The Function of Cancer*

By

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THOUGH we fully appreciate the contributions to the study of cancer by both pathologist and clinician, we might expect an investigation of the problem from the viewpoint of the physiologist to reveal something about the purpose and value of this deviation from the normal that is so commonly rated as turmoil and disorder.

The histological expressions of cancer impress us as a desperate attempt at gland production, characterized by its persistence, as a response to a persistent stimulus, by its equalization of cells in proportion to their malignancy, as indicating a singleness in the response type. While the loss of differential structure, and individualization of cells indicates a return to a simple balanced equipment in preparation for a new differentiation along lines so far not developed in the organism. Thus we may infer that the cells are responding to a new or not normal stimulus. Moreover, as the response persistently increases it cannot be adequate, and as structural differentiation has not been accomplished, the effort toward response appears to be only in the earliest stages of development.

Still the cancer process bears strong resemblance to the behavior of several glands of internal secretion, that are now established as indispensable factors in the animal economy.

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In such simple glands as the parathyroids, we observe acini production by vacuolization and death in cells located farthest from the blood supply. This process is very perfectly imitated in the cancer behavior. Yet in a higher type of gland, as the thyroid, acini production occurs by death of cells close to the blood supply. Thus as cell death is an important phase in the production of the internal secretion of the thyroid, its survival as a method of choice illustrates the adaptation of processes acquired from states of disadvantage in the established service of the organism. Thus we may conclude that the process as occurring in cancer, predicts its future place among the glands of internal secretion. And as limitation and control of activity in an established gland indicates its adequacy, so we must again qualify the cancer effort as at present inadequate in its attempted service. We may therefore infer from the histologic manifestations that cancer has a function in the process of development.

Our chemical studies corroborate this surmise and indicate also the place and value of this function. Our earliest work on the chemical significance of glands of internal secretion was directed toward the explanation of the parathyroid activity. Parathyroidectomy was long known to be followed by a set of tetany symptoms that could be ameliorated by calcium therapy. So the parathyroid glands were universally credited with a vital place in the calcium metabolism. This supposition fell short of agreement with so many experimental facts that the theory could not be sustained. Should a farmer or even a pharmacist observe an animal in the tetany of parathyroidectomy, he would certainly say the animal was poisoned. And after a careful checkup of the calcium theory we choose to direct our research along the "farmer" hypothesis.

After developing a suitable method of isolation, we

were able to isolate uniformly from the urines of parathyroidectomized dogs, toxic quantities of guanidine bases. The concentrations of these poisons were proportionate with the rapidity of development and severity of the symptoms and the earliness of fatality. We proved them the responsible factors for the symptoms and death of the animals. Thus it appeared that the parathyroids protected from a toxic agent. Our work was amply verified by Paton at the University of Glasgow whereby he earned the Triennial prize in medicine awarded by Harvard University.

Yet the guanidine bases were only incidental to the loss of parathyroid activity as we later proved by the isolation of the guanidine precursors the cyanamides, very simple fundamental metabolic interproducts. These cyanamides easily took up an ammonia radical to become the guanidines in which form they were excreted. The cyanamides are evidently products of activity of other factors than the parathyroids and were not metabolized further after parathyroid removal. So we assume that the parathyroids disposed of the cyanamides in their activity for further benefit to the organism as a whole. We cannot go further into this subject here but cannot omit it as it exemplifies an established gland activity serving as a protection of the organism against a definite toxin. Likewise we shall find evidence that the cancer behavior is a protective response to a toxic product generated within the body. The localization of the cancer effort in congested areas indicates that the exciting stimulus is distributed through the blood stream.

Clinical observation discloses the persistence of toxemia over a period even as long as twenty years previous to the advent of the growth. After the growth has come these toxic manifestations disappear completely or nearly so. After a surgical removal of the growth they return;

and with recurrence of the growth again disappear. We designate these symptoms as the pregrowth symptoms, for they differ from those consequent to the activity of the growth itself.

The pregrowth symptoms caused by the toxin-stimulus are mainly manifestations of interference with normal nerve function, and predominately with certain mechanisms of the central nervous system. Thus in a series of two hundred cases distinct mental aberration, incorrectly diagnosed as paranoia, was observed in two per cent. of cases. But the prevailing disturbance is an interference with function of the second and third nerve mechanism. Thus an optic-migraine without much or any headache or aural disturbance, or an optic-vertigo with scotomata, might express the condition. I have not been able to find a discussion of this complex in the literature and propose to take it up in a further paper. However, I may indicate the main characteristics, as they occur in fully eighty per cent. of my cases.

The points of disturbance lay both in the perception centers for optic impulses and those centers where optic impulses are conveyed into paths of motor control, of both the optic apparatus and the general musculature.

Thus visual impulses, in one case, periodically caused muscle tremors and convulsions. Covering the eyes gave relief. In several cases teichopsia gave the impression that the patient persistently saw needles and pins wherever she looked, and she was diagnosticated to be a paranoiac. Difficulty in accommodation results in a large proportion of cases in a haziness of all objects closer than or beyond a distance of usually some ten feet from the patient. In these cases attempts at accommodation give rise to a sensation of sickness but not nausea particularly. Temporary blindness of the whole or part of the visual field is common, so that a patient may run into things without

seeing them. Or a sudden general loss of sensation with blindness and a complete loss of muscle control, causing the patient to drop to the ground, without loss of consciousness, giving the impression of dying. The muscle control may be only partly lost and movements consequently be incoordinate. During these spells pin-point pupils have been reported. Great changes in visual impulses, as occurring on turning out the light or waking up in the morning, may cause a dizziness with topsyturviness of after-images or true images. In the former case turning on the light and fixing the eyes on an object relieves. In the latter case closing the eyes relieves. These occurrences come in spells of only short duration or lasting several weeks at a stretch and over a period of a few or as long as twenty years prior to the development of the growth.

Occasionally a peripheral neuritis is present. It may be mild or severe and may be associated with areas of anæsthesia and paralysis of one or more groups of muscles. But the percentage of such cases is small.

Since these symptoms, which occur in nearly ninety per cent. of my cases, let up entirely or in large part with development of the growth, its detoxicating function is evident, and resembles the detoxicating function of the parathyroids which remove the cyanamides from the blood.

The cancer cells absorb and hold the stimulus-toxin in combination without changing its chemical identity for the most part. That is, they store it. This is proven by the fact that with dissolution of the growth following our treatment, the stored toxin is again liberated with return of the pregrowth symptoms, until the growth has entirely been digested and eliminated.

The cancer cells, also in small part and continually,

alter the stimulus-toxin, but instead of changing it to a harmless or useful immune body, as the parathyroids are able to convert the cyanamides, these cancer cells only produce an even more harmful poison. Thus the cancer products cause loss of weight and strength and a progressive anæmia—the symptoms of the growth period. That this is the result of cancer-cell activity is proven by the quick cessation of these symptoms very shortly after our treatment is given. For within a week usually a gain in weight and blood count ensues, even before noticeable change in the dimensions of the growths take place. Moreover this cessation of activity is coincident with the uniform coagulation and calcification of every cancer cell in the body. And we recognize calcification to be the first stage in digestion of the body proteins. Thus the secreting activity of the cancer cells is cut short by the institution of their digestion shortly following treatment.

The type of disposal of the involuting cancer material also bears strongly on the interpretation of its function. For its digestion is the same as takes place in the development of bone or the organization of a blood clot, or even the digestion of milk. Here the first step is the production of a calcium-proteinate from which the protein can never again be reclaimed undenaturized. Thus to all intents and purposes the calcified cancer tissue is dead and prepared for removal, as occurs in the organization of a blood clot or the clearing out of the inside of the developing bone. Our slides of specimens removed at various periods following treatment show that calcification is uniformly established within two weeks and that the other steps that complete the removal process are associated with the ingrowth of angioblastic tissue, as occurs in developing bone and the removal of a blood clot. This process continues until all traces of the cancer tissue are cleaned out. Angioblastic tissue replaces the cancer

tissue and contracts down, and, undergoing autolysis, finally also disappears, only leaving a scar where mending of a destroyed wall is necessary.

The material absorbed from the involuting cancer is used in replenishing the exhausted tissues of the patient. This is exemplified in patients who, though unable to move their legs in bed from weakness, within ten days after treatment had gained sufficient strength to support their bodies, though not having been able to take food. Thus the method of removal and disposal of the involuting cancer tissue is exactly that used in serving other physiological processes.

The strongest and the sufficient proof that cancer is a response at protection against a definite toxin, however, rests with the fact that removal of the toxin from the body and destruction of the toxin source is followed by complete involution of all cancer tissue, complete healing of the regions involved, return to health with absence of growth and pregrowth symptoms, and the absence of recurrence. (Cases cured in 1918 still remain cured.) The cancer tissue then becomes obsolete and disappears when the function it attempts is performed for it.

The histologic, physiologic, and clinical relations in the development, behavior, and involution of cancer therefore, identify it with a physiological effort and a protective function, or immunizing attempt, which though inadequate at present, promises at some future time to be instituted in the animal economy as a definite function, perhaps as a gland of internal secretion like the parathyroid, and able to overcome one more opposing force in our environment. Cancer then represents an attempt at specialization of function in which all tissues now compete.

The chemistry and source of the toxin, the synthesis of

a successful anti-toxin, and the mechanism of immunity (a provision for conversion of a toxin into such chemical modification that it is harmless to the host, and destructive to its own source, the infecting agent), as exemplified in our work will be detailed in a further report.

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The Koch Treatment of Cancer*

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IN THE face of the discouraging situation shown in the cancer problem, gauged from the standpoint of permanent results with existing measures of treatment, we are deeply encouraged by the numerous channels of investigation throughout the world that indicates a different trend of thought. It is now an accepted conclusion that the causative features to be considered in cancer will be found in some infectious organism that serves as an exciting stimulus to cancer cell proliferation. We anticipate a definite report on some such discovery in the very near future.

Blindly we have been attacking cancer in its advanced stage for many generations, with surgical effort, only to find prompt recurrence after removal. Radium and the X-rays have brought us considerable encouragement and with the standardization of dosage now at hand, some remarkable advances have been made. When metastases are present, such as are commonly found in the breast, stomach and liver, and in the lower abdomen, practically nothing avails. This is the type of cancer that the world is interested in and for which it feverishly awaits the remedy.

Our belated interest in the germ theory was probably forced upon us by the failure to fully account for the origin of the scourge from embryonal, irritational or nu-

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tritional causes. Undoubtedly systematic changes wherein metabolism is markedly altered serves as a contributing influence, and nobody will deny that chronic irritation has not a place. The basic cause, however, must be in a micro-organism, similar to the type that functions in plant cancer as well as in that affecting the lower animals.

The German investigators did noteworthy work on cancer in mice and concluded their findings nearly ten years ago. Practically nothing new has been reported, although in this country we still persist in spending millions in similar research. Recent reports tend to disprove the infection theory, describe transplant work and present some interesting data on the tracing of malignant strains.

There are natural barriers to any material advance in discovery when the lower animals are compared to the human. The chemistry of man is exceedingly complex and is governed by different modifications. Physiologically, the comparison between the higher and lower animals cannot be made to advantage. Biochemical influences, so delicate in man, bring about processes of disease that are found nowhere else. Such conditions are apparent at the cancer age in every patient. Therefore, the futility of wasting too much study on animal experimentation.

Several treatment measures have recently been reported that have to do with the control and destruction of a recognized micro-organism of cancer. As a rule these agents have been presented in the form of antigens or serums. Claims for the results of such therapy have been conservative and are worthy of due credence. Experimental effort with the companion invaders, the protozoa, evidences definite points of interest. It is to be encouraged as of possible worth.

To my knowledge, the first successful attempt to destroy a recognized micro-organism of cancer by the subcutaneous injection of a synthetic of chemical structure, is the achievement of Dr. William F. Koch of Detroit, who contributes a notable paper in the preceding pages of this journal.

The reported work of Koch comes to me as the result of ten years of persistent and laborious study of cancer from its physiological side, and I believe his research is to be epoch-making. The Koch formula, as used for the control of the cancer organism is a differential poison, which exerts its destructive influence primarily upon the protoplasmic substance within the receptor, and not directly upon the micro-organism. This substance provides an unsuitable soil in which the germ cannot live. Thus the excitant stimulus to cancer is controlled and the mass soon retrogresses. Three weeks after the treatment has been instituted the mass becomes hard, due to calcification prior to absorption. The cancer effort or growth is a histological expression of nature's immunity attempt. It seems to be one of the wonders of nature. With the drain on the vital forces of the blood plasma removed, a fairly prompt tonic effect is exhibited. Apparently a specific action follows, in that the effects show only on the microbic structure and no other action is noted on surrounding structures. It remains also a notable fact that in all of our personally treated cases (Koch Formula 78 in all) we have rarely seen a new manifestation of growth after the treatment has been inaugurated. The reactions in suitable cases are profound and are of prognostic value.

Let us emphasize our statement of belief in the merit of the treatment by advancing the opinion that such measures should be advocated as a prophylactic measure against cancer in its incipient stage of infection. The

precancer period is now recognized in many instances to be associated with signs and symptoms developing over a term of many months, or years, prior to its onset. If the Koch deductions are accepted we should not hesitate in advocating this antitoxin as a routine measure. Such procedure has been adopted by several prominent surgeons and the outcome is anxiously being watched.

Of tremendous value are the contributions that have been started by Doctor Koch, and we know that his reports will receive world-wide consideration. The current paper deals with his early studies of the parathyroid gland and the toxins there concerned. These experiments directed his attention to a similar toxin stimulus in cancer. Every portion of his paper should be carefully studied in order to appreciate the further statements that are promised.

Four years ago, following the first meager reports of Koch's investigation, he was met by most unfair criticism by the local county medical society of Detroit, a defense to which was not permitted. Time has served to dissipate much of the cause for criticism, and we hope an honest expression will now be forthcoming. The weakest mind can criticise but it takes more thought to appreciate achievement.

Through the generosity of Doctor Koch, the Radium Institute of New York has been granted the use of his treatment in seventy-eight cases since October, 1923. Only patients with advanced cancer of the type untreatable by any other method were selected. Twelve cases are apparently in the cure stage. Nineteen have died. Of those who died it can be said they were all of a class that presented the limits of lost vitality. Eight of these had received previous radium treatments of such massive dosage as to alter metabolism and hasten a toxic state. In all but three of our fatal cases there showed a period of

improvement with reduction of the masses. No new growth presented in any case.

Although the space granted us is limited, we will report in abbreviated form three typical case records.

RECTAL CARCINOMA.—Archbishop R. Age 72. Referred by Drs. A. Paquet and T. Robertaille, Quebec, Canada.

Previous History.—Several years of constipation. In April, 1923, noticed obstruction. No pain. In March growth in upper rectum. *Diagnosis* Carcinoma. X-ray treatment given with evidence of control. Weight normal at 180 pounds. Colostomy performed in November, 1923. Masses in the lower abdomen located. Rectal mass size of large orange, with the rectum still partially functioning. Loss of weight 20 pounds. No removal of growth possible. Digestion fair. Confined to bed. Pains severe, requiring narcotics.

February 8, 1924—Examination by Doctor Field. Patient's favorable physical condition noted. Exploration of rectum not possible. No fecal matter coming through rectum. Blood stained, watery discharge. Pale and anemic. Pain increasing. Koch formula treatment administered.

May 2, 1924—Stormy reaction, characterized by high temperature, running to 105°. Nausea and vomiting. Spasmodic pain all over abdomen. Active discharge. Profound weakness and fear expressed for recovery.

June 21, 1924.—During past six weeks two distinct waves of reaction, with temperature not over 102°. Less pain and discharge. Rectal mass reduced to size of lemon and appears to be divided. Some fecal matter coming through rectum. Weight increased six pounds.

August 3, 1924.—Patient out walking and riding daily. Weight increased nineteen pounds. Present weight 183 pounds. Full formed bowel movements daily, during past two weeks. Very little pain. Appetite normal. Officiated at masses daily for ten days. Feels as well as ever, and sure of getting well. Examination shows a hard mass size of egg with no evidence of activity. Abdominal masses hard to locate. Operation for closure of colostomy wound deferred for a few weeks, although the case is probably cured.

Gastric Carcinoma.—Case B. S., 306 East 53d Street, New York. Age 78. Married, native of Bavaria. Cigar maker. Referred by Dr. H. Fineman and Dr. G. D. Browne, New York, N. Y.

Early History.—Irregular meals for years, gastric trouble common. Some loss of weight.

January 19, 1924.—Three months ago developed pain of colic type in stomach. Very severe pain directly on taking food. Tendency to bowel stoppage, and several days pass without any movement. Tenesmus symptom common. Has external and internal hemorrhoids. No venereal sickness. Always well. Blood never examined. No bladder trouble. No X-ray examination made. No weight lost. Complains of pain in back due to injury received in a fall. Examination shows a mass along great curvatures of the stomach, about twelve cm. long, tender on pressure. Pain radiating toward liver; liver extends two inches below free border of ribs. Tenderness around gallbladder region. Mass in lower abdomen about two by two and one-half inches, also tender to pressure. No previous treatment. Koch treatment administered.

February 2nd.—Reported cutaneous eruption around neck and shoulders. No nausea or vomiting. Food

intake liberal, with no dfficulty. Careful examination shows slight thickening remaining instead of the pronounced mass previously found. General condition greatly improved. Feels no pain or distress.

March 15th.—Examination shows no evidence of remaining growth. No digestive symptoms of pain of any kind. Patient entirely well. Only abnormality present is the nodule to the right of the umbilicus, which appears to be reduced one-half.

May 24th.—Stomach apparently normal. Digestion normal. No pain. Patient feels no need of further care. This result was entirely due to the single treatment.

August 1st.—Case remains well. No abnormal symptoms.

CANCER OF CERVIX, VAGINAL WALL AND VULVA.—Mrs. M. M. White Plains, N. Y. Age 58.

Previous History.—First referred to the Radium Institute by Dr. Robert H. Shanahan of Yonkers in July, 1920, for uterine fibroid. This condition yielded to radiation and the uterine body was reduced to apparently a normal size. Patient reports laceration during first childbirth. Operated in June, 1919, by Doctor Shanahan and small fibroid removed and cervix repaired. General health good.

August 3d.—Patient reported persistent bleeding. Examination showed an ulcerated area on the posterior border of the cervix, involving also the vaginal wall, over an area of three cm. Discharges of characteristic odor. Diagnosis confirmed by specimen as Epithelioma of Cervix.

September 13th.—After three weeks observation with evidence of increased ulceration, radium treatment was

instituted. From September 13th to November 13th, 1923, patient received three massive radium treatments, totaling 6000 milligram hours. Some relief of pain was secured and apparent control of the process.

November 13th.—Active advance of the nodular growth and ulceration on the labia majora and minora. Area on both sides about 4 cm. long. Unbearable pain evidenced. Heavy characteristic odor. Patient's physical condition poor. Ash gray color. Bowel action poor. Pelvic pressure excessive.

November 20th.—Koch treatment administered. Ulcerated area starting on opposite side of vagina, in one week developing size equal to original area on right side. Old area less painful.

November 30th.—Labia majora show numerous neoplastic nodules, slightly discolored, with similar nodules beneath skin along the right side of the neck. Ulcer on the right border of vagina practically healed, that on the left improved.

December 20th.—Report covering three visits. Continued reaction showing a multitude of small papular areas on labia majora. Surface of papules black and of melanotic type. Similar reaction noted on arm and neck without discoloration. The ulceration on lateral surface of vagina gradually healing and at present appears cured.

August 1, 1924.—No abnormal condition present. Case cured.