Chapter Two

The Use of Anticoagulant Therapy and Catalytic Agents in Vascular Thrombosis

OUTLINE

I—Pathology in Thrombosis
A. Vircho's Theory
  (1) Blood Disturbances
  (2) Figures 25, 26, 27, and 28
B. Cohnhein's Theory
  (1) Vascular Alterations
  (2) No Exhibit

II—Physiopathology - Anticoagulant Therapy in Thrombosis
A. Medication with Blood Action
B. Medication with Vascular Action

III—Clinical Observations Supporting Previous Statements
A. Surgical Thrombosis with Pulmonary Embolism
B. Berger 'a Disease
C. Coronary Thrombosis Status
D. Rheumatic Carditis Thrombosis
E. Female Pelvic Thrombosis Post Spontaneous Miscarriage

IV Summary and Conclusions

FOREWORD

Mr. Chairman, Distinguished Guests, Ladies and Gentlemen:

AGAIN I have the opportunity and the pleasure to speak to you, the members of our medical profession. Although we are small in number, we are large in ideas, and we hope, awake and alert to new scientific developments. Developments which, through interest and knowledge, have gained tremendous momentum in our day, not only from facts established by amazing therapeutical results, but also from facts promoted through a hazing of intense opposition.

Because of this opposition, many of us, and perhaps many of the new members of this philosophy, will face strong criticism. And occasionally, hatred and persecution may come to all of you who are especially well known.

But if we remember the historical trend of scientific development in this world, we will understand these repercussions; and know that all new ideas and

discoveries that have a tendency to break down classical, standard methods always invite and promote severe opposition and intense criticism.

Today I am particularly happy to be among the members of the medical profession in the wonderful, western state of Oklahoma. This community should be proud and aware of these regional conventions in which physicians with open minds convene in the American way of life, expressing themselves with freedom of speech and freedom of opportunity!

We should say that in these two days of our convention, more will be done for the care and suffering of humanity, than will be done in the total scholastic convention of the A.M.A., in which the majority of us will just take seats to listen to the same material and the same reports that we know so well. This new theory certainly places us in a precarious situation in regard to those who maintain a different point of view.

I personally consider ex-professor William Koch's philosophy so amazing and honest in results that I believe all conscientious physicians, in these states and this surrounding territory, should know of his wonderful Therapy. All doctors should be free to criticize and observe Koch's results up to the time that, by his own experience, he becomes prepared to understand Koch's Theory, and then he must speak for himself of his results among suffering humanity.

This is my own case. Seven years ago, Dr. William Koch was unknown to me. Perhaps unfortunate ignorance cost the life of many a patient, among them members of my own family. But today I am happy again, and proud of this work which I intend to carry on to the end of my time and my professional practice.

Classification:

This lecture deals with a very interesting and important subject; the anticoagulant medication in our daily practice, and of course the beneficial or injurious results when anticoagulant medications are administered to the patient afflicted with thrombosis of the vascular system.

There are diversified pathological conditions on which anticoagulants are used quite frequently. Among them, I shall mention to you the more important ones in my clinical practice-for instance:

(a)—Post surgical thrombosis with pulmonary embolism.
(b)—Coronary Thrombosis status
(c)—Endo-arteritis Obliterans (Berger's disease)
(d)—Rheumatic-carditis thrombosis from septic endocarditis
(e)—Female pelvic thrombosis

In all of these pathological conditions, the vascular system is involved. Naturally, the first question that will arise in your minds will be, "What is a thrombosis?"

A thrombosis is the formation of a plug more or less completely occluding a blood vessel or one of the heart cavities, formed in situ by coagulation of the blood, or a deposition of some of its formed elements. When this clot or a part of it becomes detached and travels to and stops in some other location, forming an obstruction, it is an "embolus."

But if this definition is a simple matter, the situation will become more and more interesting when you study the intimate problems of "why" and "how" this thrombus is formed, and here is what you call the pathology of thrombosis.

For centuries medical schools have been arguing on this subject. We are still arguing today. However, the question is not to argue, but to save patients' lives and solve their problems.

And so, it is now necessary for you to come with me on the journey over this so-called Pathology of Thrombosis, in order to secure the benefits and practical clinical conclusions, and to be sure whether or not a particular medication is useful or not in the solution of the problem. In this regard, I speak of the analysis of clinical cases.

In conclusion, I have established the framework of this lecture to include: definition, classification, pathological interpretations, and clinical results of therapeutical values in Thrombosis Pathology.

I—PATHOLOGY IN THROMBOSIS

Our sketch No. 1 divides the study of the pathology of thrombosis in two opposite theories; Vircho's Theory of blood disturbances, and Cohnhein's Theory of vascular alterations.

Vircho claimed centuries ago, that the main factor in the thrombosis process was on one side; mechanical factors with tendencies to slow down the circulation of the blood stream, and which slowness could he slight, medium or total as you will see in **Figure 25.**

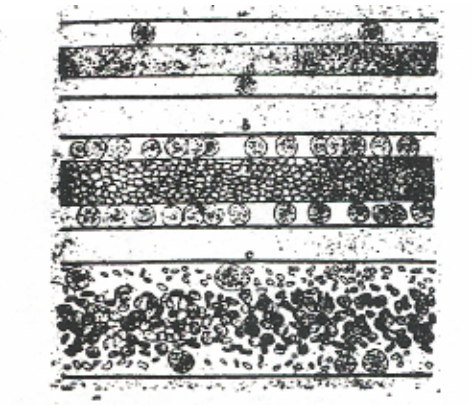

Figure 25.

Today we know from animal experimentation, that if we perform artificial cutting of the local vascular tissues, the circulation is rapidly stopped in this particular place of vascular injury without ulterior and progressive damage. This is evident in **Figure 26.**

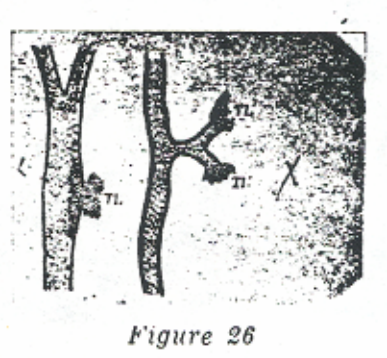

Figure 26

According to the Vircho Theory, this rapid local repair of the vascular injury takes place by a process of colloidal changes in the blood as a tissue. Among the factors of these colloidal changes, the pro-thrombin level, leucocyte ferments, calcium salts, and hepatic ferments all determine the formation of a local clot.

Today we also know that it is possible to maintain blood un-coagulated between two ligatures or sutures as long as the vascular segment remains undamaged.

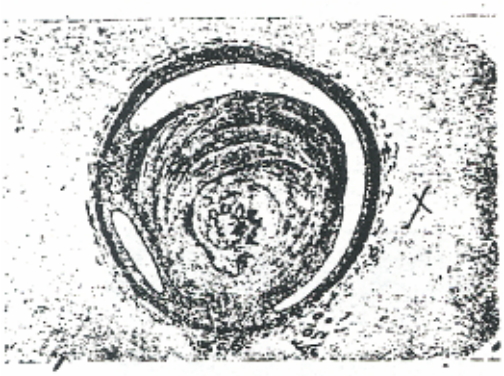

Figure 27.

But from the moment that the inside of this vascular portion receives an injury by trauma, infection, or allergy irritation, the un-coagulated blood rapidly becomes clotted. This fact leads Cohnhein to believe that the "vascular damage" is the fundamental and primary factor in the formation of the thrombus. First the condition is brought about by an endothelial inflammation provoked by infection, virus, etc., and is then advanced by a chemical disorder, (allergy manifestations).

Not long ago at a St. Louis Convention of Heart Diseases, Professor Hermans, Dr. Decher, and Dr. Schwab, of the Texas University School of Medicine, established the idea, that it was a necessity to make a complete and total revision of Coronary Thrombosis disease as a biochemical disorder.

They spoke, at that time, of the blood level balance between the glycogenic liver function and the phospho-creatinine level. These scientists claim that when the level or production of glycogenic substance in the liver and muscular tissue is not in sufficient quantity, an excess of lactic acid is formed as a result of the breaking down of the glycogenic molecule. This lactic acid remains in situ with a secondary alteration over the colloidal plasmatic stability.

In animal experimentation, in which myocardial damage is produced artificially, they always find a deficiency in creatinine molecules. The same situation occurs in a heart with myocardial thrombosis and hypertension.

Today we know the importance of a biochemical disorder and allergy in determining the endothelial vascular inflammation. Who does not remember the violent vascular manifestations of the Angio-neurotic edemas, which clinical symptoms arise suddenly, are recognized as a definite biochemical disorder, and also as the endarteritis process of pulmonary tuberculosis.

Naturally, following the inflammation, a vascular spasm takes place with transitory or permanent occlusion of the blood vessel, and also affinity exists to precipitate the colloidal elements of the blood plasma.

But if we study the ultimate development of the vascular thrombosis after it is seated inside of the vascular structure, I think we will be able to reach a final conclusion on this argument, which will point out the vascular damage as a main factor in the thrombus formation. If you look at **Figure 28**, you will see that after the thrombus is formed and located in situ as a "vascular neoplasy," a local irritation starts taking place right in the base of contact with the vascular wall, and the endothelial cells penetrate into the blood clot which gradually becomes retracted.

Figure 28.

Angioblastic formations also invade the inside of the blood clot with a final development of capillary structure, through which the blood circulation practically flows inside the blood clot. In days to follow autolysis and absorption of the thrombus material gradually takes place, carrying back to the blood stream this detritus material. The final formation of the local sear tissue takes place right in the walls of the damaged vascula.

Incidentally, Dr. Koch has described this beautiful and natural recovery of the "vascular neoplasy" in the 'recovery mechanism' of malignant tumors undergoing autolysis with the Catalytic Agent.

From the moment that the thrombus undergoes gradual absorption, by a process of cell multiplication of the blood vessel itself, no new clots are formed at that level. Despite the fact that the absorbed material is carried through the

blood stream, it is common sense to believe that the vascular alteration is the fundamental factor in the cause of thrombosis.

II—PHYSIOPATHOLOGY

Anticoagulant Therapy in Thrombosis

Let us now make a brief study of the therapeutic value and results of medications, particularly anticoagulant medications in the treatment of thrombosis.

With bases in previous dissertations, the therapy in thrombosis is divided into two groups, or more properly, two different opinions among physicians.

As you know there is a group of physicians who are in favor of medications of "blood action," or more properly, medications with direct effects on the Pro-thrombin time level, decreasing it with temporary effect. Among these medications, which are on the market, are Heparin, Decoumarin, Intercostrin, etc. The other group of physicians is in favor of using medications with direct effects over the vascular problem (vascular inflammation), among which the Catalytic Agents occupy a prominent position.

A. Medication with Blood Action

This medication is given hypodermically in repeated doses, sometimes at intervals of four hours. The necessity for repeated doses, speaks very definitely of the instability of the solution because its elimination takes place so rapidly.

As a result of the coagulation time decreasing effect, on many occasions, complications take place in the form of epistaxis, gastric hemorrhages, gingivitis, subcutaneous skin hemorrhages, etc. In some patients, these complications require urgent attention and treatment, for example, the administration of vitamin K and sometimes transfusions. All of you surely are aware of the danger of a transfusion on a patient with embolic thrombus. It is possible that this transfusion will develop more thrombus, and on many occasions will be a failure.

On the other hand, the anticoagulant therapy does not solve the distant secondary complication (fever, pain, arterial spasm, or infarction) already set by the thrombus formation. Consequently, the patient requires associated medication of Penicillin for the control of the infection, and Papaverine to prevent the spasm of the arterial segment. Neither the first nor the second has had honest results on patients. It seems that very frequently in thrombo-phlebitis of the lower extremities, Penicillin therapy is absolutely unsuccessful, even in large doses. In regard to Papaverine, this has had transitory effect only over the

spasm which belongs there, because after all the spasm is the result of the inflammatory process of the vascular endothelial coat.

B. Medication with Vascular Action

As I make an examination of the medication with vascular action, like the catalytic agents, the results present quite a different situation. The first obvious difference is that only "one single dose" is required to render the patient free of many punctures. Bringing your attention to the single dose is a digression from the point of this lecture, but I want you to recall the ''prolonged effect" of the Catalytic Agents as a matter of a chain reaction mechanism.

The principal benefit, however, is over the vascular damage. The process of "Focal infection" is removed from the vascular region without the necessity of anti-spastic medication, from the moment that the spasm is removed as soon as the local infection is wiped out.

On the other hand, the Catalytic Agents also stimulate the process of "thrombus absorption," and speed up the formation of scar tissue.

Distant complications from the thrombus infarction also received benefits from this medication, with a rapid repair process of the pathological damage. This was the case of my brother, afflicted with pulmonary embolism, followed by inguinal hernia repair.

I finally stress the fact that, if there is an underlying allergy factor, the Catalytic Agent also established a change of this pathological condition by eliminating the irritation on the vascular segment (structural allergy).

III—CLINICAL OBSERVATIONS, SUPPORTING PREVIOUS STATEMENTS

A. Surgical Thrombosis with Pulmonary Embolism

CASE: My Brother who is a Catholic Priest, white, 46 years of age was undergoing a routine inguinal hernia repair. On the third day after the operation, he developed a temperature, severe chills, and restlessness.

The surgeon failed to find a local infection in the incision, which had been healing normally. The patient was given a chest examination that showed a negative pulmonary condition, as well as a routine urinalysis for a possible kidney condition.

At the end of this temperature (seven days), the patient referred to an acute, severe pain over the left side of the hemi-thorax, complained of difficulty in

breathing, and had developed a cyanotic coloration. A half-grain of morphine was given symptomatically, and the patient was put under an oxygen tent. The examination of the lower extremities showed by palpation, a painful and inflamed vein all along the saphenous trajectory. A chest picture showed, with the findings of left costophrenic obliteration of the left pulmonary lower lobe, an infarction. This patient was given penicillin procaine, 300,000 units every four hours for a period of seven days, Papaverine injections twice a day to relieve the spasm, and Decoumarin as anticoagulants every five hours to keep the coagulation time below 30%. Despite this medication, the patient's temperature went up to 104°. He had severe dyspnea and difficult respiration and pain over the chest. Penicillin's fast resistance was considered as possibly due to the fact that the temperature became worse after the seven days.

On the morning of September 4, I received a message from my family of the seriousness of my brother's condition. After a preliminary interview with his physician, 2 cc. of Glyoxylide solution was given intramuscularly. He was practically unconscious. The next morning the temperature dropped to a hundred, with complete relief of the chest pains and difficult respiration. The cyanosis was removed to a great extent. The phlebitis and painful sensation of the leg disappeared to a great extent, and circulation was reestablished in the toes of the right foot. A week later, after the Glyoxylide medication, my brother was free from temperature, and was able to remain out of the oxygen tent for a period of two to three hours. A second chest plate was ordered seven days from the first one, and the findings revealed the total absorption of the costophrenic obliteration. He was dismissed from the hospital, convalescent, after receiving a second dose of Glyoxylide on September 14, nine days from the first dose. He has since remained well and has been engaged in church activities as a member of the Jesuit Organization.

B. Berger's Disease

CASE: This patient is white, 76 years old, male, and is afflicted with gangrene of the left foot. He had been under the doctor's care for the past two months without too much relief of his complaints—cramps, burning sensation, difficulty in walking, and swelling in his foot. After preliminary consultation with a skin specialist, it was decided to perform an amputation above the knee, due to the gangrene process on three toes, and the bottom of the plantar region.

Blood chemistry determined a negation of diabetes, and the only personal record on the history of this patient was that he was an excessive smoker, and had an allergy manifestation.

This patient was hospitalized and ready for surgery. On the next morning, his inspection showed a pale color, depression, and low resistance, which

according to his old age, was indicative of surgical shock. The surgeon was aware of this, and in my preliminary conference with him, he reluctantly denied the possibility of saving the leg of this man unless the operation was performed at once. Nevertheless, on that day the patient was moved back to his home and put under the Koch Treatment, receiving two cc. of Glyoxylide at 8 P. M. that night. Physical examination of his leg showed an offensive odor from his foot, and profuse corrupt material draining from a deep ulceration on his foot and toes. The lower extremity was cyanotic in color and palpation thermostat feelings were absent. His leg was "cool like ice," and he was under morphine, other medications, and penicillin to relieve suffering.

The next day, after the Catalytic Agent was injected, he described "throbbing sensations" in the toes, and immediate relief of the pain, to such an extent that the opiates were no longer needed. On the following day, the next improvement was in his circulation and color. The cyanosis was gradually replaced by a pinkish coloration. The temperature of his leg gradually became normal day by day, from the upper part to the ankle region. At the end of five days, the temperature of his foot was practically normal.

The following week, and at the end of nine days, he referred to some pains in the extremity, after which necrotic tissue was thrown out, particularly in the plantar region on one toe.

From a helpless man, who was unable to walk, this patient regained the use of his leg at the end of the second week. Finally, at the end of three months, there was complete recovery from receiving "one single dose of Glyoxylide." Today, as a member of the Shrine, Elks, and Kiwanis Clubs, he attends these conventions, driving his car, and enjoying practically a normal life.

C. Coronary Thrombosis Status

CASE: A 67-year-old man came into our office suffering from severe epigastric pains radiated to the chest and left arm. These pains had been so persistent that upon occasions he was unable to walk about inside his home. For months he had been under medication, but without much relief. By the time he came to the hospital, his spells had been recurring frequently. During the attacks, he turned pale with shock and there was profuse perspiration, weakness, and restlessness. A physical examination discovered a slight hypertension (167 over 105) and enlarged myocardial organs. I sent this patient to a heart specialist to make an electro-cardiogram recording. From this recording, it was possible to see that the most outstanding feature is the inversion of the T-wave, a typical manifestation of the coronary damage. I discontinued all medication on this patient and, after 48 hours of preliminary diet, administered to him 2 cc. of the Catalytic Agent. During the following months, and particularly within a few

weeks after the Glyoxylide injection, this patient was able to move around without fear of pain or distress of the chest. His blood pressure dropped from 167 to 145, and the majority of the pains and cramps in the lower extremity (calf muscles) disappeared entirely.

Three months after this injection, a second EKG was taken. The results showed continuing improvement. At the end of six months a third EKG recording was taken as evidence that he had recovered. This electrocardiogram showed the normal position of the T-wave and disappearance of the myocardial damage. The patient has remained a well man to date, eight years after his first treatment. This recovery was considered impossible by the specialists at the first examination.

D. Rheumatic Carditis Thrombosis

CASE: A 62-year-old white woman who was afflicted with a chronic rheumatic condition, and who suffered a stroke affecting the left leg and arm, was brought to me for treatment. For years she had been afflicted with rheumatic pains in the knees, shoulders, hands and ankles, from which she had not been alleviated by the standard medications.

This chronic affair suddenly became aggravating. She developed a 102° temperature at noon, chills, palpitations, and profuse perspiration. A physical examination showed organic heart murmur, typical of rheumatic carditis. She also frequently complained of pains over the heart region, and shortness of breath when she walked. Her left arm and left leg had been partially paralyzed for the previous two months, despite the lack of history of strokes of cerebral hemorrhages. Since there had been no previous strokes and the blood pressure was normal, I believed that the stroke suffered was secondary to the thrombus embolism dislodged from septic endocarditis. Therefore, I administered intramuscularly, 2 cc. of Benzoquinone (a Catalytic Agent).

The first improvement was the temperature, which became normal at the end of the third week. The pain and distress over the heart region was also improved to a great extent. In the months to follow, the partial stroke of the left arm and leg was improved to such an extent that she was able to walk without the necessity of a cane or assistance. The numb sensation and burning feeling on the hands and fingers disappeared completely, and upon a chest examination the organic murmur was practically impossible to detect.

Since the first dose of the Catalytic Agent, this patient has remained well with no recurrences of thrombosis and has carried on a normal life for the past five years.

E. Female Pelvic Thrombosis Post Spontaneous Miscarriage

CASE: A 23-year-old woman came to me as a patient afflicted with a history of spontaneous miscarriage, after which a pelvic infection was developing, as well as secondary thrombosis of the right saphenous vein. For three months she had been complaining of swelling and painful sensations in the right leg, very sensitive to palpation along the path of the saphenous vein. She had been unable to retain a job because of this condition, and was unable to walk, even a short distance. The menstrual cycles had also been irregular, with profuse hemorrhages. Upon occasions menstruation was repeated during the month to such an extent that the patient was so weakened that she was required to stay in bed. The blood count showed mild anemia of 3,000,500 of red cells and 60% hemoglobin. Occasionally, and during the evening, she complained of a slight temperature, with chills and cramps over the right leg. After a thorough examination by many physicians, a "complete hysterectomy" was proposed by a surgeon as the only solution to remove the focal infection and the hemorrhagic complications. The patient refused this because she desired to become a mother in the near future. On this condition, 2 cc. of Glyoxylide was given intramuscularly. Following the injection, she acknowledged a marked relief from the extremity pains, and the disappearance of the cyanotic coloration of her toes. The menstrual cycle of the following month was normal in duration and quantity. The chills and fever were abated. A year and one half after the first dose of Glyoxylide, she became pregnant and without any complications, gave birth to a normal child. After regaining her health, this patient has remained well for six years, and has borne two children.

IV. SUMMARY AND CONCLUSIONS

From the clinical description of the above patients afflicted with thrombosis of different kinds in the vascular system, we are impressed with the facts of the clinical results and the minimum of therapeutical measures. Coronary thrombosis particularly pays a high percent of damage among patients in this country. The anti-coagulant medications recently employed in coronary patients, do not solve the underlying factor of the disease any more than does an aspirin solve the underlying factors of the headache of hypertension patients. In surgery, thrombosis follows abdominal operations. In particular, hernia and female operations are not solved by anti-coagulant medications. It is a most interesting fact that throughout our studies of the recovery of the Obliterans Endarteritis, surgical resections of nervous plexus or resections of the external arterial cover (described twenty years ago by a French surgeon. Professor Leriche) have not yet proved to be successful measures in the recovery of this process. However, you have seen in the previous pages, the well-established case of Thrombus and

Endarteritis that obtained total recovery, even after gangrene process had been established.

I finally considered the amazing results of this therapy in vascular thrombosis, from the standpoint of the preservation of life, particularly new lives, in which the human maternal love represents one outstanding problem.

Female pelvic thrombo-phlebitis has been considered by our school of medicine one of the hopeless incurable diseases, and therefore an obstacle in the way of the maternity opportunity.

The clinical and pathological recovery under the Catalytic Agents is obtained over the infection, the circulatory obstruction, and the fertility of these patients.

I want to express my appreciation for the opportunity to speak to you, and for the kindness and attention of all of you who are gathered here today.

Oklahoma City, Oklahoma
October 5, 1949