A NEW AND SUCCESSFUL DIAGNOSIS AND TREATMENT OF CANCER 1920

BY WILLIAM F. KOCH, Ph.D., M.D.

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 urine of parathyroidectomized dogs. This finding has since been confirmed by Paton at Glasgow and by other observers. My autopsies showed in these animals extensive ante-mortem coagulation of the blood and also a coagulation of the tissue cells in the liver, lung, spleen and brain.

*(See Bibliography appended. Copyright. William Wood & Company.)

Such extensive coagulation of blood and tissues ensuing upon the loss of one physiological substance is suggestive that normal functional tissues are non-coagulative, so long as they receive and can build into their structure all the elements necessary for functionally coordinated 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case after parathyroidectomy the tissues had lost a necessary special element and had become coagulated just as blood withdrawn from its endothelial encasement becomes coagulable.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 intra-vascular and extra-vascular coagulation. This is a physiological function of the plasma to prevent hemorrhage. Likewise, the plasma of tissue cells, clot by reaction with a product of injury to the tissue cells. This function of tissue-cell plasma coagulation serves to wall off destructive processes and also to lay a bed for in-growth 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, causes some thrombin to be 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 the 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 un-clotted 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 1/2 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 intra-vascular coagulation of the blood, and therefore immediate death in the patient, were found actually to increase cancer growth and, moreover, 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 cell showed tissue death.

Fig. 1. — Section taken from the untreated squamous carcinoma.

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 hrs. after injection 3 min.— 14 sec.
24 hrs. 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 in-growth of fibroblastic tissue are shown here.

This is a digestive change in the clotted protoplasm, which accompanies the in-growth 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 carcinoma 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 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.

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

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 heartbeat, 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 likewise, as treatment proceeds rapidly passes away.

CASE 1. —The first case is selected to illustrate the healing of a vesico-vaginal 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 was examined by Dr. Garber, Dr. Hurst and Dr. W. Hackett, who gave the diagnosis of carcinoma of uterus. Wassermann, negative; R.B.C., 2,700,000; Hem., 50 percent; urine, albumin, trace; sugar and casts, negative.

April 5, 1919, laparotomy and hysterectomy performed by Dr. Walter Hackett. As much of the carcinomatous tissue as possible was removed, although the sub-renal lymph glands were infiltrated. Tissue was examined microscopically, and proved to be Adenocarcinoma of endometrial 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, and the attempt to withdraw blood by syringe failed, as the 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, of strong odor, and accompanied by the escape of urine from a vesico-vaginal fistula large enough to easily admit three fingers. At the orifice of the vagina carcinomatous nodules were visible. Moderate but exhausting hemorrhages had occurred several times a 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 101.60, 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 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.

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

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. Dr. J. H. Carstens, who stated that he found no evidence of cancer, examined her in the middle of July and the vesico-vaginal 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., 70 percent; non-coagulable 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 non-coagulable 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 n 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.

FIG. 5. —Shows the same changes as Fig. 3 and at x the in-growth of angioblastic buds

into a coagulated mass of cancer.

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, and 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 her entire body, itchy skin, clay stools, and vomiting bile. Unable to retain any food. Temperature 98.4°; pulse, 112. Abdomen so tender as to make palpation impossible. I also advised, operation and was requested to do so at once. I had her removed to the hospital, where Dr. Aldridge and myself operated her on the following morning. To our surprise we found the liver and gall bladder perfectly normal—no stones, no thickening of duct walls, etc. But the lesser curvature of the stomach was one large sausage-shaped tumor, hard in consistency, with some nodules at various spots. So much of the organ was involved and the patient was in such a weakened condition that we were both of the opinion that gastroenterostomy or any modification of such operation would be of no avail. We closed the wound and about November 1st sent her to you. At this time (August 8, 1920) she appears to be in splendid health, does her own work, and eats everything, and certainly is grateful to you.”

Fig. 6. —Shows same changes as Fig. 3, but more particularly the fibrin formation in the cancer protoplasm.

On admission to the Women's' Hospital, Detroit, November 1, 1919, her weight was 119 lbs.; R.B.C., 3,100,000; H. 60 percent; Wassermann negative, urine negative to albumin, casts and sugar; volume 7 oz. in 24 hours. Stools loose, scanty and tarry, occult blood 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 prevented 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 injection of 50 mgms. of tissue thrombin was given on the first and fourth days. Temperature running from 97° to 98°, with at times severe abdominal pain and vomiting the daily food ingested. The second period started on the eleventh day, seven days after the second treatment, 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 another 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 disappearance of the fever at the end of this period all pain left. During the last six days there was no vomiting, nor has there been since. The appetite and digestion rapidly improved, and no epigastric mass was evident on inspection. The third or convalescent period of 14 days was painless and without vomiting or gastric distress, the patient taking the regular tray. Temperature running 98° to 98 3/5°. She rapidly gained 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 percent.; 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, and ate everything.

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 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 dies 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 parietes. The meso-colon 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 on December 8, 1919. Weight 201 lbs. Urine negative to albumin and sugar. R.B.C., 3,400,000; H. 70 percent; 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 it 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 parietes, 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; age 56; normal weight about 200 lbs.

Family History. -Negative to cancer.

Past History. —Besides fevers of childhood, was well until present illness. This came on early in 1919 with constipation, pain and tenderness in lower right: quadrant of abdomen. Dr. Tupper performed an Ileostomy in November 1919, to sidetrack a large obstructing carcinoma of the ileocecal region. Examination December 1, 1919. R.B.C., 3,200,000; H., 60 percent; weight, 162 lbs.; pulse, 130; temperature, 95.2°; tarry stools. He was quite exhausted from his trip to Detroit. On December 3, the first treatment of 25 mgms. was given. On the next day he tried to walk but suffered a sinking spell. Twenty-four hours after treatment was given the temperature remained at 97°, pulse 110. Succeeding treatments of 50 mgms. of tissue thrombin given at intervals of three and four days were followed by temperature elevations which gradually came, after the ninth treatment, up to 102.5°. Two more such treatments were followed with a fever of 101.5° and 100° respectively, and the following treatment elicited no reaction at all. During this period the tenderness gradually left, and on December 31, an examination could elicit neither tenderness, rigidity, pain, or mass. The patient was able to go about as he pleased, having gained 45 lbs., and holding a temperature of 98°-98.4°. Treatment was then discontinued. In March 1920, three trial treatments 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 percent.

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 7 1/2 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 physical characteristics Dr. Friedlander, Dr. Israel and some other surgeons who happened to be present diagnosed it as carcinoma of pyloric origin. 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 later, 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. Those physicians who examined the patient favored the former diagnosis. 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 had a normal color. Weight 149 lbs. A sample of gastric juice was taken showing 0.9 percent. free HCL. R.B.C., 4,450,000; H., 90 percent. Blood analysis: Non-coagulable 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 Â¼ 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 gastric carcinoma and a gastric ulcer; that is, a carcinoma and a pre-carcinomatous 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. Dr. Watkins made the diagnosis 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 percent. 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 4D/ON 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 the 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. BI. P. 128-78 sitting. Bl. P. 128-90 standing. Heart: Apex, fifth interspace inside nipple. Dullness 3/2 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 gallbladder 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 without 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 5; 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 "inexpressibly 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. Dr. J. Davis examined her in August and in 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 areola 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 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 areola 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 cholera 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. Dr. Donald removed a specimen 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 tectum, and symptomatically in the region of lumbar and sacral plexus, 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. On 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 1/4 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.

Dr. Thompson examined her on 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 other 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 non-cancerous 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, was one 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 pulmonary 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 the dosage must be guarded. The gastric ulcer case showed no febrile reaction. 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 Sequelae. —The sequelae 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 normal non-coagulable nitrogen content of the blood after treatment, which indicates that no injury has been done to the kidney.

The isolation of the thrombin free 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.

Dr. Koch Publications

1912 – 1939

- 1912 W. F KOCH Ph. D., M. D. ON THE OCCURRENCE OF METHYL GUANIDINE IN THE URINE OF PARATHYROIDECTOMIZED ANIMALS.
- 1913 CHEMICAL CONSEQUENCES OF THE REMOVAL OF THE PARATHYROID GLANDS
- 1913 TOXIC BASES IN THE URINE OF PARATHYROIDECTOMIZED DOGS
- 1916 THE PHYSIOLOGY OF THE PARATHYROID GLANDS
- 1918 TETANY AND THE PARATHYROID GLANDS
- 1920 A NEW AND SUCCESSFUL DIAGNOSIS AND TREATMENT OF CANCER
- 1925 CANCER ITS FUNCTION AND CURE, THE EVOLUTION OF THE IMMUNITY PROCESS
- 1926 CANCER SUPPLEMENTARY POINTS
- 1926 THE PREVENTION OF CANCER
- 1927 BLOOD CHEMISTRY IN MALIGNANCY
- 1927 THE KOCH CANCER TREATMENT AND ITS INVESTIGATIONS

- 1938 NATURAL IMMUNITY VIA AEROBIC GLYCOLYSIS
- THE FUNCTION OF CANCER
- THE JOURNAL OF THE AMERICAN COLLEGE OF PROCTOLOGY

1940 – 1949

- 1939 Clinical Demonstration of the Laws of Chemical Structure that Determine Immunity to Disease, and their Application in the Treatment of Patients
- 1940 THE BASIC CHEMISTRY OF OUR DIET
- 1941 A BRIEF HISTORY OF THE KOCH SYNTHETIC ANTITOXINS
- 1941 AN EFFICIENT SINGLE DOSE TREATMENT FOR DIABETES, On A Full Carbohydrate Diet Without Insulin
- 1941 CHEMISTRY'S VICTORY OVER DISEASE
- 1941 PRINCIPLES OF THE KOCH THERAPY INTRODUCED IN 1918
- 1941 RELATION OF FOCAL INFECTION TO CANCER AND ALLERGY IN CAUSATION AND RECOVERY

1950 – 1957

- 1958 SURVIVAL FACTOR IN CANCER AND VIRAL INFECTION
- 1961 SURVIVAL FACTOR IN NEOPLASTIC AND VIRAL DISEASES
- 1963 NEOPLASTIC AND VIRAL PARASITISM THEIR BASIC CHEMISTRY AND ITS CLINICAL REVERSAL
- 1966 THE KOCH CONCEPT (FOR THE SCIENTIFICALLY KNOWLEDGEABLE)
- 1967 THE FUNCTIONAL CARBONYL GROUP IN PATHOGENESIS
- DR. KOCH'S EXPLANATION OF THE FUNCTION OF HIS REAGENTS
