideration of cell division we have to take thought of the mechanism and organization of the cell. It is well in this regard to have a model for thought in order to consider the changes which take place, exactly as the physicists have their model of the atom and the chemists have their model of the molecule. The simplest structure capable of sustaining life is the unit with which we have to do, as the physicists have to do with the atom and the chemists with the molecule.

[1] An address before the Wilmington section of the American Chemical Society, illustrated by moving pictures of cell division. October 17, 1928.

As in these two last units, the structure or organization is of importance, as the unit becomes more and more complicated, the structure becomes of greater importance. For purposes of thought, the cell may be divided into four portions: (1) the nucleus, which is alkaline (about pH 7.50); (2) the protoplasm, which is acid (about pH 6.6–6.8); (3) the semipermeable cell membrane, and (4) the environment or liquid in which it is bathed (and this in the human body consists of the blood plasma and tissue juices with a normal pH of 7.36–7.38). The cell and its environment must be considered as one.

In this arrangement, no immediate consideration is taken of the chemical substances composing the cell, and these are complicated in the extreme. The proteins of life are the most chemically specific substances known. Their variation is very wide and Abderhalden has estimated from the possibility of combination of the various amino-acids that there is a possibility of 24^{20} different combinations to form different proteins, so that the chemical combinations and chemical minuteness of the substances composing vital cells are so enormous and delicate that they stagger the scientific imagination and seem in the light of our limited knowledge to present an overpowering obstacle to the study of cell processes and function.

However, it is fortunate that nature at some stage in her complexity rejuvenates her simplicity. The cell reacts as a unit and there are certain phenomena which are common to all cells. There are regularities in the complexity of cell phenomena which make it possible to study cell processes from a physicochemical standpoint and temporarily to neglect the abstruseness of intimate chemical composition which seemed to present an insuperable obstacle.

In this renewal of simplicity, the cell may be regarded as a negatively charged particle, existing in an alkaline aqueous medium. As all life is colloid, we have, therefore, to do with a heterogeneous system of the negatively charged type and more of the nature of a suspensoid, in that alterations in the charge affect the stability of the system. Life is, therefore, the continuance of colloidal changes in an aqueous medium, and the cell is the unit of life.

There is such uniformity in nature and the reaction is so constant to constant stimuli that there must be an *equilibrium* or balance controlling the processes of life in its normality, and in its deviations in disease and age. This balance is dependent at least in some degree upon charge, as the proteins are amphoteric substances and depend for their charge upon inorganic salts and other electrolytes.

In the nucleus we have as yet little opportunity for the study of alterations in charge, but it is known that in cell division the nucleus obeys the laws of the swelling of colloids. In cell division the first noticeable changes which are produced in the cells are those of alteration in the chromosomes. These little substances are each made up of discrete particles called genes, and there are thousands of genes in each chromosome. The walls of the nucleus dissolve just before division is to take place and the tiny rods of the chromosomes form a spindle-shaped figure and into the middle of the spindle the chromosomes are drawn. They arrange themselves in an equatorial belt in two divisions and then ensues an equatorial "tug of war" until they divide, as you will see in the moving pictures, into two parts. They split lengthwise and with this division a constriction appears on the surface of the cell which spreads and gradually encircles it. This constriction cuts into the cell and it divides into two cells. After a pause of an hour or so another division takes place, and this appears at right angles to the first.

These are the processes in the nucleus which are visible in the moving pictures, but the influences outside the cell can not be thus shown. Division in the cell, as has been shown by Carrel and others, is dependent upon environmental influences. In our consideration of the colloid cell as a unit, the variations in the semipermeable membranes or surface films underlie the response of irritable tissues to stimulation. The primary reactions in stimulation to cell division are surface reactions, as is shown by their sensitivity to surface-active compounds and to changes in electrical polarization.

If a marine cell is placed in balanced sea-water, division takes place at a measurable rate. If this sea-water environment is altered by the addition of 1–1000 of sodium chloride, or if the pH of the solution is made slightly more alkaline, cell division takes place at a greater rate. If, on the contrary, 1–1000 of calcium is added or the pH made relatively more acid, division is greatly reduced or stops. Thus cell division has here been altered by changing environmental influences outside cell membrane, and nuclear division within the cell membrane has been influenced by this means. There is also alteration in cell permeability and electrical conductivity. All this shows the possibility of influencing cell division by environmental changes without destruction of the cell itself.

As cancer is a disease of cell division, the study of the environment of the cell in the human body, as shown in the blood plasma, offers considerable interest. If these changes in the environment could be shown to be pertinent in the cell division of cancer, it might open up new avenues of research and new possibilities of control of cell division in cancer.

In this disease, it is too much to hope to find a means of destroying the cancer cell alone, without the destruction of surrounding or accompanying normal cells. The so-called cancer cell offers too little difference from normal cells to expect that there should be a chemical specificity in the cancer cell which distinguishes it to such a degree from normal cells as to make it possible to attack the cancer cell alone. But it is not too much to hope that cancer cells can be restrained from division and, if this is done, the cancer cell will lose the quality which characterizes it—its power of spreading in the tissue which depends upon multiplication by division. The form of the cell is a function of time and if division can be slowed the cancer cell loses its characteristics. Like weeds in a field, if the cells can be made to cease to grow and multiply, they will not spread, even if they are not destroyed.

In this study of the environment, or blood plasma, Reding, of the Cancer Center at Brussels, has found that cancer is generally associated with a more alkaline pH[2] and with a diminution in the ionized calcium and even total calcium in the blood plasma. In other words, in cancer, a disease which is dependent upon cell multiplication, are found conditions which favor such multiplication in single-celled marine organisms. In addition, after X-rays or radium treatment, which is one of the most effective means of treatment, Reding finds there is a shift in pH (when the treatment is clinically effective) towards the relatively acid side of normal and the ionized calcium is increased in amount. In other words, the treatment which is effective in controlling cancer produces conditions similar to those in which cell division is hindered in single-celled organisms.

To the cancer research worker, these findings, if confirmed by others, will be most illuminating. They will show that it is possible to control cell division in the body by environmental changes and open up new fields in the attempt to control such cell division by the aid of chemical substances and by the alteration of equilibrium. Any cell with a definite physicochemical organization will follow a constant course of transformation if external conditions are constant, but, if these are changed, the course of transformation will also be altered. These findings, too, will give a means of biological control of the present most effective treatment of inoperable cancer, the radiation from X-rays and radium, where there are now only the rough criteria of the clinical aspects of the tumor.

And last, but by no means least important, is the finding that the physical forces of radiation by X-rays and radium produce measurable chemical changes in the blood plasma, or the physico-chemical environment of the vital system. This fact is most intriguing in that it leads to the hope that by chemical alterations in the blood it may be possible to produce effects similar to radiation, or to extend the effects of radiation by chemical means. In the moving pictures to-night you will see the effect of radiation upon cells and cell division and the sudden cessation of activity as a result of radiation. The mechanism of these effects has been thought to be upon the nucleus and chromosomes, as has been shown by Muller in his mutation experiments, but there seems to be another effect which influences the environment, and it may be that this is an effect upon the cell membrane. It may be that by altering the environment of the cell, the blood plasma, that such membrane effects may be obtained as an aid or substitution to radiation in preventing cell division.

So you see that in these problems the chemists are our hope, but it is our duty to state the problem of cancer to them in such terms as to explain the mechanism of action of the cells and in this way get the full value of their advice. The unit of life is the cell and the cell is colloid in character. Substances which may have a hope of benefiting the disease will be those which restrain cell division without complete destruction of cell function and those which will permit the cell to mature from its embryonic condition to that state where the inhibitions or restraint of the growth gradients are once more effective. Cancer is a disease of age and this is a time when cell division should be limited.

If this restraint of division can be obtained or if the influence of radiation can be extended, the hope of benefit in this disease shines brightly. In this we are gratefully in the hands of our friends, the chemists, and it is to them that we wish to state our problem in its mechanism, so that there may be an intelligent viewpoint for them to apply the knowledge which is theirs.

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[2] The work of Reding and some studies by ourselves will be published in book form under the title, "Blood Studies in Cancer," Williams and Wilkins Company, Baltimore. There will also be included a description of a new electrical pH measure and some description of the method of its use with the quinhydrone electrode. The importance of pH in the study of cancer has led the Cancer Research Committee of the Graduate School of Medicine of the University of Pennsylvania to work on the improvement and exactitude of pH measurements.

JOHN MERLE COULTER

IN the recent death of John Merle Coulter, professor emeritus of botany, of the University of Chicago, plant science has lost a profound student, an inspiring