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WEATHER—Showers, Cooler

DETROIT, MICHIGAN SUNDAY SEPTEMBER 7, 1919 ONE HUNDRED AND FIFTY-SIX PAGES FIRST NEWS SECTION PRICE EIGHT CENTS

REPORTS NEW CANCER SERUM

Professor at Detroit College Sits Medical Profession by Announcement.

DOCTORS MAKE COMMENT

Jackson Giant Proves a Hoax

Money Made By Farmer Causes Much Amusement and Public

SEEKING ROOMS FOR TEACHERS

Code Appeals to Citizens Threaten Concerns to Provide Living Quarters.

COSTS BRING HIGH PRICES

Walsh Says Wilson Admitted Pact Failure

Quotes President as Stating Tragedy of Day Was Choking of Self-Determination by Secret Treaties.

G. O. P. Senators Say Pact Change Is Too Drastic

IOWANS WANT PACT RATIFIED

G. O. P. Newspapers and Leaders Back President's Demand for No Reservations.

REPRESENT BIG MAJORITY

WILSON SAYS DELAY BREEDS BOLSHEVISM

Tells Big Des Moines Audience That "Poison May Spread to This Country" While Senate Debates Treaty.

Rule of Many by Few Must End, He Asserts; Points Out Mortification, Which Would Follow Rejection by U. S.

Wilson Pledges Life to Fight for Pact Ideals

POLICE REGAIN LOOT "LONE WOLF" STOLE

Boyle Bandit Mate Urging Him Wife to Give Up Gems.

HOWE QUITS TO FIGHT FOR PLUMB RAIL PLAN

President Wilson Man Leaves New York Post Job.

Mr. Armour's Shoes

COLLEGE FELLS ON THOSE 120 PAIRS FOR MACHREE



SAY GARY REFUSED WILSON'S APPEAL

Presidential Party Hears Final Conference in Oil.

BERLIN BAR RAIDED BY SQUAD OF POLICE

Proprietor and Manager Held for Breaking "Dry" Act

WOMAN KILLED WHEN AUTOMOBILE TIPS

Benjamin, Who Was Injured in Recent Accident.

SCOUTS DEFMAN COMPETITION IN TRADE

REPORTS BELLA KUN ESCAPES TO VILNA

HERE'S TIP FOR DETROIT TO RELIEVE HOTEL RUSH

COLUMBUS CAR SERVICE RESUMED; TO ARBITRATE

SAY GARY REFUSED WILSON'S APPEAL

PAUL M. KOCH
10 LAKECREST LANE
GROSSE POINTE FARMES, MI 48236
1-313-881-2978
FAX – 1-313-881-2978

February 17, 2009

Mr. Jon Meacham
Editor of NEWSWEEK
P.O. Box 2120
Radio City Station
NY 10101-2102

Dear Mr. Meacham:

I owe you an apology for omitting the following, a part of the September 7, 1919 Detroit Newspaper article on my father, Dr. William F. Koch, in my letter of February 9, 2009 to you. The omitted portion started on page 7 of the article: "CONFIRMED BY PHYSICIANS."

CONFIRMED BY PHYSICIANS,

The stomach, Dr. Koch, says, although important, is not necessarily a vital organ.

According to Dr. Koch, not one case of cancer in the history of the world had been cured by medical treatment until he discovered his compound.

Several Detroit physicians, whom Dr. Koch thanks in his paper for their co-operation in his cancer treatment, have confirmed Dr. Koch's statement that he has established clinical cures of cancer in specific cases.

By "clinical cured" is meant they explained, that insofar as can be determined without exploring the patients by operation to justify a positive statement that no trace of cancer remains or by waiting five years to ascertain that there is no recurrence of the cancer, the patients have been cured.

Although all spoke of Dr. Koch's treatment with that reserve which, in discussing the value of another man's discovery of a disease-treatment, marks the utterance of reputable physicians, jealous of their own professional reputations, they were unanimous in the opinion that Dr. Koch's treatment has shown remarkable results. That, from the viewpoint of the physician, caution in indorsing a "cancer cure" is natural, is emphasized by the statement of Dr. J. H. Carstens, and solemnly echoed by two others of the physicians interviewed, that "the man who discovers a cure for cancer will be the greatest man in the world."

BRILLANT CHEMIST,

Dr. Alexander W. Blain, surgeon, head of Jefferson clinic: "Dr. Koch is one of the most brilliant physiological chemists in the country. It is too early to

say he has a cancer cure, and it should not be regarded as a 'cure-all' but as an adjunct to the treatment of cancer. No cure can be established until five years have shown there is no recurrence of the disease. But what he has done is this: He has made people well who were so far gone with cancer that they had only a few weeks to live. Several patients he treated for me are working hard and enjoying life a year after they 'should have been dead.' Even if Dr. Koch gets no further with his work than he is now – and he is experimenting now with his fifteenth mixture, I believe – even if he has not discovered an absolute cure for cancer, he has added years to the lives of cancer victims. There are nearly 300,000 victims of cancer in the country and if they could all have a few years of usefulness added to their lives the saving to the country would be enormous. What he has already done is a boon to humanity and a great step forward in physiological chemistry."

CONFIDENCE IN KOCH,

Dr. Walter L. Hackett, visiting gynecologist and obstetrician, Woman's Hospital: "There is no question of Dr. Koch's sincerity and ability. It will take five years to determine whether or not he has a real cure for cancer, but I have enough confidence in his treatment to let him inject his serum into any cancer patient of mine. I had, as a patient, an old woman who was very far-gone. At Koch's suggestion I operated on her and took out such cancerous growths as were apparent. Later, the cancer grew again. Dr. Koch gave her four injections and she is now apparently entirely well. I have seen some excellent work done with radium, but never anything so remarkable as this. Dr. Koch should be given every opportunity to prove the value of his treatment."

Dr. C. Hollister Judd, president of the medical board, Women's Hospital: "When we stop to consider that one woman in every seven and one man in every 12 have cancer, the importance of the work Dr. Koch is doing can not be overrated, though it is too early to say that he has a cure for cancer. He has been working under many handicaps. The cases given him have been the 'hopeless' ones, where the surgeons saw the uselessness or impossibility of further operation, and his treatment has shown remarkable results."

SHOULD BE HELPED,

"Everything should be done to encourage him in his work. He should not be obligated to think, for instance, of expense. Yet his serum costs him $8 an injection, I believe. He ought to be given $100,000 to carry on his work and he ought to have a ward in a hospital where he could concentrate his patients. Women's Hospital is arranging to give him 12 beds. Dr. Koch's work, which is still experimental, is important in this sense; he is studying cancer physiologically rather than pathologically. That is, instead of working on the cancer tissue of a dead person, he is working on patients who are alive. There might be a question as to which method is more interesting to the physician, but there is no question of which appeals more to the patient."

Dr. J. H. Carstens: "He has apparently effected some wonderful cures, but it is too soon to say this positively. I am against publicity in the matter, as we do not want persons afflicted with cancer to flock to Detroit for treatment when they will not be able to be taken care of. Dr. Koch will get all the cases he needs."

Unless you had read the attached exhibits to my letter, which contained a full copy of this newspaper article, you would not perceived the support that Dr. Koch was receiving from a part of the local medical profession in the Detroit area in 1919. All the radiation therapy, which most cancer patients often received, would produce toxic burned cancer and normal adjacent tissue. This burned tissue and its toxic biological products and/or carcinogenic chemical would have a negative effect the body's normal chemistry. Thus the cancer patient's body would have an extra burden to metabolize and/or removed these substances from the body before they caused additional hindrance for the cancer patient taking the Koch treatment. Thus radiation therapy was counter indicated by Dr. Koch for his new form of treatment for cancer. In Detroit the radiologist, a powerful group of medical doctors, found it in their best interest to oppose Dr. Koch in every way possible because he had found that cancer patients who had received prior radiation therapy did poorly with his treatment.

It should be noted that Dr. Koch, as a part of his cancer research, studied and compared the chemistry of radiated cancer tissue with non-radiated cancer tissue and normal tissue. After the local radiologists stopped supply him with radiated cancer tissue for his cancer research, it became necessary for him to write to doctors in other cities in order for him to obtain the radiated cancer tissue that he needed for this part of his cancer research. Dr. Koch published his second cancer research paper, A NEW AND SUCCESSFUL DIAGNOSIS AND TREATMENT OF CANCER in October of 1920. His third cancer research paper, "The Function of Cancer" was published in the October 1924 issue of CANCER. In this paper he wrote about toxicity in the body and its relationship to cancer cells. This was his last medical research paper that ever made it through the censorship placed on his medical research by the J.A.M.A. in the United States.

On November 12, 1924, Dr. A. R. Mitchell, a member of the Board of Trustees for the American Medical Association wrote the following to Dr. Koch.

> "I had the pleasure of reading your article in the October number of "Cancer" and it is certainly the most intelligent and enlightening discussion of the subject I have ever read. For years I have been convinced of the utter uselessness of surgery in the true cancer cases and have made myself disliked somewhat by my opposition to surgeons going about the country lecturing upon a subject which themselves knew nothing. I hope that a little more time will prove that your work is really an epoch making work and that you will ultimately secure the full credit and profit to which your services entitles you."

I hope that you will have a better understanding of the cancer research of yesterday that is being now overlooked by the cancer researchers of today. Until the Medical profession open its eyes and reads once again and understand the truth about the independent cancer research of yesterday by cancer researchers such as Dr. William F. Koch, Dr. Albert Szent-Gyorgyi, Dr. Otto Warburg and others, there is very little chance that we will ever have a truly effective cancer treatment for cancer victims of today. Consider once again the Judy McWhorter cancer case and what the A.M.A. did to the doctor who gave her the Koch Treatment "Glyoxylide." Also consider how the A.M.A. ruthlessly treated Professor Carroll W. Allen, M.D., who had the courage to investigate

Dr. Koch and the Koch Treatment in 1924-1925 and then report his findings to his local medical society. The American Medical Association is the only medical association that I know of that has a criminal record. (AMERICAN MEDICAL ASSOCIATION v. UNITED STATES, 317 U.S, 519, January 18, 1943) Its greatest crime has been its efforts to destroy Dr. Koch and the Koch Treatment for cancer and its allied diseases. For this crime the A.M.A. has gone unpunished for nearly ninety years. The Koch medications, including Glyoxylide, could be produced today at a cost of $100.00 or less per treatment. Our Government could save billions of dollars in healthcare expenses by using the Koch Treatment, if the A.M.A. would let it. Dr. George H. Simmons and Dr. Morris Fishbein are dead; why must the American Medical Association still follow their dictates? The American patients are the ones that still suffer from the A.M.A.'s cruelty. Why must this A.M.A. fraud continue and who has the power to stop it? Or, does anyone really care?

Sincerely yours,

Paul M. Koch

Enclosures:

1) Corrected copy of Paul Koch's letter of February 9, 2009 to Mr. Jon Meacham;
2) Dr. Mitchell's letter of Nov. 12, 1924 to Dr. William F. Koch;
3) The Function of Cancer, by Wm. F. Koch, Ph.D., M.D., October "Cancer," 1924;
4) A NEW AND SUCCESSFUL DIAGNOSIS AND TREATMENT OF CANCER, by William F. Koch, Ph.D., M.D., Medical Record, October, 1920;
5) Dr. H. Edwin Lewis's letter of November 4th, 1920 to Dr. Koch in which Dr. Lewis was soliciting articles by Dr. Koch on any medical topic for early publication in American Medicine.
6) Chemical Consequences of the Removal of the Parathyroid Glands, A copy of the Editorial from the Journal of the American Medical Association, Vol. LXI, No.13, on the early medical research of Dr. William F. Koch.
7) Dr. George W. Crile's letter of June 4, 1919 offering to give cancer material to Dr. Koch for his cancer research.
8) June 10, 1947 Statement of Warren E. Miller, Attorney at Law, pertaining to Dr. Koch's offer to the United States Veterans Administration to treat veterans who were sick with Malaria. Unfortunately for the sick veterans, the Veterans Administration required prior approval from Dr. Morris Fishbein before the Koch Treatment could be used to treat these patients.

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American Medical Association

Lincoln, Nov. 12, 1924.

Dr. Willaim F. Koch,
Detroit College of Medicine,
Detroit, Mich.

Dear Doctor:

I received the material sent me a few days ago from your laboratory. This I understand was through the courtesy of Dr. Lynch. The office girl tells me that a letter came from you before the package. I did not see the letter which came during my absence and was evidently mislaid or lost.

The case on which I expected to use the material is not in favorable condition at this time. Shall I return the tube to you or to Dr. Lynch or retain it myself? I have another case which I believe is a very favorable one. The case is from another city so that I see it only once in a month or six weeks. I shall be guided by Dr. Lynch in the use of the material. Have been watching his cases at Fairbury and am convinced that whatever the substance is, it is efficient. I had the pleasure of reading your article in the October number of "Cancer" and it is certainly the most intelligent and enlightening discussion of the subject I have ever read. For years I have been convinced of the utter uselessness of surgery in true cancer cases and have made myself disliked somewhat by my opposition to surgeons going about the country lecturing upon

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American Medical Association

Lincoln,

a subject of which they themselves knew nothing. I hope that a little more time will prove that your work is really an epoch making work and that you will ultimately secure the full credit and profit to which your service entitles you.

Very sincerely,

ARM:VH

The Function of Cancer.*

By

Wm. F. Koch, Ph.D., M.D.

DETROIT, MICH.

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.

* *Reprinted from the October "Cancer"*

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 topsy-turviness 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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A NEW AND SUCCESSFUL DIAGNOSIS AND TREATMENT OF CANCER.

By WILLIAM F. KOCH, PH.D., M.D.,

DETROIT, MICH.

THE mortality from cancer has not been changed essentially by all the treatments ever used to combat it. The death rate still stands one out of eight for females, one out of fourteen for males, dying over forty. So far as the efficiency of the various treatments for cancer is concerned then, we make this observation, that no treatment yet devised meets the essential pathology of the disease.

It is the purpose of this paper to present certain physiological deductions which locate the essential pathology of cancer, and to describe a treatment that simply corrects the pathological condition on a physiological basis, and thus establishes cure. A few histories and microphotographs are selected to illustrate the various phases of the treatment.

In 1912, 1913, 1916 and 1917, I reported* the occurrence of toxic quantities of certain guanidine bases and other products of tissue degeneration in the urines of parathyroidectomized dogs. This finding has since been confirmed by Paton at Glasgow and by other observers. My autopsies showed in

*See Bibliography appended.

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these animals extensive antemortem coagulation of the blood and also a coagulation of the tissue cells in the liver, lung, spleen and brain.

Such extensive coagulation of blood and tissues ensuing upon the loss of one physiological substance is suggestive that normal functional tissues are incoagulable so long as they receive and can build into their structure all the elements necessary for functionally co-ordinated activity, and that as soon as this balanced nutrition is disturbed they become coagulable. In this case after parathyroidectomy the tissues had lost a necessary special element and had become coagulated just as blood withdrawn from its endothelial encasement becomes coagulable.

Now, two types of substances are active in the coagulation of drawn blood, the thrombokinase and the thrombin.

The thrombokinase is a product of tissue-cell injury and blood plasma is constructed to have unsaturated affinity for it, so that when this product is liberated it can react with the blood plasma and initiate clotting. Therefore, thrombokinase produces intravascular and extravascular coagulation. This is a physiological function of the plasma to prevent hemorrhage. Likewise the plasma of tissue cells clots by reaction with a product of injury to tissue cells. This function of tissue-cell plasma coagulation serves to wall off destructive processes and also to lay a bed for ingrowth of angioblastic organization tissue, thus preparing for and promoting the healing process. This coagulation process is evidently, then, a highly specialized function in all normal tissues and an activity of their functional substrate.

The type of injury that leads to the production of thrombokinase may be an active, physical or

chemical one, or a passive one, as occurred in my parathyroidectomized dogs, where failure to supply certain necessary elements (because of absence of the parathyroid activity) prevented the completion of the restoring of the cell functional substrate, and therefore the elements of this substrate already present, not being usable, were set free and were active as tissue injury or degeneration products, and initiated clotting not only of the tissue cells but of the blood as well.

The condition necessary for the initiation of coagulation in a tissue plasma, then, is the presence of a certain product of tissue-cell degeneration for which the plasma has unsaturated affinity.

The Thrombin. Now it happens in any physiological intracellular function that the initiation of a state of change and the propagation of this state are mediated by different substances, the propagation of the state being carried on by the products of the change induced, whether energy is liberated or not. We observe this in muscle and nerve cell function, and a good example is offered by blood clotting.

The process of clotting having been initiated by the kinase, some thrombin is formed by the clotting process, and this substance propagates the change of state in the fibrinogen. After blood is shed its functional substrate is removed from the nutritional support of its endothelial encasement and therefore is in the predicament comparable to the tissue of my parathyroidectomized dogs, and subject to thrombin activity. As stated above, coagulation of tissue plasma is a function of the tissue and therefore an activity of its functional substrate. The kinase acts on this functional substrate, starting the process; the thrombin, a product of the

state initiated in the tissue functional substrate, propagates the process. Thrombin cannot act on an unchanged functional substrate as is illustrated by the fact that it will not change the coagulability of circulating blood where a state of coagulation has not been initiated. It can act only on a plasma associated with a change of substrate.

Since cancer is deficient in functional substrate, at least insofar as any specialized highly differentiated function is concerned, it was suggestive that this variation from the normally constructed substrate might constitute a susceptibility to coagulation and therefore to the action of tissue thrombin. That is, the change necessary to induce coagulation existed, but the functional substrate being deficient, no thrombin product could be evolved to propagate a coagulation state throughout the cancer cell plasma, and therefore the cancer cell plasma remained unclotted until it might receive the propagator of the state that virtually existed in it.

In line with this supposition, then, thrombokinase could not initiate coagulation in a cancer cell, although not clotted, being already prepared for the activity of the thrombin.

To test out this hypothesis cancer patients were treated with tissue thrombokinase and with tissue thrombin. Amounts varying from 1/100 grm. to ½ grm. of tissue kinase and tissue thrombin being injected subcutaneously, generally in the patients buttocks, the substance being dissolved or suspended in normal salt solution in from 1 to 10 c.c.

The kinases will first be disposed of.

Quantities of the kinase insufficient to cause extensive intravascular coagulation of the blood, and therefore immediate death in the patient, were found actually to increase cancer growth and, more-

over, to cause so great a negative coagulation phase of the patient's blood that hemorrhages were profuse and the continuance of such treatment threatened the patient's life. The site of the injection

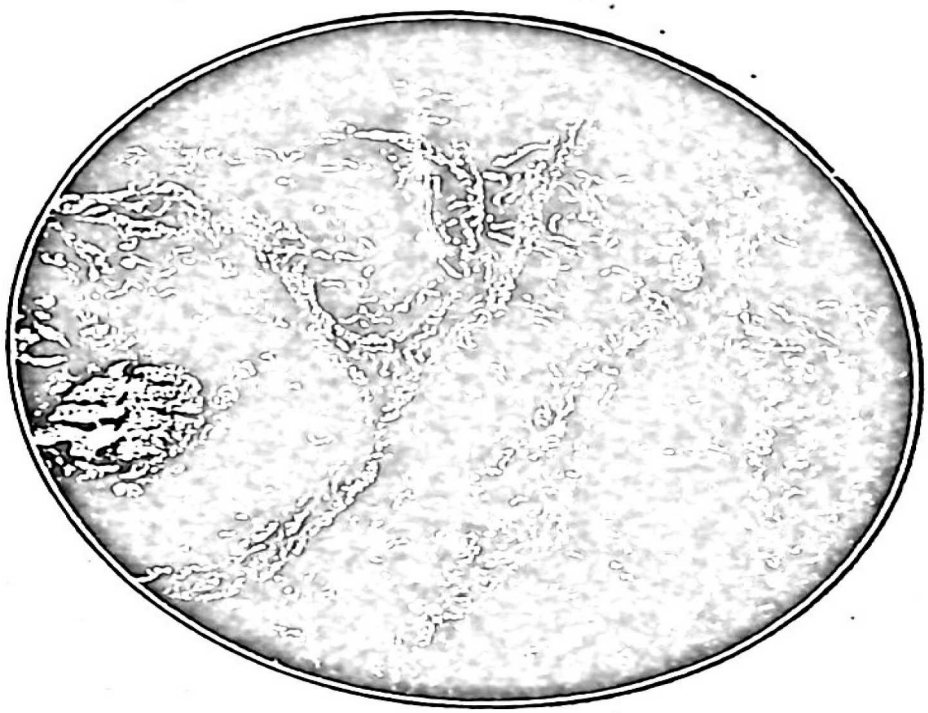


FIG. 1.—Section taken from the untreated squamous cell carcinoma.

showed tissue death. Therefore such therapy was discontinued as useless and harmful.

The use of the tissue thrombin, however, brought very different results. Locally, where injected in the hip, no sign of disturbance was produced—no more than if normal salt solution were injected.

There was no change in the patient's blood coagulation time, as the following experiment shows:

Fifty mgms. of tissue thrombin were injected subcutaneously into a healthy man of 157 lbs.

	Coagulation Time
Before injection	2 min. 40 sec.
10 min. after injection.....	2 min. 40 sec.
1 hr. after injection.....	2 min. 42 sec.
12 hr. after injection.....	2 min. 40 sec.
24 hr. after injection.....	2 min. 43 sec.

Fifty mg. of tissue thrombin were injected into a cancer patient who had not had any severe hemorrhage.

Before injection	3 min. 12 sec.
1 hr. after injection.....	3 min. 20 sec.
12 hr. after injection.....	3 min. 14 sec.
24 hr. after injection.....	3 min. 8 sec.

The microphotographs show the effect of the injected tissue thrombin upon cancer cells. These sections were taken from a large squamous cell carcinoma of the neck (Case IV, reported in the *Detroit Medical Journal*, July, 1919). The usual dose of 50 mgms. was given in the hip.

Section I was taken before treatment and shows the normal squamous cell carcinoma. Fig. 2 shows a low power magnification, and the series 3, 4, 5 and 6 show the details of the changes induced after two treatments. The most pronounced changes are firstly, a disappearance of the cells lining the basement membrane. These are the cells closest to the blood supply, the germinal cells of the cancer. Naturally the tissue thrombin reaches them first and they are the first to be destroyed. As rapidly as they disappear angioblastic tissue replaces them. Apparently the carcinomatous clumps are being devoured by angioblastic tissue just as takes place in the development of bone and in the organization of a blood clot. Investigation of the chemistry of these three phenomena reveals that they are essentially the same process.

The changes preparatory to organization of the cancer tissue are first as shown in Fig. 6, nucleolysis and a fibrin formation in the cells, and as is shown in Figs. 3, 4 and 5, a swelling of this fibrin which produces a hyalinization of the cancer protoplasm.

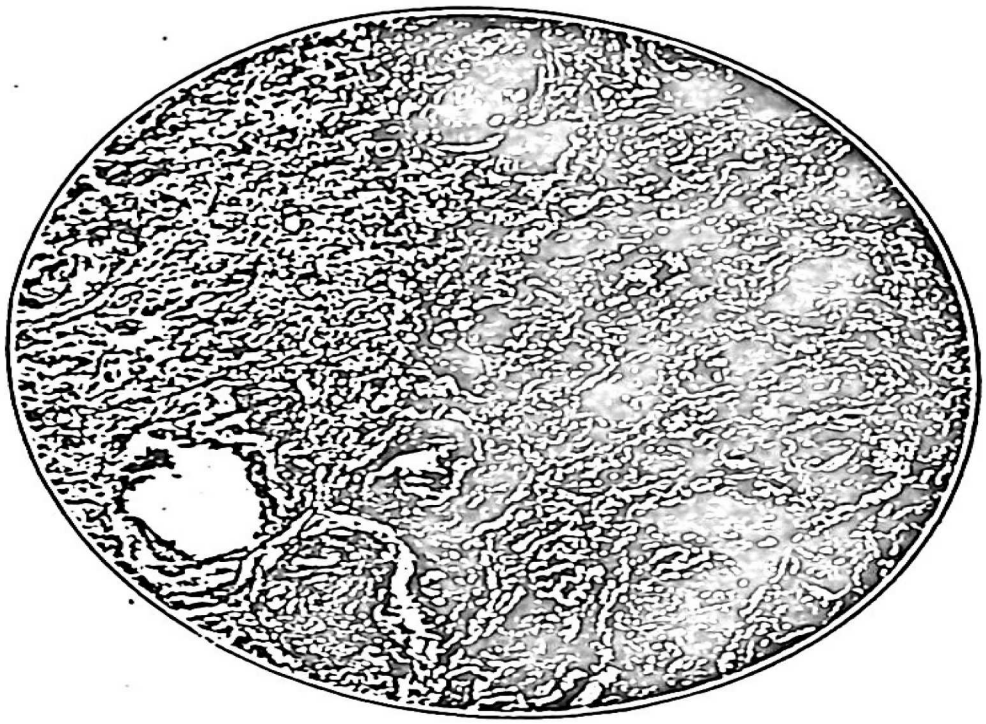


FIG. 2.—Section from the squamous cell carcinoma, removed 24 hours after the second treatment (low power). The disappearance of the malpighian layer of cells, the hyalinization of the protoplasm, and the disappearance of the nuclei of the remaining cells and ingrowth of fibroblastic tissue are shown here.

This is a digestive change in the clotted protoplasm which accompanies the ingrowth of the angioblastic tissue (shown best in Fig. 3 and Fig. 4 at x). Fig. 7 was taken from a piece of the carcinoma removed after the fourth treatment. It shows the practically

complete replacement of the carcimona by fibroblastic tissue. Whatever carcinomatous debris is left has undergone a calcification. This calcification change also occurs preliminary to bone absorption in the development of bone. Here it occurs in the



FIG. 3.—High power magnification of section (Fig. 2), showing chromatolysis, fibrin formation, and hyalin change in the cancer cells. This section shows the ingrowth of angioblastic tissue, the organization of the coagulated cancer.

last remnants of the clotted cancer which have lain unabsorbed sufficiently long to have taken up lime salts. This change is a conclusive testimony to the complete death of the cancer moreover.

CLINICAL.

The clinical features that accompany this change

induced in the cancer are for the first twenty hours after injection practically negligible. There is no change in the heart beat, in the respiration, or in the comfort of the patient. Locally, in the hip where the injection is given, there is no reaction at all. After twenty hours the injected material has been taken up by the circulation and lodged in the cancerous tissues where it now shows its work. The cancerous parts become swollen, more painful than usual, and reflexes associated with the part are augmented and fever develops, especially between twenty-four and thirty hours after injection, generally lasting from two to six hours, and as this subsides the affected parts become smaller and less tender than before treatment, and there is less pain. The patient, however, may be quite tired out for the next day, but the following day finds him much more normal and buoyant. As a rule, after two injections hemorrhages have stopped, not to return, and pain ilkewise, as treatment proceeds, rapidly passes away.

CASE I.—The first case is selected to illustrate the healing of a vesicovaginal fistula large enough to easily admit three fingers following upon the disappearance of the cancer tissue. It also illustrates the usual reaction features. This patient came under my care April 24, 1919, referred by Dr. Walter Hackett of Detroit.

Mrs. B., age 53, housewife. Normal weight, 125 pounds, five years ago. Patient's family state weight at present to be 70 pounds, having been weighed several weeks previously. *Family history*—Father died of cancer of stomach, age 61. Mother died of heart disease, age 57. No history of tuberculosis, insanity, or alcoholism in family. Four children alive and well. *Past history*—Two years ago (1917) patient noted vaginal discharge, which gradually became excessive, odorous and bloody. More notable were the occasional hemorrhages without period of menstruation. This bleeding was initiated by sudden movements, and even

came on during sleep in bed. At this time her weight was 107 pounds. In March, 1919, patient and Dr. W. Hackett amined by Dr. Garber, Dr. Hurst and Dr. Walter Hackett. who gave the diagnosis of carcinoma of uterus. sermann, negative; R. B. C., 2,700,000; Hem., 50 per cent.; urine, albumin, trace; sugar and casts, negative.

April 5, 1919, laparotomy and hysterectomy by Dr. Walter Hackett. As much of the carcinomatous tissue as possible was removed, although the subrenal lymph glands were infiltrated. Tissue examined microscopically, and proved to be adenocarcinoma of the patient. metral origin. On April 30 I found the patient very weak and anemic. She could not sit up in bed without help. It was impossible to get a satisfactory drop of blood by several deep punctures of the finger, as attempt to withdraw blood by syringe failed, and vein collapsed. Patient took about 8 ounces of milk per day and very little other food. The pain was severe enough to require between 3 and 4 grains of morphine per day. The discharge was excessive, strong odor, and accompanied by large amounts of from a vesicovaginal fistula of the vagina admit three fingers. At the orifice of the urine cinomatous nodules were visible. Moderate but easily hausting hemorrhages had occurred several times ex- week. She was given an injection of 50 milligrams of tissue thrombin in 2 c.c. of normal salt solution, April 30, 1919. Temperature, 96.2°; pulse, 110. The next day, 24 hours after treatment, her temperature rose to 101.4°; the pulse became feeble and 134. The pain in the back and abdomen was intense for 4 hours. Two grains of morphine had to be given by hypodermic injection to control it. The next day the temperature was 97.2°, and in the succeeding night an exhausting hemorrhage occurred. The blood clotted readily. This was the last hemorrhage. May 3 a similar treatment was given. Temperature, 98°; pulse, 120. In 24 hours the temperature rose to 102°, and was maintained for 8 hours. The discharge had increased considerably and had become more acrid. The patient suffered so much pain that 2 grains of morphine were necessary. On May 6 the third treatment was given, the discharge still increasing, but with less odor and no blood, accompanied by less pain than the former treatments. After 24 hours the temperature rose to 101.6°, the pulse to

103. The fever was maintained for 6 hours. The appetite started to improve after this treatment, and in four days she was able to sit up in bed without help. The succeeding treatments brought on similar reactions, but each time the fever and pain were less, so that after taking the ninth treatment, June 5, neither pain nor fever could be elicited and the patient has suffered none since, having also discontinued the

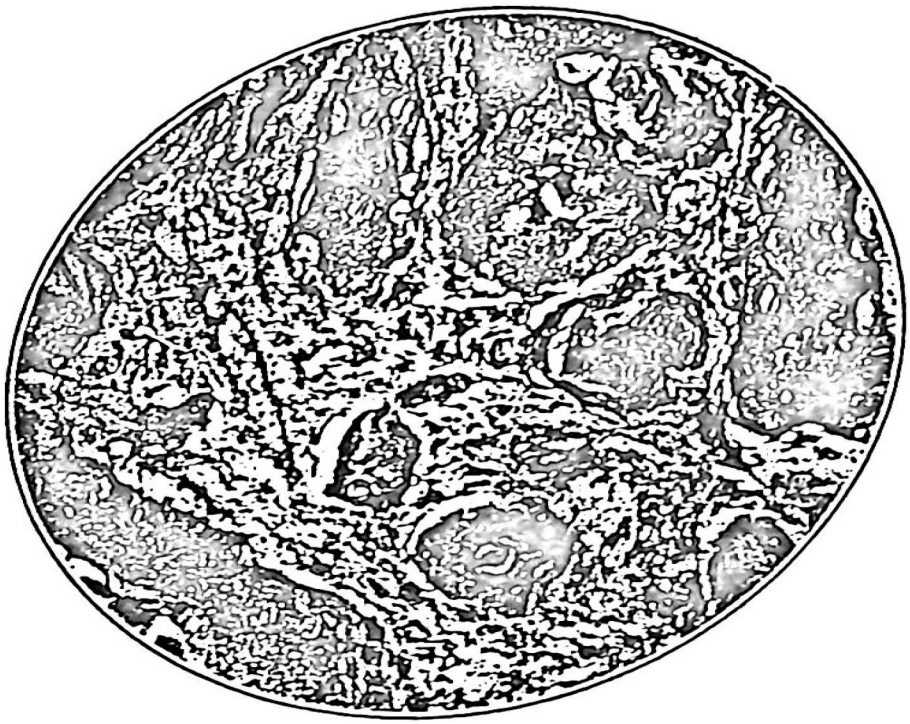


FIG. 4.—Shows the same changes as in Fig. 3.

use of morphine. The discharge had completely disappeared, and the patient was able to walk about the house and sweep the floor. She then weighed 94.5 pounds. Treatment was discontinued.

On June 30 the patient weighed 112 pounds, a gain of 42 pounds in eight weeks (since treatment was started). At this time there was slight and controllable escape of urine through the

vagina. She was examined in the middle of July by Dr. J. H. Carstens, who stated that he found no evidence of cancer, and the vesicovaginal fistula was closed so as not to admit a finger. This region he found indurated. On August 8 examination was again made and fistula found entirely closed; weight, 116 pounds. She was then active at her household duties. The blood was taken for analysis: R. B. C., 3,970,000; H.,



FIG. 5.—Shows the same changes as Fig. 3 and at x the ingrowth of angioblastic buds into a coagulated mass of cancer.

70 per cent.; noncoagulable nitrogen, 29 mgms. per 100 c.c.; alkalinity, 47 c.c., CO_2 per 100 c.c.

The alkalinity was normal and not increased, as is the rule in cancer patients. The noncoagulable nitrogen was normal, hence there was no diminution of kidney function. The patient had no symptoms of cancer, and examination elicited only some slight induration

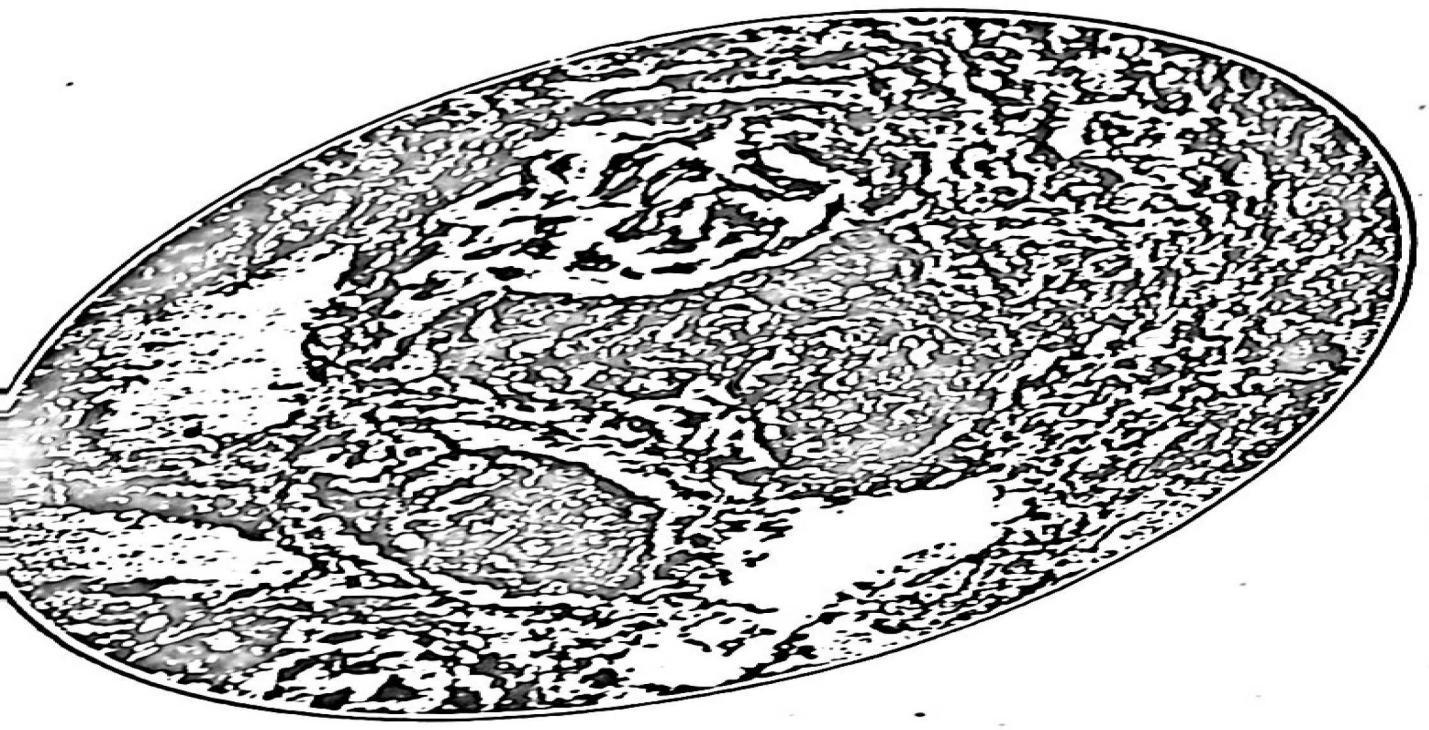
at the region of the previous fistula, which was to be expected as a result of the healing process. She was therefore pronounced tentatively cured, and remained so until November 5, 1919, when she suddenly dropped in an apoplectic stroke and died November 6 of apoplexy. Unfortunately, I was not notified of her death until two weeks later, and then an autopsy was out of the question.

CASE II.—The following case illustrates a variation from the usual type of reaction. Instead of the reaction coming on 24 hours after the treatment, in this case no febrile response occurred until twelve days after the first treatment and seven days after the second treatment. During this period a large carcinoma of the stomach, practically stenosing the pylorus, disappeared.

Mrs. P., aged 58, referred by Dr. Heavenrich of Port Huron, Mich., November 1, 1919. *Family History.*—Father died at middle age of heart trouble. Mother died at 85 years of old age. Brother died of typhoid. One sister died of pneumonia. Two sisters alive and well. No history of tuberculosis, insanity or cancer. *Chief Complaints.*—Pain in abdomen and right back, vomiting and tender mass in upper abdomen.

Past History.—Measles, whooping cough, chickenpox in childhood, well otherwise until present illness. Menses began at 14, have been normal until menopause at 49, were somewhat painful first day or two. Pregnant once; child died in infancy. No miscarriages; denies venereal infection. For past three or four years patient has been troubled with indigestion, pain coming on from two to three hours after eating, with burning pain and eructation of gas. *Present History.*—On this subject Dr. Heavenrich of Port Huron writes as follows: "She was taken ill August 1, 1919, with what was diagnosed gallstone colic. Needed opiates for relief of pain. During the following six weeks had repeated attacks—pain, nausea, jaundice. Was seen by several doctors, all of whom agreed in diagnosis and need of operation. I first saw her in September in one of these attacks. I found her emaciated and anemic, suffering severely with typical gallstone colic. Deep jaundice over entire body. Itchy skin, clay stools, vomiting bile. Unable to retain any food. Temperature 98.4°; pulse, 112. Abdomen so tender as to

make palpation impossible. I also advised o
and was requested to do so at once. I had her
to the hospital, where she was operated on the
ing morning by Dr. Aldridge and myself. To ou
prise we found the liver and gall bladder perfectly
mal—no stones, no thickening of duct walls, etc.
the lesser curvature of the stomach was one la



s same changes as Fig. 3, but more particu-
dbrin formation in the cancer protoplasm.

d tumor, hard in consistency, with some
ous spots. So much of the organ was
e patient was in such a weakened con-
were both of the opinion that gastro-
ny modification of such operation
ail. We closed the wound and about
ner to you. At this time (August
s to be in splendid health, does her

own work, and eats everything, and certainly is gra
ful to you."

On admission to the Womens' Hospital, Detroit, N
vember 1, 1919, her weight was 119 lbs.; R.B.C., 3,10
000; H. 60 per cent.; Wassermann negative, urine neg.
tive to albumin, casts and sugar; volume 7 oz. in 2
hours. Stools loose, scanty and tarry, occult bloo
negative. Retention of food very slight, apparently
all food ingested was vomited. Physical examination
revealed mass in epigastrium raised to a level of an
inch and one-half above the costal level. Palpation
showed mass to be hard and very tender, which pre-
vented outlining its borders. Light percussion showed
the dullness to extend to the umbilicus.

For descriptive purposes her stay of forty-one days
at the hospital is divided into three periods. The first,
of eleven days, was reaction-free, although an injec-
tion of 50 mgm. of tissue thrombin was given on the
first and fourth days. Temperature running from 97°
to 98°, with at times severe abdominal pain and vomit-
ing the daily food ingested. The second period started
on the eleventh day, seven days after the second treat-
ment, with a fever of 102°, dropping in 36 hours to
normal and rising for three successive days to 100°.
On the third day of this period (the fourteenth day),
a third injection was given, followed in 48 hours by a
fever of 102°, which returned to 99° in the course of
24 hours, rising again for four more days to
100° and again to 102° for a number of hours.
After a rest of two days she was given an-
other treatment, and in 48 hours another fever
of 102° was elicited, returning to normal within 24
hours and remaining there ever since. During this
period there was much pain in lower right chest and
shortness of breath and cough coming on in daily spells
and accompanying the epigastric pain. With the dis-
appearance of the fever at the end of this period all
pain left. During the last six days there was no vom-
ing, nor has there been since. The appetite and di-
stion rapidly improved, and no epigastric mass was
dent on inspection. The third or convalescent period
14 days was painless and without vomiting or
tric distress, the patient taking the regular tray.
perature running 98° to 98 3/5°. She rapidly
ed strength. On the sixth day of this period a

treatment of 50 mgms. was given, without any focal or febrile reaction. Examination of the epigastrium showed neither dullness nor rigidity and only slight tenderness. On deep palpation a suggestion of a tumor rather soft and not outlinable was found. She was kept in the hospital for eight days longer and her abdomen again examined. This time the examination was entirely negative. R.B.C. 4,000,000; H. 80 per

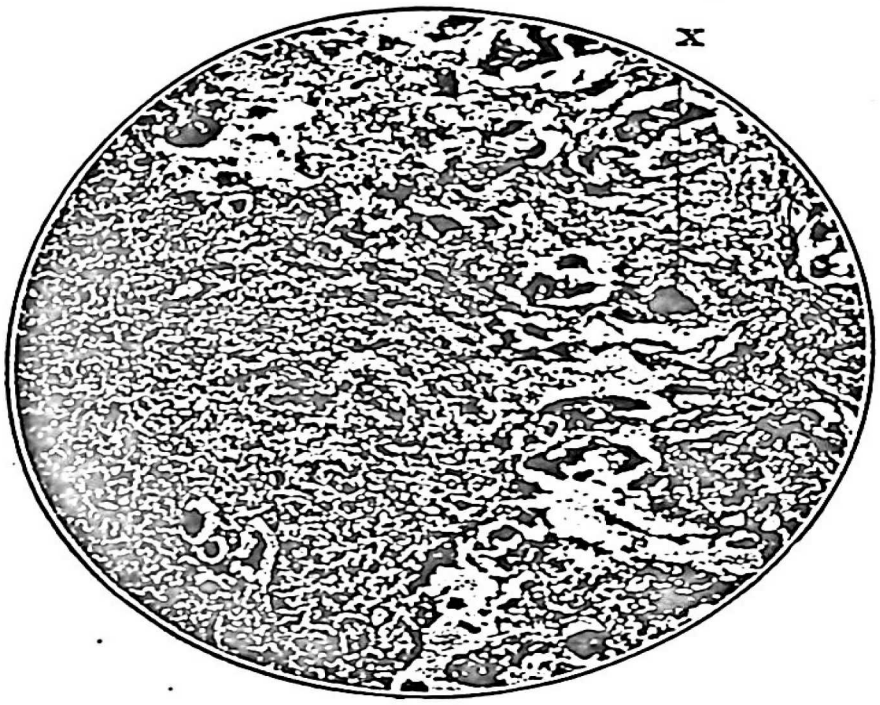


FIG. 7.—Low power view taken from a section removed after the fourth treatment, showing the fibroblastic replacement of the killed cancer. Also calcification (x) of as yet unabsorbed debris.

cent.; weight, 126 lbs. Blood analysis: Non-coagulable nitrogen, 43 mg. per 100 c.c. Alkalinity, 40 c.c. CO_2 per 100 c.c. She was discharged, tentatively cured.

In March, 1920, the patient was requested to present herself for another examination. She appeared to be in splendid health, had a good appetite, ate everything,

and weighed 142 lbs. She complained of slight distress after eating for the past week. She was given two more treatments four days apart, with slight focal reaction and a temperature of 100.2° in response to the first treatment, but no febrile reaction to the second. Within a week the indigestion had disappeared and has not returned to date. In July, 1920, her weight was 152 lbs., and she reported no trouble. Examined again August 1. Weight 159 lbs. She is still in excellent health.

CASE III—This case, with its control case and the case following, are submitted to illustrate the effect of doses of various amounts of tissue thrombin. These three cases came from the same region in Michigan, two from Bay City and one from a neighboring town. The first two are in patients of normal weight of about 200 lbs., the third a normal weight of 160 lbs. The first two have similar carcinomata of the large bowel, and the third a gastric cancer.

Mrs. B., referred by Dr. H. J. Meyers of Saginaw, Mich., January, 1920. *Family History.*—Mother died of heart failure at the age of 69 years. Father died of cancer of stomach, age 71. Two sisters died of tuberculosis. She has one son living and well. *Past History.*—Scarlet fever at 8 years, and a cervix repair operation about 25 years ago. *Present illness*, reported by Dr. Meyers, as follows: "Mrs. G. B., housewife, age 52, was first seen by me in consultation with her home physician in Bay City. This was in October, 1919. The story was as follows: A few days before, Mrs. B. had been very suddenly seized with intense abdominal pain, most marked in the upper left quadrant. There was nausea but no vomiting. The pulse became rapid and weak. There was great prostration, and the patient bordered on collapse when Dr. K. arrived and administered morphine and stimulants. This attack occurred about 3 P. M. The next morning at 2 o'clock the patient had a large hemorrhage from the bowel. Two hours afterward a second bloody stool was passed. There was no recurrence of the pain. At the time of consultation, a few days after the above attack, inquiry elicited the fact that the patient, who had been a very strong, robust woman, had lost 20 lbs. during the last few months, and that she had had a feeling of weight distress and pain in the left upper

quadrant of the abdomen. Examination failed to disclose more than a feeling of rigidity over the left rectus muscle. There was also a tender area that could be mapped out on deep pressure, but no tumor could be definitely found by external diagnostic methods. Rectal investigation for a possible source of the hemorrhage was negative. *X*-ray investigation of the upper digestive tract with the bismuth and barium meals was negative, but tracing the meal through the colon we were impressed by the fact that there was marked angulation at the splenic flexure of the colon, and that shadow seemed to thin out markedly at this point, and also that the appearance of the chemical in the descending colon was appreciably retarded. A tentative diagnosis of probable malignant trouble was made and an exploratory laparotomy was advised. On November 4, 1919, the operation disclosed the following pathology: A large irregular fusiform tumor situated at the splenic flexure of the colon. This mass was in and surrounding the lumen of the bowel, and was bound down to the posterior abdominal parieties. The mesocolon and mesenteric glands were infiltrated. The entire mass was practically inaccessible to surgical interference, and after due investigation it was decided that the tumor was inoperable. The abdomen was closed and the patient returned to bed. When the patient regained consciousness there was an excessive amount of pain resembling in character the pain she previously suffered just previous to the hemorrhage at the beginning of her trouble. The subsequent convalescence was uneventful, and she was then referred to you for treatment."

Physical examination December 8, 1919. Weight 201 lbs. Urine negative to albumin and sugar. R.B.C., 3,400,000; H. 70 per cent.; stools tarry. Wassermann negative; temperature 97°-98°. Inspection revealed upper left quadrant of abdomen to be fuller than other side. Palpation revealed same to be very tender, rigid and with dull percussion note. Patient complained of inability to lie on the left side or to touch same with her arm, and also of severe pain most of the time in that region.

Treatments of 5 mgms. each were given on December 20, 22, 29, 30, and January 2. The reaction temperature at no time rose above 99°. On January 5,

50 mgms. were given. This was followed in 24 hours by a fever of 102.5°, accompanied by the severe focal pain that had previously called attention to her sickness. Twenty other treatments were given up to July 20, each of 5 mgms. In no case did a reaction follow with a fever of over 99.4°. The last four treatments elicited no reaction whatever. On January 20, she could lie on her left side and the tenderness to pressure was very much diminished. On February 9 the soreness had entirely disappeared. By May 12 her stools had lost the tarry color. On July 6 palpation of the abdomen, as deep as the posterior parieties, elicited neither tenderness nor pain, and no suspicion of a mass could be found. She weighs at present 219 lbs., and is apparently in perfect health.

CASE IV.—As a control case Mr. H., referred by Dr. Tupper of Bay City, is selected. Occupation, banker; ge 56; normal weight about 200 lbs. *Family History.*—Negative to cancer. *Past History.*—Besides fevers f childhood, was well until present illness. This came n early in 1919 with constipation, pain and tenderness n lower right quadrant of abdomen. Iliocolostomy as performed by Dr. Tupper in November, 1919, to idetrack a large obstructing carcinoma of the ileocecal egion. Examination December 1, 1919. R.B.C., 3,200,-00; H., 60 per cent.; weight, 162 lbs.; pulse, 130; temerature, 95.2°; tarry stools. He was quite exhausted rom his trip to Detroit. On December 3, the first reatment of 25 mgms. was given. On the next day he ied to walk but suffered a sinking spell. Twenty-ur hours after treatment was given the temperature mained at 97°, pulse 110. Succeeding treatmentss 50 mgms. of tissue thrombin given at intervals of ree and four days were followed by temperature elevations which gradually came, after the ninth treatnt, up to 102.5°. Two more such treatments were lowed with a fever of 101.5° and 100° respectively, the following treatment elicited no reaction at all. ring this period the tenderness gradually left, and December 31 examination could elicit neither tenness, rigidity, pain nor mass. The patient was able o about as he pleased, having gained 45 lbs., and ing a temperature of 98°-98.4°. Treatment was discontinued. In March, 1920, three trial treat-

ments of 50 mgms. were given in one week, with neither febrile nor focal reaction, abdomen apparently normal. Weight 205 lbs. R.B.C., 4,200,000; H., 85 per cent.

The case of Mrs. B. shows that small doses are effective, but require a longer period and a larger number of treatments. This case gave the usual response to the ordinary dose. The control case of Mr. H. demonstrates that after the exhaustion had been overcome, the 50 mg. dose of tissue thrombin brings on the usual reaction, with fever at 102°, and that with larger doses fewer treatments are required.

CASE V.—The following case demonstrates the activity of large doses as 100 mgms. of the thrombin:

Mrs. Z., age 53, referred by Dr. Friedlander, March, 1919. *Family History.*—Father died of dropsy at age of 71 years. Mother died of rapidly growing tumor of uterus when 71 years old. One sister died of cancer, age 65; one brother died of cancer of the stomach at the age of 63 years. Two brothers are living, one well, age 52; the other has heart trouble, age 56. Four children, one died as baby of "cramps," one boy died of scarlet fever, age 7½ years; two children living and well—a boy, 24; a girl, 23. *Past History.*—Scarlet fever at 6; la grippe and bronchitis at 25; repair operation after childbirth, age 34; hysterectomy for malignancy, age 47; otherwise well until 14 years ago. Had burning pains in stomach after and before eating, vomited often and occasionally vomited blood, one-half pint at a time. Stomach improved somewhat until present illness. *Present History.*—February 4, 1918, had attack of severe pain, doubled up and not relieved without morphine. The spells came on every two weeks until March 24, 1919. At that time her weight was 126 lbs. Gastric analysis at this time showed absolute achlorhydria. The stools were tarry, and practically all food ingested was vomited.

On March 24, an exploratory operation by Dr. Friedlander showed a very large mass involving the liver, stomach, gall bladder and intestines. From its physi-

cal characteristics it was diagnosed carcinoma of pyloric origin by Dr. Friedlander, Dr. Israel and some other surgeons who happened to be present. No specimen was removed for microscopic confirmation because there could be no doubt of the diagnosis, and belief in the inadvisability of such procedure.

Treatment started April 8, 1919. At this time the patient could take small quantities of liquids and even this diet caused vomiting. Examination revealed a hard triangular area 11 c.m. long and 12 c.m. wide at its base just below the costal margin and extending over the epigastrium. This area was very tender and the seat of the pain. At first 50 mgms. of tissue thrombin was injected. In 24 hours a fever of 102.2°, lasting 8 hours, was elicited. There was very severe pain and vomiting of much mucus. Six days later a second injection, this time of 100 mgms., was given, followed in 24 hours by fever of 104.2° and lasting 10 hours, accompanied by very severe pain in abdomen and aching in limbs and head. Every "bone felt broken," she complained, and there was vomiting of mucus. Four days late 200 mgms. was injected, the fever rose in 24 hours to 105.4°, and after an hour dropped to 104.4°, when it soon dropped to 103° and remained for 14 hours. The pain was again severe and the universal aching was very distressing. She was then given a vacation of two weeks. On her return she weighed 136 lbs., was much stronger, having eaten fairly well and vomited mucus only twice, but no food, during the two weeks. The tenderness in the abdomen was much reduced and the tumor palpable through the abdominal wall felt about the size of an orange. She was then given three treatments of 50 mgms. at three-day intervals. The reaction started 24 hours after treatment, fever being 103.5°, 101° and 100.2° respectively, and with less severe pain and no vomiting. After the last treatment the mass on very deep palpation was about the size of an egg. Five days after the last treatment the patient developed a tetanoid condition, with stiff neck and laryngeal spasm which I cannot explain unless it was due to some guanidine products absorbed from the killed cancer or possibly to a mild tetanus infection. The former diagnosis was favored by those physicians who examined the patient. This lasted for four days, but recovery was complete only after two

weeks. At this time no mass was palpable on examination by Dr. Friedlander, Dr. Israel, Dr. Watkins and myself. She returned home in June, 1919.

In October, 1919, I examined her. No palpable mass or tenderness was found. She had no pain up to that time, was doing all her work, never felt fatigued, and her digestion was perfect. Stools, normal color. Weight 149 lbs. A sample of gastric juice was taken showing 0.9 per cent. free HCl. R.B.C., 4,450,000; H., 90 per cent. Blood analysis: Noncoagulable nitrogen, 33 mgms. per 100 c.c.; alkalinity, 52 C.C. CO_2 per 100 c.c.

March, 1920, weight 161 lbs., feeling perfectly well, no palpable mass or tenderness. She was given two injections of cephalin (0.5 gm.), which I believe promotes cancer growth. This was done to light up any hidden cancer tissue, if it were present. Patient remained well until June, 1920. Two more injections of cephalin (0.5 gm. each) were given. I heard from her July 29, 1920. Weight 163 lbs., feeling well in every way, and her stomach perfectly well except that she complained of having had pain in lower abdomen at times and occasional diarrhea, which at present has nearly cleared up. She will be examined in due time and treated with tissue thrombin, if required.

This case illustrates, in support of the former, that the size of the dose determines the extent of the reaction, and that with larger doses fewer treatments are required.

These experiments show, then, that the tissue thrombin does not behave as a ferment but acts quantitatively. Moreover, the chemical properties are not those of a ferment. This is a matter of some interest, since ferments can induce the production of antibodies when injected into the animal body. Nevertheless the conversion of at least two pounds of cancer tissue by less than ½ gm. of tissue thrombin qualifies this substance, in some measure, as a catalyst.

CASE VI.—This case is presented, with the case following, to differentiate, by the type of reaction, a gas-

tric carcinoma and a gastric ulcer; that is, a carcinoma and a precarcinomatous condition.

Mrs. S., age 72, referred by Dr. Watkins of Detroit, May 9, 1919. There is no history of cancer, tuberculosis, or insanity in the family. *Past history* shows, besides measles in childhood, a history of gastric ulcer, indigestion, intense hyperacidity, several hemorrhages 15 years ago, and the development since that time of a peculiar arthritis in the fingers and in the bones of the feet, which more recently made walking difficult and limited digital motion. *Present illness* started with abdominal pain after eating and the inability to retain food for several weeks, and, in addition, several severe gastric hemorrhages repeated at intervals of a few days. She was admitted to Grace Hospital May 6, 1919, after a severe gastric hemorrhage. The diagnosis was made by Dr. Watkins from the clinical history, *x*-ray findings and physical examination as follows: Carcinoma of the posterior wall of stomach, involving the pylorus and causing considerable stenosis. He also gave a prognosis of only a few days to live. Examination of the abdomen showed some tenderness in the epigastric region, but no mass could be palpated. Because of the anemia a transfusion of 500 c.c. of blood was given. This raised the blood count to 2,850,000, and the hemoglobin to 37 per cent. The Wassermann reaction showed slight inhibition. Patient had been having a cardiac irregularity for some time. At this time her pulse was irregular and weak, and under the control of digitalis. She was able to take a half ounce of milk and cream hourly.

She was given an injection of tissue thrombin (50 mg.) May 9, 1919. In 24 hours a fever of 101.2° developed, and the abdominal pain was intense, the heart showing signs of failure. With sufficient stimulation the heart was kept going, and three days later another treatment was given of 50 mgms. tissue thrombin. In 24 hours the temperature rose to 102.8°, with considerable gastric pain for six hours, and some cerebral disturbance, perhaps due largely to the anemia, and with pains over the body as in la grippe, for 12 hours. This typifies the reaction in this patient. She received four more treatments at intervals of several days, to which the response was less for the second last, and *nil* for the last treatment. During this period of four

weeks' treatment there was no hemorrhage, nor has there been any since, and the diet was increased to the regular tray. The pain rapidly disappeared, and she has not vomited nor had any hemorrhage since treatment started. In August, 1919, she was given a trial treatment, but neither pain nor fever could be elicited. She remains well to date, a period of 15 months, and is up and about, feeling better than she did five years ago, and without gastric symptoms, and the gainer of considerable weight.

CASE VII.—This is a gastric ulcer case, referred by Dr. H. Ulbrich of Detroit, who presents the following case history: "Mr. G., age 47 years; occupation, paint grinder, handles white lead. Father died at 73 or 74 of carcinoma of stomach (?). Mother died at 73 of pneumonia. *Past History.*—Smallpox at 12 years. Rheumatism in 1900 and in 1916. Lighter attacks in between times. *Present Illness*—Started two months ago with vomiting. Mucus aggravation morning on arising. wakens at night with dryness of mouth. Rolling in stomach ends up like a ball in hepatic region, with pains in right chest, followed by eructations, after which he feels relieved for five or ten minutes, and then the process repeats. Pain in the lumbar regions. Arises from chair with difficulty. Headaches—frontal. Vertigo. Malaise. Lost 5 lbs. that he knows of. Urination $\frac{4 \text{ D.}}{\text{O N}}$ Bowels, constipated. Sleep poor; appetite gone. Nauseated. Distress after eating. Eats bread and milk. Small amount of coffee—three cups a day and one cup of tea. Pain comes on from one to one and a half hours after meals, worse mornings than afternoons, and lasts until the following meal. Food relieves for one to one and a half hours. *Physical Examination.*—Teeth poor. Pyorrhea. Post-pharyngoceles. Enlarged turbinates, chronic rhinitis, abdomen- liver dullness at lower rib. Some pain in right iliac, slight over gall bladder. No tension of muscles, no tumor.

January 22, 1920.—Urine: Slightly acid. Sp. gr. 1030. Albumin and sugar negative. Temperature 98°. Pulse, 80. Bl. P. 128-78 sitting. Bl. P. 128-90 standing. Heart: Apex, fifth interspace inside nipple. Dullness ½ c.m. outside nipple. Heart not enlarged. Sounds

normal, no murmurs. *Lungs:* Nothing abnormal found. *Abdomen:* Some tenderness, right duodenal region. Pressure below ensiform cartilage causes pain to gall-bladder region. No tension of muscles. *Genito-Urinary:* Normal, except for slight varicocele. *Rectum:* No hemorrhoids seen. *Extremities:* No varicosity. *Differential Count:* Poly. 65.3; small, 17.3; Large, 16; transi., 1.5. *X-ray findings:* February 1, 1920. The barium meal passes through the esophagus without note. There is a slight retardation at the cardiac end of the stomach. The barium readily settles to the fundus of the stomach, the greater curvature of which is lying on a level with the umbilicus. The barium readily enters the duodenum. There is no dilatation of the stomach. No niche or incisura is visualized. The pars pylorica shows a persistent spasm which does not interfere with the passage of the barium. The duodenal cap does not show the typical appearance, but is slightly flattened. However, no niche or incisura is visualized. The peristaltic action of the stomach appears normal. The duodenum is situated in the usual position and is movable, showing no adhesion around the duodenum. Palpation over the pars pylorica causes pain. The plates verify the deformity at the pyloric end, which is persistent in all the plates taken. The further examination of the intestines and colon do not show any deviation from the normal. Roentgen Conclusions: Pyloric ulcer or carcinoma, (beginning carcinoma), most likely an ulcer."

When patient presented himself for treatment he was not able to work and felt scarcely strong enough to come to the office. Treatments of 50 mgms. of tissue thrombin were given March 3, 10, 17, 21, 24, and April 5 and 12. The first four reactions consisted only of pain in epigastric region, with increased gastric symptoms for about 6 hours during the day following the treatment. But the temperature did not vary, running from 97° in the morning to 98° in the evening. The fifth treatment brought no response, and the patient was well enough to go to work, not having vomited and having had only mild gastric distress for a week. The treatments given April 5 and 12 brought on no reaction, and at the time the patient felt as well as he ever did, being able to eat anything on the table with-

out any distress. He has had no hyperacidity, pain or vomiting since, and has gained 17 lbs. in weight.

This case demonstrates that in gastric ulcer focal pain and hyperreflexia are the only reactions to treatment, and that a febrile reaction is not attained in this condition. Contrasted with the preceding case, this fact is well brought out and the diagnostic value as well as the curative value of the treatment emphasized.

CASE VIII.—This case illustrates the reaction in a carcinoma of the breast, associated with Paget's disease.

Mrs. P., housewife, age 47. *Family History.*—Father died of old age, at 81 years. Mother died of old age at 79. One brother died of heart disease at the age of 55; another died of apoplexy at 42 years. One sister and three brothers are alive and well. One child, age 22, alive and well. *Past History*—Chickenpox before 10 years of age. One attack of rheumatism nine years ago and another two years ago, neither of which lasted more than a week. No other sickness until onset of present illness. Menstrual periods regular and not very painful. *Present Illness.*—In March, 1919, first noticed pain in the right arm, shoulder-blade and right breast, which grew worse, so that by June she could not use the right arm at housework. By this time she became rather weak and "inexpressably tired all the time," and the pain in right breast just behind nipple interfered with sleep. She became short of breath on slight exertion and coughed considerably. The tumor was first noticed in April, 1919, four weeks after the pain set in. It was about the size of a walnut, and she became cognizant of the fact that the nipple appeared fissured and smaller than the left one. She was examined by Dr. J. Davis in August and October, 1919, as well as by several general practitioners, who diagnosed the condition as carcinoma and recommended immediate radical amputation of the breast.

I first saw the patient on November 5, 1919, and found the right breast larger than the left, the nipple fissured and retracted, and exuding some blood and a slight amount of thin pus. The upper right aspect of

the nipple was eroded and the areola and surrounding area converted into a characteristic Paget's condition. Behind the nipple a very tender and hard mass about the size of an egg was found. Two other small masses, one along the outer edge of the pectoralis major muscle and one at the inner end of the third interspace of the same side, were both found to be tender and immovable. Only slightly enlarged glands could be palpated in the deeper axillary region. The left breast was normal. Her weight at this time was 157 lbs., temperature 97.4°. Wassermann negative. Blood, alkalinity, CO_2 combined, 84 c.c. per 100 c.c.

A treatment of 50 mgms. of tissue thrombin was given November 5, followed in 24 hours by a chill, fever of 102.4°, dyspnea, incessant dry cough, severe headache, smarting eyes and nausea, and a very severe burning pain in the areolar region and a severe aching pain in the tumor. This lasted five hours and eased up gradually until it disappeared. For the next few days there was less pain than she had before treatment. The second treatment was given November 9, followed by a similar reaction on the next day for four hours. After this treatment the Paget condition looked much less angry and the discharge had stopped. A third treatment was given November 14, and a similar reaction set in in 24 hours but was not as severe as the former two, and there was no dyspnea. The bleeding had stopped when she presented herself for a fourth treatment, and the Paget condition now looked like a mild eczema that was nearly healed. She still had a mass about the size of a walnut behind the nipple, but it was less painful and did not interfere with sleep, and the pain in the arm and shoulder had practically disappeared. Palpation could not locate another mass. After eleven more treatments with rather mild reactions, the pain, tenderness and mass had entirely disappeared, the nipple had gradually returned to its normal position, and the entire areolar region had become normal. A slight deficiency was left in the upper right corner of the nipple and the breast as a whole is noticeably smaller than the left breast.

I sent her to Dr. R. Wollenburg on March 5, 1920. He reported that he found her in perfect health, with normal breasts. I also sent her to Dr. James Davis, January 25, May 5, and July 26, 1920, for examination.

He reported not being able to find any suspicious tissue after thorough examination.

Patient has been given several treatments at intervals of four weeks without any reaction following, and has now remained tentatively cured six months. She has gained six pounds, and reports that she is not fatigable and can use her arm at washing cloths, etc., without any pain and as well as she ever could. Blood alkalinity, CO_2, combining power 57 c.c. per 100 c.c.

CASE IX.—The following case is presented to illustrate the type of response elicited in a rapidly growing squamous-cell carcinoma in a young patient.

Mrs. W., age 33, normal weight 130 lbs., three years ago. Referred by Dr. F. E. Thompson. *Family History.*—Father alive and well, age 75. Mother, age 68, alive and well. Mother's sister died of cancer of the stomach at the age of 68. Two sisters died in infancy, one of colera and one of dropsy. Another sister died of diphtheria when 5 years old. One brother died of diphtheria, age 8. *Past History.*—Measles, mumps, pertussis and diphtheria in childhood. Well until present illness. *Present Illness.*—Started in June, 1919, with severe pain in lower back and a urinary frequency of every 30 minutes, accompanied with severe pain on micturition, and severe, constant headache. Patient was "very tired and weak all of the time." Several times a day deep, cutting pains occurred in lower abdomen. Discharge was excessive, somewhat bloody, but not very odorous. She consulted Dr. F. E. Thompson and also Dr. Wm. Donald on October 1, 1919, who diagnosed the condition as carcinoma of the cervix. A specimen was removed by Dr. Donald for microscopic confirmation. The diagnosis returned was squamous-cell carcinoma of the cervix uteri.

On November 19, a vaginal hysterectomy was performed by Dr. F. E. Thompson. The tissue removed was examined microscopically and diagnosed squamous-cell carcinoma. For the first two weeks after operation, patient appeared to improve, but in the following two weeks this improvement gave place to a rapid decline. The rectum became so painful that the sitting posture was impossible. The very severe pain that developed in the abdomen increased, so as to cause reflex paralysis of the limbs and inability to either walk, turn over in bed, or reach for things. This was accompanied

by intense pain in the hips and thighs, constipation and loss of appetite. The patient was examined by Dr. Thompson on December 20, as well as by myself, and found to have carcinomatous recurrence between the vagina and the rectum, in the rectum, and symptomatically in the region of lumbar and sacral plexes, and in the liver.

She presented herself for treatment December 21, 1919. She could not walk; weight 115 lbs. A treatment of 50 mgms. of tissue thrombin was given at 9 P. M., December 21, 1919. On the next day at 10 P. M., 25 hours after treatment, the patient awoke with fever of 104.3°; pulse, 120; intense headache, backache, grippy pains all over the body, and nausea all night until 10 A. M. next day. Within 3 hours after its onset the temperature rose to 105.2°, and did not fall below 104° until after 9 A. M. the next day. A drenching sweat followed the fever and the patient then felt much better than she had for the past four weeks. December 23, a second treatment of 25 mgms. was given. This was followed in 24 hours by a fever of 102°, lasting from 11 P. M. to 5 A. M. of the next day and accompanied by the other features of the former reaction, but not so severe. After the reaction subsided the patient could turn over or lie in bed on either side and was able to take a few steps. On the next day she could limp about, had a better appetite, and her bowels moved without so much pain. On December 28, 5 days after the second treatment, she walked ¼ mile without limping, and was without any pain whatever. Temperature 98.2°, pulse 80. On December 30, 1919, January 2, 6, 10, 12, and 27, 1920, she received additional treatments. The reactions gradually let up in severity after four of these treatments and then did not occur again.

She was examined by Dr. Thompson April 5, 1920, and no suspicious tissue could be found. She was likewise examined May 18 and July 1, and pronounced cured by Dr. Thompson (tentatively cured, of course). She was given a trial treatment July 16, 1920, but no reaction was elicited. The patient is perfectly well to date, her present weight being 149 lbs. She works hard all day without fatigue, pain, discharge, or any signs or symptoms of cancer.

DISCUSSION OF CASE HISTORIES.—*The Reaction.*

Every carcinoma case presented, generally 24 hours after the treatment, developed a febrile reaction, accompanied by increased focal pain and hyperreflexia of the affected part. Moreover, a systemic intoxication is expressed in the grippy feeling accompanying the reaction. These phenomena are no doubt due to the swelling of the coagulated tissue and to oxidation of the absorbed products. That these products are to some extent toxic is illustrated in the case of Mrs. Z., who had severe reactions from the large doses given and who developed a temporary tetanoid condition.

I might cite briefly in this connection a case of very extensive carcinoma of the ovary. Mrs. W., referred in August, 1919, by Dr. Larson. This patient, from sheer exhaustion, was barely able to move about in bed, and after receiving three treatments died in a reaction from the intoxication of absorption of the killed cancer tissue. Autopsy showed that the large mass was entirely caseated and could be torn to bits without resistance. This toxic reaction has a diagnostic value, since it occurs constantly in cancer patients. I have not been able to obtain either a focal or a febrile reaction by injecting as much as 2,000 mgms. of the tissue thrombin in healthy men, or in noncancerous patients with gummata, tabes or tuberculosis. Moreover the focal reaction is of value in determining the distribution of the cancer tissue. For instance, those cases of breast cancer with pulmonary involvement develop dyspnea and dry cough during the reaction, as in the case of Mrs. P. I may cite as an illustration of the possible severity of a focal reaction the case of Mrs. S., referred by Dr. J. H. Carstens in October, 1919. This patient weighed about 170 lbs. *X*-ray plates showed marked

pulmonary involvement in both lungs and a dilatation of the heart, especially on the right side. In her right breast was a hard mass 9 c.m. long and irregularly 4 c.m. thick. The skin was movable above it. In the left axilla were a mass as large as a lemon and also several smaller masses. The left breast had been removed two years previously; the scar remaining appeared healthy.

This patient suffered quite severe dyspnea, the respiration running generally around 38, while the heart rate was variably 140. She was very cyanotic and the slightest exertion brought on intense dyspnea. Cough was incessant. The patient could not repeat more than two letters of the alphabet without taking breath. She was given six treatments, of 10 mg. each, weekly. The improvement in respiration was so marked that she could get up and walk about, only breathing twenty-eight times per minute. In the meantime the mass in the right breast disappeared, and the mass in the left axilla had diminished in size to that of a walnut. During the reaction periods she required constant stimulation, and even then the cough and dyspnea were almost unbearable. Her reaction temperature varied between 101° and 102°. After having improved so markedly, I risked a treatment of 50 mg., which proved to be too much for the patient, and she died in a reaction of cardiac failure. There was sufficient cancer left in the lungs, no doubt sufficiently swollen during the reaction, to obstruct the pulmonery circulation and cause failure of the right ventricle. An autopsy was not obtainable.

This illustrates that in very extreme cases the focal reaction also may be dangerous and that here the dosage must be guarded.

The gastric ulcer case showed no febrile reac-

tion. We therefore now possess an additional means of characterizing cancer by the febrile reaction elicited by this treatment and, since this depends upon the chemical and physiological properties of the cancer tissue, it depends upon the intrinsic essential structure of the cancer and is therefore more valuable as a diagnostic feature than the microscopic characteristics. Furthermore, a good thermometer is the only instrument needed to estimate the fever and the personal equation for error cannot be so great as that to which the pathologist is subject.

The Results of Treatment.—These are, as illustrated by the cases presented, disappearance of the tumor and its attendant cachexia, return to normal of the blood chemistry—the alkalinity, for example; increase in the blood count and hemoglobin content—a doubling of the blood count in four weeks, for instance; increase in weight to normal or above normal, as in the case of Mrs. W.—often an increase of 40 lbs., cited in Cases I and IV; complete disappearance of pain and soreness and return of function, as in the case of Mrs. Z., where a previous achlorhydria gave place to a 0.9 per cent. HCl content in the gastric juice, incident, of course, to the return of the blood alkalinity to normal. The rapid recuperation of the patient after the carcinoma has disappeared, and the loss of easy fatigability, as demonstrated by these cases, are also significant.

The Sequelæ.—The sequelæ are also physiological. In a region as the breast of Mrs. P. (Case VIII), a deficiency exists in place of the cancer tissue. In a region where there is a necessity for replacement of the cancerous area by scar tissue this takes place, as in the case of Mrs. B. (Case I), where a

large vesico-vaginal fistula was entirely replaced by scar tissue and the deficiency made good.

That the tissue thrombin itself is not injurious to the patient is illustrated in the cases presented by failure to obtain a reaction after the cancer tissue has disappeared, by the steady gain in weight during treatment and by the increase in the blood count and in the hemoglobin content during and after treatment, and by the normal noncoagulable nitrogen content of the blood after treatment, which indicates that no injury has been done to the kidney.

The isolation of the thrombin free from products that are injurious and that promote cancer growth is a matter of great difficulty and only after over three years of constant experiment have I succeeded in working out the only two possible methods that can yield a useful product.

The chemistry of the thrombin, its isolation and certain synthetic work will be reported in some chemical journal. I owe my deepest gratitude to the clinicians who have cooperated with me so kindly in this work.

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355 SHERIDAN AVENUE.

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H. EDWIN LEWIS, M.D.
EDITOR
IRA S. WILE, M.D.
ASSOCIATE EDITOR

November 4th, 1920.

Dr. Wm. F. Koch,
355 Sheridan Ave.,
Detroit, Michigan

Dear Doctor:-

We have been much impressed with a most interesting and valuable article by you which appeared in a recent issue of the Medical Record, and are taking the liberty of writing to you to solicit a contribution from you on any medical topic for early publication in American Medicine.

As you may know American Medicine is one of the most widely read and quoted medical journals in America and assures you an audience that is not exceeded by that of any other high class medical monthly.

We are constantly striving to make American Medicine helpful and inspiring to the thinking medical men of the country and it is because we believe any article you may send us will aid us in these efforts that we are asking you to become a regular contributor to our pages.

Hoping you have something in hand you can send us in the near future, and assuring you that we will "leave no stone unturned" to make our relations most pleasant and satisfactory, we remain,

Faithfully yours,

The Editors of American Medicine

H. Edwin Lewis

Editor-in-Chief

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CHEMICAL CONSEQUENCES OF THE REMOVAL OF THE PARATHYROID GLANDS

The complete removal of the parathyroid glands is attended with fatal consequences. This experimental fact speaks decisively with regard to their importance for the maintenance of the bodily functions; it does not, by itself, give any indication of the mode in which the parathyroidal tissue determines the healthy continuance of the normal processes in the organism. As has been done in the case of other so-called glands with internal secretion, so here we may assume that they act in one of several ways —either they furnish some regulatory or stimulating product (a hormone) which is distributed to appropriate parts of the body, or they may act as antitoxic agencies, neutralizing, modifying or destroying products which would otherwise be harmful to the individual.

The most prominent symptoms of abnormality which attend the removal of the parathyroids are perhaps those of tetany. This is of itself suggestive, though by no means demonstrative, of the participation of a toxic agent in the physiologic events caused thereby. The discovery of toxic bases in large quantities in the urine of parathyroidectomized dogs by Dr. Koch[2] at the University of Michigan is therefore of more than passing interest. In every case studied methylguanidin was present in the secretion of the kidneys. When this substance was found in smaller quantities, other guanidin bases were present, so that the excreted guanidin nitrogen approached a constant. In addition to these bases others were observed, namely, beta-imidazolylethylamin, cholin, neurin and unidentified bases, although these were not distributed uniformly in the cases studied.

The histologic picture which appears in the tissues of parathyroidectomized animals is one of cellular disintegration, particularly in such organs as the liver, kidney and brain. Various degrees of chromatolysis are observed in the nuclei, and in some places the latter disappear entirely in large areas. Koch suggests that the passive protein destruction which must accompany such tissue changes may give rise to basic products and thus account for the unusual compounds excreted. Inasmuch as in animals which have been operated on the specific toxic symptoms can be provoked by the feeding of digested protein, it may be that the toxic effects are initiated by products of intestinal or even of parenteral digestion. Normally these derivatives are incorporated in some cell molecule or stored up in some form. In the case of parathyroidectomized animals after feeding digested proteins, it is suggested that the products remain free and act as toxins. In animals operated on when no feeding occurred the symptoms increased in violence with short intermissions until death. The intensity of the symptoms doubtless followed the rate of disintegration of body protein. The pathologic condition would thus appear to be a failure on the part of the cells to build up their protein. This part of the metabolism of the cell, Koch reminds us, is regarded as the function of the nucleus. Such indications, together with the formation of free "nuclein" components, point to a nuclear atrophy. The histologic findings, moreover, show an active "nuclein" degeneration. The reputed relation of the parathyroid to calcium metabolism and the theories of glandular function built up on it have not made effective progress of late. One is not justified at present in saying that these are quite unfounded. Doubtless in the complex disturbances set up by so serious an operation as the complete exclusion of vitally important glands the interrelated consequences are varied and numerous. The outcome of the discovery of the toxic bases in the urine is the suggestion of Koch that the parathyroid secretion appears to be concerned also with anabolic processes related to the synthesis of nuclear contents. Whether or not such a hypothesis can be further substantiated remains to be seen; in any event the final successful isolation of recognized toxic chemical products of traceable origin has paved the way to definite conceptions and specific lines of inquiry where hitherto the explanations have been vague and the outlook unpromising.

[2]Koch, W. F.: Toxic Bases in the Urine of Parathyroidectomized dogs, Jour. Biol. Chem., 1913, xv, 43.

GEORGE W. CRILE M.D.
1021 PROSPECT AVENUE
CLEVELAND

June 4, 1919

Dr. Wm. F. Koch,
Detroit College of Medicine and Surgery,
Detroit, Mich.

Dear Doctor Koch:

I shall be only too glad to give you the cancer material and as a matter of fact in certain cases in which no indication for x-ray treatment is given I could give a few treatments before excising the cancer. You may consider that at Lakeside Hospital we shall cooperate with you to every extent.

Sincerely yours,

GWC:HO

LAW OFFICES
WARREN E. MILLER
SUITE 1012 BARR BUILDING
910 SEVENTEENTH STREET N.W.
WASHINGTON 6, D. C.

TELEPHONE
NATIONAL 0995
IN REPLY PLEASE REFER TO

June 10, 1947

STATEMENT OF WARREN E. MILLER

This is to certify that while the undersigned was National Commander of the Army and Navy Union, U. S. A., during the winter of 1943-1944, he met and talked with Dr. William F. Koch, who explained his revolutionary treatments.

Among the deseases which Dr. Koch explained his preparation would cure was the desease of Malaria, which at that time was causing great concern among our troops in the South Pacific. The undersigned had previously been informed of Dr. K$_o$ch's work. As a result of conversation with Dr. Koch, the possibilities of his treatment if used by the government in treating Malaria among members and former members of the armed forces were apparent to the undersigned; and at my urgent solicitation, Dr. K$_o$ch agreed, on the spur of the moment, to accompany me to the Office of the Medical Director of the United States Veterans Administration, Dr. Griffith.

I introduced Dr. Koch to Dr. Griffith, explained briefly the possibilities of the government's using Dr. K$_o$ch's treatment, and Dr. Koch volunteered to make it available to government physicians. Dr. Griffith phoned one of the members of his staff, and Dr. Koch and I were ushered to their desks, where Dr. Koch explained his formula or method in technical terms to the physicians on Dr. Griffith's staff and another who was sitting at the next desk. When they realized the claims Dr. K$_o$ch had made for his method of treatment, they asked if he had taken the matter up with Dr. Fishbein of the American Medical Association and suggested that he do so immediately. Dr. Koch then discontinued his enthusiastic explanation of his method of treatment and seemed chagrined that these high-ranking medical officers of the United States Veterans Administration should ask him to take the matter up with Dr. Fishbein. They went along to state that the Veterans Administration could not use on disabled war veterans a method of treatment that was in an experimental stage and had not been approved by the American Medical A$_s$sociation.

Dr. Koch's presentation of his method of treatment seemed to be beyond the comprehension of these physicians. He went into the chemistry of the matter, and apparently they could not follow him in his explanation.

Warren E. Miller
WARREN E. MILLER