THE PATHOLOGY OF SINUS THROMBOSIS.

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Most thrombi are described as consisting of a head, a neck and a tail. The head is usually white in color, the neck is mixed white and red, and the tail is red. The tail usually forms the bulk of the thrombus. The head of the thrombus is composed almost entirely of blood platelets. Blood platelets are small disc-shaped nonnucleated bodies, which are normally present in the blood. According to J. H. Wright of Boston, they arise from the giant cells of the bone marrow and the spleen.

The free surface of the head portion of the thrombus is covered with ripple-like markings. A longitudinal section of this portion of the thrombus shows that these delicate surface elevations are the summits of a framework of beams. The beams are composed of blood platelets, and are surrounded by a border of polynuclear leucocytes. The spaces between the beams are filled with red blood cells. There is no fibrin. The nearer we approach the free extremity of the head portion of the thrombus, the broader the beams become, and the narrower the furrows between the beams, until finally at the tip of the head portion the beams unite into a solid white mass of blood platelets. The beams are transverse to the long axis of the vessel, or oblique. They grow outward from the vessel wall. In the neck portion of the thrombus the furrows containing red blood cells, which lie between the beams, become wider. The neck portion of the thrombus is mixed red and white, because of the admixture of red blood cells with the blood platelets. The tail portion of the thrombus is red and consists of an irregularly arranged mass of red blood cells, leucocytes, blood platelets and fibrin. It resembles postmortem clot, microscopically. The portion nearest the neck is the densest portion. Here, suggestions of lamellæ can still be seen. As we approach the end of the tail the structure of the

thrombus approaches, more and more, that of normal blood.

The head portion of the thrombus is formed first. This is laid down while the blood is flowing through the vessel. When the thrombus has grown sufficiently large to completely obstruct the lumen of the vessel, the blood column becomes stationary peripheral to the thrombus, up to the place where the first anastomosing branch enters the vessel. This column of blood becomes completely coagulated in a short while. This forms the tail of the thrombus. The neck is the intermediate portion between the head and the tail of the thrombus.

A white thrombus is formed by a sticking together of the blood platelets, and is called by Eberth and Schimmelbusch a "conglutination thrombus." A red thrombus is produced by ordinary clotting of the blood, and is called a "coagulation thrombus." A blood platelet thrombus can only occur in a flowing bloodstream, and a red thrombus can only occur in stagnant blood. Very long white thrombi occur when the blood continues to flow through the vessel for a long time after the onset of the thrombus formation.

One of the factors in the formation of a white thrombus is a slowing of the bloodstream and the formation of eddies. Aschoff reproduced structures similar to the beam formation in white thrombi by placing dams and weirs in the course of a flowing stream of water, in which were suspended particles of sawdust. As a result of the slowing of the current of water and the formation of whirlpools and eddies, the sawdust was deposited at the dams and weirs in the form of ripples and net-like elevations.

The slowing of the blood current in the vein allows the blood platelets to be deposited on the wall of the vein, in the form of ridges. Before complete cessation of the bloodstream the system of platelets is covered by a layer of leucocytes. This is due to the fact that when the bloodstream is slowed the white blood corpuscles, being of lighter specific gravity than the red, tend to travel at the margin of the bloodstream and thus are deposited on the beams of blood platelets. When the thrombus fills the lumen of the vessel, the formation of the primary thrombus stops, as no new blood platelets can be carried past.

A slowing of the blood current is favored in certain parts

of the venous system, where there is a widening or bending of the vein, or where there is pressure from a large column of blood, as in the leg when the body is upright. There is a slowing of the current when there is pressure on the vein from without. These factors play a more important part when there is a defect in the heart's action, leading to a general slowing of the bloodstream in the venous system.

In addition to slowing of the bloodstream there are three other factors which play an important rôle in the causation of thrombi. These are an increased agglutinability of the blood platelets, an increased coagulability of the blood plasma and changes in the vessel wall. That slowing of the blood current alone does not cause thrombus formation was proven by Baumgarten, who showed that a stationary column of blood in a doubly ligated vessel did not thrombose. In thrombosis of infective origin there is an inflammation in the vessel wall and destructive changes in the endothelial lining of the vessel. It is likely that the bacteria in the vessel wall set free toxins which pass through the intima into the blood. These toxins, as well as the juices set free by the destroyed endothelial cells, probably act upon the blood platelets in such a way as to increase their agglutinability. An increase in the coagulability of the blood is probably also brought about in this way.

Clotting *en masse* is called coagulation thrombosis. To produce a thrombus of this type, complete stoppage of the bloodstream and an increase of fibrin ferment in the blood are essential factors.

That destruction of the endothelial lining of a vessel is not the only factor necessary to produce a thrombus is shown by the fact that thrombosis is very rare in extensive atheromatous disease of the aorta.

The thromboses which occur after operations are due, in part, to the slowing of the blood current which results from loss of blood at the operation, weakening of the heart action, general prostration and confinement to bed. Another important factor is the change produced in the blood platelets by the infection.

Eberth and Schimmelbusch produced thrombosis experimentally by injuring vessel walls and interfering with the circulation. By ligating a vessel for a while, the intima was torn,

After releasing the ligature and allowing the blood to flow through the vessel for a quarter of an hour, the vessel was incised and examined. It was found that all the prominent portions of the inner surface of the vessel were covered by adherent masses of blood platelets. After cauterization of a vessel with silver nitrate and destruction of portions of the intima, similar results were obtained.

In a punctured or incised wound of a vessel wall, in which the bleeding was allowed to stop of its own accord, the opening was found to be stopped up by a plug of blood platelets which protruded into the lumen of the vessel.

Jakowski found that by injecting bacteria into the circulation and at the same time producing a disturbance in the circulation or a slight traumatism in a vein in some other part of the body (for example, by ligation), a thrombus was produced at the point of ligation, in most cases.

Talke exposed vessels in cats, dogs and rabbits. Pure cultures of staphylococci were placed in contact with the vessel walls and the skin sutured over them. The neck or leg vessels were usually used. After nine to seventy-four hours, the animal was killed. The affected portion of the vessel was removed and examined. Forty-four vessels were experimented upon in thirteen animals. Thirteen arteries and thirty-one veins were used. The femoral and carotid arteries and the jugular and femoral veins were employed. In thirty-three cases thrombosis was found, and in eleven, none.

Bacteria were found in fifteen of the thrombi. In the remaining eighteen, numerous bacteria were present in the periadventitial tissue. In six of these latter cases the bacteria extended to the middle layers of the externa. In three, they extended to the outer layers of the media. In eight, they reached as far as the middle layers of the media, and in one case there were bacteria in the intima. The bacteria were present almost exclusively in the interlamellar clefts and lymph spaces, but not in the vasa vasorum. Very few bacteria were found free in the tissues. The progress of bacteria could be followed through the lymph spaces in the externa, media and intima, and finally into the thrombus. The bacteria were present mostly in the peripheral portions of the thrombi. The

youngest thrombi contained no bacteria. The older thrombi contained bacteria in most cases. These facts seem to show that the thrombus is formed before the bacteria reach the bloodstream. The thrombus may even be formed before there are any marked changes in the intima. The bacteria in the vessel wall produce changes in the tissue fluids. This changed tissue fluid and the bacterial toxins enter the circulation and cause the blood platelets to become more viscous and adhere to each other and to the vessel wall. Changes are also produced in the blood serum. In this way the thrombus is formed. The bacteria then enter the thrombus, either directly from the vessel wall or through the circulation.

Stenger exposed the sigmoid sinus in a dog, and placed over the sinus a tampon containing streptococci. The streptococci were obtained from a suppurating ear, and were made more virulent by passage through several animals and cultivation in very alkaline Aronson bouillon. No thrombus was formed in the sinus. In another dog he placed an infected tampon within the sinus. There was no thrombosis. In a third dog one-fourth cubic centimeter of a bouillon culture of streptococci was injected into the sinus. There was no thrombosis, and the heart blood was sterile three days later. In a fourth dog, the wall of the sinus was scarified with a scalpel before an infected tampon was applied. This dog died two days later. An abscess was found over the sinus, and there was an extensive thrombosis in the lateral and superior petrosal sinuses. A portion of the thrombus was broken down, and contained streptococci and staphylococci. A pure culture of streptococci was obtained from the heart blood.

Stenger drew the following conclusions from his experiments:

1. The greatest protection against infectious thrombosis is the vessel wall itself. Bacteria which pass through a healthy vessel wall are destroyed in the circulation. The nonmechanical thrombus is preceded by disease of the vessel wall and subsequent change in the blood.
2. Bacteria do not cause thrombosis by settling upon the intima; the thrombus is caused by inflammatory changes in the blood, which are indirectly caused by bacterial invasion.
3. Thrombosis occurs before bacteria enter the circulation.

The infection of the thrombus is secondary.

Haymann infected the superior longitudinal sinus in twenty dogs, and the lateral sinus in six monkeys. He placed a tampon soaked in a culture of streptococci or staphylococci in contact with the sinus wall, and left it in place for varying lengths of time. He reached the following conclusions:

1. Infectious sinus thrombosis is best produced experimentally by the application of an infected tampon to the outer wall of the sinus. The rubbing on of cultures, even after injury to the sinus wall, does not usually produce thrombosis.

2. Bacteria can reach the circulation without the intermediation of a thrombus.

3. Sinus thrombosis usually occurs as a parietal clot, which becomes obturating after a variable time. Rarely, the entire blood column may clot at once.

The length of time between the application of the infection to the outer sinus wall and the beginning of clot formation varies within wide limits. The time from the beginning of the formation of the parietal clot until it becomes obturating also varies considerably.

4. Thrombi may contain bacteria as soon as they are formed, or the bacteria may enter the thrombus secondarily. Bacteria usually enter the thrombus from without, but they may enter it from the circulation. The number of bacteria in a thrombus varies greatly. The ends are usually more benign, but this is not always so. Moderate numbers of bacteria are no bar to organization of the thrombus.

5. Thrombi may remain parietal and organize thus.

6. The growth of thrombi is usually centrally directed. Discontinuous thrombi may occur through the fact that thrombosed dural veins may enter into nonthrombosed areas of the sinus, and thus produce new thrombi.

7. There is a marked tendency to spontaneous healing of thrombi. The healing usually starts early.

8. From the macroscopic appearance of the sinus wall it is impossible to judge the contents of the sinus.

9. Aseptic compression or incision of the sinus produces no thrombosis.

10. Injection of bacteria into the circulation, with aseptic compression or incision of the sinus, produces thrombosis.

Most thrombi are infectious. But a few are not infectious. These latter are called marantic thrombi and are primary. They are located most commonly in the superior longitudinal sinus and occur usually in individuals who are in a very weakened condition. They occur most commonly in very young children and old people. They probably occur as the result of a slowing of the bloodstream and changes in the constitution of the blood. The thrombi are almost always mural and they never suppurate. They either organize or become absorbed. The thrombi may extend into the cerebral veins and produce localized cortical cerebral lesions.

Infectious sinus thrombosis is due either to compound fracture of the cranial bones or to a localized inflammatory lesion in some part of the head. Inflammatory processes in the scalp may cause a thrombosis of the superior longitudinal sinus. Inflammations on the face, in the orbit or about the tonsils may give rise to a thrombosis of the cavernous sinus. The most common cause of sinus thrombosis is suppurative disease in the middle ear and mastoid. This gives rise to thrombosis of the lateral sinus and jugular bulb. Several cases have been reported, of suppurative adenitis in the neck causing a thrombosis of the internal jugular vein, which extended up into the jugular bulb and sigmoid sinus. Injuries to the sigmoid sinus or jugular bulb in the course of a mastoid operation may give rise to a sinus thrombosis.

Thrombosis of the lateral sinus resulting from middle ear and mastoid disease may come about in one of several ways.

1. The inner table of the mastoid over the sinus may be diseased and an abscess form between the sinus and the inner table. This results in an inflammation of the outer sinus wall, which in turn leads to the formation of a thrombus within the sinus.

2. The inner table over the sinus may be diseased and cause an extension of the inflammatory process to the sinus wall without the intermediation of a perisinus abscess. The phlebitis results in a thrombus formation.

3. A thrombus may form in one of the smaller veins of the mastoid process and extend into the lateral sinus.

The pathologic changes in sinus thrombosis are the same as in thrombosis of veins in other parts of the body, with the

exceptions caused by differences in the structure of the sinus wall. Differences in location also give rise to variations in the pathologic changes. The sinuses differ from veins principally in the fact that they have no muscular coat, and that in most cases they are adherent to bone.

The inflammatory changes in the sinus wall consist of thickening of the entire sinus wall due to round celled infiltration, dilatation of the vasa vasorum, and necrosis of some of the cells, especially of the endothelial cells in the intima. There may be smaller and larger abscesses in the sinus wall. There are numerous bacteria in the sinus wall. The thrombus is adherent to the intima. The thrombus usually contains bacteria, but it may be sterile. It may be broken down in places. It may be partly or entirely organized. It may be broken down in parts and organized in other parts. The outer surface of the sinus may be covered with plastic exudate. There may be an abscess between the outer surface of the sinus and its bony covering. When this is the case the sinus wall is **enormously thickened and covered** with shaggy granulations. Sometimes the thrombus breaks down, and a portion of the outer sinus wall becomes necrotic and breaks down, with the result that the abscess within the sinus communicates through the fistula in the sinus wall with the perisinus abscess. In some of these cases the pus may find its way through the mastoid canal alongside of the emissary vein to the outer surface of the skull and cause a localized edematous swelling in this situation, or it may pass through the posterior condyloid foramen and give rise to a cellulitis in the deep tissues of the neck in the region of the posterior cervical triangle.

The inner or visceral wall of the sinus may undergo the same changes as the outer wall. When this occurs there is usually an extension of the inflammatory process to the pia, resulting in the formation of adhesions between the sinus wall, the pia and the surface of the brain. In some cases a diffuse leptomeningitis results. Sometimes the inflammatory process extends into the substance of the brain and gives rise to a brain abscess. This is especially common in the cerebellum.

The saccus endolymphaticus lies in the visceral wall of the sigmoid sinus. When a suppurative labyrinthitis results in a saccus empyema, the infection may spread from the sac-

cus in both directions, giving rise to a sinus thrombosis and a cerebellar abscess.

Sinus thrombosis may cause alterations in the brain tissue and meninges in other ways than by direct extension of the inflammatory process from the sinus wall. The thrombus may extend from the sinus into some of the pial and cerebral veins. Thrombosis of the cerebral veins may result in the occurrence of spots of hemorrhagic softening in the brain. Heilbronn reported a case of sinus thrombosis with general cerebral symptoms. Autopsy showed an extension of the clot from the lateral sinus into the vena magna Galeni and the small basal cerebral veins, with spots of hemorrhagic softening in both optic thalami. In another case of sinus thrombosis there were disturbances of speech. In this case he found multiple small lesions in the medulla. Extension of the thrombus into the pial veins may cause a serous meningitis or an edema of the brain. In a third case of sinus thrombosis described by Heilbronn, there was a sudden onset of aphasia and agraphia after several hours of coma. The next day the aphasia and agraphia disappeared. These symptoms were due to an extension of the clot from the lateral sinus to the large pial veins which surround the temporosphenoidal lobe and drain it. There were no localized lesions in the brain. The symptoms were caused by an edema of the temporosphenoidal lobe which disappeared as soon as a collateral circulation was established.

The inflammatory process which extends from the sinus to the meninges sometimes gives rise to an involvement of one or more of the cranial nerves. This is especially true of the third, fourth and sixth nerves. The nerves become inflamed as the result of a direct extension of the inflammatory process from the meninges. In thrombosis of the cavernous sinus the inflammatory process spreads directly from the thrombus to the nerves which lie in the wall of the cavernous sinus.

Inflammation of the optic nerve occurs with sinus thrombosis. When the thrombus is in the lateral sinus, the inflammation of the optic nerve is probably due to an extension of the meningitis. When the thrombus is in the cavernous sinus the changes in optic nerve may be due either to the accompanying meningitis or to edema resulting from obstruction to the

circulation.

Thrombi in the sinus may be partial or complete. The partial thrombus is called parietal or mural, and the complete thrombus is called obturating. There is no apparent reason why some thrombi should be parietal and others obturating. Most of the thrombi that come to operation are obturating. All thrombi begin as parietal thrombi, and some finally become obturating. Parietal thrombi are no doubt frequently overlooked at operation. Leutert believes that parietal thrombi occur more commonly with acute otitis and obturating thrombi with chronic otitis. But the experience of most otologists today is that either form of thrombus is apt to occur with equal frequency in acute and chronic otitis.

According to Brieger, "a parietal thrombus in the sinus can only be assumed, when it is demonstrated; but even in cases which are positive anatomically, the proof of the presence of a parietal thrombus must be completed by the further proof that the thrombus is so situated that it took its origin from the ear, and is so constituted that it can produce general sepsis and metastases." He believes, for example, that in cases of otitic general sepsis, in which autopsy shows a small partly organized parietal thrombus attached to the cerebellar wall of the sigmoid sinus, the thrombus is not the cause of the general sepsis. A thrombus of this kind is too insignificant and contains too few bacteria to keep up a general sepsis, and furthermore, a thrombus in this situation is usually not an extension from the middle ear suppuration, but is due to incision and tamponade of the sinus.

The thrombus is most commonly located in the sigmoid portion of the lateral sinus. It varies in size from a fraction of an inch to the entire length of the lateral sinus. It may extend down into the bulb, and even for a variable distance into the internal jugular vein. It may even occasionally reach the upper part of the innominate vein. It may extend upward as far as the torcular, and even cross over into the opposite lateral sinus. It may extend into the superior longitudinal sinus, the occipital, the straight, the superior or inferior petrosal sinuses. It may extend into the mastoid emissary or the posterior condyloid vein.

There may be a primary thrombosis in the jugular bulb,

without involvement of the sigmoid sinus. It is easy to understand how the inflammatory process may pass directly from the middle ear through its floor to the wall of the jugular bulb, especially when the floor of the middle ear is very thin or even wanting altogether. Leutert does not believe that primary bulb thrombosis occurs as the result of extension through the floor of the middle ear. He thinks that it is due to bacteria which enter the bloodstream through the wall of the sigmoid sinus, and passing downward, find a favorable spot for clot formation in the bulb. Here the bloodstream curves and forms a whirlpool. The lumen of the bulb is narrowed at its outlet. The blood current is forced back from the internal jugular vein during deep expiration.

Occasionally the thrombus is located in the inferior petrosal sinus, without involvement of the other sinuses. The veins of the internal ear empty into the inferior petrosal sinus, and suppurative disease in the labyrinth may give rise to a thrombosis of the inferior petrosal sinus. Necrotic processes of the petrous pyramid may also result in a thrombus formation in this location. Schwartz reported two cases, Jansen reported four cases and Beyer reported one case of primary thrombosis of the inferior petrosal sinus. The writer reported one case of thrombosis of the inferior petrosal sinus complicating a chronic suppurative labyrinthitis. In this case, the thrombus extended from the inferior petrosal sinus into the cavernous sinus.

The thrombus may be situated primarily in the cavernous sinus. This occurs as the result of an infectious process about the face, in the throat or in the orbit. A thrombus may extend into the cavernous from the lateral sinus through the superior or inferior petrosal sinus. A thrombus in the cavernous sinus is rarely limited to one side. It usually extends, in a few days, through the circular sinus to the opposite cavernous sinus.

A thrombus may occur in the superior longitudinal sinus as the result of an infectious process in the scalp or nose.

We sometimes find, in operations for jugular resection, that the internal jugular vein is empty and reduced to a thin cord. When this occurs it is sometimes very difficult to find the vein. It can easily be mistaken for a nerve or a piece of fascia. The

reason for collapse of the vein is not very clear. It is generally thought to occur when the thrombus extends down from the jugular bulb into the internal jugular vein past the point of entrance of the facial vein into the latter. But it is difficult to understand why the blood should not pass upward from the subclavian to the lower limit of the thrombus in such cases. It is probable that a periphlebitis and phlebitis of the internal jugular is the cause of the obliteration of the vein.

Kramm and Passow reported several cases of obliteration of the sigmoid sinus without thrombus formation at the site of the obliteration. In these cases a perisinus abscess compressed the sinus until the walls were in apposition. There was an inflammation of the outer wall of the sinus with a thickening of the wall. When the inflammation reached the intima, the latter became adherent to the opposite wall. There was no thrombus formation, because, at the time when the inflammation reached the intima, there was no longer any blood passing through the sinus.

The following are the possible end results of a thrombus in the sinus:

1. The patient dies of general sepsis before the clot breaks down.
2. The clot breaks down in the center, and the pus finally breaks through the outer wall of the sinus, so that the abscess within the sinus communicates with the perisinus abscess.
3. The pus within the sinus breaks through the visceral wall of the sinus and produces a cerebellar abscess or a meningitis.
4. The thrombus organizes and results in obliteration of the sinus.
5. Part or all of the thrombus becomes absorbed, resulting in recanalization of the sinus.

In sinus thrombosis, bacteria pass from the thrombus into the general circulation, where they can usually be demonstrated. The streptococcus hemolyticus and the streptococcus mucosus are the organisms most commonly found. Occasionally other organisms are found. The presence of bacteria in the blood is determined by blood cultures.

Leutert believes that every case of otitis that has a bacteri-

emia is due to sinus thrombosis. Libman believes that there is a bacteriemia at some time in all cases of sinus thrombosis except those that are aseptic from the beginning and remain so. Brieger reported a few cases of pyemia with metastatic abscesses originating from middle ear suppuration, in which postmortem examination showed no thrombus in the sinuses or jugular bulbs. He believes that, although it is possible for an otitic pyemia to occur without sinus thrombosis, yet these are the exception, and the vast majority of cases have a sinus thrombosis. Kobrak reported several cases of general sepsis with otitis, in which no thrombus was found in the sinuses. Haymann, in the course of his experimental work on thrombosis in dogs and monkeys, found bacteremia without sinus thrombosis in a few cases. There seems to be no doubt that cases of otogenic general infection do occur without sinus thrombosis, but they occur very rarely. As a general working rule, we may assume that otogenic general infections are due to sinus thrombosis.

There are several conditions besides sinus thrombosis in which bacteriemia occurs. These are meningitis, tonsillar infections, acute bacterial endocarditis, scarlet fever, typhoid fever, pneumonia and erysipelas.

In cases of sinus thrombosis, bacteria may not be found in the circulation at all times. Sometimes two or three cultures must be taken before bacteria are found. Libman found that bacteria are most apt to be found either during or immediately after a chill.

Multiplication of bacteria in the blood rarely occurs. Libman found that the circulation often becomes free of bacteria within a few hours after the thrombus is removed from the sinus and the internal jugular vein ligated.

When fragments of infected clot are broken off from a thrombus in the sinus and carried into the circulation, they are caught in the pulmonary capillaries and produce metastatic foci in the lungs. When there are free bacteria in the circulation, they can pass through the capillaries of the lung and enter the systemic circulation. Under these circumstances they are more apt to produce metastatic foci in the joints, muscles and subcutaneous tissues.

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