THESIS FOR THE DEGREE OF M.D.

on

THROMBOSIS AND PULMONARY EMBOLISM.

An investigation of their origin, incidence and causation.

by

J. Greenstein  M.B. Ch.B. (Edin.)
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Photographs and Microphotographs.
The work on this thesis was carried out at the British Post Graduate School, Hammersmith Hospital, London - and completed in Johannesburg, South Africa.

During thirteen years of private practice in a small village in South Africa where mechanical or biological aid to diagnosis was unobtainable (but when absolutely essential could only be obtained by sending either the patient or a specimen to a distant town) I had to rely, as the vast majority of country practitioners do, on the old and perhaps the best method of diagnosis viz:- by utilising all the senses. My limited knowledge of Medicine, Surgery and Gynaecology was heavily taxed and very often I had to rely on judgment based on experience rather than on a thorough knowledge and understanding of disease in progress. It was under such circumstances, often trying, that I realised the importance of a thorough knowledge of Pathology commonly known as the "Grammar of Medicine and Surgery".

During my student days, the subject of Pathology was studied during the middle of the course with the result that at graduation the new medico was crammed with signs, symptoms and treatment. The knowledge of the basic principles of Surgery, Medicine and Gynaecology had by this time evaporated to a great extent, and the process of disease was considered rather from the point of view of signs and symptoms exhibited by the patient.

It was due to this unsatisfactory understanding of disease in general that I decided to revert to a thorough study of Pathology. The British Post Graduate School offered excellent facilities for such study in the department of Pathology/
Pathology under the able and sympathetic guidance of Prof. J. H. Dible.

During the course of my studies, in a conversation with Dr. T. H. Belt - senior lecturer in Pathology at the School - on the subject of Cardio-Vascular disease, which interested me greatly, Dr. Belt suggested that I investigate the origin, incidence and causation of Thrombosis and Pulmonary Embolism.

I gladly undertook to do this. In spite of the difficult conditions that war brings in its trail, the research departments of the School carried on their different branches of study so that the torch of science could be kept alight, and the British tradition of Scientific research maintained. Many research students had to give up their work, but a few remained and carried on.

It is with the greatest pleasure that I wish to record my appreciation of the School for the facilities that were granted to me during my studies, and during the course of my investigations. Unfortunately, owing to circumstances, I was compelled to return to South Africa sooner than I expected. Here, however, I was fortunate in obtaining permission from Prof. R. H. Mackintosh - head of the Department of Forensic Medicine of the Witwatersrand University - to continue my work in his Laboratories and was permitted ready access to the Mortuary. The work on Hearts, Thrombo-Angiitis Obliterans and the closure of the Ductus Arteriosus, was carried out in this department. I greatly appreciate the assistance of Prof. Mackintosh. His profound knowledge of world scientific literature has enabled me to peruse articles of extreme interest which greatly assisted me in my work. Most of the slides and specimens were photographed in this department.

I wish to record my appreciation, thanks and gratitude/
gratitude to Prof. J. H. Dible for his encouragement, inspiring lectures and ready assistance in my studies, and particularly for his readiness to discuss problems connected with my work. To Dr. Belt I am grateful for assistance and encouragement. He has done a good deal of work on this subject and has published several papers dealing with it. To these articles constant reference is made. The origin of thrombosis in its relation to pulmonary embolism as shown in this thesis will, I think, furnish the necessary link to complete the subject.

While most of the work - PostMortems, dissections, fixation, embedding and cutting of tissues, and staining - was carried out by myself, a great deal of assistance was readily given me by the laboratory technicians, J. Baker and J. Griffin - at Hammersmith - to whom I wish to express my thanks. I also wish to thank Mr. E. V. Wilmott for the Photographic work.

In conclusion, reference must be made to the number of occasions that I have been compelled to give quotations without verifying these from the original articles because these are unobtainable in this country. I have no hesitation, however, in accepting the quotations given by reputed research workers as entirely correct.

Johannesburg.
June, 1941.
"The Vascular System in an animal" says John Hunter, "is, in some degree, to be considered as the efficient part of the whole animal respecting itself, every other part of the body being more or less subservient to it and depending upon it for existence and support."

Of all diseases that the human body is subject to, Cardio-Vascular diseases are the most important and at the same time the most fascinating from the point of view of study and conjecture. Ability to work, comfort, happiness, long life, yea life itself, depends on the proper function of the Arterial and the Venous systems. Any departure from the healthy, normal, physiological state, immediately reacts on the body as a whole with varying consequences, but leading inevitably to disaster. While most of the other systems of the body can be adjusted artificially by different methods of treatment and the patient can eventually recover showing very little departure from the normal, this is hardly possible with cardio-vascular lesions by reason of the fact that the proper function of the body, nay, of each cell, depends on its proper blood supply. A blockage of an artery by an embolus or thrombus, a thrombosis of a vein, a rupture of an artery etc., have not only their immediate dangers such as cardiac infarction, gangrene of an extremity, or pulmonary embolism etc., but if recovered from inevitably leave a devastating effect which makes life hardly worth living.

It is often stated that "a person is as old as his arteries". The obvious inference is, if the arterial system could be effectively prevented from taking on the arteriosclerotic nature and thus permit a free, easy and full blood supply to reach every part of the body, life could be prolonged.
Unfortunately, factors such as stress, strain, anxiety and economic conditions, all of which are supposed to influence, by one means or another, degenerative changes in the arteries, are beyond the control of the individual under the present social and economic system. The veins, too, suffer similar degenerative changes, and it is as important to have a healthy venous system as it is to have a healthy arterial system.

Very little attention in the past has been paid to the veins. How far do veins influence degenerative change in arteries? This is a question that requires intensive study and elucidation. An attempt has been made in this study to point out certain relationships that exist between arteries and veins as found Post Mortem. Certain conclusions were drawn from these findings. These, however, are mere indications for further study and research. One part of the circulatory system cannot be adequately studied without reference to the other system. Thus capillaries, arteries, veins and heart must be taken into consideration when discussing the question of the venous circulation.

The veins act as return channels for the blood and thus if there is a pathological state which impedes the adequate return flow, as for example, varicosity, the destruction or non-proper functioning of the valves or occlusion by thrombosis, it follows that the heart, which acts as a pressure pump, will fail in its function of distribution of blood to the tissues for their metabolic needs.

Physiologically, the veins are liable to undergo changes and variations according to the needs of the body, and thus are able to control the inflow of blood into the heart. The local relationship between arteries and veins, and nervous reflexes originating in veins when the latter are in a pathological state, and the transmission of these reflexes by way of the sympathetic to arterioles, are of extreme importance.
in so far that contraction of arterioles reduces the volume of blood passing to the tissues, nutrition is interfered with, and oedema often follows as a consequence. Further the presence of direct channels by means of vasal vessels connecting artery and vein, as shown by Winternitz, is of importance in so far that direct infection does spread from vein to artery. The veins are considered to be more prone to infection than arteries, and thus because of the channels existing between artery and vein, spread of infection is inevitable, with consequent irritation and pathological change in the wall of the artery. Thus the venous system is perhaps of prime importance in the development of arterial disease.

A knowledge of the part played by thrombosed veins, and the origin and causation of the thrombus should materially assist us in combating not only the immediate dangers threatening a patient, but prevent remote sequelae which make life unpleasant, uncomfortable and at times unbearable.

It has been my object to establish the incidence of thrombosis and the dangers following in its trail, and if note will be taken of the extraordinary high incidence of thrombosis found in this investigation, and the treatment as indicated in a special chapter carried out to prevent thrombosis, this thesis will have served its purpose in contributing to a small degree towards the solution of a difficult problem and the dangers threatening the human body by one part of the Cardio-Vascular system.

In conclusion I should like to mention that it was not my original intention to produce such a bulky work. I intended to keep within the limits prescribed by the University. As the work proceeded, however, problems arose from observations made which led to further study and investigation, and thus
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the work became more extensive and the contents increased in size. Passing reference only is made on subjects such as Thrombo-Angiitis Obliterans and the physiological closure of the Ductus Arteriosus. A detailed study is now being conducted and will form a subject for future articles.
The name Embolia was first used by Virchow, who defined it as "a detachment of larger or smaller fragments from the end of a softening thrombus, which are carried along by the current of blood and driven into remote vessels". Now we use the term Embolus in a much wider sense, and define it as "a foreign body circulating in the blood stream, and arrested as soon as it reaches a blood vessel too small to give it passage". - Dible and Davie. There are different types of foreign bodies which are liable to circulate in the blood stream, all of which can give rise to signs and symptoms similar in nature and produce effects equally injurious to the system. Thus we classify Emboli under the following headings: -

1. **Fat Embolus.**

This consists of globules of fat gaining access to the blood stream as a result of extensive fractures of bone, particularly in adipose persons. The amount of fat entering the circulation may be in a sufficiently large quantity to cause extensive plugging of Pulmonary capillaries and bring about collapse and death.

2. **Air Embolus.**

This somewhat rare condition is due to air being sucked into veins during an operation (minor or major), particularly when such operations are carried out in the region of the Internal Jugular vein or other large veins near the heart. The air entering the right auricle and ventricle is churned up with the blood by cardiac contractions into a foamy mass, thus - CAUSING -
2. causing sudden death by blocking the passage of blood into the Pulmonary Arteries. Two such cases of sudden death are reported by Dible, Hewer, Ross and Walsh. The operations performed were of a minor nature.

Case I. In the course of treatment of a urethral stricture after the passage of a bougie, which produced a slight haemorrhage, an air inflating urethroscope was passed and air introduced. The patient collapsed and died suddenly. At Post Mortem, air bubbles were found in the Pulmonary Arteries.

Case II. Air was introduced by means of a catheter into the Fallopian tubes to test for patency in the case of sterility of a married woman. The Fallopian tubes were found to be patent, and on withdrawal of the catheter after the introduction of 150 c.c. of air, a trickle of blood was noticed flowing from the os. The patient collapsed suddenly and died.

At Autopsy, the right auricle, ventricle and Pulmonary arteries were found to be full of air. The authors mention the volume of 150 c.c. of air introduced into the Fallopian tubes. This large volume of air is not necessarily the amount that entered the veins, a good deal, if not most of it, entered the peritoneal cavity. Some authorities consider that a volume of 5 c.c. is sufficient to produce a fatal result if the latter volume is introduced into the venous circulation.

3. Tumour Embolus.

A malignant tumour may invade a vein and set up a thrombosis at the site of invasion by its effect on the wall of the vein, and an embolus may be detached and swept away by the blood stream, producing the mechanical results of an embolus. On the other hand, a few living malignant cells may enter the blood stream, either by invasion of a blood vessel through spread of the growth, or by trauma which ruptures small thin blood vessels in the growth, causing the entrance of tumour cells into the circulation. In the latter case, no mechanical effects are produced, but the danger from such emboli is the setting up of secondary growths.
4. **Bacterial Embolus.**

Clumps of Bacteria may act as emboli, but these are always in association with thrombi. A thrombus infected with pyogenic bacteria softens, breaks up, and is discharged into the fragments circulation, being arrested when the/ reach the capillaries of the lungs—when the thrombus is on the venous side, or kidneys, liver, skin etc.—when the thrombus is on the arterial side, setting up secondary abscesses.

5. Lastly, Embolism caused by a thrombus having detached itself from its seat of origin, swept by the current and arrested in the Pulmonary arteries, causing sudden death if the embolus is large enough to occlude the Pulmonary circulation, or giving rise to distressing symptoms if the embolus is small and lodges in the smaller branches of the Pulmonary tree.

This last type of Embolism is the predominant type encountered in Pulmonary obstruction, and owing to the tragic consequences that follow such obstruction after operations, during puerperium, during the course of medical treatment, the incidence, origin and causation of Pulmonary Embolism is occupying an increasing interest in the world of medicine and surgery. The reasons for such interests are manifold.

(i). The tragic consequences of Pulmonary Embolism following operative procedure, childbirth, fractures, phlebitis, injection of veins for varix and medical cases confined to bed as a result of heart, arterial and debilitating diseases.

(ii). The late sequelae of Pulmonary Embolism which Belt terms "Chronic Embolisation" of Pulmonary arteries with its resulting disability and chronic ill health.

(iii). The increase in incidence.

(iv). The possibility of saving the patient by means of medical or surgical procedure if only the condition of thrombosis is recognised sufficiently early.

(v). The prevention of development of thrombosis by instituting prophylactic measures.

(vi). The social aspect of the problem.
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The relationship that exists between Pulmonary Embolism causing sudden death, haemorrhagic infarcts of the lungs, chronic embolisation with its sequelae and venous thrombosis has long been recognised. Virchow, as far back as the middle of last century, said, "I long entertained doubts whether I ought to consider the metastatic inflammation of the lungs one and all as embolical, because it is very difficult to examine the vessels in the small metastatic deposits, but I am continually becoming more and more convinced of the necessity of regarding the mode of origin of emboli as thrombi from the periphery of the body". Aschoff agrees with this point of view. He states "the majority of Pulmonary Emboli have their seat of inception in the Vena Femoralis". Belt has demonstrated in 116 cases out of 155 (74.8%) the source of emboli in the peripheral veins (94 in pelvic and leg veins and 22 in other parts of the body). Giertz and Craffoord state "According to modern experience, clinical as well as patho-anatomical lung emboli are believed to consist of entire thrombi, or larger or smaller portions of thrombi formed in the peripheral veins, and only quite exceptionally built up in the lung. Thrombus formation in the veins is necessary for emboli to occur, therefore in all cases of emboli, we must assume the presence of venous thrombosis, even though it is impossible to demonstrate in all cases of emboli such thrombosis".

In this connection, i.e. inability to demonstrate thrombosed veins in some cases of Pulmonary Embolism, it can be pointed out - a fact which will be indicated more fully later - that it often happens that practically the whole thrombus can be dislodged from a vein, and found as an embolic mass occluding the Pulmonary arteries without any obvious trace in the veins of the legs unless careful dissection of the latter, including the Plantar veins, is made. It is only then that the source of the embolus can be established. Lindsay, in a collected series of 31,428 post operative cases, found 114 instances of Pulmonary Embolism, i.e. a mortality rate of .3%.

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He quotes Rupp, who, in 22,689 cases, found a mortality from Pulmonary Embolism 2.26%, and in 13,000 autopsies on medical cases 1.3%, i.e. four times as great following operations. Lindsay further states that in 42% thrombosis was found in the pelvic vein. 47% in gynaecological cases with Pulmonary Embolism showed thrombosis in the Pelvic, Iliac and Femoral veins. This low incidence of thrombosis in the veins the author attributes to the fact that no full post mortem examinations were performed. As a rule, autopsy examinations are performed after permission is obtained from relatives, and then it very often happens that a limited examination is permitted. A complete dissection of the veins of the legs is therefore seldom performed with the result that the origin of the embolus is not always established with absolute accuracy. As it will be shown later, in a consecutive unselected series of 100 autopsies, the legs were in all cases examined for thrombosis, irrespective of the presence or absence of emboli in the lungs, and in a second series of 75 cases, the legs were examined in instances where emboli were found. From these two series, it will be seen that in all cases where emboli were found in the lungs, the veins in the legs were found thrombosed. From that, it will be concluded that a thrombus found in the Pulmonary arteries, whether big, causing sudden death, or small, causing haemorrhagic infarcts, is of an embolic rather than of an autochthonous nature.

The possibility of an autochthonous thrombus in the Pulmonary veins and arteries must not, however, be ruled out as a possible occurrence. In a disease such as thrombo phlebitis migrans, the possibility of a segment of a Pulmonary vein being involved in the general process of the disease is quite understandable. The nature of the disease being that of a primary involvement of segments of veins in different parts of the body at different times, it is quite possible that segments of Pulmonary veins become affected in a similar manner, the Pulmonary arteries becoming involved in the thrombotic process.
A microscopic examination, however, will establish the diagnosis without difficulty - the picture in phlebitis migrans being different from that of an ordinary embolic thrombus. Moorhead and Abrahamson and Ryle point out, however, that pulmonary involvement with haemoptysis is due to thrombosis of the Pulmonary veins.

With this exception, it is generally agreed that a thrombus found in the Pulmonary arteries is secondary to a thrombosis in the peripheral veins.

Giertz and Crafoord have found that in the period 1922-1927, there was an increase in the number of cases of Pulmonary Embolism from 21 to 61 cases in a hospital where there was a pretty constant number of admissions. Lockhart Mummery also suggests an increase in the incidence. Burke too emphasizes the importance of an increase in thrombosis and Embolism, particularly since the World War. Fahrr, quoted by Ochsner and de Bakey, found an increase in over ten times in the 13-year period 1913 to 1926. Victor Bonney, however, disputes this increase, and suggests that there was actually a decrease.

It is suggested that the increase is probably due to an increase in the number of operations, better facilities for diagnosis, lengthening of the average life expectancy, increase in hospitalisation of patients with a more widespread resort to recumbency, greater use of intravenous therapy and diuretics, and lastly, as suggested by Ochsner and de Bakey, an increased vascular irritability, which may be the result of the markedly increased use of tobacco. This increase, therefore, must take on a social character. For, apart from the acute obstruction caused by Pulmonary Embolism, which frequently, after quite a trivial operation or minor injury, ruthlessly deprives an apparently healthy human being of life, and the combating of which must therefore be a personal concern of every active surgeon - the bodily discomfort and chronic ill health which a patient suffers after a thrombosis, which may drag on for years, and which necessitates a prolonged stay in the hospital with
increased expense to the community at large, and reduction in income for the patient must have its social repercussions.

The relationship between Venous intervascular clotting and Pulmonary Embolism is, according to the views expressed by various and noted authorities, fairly conclusive, i.e. that a thrombus found in the lung has its origin in a peripheral vein, and that it is there as an embolus. Ribbert, however, quoted by Belt, was the chief protagonist of the alternate view, namely: "That a clot found in the Pulmonary arteries was autochthonous rather than embolic", and his pupil, the late Professor Klotz, who held this view, was only convinced of its embolic nature after a large number of autopsies.

In order to understand the whole problem of Thrombosis and its sequelae, a consideration of intervascular clotting, both physiological and pathological, is necessary.

Definition.

Martin Silverberg defined thrombosis as "the intervital partial or complete obstruction of a vessel by a clot due to changes in the pre-existent constituents of the blood. These may affect either cellular elements or plasma, or both of these substances. The phenomenon is preceded by or associated with disturbances in the chemical constitution, or in the circulation of the blood with inflammatory processes or injuries to the vascular wall". While thrombosis occurs in capillaries, arteries and veins, we are concerned here mainly with venous thrombosis.

Venous Vascular occlusion has been termed Thrombophlebitis, thus indicating an inflammatory condition as an essential factor in the process. As however the condition I am dealing with showed, in the vast majority of cases, no evidence of inflammatory reaction, either in or around the wall of the vein, or in the clot itself, the condition will be referred to as Phlebo-thrombosis. The latter, as Barker calls it a "Maurantic Thrombus".
can be defined as a partial or complete venous occlusion by an intervascular clot which is unassociated with inflammation. The clot is generally loosely attached to the wall of the vein.

Thrombophlebitis can be defined as a partial or complete venous occlusion by an intervascular clot which is associated with or dependent on an inflammation of the wall or perivenous tissue. The thrombus is invariably firmly attached to the wall of the vein. The importance of this distinction lies in the fact that emboli are more liable to break off from a loosely attached thrombus than from one which is firmly adherent to the wall of the vein.

Historical.

The term thrombosis, according to Silverberg, was originally used by Hippocrates (460-370? B.C.) and Galen (129-201 A.D.) as a coagulation of blood, in particular that following haemorrhages in the tissues. John Hunter (1728-1793) considers that the clot found in a vessel is pus and coagulating lymph, which has been secreted by the wall of the vessel and pushed into the lumen. This occurs, according to him, after the inflammatory process had subsided and "a new disposition alters these vessels to their suppurative state." Thus he establishes the fact that a primary suppuration of the vein is necessary for thrombosis to occur. Cruveilhier, on the other hand, considers that the first effect of phlebitis is the coagulation of the blood and its adherence to the wall of the vessel, thus indicating that a primary purulent inflammation did not occur. He points out that the capillary venous system is the source of all inflammation as well as of all normal and morbid secretions, death of the largest number of those who succumb to wounds or surgical operations is due to Phlebitis. He even produced coagulation of the blood experimentally in animals by introducing a wooden splint or some chemically irritating substance. Lobar Pneumonia he attributed to capillary phlebitis, the latter coinciding with some phlebitis more or less distant, giving rise to pus. In the case where the distant phlebitis is not present,
he suggests that "one should break the bones that have been fractured or amputated, where one will find that the spongy tissue is more or less infiltrated with pus". He further observed that clots found in the Pulmonary arteries were hard and lightly adherent to the wall, and on section, a white discoloured area is found which he considered to be pus.

Virchow, however, considers that "before a trace of inflammation is visible, we find a clot." He thus considers that phlebitis is secondary to thrombosis, although he did not deny the fact that phlebitis could be a cause of thrombosis "in consequence of formation of inequalities, elevations, depressions and even ulceration upon the inner wall which favours the production of a thrombus." Emboli, as already indicated, he considers as due to fragments of thrombus having broken off and carried by the blood current to the Pulmonary vessels. He makes the interesting observation that in some cases, the first indication of venous thrombosis is a metastatic deposit. Furthermore, he emphasizes the importance of slowing of the blood stream due to mechanical hindrance as a contributing factor in thrombosis of the veins. This latter point will be more fully discussed when the veins of the lower extremities are considered in relation to thrombosis.

Rokitansky points to the importance of fibrin in thrombosis. He considers that primary inflammatory or chemical alteration in the blood itself is characterized by a quantitative excess in the production of fibrin, which is at the same time qualitatively impaired, and is manifested by a high degree of coagulability of the blood.

Aschoff has laid stress on slowing of the blood stream, backward flowing and eddy making. In support of this assumption, he points out that the situations most predisposed to thrombosis are the veins of the legs, proximal part of the Femoral vein, where large valves are present, Pelvic plexuses, venous network in the Dura Mater, and auricles. He lays down certain conditions for the localisation of a thrombus:
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(1) **Continued increase in venous pressure** in the veins of the legs when upright; or in the pelvis from downward pressure of intestines, which cause a physiological widening of the veins, thus slowing of the blood stream with the consequent deposit of blood platelets near the valves "just as particles floating in a stream of water with a changing velocity may be sifted to the bottom."

(2) **Mechanical obstruction:** - Pāupert's ligament, bend in the Iliac veins, the crossing of the Iliac artery over the left Iliac vein. Other factors which contribute towards retardation of the blood stream have been emphasized by various investigators. These are:

(a) **Immobility of the legs after operations.** In view of the fact that the venous return from the lower extremities depends largely on muscular activity to propel the blood, after an operation, injury or childbirth, the lower limbs are immobilized due to quiet rest. Professor Gray Turner, when discussing the incidence of Pulmonary Embolism, often remarked that cases exposed to this complication are those of the "Angelie" type, i.e., those who lie quietly, trouble the nurses least and vomit little.

(b) **Increase in abdominal tension** as a result of meteorism. Friemann Dahl stresses the importance of diaphragmatic movement on the venous circulation. After operation, the venous circulation is prolonged. His investigations show that from one to twelve days after operation, the movements of the diaphragm are reduced. He investigated twenty operated and forty medical cases while in bed by Venography. In both sets he found a prolonged blood circulation. In the abdomen, the circulation through the veins depends on

(i) the muscular activity of the abdominal muscles and
(ii) respiration.

After an operation, the muscles of the abdominal wall are thrown out of action, due possibly to (1) pain and (2) tight bandaging, the latter causing intra-abdominal tension with
pressure on the abdominal veins, resulting in retardation of the venous flow, the former retarding abdominal respiration.

Respiration assists the flow of blood in two ways:-

1. Negative pressure during inspiration draws blood into the thorax.

2. As the diaphragm descends, it raises the intra-abdominal pressure, and by vis-a-tergo propels the blood from the abdomen into the thoracic veins.

After operation, respiration is generally impaired with the consequent lack of suction on the abdominal veins.

In support of this blood stasis theory, many investigators lay stress on the fact that it is seldom that a thrombosis of the veins of the upper extremities occurs.

Fowler's position, practised after operations, encourages retardation of the blood stream as a result of flexion of the thighs at the hip, and of the legs at the knees, causing compression of the Femoral vessels beneath the Inguinal ligament, and the Popliteal vessels in the Popliteal space.

Recumbency is suggested by Laplace and Nicholson as a contributory cause of death in elderly persons. In 34 cases between 60 and 83 years of age, 17 died, ten from the effects of recumbency, i.e., from forced immobility. Many surgeons have recognised the detrimental effect of recumbency on elderly patients after operations. Every attempt is made to encourage such patients to leave their beds much earlier than usual.

CARDIAC INCOMPETENCE.

Cardiac incompetence is considered to be a very important factor in thrombosis and embolism. Burke has shown that in 648 cases of thrombosis in medical and surgical cases, 444 (68.5%) were patients suffering from primary and secondary cardiac incompetence. Belt gives figures of 36 instances of venous thrombosis in 83 autopsy cases of Congestive Heart Failure, i.e., 43.4%, and 49 cases of impaired cardiac function in 56 autopsy cases of pulmonary embolism, i.e., 87.5%.
Blumgart and Weiss have shown experimentally that in cardiac insufficiency, the circulation time is prolonged, and that the velocity of venous return is reduced in 40% of cases following surgical operations. Kvale, Smith and Allen have studied in 31 patients the effect of operation on the venous circulation time. They found that there was a distinct decrease in the circulation time during the first 48 hours, and from then onwards, an increase. Sympathectomy, as well as an increase in temperature, speeds up the venous circulation. Hypertension slows it in the lower extremities. Elevation of an extremity increases the venous blood flow, but when the patient is in an upright position, the speed of the flow of the arterial blood is decreased, due to orthostatic vaso-constriction in the lower extremities. These experimental observations are of great significance as they indicate that there is a definite relationship between retardation of the blood flow and venous thrombosis.

"Cardiac competency" says Burke, "is the greatest single defence against thrombosis, and its lack is the greatest single danger. It is the condition of decompensation, and not whether its cause is degenerative or inflammatory, nor age of patient."

**Thrombosis Due to Infection.**

Infection, where it is present as a cause of thrombosis, has been, and is considered a most important etiological factor. Hunter, Cruveilhier, Virchow and Aschoff all agree that infection brings about coagulation of the blood. The distinction, however, must be made between Thrombophlebitis and Phlebothrombosis. In the former, where phlebitis is the dominating factor, infection is considered as the direct cause of the thrombosis. In the latter, however, there is still a great deal of controversy and disagreement. "Thrombosis" says Aschoff, "is a function of a number of variables." More than one factor is necessary before clotting of the blood can take place. Welch too considers that more than one factor is necessary for the occurrence and propagation of venous...
13. Thrombosis. These, according to him, are three in number:

i. Local injury to a vein, either toxic, infectious or degenerative,

ii. Some alteration in the constituents of the blood and

iii. Venous stasis.

Giertz and Craffoord, although they consider bacterial infection unlikely to be a cause of thrombosis, point out, however, that thrombotic and embolic cases have periodically aggregated in large numbers which tended to keep in certain wards. As a consequence, they treated all their thromboembolic cases from the point of view of infection, isolated them and disinfected all their bed-clothes. Hochenegg, quoted by Giertz and Craffoord, attributed thrombosis to an acute infectious catarrh of the sigmoid flexure.

Bargin and Barker report six cases of chronic ulcerative colitis with three deaths due to massive thrombosis, caused by local infection, general toxaemia, alteration in the blood and venous stasis.

In puerperal cases, Phlegmasia Alba Dolens is considered to be due to phlebitis, causing thrombosis of the deep veins of the legs.

Phlebitis in varicose veins, followed by thrombosis, is an everyday occurrence.

Phlebitis Migrans is a disease of an inflammatory nature in the wall of the vein, occurs in short segments and has a tendency to recur, and is associated with Thrombo Angiitis Obliterans. Barker selected 79 out of 101 unselected cases suffering from Idiopathic thrombophlebitis, which showed no other constitutional disease. Out of the 79 cases, 40 had recurrent attacks and 39 had single attacks. Out of the 40 cases, 12 showed acute infarction of the lung and 17 showed recurrent attacks of Pulmonary Infarction. Two died from a clinical picture of Pulmonary Embolism - both had two previous attacks of pulmonary infarction. He suggests that these pulmonary infarctions were caused by emboli from thrombosis.
of the veins of the legs.

As suggested above (Page 5), however, the possibility of an involvement of segments of the Pulmonary veins in the general process of the disease with thrombosis of the Pulmonary arteries might give rise to clinical symptoms similar to those produced by emboli. Barker suggests that the lesions in the veins occur as a result of hypersensibility of the venous tissue due to injury by toxins. Thus he found foci of infection in 31 cases out of the 40, and in 22 cases out of the 39 in tonsils, prostate, cervix and middle ear. Kletz too suggests a blood borne infection from some cryptic focus.

Cultures from thrombosed veins and thrombi by various investigators proved sterile. Barker cultured the veins with a negative result. Brown collected 87 cases of post operative phlebitis, 33% of which showed pulmonary infarction. Culture of portions of the inflamed vessels yielded no organisms.-

Govaerts considers that a relatively avirulent micro-organism might be introduced into the blood. These organisms adhere to the blood platelets and leucocytes. Normally the leucocytes phagocytose the micro-organisms, but it is possible that they may, under certain circumstances, remain and form a nidus for subsequent thrombosis. He has also shown that intravenous injection of avirulent micro-organisms produced changes of a physio-chemical nature which consists of a decrease in the electric charge, and is usually associated with a change in albumin globulin ratio of the plasma protein, in that the globulin becomes relatively increased, resulting in an increased agglutinability of the platelets and other formed elements of the blood, thus favouring thrombosis.

Vascular invasion of such avirulent micro-organisms might arise from such foci of infection in the body, and in such instances, it is impossible to obtain these micro-organisms by culture, and hence the possibility of infection might be overlooked.

Rosenow, in his bacteriological investigations into...
thrombosis and embolism, claimed that he could demonstrate by means of a "special method" diplococci in five cases of recent post-operative pulmonary embolism, and in one case of portal thrombosis. He also claims to have demonstrated the same type of organism microscopically within a thrombus, embolus or infarct in 23 out of 25 additional cases. He considers the organism to be of low virulence, which often shortens the coagulation time of the blood of animals after repeated intravenous injections. He was able to produce thrombi sometimes associated with pulmonary embolism, which resembled the thrombi in man. He further states that production of a local focus, such as in the eye, teeth or even subcutaneous injection sufficed to incite the formation of thrombi. Thus, according to Rosenow, stasis and other factors attributed to thrombosis are contributory rather than primary - the primary being a diplococcus, the number of which are relatively small and difficult to isolate. He suggests a specific inoculation with a vaccine prepared from this organism as a means of prevention.

In Thrombophlebitis, the lesion in the vessel wall is the result of bacterial invasion, the offending micro-organisms are usually virulent. Winternitz and Le Compte have carried out interesting experiments on the role played by bacterial infection in the pathogenesis of the more chronic forms of vascular disease. They injected different types of organisms of different virulence into the adventitia of the Femoral vessels, Jugular veins and Carotid artery. By varying the virulence of the organisms and duration of the experiment, lesions in both arteries and veins were obtained, ranging from acute suppurative and proliferative reactions with thrombosis, to old fibrous intimal plaques. They encountered venous lesions more frequently than arterial. This is attributed to the fact that veins have a weaker structure and are exposed more to injurious substances. In cases where mildly pathogenic organisms, such as Bacillus Pyocyaneus were injected into the
adventitia of the Carotid arteries and veins, the veins showed lesions, whereas the arteries, except once, showed no lesions. With Streptococcus Viridans, they obtained venous lesions, but no arterial. From these experiments, it would appear that arteries are more resistant to infection than veins, especially when the organism is of low virulence.

A very important observation was made by the same authors during the course of the above experiments. They noted that an occasional extension of the infection between vein and artery occurred without affecting the tissue lying between. This they attributed to a free communication between the Vasa Vasorum of the vein and artery, and demonstrated this communication by injecting dilute India ink into a vein which was tied at one end, without injecting the accompanying artery.

If this anatomical relationship exists between artery and vein, then Buerger's emphasis on the relationship between vein and artery in Thrombo Angiitis Obliterans has a definite basis. He suggested that patients showing symptoms of Phlebitis Migrans should be watched for development of Thrombo Angiitis Obliterans. He stresses the importance of inflammation in the veins as the initial process of the disease. By conducting a series of experiments on healthy persons, he proved that Thrombo Angiitis Obliterans is an infectious disease. Thus he inoculated doubly ligated veins in healthy persons, clot and scraping from an acutely inflamed vein of a case of Phlebitis Migrans of the Thrombo Angiitis variety. In four out of eight cases, he reproduced a thrombo phlebitis with foci of miliary giant cells typical of Thrombo Angiitis Obliterans. If the observation made by Winternitz and Le Compte be accepted, and Buerger's contention that Thrombo Angiitis Obliterans is an infectious disease, the primary infection being in a vein, then the spread from vein to artery through the communicating vasal vessels can be accepted as a possible mode of spread of the disease.

No micro-organism has so far been isolated to account for the inflammatory cells observed histologically. Hauswirth...
and Eisenberg, however, while agreeing with Buerger that Thrombo Angiitis Obliterans begins in the veins, suggest that the inflammatory process noted in the veins is really a terminal process, occurring after the vessels have become thrombosed and devitalised.

**NON-INFECTED THROMBOSIS.**

Phlebothrombosis or venothrombosis, on the other hand, shows no inflammatory change in the wall of the vein, the thrombus is bland and there are no clinical manifestations. The first indication is often an infarct in the lung or a massive pulmonary embolus causing sudden death. The incidence of Phlebothrombosis, irrespective of complications, has not been sufficiently investigated. The object of this investigation is to enquire into the incidence of such thrombosis in a series of consecutive unselected cases brought to Autopsy at the Hammersmith Hospital British Post Graduate School, London. The procedure adopted will be discussed later. Owing to the absence of firm fixation of this type of thrombus to the vessel wall, the danger of embolism is far greater than in Thrombophlebitis, where the thrombus is firmly fixed to the wall of the vein. Belt observed that approximately 10% of autopsies upon adult individuals show Pulmonary Embolism, and that it is more common in medical than in surgical cases. Thrombosis of the legs and pelvic veins, according to him, is the chief source of dangerous Pulmonary Emboli.

**TRAUMA.**

Trauma, whether operative or non-operative, has been considered an important predisposing cause of venous thrombosis. There is nothing more tragic in medicine than a fatal pulmonary embolism terminating the life of a patient who has been successfully operated upon, is convalescing satisfactorily and is about to be discharged, or a woman after childbirth who suddenly develops a white leg and is in hourly danger of sudden death, or a young healthy boy suffering from a fractured leg smitten down without warning. Direct injury to vessels during
operative procedure, a mild form of infection in the wound, changes in the blood resulting from absorption of toxic products, increase in the blood platelets, liberation of Thrombokinase, adiposity, age, apart from venous stasis as a result of recumbency, immobility, insufficiency of the heart already mentioned, have been attributed as factors in the causation of thrombosis.

Surgeons agree that most patients contracting post-operative Thrombo-Embolic disease have clean wounds and show no evidence of infection. Giertz and Craffoord state that out of 38 surgical cases who developed thrombosis, 31 showed clean wounds. This is the experience of most surgeons. Injury to the vessel wall during an operation, according to Lockart Mummery, is not a factor in the production of thrombosis. Often there is no relationship between the wound and the thrombosed vein. In an operation as high as the gall bladder or breast, the thrombosis is found in the vessels of the legs.

CHANGES IN THE VESSEL WALL.

Direct changes in the vessel wall is an important if not an essential factor. Abrasion of the endothelial lining due to toxic, infectious or degenerative causes initiates the thrombotic process. Such changes in the vessel wall are considered by some authors to be due to alteration or interference with the intramural vascular nutrition.

NUTRITION OF THE BLOOD VESSELS.

The walls of the arteries and veins are provided with their own blood supply - through the Vasa Vasorum. According to Maximow and Bloom, these vasal vessels originate from the small arteries adjacent to the vessel, and form a capillary network in the adventitia. These penetrate as far as the external layer of the media in arteries; in veins they are generally more abundant and may even penetrate up to the intima.

Ramsey, Geiser and their co-workers in their studies on the Pathology of Vascular Disease, consider that there are
three possible mechanisms by which the vessels obtain their nutrition:

(i). Through the Vasa Vasorum
(ii). From the lumen of the vessel by imbibition
(iii). By way of a canal system communicating directly or indirectly with the Vasa Vasorum or the lumen.

In a very extensive review on the literature of this subject, they bring evidence of two schools of thought in connection with the pathogenesis of vascular disease:

1. Those who believe that the Vasa Vasorum is the main nutritive supply to the vessels, i.e., supplying all coats. All vascular pathology is therefore secondary to disease of the Vasa Vasorum. Specifically included in the Vasa Vasorum are lymphatics as well as arterial and venous blood channels. They believe that disease of the intima is secondary to disease of the vasal vessels, and that the degenerative changes in the intima are dependent upon disturbances in the nutrition, brought about by changes in the Vasa Vasorum. Thus inflammatory reaction of the intima and inner media is due to an inflammatory condition in the Vasa Vasorum and that the proliferative changes in the intima are the result of diminished blood supply from the Vasa Vasorum or canals - this process being similar to fibrosis occurring in other organs when blood supply is inadequate. A good example of such fibrosis where nutrition is interfered with or inadequate is found in myocardial fibrosis, where the blood supply is cut down either by a gradual reduction in the lumen, due to atheromatous change in the Coronary Arteries or the Coronary ostia being narrowed by syphilitic change.

2. Those who believe that nutrition is derived from the lumen of the vessel and regard the "lumen as the source of injurious agents, deliterious mechanical influences and cellular elements." When these agents have been deposited on the intima in sufficient numbers, an impairment of nutrition occurs secondarily. This factor is the result rather than a cause of intimal pathology. Thus they quote Rindfleish as having stated that "the intima..."
is so dependent upon the lumen for its nourishment that if it be cut off from it - as for example by a thrombus - necrosis results." Most emphatic is Köster, quoted by the above authors. He says "we may assume without doubt that the intima derives its nutritious substances from the blood which flows past it and not from the Vasa Vasorum." Short has recently published his preliminary observations on the vascular supply of the Femoral vein. According to his findings, the intima receives its blood supply from a capillary Plexus lying on the medial side of the Internal Elastic Lamina, and that in the normal vein the intima contains no vasa. In Phlebosclerosis and Thrombosis, however, vasal vessels are found in the intima, these vessels being derived from the Flexus. In the case of a thrombus, these ingrowths of vasa establish communication with endothelial lined spaces which form around the original scaffolding of platelets in the thrombus. The edge of attachment of the thrombus to the vessel wall is the point of the vasal invasion. The internal elastic lamina becomes disorganised.

In their own investigations, Ramsey and her co-workers, who carried out a series of experiments (i) simple double ligation of a vessel after blood had been milked out from the ligated portion to avoid the reaction due to thrombus formation; and (ii) subsequent injection in the lumen of the ligated portion of the vessel/one of a series of injurious agents, such as (a) streptococcus Viridans; (b) Tubercle Bacilli and (c) cholesterol, the authors point out that "they cannot throw any light on the mechanism which determines where the initial reaction occurs, whether in the outer tissue of the vessel, or in the intimal surface." They make their interesting and significant observation that "the initial reaction is an accumulation of polymorphs in the adventitia and connective tissue surrounding the vessel and the progression of these cells from without inwards to the lumen." In no instance was the immediate reaction seen to occur in the intima or to involve the intima to any great extent. The cellular proliferation -
proliferation which uniformly appeared to originate in the intima was a late reaction. They could not identify the cells whether they were endothelial or from cellular elements comprising the intima.

These observations will be taken into consideration when the etiology of thrombosis and phlebosclerosis will be discussed.

INJECTION OF VARICOSE VEINS.

Direct and deliberate thrombosis in veins has been practised as a method of treatment of varicose veins. The action is essentially a sclerosing process, involving all the coats of the vein - none of the solutions used has a coagulating action on the blood itself. It is limited to chemical irritation of the intima, resulting in the destruction of the endothelium. Round cell infiltration, fibroblastic proliferations and a gradual sclerosis of the media, adventitia and sometimes the perivenous connective tissue takes place. The thrombus that forms is usually attached firmly to the wall. In spite of this attachment, fatal cases of embolism due to direct separation of a thrombus without any bacterial infection have been recorded. Silverman, in a review of literature on injection of varicose veins, collected twenty cases of Pulmonary Embolism, including one of his own which was fatal. Out of these twenty cases, fifteen were fatal and five recovered. He notes that most of these cases were confined to bed owing to one cause or another. The Pulmonary Emboli encountered in these cases can therefore be attributed to recumbency, sluggish circulation and inactivity, all of which encouraged thrombosis of a propagated type. It is interesting to note that the reason attributed for the failure to produce experimental thrombosis in animals is the fact that animals get up and move about after the operation, thus preventing a sluggish and retarded circulation.

Kilbourne records five fatal cases in 53,000 injections from Pulmonary Embolism, i.e. .009%. Compared with excision of varicose veins, he quotes Berntsen who, in a series of 376 operations, had 27 cases, i.e. 7.2% of Pulmonary Embolism. Dean and Dulin record two fatal cases from Pulmonary Embolism.
in a series of six hundred injections. Both cases were not ambulatory (one suffering from heart disease and the other from sepsis).

From this data we can conclude that the injection method is by far the safest, compared with operative procedure. If due precautions are taken to avoid rest in bed after injections, i.e. to encourage the circulation by movement, the probabilities are that very few, if any, cases of Pulmonary Embolism would occur.

**ADIPOSITY OR OBESITY.**

According to statistical data, adiposity or obesity plays an important part in Pulmonary Embolism and Thrombosis. Snell, in a study of 156 obese patients, who died after operation, found 48 cases (30.8%) who died as a result of thrombosis and embolism. Only five cases out of the 48 showed phlebitis. Gertz and Craffoord, in 239 cases of thrombo-embolic disease, found 63 or 26.3% who were definitely obese. Collins, in a collected series of 316,060 cases by fifteen different authors, found 271 instances of Pulmonary Embolism (53%), 173 of which (63.8%) were recorded as obese.

The cause for such a high incidence of Pulmonary Embolism in obese people has been attributed by Snell to (i) difficulty of operation with undue trauma (ii) circulatory retardation and (iii) liberation of large quantities of thromboplastic lipid substances.

**AGE.**

The age of the patient is important. In Belt's series of 25 cases suffering from congestive Heart failure with Pulmonary Embolism the ages vary from 18 to 77 years, with an average of 53 years. In 16 cachectic and debilitated people with thrombosis and embolism, the ages varied from 24 to 90 years with an average of 58 years. In a group of fifteen convalescent cases with sudden death from massive pulmonary embolism, the ages varied from 39 to 76 years with an average of 59 years. In McCarthy's 73 cases of Pulmonary Embolism, the ages varied from
Torres gives 25 cases of phlebitis complicating gynaecological operations, fifteen of these (60%) were over forty years. Out of seven cases of fatal Pulmonary Embolism, five were above forty years, one 38 years and one younger.

Stitch found that 83% of all emboli were in patients over forty years, 66% of all emboli were in patients over fifty years and 20% of all emboli were in patients over seventy years.

In Collins' series, 65.7% were over forty years and 42.8% were over fifty years. Snell gives 55 years as the average age in 156 patients. In 113 cases of thrombosis and embolism (76 post operative and 37 medical), Miller and Rogers found the average age to be 49.7 years. (The low average age of this series is due to the fact that one case was a child of one year and ten months, suffering from Sarcoma of the kidney).

Henderson collected 313 cases of Pulmonary Embolism, the average age of which he found to be 53.2 years. Sproul gives the highest incidence in the sixth decade.

From these statistical data it appears that the incidence of thrombosis increases with advancing age. Most cases are found between forty and sixty years, rarely before forty and few past seventy years. The low incidence after seventy years is attributed to the fact that few people live beyond that age and also because few undergo operations at about that age. The predisposition to thrombosis in elderly people is chiefly attributed to the bad condition of the heart, thus encouraging circulatory retardation, dehydration of the tissues, increase in blood pressure, etc.,

SEX does not appear to have a direct influence on the incidence of thrombosis. From statistical data, from the point of view of operative cases, there appears to be a greater number of females liable to thrombosis and embolism. Thus Collins gives the number as 61.5% females. A great deal seems to depend upon the type of operation performed, and as females are more liable to pelvic trauma, viz. gynaecological operations and childbirth, the incidence among females would be expected...
to be higher. The likelihood of thrombosis developing after abdominal operations appears however to be the same for both sexes.

**ANAESTHESIA** does not appear to play any role in the development of thrombosis. Hernia operations, which are mostly performed under local anaesthesia, claim a good percentage of thrombo-embolic disease. Miller and Rogers carried out investigations on 65 cats, using Ether anaesthesia in some and keeping the animals under for as long a period as three hours, but failed, except in one case, to produce thrombosis by "ordinary bruising, clamping, perivascular infection, injection of muscle extract and muscle tissue." The majority of postoperative lung complications, excluding bronchitis, according to Lockhart Mummery, were really the result of infarction of the lung and many cases that used to be called "Ether Pneumonia" were really due to small emboli.

**DEHYDRATION** is recognised as a cause of thrombosis. Sweating after operations, anaemia due to haemorrhage, e.g. from bleeding uterine polypi, vomiting, diarrhoea etc., all predispose to thrombosis. The factor responsible for thrombosis is attributed to an increased viscosity of the blood.

**DEBILITY.**

Debilitating and wasting diseases predispose to thrombosis. Cancer, tuberculosis and general toxaemia are the chief among such diseases. Cancer, as will be seen from my investigations, is one of the chief causes predisposing to thrombosis.

Trousseau, as quoted by A.P. Thompson, emphasized the relationship between cancer and thrombosis, and stressed the fact that the first sign of cancer of the stomach is frequently a peripheral phlebitis. The following is a translation of Trousseau's remarks. "When you are undecided about the nature of a disease of the stomach, when you hesitate between a chronic gastritis and simple ulcer and a carcinoma, a phlegmasia Alba Dolens occurring in the leg or in the arm will put an end to your indecision and you will be able to assert positively that a cancer is present." In Burke’s series, there were...
25.

187 cases of cancer out of 648 cases of thrombosis (28.8%). He suggests that cancer may exert a thrombotic influence in several different ways:

1. Indirectly through its general or constitutional effect on the patient such as altered resistance and metabolism, debility, secondary anaemia, infection, etc.

2. Through its interference with adequate liver production of Heparin.

Heparin, according to Howell, is present in small traces in the blood, comparable to hirudin secreted by leeches and other blood sucking animals. This substance is an anticoagulant and termed by him "Antiprothrombin." It is combined with prothrombin in the circulating blood and acts as a protective or inhibiting agent against the conversion of prothrombin into thrombin. The conversion to thrombin only takes place after thromboplastin has been made available for neutralisation of heparin, thus liberating prothrombin which can then react with calcium to form thrombin.

In the opinion of Quick, however, there is not sufficient evidence that prothrombin is bound or has to be freed before it can then become active. He suggests and produces evidence, that the action of Heparin and thromboplastin are entirely independent of each other, the former by reacting with a constituent present in the plasma, giving rise to a true antithrombin, the latter reacting with prothrombin producing thrombin. The thromboplastin, according to him, antagonises the anticoagulant action of Heparin by accelerating the conversion to thrombin of prothrombin and that the thrombin is the true antagonist of the inhibitory substance heparin produces in the blood.

Heparin has been extracted from the liver and certain other tissues, and in the case of damage to the liver, it is suggested that there is an interference with the production of this anticoagulant substance and hence the predisposition of the blood in the case of carcinoma to thrombosis.

3. Directly by its encroachment of vessels, i.e. by pressure,

- INVASION -
invasion of the wall, dissemination and dispersal of cancer cells by the blood stream.

**VASO CONSTRICTION.**

Inflammatory reaction in the wall of the vein has been discussed under infection and it has been pointed out how a perivenous infection spreads by means of the vasal vessels to the wall of the vein. There is therefore a relationship between perivascular inflammation and thrombosis. This relationship is not often discernible, but when present, is a case of thrombosis.

The signs and symptoms relative to thrombophlebitis giving rise to clinical manifestations are fever of a hectic type, pain which is quite prominent, being limited to the involved veins, oedema, change in colour and alteration in the peripheral temperature. Those in which the superficial veins are involved there is redness, due to an increase in vascularity in the region of the inflamed vein, such as seen in thrombophlebitis of the saphenous veins and pallor or cyanosis when the deeper veins such as the Femoral or Posterior Tibial veins are involved. Phleghmasia Alba Dolens is an example of the latter type. The peripheral temperature of the leg in involvement of the superficial veins is increased particularly in the area involved whereas the temperature in the case where the deeper veins are involved is decreased.

There is a good deal of controversy and speculation concerning the reason for the pain, oedema and change in temperature. Mechanical blockage produced by an intravascular clot as well as obliteration of lymphatic channels by an inflammatory perivenous lesion was considered as a cause for such clinical manifestations. Lately, however, the conception has been changed in favour of a disturbed physiology, viz. on the basis of Vaso Constriction.

Leriche in France was the first one to suggest that the mechanism of development of clinical manifestations of thrombophlebitis is the initiation of a vaso-motor reflex as a result
Fig. 1.—Diagrammatic representation of the mechanism of development of the clinical manifestations of thrombophlebitis. Impulses (depicted by arrow) originating in the thrombosed venous segment set up a vasomotor reflex resulting in generalized vasospasm of the involved extremity.

Fig. 2.—Diagrammatic representation of the mechanism of relief of the clinical manifestations after procaine hydrochloride block in cases of thrombophlebitis. Block of the sympathetic ganglia with procaine hydrochloride interrupts the vasoconstrictor impulses and results in breaking of the vasomotor reflex.
of impulses originating in the thrombosed venous segment. The process was \textit{veno-spasmod coagulation and arterial spasm}. He came to that conclusion as a result of relief from pain and oedema by resection of chronically adherent, chronically thickened occluded iliac veins. Later, he and Kunlin treated cases of post operative phlebitis by means of Proca in hydrochloride block of the lumbar sympathetic ganglion (Diagrams I and II - Ochsner and De Bakey - Arch. Surgery February, 1940).

\textbf{Diagram I} illustrates the vaso spastic impulses originating in the thrombosed segment of a vein and the vaso motor reflex resulting in generalised vaso-spasm involving arterioles and venules.

\textbf{Diagram II} illustrates break in the reflex in the sympathetic ganglion by injection of Proca in hydrochloride.

Investigations by many authorities have been carried out to substantiate this important conclusion, particularly in connection with the development of oedema of the limb or limbs involved. Zimmerman and De Takats are of opinion that the oedema is due to venous obstruction caused by a clot, i.e. a mechanical obstruction. Homans believes that two factors are concerned in the production of oedema (i) venous stasis and (ii) lymphatic involvement in the inflammatory exudate engulfing large trunks which course about the great blood vessels. Any infection carried by the lymphatic stream from the legs, the genitals or anal region must pass the lymphatic vessels and glands about the Iliac blood vessels. Ligation of the Femoral vein does not cause swelling, but if adjacent lymphatics in the region of Pauparts Ligament are obstructed, cold swollen legs result.

Payne considers that arterial, venous and lymphatic elements are essential for the preservation of normal circulation. Venous obstruction, according to him, may be followed by temporary swelling and oedema of the limbs, but the oedema does not persist. Reichter has shown that when tissues are divided around vessels, oedema appears below the point of section. This oedema begins to subside on the fourth day after the operation,
Fig. 1.—Diagram of normal physiological relationship of intravascular and perivascular fluids. As indicated by the arrows, normally there exists a balance between the amount of fluids leaving the blood vessels and entering the tissues and that leaving the tissues and entering the blood and lymphatic vessels.
that is, when the lymphatics begin to regenerate and cross the field of operation. On the seventh and eighth day, the oedema has completely subsided. If veins are ligated after the fourth day of operation, no swelling occurs. He further points out that oedema may follow cellulitis of the subcutaneous tissue, Inguinal adenitis and pyogenic tuberculosis or other chronic type of infection or elephantiasis of the Filarial type. Because of these experimental results, he concludes that perivascular lymphangitis is a primary condition followed by phlebitis and secondary thrombosis of vessels.

Ochsner and De Bakey have made extensive experimental investigations. They have come to the conclusion that the oedema can be explained on the basis of Vaso Constriction resulting from impulses originating in the involved venous segment, originally propounded by Leriche. They believe that vaso-spastic influences affect both arterioles and veins. By producing a chemical endophlebitis, they obtained a marked arteriolar vaso-spasm of such a severe degree that pulsations were lost. De Takats considers that acute vaso-spasm accompanying thrombo-phlebitis or lymphangitis may be mistaken for peripheral embolism. He cites two cases which were diagnosed as peripheral embolism and which turned out to be venous thrombosis. Montgomery and Ireland actually explored two cases which were considered to be peripheral embolisms. At operation all that was found was an acute spastic condition of the arteries.

Due to vaso-spasm affecting arterioles and venules, the relationship between intravascular and perivascular fluid is upset.

Normally the interchange of fluids between vessels and tissue is balanced (Diagram III). The passage of fluid from the vessels to the tissues depends upon the difference in filtration pressure between the intravascular and perivascular spaces. It is greater in the former. The passage of fluid from the perivascular to the intravascular spaces
depends upon (i) the osmotic pressure which is greater in the latter and (ii) the lymph flow. If there is an increase in the venous pressure, the filtrations pressure is increased and we get an increase in flow from the vascular to the perivascular spaces.

As already mentioned, vaso constrictor impulses originating in a thrombosed segment affects the venous as well as the arterial side of the vascular tree. Venous spasm together with the mechanical blockage by a thrombus of the involved segment gives rise to a marked increase in the venous pressure, thus augmenting the filtration pressure which increases transudation of fluid into the perivascular spaces. Ochsner and De Bakey have found an increase in the venous pressure from four to five times that of normal in eight cases of thrombophlebitis with oedema.

The other factor which influences oedema is the flow of lymph. Homans and Reichter have pointed out the importance of lymphangitis in the formation of oedema. The persistence of oedema following the subsidence of inflammation has been attributed to obliteration of the lymph channels together with blocking of veins, both of which mechanically interfere with the venous and lymphatic drainage. This oedema, if allowed to persist, encourages perivascular fibrosis which also contributes towards its maintenance with the result of a chronic oedematous state of the legs.

Arteriolar pulsation influences oedema. Parsons and McMaster have investigated this problem. They pointed out that in cardiac patients lying in the horizontal position, the lymph flow from the legs is poor. They attribute this to the poor pulsation as well as to the poor flow of blood, which according to them influences the movement of fluid into the lymphatics and along them.

Vaso spasm of the arterioles following impulses originating in a thrombosed segment of a vein obliterates the pulse and thus contributes to the retention of fluid in the perivascular spaces. Stagnation of tissue fluids also brings about
Fig. 2.—Diagram of production of edema in thrombophlebitis. As shown by the arrows, there is a greater amount of fluids leaving the blood vessels and entering the tissues than that leaving the tissues and entering the blood and lymphatic vessels. The increased transudation of fluids from the vascular system into the perivascular spaces is due to several factors. As a result of vasoconstrictor impulses initiated in the thrombosed venous segment there is produced a reflex vasoconstriction involving both the arterial and the venous elements of the vascular tree. Thus there occurs marked increase in venous pressure with consequent augmentation of filtration pressure and relative anoxia of capillary endothelium, both of which favor an increased transudation of vascular fluid into the perivascular tissue. The marked diminution of peripheral pulsations consequent to vasospasm and increased venous pressure results in a decrease in lymph flow and a stagnation of tissue fluids.

Fig. 3.—Diagram of mechanism by which procaine hydrochloride block produces improvement in thrombophlebitic edema. Interruption of the vasoconstrictor impulses results in a decrease in venous pressure, increased vascularity and increased peripheral pulsations. The diminished venous pressure results in a decreased filtration pressure and thus tends to prevent the increased transudation of vascular fluid into the perivascular spaces. Increased vascularity reestablishes normal oxygenation of the vascular endothelium and permits return of normal permeability, which prohibits excessive transudation. Increased pulsations favor removal of perivascular fluids by increasing lymph flow.
an accumulation of proteins in the retained fluid with the result that the osmotic pressure in the perivascular fluid practically approaches the osmotic pressure within the vessels. This tends to prevent the reabsorption of fluid from the tissues.

Owing to the vascular spasm and diminished vascularity another factor contributes towards oedema, namely, Anoxia of the Capillary Endothelium. This tends to favour an increased permeability of the endothelium and consequently increases the transudation of vascular fluid into the perivascular spaces. (Diagram IV).

From the above observations it is obvious that a vicious circle is set up, which if attended to at an early stage in the disease, could be broken and the sequelae avoided. This vicious circle can be broken by:-

1. Natural means and
2. Artificial means.

In the case of (1), it occurs by the natural subsidence of the perivascular inflammation with the resultant cessation of afferent impulses from the inflamed segment and the early restoration of blood and lymph flow.

In the case of (2), it occurs by artificially breaking the circle at an early stage by means of blocking the path either by sympathectomy or by blocking the sympathetic ganglion with Procain Hydrochloride. (Diagram V).

The latter method is now adopted. Cases have already been reported where this method of treatment was carried out. Thus Ochsner and De Bakey have reported seventeen cases of thrombophlebitis which have been treated by Procain Hydrochloride sympathetic block. The results they obtained were "quite dramatic". There was immediate relief of pain within fifteen to twenty minutes in six cases. Eight of the remaining eleven required a second injection and three a third. All obtained complete and permanent relief. The temperature subsided rapidly and the stay in the hospital was reduced considerably. Oedema subsided completely in eight days in more than half of the cases.
and the remaining ones within twelve days.

The results obtained are extremely encouraging and the future suffering from the immediate and after effects of thrombo-phlebitis should thus be eliminated.

Applying the same principle of vaso-spasm in the case of Thrombo Angiitis Obliterans, a sympathetic block was introduced in a patient under my care in the Johannesburg Non European Hospital, the favourable result of which will be discussed later.
A thrombus can be defined as a clot formed from the elements in the circulating blood during life. All elements, platelets, fibrin, leucocytes and red cells may enter into its formation. There are quite a number of different conditions which may bring about thrombosis in the blood stream. Aschoff considers these conditions under the following headings:

a. Changes in the blood plasma (diminished or increased coagulability).
b. Changes in the blood elements (increased or diminished power of agglutination).
c. Changes in the blood flow (slowing and formation of eddies).
d. Changes in the vessel wall (endothelial damage).

Not all conditions are required to produce thrombosis. Sometimes one factor, sometimes another factor plays the principal role.

Under changes in the blood plasma, the following conditions can be considered:

1. Increased viscosity found in dehydration and Polycythemia Vera.
2. Increase in fibrinogen and relative globulin rise and increase in lactic acid as a result of anoxia and slow metabolic rate.

The changes in the blood elements consist chiefly of an increased platelet count, increased leucocyte count and an increased agglutination tendency.

Changes in the blood flow, as has already been mentioned, consists principally in slowing, backward flowing and eddy formation. It must be emphasized that it is not stagnation but retardation which brings about thrombosis. Thackrah, as far back as 1819, ligated the Jugular vein of a living dog and after three hours, found that the blood had not clotted in the ligated segment. McLean crushed a vessel and applied simultaneously micro-organisms to the place of injury; thrombosis occurred only in those in which there was oscillation of the blood flow. Numerous investigators have since corroborated
the correctness of this observation. Welch – quoted by Miller
and Rogers – said "that a stationary column of blood included
in an artery or vein between two carefully applied aseptic
ligatures within the living body may remain fluid for weeks."

Changes in the vascular endothelium play an important part
if not a prominent role in the development of phlebothrombosis
and thrombophlebitis. In the latter, the changes are definitely
organic, being associated with inflammation and even actual
destruction of the intima. In the former, it is more functional
in nature in so far that no actual lesion or breach in the
endothelium can be established, although it is considered by
some authorities to be present somewhere, the actual abrasion
being difficult to locate. Thus Cohnheim points out that injury
to the lining of a blood vessel favours, if not essential to,
thrombosis. Damage to the endothelial lining of a vein may be
toxic, cachexic or degenerative. These would predispose to
thrombosis.

The importance of the endothelial cells of the intima is
stressed by Ritter, as quoted by Chsner and De Bakey. He main-
tains that the endothelial cells serve not only as a lining to
the vessel but have an active function, viz.,

(i). Nutrition
(ii). Secretion
(iii). Absorption and
(iv). Phagocytosis.

If the cells are damaged by toxins, proteins etc., absorp-
tion of protein metabolites, bacteria, toxins, pigment and metal
is facilitated and augmented. These latter substances predispose
to thrombosis. In the opinion of Chsner and De Bakey, endo-
thelial changes can also occur as a result of stimulation of the
sympathetic nervous system during operative procedure apart
from arteriolar vaso constriction.
THE MORPHOLOGICAL STRUCTURE OF A THROMBUS.

Given the predisposing causes, the blood clots within a vessel and a thrombus is formed. It begins by a deposition and agglutination of platelets on the wall of the blood vessel. The number of these platelets grow as they pass by in the coursing stream. They produce elevated ridges or laminae which run transversely across the blood stream, i.e. transverse to the long axis of the vessel and anastomose freely with one another. They form the framework or skeleton of the thrombus. On the surface, these lamellae of platelets are greyish white, project slightly and are known as the "Lines of Zahn." As the platelets get piled up, the lumen of the vessel gradually gets narrower and the blood flow gets slower and the platelets become covered by a layer of leucocytes. This is explained by Eberth and Schimmelbuch as being due to the fact that when the blood stream slows, white corpuscles, being lighter in specific gravity, tend to travel to the margin of the blood stream, and so are found closely in contact with the vessel wall. At the same time, thromboplastin is liberated by the platelets and the injured endothelial wall, and fibrin is deposited. In this process, red blood corpuscles become entangled and we get a solid mass of blood clot. As soon as the lumen is closed by this type of platelet clot, there is left a stagnant column of blood to the next anastomosing vessel which undergoes complete coagulation in which there are hardly any platelets. This is red thrombus, resembling a post mortem clot and consists of red and white corpuscles, platelets and fibrin. The first part of the thrombus, which is white and consists mainly of platelets, is known as the head; the second part which is mixed - white and red - is known as the neck, and the third part - the propagated part - is known as the tail and may form the bulk of the thrombus - or, as the Germans call it, Kopfteil, Halsteil and Schwantzteil.

The white thrombus, because of the destruction of the...
endothelium of the vessel wall becomes firmly attached to the wall and has little tendency to become detached. The red thrombus, however, is only loosely attached to the vessel and is liable to detach itself and give rise to a massive pulmonary embolism. It is this type of thrombus that occurs in phlebothrombosis and hence the frequency of pulmonary embolism. If a thrombus becomes infected particularly with haemolytic streptococci, it undergoes liquefaction as a result of liberation of tryptic ferments following the destruction of polymorphonuclear leucocytes, emboli become detached and produce distant metastasis.

THE MECHANISM OF THROMBOSIS.

Circulating blood contains three essential factors for coagulation:--

1. Fibrinogen
2. Prothrombin
3. Calcium salts.

Under normal circumstances, blood is prevented from coagulation by an inhibitory substance known as Heparin. The antagonist to this anticoagulant - thromboplastin - is not free in the blood but is widely distributed in the body and is present in high concentration in the brain, lungs and thymus. It is liberated whenever tissue cells are ruptured or injured. In normal clotting, the important source is the disintegrating platelets. The views with regard to Heparin or the inhibitory substance it produces in the plasma as expressed by Howell and Quick have already been referred to on Page 25. Whatever view is accepted, the mechanism of coagulation of blood, apart from its relation to Heparin, may be expressed as follows:--

i. Prothrombin + Thromboplastin + Calcium = Thrombin.

ii. Fibrinogen + Thrombin = Fibrin.

Prothrombin is only present in the blood plasma, and according to Quick, human blood contains a large excess of this factor and 80% can be lost before a haemorrhagic condition can become manifest.

- QUICK -
Quick has evolved a method whereby the amount of prothrombin present in the blood can be estimated. He found that there is a direct ratio between the speed of clotting and the quantity of thrombin present in the blood - the amount of thrombin formed is dependent upon the concentration of prothrombin present in the blood. In view of the constant relationship of prothrombin to thrombin in the presence of thromboplastin and calcium, he concluded that "the coagulation time of blood or plasma can be employed as a measure of the prothrombin concentration, if the other factors in the clotting process is made constant." On this basis, he evolved the quantitative test for prothrombin.

Smith, Warner and Brinkhause have shown that the liver is vitally concerned with the manufacture of prothrombin. In disease of the liver such as Acute Yellow Atrophy, haemorrhage is a constant finding and this has been attributed to depletion of fibrinogen. This depletion of fibrinogen, however, is disputed by Quick, Stanley Brown and Bankroft, who point out that the "haemorrhagic diathesis in the presence of jaundice is not the result of any alteration in the amount present in calcium, fibrinogen, platelets, bilirubin or thromboplastin, but depends on the lack of prothrombin". In experimental liver damage by chloroform anaesthesia, Smith, Warner and Brinkhause found that prothrombin was affected even more than the fibrinogen, and later, together with Quick, verified this observation on starved dogs and light chloroform anaesthesia, when it was found that the prothrombin rapidly decreased and reached its lowest level in 48 hours after which it returned gradually to normal.

Recently a food accessory substance, Vitamin K, which is fat soluble, was discovered by Dam in Copenhagen (quoted by Quick). It is considered an essential substance for the proper clotting of blood. Chicks, given a diet lacking in this Vitamin developed severe deficiency of prothrombin and severe haemorrhage. Hawkins and Brinkhause observed that if a dog is deprived of bile by means of a bile fistula, a haemorrhagic disease developed, and that it was cured by feeding the dog with bile. This, according to Smith, Warner, Brinkhause and Seegers, is due to
the fact that Vitamin K requires the presence of bile salts in the intestine for its absorption, and in the absence of bile salts, a haemorrhagic condition develops as a result of severe depletion of prothrombin. Vitamin K therefore is essential for the synthesis of prothrombin.

As mentioned above, the liver plays an important role in the synthesis of prothrombin and it is believed that the organ is essential for the conversion of Vitamin K into the prothrombin component. Damage to the liver, or biliary fistulae with loss of bile externally, or obstruction to the biliary ducts prevents bile from entering the intestine and causes a prothrombinopenia in patients. When such a decrease in prothrombin is solely due to inadequate absorption of Vitamin K, a rapid response is obtained by giving a concentrate of Vitamin K and bile salts.

There are four factors required for the absorption of Vitamin K:-

(i). Proper diet;
(ii). Bile salts;
(iii). Healthy bowel;
(iv). Normal liver.

Butt, Snell and Osterberg have shown that intestinal disorders, such as chronic ulcerative colitis, non tropical sprue, post operative gastric retention and gastro-colic fistulae, interfere with the normal absorption of Vitamin K, which bring about a fall in the prothrombin concentration of the blood. Treatment with Vitamin K and bile salts is of benefit.

A damaged liver is of practical importance to the surgeon in so far that he is often called upon to operate on patients suffering from Jaundice. The choice of an anaesthetic, the danger of severe or fatal haemorrhage have to be taken into consideration. Two tests have been made available by Quick:-

1. The Prothrombin concentration of the blood
2. Hippuric Acid test for determining the liver function.
The prothrombin test will be discussed later.

The Hippuric acid test is based on the principle that when Benzoic Acid is administered, it combines with Glycin, producing Hippuric Acid, which is excreted in the urine. The formula is:

\[ \text{Benzoic Acid} + \text{Glycin} = \text{Hippuric Acid}. \]

This reaction takes place in the liver, and in damage of the liver, the excretion of Hippuric Acid is reduced. This gives a measure to the extent of which the liver is damaged. Clinically, it is often found that in cases of biliary obstruction and liver damage, the administration of Vitamin K plus bile salts is ineffective in raising the prothrombin level of the blood, this being due to liver damage, and Quick suggests that in addition to Vitamin K administration, the liver function should be improved by means of glucose, calcium salts and gelatine.

Recently, the haemorrhagic diathesis noted in the new born has been attributed to a deficiency in Vitamin K. All the available prothrombin is quickly used up after the infant's birth and is not replaced until it receives Vitamin K. Quick suggests that normally the entrance of bacteria into the alimentary tract is an important factor in supplying Vitamin K in the first few days of life, thus restoring the prothrombin level. It is now practically certain that the haemorrhagic disease of the new born is caused by the delay in the restoration of the prothrombin level. To restore the prothrombin level in such cases, a transfusion of fresh blood from the mother used to be practised. This procedure provided the required prothrombin and tided over the infant during a dangerous period. Now, however, Vitamin K is administered. This acts as a specific cure. Niggard reports three cases suffering from haemorrhagic disease treated with Vitamin K, and found the therapeutic effect equal to that of blood transfusion.

The temporary relief obtained in haemorrhagic disease in adults when treated by transfusion is attributed to the fact that plasma contains an excess of prothrombin, and that only
a small fraction is required to give a normal clot.

Zeigler, Osterberg and Hovig have shown lately that stored blood decreases in the prothrombin potency over a period of time to a level of 40% of the original content, and consequently, old banked blood is not a suitable agent for the purpose of raising the prothrombin level in patients that require it. This is corroborated by Quick, who states that stored blood is inferior to fresh blood for controlling bleeding in Jaundice.

These observations are of practical importance in so far that the question of using stored blood will become a major problem in the present war.

Andrus and Lord have successfully treated cases of pro-thrombin deficiency with a Naphthoquinone compound. They found this to be an effective means of restoring the plasma prothrombin level in the absence of severe liver damage. They noted that there were no toxic effects and that a single injection restored the prothrombin level of the plasma by as much as 48%, the effect of which was evident as early as eight hours after injection and lasted for as long as a week.

**THROMBOPLASTIN.**

As mentioned above, this substance is found in high concentration in the brain, lungs and thymus. It is liberated when tissue cells are ruptured or injured, and by disintegrating platelets. Quick attributes the following properties to it.

1. It has a fixed degree of affectivity. The clotting time by the prothrombin test reaches a minimum which cannot be shortened by the addition of more thromboplastin. The minimum clotting time is the same whether the extract is from the lung, thymus or brain.

2. It activates prothrombin and fails to clot purified fibrinogen or plasma from which the prothrombin has been removed by Aluminium Hydroxide cream.

3. Its activity decreases with increasing temperature, but it does not completely inactivate it.
As it has already been mentioned, thromboplastin accelerates the conversion of prothrombin to thrombin in the presence of calcium salt (Quick) or neutralises or inactivates Heparin which is combined with prothrombin, liberates prothrombin, which then is activated by calcium to form thrombin (Howell). The question of the conversion of prothrombin to thrombin by thromoplastin is, however, still not solved.

**BLOOD PLATELETS OR THROMBOCYTES.**

The participation of blood platelets in the early stages of thrombosis has already been mentioned. From a historical point of view, it is interesting to recall that it was Bizzozero in 1882 who was the first to name these cells "blood platelets" or "thrombocytes", and who emphasized their importance in blood coagulation by their disintegration and liberation of a coagulative ferment. Later, Eberth and Schimmelbuch studied the blood platelets in the small Mesenteric vessels of the dog and confirmed the observation of Bizzozero. They found that when the rapidity of the stream diminished, there were a large number of leucocytes along the peripheral zone of the capillaries and venules. The Axial column consisted of red cells and platelets. As the stream slackened further, large numbers of blood platelets gradually appeared at the peripheral zone and began to agglutinate. They also noticed that a slight trauma of the lumen of the vessel under observation was followed by adhesion of the platelets to the site of injury and thus formed a thrombus. The participation of the blood platelets in the early stages of thrombosis is therefore of primary importance. By an alteration in the physical relationship between them and the vessel wall whereby the blood platelets become adherent to the vessel wall, and the liberation of thromboplastin by their disintegration, clotting is set in motion.

Could post operative thrombosis be attributed to an increase in the blood platelets count as well as a liberation of an
excess amount of thromboplastin from the injured tissue in the operated area? Dawbarn, Earlam and Evans investigated the platelet rise in post operative cases. They have found that there is a general tendency for the platelets to increase after a surgical operation and parturition. They noted that the rise begins about the sixth day and reaches the maximum about the tenth day and gradually reaches the normal in about three weeks. This corresponds to the clinically observed post operative thrombosis and embolism. They have also noted that the severer the operation, the greater the rise. With this rise in count, they have found that the coagulation time was slightly shortened. The reason for such a rise they find difficult to assess, but suggest that it is a natural phenomenon "a physiological response on the part of the bone marrow comparable to early leucocytosis," and attributed this response to "absorption of tissue products resulting from trauma during the operation."

The Spleen is considered to be an important organ for the destruction of platelets. An investigation was carried out by Evans, on eleven splenectomised cases. He found:

1. The platelets showed a considerable rise in ten;
2. The clotting time showed a rough parallelism to the platelet level;
3. The clot retraction seemed more proportional to the platelet count.

The part played by platelets, once a thrombus is formed, has been studied by Tocantins. He found important differences between platelet rich and platelet poor thrombi. In platelet rich clots, according to him, the fibrin is bound together by large firm knots, while in the platelet poor clots, the fibrin is in the form of separate needles loosely placed one over the other. These knots are clumps of intact platelets in the interior of the clot, which converge towards the fibrin needles as soon as they are laid down, adhere to them, and by so doing, "the needles become twisted, bent, shortened and more closely knit." This is due to a mechanical action of the platelets...
together with the natural contractility of the fibrin. In this way, the clot is strengthened, becomes more rigid, firm and elastic and undergoes the visible reduction in volume known as Syneresis.

This observation is of importance in so far that it gives us an understanding of the danger of the red or propagated thrombus which is normal or rich in platelets. The action of the platelets in the interior of the clot causing a Syneresis, prevents or delays the adhesion of the clot to the vessel wall. We have thus a free oscillating soft thrombus - compared with the white, more firm and adherent clot (which is chiefly composed of platelets with little fibrin) - which floats in a moving stream, and is liable to be detached and carried away on the slightest muscular movement or exertion. A sudden reduction in pressure within the vein itself, as for instance by lifting a leg suddenly and thus emptying the vein of blood, may, by suction, pull such an unattached, retracted, soft, elastic thrombus away from the adherent portion, and cause a massive pulmonary embolism.

These are the views expressed by various authors found in literature on the subject of the origin, incidence and causation of Thrombosis and Pulmonary Embolism. Now we shall proceed with the investigation carried out and see how far the conclusions arrived at agree with those found in literature.

The subject has been divided into:-
I. Thrombosis.
   a. Thrombophlebitis
   b. Phlebo- or Venosclerosis
   c. Arterial disease in relation to Thrombosis.
II. Pulmonary Embolism.
III. Fate of a Thrombus.
IV. Short Note on Treatment.
V. Discussion.
VI. Summary.
Thrombosis is of particular significance in so far that it can give rise to grave danger, both as regards life and subsequent morbidity. The danger to life is through fatal massive pulmonary embolism and subsequent morbidity through chronic oedema of the legs with impairment of the circulation in the lower extremities and chronic embolisation with its effect upon the lungs and heart. Such chronicity is a constant source of ill health. It is only in cases where Pulmonary Embolism has drawn the attention of the Physician, Surgeon or Pathologist to a thrombosis somewhere in the body that investigations have been instituted to ascertain the source of the embolus and an attempt made to establish the etiology for the thrombosis. Statistical data in the majority of investigations has been based on:

(i). The presence of Pulmonary Emboli, either massive, causing sudden death, or recurrent, giving rise to distressing symptoms.

(ii). An outspoken thrombo-phlebitis, i.e. an obvious inflammatory condition of the veins with thrombosis, giving rise to typical clinical symptoms such as oedema, pain, a general rise in temperature, a rise in surface temperature of a limb, etc. Few authoritative and comprehensive investigations have been carried out to establish the incidence of thrombosis accompanying or following disease in general. Investigations have been directed chiefly to post operative thrombosis and those following childbirth and other conditions such as trauma. What part thrombosis plays in general and what part Pulmonary Embolism contributes towards immediate cause of death in patients suffering from acute or chronic disease has not been FULLY.
fully investigated. Similarly, their contribution towards the ultimate cause of death in patients who have recovered from a serious illness or operation and have had an undetected thrombosis with minor Pulmonary Embolisation to which they did not succumb, has likewise not had sufficient attention. Further when the existence of a thrombosis is definitely suspected, the investigations carried out are often incomplete for some reason or another, and thus the true origin of the thrombosed segment of vein is not established.

Thrombi have been located in various veins in the body to account for embolism. The veins mentioned by various authorities are Prostatic, Pampiniform Plexus, superficial leg veins, long and short Saphenous, Femoral, Ovarian, common and external Iliacs, Superior Vena Cava, Renal and several others. The impression that one gets from literature is that when an embolus in the lung is located post mortem, the Pelvic veins are inspected, and in some cases, the Femoral veins displayed, and if a thrombus is found in these areas, no further investigation is made. Leg veins are sometimes examined, but not in the majority of cases. No clear idea, therefore, is obtained where and why a thrombus originated.

The object of this investigation has been to ascertain and establish the incidence and origin of thrombosis, the veins involved, whether emboli are present or not, whether recent or old thrombosis, and the possible cause of such thrombosis, in all cases coming to autopsy, irrespective of suspected or unsuspected thrombosis.

**MATERIAL USED.**

One hundred consecutive unselected cases that came to autopsy were examined. A full post mortem examination was carried out in each case, the pathological conditions of the various organs noted and the cause of death established. The Posterior Tibial Veins with their muscular tributaries were dissected from the Popliteal fossa to the Malleolar region - FIG. -
In a good number, the Femoral vessels, Inferior Vena Cava and often the Plantar vessels were dissected as well. In each case, both lower extremities were investigated. In addition, in a second series of 75 cases following on the first 100, the leg veins were examined in those cases which showed Pulmonary Emboli post mortem. This was done to substantiate the findings of the previous series.

In considering whether the findings and conclusions in these cases are general or merely local, it should be pointed out that the Hammersmith Hospital (British Post Graduate School where these investigations were carried out) caters for all diseases of all ages, but of great importance is the fact that to it is attached a chronic sick home which admits neoplastic, cardiac and chronic cases. A good number that came to autopsy were from this institution. Also, mention should be made that these investigations were carried out during the months of November to April, i.e. during the height of winter.

The Posterior Tibial Vessels having been exposed, were carefully examined macroscopically for the following:

i. Were they empty or full?

ii. Were they varicose, tortuous, soft or hard?

iii. Was the content liquid blood, semiliquid, soft, firm or brittle?

iv. If clotted, whether post mortem or ante mortem. Whether free, mildly or firmly adherent to the wall of the vessel.

v. Whether the thrombus was red, mixed or white.

vi. How far the thrombosis ascended or descended the limb.

vii. Whether muscular tributaries were thrombosed.

viii. If an embolus in the lung was found, the possible site of detachment was sought for and established, by comparing the colour, firmness and brittleness of the embolus with the remaining portion of the thrombus in the vein.

ix. A general inspection of the other veins in the body;
particular note being taken of the Femoral, Pelvic and Prostatic veins.

x. The state of the arteries.

xi. The limbs were inspected for oedema, atrophy of the muscles and any other abnormality.

Having removed the vessels - the Posterior Tibial with their branches and tributaries and occasionally the Plantar and Femoral with surrounding tissues - the whole mass was placed lengthwise in a bath containing 10% Formol Saline and left there to fix for a minimum period of 48 hours (Fig. 2).

**FORMOL SALINE:**

- 10 c.c. Commercial Formaldehyde
- 90 c.c. Normal Saline

This is stored in a bottle with chalk to keep the solution neutral. The clear supernatent fluid was used.

When fixed, sections were taken from different areas.

1. From the area where the Posterior Tibial becomes the Popliteal vein. This was labelled area one.

2. From an area midway between its commencement and its bifurcation at the Malleolar region. At almost the same level or a little higher at the thickest part of the calf muscles, several blocks were taken of muscular branches. This area was labelled two.

3. From an area in the neighbourhood of the ankle. This was marked three.

4. On numerous occasions, the Medial Plantar vessels were dissected and blocks taken.

5. On quite a number of occasions, blocks were taken from the Inferior Vena Cava, Renal, Femoral or any other veins that were of interest.

6. In all cases, the small Saphenous vein was dissected, fixed and blocks taken from the three areas corresponding to the Posterior Tibial vessels.
DECALCIFICATION.

All the blocks taken consisted of artery, vein and perivascular tissue. In a great number of cases, the arteries were atheromatous, with dense calcium deposit - especially of the Mönckeberg type, and in several cases, bone formation was actually noted in the calcified areas. These blocks were decalcified prior to dehydration. Jenkins' solution was used.

JENKINS' SOLUTION:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>%</th>
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<tbody>
<tr>
<td>Pure Hydrochloric Acid</td>
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</tr>
<tr>
<td>Glacial Acetic Acid</td>
<td>3%</td>
</tr>
<tr>
<td>Chloroform</td>
<td>10%</td>
</tr>
<tr>
<td>Water</td>
<td>10%</td>
</tr>
<tr>
<td>Absolute Alcohol</td>
<td>ad 100 c.c.</td>
</tr>
</tbody>
</table>

The blocks remained in this solution for one to two weeks, or if necessary, longer.

All blocks were dehydrated in the following manner:-

1. In Methylated spirit for twenty-four hours.
2. Three changes in absolute alcohol
   i. For a period of not less than three hours
   ii. For a period of not less than four hours
   iii. Overnight.
3. Two changes in chloroform
   i. All day
   ii. Over night.

EMBEDDING.

Cakes of Paraffin wax with a melting point of 55°C was used. This was melted in an oven at about 58°C. The blocks were immersed in the melted wax and three changes made in order to impregnate the tissue.

i. During morning - four hours.
ii. During afternoon - five hours.
iii. Over night.

The blocks were then embedded in melted wax and immersed in cold water, so that hardening took place rapidly to avoid crystallization.

The impregnation with the wax gave the tissues a supporting medium to permit thin sections 2½ to 3μ to be cut.
GELATINE EMBEDDING.

This method was used to demonstrate fat. The lipoid content of tissue can be preserved and suitably stained. The method employed was as follows:-

The block after removal from Formol-saline was thoroughly washed in running water all day. It was then transferred to a Gelatine mixture made up of:

- Gelatine 15gm.
- Glycerine 15 c.c.
- Tap water 70 c.c.

and left overnight in an oven at 58°C. In the morning, the block was removed and placed in a small dish containing a fresh gelatine mixture and allowed to cool for an hour or two, at room temperature. After it was set, the gelatine block was placed in 5% formalin for two days to harden. When hardened, the surplus gelatine was trimmed off and sections cut on the freezing microtome about 7½ to 10µ in thickness.

Whenever a clotted vein was encountered, the wall was slit for a short distance while the vein was still in situ, and the nature of the clot examined. Little difficulty was encountered in establishing whether the clot was ante or post mortem. The essential points for differentiation were considered to be:

POST MORTEM CLOT.

This was recognised by its red colour, gelatenuous consistency, surrounded by an elastic translucent yellowish jelly-like substance, free in the vessel, often floating in serum, and easily removed, leaving an empty, clean, shiny-walled lumen. Often the clot was noted to be denser and red in its posterior or dependent portion, and yellow in its upper anterior portion. These two distinct layers are due to the denser, red corpuscles falling to and settling at the bottom, and the yellow layer due to white corpuscles, platelets and plasma serum rising to the top. Such a clot can often be demonstrated in the Pulmonary Artery. When such a clot is removed carefully while the heart and lungs are in situ - the right ventricle having previously been slit open - the arterial tree of the Pulmonary Artery can
be demonstrated when the clot is placed in water. The various branches of the clot representing the different branches of the Pulmonary Artery are seen floating like tentacles from a parent trunk. (Fig. 3).

Post Mortem clots appear at different times, the average being about three hours after death. When circulation ceases, coagulation takes place slowly for the intact endothelium lining the heart and blood vessels, prevent rapid clotting. The red blood corpuscles have time to fall to the bottom and hence the reason for the separation into two distinct layers.

It often happens, however, that post mortem clotting is delayed for some considerable length of time, the blood remaining fluid for 24 hours or longer. This condition is generally found in cases of asphyxia or where impeded respiration contributes towards the cause of death, or Coronary Thrombosis causing respiratory distress without causing instantaneous death.

These cases generally show marked cyanosis of the head, face and even upper part of the chest, and the blood is generally dark and fluid.

The explanation for this delay in clotting has been given by Lenggenhager, who attributes this to an increase in CO₂ in the blood, causing the fibrinogen to be rapidly removed.

The following is an extract from the article:

ANTEMORTEM CLOT.

The antemortem clot, however, even if only recent differs distinctly from the above. It is white or greyish in colour or red. It is firm, inelastic, friable and granular on the surface. It fills the lumen and is attached firmly or lightly to the whole or partial circumference of the vessel wall. If an attempt at removal is made it breaks easily, portions may remain attached to the wall and the surface of the endothelium of the removed portion of the clot is rough and dull looking. The red or propagated thrombus, may present some difficulty in being differentiated from a post mortem clot, but if the vein is slit open for some distance, some indication of its antemortem character e.g. light adhesion to the wall, greater friability than elasticity etc., will invariably be found.

Muscular tributaries were often found thrombosed, dilated, thin walled (varicosed) and when cut across the thrombi were firm, friable and could be squeezed out without great difficulty from the lumina. On the surface greyish ridges were invariably noticed.

The three types of antemortem thrombi described in the first part were often encountered, depending upon the conditions under which the thrombi were laid down. (FIG. 4).

1. The white was found where the stream is more rapid. It is the first part of a thrombus formed on an inflamed or injured vein - the "Kopfteil" as the Germans call it. The vegetation on a heart valve is an example of a typical white thrombus. This type was invariably firmly adherent to the wall of the vessel, was firm in consistency, and left a ragged area on the endothelium when removed. This type seldom gives rise to emboli because of its firm attachment to the wall.

2. ........
2. The mixed type could often be identified. It follows on the white and is formed in a slower stream. It is greyish red in colour, inelastic, friable and granular on the surface. This granularity being due to platelets, being deposited on the surface forming ridges. It fills the lumen completely or partially and is firmly or lightly attached to the whole or partial circumference of the wall according to its age. If an attempt at removal is made, it breaks easily, portions may remain attached to the wall and the endothelium, exposed after removal, is rough and dull looking. This type because of its light attachment often gives rise to emboli. A good example of such a thrombus is often encountered in an aneurysmal dilatation e.g. Aorta. In such an aneurysm the stream is slow and the thrombus is slow in forming (FIG.5). It shows a laminated structure (FIG.5a) where layers, differing in colour, are prominent. This is due to layers of platelets alternating with layers of fibrin, leucocytes and red cells.

3. The red thrombus - almost resembling a post mortem clot - is also known as the propagated thrombus. It is formed in a very slow moving almost stagnant stream and follows on the mixed type. It is very loosely attached to the wall, fills the lumen and conforms to its circumference. The end, as it is being propagated, is generally loose and thus can flutter in the moving stream. It is firmer than the post mortem type and friable. It may or may not have ridges on the surface. This is the most dangerous type of thrombus and is the one that gives rise mostly to emboli. When removed the endothelium of the vessel is generally somewhat dull looking, but it may even be shiny.

Macroscopic . . .
MACROSCOPIC APPEARANCES.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ante Mortem</th>
<th>Post Mortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions in which formed</td>
<td>Heart disease, debility, cancer, post oper., puerperium, phlegmon etc.</td>
<td>In all cases - delayed in asphyxia etc.</td>
</tr>
<tr>
<td>Types</td>
<td>white, mixed and red.</td>
<td>Red.</td>
</tr>
<tr>
<td>Colour</td>
<td>white, greyish red or red (according to type)</td>
<td>Red, surrounded by yellowish translucent substance.</td>
</tr>
<tr>
<td>Relation to lumen</td>
<td>Fills lumen completely or partially, and may float.</td>
<td>Floats in lumen.</td>
</tr>
<tr>
<td>Shape</td>
<td>Conforms to shape of vessel.</td>
<td>Always round.</td>
</tr>
<tr>
<td>Attachment to wall</td>
<td>Always firmly or lightly attached to wall.</td>
<td>Always free and generally surrounded by serum.</td>
</tr>
<tr>
<td>Removal</td>
<td>Difficult, breaks easily.</td>
<td>Easy.</td>
</tr>
<tr>
<td>Surface</td>
<td>Granular.</td>
<td>Smooth.</td>
</tr>
<tr>
<td>Structure</td>
<td>Laminated or uniform.</td>
<td>Two distinct layers, (1) red (II) yellowish translucent.</td>
</tr>
<tr>
<td>Endothelium of vessel</td>
<td>Dull, ragged looking may be shiny if thrombus of red type.</td>
<td>Always smooth and shiny.</td>
</tr>
</tbody>
</table>

In all cases blocks of the vessels with their contents were examined microscopically, the object being to establish without any doubt the nature of the clot i.e. antemortem or postmortem. The sections cut were suitably stained by different methods in order to demonstrate various cells, fibres, elastic tissue etc., required for the investigation. The following were the stains used, and the methods adopted were those described in "Mallory's Pathological Technique" with certain variations according to requirements.

(1)......
Post Mortem Clot -- Microphotograph.

Note homogeneous distribution of cells. This resembles a red or propagated thrombus.
(1) Haematoxylin and Eosin.
(2) Weigert's Stain for elastic tissue - a special modification was used in the laboratory at Hammersmith.
(3) Verhoeff Stain for elastic tissue.
(4) Van Gieson's Stain for Collagen and muscle tissue.
(5) Von Kossa's Stain for calcium.
(6) Perl's Stain for Iron.
(7) Scharlet R for fat.
(8) Mallory triple Stain.

MICROSCOPICALLY the differentiation between antemortem and postmortem thrombi was considered primarily on the basis of attachment of the thrombus to the vessel wall i.e. where there was evidence of organisation. In an older thrombus no difficulty was encountered - well marked organisation is sufficient for one to conclude that the thrombus is antemortem. In the more recent types however, there was some difficulty in view of the fact that a red or propagating thrombus closely simulates a postmortem clot. Apart from the fact that a vein when clotted will show at some place or another a light attachment to the wall if searched for deep enough, there are other distinctive features in the microscopic picture which assists/giving additional evidence.

A POST MORTEM clot shows :-

(i) A deep red portion which consists of a homogeneous distribution of red cells, leucocytes and platelets in what appears to be their normal distribution in the blood.

(ii) A layer of loose web-like structure consisting of fibrinous threads practically free of cells, (FIG. 6)

ANTEMORTEM THROMBUS.

(i) The white type consists mainly of platelets. The red cells which might have originally become adherent to the wall have been washed off by the current of blood. It is invariably firmly attached to......
to the wall by well organised granulation tissue.

(ii) The mixed type consists of all elements in the blood that go to make up a thrombus. It is invariably attached to the wall of the vessel, the firmness of the granulation tissue depending on the age and extent of the organisation. It shows generally a laminated structure; layers differing in colour alternate. This lamination is formed during life and is due to slow streaming blood. The layers consist of platelets with layers of fibrin, leucocytes and red cells.

(iii) The red thrombus is made up chiefly of red cells and fibrin with a few leucocytes. It may adhere to the wall of the vein by very recent granulation tissue, often it lies free in the lumen.

For our purpose no clot was considered antemortem unless there was definite evidence of attachment to the wall of the vessel and commencing organisation. (Fig. 7)

The laminated appearance of the clot was considered as additional evidence, but not by itself as proof of its antemortem character. Any doubtful case was discarded.

Cells laden with brownish pigment - haemosiderin - was always considered as definite proof of an antemortem thrombus. (Fig. 8).

### MICROSCOPIC APPEARANCES.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Antemortem</th>
<th>Postmortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>chiefly platelets</td>
<td>Homogeneous distribution of red cells, leucocytes and platelets</td>
</tr>
<tr>
<td>Mixed</td>
<td>All blood elements</td>
<td>Two separate distinct layers: (i) red cells (ii) web-like fibrinous threads with practically no cells.</td>
</tr>
<tr>
<td>Red</td>
<td>Chiefly red cells</td>
<td>No organisation.</td>
</tr>
<tr>
<td>Lamination</td>
<td>Layers alternate in colour; layers of platelets, and layers of red and white cells and fibrin.</td>
<td>No organisation.</td>
</tr>
<tr>
<td>Organisation</td>
<td>Round margin with Vascularisation.</td>
<td>No pigment.</td>
</tr>
<tr>
<td>Iron</td>
<td>Haemosiderin pigment depending on age.</td>
<td></td>
</tr>
</tbody>
</table>
A striking, almost constant finding in the course of microscopic examination was a thickening of the endothelium of the Posterior Tibial Veins, which took the form of irregular patchy proliferation of the intima. (FIG. 9). The possibility that this proliferative thickening might be a fibrosed old thrombus and that it might have a bearing on the etiology of thrombosis, an investigation was simultaneously carried out to establish the nature of this pathological state of the veins and will be discussed fully under the heading Phlebosclerosis.

Often veins were found to be cord-like, hard greyish in colour and when cut across transversely, the lumen was found to be either completely or partially occluded, or divided into several compartments separated by fairly thick partitions. In the individual compartments recent clots were often encountered, the type of which could only be established microscopically. These partitions, as will be shown later, are trabeculae, or old fibrosed thrombi, and the compartments are canals which have formed by retraction of the clot during the process of organisation and fibrosis. These compartments act as channels, thus re-establishing the circulation to a certain extent through a completely thrombosed vein. (FIGS. 57 to 66.)
ANALYSIS OF THE CASES UNDER INVESTIGATION.

100 cases were examined.

The cases have been placed in five distinct groups. According to the nature of the disease to which the patient succumbed.

(1) Those in which the state of the Heart was of such a nature that clinically the direct cause of death was attributed to the pathological state of the heart. Thirty two cases fall under this group.

(2) Cases in which the predominant feature was Malignant disease inoperable in character, the patient cachectic and debilitated. Thirty one cases fall under this group.

(3) Cases in which Arterial disease played the Chief part in the immediate cause of death. Thirteen cases were examined.

(4) Miscellaneous cases which were twenty two in number. The cause of death assigned were other than the above.

(5) Sudden death due to Massive Pulmonary Embolism following operation. Two cases were encountered.

TABLE 6 shows the final analysis.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1504</td>
<td>51</td>
<td>F</td>
<td>Medical</td>
<td>Thrombosis of Saphenous and Post.Tibial to Planter Veins</td>
<td>No abnormality</td>
<td>Intimal Proliferation</td>
<td>Old and recent + old and recent</td>
<td>430 gms. Hypertrophied</td>
<td>+</td>
<td>Oedema of legs</td>
<td>Hypertensive heart</td>
</tr>
<tr>
<td>1506</td>
<td>57</td>
<td>M</td>
<td>Medical</td>
<td>Recent thrombosis</td>
<td>Slight Atheroma</td>
<td>Thin walled</td>
<td>Old and recent</td>
<td>-</td>
<td>610 gms.</td>
<td>Chronic Bronch. Cardiac and Emphysema</td>
<td></td>
</tr>
<tr>
<td>1508</td>
<td>33</td>
<td>F</td>
<td>Medical</td>
<td>Thrombi appeared like Post Mortem clots</td>
<td>Normal</td>
<td>Thin walled</td>
<td>Old and recent</td>
<td>-</td>
<td>460 gms.</td>
<td>Mitral Stenosis</td>
<td></td>
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<tr>
<td>1520</td>
<td>52</td>
<td>F</td>
<td>Medical</td>
<td>No thrombosis</td>
<td>Atheroma</td>
<td>Patchy Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>Congestive Heart Failure</td>
<td></td>
</tr>
<tr>
<td>1522</td>
<td>39</td>
<td>F</td>
<td>Medical</td>
<td>In muscle older In Post.Tibial more recent</td>
<td>No abnormality</td>
<td>Thin in muscle</td>
<td>Marked org. in muscle recent in P.T. Veins</td>
<td>-</td>
<td>836 Hypertrophied</td>
<td>Patent Intervent. Septum</td>
<td></td>
</tr>
<tr>
<td>1536</td>
<td>31</td>
<td>F</td>
<td>Medical</td>
<td>Recent thrombosis</td>
<td>No abnormality</td>
<td>Intimal Proliferation</td>
<td>Old and recent (small microscopic)</td>
<td>620 gms.</td>
<td>+</td>
<td>Infarcts in lungs</td>
<td>C.H.F. Coronary Thrombosis</td>
</tr>
<tr>
<td>1537</td>
<td>48</td>
<td>M</td>
<td>Medical</td>
<td>Thrombosis of Post.Tibial and Plantar Veins</td>
<td>Atheroma</td>
<td>Intimal Proliferation (facing atheroma)</td>
<td>Old and recent in right None in left</td>
<td>520 gms.</td>
<td>+</td>
<td>Aortic Stenosis due to old infect. Endocarditis (Ed. of ankle)</td>
<td>C.H.F. Aortic Stenosis</td>
</tr>
<tr>
<td>Case No.</td>
<td>Age</td>
<td>Sex</td>
<td>Medical or Surgical</td>
<td>Macroscopic State of Arteries</td>
<td>State of Veins</td>
<td>Type of Thrombus</td>
<td>Emboli</td>
<td>Condition of Heart</td>
<td>Iron</td>
<td>Other Abnormalities</td>
<td>Cause of death</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
<td>-----</td>
<td>---------------------</td>
<td>-------------------------------</td>
<td>---------------</td>
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<td>--------------------</td>
<td>------</td>
<td>--------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>1539</td>
<td>61</td>
<td>F</td>
<td>Medical</td>
<td>Recent Thrombosis</td>
<td>No abnormal-</td>
<td>Thin walled</td>
<td>-</td>
<td>420 gms.</td>
<td>-</td>
<td>-</td>
<td>Broncho Pneum. and C.H.F.</td>
</tr>
<tr>
<td>1541</td>
<td>77</td>
<td>M</td>
<td>Medical</td>
<td>Recent thrombi</td>
<td>Mönckeberg</td>
<td>Slight Proliferation</td>
<td>Very recent</td>
<td>415 - dill. and hyper.</td>
<td>+</td>
<td>-</td>
<td>Hypertension</td>
</tr>
<tr>
<td>1543</td>
<td>68</td>
<td>F</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>No abnormal-</td>
<td>Varicose</td>
<td>-</td>
<td>410 gms.</td>
<td>-</td>
<td>-</td>
<td>C.H.F.</td>
</tr>
<tr>
<td>1546</td>
<td>46</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>No abnormal-</td>
<td>Varicose</td>
<td>-</td>
<td>380 gms.</td>
<td>-</td>
<td>-</td>
<td>C.H.F.</td>
</tr>
<tr>
<td>1548</td>
<td>57</td>
<td>F</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>No abnormal-</td>
<td>-</td>
<td>-</td>
<td>Soft and Flabby</td>
<td>-</td>
<td>-</td>
<td>C.H.F. Bronch.Pneumonia</td>
</tr>
<tr>
<td>1549</td>
<td>54</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>No abnormal-</td>
<td>-</td>
<td>-</td>
<td>440 hypertr.</td>
<td>-</td>
<td>-</td>
<td>Acute Bronch. C.H.F.</td>
</tr>
<tr>
<td>1550</td>
<td>70</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Atheroma</td>
<td>Fibrose</td>
<td>Old calcium deposit</td>
<td>450 Fibrosis of myocardi</td>
<td>-</td>
<td>Cor.Pulmonary &amp; C.H.F.</td>
<td></td>
</tr>
<tr>
<td>1555</td>
<td>53</td>
<td>F</td>
<td>Medical</td>
<td>Thrombosis in leg veins and it hepatic veins</td>
<td>No abnormal-</td>
<td>Thin Intimal Proliferation</td>
<td>Old and recent</td>
<td>450 Cor. Pulmon.</td>
<td>-</td>
<td>-</td>
<td>Rheumatic Endocarditis</td>
</tr>
<tr>
<td>1558</td>
<td>59</td>
<td>M</td>
<td>Medical</td>
<td>Both leg veins thrombosed</td>
<td>No abnormal-</td>
<td>Thin</td>
<td>Recent</td>
<td>Hypertrophied.</td>
<td>-</td>
<td>-</td>
<td>Acute Lobar pneumonia</td>
</tr>
</tbody>
</table>

TABLE 1 - HEART (Continued)
<table>
<thead>
<tr>
<th>Case No</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1559</td>
<td>57</td>
<td>M</td>
<td>Medical</td>
<td>Thrombosis in muscle and leg veins</td>
<td>No abnormality</td>
<td>Thin in 2</td>
<td>Recent in muscle veins</td>
<td>-</td>
<td>385 dilated</td>
<td>-</td>
<td>T.B. Lungs</td>
<td>Acute Broncho pneumonia</td>
</tr>
<tr>
<td>1563</td>
<td>52</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombi</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>Cor. Pulmonali</td>
<td>-</td>
<td>Chr. Bronch. and Emphysema</td>
<td>Rheumatic Arthritis</td>
</tr>
<tr>
<td>1566</td>
<td>59</td>
<td>M</td>
<td>Medical</td>
<td>Thrombi in muscle veins only</td>
<td>Arteritis</td>
<td>Thin varicosed</td>
<td>Recent</td>
<td>-</td>
<td>-</td>
<td>Myocarditis</td>
<td>Focal Central Liver Necrosis</td>
<td></td>
</tr>
<tr>
<td>1567</td>
<td>50</td>
<td>M</td>
<td>Medical</td>
<td>Thrombosis in muscle veins only</td>
<td>Slight Atheroma</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>380 gms.</td>
<td>-</td>
<td>Chr. Bronch. and Emphysema</td>
<td>Rheumatic Endocarditis</td>
</tr>
<tr>
<td>1570</td>
<td>67</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Atheroma</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>360 gms.</td>
<td>-</td>
<td>Chr. Bronch. and Emphysema</td>
<td>Cor. Pulmonali C.H.F.</td>
</tr>
<tr>
<td>1576</td>
<td>60</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Atheroma</td>
<td>No Abnormality</td>
<td>-</td>
<td>-</td>
<td>360 gms.</td>
<td>-</td>
<td>Chr. Bronch. and Emphysema</td>
<td>Cor. Pulmon. C.H.F.</td>
</tr>
<tr>
<td>1578</td>
<td>76</td>
<td>F</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Atheroma</td>
<td>Thin</td>
<td>-</td>
<td>-</td>
<td>Fatty infiltration</td>
<td>-</td>
<td>Chr. Bronch. and Emphysema</td>
<td>Acute Broncho pneumonia</td>
</tr>
<tr>
<td>1582</td>
<td>44</td>
<td>F</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>Left Hypertrophy</td>
<td>-</td>
<td>Uraemia</td>
<td>Malignant Hypertension</td>
</tr>
<tr>
<td>1585</td>
<td>73</td>
<td>M</td>
<td>Medical</td>
<td>No recent thrombosis</td>
<td>Little Atheroma</td>
<td>Thin and Varicosed</td>
<td>Old and coec- cluding veins</td>
<td>-</td>
<td>480 Dilatat- ion and Fatty Infiltration</td>
<td>-</td>
<td>Bronch. &amp; Emphysema</td>
<td>Acute Broncho pneumonia</td>
</tr>
<tr>
<td>1588</td>
<td>72</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Atheroma at R 2 occlusion by Thrombus</td>
<td>Prolif.&amp; mid- dle Hypertrophy</td>
<td>-</td>
<td>-</td>
<td>Cor. Pulmonali</td>
<td>-</td>
<td>Bronch. &amp; Emphysema</td>
<td>C.H.F.</td>
</tr>
</tbody>
</table>

TABLE 1 - HEART (Continued).
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other abnormalities</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1593</td>
<td>65</td>
<td>F</td>
<td>Medical</td>
<td>No Thrombosis No abnormal-</td>
<td>No abnormal-</td>
<td>No abnormal-</td>
<td>-</td>
<td>-</td>
<td>Rt. side Hypertrophy</td>
<td>-</td>
<td>Bronch. &amp; Emphysema</td>
<td>C.H.F.</td>
</tr>
<tr>
<td>1594</td>
<td>53</td>
<td>M</td>
<td>Medical</td>
<td>Thrombosis of Monckeberg</td>
<td>Intimal Pro</td>
<td>Recent</td>
<td>Multiple small, adher-</td>
<td>-</td>
<td>650 gsm Hypertroph-</td>
<td>-</td>
<td>Oedema of legs</td>
<td>C.H.F.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post. Tib. veins</td>
<td>lation Phlebitis</td>
<td></td>
<td>ent Infarction</td>
<td></td>
<td>yed</td>
<td></td>
<td></td>
<td>Essential Hypertension</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Post. Tib. and ity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>yed</td>
<td></td>
<td></td>
<td>Cirrhotic Liver</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Plantar veins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bronchitis and</td>
</tr>
<tr>
<td>1596</td>
<td>60</td>
<td>M</td>
<td>Medical</td>
<td>No ThrombosisMonckeberg</td>
<td>Intimal Pro</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>Chon. Glom.</td>
<td>Acute Pericarditis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post. Tib. veins</td>
<td>lation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nephritis</td>
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<tr>
<td>1597</td>
<td>72</td>
<td>M</td>
<td>Medical</td>
<td>No ThrombosisMonckeberg</td>
<td>Intimal Pro</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>Chon. Glom.</td>
<td>Acute Pericarditis</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Post. Tib. veins</td>
<td>lation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nephritis</td>
<td></td>
<td></td>
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</table>

**ANALYSIS:**

<table>
<thead>
<tr>
<th>No. of Cases Examined</th>
<th>Cases with Thrombosis</th>
<th>Percentage</th>
<th>Cases with Embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>16</td>
<td>50%</td>
<td>7</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
<td>63.6%</td>
<td>44</td>
</tr>
</tbody>
</table>

C.H.F. = Congestive Heart Failure.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron Other abnormalities</th>
<th>Cause of death</th>
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<tr>
<td>1494</td>
<td>76</td>
<td>M</td>
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<td>No Thrombosis</td>
<td>Atheroma</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>4/20 Fibrosis</td>
<td>- Gastrostomy sudden from Coronary Disease</td>
<td>Carcinoma of oesophagus</td>
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<tr>
<td>1498</td>
<td>66</td>
<td>M</td>
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<td>Monckeberg</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>- ?</td>
<td>Bronchogenic Carcinoma</td>
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<td>Slight Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>- ?</td>
<td>Carcinoma of Breast</td>
</tr>
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<td>No abnormality</td>
<td>Thin</td>
<td>In muscle L in muscle veins R</td>
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<td>?</td>
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<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>In order X Ray Treatment</td>
<td>Carcinoma of Hypopharynx</td>
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<td>Thrombi in muscle and Post-Tib-vein</td>
<td>Monckeberg Sclerosis</td>
<td>Thin Fibroased</td>
<td>Recent</td>
<td>-</td>
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<td>- Pyelonephritis</td>
<td>Carcinoma of Uterus Hysterectomy</td>
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<td>Thrombosis in Post. Tibial and left Femoral veins</td>
<td>Medial Hypertrophy and atheroma</td>
<td>Thin Fibroased</td>
<td>Old and recent + Pericardial adhesion</td>
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<td>Metastasis in Kidneys and adrenals</td>
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<td>Left Post. Tibial Thrombosed</td>
<td>Atheroma</td>
<td>Normal</td>
<td>Old Canal, and recent</td>
<td>-</td>
<td>?</td>
<td>+ Saphenous thrombosed</td>
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<td>Case No.</td>
<td>Age</td>
<td>Sex</td>
<td>Medical or Surgical</td>
<td>Macroscopic</td>
<td>State of Arteries</td>
<td>State of Veins</td>
<td>Type of Thrombus</td>
<td>Emboli</td>
<td>Condition of Heart</td>
<td>Iron</td>
<td>Other abnormalities</td>
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<td>1523</td>
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<td>Leg Veins thrombosed</td>
<td>Marked Atheroma</td>
<td>Varicose</td>
<td>Organised and recent from Plantar upwards. Older in muscle</td>
<td>-</td>
<td>240 Myocardial fibrosis</td>
<td>-</td>
<td>Calf muscle vein older thrombi.</td>
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<td>Recent in muscle</td>
<td>-</td>
<td>-</td>
<td>440 gms (Hypertrophied)</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>1530</td>
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<td>M</td>
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<td>Monckeberg almost occluded</td>
<td>Intimal Proliferation with hypertrophy of media</td>
<td>-</td>
<td>-</td>
<td>?</td>
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<td>Monckeberg</td>
<td>Varicose</td>
<td>Recent in muscle loose in Post.Tib.</td>
<td>+</td>
<td>410 gms.</td>
<td>-</td>
<td>Obstructive Jaundice (metastasis in Liver)</td>
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<td>Intimal Proliferation with medial Hypertrophy</td>
<td>In muscle veins organic. more advanced</td>
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<td>-</td>
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<td>Case No.</td>
<td>Age</td>
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<td>Medical or Surgical</td>
<td>Macroscopic</td>
<td>State of Arteries</td>
<td>State of Veins</td>
<td>Type of Thrombus</td>
<td>Emboli</td>
<td>Condition of Heart</td>
<td>Iron</td>
<td>Other Abnormalities</td>
</tr>
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<td>1535</td>
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<td></td>
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<td>Organised and recent</td>
<td>-</td>
<td>Normal</td>
<td>-</td>
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<td>Normal</td>
<td>Varicosed</td>
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<td>Atheroma</td>
<td>Fibrosed</td>
<td>Organised &amp; canalised Phlebolith</td>
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<td>Mönckeberg</td>
<td>Some thin</td>
<td>Some hyper-trophied Media</td>
<td>+</td>
<td>Normal</td>
<td>-</td>
<td>Cystostomy</td>
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<td>Normal</td>
<td>Thin and fibrosed</td>
<td>Recent in large veins older in muscle veins</td>
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<td>Pericardial effusion</td>
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<td>Secondary in Spine and chest</td>
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<td>Atheroma</td>
<td>Prostatic plexus thrombosed</td>
<td>No thrombi in leg veins</td>
<td>-</td>
<td>?</td>
<td>+</td>
<td>Broncho Pneumonia</td>
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<td>74</td>
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<td>Medical</td>
<td>Thrombosis in varicosed muscle veins</td>
<td>Atheromatous and thrombosed</td>
<td>Intimal Proliferation</td>
<td>Recent in area ii</td>
<td>-</td>
<td>?</td>
<td>+ in arterial thrombosis X Ray treatment and cachexia</td>
<td>Carcinoma of breast</td>
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<td>Case No.</td>
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<td>Sex</td>
<td>Medical or Surgical</td>
<td>Macroscopic</td>
<td>State of Arteries</td>
<td>State of Veins</td>
<td>Type of Thrombus</td>
<td>Emboli</td>
<td>Condition of Heart</td>
<td>Other Abnormalities</td>
<td>Cause of Death</td>
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<td>1564</td>
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<td>-</td>
<td>-</td>
<td>Hypertrophy and dilatation of right heart</td>
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<td>Post Mortem Clots in both legs</td>
<td>Atheromatous</td>
<td>Varicose</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>Intestinal obstructions</td>
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<td>Medical</td>
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<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>Pericarditis</td>
<td>-</td>
<td>Metastasis in Liver, Spine and Pleura</td>
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<td>Thin and fibrosed</td>
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<td>-</td>
<td>?</td>
<td>-</td>
<td>Secondary in Gastric and Mediastinal glands</td>
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<td>76</td>
<td>M</td>
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<td>Planter and leg veins thrombosed</td>
<td>Atheromatous</td>
<td>Intimal Proliferation and Varicose</td>
<td>Recent</td>
<td>-</td>
<td>Myocardial Fibrosis and adherent Pericardium</td>
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<td>No abnormality</td>
<td>Intimal Proliferation</td>
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<td>-</td>
<td>Congestive Heart Failure</td>
<td>-</td>
<td>Chronic Bronchitis and Emphysema</td>
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<tr>
<td>1589</td>
<td>72</td>
<td>M</td>
<td>Surgical</td>
<td>Leg veins not examined</td>
<td>Mönkesberg</td>
<td>Phlebitis of Renal Vein</td>
<td>Septic thrombosis Recent + Septic infarcts 180 gms.</td>
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<td>X Ray Therapy Essaciated Pylemonophritis</td>
<td>Carcinoma of Cervix</td>
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<td>1598</td>
<td>71</td>
<td>F</td>
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<td>No thrombosis</td>
<td>Atheromatous</td>
<td>Thin and Varicose</td>
<td>-</td>
<td>-</td>
<td>No abnormality</td>
<td>-</td>
<td>Swollen right arm. Secondary in Spine and legs</td>
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TABLE II: CARCINOMA (Continued).
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<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of Death</th>
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<tbody>
<tr>
<td>1600</td>
<td>50</td>
<td>M</td>
<td>Medical</td>
<td>Both legs thrombosed from Plantar to Inferior Vena Cava</td>
<td>Atheromatous</td>
<td>Thin and Varicose</td>
<td>Recent</td>
<td>+</td>
<td>Normal</td>
<td></td>
<td>Metastasis in Liver</td>
<td>Carcinoma of Tail of Pancreas</td>
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**ANALYSIS:**

<table>
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<tr>
<th>No. of Cases Examined</th>
<th>Cases with Thrombosis</th>
<th>Percentage</th>
<th>Cases with Emboli</th>
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<tbody>
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<td>31</td>
<td>18</td>
<td>58%</td>
<td>6</td>
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<td>6</td>
<td>6</td>
<td>48%</td>
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<td>25</td>
<td>12</td>
<td>75%</td>
<td>4</td>
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<tr>
<td>8</td>
<td>6</td>
<td>75%</td>
<td>-</td>
</tr>
<tr>
<td>23</td>
<td>12</td>
<td>52%</td>
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Secondary Cardiac:

Deducting Secondary Cardiac:

Cases treated Surgically:

do. do. Medically:

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TABLE 11 - CARCINOMA (Continued)
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1495</td>
<td>77</td>
<td>F</td>
<td>Medical</td>
<td>Thrombosis of left Fem. and Post. Tibial Veins</td>
<td>Atheroma and practically occluded by organising Thrombus</td>
<td>-</td>
<td>Trabeculated and recent thrombus</td>
<td>-</td>
<td>375 Hypertrophied</td>
<td>-</td>
<td>5 day gangrene of left leg Matting of art. and veins</td>
<td>Cerebral thrombosis and softening</td>
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<td>1497</td>
<td>77</td>
<td>F</td>
<td>Medical</td>
<td>Tortuous cordlike veins</td>
<td>Mönckeberg and thrombi</td>
<td>Thrombus</td>
<td>Old Phlebolith</td>
<td>-</td>
<td>420</td>
<td>in art. thromb-</td>
<td>Matting of art. and veins</td>
<td>Cerebral thrombosis</td>
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<td>Medical</td>
<td>Thrombosis in lower parts of Post. Tibial Veins</td>
<td>Mönckeberg</td>
<td>Intimal Proliferation</td>
<td>Old organised and recent thrombus</td>
<td>+ old and recent</td>
<td>Small, mural thrombus and myocardial infarct</td>
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<td>Ascitis and Pleural effusion</td>
<td>Coronary Disease</td>
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<td>Muscle Veins and Saph. (left) thrombosed</td>
<td>Mönckeberg</td>
<td>Intimal Proliferation</td>
<td>Recent in Saphenous none in Post. Tibial</td>
<td>-</td>
<td>480 gms. Myocardial infarct</td>
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<td>Hypertrophy of left Ventricle</td>
<td>Coronary Disease</td>
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<td>Arterio Sclerosis</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>Hypertrophy of left Ventricle</td>
<td>-</td>
<td>-</td>
<td>Spontaneous haemorrhage in brain</td>
</tr>
<tr>
<td>1518</td>
<td>57</td>
<td>M</td>
<td>Medical</td>
<td>No Thrombosis</td>
<td>Arterio Sclerosis</td>
<td>Normal</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>Spontaneous haemorrhage in brain</td>
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<tr>
<td>1528</td>
<td>76</td>
<td>M</td>
<td>Medical</td>
<td>Rt. Saphenous dilated and calcified</td>
<td>Mönckeberg</td>
<td>Calcification of Saphenous</td>
<td>Recent in muscle veins</td>
<td>-</td>
<td>?</td>
<td>Arterio Sclerosis Emaciated and dehydrated</td>
<td>Cerebral Thrombosis</td>
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</tr>
<tr>
<td>Case No.</td>
<td>Age</td>
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<td>Medical or Surgical</td>
<td>Macroscopic</td>
<td>State of Arteries</td>
<td>State of Veins</td>
<td>Type of Thrombus</td>
<td>Emboli</td>
<td>Condition of Heart</td>
<td>Iron</td>
<td>Other Abnormalities</td>
<td>Cause of Death</td>
</tr>
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<tr>
<td>1561</td>
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<td>Hönckeberg</td>
<td>Intimal Proliferation</td>
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<td>-</td>
<td>?</td>
<td>-</td>
<td>Arterio Sclerosis</td>
<td>Cerebral Thrombosis</td>
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<td>Left Femoral to Plantar thrombosed Right lower part of Post Tibial thrombosed</td>
<td>Arterio Sclerosis with occlusion</td>
<td>Intimal Proliferation Thin in Muscle</td>
<td>Old with superadded recent (massive)</td>
<td>No abnormality</td>
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<td>Intermittent Venous Occlusion</td>
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<td>?</td>
<td>-</td>
<td>Myocardial Fibrosis</td>
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<td>Atheroma</td>
<td>Intimal Proliferation</td>
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<td>-</td>
<td>?</td>
<td>-</td>
<td>Syphilis</td>
<td>Ruptured Aneurysm of Aorta</td>
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<td>? Post Mortem Clot</td>
<td>Hönckeberg</td>
<td>Intimal Proliferation</td>
<td>Old and recent</td>
<td>-</td>
<td>Myocardial fibrosis</td>
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<td>Coronary thrombosis</td>
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**ANALYSIS:**

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<thead>
<tr>
<th>No. of Cases Examined</th>
<th>Cases with Thrombosis</th>
<th>Percentage</th>
<th>Cases with Embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>7</td>
<td>53.8%</td>
<td>2</td>
</tr>
<tr>
<td>Secondary Cardiac</td>
<td>5</td>
<td>38.5%</td>
<td>1</td>
</tr>
<tr>
<td>Deducting Secondary Cardiac</td>
<td>8</td>
<td>62.5%</td>
<td>1</td>
</tr>
<tr>
<td>Case No.</td>
<td>Age</td>
<td>Sex</td>
<td>Medical or Surgical</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
<td>-----</td>
<td>-------------------</td>
</tr>
<tr>
<td>1500</td>
<td>55</td>
<td>F</td>
<td>Medical</td>
</tr>
<tr>
<td>1509</td>
<td>79</td>
<td>F</td>
<td>Medical</td>
</tr>
<tr>
<td>1511</td>
<td>69</td>
<td>F</td>
<td>Medical</td>
</tr>
<tr>
<td>1513</td>
<td>44</td>
<td>F</td>
<td>Medical</td>
</tr>
<tr>
<td>1517</td>
<td>69</td>
<td>M</td>
<td>Surgical</td>
</tr>
<tr>
<td>1521</td>
<td>75</td>
<td>M</td>
<td>Medical</td>
</tr>
<tr>
<td>1526</td>
<td>49</td>
<td>F</td>
<td>Medical</td>
</tr>
<tr>
<td>1527</td>
<td>50</td>
<td>M</td>
<td>Medical</td>
</tr>
<tr>
<td>1529</td>
<td>77</td>
<td>M</td>
<td>Medical</td>
</tr>
<tr>
<td>1530</td>
<td>79</td>
<td>F</td>
<td>Medical</td>
</tr>
</tbody>
</table>

**Table IV - MISCELLANEOUS**

Group of cases in which the primary cause of death was attributed to other than Heart, Arterial, or Carcinoma.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1533</td>
<td>45</td>
<td>M</td>
<td>Surgical</td>
<td>Red Thrombi in veins</td>
<td>No abnormality</td>
<td>Intimal Proliferation</td>
<td>Recent</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Resection of Stomach Chronic Peptic Ulcer</td>
<td>Peritonitis</td>
</tr>
<tr>
<td>1542</td>
<td>43</td>
<td>F</td>
<td>Medical</td>
<td>Post Mortem Clots</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>350 Fatty</td>
<td>-</td>
<td>Cirrhosis of Liver</td>
<td>Spontaneous haemorrhage in brain</td>
</tr>
<tr>
<td>1545</td>
<td>56</td>
<td>M</td>
<td>Surgical</td>
<td>Red recent thrombi</td>
<td>Atheroma</td>
<td>Intimal Proliferation</td>
<td>Very old and fibrosed lumen trabecular and recent</td>
<td>-</td>
<td>260 gms. Normal</td>
<td>-</td>
<td>Amyloidosis of spleen, kidney, adrenals, and small bowel</td>
<td>Peritonitis</td>
</tr>
<tr>
<td>1547</td>
<td>55</td>
<td>M</td>
<td>Medical</td>
<td>No thrombi</td>
<td>No abnormality</td>
<td>Intimal Proliferation</td>
<td>Left old Rt. no obvious</td>
<td>-</td>
<td>310g Myocardial Fibrosis</td>
<td>-</td>
<td>Steatorrhea</td>
<td>Actinomycosis</td>
</tr>
<tr>
<td>1556</td>
<td>28</td>
<td>F</td>
<td>Medical</td>
<td>No thrombi</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Peritonitis</td>
</tr>
<tr>
<td>1557</td>
<td>72</td>
<td>F</td>
<td>Medical</td>
<td>No thrombi</td>
<td>No abnormality</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Simple Pericardial effusion</td>
<td>Myxoedema</td>
</tr>
<tr>
<td>1560</td>
<td>76</td>
<td>M</td>
<td>Medical</td>
<td>No thrombi</td>
<td>Medial degeneration</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>Hypertrophy of left Ventricle</td>
<td>-</td>
<td>Bronchitis</td>
<td>Uraemia</td>
</tr>
<tr>
<td>1575</td>
<td>77</td>
<td>M</td>
<td>Medical</td>
<td>No thrombi</td>
<td>Mönckeberg</td>
<td>Intimal Proliferation</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>T.B. Pulmonary</td>
<td>Fatal haemoptysis</td>
</tr>
</tbody>
</table>

**TABLE IV - MISCELLANEOUS (Continued).**
## TABLE IV – MISCELLANEOUS (Continued)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Medical or Surgical</th>
<th>Macroscopic</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Emboli</th>
<th>Condition of Heart</th>
<th>Iron</th>
<th>Other Abnormalities</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1587</td>
<td>65</td>
<td>M</td>
<td>Medical</td>
<td>Left Veins thrombosed R doubtful</td>
<td>No abnormality</td>
<td>Varicose and Intimal Proliferation</td>
<td>Recent</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>340 gms. Myocardial Fibrosis</td>
<td>Traumatic haemorrhage in brain</td>
</tr>
<tr>
<td>1601</td>
<td>53</td>
<td>F</td>
<td>Medical</td>
<td>Veins thrombosed to Femoral</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>Recent</td>
<td>+</td>
<td>440 gms. Acute dilation of right side</td>
<td>-</td>
<td>Broncho Pneumonia</td>
<td>Perforated Peptic Ulcer</td>
</tr>
<tr>
<td>1602</td>
<td>60</td>
<td>M</td>
<td>Surgical</td>
<td>Thrombosis from Plantar to Iliac Veins</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>Recent</td>
<td>Old and Recent</td>
<td>Recent</td>
<td>+</td>
<td>330 gms. appeared healthy</td>
<td>T.B. Spine and Kidney and Uraemia</td>
</tr>
<tr>
<td>1606</td>
<td>51</td>
<td>M</td>
<td>Medical</td>
<td>No thrombosis</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>-</td>
<td>Pyelonephritis Splenomegaly Jaundice</td>
<td>Cirrhosis of Liver</td>
</tr>
<tr>
<td>1607</td>
<td>15</td>
<td>F</td>
<td>Medical</td>
<td>No thrombosis</td>
<td>No abnormality</td>
<td>No abnormality</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
<td>-</td>
<td>T.B. Meningitis</td>
<td></td>
</tr>
</tbody>
</table>

### ANALYSIS:

<table>
<thead>
<tr>
<th>No of Cases Examined</th>
<th>Cases with Thrombosis</th>
<th>Percentage</th>
<th>Cases with Emboli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases treated Surgically</td>
<td>22</td>
<td>4</td>
<td>36.4%</td>
</tr>
<tr>
<td>Cases treated Medically</td>
<td>18</td>
<td>4</td>
<td>100%</td>
</tr>
</tbody>
</table>

Out of the 8 cases with Thrombosis, 6 had Peritonitis and 2 Cystitis.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Type of Operation</th>
<th>State of Arteries</th>
<th>State of Veins</th>
<th>Type of Thrombus</th>
<th>Recent and Old Emboli</th>
<th>Condition of Heart</th>
<th>Type of Emboli</th>
<th>Other Causes of Death</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1574</td>
<td>54</td>
<td>F</td>
<td>Cholecystectomy</td>
<td>Varicosed</td>
<td>+</td>
<td>Recent</td>
<td>+</td>
<td>Right old</td>
<td>Stout</td>
<td>Pulmonary Embolism</td>
<td>1</td>
</tr>
<tr>
<td>1590</td>
<td>56</td>
<td>F</td>
<td>Neprolithotomy</td>
<td>Varicosed</td>
<td>+</td>
<td>Recent</td>
<td>+</td>
<td>Right old</td>
<td>Stout</td>
<td>Pulmonary Embolism</td>
<td>1</td>
</tr>
</tbody>
</table>

Cases treated surgically but placed with their respective groups under the primary cause of death.
### TABLE VI - Analysis of 100 cases in respect of Thrombosis and Embolism.

<table>
<thead>
<tr>
<th>No of Cases Examined</th>
<th>Males</th>
<th>Females</th>
<th>Medical</th>
<th>Surgical</th>
<th>Thrombosis</th>
<th>Emboli</th>
<th>Average Age</th>
<th>Per Cent Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart (Table 1)</td>
<td>32</td>
<td>20</td>
<td>12</td>
<td>32</td>
<td>-</td>
<td>16 (10 Males) (6 Females)</td>
<td>7 (4 Males) (3 Females)</td>
<td>57.4 yrs.</td>
</tr>
<tr>
<td>Carcinoma (Table II)</td>
<td>31</td>
<td>19</td>
<td>12</td>
<td>23</td>
<td>8</td>
<td>18 (12 Males) (6 Females)</td>
<td>6 (5 Males) (1 Female)</td>
<td>63.8 yrs.</td>
</tr>
<tr>
<td>Arterial (Table III)</td>
<td>13</td>
<td>9</td>
<td>4</td>
<td>13</td>
<td>-</td>
<td>7 (3 Males) (4 Females)</td>
<td>2 (1 Male) (1 Female)</td>
<td>66.8 yrs.</td>
</tr>
<tr>
<td>Miscellaneous (Table IV)</td>
<td>22</td>
<td>12</td>
<td>10</td>
<td>18</td>
<td>4</td>
<td>8 (6 Males) (2 Females)</td>
<td>4 (2 Males) (2 Females)</td>
<td>57.4 yrs.</td>
</tr>
<tr>
<td>Operative (Table V)</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>2 (2 Females)</td>
<td>2 (2 Females)</td>
<td>55.0 yrs.</td>
</tr>
<tr>
<td>Cases:</td>
<td>100</td>
<td>60</td>
<td>40</td>
<td>86</td>
<td>14</td>
<td>51 (31 Males) (20 Females)</td>
<td>21 (12 Males) (9 Females)</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE:** If Secondary Cardiac insufficiency is considered as a contributory factor to the causation of Thrombosis, the tables would show an incidence of Thrombosis in:

- **Cardiac**: 63.6%
- **Carcinoma**: 43%
- **Arterial**: 25%
CLASSIFICATION.

No clear cut classification of the cases into definite groups was absolutely possible. Some difficulty was experienced in placing the cases in their respective groups. Particularly was this so with the Heart group. All those placed in group one were considered as primary cardiac conditions. An examination of the other groups revealed that a fair number of the cases showed secondary or concomitant cardiac insufficiency. This is a fact which must be taken into consideration when assigning the relative etiological factors responsible for thrombosis. Thus in group two out of 18 cases with thrombosis at least six cases were definitely recorded as having cardiac abnormality. In group three there were five cases with cardiac involvement. In group four at least one case of the eight was secondary cardiac. In group five both cases showed fatty hearts.

In group one, out of thirty two cases, 16 or fifty per cent. showed thrombosis of the veins of the legs. In group two, out of 31 cases 18 or 58 per cent. showed thrombosis.

In group three, out of 13 cases 7 or 53.85 per cent. showed thrombosis.

In group four, out of 22 cases 8 or 36.4 per cent. showed thrombosis.

Leaving group five out of consideration, groups two and three show a higher incidence of thrombosis than group one. But if secondary cardiac conditions are taken into consideration as factors encouraging thrombosis, then the incidence of thrombosis in conditions...
conditions associated with cardiac insufficiency, far outweighs the incidence in the other two groups mentioned. Thus 12 cases would have to be added to group one making a total number of cases with cardiac insufficiency forty-four (32 + 12) with 28 cases of thrombosis (16 + 12) i.e. 63.6%.

The number of cases examined and the incidence of thrombosis in groups 2 and 3 would drop to 25 (31 - 6) with 12 cases of thrombosis (18 - 6) i.e. 48%, and 8 cases (13 - 5) with 2 cases of thrombosis (7 - 5) i.e. 25% respectively.

According to table 6 the three major conditions in which thrombosis is a common occurrence are in order of frequency:-

(i) Carcinoma with 58%
(ii) Arterial disease with 53%
(iii) Cardiac with 50%

If, however, we take into consideration the secondary cardiac conditions, we have an amended table in the following order of frequency :-

(i) Cardiac with 63.6%
(ii) Carcinoma with 48%
(iii) Arterial with 25%

This is a striking finding, particularly so as in the vast majority of cases no clinical evidence of venous thrombosis was manifest. In 12 cases only was oedema of the legs and ankles noted. I do not however place great reliance on this figure as no careful observation was made in each case, because the relationship of oedema to thrombosis was not fully appreciated until the work was fairly well advanced. It is however interesting that where oedema was noted in my records 7 cases with thrombosis belonged to the Heart group, one to the arterial group and two to the carcinoma group. It can however be stated, that in the vast majority of cases where thrombosis occurred no obvious oedema was noted.

Oedema . . .
OEDEMA as a clinical sign in thrombosis has been discussed above and the views put forward by the various authors mentioned. It was noted that three factors are associated with this condition:

(i) Mechanical blockage by a thrombus.
(ii) Lymphatic blockage by perivenous inflammation.
(iii) Vasocostriction of arterioles and venules as a result of impulses initiated in a thrombosed segment of a vein.

It was also noted that when thrombo-phlebitis affects the deep veins, oedema occurs, but not so when the superficial veins such as the Sapheni were involved.

Only 4 cases of thrombo-phlebitis were encountered in my series.

1. Case No. 1515. A male aged 79 had recurrent epigastric pains for about 3 years. This was attributed to cholecystitis and choledolithiasis. He also suffered from generalised Arterio-sclerosis, heart disease and auricular fibrillation. He had pain in the right leg in a line corresponding to the lesser Saphenous Vein. There was no obvious oedema of the leg. He died suddenly.

At post mortem a fresh infarction on the left side of the Interventricular Septum was found due to Coronary thrombosis. The Sapheni of both legs were thrombosed, the thrombi were adherent to the vessel wall.

Microscopically recent thrombosis with commencing organisation were found. All the coats of the wall as well as the perivenous tissue were infiltrated with inflammatory cells. The Posterior Tibial Veins were neither thrombosed nor inflamed.

2. Case No. 1594. A male aged 53 years suffered from Conjestive Heart Failure due to essential Hypertension. Both legs were extremely oedematous.

At . . . .
At postmortem the Posterior Tibial Veins, Plantar and Femoral Veins were found thromboseed. Microscopically the veins were markedly infiltrated with inflammatory cells - lymphocytes, polymorphs and plasma cells. There were haemorrhages and degenerative change in the muscle fibres in the media, proliferative and supplicative changes in the intima. The thrombus was of the white mixed type. Commencing organisation and vascularisation was noted round the periphery of the thrombus. (FIG. 10, 11, and 12).

Emboli were found in the lungs and appeared to be of some duration as shown by the state of organisation.

The swelling of the legs might be attributed to cardiac failure, but owing to the acute inflammatory condition of the wall of the vein and the perivascular tissue it is, according to Homans, primarily an oedema due to an acute lymphangitis and phlebitis, but vaso- constriction and mechanical blockage must, of course, also be taken into consideration.

The small emboli found in the lungs were definitely older than the thrombi in the veins and can be accounted for by a thrombosis of the veins as a result of the cardiac failure prior to the onset of the phlebitis.

3. Case No. 1696. This case illustrates a thrombo-phlebitis commencing in the Renal Veins and spreading to the Inf. Vena Cava and involving the venous system in the lower part of the body. A young girl 18 years old was ailing for six months with rather obscure symptoms localised in the left loin.

Her . . .
Her condition was thought to be a subphrenic abscess. An exploration revealed no pus. A basal pneumonia of the left lung appeared about two weeks after the onset of the illness, which was attributed to the spread of the subphrenic abscess. The lung cleared up. Later, marked swelling of the legs appeared. Albumin in the urine was noted.

At postmortem, the heart weighed 280 gms. and on the mitral valve there were recent beady, pale, friable clusters of warty vegetation, which did not appear crumbly thrombotic excrescences of bacterial endocarditis. There were no old thickening or stenosis of the mitral cusps. The other valves appeared normal.

The left lung was firmly adherent to the diaphragm and tore on removal showing friable, reddish consolidation as from healing suppuration. The Pulmonary arteries on both sides showed small, greyish, embolic masses in the tertiary branches. Some of these appeared old.

The venous system, from the point where the Inferior Vena Cava enters the right auricle down to the Plantar veins, were thrombosed. On separating the heart from the Inferior Vena Cava a grey thrombus was found protruding about a quarter of an inch into the right auricle from the Inferior Vena Cava. About three quarters of the circumference of the lumen was filled with this greyish, firm, friable thrombus which was adherent to the wall. The anterior quarter was empty and apparently provided a little space for the flow of blood. At or about the entrance of the Renal veins the whole lumen was obliterated by thrombus. The wall of the Inferior Vena Cava was thickened and indurated and the vessel as a whole was constricted

as ...
as from long standing thrombosis.

The Renal Veins were completely occluded by greyish, firm thrombi which appeared to be oldest at about the level of their exit from the kidneys.

As the thrombosis extended downwards it changed in colour to red, was softer and less firmly adherent to the wall - a retrograde thrombosis.

The left Ovarian vein was thrombosed. The kidneys were large, swollen, yellowish as from fatty degeneration. On the cut surface they appeared in a state of early infarction.

**MICROSCOPIC EXAMINATION**

Inferior Vena Cava 2" from the mouth. An organising thrombus with vascularisation, attached to one part of the wall. The Intima showed no proliferative change and the elastic layer was thin.

The Media. The circular muscle fibres adjacent to the internal elastic lamina adjoining the organising attached thrombus had practically disappeared and was replaced by fibrous tissue. The part of the vein which had no thrombus attached to it, appeared normal.

The Adventitia showed thick bundles of longitudinal muscle fibres with thick bundles of collagen fibres in between them.

There was a marked cellular infiltration consisting of lymphocytes and mononuclear cells in both the media and adventitia.

Inferior Vena Cava 3" below. The whole vessel was occluded with organising thrombus. It was further advanced in its organisation than the portion above. Inflammatory cells were numerous round the margin and were laden with brown pigment which gave the Perl reaction for Iron - haemosiderin.

Left Common Iliac. There was fibrosis round the edge of the thrombus. There was marked disappearance...
of muscle fibres in the media and adventitia which was replaced by fibrous tissue. There was a very dense layer of fibrous tissue between vein and artery.

**Left Ovarian Vein.** There was recent thrombosis with commencing organisation. The media and adventitia appeared quite normal. No inflammatory cells were seen in the wall.

As we descended the thrombosis became more of the red type, the wall of the vein showed little change with no inflammatory reaction and when the left Plantar was reached there was no thrombosis.

**Left Renal Vein.** This was completely occluded by thrombus, half of which was well organised and canalised and the rest was hyalinised and was showing organisation. Haemosiderin pigment was present in the organising part. The wall showed replacement fibrosis.

**Right Renal Vein.** There was recent thrombosis with evidence of commencing organisation. There were a few inflammatory cells in the wall. No haemosiderin was present.

**The Lungs** showed recent as well as older emboli lodged in the small Pulmonary branches.

The origin and process of thrombosis is well illustrated in this case. From the macroscopic appearances, corroborated by microscopic findings, it can be conclusively stated that the place of origin of the thrombosis was in the Left Renal Vein due to an infection. From there it spread to the Inferior Vena Cava, the Left Ovarian Vein and then upwards and downwards. The state of the organisation of the thrombus was more advanced in and in the neighbourhood of the Renal vessels. The further away from the Renal Veins, the more the thrombus resembled the propagating ...
propagating the red type. The haemosiderin pigment present in early thrombosis and absent in the very recent, old and fibrosed areas (haemosiderin and its relation to age of a thrombus will be discussed later), the gradual disappearance of inflammatory cells from the wall of the vessels as we proceed downwards, the replacement fibrosis in the wall of the veins nearer the kidneys, and the practically healthy state of the walls the further away from the source of infection; the tailing off of the thrombus as we approach the Malleolar region; the microscopic absence of thrombosis in the lower end of the Posterior Tibial and Plantar Veins (though these vessels were noted to be thrombosed in situ before dissection and apparently were squeezed out inadvertently during dissection and fixation;) all the above indicate that thrombosis had commenced in the Left Renal Vein and extended upwards and downwards.

The clinical symptoms of the Left lobar consolidation attributed originally to a spread of a Left Subphrenic abscess can be attributed to an embolus having detached itself from the main thrombus and found its way into the Pulmonary artery of the left lower lobe where it set up an infarct, pleurisy and pneumonic consolidation. The possibility of a spread from a periphlebitis of the Left Renal Vein by way of lymphatics through the diaphragm to the left lower lobe of the lung cannot however be excluded, but the fact that the lung showed recent as well as old emboli in the small branches of the Pulmonary artery is highly suggestive that the consolidation was embolic in origin.

The marked oedema of the lower extremities can be attributed mainly to the mechanical obstruction by thrombosis of the main venous channels including the Inferior Vena Cava.

Case...
Case 4 No. 1517.

A male aged 69 suffered from retension of urine due to an enlarged prostate. A cystotomy was performed for relief.

At autopsy a perivesical infection was found. The prostate was enlarged and the prostatic plexus of veins was thrombosed.

The Right Leg was oedematous, the small Saphenous vein empty but thick. The Posterior Tibial and muscle veins were thrombosed.

The Left Leg showed no oedema. The small Saphenous was thick and thrombosed. The Posterior Tibial and muscle veins were thrombosed.

MICROSCOPIC EXAMINATION.

The Left Small Saphenous showed an acute inflammation of all the coats including the perivenous tissue. There was haemorrhage in the media and recent thrombus occluded the vessel.

The Left Posterior Tibial and muscular tributaries showed a recent red thrombosis, but no infection of the wall of the perivascular tissue.

The Right Saphenous showed no thrombosis and no inflammation.

The Right Posterior Tibial vein was markedly and acutely inflamed. The adventitia and media of the wall were acutely oedematous. The muscle fibres were widely separated by oedema and the connective tissue between the muscle fibres showed active proliferation. The Intima was in a state of proliferation.

The thrombus which occluded the lumen showed commencing organisation.

This........
This case shows (i) that oedema is associated with periphlebitis or lymphangitis and phlebitis of the deep veins but not of the superficial veins and (ii) that thrombosis without phlebitis and lymphangitis does not necessarily give rise to oedema.

These four cases illustrate that oedema of the lower extremities, as indeed in other parts of the body, depends upon an inflammatory condition of the veins, and upon the particular veins which are affected, whether superficial or deep. Thus in the case of the saphenous no oedema is present. In the deep veins e.g. Posterior Tibial, Femoral etc., oedema is present if the veins are inflamed. Thrombosis in the deep veins without inflammation need not necessarily give rise to oedema.

**SUPPURATIVE PHLEBITIS.**

If the inflammation is due to pyogenic bacteria, the infection spreads to the thrombus. The polymorphs secrete an enzyme, which liquifies the thrombus and septic emboli usually, if not invariably, occur. (FIG. 13)

*Lymphatic obstruction.* This was not investigated but the inflammatory reaction noticed in the perivenous tissue is suggestive of a lymphatic involvement. Homans, who, on several occasions explored surgically the veins in cases of oedema following thrombo-phlebitis found the veins surrounded by inflammatory exudate. This exudate he maintains, engulfs the lymphatic vessels, thus adding lymphatic obstruction to the already occluded vessel. He also maintains that inflammation when present, is a cause of thrombosis, and that thrombosis does not occasion a perivascular inflammation. The frequency of infection in the legs, genitals, anal region, prostate etc. - the lymphatics ...
lymphatics of which course about the Iliac and Femoral vessels constitute a reasonable explanation for the frequent occurrence of thrombosis in the lower extremities.

Oedema, however, is frequently met with in cases where there is no obvious or actual (microscopic) inflammation of the veins. In thrombosis of the _maurantian type_ the lymphatics are normal. Here, however, the elevation of the venous pressure is responsible for the oedema. It causes an enormous transudate of tissue fluid which the lymphatic channels are unable to carry away.

The third view as a cause of oedema brought forward by Leriche and confirmed by Ochsner and DeBakey is _vaso-constriction_. The latter have demonstrated clinically the benefit of Lumbar-Sympathetic block in such cases.

Two cases of Thrombo-Phlebitis came under my care. One was treated by lumbar-sympathetic block and the other by the old conservative treatment.

**CASE 1.** An African male, age 18, was admitted into Hospital with a history of pain, tenderness and swelling of the right leg for seven days. The pain was worse at night and during walking. On examination, his temperature was 101°F., Pulse 116. The right leg was tense, oedematous and painful. The surface temperature was reduced compared with the left leg, and the Dorsalis Pedis Artery was very faint - in the left foot the artery was full and strong. The measurements of the thickness of both legs were taken. No other abnormalities were noted.

For four days the patient was kept in bed at rest, with local Ichthyol applications. Although the temperature dropped, the pain and oedema did not subside. On the evening of the fourth day after admission, the temperature suddenly rose again to 101°F. On the morning of the fifth day, the 2nd, 3rd and 4th Lumbar Sympathetic Ganglia were injected with 2% Novocaine.

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**Results.**
RESULTS: Within half an hour the leg was distinctly warmer than the right, the pain diminished and the Dorsalis Pedis Artery was more distinct and full. Within 24 hours the leg was less tense, hardly any pain and the swelling was reduced by at least half an inch. The temperature began to drop and was subnormal on the third day. On the seventh day after injection, the leg appeared normal and the patient allowed up. He was discharged on the thirteenth day after admission.

The second case. A woman, age 21, was admitted into Hospital with a history of three weeks of pain and swelling of the left leg. Tenderness was elicited along the Posterior Tibial and Femoral vessels. The temperature was 100.6°F, and pulse 110. No other abnormalities were noted.

TREATMENT: She was kept in bed quietly with Ichthyol applications to the leg and foot and the foot of the bed was raised. The pain and swelling did not subside and on the fourth day after admission she was given M & B gr. XX a day for five days when she suddenly developed a high temperature (104°F.) and a rash which simulated Measles. This was attributed to the M & B. The latter was stopped immediately and the rash disappeared within three days. On the sixth day after the onset of the rash the temperature was normal again. By that time the swelling and pain in the leg had not yet completely subsided but the symptoms and physical signs were less marked. On the sixteenth day after admission, i.e. five and a half weeks after the onset of the illness the patient left the hospital - at her own request - apparently free from pain and swelling of the leg.

The second case was really kept as a control. It is obvious from a comparison of the two cases, although insufficient to draw any definite conclusions, that in the first instance the Lumbar Sympathetic block was of considerable benefit. The duration of the illness, as demonstrated by the rapid disappearance of the pain, was shortened, the
subsidence of the Oedema was rapid, the return of pulsation in the Dorsalis Pedis Artery was almost instantaneous and remained so.

In the first case the duration of the illness was twenty-three days - from the commencement of the illness to the discharge from the Hospital, (although he could have been discharged several days earlier). Case No. 2 lasted nearly six weeks although she could have still remained in Hospital for several days longer.

Vaso-Constriction in thrombophlebitis appears to play an important role in the manifestation of the signs and symptoms and lumbar sympathetic block should be instituted as a form of treatment in all cases.

Applying the same principle of Vaso-Constriction to Thrombo-Angiitis Obliterans, a lumbar sympathetic block suggests itself for relieving symptoms. The element of spasm in this tragic disease is much more obvious than in Thrombo-Phlebitis. The pathology differs considerably from ordinary Thrombosis, and the histological picture is also different.

The disease attacks chiefly young people between the ages of 20 and 40, is insidious in its onset, first the appearance of a Phlebitis Migrans and later the appearance of intermittent claudication of the calves of the legs or upper extremities. This is followed later by gangrene, commencing generally in one or other of the toes. In the past, several methods of treatment were adopted e.g. amputation at a high level, Arterio-Venous anastomosis, various types of exercises etc. Since the recognition of the spastic element in the condition - this being brought about by a reflex initiated in the veins by the phlebitis migrans which apparently takes the form of a thrombo-phlebitis - more attention has been directed towards relief of spasm. Vaso-dilators have been tried with apparently
apparently little success.

In this condition both artery and vein are affected — an arteritis and periarteritis, a phlebitis and periphlebitis. Since Buerger's original description of the pathological changes in arteries, he described the occurrence of similar changes in veins in a subsequent article. He says "in the veins, too, the thrombosis seems to take place in attacks, for we not uncommonly encounter various stages of the process in the two Venae Comites following an artery. (Figs. 14 and 14a). In the same field we see arteries and veins thrombosed. (i) Very recent closure of an artery showing hyalin thrombus in the centre and a peripheral zone of organisation bordering on the intima.

(ii) Another small artery completely occluded by an organising thrombus with vascularisation and canalisation.

(iii) Marked fibrosed thrombi in veins of a larger and smaller calibre. (Fig. 15 and 15a).

(iv) The remarkable collateral circulation as shown by the numerous thick walled blood vessels in the perivascular and matted fibrous tissue.

(v) Subcutaneous vessels. These were taken from just under the skin. They felt cord like and from the picture note their thickness and their almost occluded state. (Fig. 14a).

From the pictures it is obvious that the vein contains a much older thrombus which is almost completely fibrosed. (The cellular elements having practically disappeared). The arteries (Figs. 16 and 17) contain recent organising thrombus. The striking feature is the absolute and perfect preservation of the internal elastic layer, the healthy state of the media which shows rather thickened dilated and proliferating vasal vessels.

The ...
The organising thrombi in different sections show definite differences in age. The blocks taken from the lower parts of the vessels, e.g. Planter, show older thrombi than those taken from the Popletial. Haemosiderin is still present though in smaller amount.

All the coats of the vessels are infiltrated with cells chiefly round mononuclear cells and occasionally polymorphs are seen. (Fig. 19). There is no oedema and separation of muscle fibre, there is no necrosis and no haemorrhage. There is a marked proliferation of endothelial cells lining the vessel wall. These are seen leaving the margin and migrating into the thrombus where at first they become thicker, spindle shaped and more bulky, later they take on a more elongated form and the characteristics of fibroblasts. (Fig.20).

In addition the organising mass is crowded with plasma cells which also appear to be taking on the character of fibroblasts. (Fig.18). There are large phagocytes with brownish haemosiderin pigment. Occasionally a foreign body giant cell is seen near the periphery in the organising thrombus. (Fig. 20).

The vascularisation in the organising thrombus is profuse. The adventitia and media are also crowded with old dilated and new growing blood vessels. The latter are clearly seen penetrating deep into the media and are found even near the Internal Elastic layer. (Fig.19). Often we encounter downgrowths of vessels from the "Sublamellar Plexus" which link up with big blood channels in the organising thrombus. (Fig.20)

The vessels are thick walled, some small, some large and some elongated, most contain blood and are spread uniformly throughout the thrombus. Some show complete occlusion, their endothelial lining cells being quite prominent and often take on the form of mononuclear giant cells. The occlusion appears to take place as a result of concentric growth. Often these endothelial ...
endothelial cells are seen several layers deep in the wall of these channels. Once the vessels are closed these cells appear to assist in the fibrosis of the organising thrombus thus taking on a similar function of endothelial cells lining the vessel wall. (Fig.18).

The intervening tissue between the arteries and veins consists of thick layers of fibrous tissue which bind together artery, vein and nerves in a firm dense fibrous mass. In this mass of fibrous tissue the striking feature is the number of blood vessels present. On the whole the perivascular tissue is crowded with numerous large and small thick walled blood vessels much thicker and larger than found normally. Some show organising thrombi while others are clear. Surrounding these thick vessels are numerous round lymphocytic looking cells. These vessels constitute the collateral circulation when the main channels become occluded by the thrombotic process.

Thrombo-Angiitis Obliterans is a progressive disease and so long as the collateral channels which have been opened up can carry on their functions of supplying blood to the tissues (the major vessels having been obliterated) gangrene is averted, but when these smaller channels also become engulfed in the process, gangrene sets in.

The histological picture is totally different from the picture seen in an ordinary thrombosed vein.

<table>
<thead>
<tr>
<th>THROMBO-ANGIITIS OBLITERANS</th>
<th>PHLEBO-THROMBOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrence.</td>
<td>From Fifth Decade in Cardiac and Debilitated et</td>
</tr>
<tr>
<td>Signs &amp; Sym:</td>
<td>May have none.</td>
</tr>
<tr>
<td>Gangrene</td>
<td>No gangrene.</td>
</tr>
<tr>
<td>Elastic Layer</td>
<td>Fragmented &amp; degenerated.</td>
</tr>
<tr>
<td>Vessels</td>
<td>Thin; chiefly round margin.</td>
</tr>
<tr>
<td>In young between 20-40</td>
<td>Endothelial</td>
</tr>
<tr>
<td>Phlebitis Migrans &amp; intermittent claudication.</td>
<td></td>
</tr>
<tr>
<td>THROMBO-ANGITIS OBLITERANS</td>
<td>PHLEBO-THROMBOSIS</td>
</tr>
<tr>
<td>---------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td><strong>Endothelial &amp; Sub-Endothelial Layers</strong></td>
<td>Marked proliferation.</td>
</tr>
<tr>
<td>Media</td>
<td>Intact, proliferation of Vasal Vessels, hypertrophied muscle fibres.</td>
</tr>
<tr>
<td>Inflammatory Cells</td>
<td>Throughout all coats and perivascular tissue.</td>
</tr>
<tr>
<td>Collateral Circulation</td>
<td>Marked.</td>
</tr>
<tr>
<td>Haemosiderin</td>
<td>Present</td>
</tr>
<tr>
<td>Giant Cells</td>
<td>Present</td>
</tr>
<tr>
<td>Arteries &amp; Veins</td>
<td>Both thrombosed.</td>
</tr>
<tr>
<td>Vasal Vessels</td>
<td>Thick walled. <strong>Endothelium</strong> several layers deep.</td>
</tr>
<tr>
<td>Perivascular Tissue</td>
<td>Dense</td>
</tr>
</tbody>
</table>

The sections shown above are for the purpose of comparison, and were taken from a limb which was amputated at the mid-thigh because of the rapid spread of gangrene.

Can gangrene be averted and a limb saved and can the progressive nature of the disease be arrested?

The Etiology of the disease is as yet unknown. Some 38 consider it bacterial. Buerger himself has carried out experiments and transplanted the disease from man to man. Tobacco and ergot poisoning have been blamed. Not knowing the etiology it is difficult to see how the progress of the disease can be arrested. However, an attempt is at present being made to avert gangrene as long as possible and encourage collateral circulation. A certain amount of success has accompanied such attempts. The basis of the modern treatment is to relax the spastic condition of the vessels. Tobacco is forbidden, special graduated exercises are prescribed, the head of the bed is raised to assist the blood circulation by gravity.

Intermittent . . .
Intermittent venous occlusion, vaso-dilators such as alcohol, Papaverin and Aminophyllin are prescribed. Sympathetic block and even sympathectomy is now being considered.

The treatment of such a case has been under my supervision in the local hospital.

An Indian - the condition is very rare amongst this race, age 36, developed about one year ago typical signs of symptoms of Thrombo-Angiitis Obliterans. All forms of treatment were carried out, but gangrene of the third and fourth toes developed. Severe pain was controlled by Omnopon, and other opiates. The toes sloughed off and healthy granulation tissue covered the wounds. At the same time the pain ceased. Hardly had these wounds healed than the second toe showed signs of impending gangrene. At this stage a lumbar sympathetic block was considered advisable. This was done. The surface temperature of the foot and toes was taken before and after the block. There was a marked variation in temperature. Within five minutes the surface temperature of the big toe of the affected limb rose 3°F. The foot definitely became warmer and the patient volunteered the statement that the pain was disappearing gradually and that he was able to lie flat on his back quite comfortably - a thing which he could not do before, when sitting was the most comfortable position. That night he slept well without medication. The effect lasted for eighteen hours when the pain gradually returned. Thereafter intermuscular Aminophyllin injections were given every day and the ulcer on the second toe healed remarkably quickly. The treatment is still proceeding and in view of the beneficial effect of a block and vaso-dilator injections, sympathectomy is the next likely stage in the treatment.
Out of the fifty-one cases which showed thrombosis of the veins, four had phlebitis, the rest showed no inflammatory change in or around the vessels. In the latter, if the thrombus was recent, it was of the red type, lightly adherent in parts to the wall of the vessel where commencing organisation was apparent. A thrombus in a vessel is not tolerated; it acts as a foreign body, and reactive changes leading to organisation is soon set up. Thus the extent to which organisation is present will more or less indicate the age of the thrombus. The process of organisation is well illustrated in the photographs shown further on. Thus taking a normal vessel where the coats show no abnormality, a very recent red thrombus is a homogenous hyaline and acidophile (as shown by haematoxylin and eosin) mass filling the vessel and attached at one point or another to the vessel wall. In the early stages elongated or spindle shaped cells are seen migrating from the subendothelial layer into the clot, some of these cells are even seen passing through the thick wavy elastic lamella which is often found fragmented in parts. These spindle shaped cells are often seen arranged in layers at right angles to the intima, i.e. indicating a growth into the clot from the endothelial, subendothelial and possibly from the fibrous tissue in the area of the "Sublamellar Plexus of Short". Between these cells are small bundles of collagen fibres in which empty spaces are seen. These spaces in the early stages are small clear often slit like and at first have no lining. Soon however, bulky spindle shaped cells, some showing long protoplasmic processes are seen in the process of migration towards these spaces and encircle them. As soon as they have arranged themselves they become thinner, more elongated and form an endothelial lining to the clear space. These apparently now become new blood vessels. Both media and adventitia
adventitia are absent. At first no elastic tissue appears to be present. As the organisation proceeds elastic tissue makes its appearance in the wall of these thin walled vessels.

During the early stage of organisation the organising area is very cellular, consisting of fibroblasts, angioblasts and plasma cells. The organisation proceeds from the margin towards the centre. In time the area round the edge becomes less cellular, more fibrous, less vascular, whereas towards the centre the active forces of organisation are in full swing. When the whole process is complete the lumen of the vessel is completely occluded by a fibrous layer, with larger or smaller spaces lined by a single layer of flattened endothelial cells. This is known as the process of canalisation, and by this means the circulation is somewhat re-established.

A clot has a natural tendency to retract by virtue of the contractility of the fibrin as well as by the mechanical action of the platelets (Tocantins). In the process of contraction large spaces are formed. These soon take on an endothelial lining, the cells being derived from the reflection of the endothelium lining the vessel wall. The trabeculation so often encountered in old organised thrombosed veins is constituted as a result of the contraction of the original clot, canalisation of the thrombus and separation of the lumen into separate compartments by these fibrous bands. The vein in these cases is thick, distorted and cord like, the perivascular tissue is fibrosed and the vein matted firmly to the corresponding artery. The nerve is often found included in this fibrosed mass.

The Capillary vessels in the thrombus which are so conspicuous around the margin are derived from the Vasa Vasorum. They enter the thrombus at the point of attachment to the wall by a descent of angioblasts. According to Short there is an ingrowth of capillaries from the "Sublamellar Flexus". These
vascular vessels anastomose with the large endothelial lined spaces - the only instance where such communication takes place. (Fig. 20).

Another important factor when considering the age of a thrombus is the presence of iron or haemosiderin pigment. The pigment is yellowish brown and gives the Perl reaction with H.CI. and Potassium Ferrocyanide. It is found in conditions where there is blood destruction; i.e. in haemorrhage where there is a local destruction of red cells, and in haemolytic disease where there is a general destruction. In thrombosis the red blood corpuscles break up and the iron is taken up by histocytes (reticuloendothelial cells). It is these pigment laden cells that we see in the pictures. Eleven cases were found to contain this pigment. All were found to be in cases where the process of organisation was well advanced, but not replaced completely by fibrous tissue. It is found chiefly around the advancing organising margin, the deeper the organisation proceeds, the deeper do we find the pigment. In very recent thrombi with little organisation or complete and well developed organised thrombi of considerable duration, no pigment was found. This indicates that some time must elapse after a thrombus had formed before the pigment makes its appearance and that when the organisation of the thrombus is complete, the iron pigment has been completely removed and no trace is left.

A knowledge of the time of the appearance and disappearance of iron pigment in a thrombus would be of considerable help in assessing the age of a thrombus. No such data however, has come to my knowledge. Professor Mackintosh, of the Forensic Medicine Department of the University of the Witwatersrand, Johannesburg; however, informs me that from his own observations in medico legal cases which come to autopsy as a result of injury to the brain where haematomata are responsible or contribute to the cause of death; the earliest appearance of haemosiderin
haemosiderin in a thrombus is on the seventh day after injury and the longest period when the pigment is still found to be present is three months after the injury. Prior to the seventh day and subsequent to the end of the third month no pigment is found. If we were to take the age of a thrombus in a vein within these limits then the so-called recent thrombi fall within the first week, those with pigment between the first week and the end of the third month, and old organised thrombi without pigment beyond the third month.

The amount of pigment present could also assist in assessing the age of a thrombus. As the pigment is being continuously and rapidly removed, the greater the amount of pigment present the younger the thrombus. The amount would however vary with the type of thrombus. In a red thrombus one would expect a greater amount of pigment than in a mixed and very little if any at all in a white thrombus. Thus in assessing the age of a thrombus one would have to take into consideration the following:

(i) The amount of organisation, i.e. the amount of fibrous tissue and cellularity.

(ii) The presence, absence and amount of haemosiderin pigment.

(iii) The type of thrombus - white mixed or red.

(iv) The state of the vein. A hard distorted cord like, trabeculated vein with dense perivenous connective tissue binding together artery vein and nerve is an obvious indication of old standing thrombosis.
An analysis of the condition in which the thrombi were found might suggest a possible etiological factor in thrombosis. For this purpose thrombi are classified into three groups. (a)

(a) Recent. Under this heading are included thrombi which microscopically show a hyalinised thrombus, commencing organisation and no haemosiderin pigment.

(b) A recent thrombus superimposed on an older thrombus, the latter containing haemosiderin pigment or is completely fibrosed.

(c) Old organised and canalised thrombi.

<table>
<thead>
<tr>
<th>TABLE VII.</th>
<th>Recent Th.</th>
<th>Old</th>
<th>Recent Th.</th>
<th>Old</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table I. (Heart Group)</td>
<td>7</td>
<td>7</td>
<td>2</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Table II (Carcinoma)</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Table III (Arterial)</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Table IV (Miscellaneous)</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Table V (Operative)</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

This table shows that sixteen cases with thrombosis in the Heart Group, seven belong to Group (a), seven belong to Group (b) and two belong to Group (c).

In Table II:

- fourteen cases belong to Group (a),
- two cases belong to Group (b) and
- one case belongs to Group (c).

In Table III:

- two cases belong to Group (a),
- four cases belong to Group (b) and
- one case belongs to Group (c).

In Table IV:

- four cases belong to Group (a),
- three cases belong to Group (b) and
- one case belongs to Group (c).

In Table V:

- one case belongs to Group (a),
- one case belongs to Group (b).
We can simplify Table VII by considering (a) alone and (b) and (c) together. We thus have:

**TABLE VIII.**

<table>
<thead>
<tr>
<th>Table</th>
<th>Recent Thr.</th>
<th>Old Thr.</th>
<th>No of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Heart Group)</td>
<td>7</td>
<td>9</td>
<td>16.</td>
</tr>
<tr>
<td>II (Carcinoma)</td>
<td>14</td>
<td>3</td>
<td>17.</td>
</tr>
<tr>
<td>III (Arterial)</td>
<td>2</td>
<td>5</td>
<td>7.</td>
</tr>
<tr>
<td>IV (Miscellaneous)</td>
<td>4</td>
<td>4</td>
<td>8.</td>
</tr>
<tr>
<td>V (Operative)</td>
<td>1</td>
<td>1</td>
<td>2.</td>
</tr>
</tbody>
</table>

This table shows that of the sixteen cases with thrombosis in:

- Table I, seven belong to Group (a), nine belong to Groups (b) plus (c).
- Table II, fourteen belong to Group (a), and three belong to Groups (b) plus (c).
- Table III, two belong to Group (a) and five belong to Groups (b) and (c).
- Table IV, four belong to Group (a) and four belong to Groups (b) and (c).
- Table V, one belongs to Group (a) and one belongs to Groups (b) and (c).

The number of old organised thrombosed veins in Tables I, III and IV, is somewhat striking. From these figures it is obvious that patients suffering from Heart and Arterial disease are liable to thrombosis of their leg veins, which does not manifest itself clinically and does not appear to interfere seriously with their state of health. They walk about and carry on their normal work as best as they can until the heart fails, when confinement to bed encourages a thrombosis which becomes superimposed on the old organised thrombus. A possible pulmonary embolus assist in the final failure of the heart.

The Carcinomatous Group (Table II) is in striking contrast to the Heart and Arterial Groups. Fourteen out of the seventeen cases show recent thrombosis and only three cases have old organised thrombi.
The conclusion that one must inevitably arrive from the above figures is that patients suffering from heart disease are liable to thrombosis of the leg veins by virtue of the chronicity of the condition and the repeated confinement to bed due to circulatory failure. Myocardial weakness and insufficiency leads to slowing of the circulation, muscular activity is lessened and the blood stream in the leg veins is retarded. Under such conditions thrombosis is encouraged. In the early stages of the disease, however, the latent power of recuperation of the myocardium is great and the patient after a prolonged stay in bed recovers as a result of myocardial compensation. By this recovery the contracting power of the heart, and the velocity of the blood stream is increased and the circulation is restored, thus preventing a continuation of the thrombotic process. The part of the vein which did thrombose, organises and canalises. Such attacks recur, the thrombosis proceeds upwards in the leg in the direction of the blood stream and may again be stopped by recovery. Sooner or later the final stage is reached, when the heart has exhausted all its compensatory reserve and the patient is confined to bed dying from circulatory failure. Thrombi in the final stages are superimposed on the old organised and canalised thrombosed veins. This is clearly shown in Table VII where seven out of nine cases show recent thrombi superimposed on old organised thrombi. Seven cases in the Heart Group show recent thrombosis only, thus indicating, that these developed in the final stage of the disease, apparently the previous attacks were not severe enough to cause circulatory failure and for thrombosis to develop.
The Arterial Group (Table III) shows five out of seven old thrombosed veins. If one takes into consideration the fact that arterial disease (apart from the local effect and the relationship of vein and artery which we will discuss later) also affects the Coronary Arteries, which owing to change atheromatous/and gradual narrowing of the lumina depletes the myocardium of an adequate blood supply with consequent myocardial fibrosis. The latter state of the heart leads to myocardial weakness and circulatory retardation which is a potent contributory factor in encouraging thrombosis if we accept the school of thought led by Aschoff.

The Carcinomatous Group (Table II) with its fourteen cases of recent thrombosis and only three of the old organised type is of interest in so far that it shows that the thrombosis is of a terminal nature, being due to debility causing a terminal cardiac and generalised weakness with circulatory retardation. This is borneout by an investigation of the clinical history. Patients suffering from malignant disease are able in the early stages to move about, their hearts are generally sound, the pulse is good and the blood flow fairly rapid. It is only in the terminal stages of the disease that pain, exhaustion and cachexia compels such patients to take to their beds.

Has the primary site of malignant disease any bearing on thrombosis?

An analysis of the Carcinomatous Group regarding the relation of the site of malignancy to thrombosis reveals the following data:

<table>
<thead>
<tr>
<th>Thrombosis</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above Diaphragm</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Abdomen</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Pelvis</td>
<td>6</td>
<td>9</td>
</tr>
</tbody>
</table>

This
This table shows that thrombosis occurs more often where malignancy is below the diaphragm and most often when it is in the pelvis. But eight out of fifteen (53.3%) cases above the diaphragm is rather a large number to pass over unaccounted for and an analysis of the eight cases reveals that four (i.e. 1512, 1514, 1531 and 1544) show metastases in the abdomen, and the other four (i.e. 1524, 1553, 1562 and 1584) show in three cases direct evidence of cardiac insufficiency and one extreme cachexia with treatment by X-ray, the latter according to some authorities encourages thrombosis.

Thus the conclusion that one can derive from this table is that malignant disease in the pelvis and abdomen has a direct bearing on thrombosis of the veins in the lower extremities. This is brought about in all probability by direct pressure on the walls of the veins causing retardation of the blood stream. Another possibility is injury to the endothelial lining of the veins in the pelvis by apposition of the walls due to pressure and a retrograde thrombosis down the Femoral and Posterior Tibial veins. This latter possibility is analogous to the pressure sustained by the veins in the calves of the legs when the patient, who is confined to bed and is lying in the recumbent position with his calves pressing against the mattress.

In the Arterial Group (Table III) out of thirteen cases, seven showed thrombosis (53.8%). The striking feature here is that in five out of the seven cases the veins showed thrombosis of old standing, viz. fibrosis, canalisation, trabeculation and even phlebolith formation. In no thrombus was haemosiderin found. There were only two cases of recent thrombosis. In one 1515, there was an outspoken phlebitis of the small Saphenous and in the second 1528, a recent thrombosis in the muscle veins only. In the latter calcification of a thickened intima in the Saphenous vein was found - a rare occurrence and the only case noted.
noted. According to this table a definite relationship must exist between arterial disease and thrombosis of veins. The nature of such relationship will be discussed under Phleboscle-
rosis.

In the Miscellaneous Group (Table IV), eight out of the twentytwo cases showed thrombosis. The cases in this group fall under infection, exsanguinaion, or debility, all of which encourage thrombosis. It is interesting to note that there were four surgical and four medical cases. Six cases out of the eight consisted of: four cases of Peritonitis, and two cases of haemorrhagíc cystitis with a fair amount of sepsis round the bladder. This would lead one to support the view that as a result of the absence of abdominal respiratory movements (in localised infection in general and peritonitis in particular abdominal respiration is arrested) the circulation is slowed and thus thrombosis encouraged.

Surgical.

In this group there are two cases only. Both were apparently good operative risks. Both died on the fifth day after the operation from massive Pulmonary Embolism. In both cases the leg veins were thrombosed. Both patients were stout. In the one case 1574, a Cholecystectomy was done and in 1590 a Nephrolithotomy. The heart in each case showed no undue abnormality.

Actually there were more than two operative cases, but owing to the fact that operation was undertaken as a pallia-
tive measure the cases were placed in their respective groups; i.e. under the primary and main causes of the patients illness. Thus in Table II, out of thirtyone cases eight were treated surgically, six of which showed thrombosed veins and the striking feature in all the cases was the fact that the thrombi were of a recent nature, thus indicating that certain definite factors operate in the production of thrombosis after surgical treatment in
in chronic and debilitated cases. In two cases only were emboli found in the lungs.

In Table IV there are four surgical cases, all of which had thrombosed veins, the thrombi in three instances were recent, superimposed on old organised thrombi, and one of a recent nature only.

Thus altogether there were twelve surgical cases, ten of which showed thrombosis, excluding Group V with two surgical cases.

In Table II (Carcinomatous) 8 surgical with 6 thrombosis.

In Table IV (Miscellaneous) 4 surgical with 4 thrombosis.

The conclusion is that in cases suffering from carcinoma, operative procedure of a palliative nature has an incidence of 75% of thrombosis in cases which show no sepsis, and that where sepsis in the peritoneal cavity or pelvis is present the development of thrombosis in the legs is according to the figure 100%.

In Table III there were no surgical cases but in one case, 1565, the cause of death was a massive pulmonary embolus. This was attributed to Intermittent Venous Occlusion, a form of treatment undertaken in peripheral vascular disease, the principle of which is based on:

(a) The mechanical filling and stretching of the vascular tree, thus encouraging collateral circulation.

(b) The chemical vaso-dilatation as a result of reactive hyperaemia following the release of the constriction, thus saturating the tissues and venous blood with oxygen.

(c) The increase in capillary pressure and

(d) The increase in the flow of lymph.

(De Takats, Hick and Coulter)

This method of treatment has been applied with little discrimination in vascular diseases especially in Thrombo Angiitis Obliterans and Arterio-Sclerosis.

The . . .
The danger of intermittent Venous occlusion - a process in which veins are compressed no matter how lightly even to 40 m.m. of mercury and relaxed at regular intervals of one to two minutes for half an hour several times a day - can easily be understood if we remember that very recent thrombi, lightly attached to the wall can be dislodged from inflamed and degenerated vessels by repeated manipulation. Case 1565 illustrates this point.

A female, age 76, was admitted to hospital suffering from transient hemiplegic turns for 12 years. She had intermittent claudication for 7 to 8 years. The arteries were markedly sclerotic and there was impending gangrene of the right great toe. She was treated by intermittent venous occlusion, the pressure being applied in the middle of the thigh. Thirteen days after admission she suddenly collapsed in the bath room, became cyanosed and breathless and died within a few minutes. At autopsy both lungs showed large as well as small pulmonary emboli in different stages of organisation - thus indicating repeated pulmonary embolisation for days prior to the final massive attack.

In the lower extremities the left Femoral, Posterior Tibial and Plantar veins were thrombosed whereas on the right side there was no thrombus in the Femoral and the upper part of the Posterior Tibial - the main thrombus apparently having become dislodged by the treatment and carried away to the lungs plugging the Pulmonary Arteries.

In view of this method of treatment being universally recognised, the danger of thrombosis and pulmonary embolism must be emphasised. Buerger in his article on Veins suggested a test "by means of which we could learn something about the sufficiency of the deep veins". He put forward this suggestion in connection with Arterio-Venous Anastomosis. The test could
could, however, be equally well applied prior to instituting intermittent venous occlusion, as an unhealthy vein such as one which shows a marked intimal proliferation or an old thrombotic partially occluded vein, may have its endothelial lining damaged during the process of compression and relaxation, thus creating an injured surface on which a thrombus could easily develop. The test suggested is as follows:

The limb is allowed to hang and watched for the advent of erythema. When a fair degree of cyanosis has become established (after about 5 to 10 minutes), the veins are obliterated above the knee by means of a bandage. The limb is then raised high and the bandage loosened just enough to remove pressure from the deep but not from the superficial veins. If the cyanosis is slow in disappearing or fails to disappear, it may be concluded that the function of the deep veins is impaired.

From our point of view if a vein is partially or completely occluded it is an unhealthy vein and liable to damage by the least trauma, i.e. careless repeated compression. If intermittent venous occlusion is absolutely essential for treatment, we would be in a position to judge by means of this test, what pressure to use below 60 to do the least amount of damage to the diseased veins or at least try to adopt methods for the prevention of thrombosis.

INCIDENCE.

The incidence of thrombosis varies widely according to different investigators and the method used for investigation, whether clinical or post mortem. The incidence of 51% is high compared with the figures given by other authors. Sproul in 4258 autopsies found 617 or 14.4% thrombosis in "heart, arteries or veins". Dietrich (quoted by Aschoff) during the last war found in 1400 autopsies, 11% of the cases thrombosed in association with sepsis. Wantock (quoted by Ochsner and DeBakey) found 7.7% thrombosis (367 cases in 4729 autopsies). Burke found
in 2613 autopsies, 648 cases or 24.7% with thrombosis, of which 427 were medical, 195 surgical and 26 miscellaneous.

The nearest approach to my figures are those shown by the latter. Medical cases showing 16%. This marked discrepancy between my figures and those of others might be accounted for by the greater number of medical cases that came to autopsy under my observation and also because of the chronic sick home that is attached to the hospital.

**AGE.**

Tables showing age incidence in the different groups.

**Table X.**

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Heart</th>
<th>Carcinoma</th>
<th>Arterial</th>
<th>Misc.</th>
<th>Operative, included</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40, 3</td>
<td>31-40, 0</td>
<td>31-40, 1</td>
<td>31-40, 0</td>
<td>0</td>
<td>31-40, 4</td>
</tr>
<tr>
<td>41-50, 2</td>
<td>41-50, 4</td>
<td>41-50, 0</td>
<td>41-50, 1</td>
<td>0</td>
<td>41-50, 7</td>
</tr>
<tr>
<td>51-60, 7</td>
<td>51-60, 4</td>
<td>51-60, 0</td>
<td>51-60, 4</td>
<td>51-60, 2</td>
<td>51-60, 17</td>
</tr>
<tr>
<td>61-70, 2</td>
<td>61-70, 3</td>
<td>61-70, 0</td>
<td>61-70, 2</td>
<td>0</td>
<td>61-70, 7</td>
</tr>
<tr>
<td>71-80, 2</td>
<td>71-80, 7</td>
<td>71-80, 5</td>
<td>71-80, 1</td>
<td>0</td>
<td>71-80, 15</td>
</tr>
<tr>
<td>80+</td>
<td>80+</td>
<td>80+</td>
<td>80+</td>
<td>1</td>
<td>80+</td>
</tr>
</tbody>
</table>

**Table XI.**

**Table XII.**

Chart for Table XI.
Tables X, XI and XII show the incidence of thrombosis in my series. It will be noticed that there are no patients under 30 years showing thrombosis. The majority of cases fall between 51 and 60 years. This agrees with the various investigators through Sproul gives the highest incidence in the sixth decade. The 71 to 80 group shows a remarkably high number, i.e. 15. This high incidence is due to the high incidence of the aged patients in the chronic sick home who have passed the age of 70 years. The low incidence in patients beyond 70 years is attributed by other authorities to the fact that few people live beyond that age and also because few undergo operation. Of the individual groups the carcinomatous group contributes the highest number beyond the age of 70, the arterial next with 5. The heart group shows the highest incidence in the fifth decade. The average age is shown in Table VI.

**SEX.**

Table XIII showing sex incidence.

<table>
<thead>
<tr>
<th></th>
<th>Examined</th>
<th>Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Heart (Table I)</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Carcinoma (Table II)</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Arterial (Table III)</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Miscel. (Table IV)</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Operative (Table V)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
<td><strong>40</strong></td>
</tr>
</tbody>
</table>

In the 100 cases examined, 60 were males and 40 females. Thrombosis occurred in 31 males and 20 females. The proportion of males to females corresponds to the proportion of cases examined. Sex therefore does not appear to have a direct influence on the incidence of thrombosis.

**Anaesthesia:** Anaesthetics as a direct factor predisposing to thrombosis was not investigated but as indicated above it does not appear to play a part.

Dehydration
Dehydration and Viscosity of the blood is recognised as a cause of thrombosis. Thus sweating after operations, incessant vomiting, diarrhoea, haemorrhage, all tend to increase the viscosity of the blood and thus slow the circulation which predisposes to thrombosis.

Polycythemia Vera in which the viscosity of the blood is increased, predisposes to thrombosis. Portal thrombosis is often found as a complication of this disease and according to Harrop and Wintrope, the viscosity of the blood is 5 to 8 times that of normal blood and is due to an access of red cells over plasma. 11.5 millions of red cells are required according to these authors, to pack completely 1 c.c. of blood and nobody could live with his or her blood consisting of all cells and no plasma. In a case that came under my observation the number of red cells per c.c. was 10 million and the Portal and leg veins were thrombosed. The clinical history as well as the autopsy finding is given as an illustration.

Case 1639: A woman, aged 62, was admitted into hospital with a history of weakness, vomiting and diarrhoea for two months prior to admission. Frequency of micturition - every half hour - with pain and haematuria. There was ascitis. Six months previously she had a stroke with a right hemiplegia from which she completely recovered. Five months previously had an attack of biliary colic and jaundice. Liver and spleen were enlarged. Blood pressure 170/120 and blood count 8,500,000. The last count - 4 days before death, was 10,000,000.

Autopsy: The right coronary artery showed occlusion by organising thrombus. The Posterior Tibial Veins of both legs were thrombosed.

Lung.
These showed multiple small emboli in the secondary and tertiary branches of the pulmonary arteries.

The Liver, was large, firm and was adherent firmly to the tissue below and the diaphragm above. On section the right lobe showed dark areas mottled with pale yellow areas almost as if it were infarcted. The Portal veins were thick and some showed complete occlusion by organised thrombus.

Microscopic Examination.

The Posterior Tibial Veins and Portal Veins contained thrombi in a state of organisation, some older and some more recent.

The Bone Marrow showed Normoblastic and Myelocytic reaction.

**PROTHROMBIN CONCENTRATION.**

Clotting of the blood depends on the formation of thrombin which in turn depends on the presence of Prothrombin. According to Quick, the clotting time is proportional to the concentration of prothrombin provided that thromboplastin, Calcium and Fibrinogen are made constant. On this basis he developed his quantitative test for prothrombin in the blood. He evolved a principle that the coagulation time of the blood or plasma can be employed as a measure of the prothrombin concentration if the other factors in the clotting process are made constant.

According to his chart blood or plasma containing

<table>
<thead>
<tr>
<th>Prothrombin concentration (%)</th>
<th>Clotting time (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>11-12 seconds</td>
</tr>
<tr>
<td>80%</td>
<td>13½</td>
</tr>
<tr>
<td>60%</td>
<td>15½</td>
</tr>
<tr>
<td>50%</td>
<td>17</td>
</tr>
<tr>
<td>40%</td>
<td>19½</td>
</tr>
<tr>
<td>30%</td>
<td>21½</td>
</tr>
<tr>
<td>20%</td>
<td>23½</td>
</tr>
<tr>
<td>10%</td>
<td>26½</td>
</tr>
<tr>
<td>5%</td>
<td>28½</td>
</tr>
</tbody>
</table>

Bearing this in mind an attempt was made to find out whether patients suffering from carcinoma show any alteration in the prothrombin concentration in their blood. Fourteen cases were investigated.
investigated, nine cases suffering from carcinoma; two from kidney disease, two from cholecystitis - the latter were about to undergo surgical treatment, and one suffering from chronic T.B. Osteitis of the right foot. The procedure closely followed that adopted by Quick.

**Material Used.**

1. \(\text{M/10 Sod. Oxalate} \) (1.34 gms. anhydrous Sod. Oxalate dissolved in 100 c.c. of distilled water).

2. \(\text{M/40 Calcium Chloride} \) (1.11 gms. of anhydrous calcium chloride dissolved in 400 c.c. of distilled water).

3. **Thromboplastin.** Fresh rabbits brain after removing all blood vessels by stripping off the pia was masserat in a mortar and a little physiological Sod. Chloride solution was added to it. 4.5 c.c. of blood was drawn from a patient and mixed immediately with .5 c.c. of Sodium Oxalate solution. The blood was then centrifuged for 10 minutes and the plasma used. Four small tubes placed in a stand and immersed in a water bath at 37°C were taken and two drops of plasma were placed in each of the test tubes and a further two drops of thromboplastin added to each. With a stop watch ready two drops of calcium chloride were added and the time taken by the plasma to clot gave the measure of prothrombin concentration in the plasma and thus a measure of the coagulation of the blood was obtained.

The average time recorded for the plasma to clot in the fourteen cases were:

<table>
<thead>
<tr>
<th>Carcinoma</th>
<th>Kidney</th>
<th>Cholecystitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>Hydrenephrosis</td>
<td>20.3 secs.</td>
</tr>
<tr>
<td>Breast</td>
<td>Pharynx</td>
<td>16.0</td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td>19.5</td>
</tr>
<tr>
<td>Pharynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

According to Quick's chart these findings show a prothrombin concentration below 50%, an indication of a tendency to bleeding rather than a tendency to clotting.

(A patient may lose as much as 50% of his prothrombin concentration before its effect on the blood is manifest). I hesitated to accept my findings as a true reflection of the prothrombin concentration but on enquiry from different workers in the Haematological Department I was informed that almost invariably
readings of the clotting time by the same method is generally between 20 and 21 secs. I am not in a position to account for the wide margin of error; but I can only conclude from these findings that the prothrombin concentration in cases of cancer in general bears no relation to the thrombosis so frequently found at autopsy.

One must bear in mind however the fact that extensive damage to the liver by secondary carcinoma or chloroform anaesthesia causing temporary damage to the liver (the latter plays an important part in the synthesis of Prothrombin) alters the prothrombin concentration in the blood. Under such circumstances the tendency should be towards haemorrhage rather than thrombosis. Jaundice - due to liver damage, obstruction to the bile flow by tumour or other conditions, is a recognised condition causing a haemorrhagic diathesis and one would not expect a thrombotic condition of the veins. Out of six cases with marked jaundice, however, five showed thrombosis of the leg veins. The explanation must be looked for in other directions such as exsanguination, dehydration, cachexia and circulatory retardation.

Table XIV - Thrombosis in Cases of Jaundice.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Disease</th>
<th>Condition of Liver</th>
<th>Other Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1502</td>
<td>Carc. of Stomach</td>
<td>Obstruction due to tumour.</td>
<td>Haematemesis.</td>
</tr>
<tr>
<td>1500</td>
<td>Cirrhosis of Liver.</td>
<td>Cirrhosis</td>
<td>Ascitis.</td>
</tr>
<tr>
<td>1531</td>
<td>Retroperitoneal Lymphosarcoma</td>
<td>Obstruction due to tumour</td>
<td>Severe vomiting for three weeks.</td>
</tr>
<tr>
<td>1606</td>
<td>Cirrhosis of Liver.</td>
<td>Cirrhosis (No thrombosis).</td>
<td></td>
</tr>
</tbody>
</table>

Sproul found a high incidence of venous thrombosis in cases associated with carcinoma of the pancreas and puts forward ...
the suggestion that the increased coagulability of the blood is due to the lack of digestion of fat resulting in an increased absorption of Vit. K. from the intestines. (Vit. K. is a fat soluble substance and is absorbed from the intestinal tract in the presence of bile and is responsible for the level of prothrombin in the blood.)

**CHANGES IN THE BLOOD.**

No blood investigation (apart from the prothrombin concentration) was carried out to establish some of the factors known to influence its coagulability. Thus it is considered that an increase in polymorphs, platelets and a disturbance in the Albumin-Globulin ratio contribute at one time or another towards thrombosis. The relationship of albumin to globulin is changed, the shift being towards a relative increase in globulin, there being an actual decrease in albumin. The albumin fraction is most important in relation to oedema. Nutritional oedema is often encountered among the Bantu in South Africa, this being due to lack of intake of proteins. The critical level appears to be 2.5% (normal 4.6 to 6.7%) below which oedema appears. In the chronically ill person, as for example in Cachexia due to malignant disease, is it not possible that the lack of intake of food in general, thus reducing the protein intake, might give rise to this relative increase in globulin which favours the agglutinability of platelets and other formed elements of the blood7. As an etiological factor in thrombosis in general this might possibly be the case, but as a factor in thrombosis of the lower limbs only this must be discounted. For if this were the case, one would encounter more often a generalised thrombosis in the venous system, the blood having acquired an increased tendency to coagulation. In my series no generalised thrombosis was found (except in cases of polycythemia Vera and renal vein thrombosis). If, however, there are other more potent factors, such
such as phlebitis, retardation of the blood stream, endothelial
damage, then it is possible that an alteration in the globulin
concentration in the blood plasma causing a less stable colloid
equilibrium might contribute towards a thrombosis.

**THE SITE OF THROMBOSIS.**

Thrombosis can occur in any vessel in any part of the
body provided the local factor is there. In all cases investigat-
ged, the thrombosis was found in the lower extremities and
almost invariably in both legs. The Posterior Tibial and
muscular tributaries were involved, never were the anterior
veins found thrombosed. Often the Plantar veins were involved
as well, but in only a few cases were the latter dissected and
investigated. The Femoral, Iliacs, Infer. Vena Cava, prostatic
as well as the ovarian veins were frequently found involved.
In several cases the muscular branches of the calves of the legs
were found thrombosed without any evidence of thrombosis in the
Posterior Tibial Veins. Where the Femoral vein was found
thrombosed the Posterior Tibial and its muscular tributaries
were likewise thrombosed. In no instance were the Femoral
veins alone found thrombosed. Neumann found that 75% of
thrombosis in the thigh veins were combined with the leg veins
and he asserts that a solitary thrombosis of the Femoral vein
never exists alone. He further claims that thrombosis of the
thigh and calf veins without plantar thrombosis is less frequent.
Most thrombi according to him are found in the legs and feet.

It has already been stressed that circulatory retardation
is one of the most important factors in precipitating Venous
thrombosis. Such retardation can be brought about apart from
the slowing of the circulation due to heart insufficiency by:

(i) Recumbency.
(ii) Immobility.
(iii) Hypnoeas after an anaesthetic.
(iv) Increased abdominal tension due to meteorism
     or tight bandaging.
(v) Pressure of tumour on veins, and
(vi) Anatomic.

All except (vi) have been discussed.
The anatomic factors predisposing to thrombosis can be appreciated if the relationship of the veins in the abdomen and the lower extremities to other structures is examined.

The flow of blood from the lower extremities to the heart is propelled chiefly by muscular action and is assisted by negative pressure within the thorax. Any interference with the muscular activity; any pressure on the veins or hypopnoea, will cause retardation of the venous flow. The Inferior Vena Cava is formed by the union of the two common Iliacs on the right side of the fifth Lumbar Vertebra and ascends on the right side of the Aorta. The right common Iliac Artery crosses the left common Iliac vein at almost a right angle. The Hypogastric arteries cross the external Iliac veins. There is thus a possible pressure exerted on the veins, particularly on the left common Iliac vein at the point where the artery crosses it. In addition the presence of the Sigmoid Colon and Rectum on the left side might exert pressure on the left common Iliac vein. (This relationship is a possible source of infection setting up a thrombo-phlebitis).

In the Femoral region we have Paupart's Ligament which can exert pressure on the veins, particularly when the patient is in the Fowler's position. In addition numerous large and small tributaries enter the Femoral vein and the external Iliac veins in different directions confusing the current by "backward flowing and eddy formation". The valves in these areas are large. They assist normally the return flow of blood by preventing its reflux. When there is a widening of the veins, as for example in varicosities, the blood stream is slow and there is a tendency towards a deposition of blood platelets near the valve. (Figs. 21 and 22). Lower down, in the Popliteal region the popliteal vein is liable to compression particularly when the legs are flexed at the knee. Here too, in the upper part of the calf muscles several plexuses drain the muscles and enter the popliteal vein
where similar confused currents occur. Lastly when the patient is in the recumbent position, the calves of the legs are pressed against the mattress, not only retarding the blood flow but compressing the veins and possibly injuring the endothelial lining.

It is practically unanimously agreed that thrombosis takes place more often on the left side than on the right due to the difference in the anatomical relationship of the veins on the two sides. Thus Payne in an analysis of 86 cases of Femoral Thrombosis found 64 unilateral and 21 bilateral. Of the former 46 were on the left side and 18 on the right. In my series practically all were bilateral. The two cases with fatal Pulmonary Embolism following operation show bilateral thrombosis in the Posterior Tibial veins and muscle tributaries. In the absence of microscopic examination however these would have been recorded as unilateral. Thus 1574 showed a recent thrombus in the left distal half of the Femoral down to the Plantar vein, whereas the right vein showed no thrombosis. Microscopic examination of the right calf veins however showed recent thrombosis. In Case 1590 the right veins were thrombosed from the Plantar to the middle of the Femoral, but the left showed no thrombosis. Microscopic examination however revealed on the left side old thrombosed organised and canalised veins.

The rest of the series showed bilateral thrombosis in the Posterior Tibial and calf muscle veins. Often the muscular veins showed evidence of thrombi being older than those in the Posterior Tibial or Femoral veins.

The evidence thus produced indicates that in these types of cases, particularly those belonging to the heart and carcinomatous groups (Tables I and II) the thrombosis is bilateral, that the calf muscles appear to be the first to suffer.
suffer, and that from there thrombosis spreads with the blood flow to the main trunks they drain in, and if favourable conditions exist spread upwards and downwards. (Fig. 23). The picture of the Posterior Tibial vein, Case No. 1572, is of interest. (Fig. 24). Four separate small round thrombi of different age are seen. These have apparently converged to the main vein from four separate tributaries and have continued upwards with the stream. It has been pointed out that whenever a thrombus meets a rapid stream, further thrombosis is discouraged. In cases of debilitating diseases however the blood stream is generally slow in the lower extremities and the thrombus once commenced continues to spread.
CHAPTER III.

PHLEBO- or VENO-SCLEROSIS.

A striking feature in this investigation has been the extraordinary number of veins encountered showing intimal thickening and narrowing of their lumina. Two types were found:

(1) The small Saphenous was found on innumerable occasions thick and cord-like with a very narrow lumen which occasionally was almost occluded. (Fig. 25)

Histological Examination.

The entire circumference of the vein is involved. Finger-like projections are found protruding into the lumen thus narrowing it. There is no demarcation between intima and media by an internal elastic layer. Instead there is a definite boundary between the media consisting of circular muscle fibres and the projections consisting of bundles of longitudinal muscle, surrounded by thick and dense fibrous tissue. (Figs. 26 & 27). These muscle bundles reach the apex of each projection which is lined by a single layer of flattened endothelium. Scattered sparsely between the muscle bundles and the connective tissue are thin wavy strands of elastic tissue. (Fig. 28). There are no well marked blood vessels, but numerous clear cleft-like sinusoids, lined by flattened endothelial cells in the connective tissue between the muscle bundles.

The Media is thick, consists of circular muscle fibres separated by fibrous tissue. Vasal vessels are not prominent.

The Adventitia is much thicker than the media and consists of dense, thick collagenous bundles with an elastic tissue network. The vasal vessels are thick and stand out quite prominently. No inflammatory cells were found in any of the veins except in those which showed an outspoken phlebitis.

(11). The second type was found in the deep veins.

HISTOLOGY
HISTOLOGY.

The thickening is entirely due to intimal proliferation and is patchy in distribution. The line of demarcation between media and intima is well indicated by the original layer of the internal elastic lamella. There are patches of thickening in one or several places round the intima leaving some areas quite unaffected and healthy. Occasionally projections or plaques are found encroaching on the lumen and narrowing it considerably. These plaques consist entirely of fibrous tissue with layers of strands of elastic tissue branching in all directions and forming a wide, loose network and anastomosing freely with each other. They are dense near the internal elastic lamella, become looser as they proceed inwards where fibroblasts are more distinct and stand out clearly in layers of flat spindle shaped cells. These latter cells project strands from each pole and are considered to be elastic fibrils. There is no definite clear layer of cells lining these plaques, but sometimes long spindle shaped, sometimes irregular shaped polygon cells are found on the margin and appear to be actively proliferating. At the base, cells are seen perpendicular to the internal elastic layer thus simulating the migration of fibroblasts into a thrombus.

The origin of these latter cells has not been fully established, but they appear to spring from the subendothelial layer of connective tissue and the endothelial cells. The origin of the elastic tissue seen in these plaques appear to be twofold:—

(i) From the splitting of the internal elastic lamina.

(ii) From proliferating connective tissue cells.

Robertson F. Ogilvie claims that in endarteritis obliterans (which according to him resembles phlebsclerosis) the new elastic tissue is formed by proliferating connective tissue...
tissue cells, and do not represent elastic tissue split off from the internal elastic lamella as occurs in hypertrophic sclerosis in arteries. Figure 29 shows the manner in which the internal lamella is split and grows inwards giving off numerous branches, and Figure 30, a high power shows the growth of elastic tissue in area D in figure 29.

The Histogenesis of Elastic Tissue has not been settled. According to Maximov and Bloom, supported by Schaeffer J. Parsons elastic fibres and collagen fibres probably arise in or from a common precursor. The origin of the latter is:-

(i) From a direct transformation of the cell processes of the fibroblasts; and

(ii) From a liquid or semi-liquid intercellular substance secreted by the cells which become condensed or crystallised. Once these elastic tissue fibres are laid down they branch in all directions, become more numerous, thicker and have a tendency to arrange themselves in wavy layers parallel to the internal elastic lamella, probably due to mechanical forces.

I have on numerous occasions observed long processes from fibroblasts emanating from each pole, and when stained appropriately, took on the elastic stain. The conclusion, therefore, that I am prepared to draw from these observations is that the elastic tissue found in the intimal proliferation in Phlebosclerosis is:-

(i) From fibroblasts originating in the subendothelial layer and possibly endothelial cells.

(ii) From the splitting of the internal elastic lamella.

The vessels in the plaques are small, and their walls thin and lined by a single layer of endothelium. They are few in number and tend to disappear with the older type of proliferated intima. The source of these vessels, according to Short are twofold:

(i) From/
From loops of the Sublamellar plexus which lie nearest to the internal elastic lamella.

(ii) From a localised growth of Vasa which burrows through the internal elastic lamella and invades the intima.

The Media shows an increase in fibrous tissue, and a disappearance of muscle fibres - a replacement fibrosis.

The two types described above are different. The superficial small Saphenous is in an hypertrophic state, the deep Posterior Tibial Veins in a degenerative state.

Has a Phlebosclerotic Vein a bearing on Thrombosis?

An analysis of the state of the veins in the different groups shows a remarkable number of veins with intimal proliferation, most of which are associated with thrombosis.

 VEINS showing abnormalities in their walls.

<table>
<thead>
<tr>
<th></th>
<th>Intimal Proliferation</th>
<th>Varicosity</th>
<th>Normal</th>
<th>Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart (Table I)</td>
<td>12</td>
<td>13</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Carcinoma (Table II)</td>
<td>11</td>
<td>14</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Arterial (Table III)</td>
<td>9</td>
<td>1</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Miscel. (Table IV)</td>
<td>12</td>
<td>1</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Operative (Table V)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

This Table shows that:

in the Heart Group there were 25 cases with abnormal veins of which 16 were thrombosed.

in the Carcinoma Group there were 25 cases with abnormal veins of which 18 were thrombosed.

in the Arterial Group there were 10 cases with abnormal veins of which 7 were thrombosed.

in the Miscel. Group there were 13 cases of abnormal veins of which 8 were thrombosed.

in the Operative Group there were 2 cases of abnormal veins of which 2 were thrombosed.

As already mentioned the endothelium of a vessel serves not only as a lining but functions such as nutrition, secretion, absorption, ...
absorption and phagocytosis are attributed to it. In
the lower extremities an increase in venous pressure due
to cardiac failure, erect posture or any other abnormality
which may retard the return flow of blood would lead to
adaptive changes in the veins, and set in motion degenerative
and proliferative changes. At first there is hypertrophy
of the muscle fibres in the media, later degenerative changes
with replacement fibrosis set in. Nutrition of the vessel
wall must be interfered with, and there is a consequent weakening
of the wall of the vein thus assisting in the degenerative
and fibrotic changes in the media and the intima. Elastic
tissue shares in the degenerative process. The veins having
lost their elasticity and muscular contracting power, dilate
still more under extra pressure and become thin and varicose.

**Chronic infection** of a vein leads to degenerative
change and replacement fibrosis. If the inflammation
happens to be of a mild nature, a phlebosclerotic condition
can easily be established without obvious clinical manifesta-
tions, the intimal proliferation being due to chronic stimulation.

Phlebosclerosis may therefore arise under three distinct
conditions:

(i) An increase of venous pressure which leads
first to hypertrophic and later degenerative
changes, and finally to replacement fibrosis in
the media.

(ii) Nutritional interference - the intimal growth
is stimulated by passive contraction of the veins.

(iii) Inflammation leading to weakening of the walls;
chronic stimulation and eventual fibrosis. Such
chronic inflammation would also stimulate the
nerves in the adventitia which would lead to
vaso constriction. Such spasm raises the venous
blood pressure with consequent intimal proliferation
and fibrosis.
Venous blood contains numerous toxins if retarded in its return, can act more powerfully on a degenerated vein and create conditions suitable for thrombosis. Degenerated endothelium will react more easily to the least trauma which can occur when the veins of the legs are pressed upon by the mattress, their blood squeezed out and their endothelial lining pressed into apposition.

We can conclude therefore that a Phlebosclerotic condition of a vein is favourable to thrombosis.

Is there any relationship between Arterial degeneration and Phlebosclerosis?

Arterial degeneration and its relation to Veins.

An analysis of the arteries in the different groups shows:

<table>
<thead>
<tr>
<th>Table XVI.</th>
<th>Atheroma</th>
<th>Monckeberg sclerosis</th>
<th>No change</th>
<th>Phleboscl.</th>
<th>Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart (Table i.)</td>
<td>10.</td>
<td>5.</td>
<td>16.</td>
<td>12.</td>
<td>16.</td>
</tr>
<tr>
<td>Carcinoma (Table ii).</td>
<td>14.</td>
<td>8.</td>
<td>8.</td>
<td>11.</td>
<td>13.</td>
</tr>
<tr>
<td>Arterial (Table iii)</td>
<td>8.</td>
<td>9.</td>
<td>0.</td>
<td>9.</td>
<td>9.</td>
</tr>
<tr>
<td>Miscel. (Table iv)</td>
<td>3.</td>
<td>9.</td>
<td>12.</td>
<td>12.</td>
<td>8.</td>
</tr>
<tr>
<td>Operative (Table v.)</td>
<td>0.</td>
<td>0.</td>
<td>2.</td>
<td>0.</td>
<td>2.</td>
</tr>
</tbody>
</table>

We have thus in:

The Heart Group 15 cases with arterial disease, 12 showing Phlebosclerosis.

" Carcinoma " 22 " " " " 11 " " "
" Arterial " 13 " " " " 9 " " "
" Miscel. " 12 " " " 12 " " "
" Operative " 0 " " " 0 " " "

Such evidence points to a definite association between the two conditions.

Winternitz et al. have pointed out that there is a fairly free communication between the Vasa Vasorum of the Femoral Artery and Vein. Presumably such a vascular pathway exists between the Post. Tibial Art. and Vein. Thus any infective or sclerotic process present in the arteries would by the existing vascular pathway be transmitted to the concomitant vein, producing . . .
producing an irritation leading to proliferation of the intima. Irritation in the wall of an artery, (as it must inevitably be present when it is in a degenerating state) would cause an irritation in the corresponding vein by way of the sympathetic and thus lead to proliferative change in the intima. The matting of the arteries and veins by dense fibrous tissue is quite a common finding, and is usually associated with marked arterio-sclerotic change in the arteries. Such dense fibrosis interferes with the proper blood supply to the walls of the vessels and causes a constant irritation to the nerves as well.

The conclusion that can be drawn from the above is that owing to the intimate relationship that exists between artery and vein, any pathological condition (in it could be included the normal physiological process which accompanies advancing age) that exists in an artery would be transmitted to a vein, and proliferative and degenerative changes take place as described above. (Figs. 31 & 32.)

As has already been pointed out, the proliferative change in the veins is not concentric but patchy. It occurs at different places round the margin, leaving areas which remain healthy. This is explained by Winternitz and his co-workers as due to "the vasai communication between artery and vein occurs either longitudinally or transversely, therefore an arteritis need not be exactly opposite a phlebitis of an adjacent vein".

The relationship between arterial disease, phlebosclerosis and thrombosis can be appreciated if these factors are taken in full consideration. In a vein, no complete occlusion was encountered where intimal proliferation alone was responsible for the closure. Invariably the formation of a thrombus assisted in the ultimate occlusion. Thus while occlusion of a vein by a thrombus only with organisation and fibrosis was often encountered without any evidence of previous intimal proliferation, in phlebosclerosis occlusion of . . .
of the lumen was found to be twofold:

(i) Primarily proliferating intima, and
(ii) Organised thrombus.

It is interesting to note that in the case of the Ductus Arteriosus, Hypogastric Arteries and Umbilical Vein the physiological closure is by proliferation seldom assisted by thrombosis. The process involved in this physiological closure is at present under investigation. The pictures are given for the purpose of comparison, Figs. 33, 34, 35, and 36.
Pulmonary Embolism is a comparatively frequent occurrence and is intimately connected with Peripheral Thrombosis. Table VI. shows this relationship. Out of 100 cases examined seriatim 51 showed thrombosis in the leg veins and in 21 Pulmonary Emboli were found. The bulk of the cases were medical, only two were surgical. Leaving the surgical cases out of consideration and considering the medical cases only, we arrive at a true estimate of the incidence of thrombosis and embolism in medical cases.

Thus in 98 medical cases, 49 showed thrombosed veins i.e. 50%, and 19 showed emboli i.e. 19.3%. Following on the first 100 cases, I examined a further 75 which came to autopsy. 11 cases of Pulmonary Embolism were found. In this series, however, the examination was concerned chiefly with Emboli in the lungs and the veins in the legs were only examined when emboli were found. Invariably, whether the emboli were recent or organised, the leg veins showed corresponding thrombi. Thus in recurrent embolisation the leg veins were well organised and canalised and in some cases completely fibrosed. Two in this latter series were of the massive type and followed directly on operation. One case (1659) 23 days after operation and the second case (1670) eight days after operation. The rest were medical cases. To compare the latter with our first series we find:

First Series 21 cases with emboli in 100 autopsies i.e. 21%
Second Series 11 " " " 75 " " 15%
Medical
Medical cases only.

First Series 19 cases with emboli in 98 autopsies i.e. 19.3%
Second Series 9 " " " 73 " " 12%

There is thus a fairly wide margin between the two series.
This can be explained on the ground:
(i) there were fewer cases in the second series (75 instead of 100)
(ii) the first series were examined during the height of winter - between November and March -, and the second lot between March and May.

The incidence of thrombosis according to some authorities is greater during the winter months. This is explained on the assumption that during the cold weather there is a greater stimulus to vasospasm which is particularly marked in the lower extremities. Vasospasm, as has already been pointed out, produces vascular retardation which is an important factor in thrombosis. In the summer, the warm weather produces vaso-dilatation and thus a better blood circulation.

Taking all the 175 cases in which the lungs were examined for emboli we find 32 cases with Pulmonary Embolism i.e. 18%, and if we leave out the four surgical cases, we find an incidence of 16% in medical cases, 18% in all autopsies and 16% in medical cases only are higher figures than those shown by other investigators.

The incidence of Pulmonary Embolism varies remarkably in literature. It depends whether the investigation was carried out on surgical cases, medical and surgical, whether the figures were based on clinical signs and symptoms and whether verified at autopsy.

Most of the figures found in literature are taken from surgical cases. In a collected series of 316,060 surgical cases, Collins found an incidence of .53%. In the same series there were 33,223 autopsies, among which, 891 showed Pulmonary Embolism i.e. 2.68%. Lister in 4000 operated cases taken at random found 207 cases with Pulm. Embol. i.e. 5.3%. Barnes estimates that at least 3,068,000 people would die from Pulmonary/
Pulmonary Embolism in the United States of America, basing the population at 130,000,000 i.e. 2.3%. McCartney found 73 cases of Pulmonary Embolism in 9275 autopsies i.e. .78%. Lindskog, in 1215 consecutive major operations found 106 Pulmonary complications, 12 of which were due to Pulmonary emboli - an incidence of .98%. Belt shows an incidence of 14.6% of Pulmonary Embolism in all autopsies. In my series there are four surgical cases with fatal Pulmonary Embolism in 175 autopsies i.e. 2.3%, and 32 cases with Pulmonary Emboli in all deaths i.e. 1.8%.

Pulmonary complications is a fairly common occurrence in convalescents. Lockhart Mummery records an incidence of 5.6% in the Middlesex Hospital and 1.2% in the Mayo Clinic. Lindskog gives an incidence of 106 cases in 1215 i.e. 8.7%. Lockhart Mummery concludes that the majority lung complications excluding Bronchitis, are the result of infarction of the lung, a conclusion fully justified in view of the frequency of thrombosis of the leg veins shown in my figures. As already pointed out, symptoms indicating thrombosis in the legs are rare unless there is an outspoken thrombophlebitis. Often the first indication of the presence of thrombosis is the appearance of sudden and distressing pulmonary symptoms. This may terminate in sudden death or cause such distressing symptoms which lead one to suspect an Embolus.

HISTORY OF SURGICAL CASES WHO DIED FROM PULMONARY EMBOLISM.

I. Case No. 1574. A stout woman aged 54 years and weighing 125 lbs. was operated for Cholecystectomy. Post operative progress was satisfactory. On the 5th. day after operation she suddenly collapsed after drinking morning tea and died within 25 minutes.

Autopsy. Large, coiled, cylindrical emboli were found completely blocking both main branches of the Pulmonary Artery. That of the right side was about six inches long and the diameter of a lead pencil. It was dark red in colour - a typical stagnation thrombus - about the calibre of the lower end.
end of the Femoral Vein. No true infarct was found in the lungs. (Fig. 37)

In the lower extremities, the distal half of the left Femoral and the Posterior Tibial Veins were thrombosed. The right side showed no thrombosis.

Microscopically the thrombus in the left vein was recent, slightly attached to the wall and of the red type. There was no evidence of inflammation.

In this case thrombosis occurred in the left lower extremity showing no obvious external signs. It spread upwards and being of the soft propagating type, became detached on movement while drinking tea and constituted a fatal Pulmonary Embolus.

2. Case No. 1590. A stout woman aged 56 years and weighing 9 st. 13 lbs. suffered from pain in the left loin for over ten years. For two years she suffered from headaches and dry tongue. On the 30/1/40 she was operated on for Nephrolithotomy and Pyeloplasty. On the 3/2/40, i.e. on the 5th. day after the operation, she became drowsy and restless and died.

At autopsy, a large Pulmonary Embolus was found at the bifurcation of the Pulmonary Artery. Small emboli were also found in the smaller Pulmonary branches. (Fig. 38)

Death was gradual, the time from the onset of the drowsiness to death was not stated in the records. The fact that small independent emboli were found in the small branches suggests that there must have been a shower of small emboli before the massive embolus finally blocked the main Pulmonary branches.

The veins in the right leg were found thrombosed from the Plantar to the middle of the Femoral. The left vein showed no obvious thrombosis.

Microscopic...
Microscopic Examination.

The right Post. Tibial vein showed no recent thrombosis. The left Post. Tibial vein showed evidence of organised thrombi and the muscle veins were thrombosed with evidence of organisation. There was no evidence of inflammatory reaction.

3. Case No.1670. A male, 77 years, suffering from carcinoma of the colon was operated on for Sigmoidostomy. On the 8th. day after operation he suddenly became cyanosed and breathless and died within six hours.

At autopsy large were found plugging the secondary branches of the Pulmonary Arteries.

Thrombosis of the left leg veins was found.

Microscopically, the thrombus was of recent nature.

4. Case No.1659. A woman aged 7 was operated on for Colporrhaphy on the 15/3/40. She progressed favourably until the 27/3/40 when she suddenly collapsed and developed a severe pain in the lower part of the right side of the chest. On the 3/4/40 she was quite well again and was permitted to sit up.

On the 6/4/40 she became suddenly breathless, and on the 7/4/40 she collapsed while on a bed pan and died within a few minutes.

Post Mortem Examination. An embolus was found blocking the Pulmonary Artery. The lower lobe of the right lung showed older emboli plugging the smaller vessels.

The veins in the legs were thrombosed. The left, as high as the External Iliac, the right from the Plantar to the middle of the Post. Tibial vein. There was no evidence of inflammation.

This case illustrates repeated embolisation. The first warning appeared on the 12th. day after operation. She recovered from this attack rather quickly and was allowed up 7 days later, i.e. on the 19th. day. The next day she had another attack, this time apparently larger emboli blocked larger arteries but as yet not of sufficient size to cause death. It was only a day later i.e. on the 21st. day after operation that the final attack...
attack came, to which she succumbed.

The emboli in the first two attacks could have originated in either of the legs, but the final and fatal embolus must have come away from the right side, it having become detached at about the middle of the Post. Tibial vein.

Recurrent embolisation is often encountered, and because of the obstruction to the Pulmonary circulation, the effect upon the heart must inevitably cause distressing symptoms, of the Cor-Pulmonale type with ultimate heart failure.

An instance of such a condition is illustrated in Case No. 1624. A male, 58 years of age, suffered from indigestion. He was taken to the X-ray room for examination, where he suddenly collapsed and died within 15 minutes.

At autopsy numerous Pulmonary branches were found almost totally occluded by organised emboli. Recent emboli were also found. Gross Emphysema was present in the lungs.

In the right leg a thrombus was found entering the Post. Tibial vein from a tributary in the calf muscle at level 2.

Microscopically, the thrombus was found organised.

The veins of the left leg were not examined.

The heart weighed 450gms. The right Ventricle was Dilated and Hypertrophied.

In this case, gross emphysema coupled with widespread occlusion of the smaller branches of the Pulmonary Artery by organised emboli must have considerably embarrassed the right side of the heart, so that a fresh shower of emboli exerted an extra strain on the heart causing it suddenly to fail.

It further illustrates, that cardiac insufficiency leads to recurrent thrombosis - in this case the calf muscle veins only were affected. No history is available as to his previous health, but, judging by the state of the organised thrombi and emboli the process must have recurred on several occasions, (Fig. 39 & 40.)
As in the veins so in the lungs, an embolus once lodged in the Pulmonary artery acts as a foreign body and initiates the process of organisation, canalisation and ultimate fibrosis, and occlusion of the artery. Repeated embolisation is quite a common occurrence, more so than hitherto emphasised, and because of that, to quote Belt "from a clinical point of view Pulmonary Embolism is rarely if ever regarded as a cause of chronic disease. The usual picture is more or less acute illness which passes fairly quickly from one episode to another and ends either in death or recovery in a matter of days or weeks." It can well be understood, how in cases of heart disease, a vicious circle is set up. Circulatory failure initiates thrombosis in the veins, small emboli detach themselves lodge in the smaller branches of the Pulmonary Arteries, affect the heart in a manner already described and add to the already overburdened myocardium an extra strain, to which ultimately the patient succumbs. (Fig. 41 & 42.)

A similar process of trabeculation in the Pulmonary Arteries as in the veins often takes place. An embolus by virtue of it being a recent thrombus, retains its contracting power in the early stages of organisation, becomes attached at its both ends to the vessel wall, the intervening portion retracting, leaving a clear space between it and the wall. A cord-like structure is thus formed, running longitudinally and in the direction parallel to the blood stream. Such trabeculae, sometimes thin sometimes thicker, are often encountered. The possibility that these trabeculae are the end result of autochthonous thrombi in the Pulmonary Arteries cannot entirely be ruled out, but a search in the leg veins will invariably disclose a similar condition of trabeculation, or at least old standing organised thrombosed veins. (Fig. 43.)
Fig. 1.—The afferent impulses travel mainly in the vagus and radiate back to the lung as bronchoconstrictor and bronchosecretory fibers. They may constrict the coronaries, produce vagal inhibition of the heart and depress blood pressure. They can radiate to the upper gastrointestinal tract and produce colics, increased peristalsis and reverse peristalsis. The plug may produce a stimulation of the sympathetic vasoconstrictors or a more general sympathetic stimulation through the dilatation of the right heart (Bainbridge reflex). The hypertension in the right heart and in the pulmonary artery seems to be the main stimulus for these widespread reflexes, although the rise in intrapulmonary pressure, the congested lung and the irritated pleura all have been shown to act as reflexogenic factors. From Surgery 6: 339 (Sept.) 1939.
PHYSICAL SIGNS AND SYMPTOMS OF PULMONARY EMBOLISM.

While we are concerned mainly with the pathological condition of Thrombosis and Pulmonary Embolism and their post-mortem findings, for the purpose of completeness, the symptoms, from a clinical point of view, exhibited by Pulmonary Emboli are included. The following remarks are based on observations made and experiments carried out by prominent research workers in this field.

De Takats and his co-workers emphasise two types of symptoms caused by emboli of different sizes.

(i) **Syncopal type** caused by a large embolus. It obstructs the main Pulmonary Artery and exhibits pallor, fall in blood pressure - as suggested by a weak rapid pulse - shock, restlessness and retro-sternal pain.

(ii) **Asphyctic type** brought about by multiple small emboli and characterised by cyanosis and dyspnoea.

The symptoms exhibited by these two types are attributed to mechanical factors viz:- complete or partial obstruction, death being due to reduction in the effective blood volume, or right heart failure of the Cor Pulmonale type.

Lately, another important factor in the causation of death has been brought into prominence viz: - a reflex mechanism initiated by an embolus lodged in the Pulmonary Art. This acts on the same principle already described in connection with the production of symptoms in thrombophlebitis of the leg veins. In the case of the lung, it is based on the fact that the Pulmonary Vascular bed is richly supplied by sensory receptors and that the Pulmonary and Bronchial vascular systems possess strong vaso-constrictor mechanism which is under sympathetic control. (Diagr. VI). It has been proved experimentally on rabbits that distal to the plugged artery, the ...
the capillaries of the alveoli and small bronchi are filled with blood and that the trachea and larger bronchi are filled with bloody mucus. This congestion, according to Harrison et al., stimulates vagal reflexes. They proved this by experiments on dogs in whom they produced Pulmonary congestion artificially and observed the effect on the respiratory rate with the Vagi intact and with the Vagi severed. They found that where the Vagi were intact there was a marked increase in the respiratory rate, whereas in cases with bilateral vagotomy there was no significant change. From these experiments, these authors concluded that Pulmonary afferent fibres of the Vagus are extremely sensitive to Pulmonary congestion.

The Vagus also constricts the smooth muscle of the Coronaries, hence stimulation of the Vagus would lead to Coronary constriction, ischaemia of the myocardium, infarction and death. This view was emphasised by Jackson and Jackson in 1937, who pointed out that cases with symptoms attributed to Coronary Thrombosis are really due to Pulmonary Embolism. Friedberg and Horn confirmed this in their investigations on myocardial infarctions. In 1000 autopsies they found 31 myocardial infarcts, 28 of which i.e. 31% showed no Coronary Thrombosis, and in 12 cases out of the 28, Pulmonary Emboli were found, i.e. 43%. These latter authors believe that in cases of Pulmonary Embolism, coronary insufficiency occurs because (a) the attendant shock, (b) vagal inhibition of the heart, and (c) depression of the blood pressure.

Constriction of the Coronary Arteries in cases of recurrent Pulmonary Embolism with consequent ischaemia and myocardial change can now be understood. Such repeated occurrences of Pulmonary Embolisation in Heart cases and Cases with Arterial disease, who, as tables 1 and 3 show, often have thrombosed veins, might well lead to repeated myocardial infarcts and morphological myocardial change. Thus in a weakened
weakened heart, a final shower of emboli might produce an acute myocardial ischaemia with sudden death. Such an occurrence might be facilitated if the Coronary Arteries are already narrowed by arterio-sclerotic change.

In the human being it is assumed that the action of multiple small emboli act in a similar manner in the production of symptoms as those produced experimentally in dogs. Thus on the basis of Vagal stimulation, Atropin and Papaverin have been used successfully to counteract the alarming and dangerous symptoms, the former by blocking the Vagal impulses, the latter by relaxing the smooth muscle in the Coronary Arteries. Collins records 9 cases out of 10 with Pulmonary Embolism treated successfully with Atropin and Papaverin (Spasmalgin).

The diagnosis of Pulmonary Embolism in medical cases such as those described in this investigation, is difficult. It is generally obscured by the symptoms of the primary disease. In no case in Groups 1, 2, 3 & 4 was Pulmonary Embolism diagnosed antemortem. The emboli were accidental findings. The four surgical cases were sent to autopsy with definite diagnosis of Pulm. Embolism.

Definite Electro-cardiac changes in Pulmonary Embol. have recently been reported. In a well illustrated article De Takats et al. gives an interesting report on his findings. Such electrographic assistance might usefully be employed not only in cases where such emboli are suspected, but also in cases where embarrassment of the heart occurs in the course of a long chronic illness.
METHOD USED IN THE EXAMINATION OF THE LUNGS FOR PULMONARY EMBOLI.

In order to detect emboli in the lungs, it is necessary to adopt a procedure whereby ready access is obtained to the larger and smaller Pulmonary branches. For this purpose a special technique described by Belt and introduced by him at the British Post Graduate School, was adopted. He calls this technique the "German Method."

The chest is laid open and the heart and lungs exposed. An incision is made in the Right Ventricle and with a pair of scissors, is carried upwards along the Pulmonary Artery, laying it open in situ. Emboli of large size which lodge in the hilus can easily be detected. If no embolus is encountered, the lungs are separated at the hilus and removed for further investigation. It is then placed horizontally on the table, hilus down. An incision is made with a long knife down the middle of the dorsal surface from the apex to the base until the knife encounters, but does not sever the hilus structures. The lung is thus opened up and the main trunk of the Pulmonary Artery is exposed in the depth of the cut. With small scissors the branches of the arteries can be laid open horizontally almost to their termination without any difficulty. (Fig. 44.)

The object of this method is to lay open the secondary and tertiary branches of the Pulmonary Artery longitudinally. In this way the smallest branches can be opened and a thrombus, if present, can be traced to its termination and the morphology of its structure — whether autochthonous or embolic can be studied.

THE IDENTIFICATION OF AN EMBOLUS.

The identification of an embolus in contradistinction to an autochthonous thrombus or a post mortem clot, may not always be easy. There are certain features which, if remembered, will assist in its identification.
An Embolus may be free in the lumen, coiled, twisted, impacted, or riding a bifurcation. It may have branches which do not correspond to the vessel in which it lies. It is generally the red propagated type encountered in the thrombosed veins where it is formed in a slow moving stream. When such an embolus is compared with the original thrombus in a vein it generally resembles it in morphological structure. It does not conform to the shape of the vessel in which it lies, unless there is a superadded thrombosis which forms round it when impacted already in the Pulmonary Artery.

An autochthonous thrombus however, differs from the above considerably. It conforms to the shape of the vessel, it is securely attached to the wall, and shows the characteristics of an ante-mortem thrombus. It is greyish or light pink, being composed chiefly of platelets and white cells because it is laid down in a faster moving stream. It cannot be removed easily, is friable and breaks when an attempt is made at its removal.

A Post Mortem Thrombus is elastic, red with a greyish-yellow layer, shiny when washed in water, free in the lumen etc.

**Comparison between thrombi found in the lungs.**

<table>
<thead>
<tr>
<th>Conditions in which found.</th>
<th>Autochthonous thrombus</th>
<th>Post mortem thrombus</th>
<th>Embolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Types</td>
<td>Mixed</td>
<td>In all cases, delayed in asphyxia</td>
<td>Associated with thrombosed veins</td>
</tr>
<tr>
<td>Colour</td>
<td>Greyish-red or light pink</td>
<td>Red surrounded by yellowish transluce subst.</td>
<td>Red</td>
</tr>
<tr>
<td>Surface</td>
<td>Granular and dull</td>
<td>Smooth &amp; glossy, Granular</td>
<td></td>
</tr>
<tr>
<td>Consistency</td>
<td>Firm, friable</td>
<td>Elastic, soft, Firm friable</td>
<td></td>
</tr>
<tr>
<td>Relation to lumen</td>
<td>Fills completely or partially</td>
<td>Free or float, recent</td>
<td>Free if always round.</td>
</tr>
<tr>
<td>Shape</td>
<td>Conforms to shape of vessel</td>
<td></td>
<td>Does not conform to shape of vessel</td>
</tr>
</tbody>
</table>
### Autochthonous thrombus

| Attachment to wall. | Always firmly or lightly |
| Structure. | Laminated or uniform. |
| Endothelium. | Dull & ragged. |

### Post Mortem thrombus

| Artery & vein contain clot. |
| Always free. |
| Two layers: (i) red (ii) yellow transluscent. |
| Laminated or uniform. |
| Shiny & smooth. |

### Embolus

| Artery blocks vein free. |
| Generally free. |
| Laminated or uniform. |
| Smooth often shiny. |

### MICROSCOPIC

| Structure. | Mixed. |
| Homogeneous distribution of cells. |
| Red cells surrounded by platelets & leucocytes. |
| Attachment. | Evidence of Free no organisation. |
| Free or evidence of commencing organisation. |

A Pulmonary Embolus, in essence, is an antemortem thrombus having detached itself, partially or completely, from a vein in any part of the body and carried by the blood stream by way of the Inferior or Superior Vena Cava to the right heart, and thence into the Pulmonary Artery and its branches. Occasionally, in the presence of a patent Foramen Ovale, an embolus from the venous side may be found obstructing a vessel and causing an infarct in an organ or tissue on the systemic (arterial) side of the circulation. Such an Embolus is known as a PARADOXICAL EMBOLUS.
THROMBOSIS IN THE HEART CHAMBERS.

The heart is often referred to as a site for thrombosis, particularly in the case of heart failure and auricular fibrillation. The apex of the right auricle is said to be the place where it is usually found. This has not been my experience. In no case of Pulmonary Embolism was the origin of the thrombus traced to the heart. In one case a thrombus, which appeared to be ante-mortem, was found in the apex of the right auricle, but on microscopic examination it proved to be post-mortem in type.

Blood clots are frequently encountered in the auricles and ventricles. Because of their firm adhesion to the wall they suggest an ante-mortem nature. They lie on the posterior wall of the ventricular or auricular cavity, filling the interstices between the chordae tendineae and trabeculae carneae which they surround. When an attempt at removal is made, the elasticity of the clot determines its nature, and the endocardial surface remains smooth and glossy.

An ante-mortem thrombus in the heart has a definite pathological basis - except if it is lying loose in the ventricle or auricle and is obviously an embolus from a distant vein. Invariably it is a mural thrombus, having originated in the myocardium as a result of an infarction, necrosis or fibrosis. The cause is generally found in the pathological state of the Coronary Arteries. The conditions encountered in the latter which give rise to myocardial degeneration can briefly be summarised under the following headings:-

(i) Stenosis of the Coronary ostia due to Syph. Aortitis. (Fig. 45 & 45a.)

(ii) Narrowing due to arterio-sclerotic change - the mural thrombus is generally found at the apex. (Fig. 46 & 46a & 46b.

(iii) Thrombosis on an atheromatous plaque to which the patient has not succumbed immediately.

(iv) Constriction due to Vagal reflexes originating in the lungs and giving rise to gradual ischaemia and fibrosis of the myocardium.

(v) Large pedunculated thrombi in the first part of the Aorta near the valves blocking one or other of the orifices. Several such cases have been encountered lately in an investigation on sudden death from heart failure. (Figs. 47, 48, 48a.)

Such ...
Such antemortem thrombi are intimately associated with the walls of the auricles or ventricles. Once started, they grow by gradual piling up of layers of fibrin and cells in the characteristic laminated appearance and often fill the chamber half or even two-thirds its volume capacity. Under such circumstances an embolus from the right side of the heart can easily break off and lodge in the Pulmonary Artery.
CHAPTER V.

FATE OF A THROMBUS.

Once a thrombus is formed in a vein artery or anywhere else, it acts as a foreign body and the process of organisation commences immediately. In order to appreciate the process, a series of microphotographs taken from the sections in the course of this study are included.

Soon after its formation the thrombus loses its cellularity and becomes a hyaline mass. (Figs. 50 and 50a.) Organisation soon commences at one or more points round the intima. The agglutinated platelets adhere to the intimal lining of the vessel, the hyaline thrombus becomes less acido-phile, and at the point of attachment a markedly cellular activity is noticed. Long spindle shaped cells are seen arranged in parallel layers perpendicular to the Internal Elastic Lamella and descending into the thrombus. (Figs. 51 and 52.)

The intimal lining is no longer discernible and the endothelial cells appear as if they are migrating into the thrombus. No doubt the very thin subendothelial layer, which consists of connective tissue cells participates in the proliferative activity. The Internal Elastic Lamella is thickened and splits into several layers, and in parts shows fragmentation. On the medial side of the Internal Elastic layer there is a marked cellular activity. This is the area which contains the Sublamellar Plexus of vessels of Short. It is in a state of great activity and cells from this area are often seen migrating into the organising mass through cracks in the fragmenting elastic lamina. The process in this area is well illustrated in Fig. 10 D. Figs. 53 & 54. show a similar process of commencing organisation, fibroblastic proliferation and ...
and the formation of small thin blood vessels and large sinus-like spaces. Here the thrombus is formed on a Phlebosclerotic intima.

The evidence from these pictures as well as from many others which have been studied is, that genetically these fibroblasts in the organising mass are derived from the endothelial, subendothelial layers and sublamellar area of Short. It should, however, be pointed out that according to Ramey et al. who, in their experimental work on the effects of injections into the walls of vessels by Tubercles and colloidal Cholesterol, i.e. substances which produce chronic irritation and proliferation of the intima, state that "cellular proliferation uniformly appeared and originated in the intima," but are not prepared to state "that these cells are genetically derived from the endothelium, but that only the first evidence of proliferation consists of cells adjacent to the Internal Elastic Lamella and in many cases indistinguishable from the cellular elements comprising the intima."

There is possibly another source from which these cells are derived. I have noticed on numerous occasions a plasma cell infiltration in the wall of the vein which cells often appear to assume a fibroblastic role. This is particularly well marked in the physiological obliteration of the lumina in the vessels like the Ductus Arteriosus and Hypogastric Artery in infants. These Plasma cells are particularly well marked round the Vasal vessels. It is highly probable that these cells participate in the organising process, having migrated, together with the large phagocytic cells - which are often found loaded with haemosiderin pigment - , from the Vasal vessels.

A very striking feature in the organising process is the presence of numerous thin-walled capillaries, some fully formed, others in the process of formation. This growth of
capillaries is first seen at the margin of the vessel at the point of attachment of the thrombus. They are derived according to Short from the Sublamellar Plexus on the medial side of the Internal Elastic Layer. Fig. 55 shows such vessels in the process of formation. Cells are seen travelling towards a clear space which they seem to surround and arrange themselves round it forming an endothelial lining. (A). Fibroblasts eventually surround these vessels, strengthen their wall which have no other coats (B). (C) shows a space filled with blood cells but as yet has no clear endothelial lining. (D) Angioblasts forming blood vessels.

Larger spaces are also encountered. These spaces are due to retraction of the thrombus and follow the platelet scaffold. They are lined by endothelial cells which are derived from the endothelial lining of the main vessel. The vasal vessels, according to Short, anastomose with these spaces. (Fig. 20).

As the organisation of the thrombus proceeds inwards from the margin, the deeper areas in the thrombus become involved in the process of organisation. The older marginal areas become more fibrous and the vasal vessels thicken and eventually become obliterated. Fig. 56. shows four such vessels in different stages of obliteration. Elastic tissue in the walls of these vessels is quite prominent. Although there is no evidence of elastic tissue in the wall of a vessel when it forms originally, it appears to develop at a later stage. I could find no evidence of elastic tissue in an organising thrombus, in contradistinction to a proliferating intima in Phlebo-sclerosis which abounds in such wavy elastic strands. The elastic tissue in a vessel wall in a thrombus must therefore take its origin either from:-

(i) the fibroblasts which surround the vessel wall giving it additional strength
(ii) the Angioblasts which must have an inherent quality to form elastic tissue by secreting a liquid or semiliquid intercellular substance which becomes condensed and crystallised elastic tissue.
The further advance in the organising process is fibrosis, retraction, leaving large spaces which are lined by endothelium and thus to a certain extent restoring the circulation, and finally obliteration of the Vasal vessels. (Figs. 57 & 58.) When such thrombosed, organised and canalised vessels are cut transversely the partitions separating the spaces are known as trabeculae. (Figs. 59, 60,61,62,63,64.) Fig. 65 shows a recent thrombus forming on a small trabeculus. Fig. 66 shows an old thrombus and a more recent one. Fig. 67 shows a trabeculus attached to the wall with the endothelium reflected from the intima onto the trabeculus. Fig. 68 shows the appearance of a cicatricial trabeculated vein.

(by permission of Dr. T.H. Belt.)

Finally, a deposition of Calcium is sometimes encountered. Normally i.e. in ossification, the calcium salts are deposited diffusely in osteoid tissue. In disease the process is known as calcification, the lime salts being deposited in clumps of granules in tissue which is dying or is dead or in which no cells are present. In thrombi stony nodules are often encountered. These are known as Phleboliths and consist of lime salts - Calcium Carbonate and Calcium Phosphate deposited in the same proportions as are found in bone. Such a deposition of lime salts taking place in a hyaline thrombus is purely a physical process being due to absorption of these salts from the blood by the degenerated tissue. Figs. 69 & 70 show a Phlebolith in the process of formation.

Fatty degeneration is considered as a cause of calcium deposit. Fat is hydrolised, liberating fatty acids which unite with Calcium forming Calcium soap, which later changes to Calcium Carbonate and Calcium Phosphate. Such calcification is very frequently encountered in atheromatous plaques in arteries. In veins no such change appears to take place. No fatty change is found in the wall of the veins. On numerous occasions have sections of degenerated veins been stained for fat...
fat with negative results. In only one instance was calcification of the wall of a vein encountered and in this case also no fat could be found in the wall of the vessel when appropriately stained. The deposition of Calcium in this instance I attribute to adsorption of calcium salts from the blood. In the adjacent artery there is a marked Calcium deposit in the media; in one area there is actual bone formation. (Fig. 71.)
Once we appreciate the conditions under which Thrombosis occurs and the places where it is most likely to occur, it is obvious that our first attention should be directed towards preventing its development. In all cases whether medical, surgical or gynaecological the forces which encourage thrombosis are practically the same. Apart from outspoken thrombophlebitis no inflammatory reaction is found in the walls of the veins or perivenous tissue which encourages firm adhesion of the thrombus to the wall. It is a Phlebothrombotic condition in which the adhesion of the thrombus to the wall, in the early stages is very mild, or may even lie free in the lumen.

In view of the fact that we consider a lesion in the vein as a primary essential for the commencement of the building of a thrombus, our first attention should be directed towards avoiding pressure on veins. The patient must therefore be instructed to keep his or her legs in such a position where little pressure is exerted on the calf muscles. Tight abdominal bandages after operation must be discouraged and meteorism avoided. Pressure by pillows behind the knees and Fowlers position must be discouraged. Increase in the circulation must be encouraged. Stimulation of the heart, if it shows signs of weakness, must be persistent and continuous. The veins must be kept filled with blood by encouraging the circulation so as to avoid collapse. The return flow of blood must be assisted by elevation of the foot of the bed from eight to ten inches. Muscular movements must be insisted on soon after operation in debilitated or heart patients who are confined to bed. For this purpose, a bicycle pedal arrangement is attached to the foot of the bed and the patient pedals for five minutes a day, starting on the third day.
after operation during the period of confinement to bed. Massage of the calves and thigh muscles must be carried out once or twice daily. Dehydration should be avoided and if necessary actively combated. Hypopnoea should be avoided by instructing the patient to take deep breaths frequently when awake or if necessary stimulate respiration by CO₂ and O₂ inhalation. The patient must be kept warm and perhaps heat tents applied to the abdomen thus producing vaso-dilatation of the peripheral vessels. A low protein diet is advisable in the early post operative days to avoid hyperproteinaemia which increases the coagulability of the blood. Prolonged stay in bed should be avoided particularly in elderly patients who are liable to suffer from "recumbency shock."

If a thrombosis has developed or is suspected, elevation and immobilisation of the limb is essential in the early acute stages. The lymph and blood flow must be encouraged and the limb kept warm. The best result is obtained by blocking the Lumbar Sympathetic Ganglion with 2% Novocaine, thus relieving vaso-spasm and increasing the arteriolar and lymphatic flow.

Surgical treatment is occasionally necessary. This consists in ligation and excision of part of the vein.

In Pulmonary Embolism, Atropine gr. 1/2, and Papaverine Hydrochloride gr. 1/60 should be given intravenously.

Embolectomy is occasionally practised. Crafoord C. records two successful cases, and Henry describes three cases on whom attempts were made to remove emboli from the Pulmonary Artery. Success of such an operation depends on the speed and the skill of the operator and most important of all is the supply of blood to the brain. The Medulla cannot tolerate lack of circulation for any length of time - some claim 5 minutes as the maximum. Success therefore might result more often if the Medulla is kept supplied with perfused blood at normal pressure directly up the Carotid trunk while the operation is in progress. This suggestion which I put forward to Mr. Henry is embodied in his article on the subject as a possible trial in future operations.

- DISCUSSION -
It is surprising how little attention is being paid to thrombosis as a complication in disease. Few realise how frequently one encounters such conditions in medical cases in general, and in certain cases in particular. Attention in the past has chiefly been focussed on surgical, traumatic and puerperal cases because of the grave Pulmonary complications that frequently arise as a result of it. Four deaths from massive Pulmonary embolism in 175 autopsies i.e. 2.2% is a high incidence, though it does not reflect accurately the true incidence of Pulmonary embolism if surgical cases only were considered. Statistical data accumulated by recognised authorities show an incidence of .2% to .3% in purely surgical cases which are good operative risks. In cases where the patients are suffering from chronic and debilitating disease surgery, generally of a palliative nature, is a grave risk from the point of view of thrombosis. From the figures shown, 75% in cases of carcinoma run that risk compared with 52% if the patients are left alone. With the development of Peritonitis or perivesical infection thrombosis invariably occurs.

The striking feature in this investigation is the number of medical cases found that are liable to thrombosis. Their order of incidence is according to Table VI: -

(i) Carcinoma 58%
(ii) Arterial 53%
(iii) Heart (Primary) 50%

When, however, the cases showing secondary cardiac involvement in the other groups are added to the cardiac group 1. (an essential adjustment in view of the considered etiology of thrombosis), the figures are materially altered and their order of incidence changed thus:

(i) Heart (primary & secondary) 63.6%
(ii) Carcinoma 48%
(iii) Arterial 25%

The etiological factors have been discussed under their different...
different headings. Most prominent stands out Cardiac Insufficiency. This is particularly well borne out by the fact that cardiac cases have, in the vast majority of cases, old, organised and canalised thrombosed veins. Bilateral thrombosis in the lower extremities was almost invariably encountered. The distance of the extremities from the heart, the low systolic pressure, the weak arteriolar pulsation and the poor lymph flow, the anatomical relation of the veins to ligaments and other structures, the general varicose condition of the veins and the inability of the valves to function properly and the increase in the venous pressure, all predispose to retardation of the blood flow and facilitate the agglutination of platelets and red blood corpuscles, particularly in the neighbourhood of the valves. Unhealthy veins, such as are found in Phlebosclerosis and in association with arterial disease, are predisposed to thrombosis by virtue of anoxia due to slow circulation and interference with the proper nutrition of the wall—particularly the intima of the vessel—thus predisposing them to poisonous substances circulating in the blood with consequent degeneration, disintegration and injury of the endothelium.

The other factors discussed which influence thrombosis are:

(i) Injury to the intima—traumatic or inflammatory.
(ii) Carcinoma and general debility.
(iii) Changes in the chemical condition and composition of the blood.
(iv) Age
(v) Adiposity.

It is hardly possible to conceive that an increase in the platelets, an increase in the thromboplastin and an alteration in the Albumin-Globulin ratio could initiate a thrombosis in the lower extremities, avoiding the rest of the venous system. The fact that the lower extremities are constantly affected, without evidence of thrombosis in the upper part of the body, strongly suggests that a local factor initiates the thrombosis, some of the other factors assist in its further
This local factor is considered to be an injury to the endothelial lining at one point or another in the veins of the lower extremities. I consider that the veins in the calf muscles constitute the place of origin of thrombosis in medical as well surgical cases. Considering the posture of the patients who are confined to bed, we find that generally they lie on their backs, invariably quiet with very little movement and with the calves of the legs pressed against the mattress. The veins thus suffer compression; the blood is emptied and the endothelial lining brought into apposition with consequent damage to the intima. In addition the muscular venous tributaries are invariably found thin walled and varicose. Little resistance is thus offered to compression. The unhealthy state of the walls, particularly in association with Phlebosclerosis, would under these circumstances suffer further degeneration thus giving rise to foci for thrombosis. The fact that the Anterior Tibial vein or veins on the dorsum of the legs never appear to suffer thrombosis in these debilitated and cardiac cases indicates the importance of posture and compression of the veins.

The further development of the thrombus appears to proceed in the direction of the blood stream and once such a thrombus reaches a larger vein its progress might be arrested if the blood flow is rapid; if however the circulation is slow as a result of cardiac insufficiency or a narrowed lumen by Phlebosclerotic change, the thrombosis proceeds upwards as well as downwards. Initial Plantar vein thrombosis is, according to Neumann, a fairly frequent occurrence; but in my series of cases examined, the thrombi in these veins appeared much more recent than those in the Post. Tibial and muscular tributaries thus suggesting an ascending thrombosis in the first instance followed later by a spread downwards. Further/
Further evidence in support of thrombosis originating primarily in the calf muscles is found in the fact that, the thrombi in the Post. Tibial veins in the cases under discussion were invariably of an older nature than those found in the Femoral or Pelvic veins. In no case were thrombi found in the Femoral veins without thrombosis in the Posterior Tibial veins, whereas in many cases the Post. Tibial veins were thrombosed without the Femoral veins being involved.

With the exception of outspoken thrombophlebitis, none of the veins examined showed any evidence of inflammatory reaction. The cellular activity in the two conditions in the organising thrombus is markedly different. In Thrombophlebitis the organisation is very active with numerous plasma cells, round cells, phagocytic cells, polymorphs, oedema of the wall and marked activity of newly forming thin walled blood vessels. In Phlebothrombosis the activity is slow, fewer cells, no oedema in the wall of the vessel, no polymorphs and very few actively growing blood vessels.

Oedema appears to be a rare symptom in Phlebothrombosis, unless the Inferior Vena Cava is involved. In Thrombophlebitis, it depends on whether the superficial or deep veins are involved. In the case of the Saphenous vein, there is merely a local reaction. When however, the Femoral and Posterior Tibial veins are involved oedema is invariably present.

Involvement of the lymphatics is important. Perivascular inflammation in Thrombophlebitis involves the lymphatics which become blocked and drainage is stopped. This together with mechanical obstruction by a thrombus gives rise to severe oedema. In Phlebothrombosis however, the lymphatics are free and are able to drain the legs with the result, that in spite of mechanical obstruction by thrombosis, no oedema occurs. When the larger main trunks are involved e.g. the Inferior Vena Cava, oedema is present and is entirely due to...
Pelvic veins have often been found thrombosed particularly round the Prostate. In view of the frequent occurrence of infection in and around the Prostate, tubes and ovaries, a mild chronic infection might often account for a thrombosis which often remains localised but may spread to the Inferior Vena Cava. Some authors, Goverts and Rosenow consider that thrombosis in these non inflammatory veins is due to a relatively avirulent organism introduced into the blood from a focus of infection somewhere in the body. The organisms may either (i) form a nidus of infection on the intima of a vein and thus produce thrombosis, or (ii) by alteration in the physico-chemical nature of the blood which is associated with a change in the albumin globulin ratio. Pressure by Pelvic viscera, tumours, gravid uterus, all are liable to injure the intima of the vessels and initiate thrombosis.

Age is an important factor. The incidence of thrombosis increases with advancing age. The heart and operation cases show an average of 57 and 55 years respectively, the carcinoma group shows an average of 63.8 years and the arterial group 66.8 years. As a person advances in age the velocity of the circulation decreases, the tissues become dehydrated and muscular activity is reduced. With confinement to bed these factors become more marked and the blood stream further retarded.

Sex does not appear to have an influence on thrombosis. In surgical cases however, owing to the more frequent pelvic operations and the exposure to chronic infection, the consensus of opinion is that there is a preponderance of thrombosis among females.

The prothrombin level in the blood was estimated in a number of cases corresponding to the types of cases where thrombosis was found. No conclusive evidence could be deduced to consider a reduction in the prothrombin level as a cause
for thrombosis in these cases. Four cases however, showed a definite reduction in the prothrombin concentration, if the figures of 19 & 20 seconds be taken as a possible normal clotting time.

PULMONARY EMBOLISM.

It has long been recognised that there is a definite relationship between thrombosis and pulmonary embolism. Most of the authorities agree with this point of view originally enunciated by Virchow in the middle of last century. Klotz however, following the teaching of Ribbert, maintains that thrombi found in the Pulmonary Arteries were autochthonous rather than embolic. Following convincing proof of their embolic nature, Klotz later accepted the evidence that thrombi were responsible for such emboli. The only possible exception where thrombi might originate in the Pulmonary Arteries is where the veins in the system are subject to thrombosis by virtue of their local pathological condition e.g. trauma, or a generalised condition where the veins are susceptible to unknown toxins or bacteria e.g. Phlebitis Migrans followed by Thrombo-Angiitis Obliterans. In such conditions the arterial thrombosis in the lungs is followed on venous pulmonary thrombosis i.e. both vessels are affected. In an embolic condition however, the Pulmonary Arteries contain emboli but the veins - unless there is an infarct - need not necessarily be involved. Polycythemia Vera or conditions of extreme dehydration which because of extreme viscosity of the blood, might give rise to a generalised thrombosis in which the Pulmonary Arteries and Veins might share.

Against the autochthonous nature of a thrombus found in the Pulmonary Arteries, the question of the rapidity of the blood flow through the Pulmonary vessels might be considered and compared with the rapidity of the stream in the lower extremities. Whereas the blood in the limbs can be retarded in its flow by rest, recumbency, muscular inactivity,
pressure, anatomical obstruction etc., the flow through the Pulmonary vessels is kept at a fairly rapid rate by virtue of respiration, and if we accept the view of Aschoff and his school that retardation and eddy formation in the bloodstream encourages thrombosis, the autochthonous nature of a thrombus found in the Pulmonary Arteries must, on general lines, be disregarded.

In 175 cases examined post mortem 32 cases with emboli were found i.e. 18%. All these cases revealed on macroscopic verified by microscopic examination, thrombosis of the lower extremities. No cases were encountered with emboli in the lungs and at the same time showing thrombosis in any part of the body without thrombosis in the lower extremities. 18% is a high figure compared with the figures of other authorities. The nearest figure is that shown by Belt. Consideration, however, must be given to the fact that these investigations were carried out in the height of winter and the early part of Spring, a factor which is considered by some authorities to influence thrombosis by superficial vaso-constriction. Another factor which must be borne in mind is the number of cases drawn from the chronic sick home which is attached to the Hospital. Both these factors contribute no doubt to the higher incidence of thrombosis in my investigations.

In my series, only four cases were surgical, the rest were medical. No puerperal and only one traumatic cases were encountered. It is obvious therefore that medical cases predominate, the explanation being found in the preponderance of venous thrombosis in medical cases due to well defined causes which predispose to thrombosis in the lower extremities.

Pulmonary complications in convalescent patients is quite a common occurrence. This, in the past, has been attributed to other than embolic causes e.g. Broncho Pneumonia, Other Pneumonia etc. No signs or symptoms in the majority of cases manifest themselves to indicate thrombosis in the peripheral . . .
peripheral veins, hence the difficulty at times in the diagnosis of either condition. Clinically the electrocardiograph is at present used to assist in the diagnosis, but here too difficulties arise owing to the similarity of the tracing in Coronary Thrombosis.

Recurrent attacks of distressing Pulmonary symptoms due to small and repeated emboli is often encountered. The condition lasts for a few days and then passes off leaving occluded vessels in infarcted areas of lung tissues, which sooner or later has a back pressure effect on the right side of the heart with ultimate development of a Cor Pulmonale. That the occurrence of such recurrent attacks is frequent is exemplified by the repeated encounter of old organised and canalised Pulmonary Arteries as well as the frequent finding of cord-like trabeculae running in a longitudinal direction in the larger and smaller Pulmonary branches. The veins in the legs are invariably associated with such chronic embolisation and show such cord-like trabeculae as well.

The question of vagal reflexes initiated in a congested lung and irritated pleura by embolic plugs and constriction of the Coronary Arteries and vagal inhibition of the heart has lately been brought to the fore and is receiving more and more attention. As a result of the work by De Takats, Harrison and Friedberg and Horn it is now known that many cases of death attributed to Coronary thrombosis are really due to Pulmonary Infarction. Such findings are of considerable importance in so far that, knowing the conditions under which thrombosis arises, the possibility of cardiac symptoms arising in the course of these conditions must be borne in mind and direct treatment towards preventing such an eventuality.
Summary.

1. The origin, incidence and causation of thrombosis and pulmonary embolism is discussed and the literature reviewed.

2. The investigation was carried out during winter months and the early spring at the Hammersmith Hospital, British Postgraduate School, London, to which is attached a chronic sick home.

3. The incidence of thrombosis in the posterior tibial and calf muscle veins in 100 unselected consecutive cases was found to be 51.5% and that of pulmonary embolism 21%. In an additional 75 consecutive autopsies, 11 cases of pulmonary embolism were found, giving an incidence of 18% in 175 cases. The investigation was verified by microscopic examination taken from different areas in the leg veins and pulmonary arteries.

4. The incidence of thrombosis was divided into different groups according to the nature of the illness:
   
   (i) Those suffering from primary and secondary cardiac disease. . . . . 63.8%.
   (ii) Those suffering from carcinoma, general debility, cachexia etc. . . . . 48%.
   (iii) Those suffering from arterial disease. . . . . 25%.
   (iv) Miscellaneous diseases. . . . . 36.3%.
   (v) Surgical cases with good operative risk. . . . . 2.3% (4 in 175 autopsies)

5. Thrombosis occurred more often among medical than surgical cases, and was almost invariably bilateral. When debilitated cases are subjected to operation 75% develop thrombosis of the leg veins. Where peritoneal and perivesical sepsis develops after an operation, thrombosis invariably occurs.

6. Cardiac cases show old thrombosed veins, often with superadded recent thrombi, whereas carcinomatous cases show mainly recent thrombi.

7. The origin of a thrombus is in the veins of the calf muscles.
8. An injury to the endothelial lining of a vein is essential to initiate thrombosis. This occurs in the veins of the calf muscles and is due to compression, occurring as a result of pressure by the mattress on the calves while the patient is in the recumbent position.

9. Cardiac insufficiency, slowing and retardation of the blood flow are essential factors in the further development of a thrombus, all other factors are contributary.

10. Phlebosclerosis is a constant finding in elderly people. Its presence facilitates thrombosis.

11. The thrombus is generally of a mixed or red type, often resembling a post mortem clot.

12. Cells participating in the organising process in a thrombus are derived from:

   (a) The endothelium.
   (b) Subendothelial connective tissue.
   (c) From the connective tissue of the "Sublamellar Plexus of Short."
   (d) Possibly from plasma cells taking on a fibroblastic character.

13. Elastic tissue is present in the proliferating intima of veins in Phlebosclerosis but absent in an organising thrombus. In the former it is derived from:

   (i) The splitting of the Internal Elastic Lamella,
   (ii) From fibroblasts.

14. The relationship of arterial disease, Phlebosclerosis and Phlebothrombosis is discussed.

15. A case of Thrombo-Angiitis Obliterans is reported and the relationship between artery and vein is discussed. The points of difference between this condition and an ordinary thrombosed vein is noted and treatment discussed.

16. One case of calcification of the intima of a vein is reported.

17. Age is important. There were no cases under 30 years of age. The high incidence in the 7th decade in the carcinomatous and arterial groups is attributed to the chronic sick home which contributed a fair proportion of the cases. In the heart, miscellaneous and operated cases the highest incidence ...
139.

incidence is in the 5th decade.

18. Sex has no influence on the incidence of thrombosis.

19. The highest incidence in cases of malignancy is when the primary is in the pelvis 66.6%; next when the primary is in the abdomen 57%; and lastly when the primary is in above the diaphragm 53.3%.

20. In Jaundice thrombosis is due to extreme debility, recumbency, exsanguination and dehydration.

21. The difference in the process of organisation of a thrombus and occlusion of the lumen in a vessel on the one hand and the physiological closure of the Ductus Arteriosus Umbilical vein and the Hypogastric Artery in an infant on the other hand, is indicated.

22. The prophylaxis and treatment of thrombosis and Pulmonary Embolism is discussed. Lumbar Sympathetic block is recommended in cases of thrombosis in the veins of the legs.
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PHOTOGRAPHS

and

MICROPHOTOGRAPHS.
Thrombosed veins in the right leg.

1. Area 1. A. Popliteal vein and Artery.
3. Area 3. C. Peroneal vein (not thrombosed)
D. Muscular tributaries.

Thrombosed veins dissected from Fig. 1.

Post mortem thrombus removed from right Ventricle and Pulmonary Artery.

A. Stringy yellowish grey elastic mass of fibrin.
B. Thrombus in the main Pulmonary trunk.
C. Red clot from right and left Pulmonary Arteries and their branches.
**Fig. 4.** (Page 50.)

Antemortem Thrombi attached to wall of Femoral Vein
(by permission of Dr. T.H.Belt)

A. Mixed Thrombus.
B. Red propogated Thrombus.

**Fig. 5.** (Page 51.)

Aorta cut open to show two aneurysms filled with antemortem thrombus.

A. Aneurysm opened to show laminated appearance of thrombus.
B. Thrombus completely filling aneurysm and extending into lumen.

**Fig. 5a.** (Page 51.)

Microphotograph from Fig. 5, showing lamination of antemortem thrombus.

A. White layer represents clumps of platelets.
B. Darker layers represent masses of red corpuscles and fibrin.

(H&E x 12.)
Fig. 6. (Page 53.)
Microphotograph of Post Mortem Clot.
A. Fibrinous layer constituting the elastic mass.
B. Red portion which consists of red corpuscles & platelets. (H. & E. x 12.)

Fig. 7. (Page 54.)
Recent antemortem thrombus showing attachment to wall of vessel at point A. (H. & E. x 12.)
Fig. 8. (Page 54.)

Occlusion of Small Saphenous Vein by two distinct types of organising and canalising thrombi. Note Vasal vessels, thin walled, and Haemosiderin pigment around margin of more recent thrombus.

A. Older thrombus.
B. More recent thrombus.

( H. & E. x 80.)

Fig. 9. (Page 55.)

Phlebosclerotic Vein with propagated thrombus free in the lumen.

A. Artery. B. Vein. C. Internal Elastic layer.
D. Media. E. Thickened Intima.

(Weigert's Elastic Stain x 12.)
**Fig. 10.** (Page 60.)

**Thrombo Phlebitis.**

A. Adventitia with numerous inflammatory cells.
B. External Elastic layer splitting and breaking up.
C. Media. Markedly oedematous, muscles widely separated and infiltrated with numerous cells.
D. Sublamellar layer of "Short" showing marked proliferative change.
E. Internal Elastic layer splitting and disintegrating
F. Commencing agglutination of cells in the lumen.  
   (Weigerts Elastic Stain x 80.)

**Fig. 11.** (Page 60.)

High power of Fig. 10.
A. Media - muscle fibres widely separated by oedema.
B. Sublamellar Plexus.
C. Internal Elastic Lamella.  
   (Weigerts Elastic Stain x 400.)

**Fig. 12.** (Page 60.)

Inflammatory change in the wall of some duration.
A. Media showing numerous polymorphs and marked fibrosis.
B. Disintegrating Internal Elastic Lamella.
C. Thrombus.  
   (Weigerts Elastic Stain x 240.)
Fig. 13. (Page 66.)

Suppurative Thrombo-Phlebitis.

Fig. 14. (Page 70.)

Thrombo Angitis Obliterans.
(Section from mid thigh.)
A. Femoral Artery partially occluded with recent organising thrombus. Note concentric arrangement of thrombus and hypertrophied media.
C. Small artery occluded with recent organising thrombus. Note hypertrophied media.
D. Small thickened vessels establishing a collateral circulation in a matted intervascular dense mass of fibrous tissue. (H. & E. x 8.)

Fig. 14a. (Page 70.)

Section from Post. Tibial vessels.
A. Artery. B. Veins. C. Small Artery.
D. Small hypertrophied subcutaneous vessels. These constituted the collateral circulation. (H. & E. x 10.)
Small vein showing fibrosed thrombus occluding lumen. (H.& E. x 80.)

Small vein occluded with dense fibrous tissue. Note elastic tissue separating fibrosed thrombus into different compartments which apparently were originally canals.

A. External elastic layer.
B. Thickened media.
C. Internal elastic layer.
D. Fibrosed thrombus.

(Verhoeff stain. x 80.)
**Fig. 16.** (Page 70.)
Organising thrombus in a small artery.
( H. & E. x 80.)

**Fig. 17.** (Page 70.)
Organising thrombus in a small artery.

A. Internal Elastic layer.
B. Histiocytes loaded with Haemosiderin pigment.
C. Media -- hypertrophied, intact and infiltrated with cells.
D. Numerous intact thickwalled vasal vessels in thrombus.
   ( Verhoeff Elastic Stain. x 80.)

**Fig. 18.** (Page 71.)
Vascularisation of a thrombus.
A. Vasal vessels. Note thick wall with several layers of cells.
B. Histiocytes with haemosiderin pigment.
C. Mononuclear cells -- lymphocytes and plasma cells.
D. Cells taking on the character of fibroblasts.
E. Vasal vessels in the process of occlusion.
   ( H. & E. x 400.)
Fig. 19. (Page 71.)
Downgrowth of Vasal vessels from adventitia to media.
A. Adventitia.  B. Media.  C. Vasal vessels.
(H. & E. x 400.)

Fig. 20. (Page 71.)
A. Internal Elastic layer.
B. Vessel growing from sublamellar plexus and communicating with canal in thrombus.
C. Canal.  D. Giant cell.
(Verhoeff Elastic Stain x 400.)
Figs. 21 & 22. (Page 96.)

Formation of a thrombus near a Valve.
A. Valve.  B. Recent thrombus.
C. Older thrombus organizing.

( H.& E. x 80.)
Fig. 23. Page 98.
Thrombus from a tributary entering a vein.
A. Wall of vein.
B. Thrombus. Note lamination.
( H. & E x 80.)

Fig. 24. (Page 98.)
Separate thrombi from small tributaries in Posterior Tibial Vein.
( H. & E. x 12.)
Phlebo- or Veno-Sclerosis.

Fig. 25. (Page 99.)
Small Saphenous Vein, uniformly thickened, showing finger-like projections in lumen.
( H. & E. × 10.)

Fig. 26. (Page 99.)
Projection.
A. Adventitia.
B. Media, hypertrophied muscle fibres.
E. Elastic strands.
(Verhoeff Elastic stain × 80.)

Fig. 27. (Page 99.)
Base of projection.
A. Media - circular muscle fibres.
B. Dense connective tissue.
C. Long muscle bundles.
( H. & E. × 400.)

Fig. 28. (Page 99.)
Apex of projection.
A. Muscle bundles.
B. Flattened Endothelial cells.
C. Sinusoids.
( H. & E. × 400.)
**Fig. 29.** (Page 101.)

**Intimal Proliferation.**

A. Thickened Intimal Plaques.
B. Internal Elastic layer.
C. Splitting of Internal Elastic layer and growth of elastic tissue into intimal plaque.
D. Formation of Elastic tissue.

(Weigert's Elastic Stain x 28.)

**Fig. 30.** (Page 101.)

Growth of Elastic tissue from fibroblasts.
High power area D. in Fig. 29.

(Weigert's Elastic Stain x 240.)
Fig. 31. (Page 105.)
Arterial degeneration, Phlebo-sclerosis and thrombosis.
A. Artery showing Mönckeberg Sclerosis.  
B. Vein.  C. Intimal proliferation.  
D. Old thrombus organised and canalised.  
(Verhoeff Elastic Stain.  x 12.)

Fig. 32. (Page 105.)
A. Artery showing Mönckeberg degeneration.  
B. Vein thin walled with recent thrombus.  
C. Fibrosed intervascular tissue matting artery and vein.  (H. & E.  x 50)
Fig. 33. (Page 106.)

Etiological closure of the Hypogastric Artery, Umbilical Vein and Ductus Arteriosus.

**Hypogastric Artery.**

A. Proliferating Intima.
B. Proliferating Subendothelial layer.
C. Internal Elastic layer, thick, split and much of it in the proliferating subendothelial layer.
D. Media. (Weigert's Elastic stain. x 240.)

**Umbilical Vein.**

Fig. 34. (Page 106.)

A. Intimal Proliferation.
B. Remains of lumen with a little blood showing commencing agglutination of blood cells possibly assisting in final occlusion.
C. Media. (H. & E. x 112.)
Ductus Arteriosus -- 8 days old.

Fig. 35. (Page 106.)

A. Intimal Proliferation.
B. Media thick with extraordinary amount of elastic tissue.
C. Adventitia.
D. Internal Elastic layer.

(Verhoeff elastic stain. x 80.)

Fig. 36. (Page 36.)

Proliferating intima from Fig. 35. - High Power. Note downgrowth of cells.
A. Internal Elastic layer.

(Verhoeff Elastic Stain. x 400.)
Pulmonary Embolism.

Fig. 37. (Page 110.)
Embols blocking Pulmonary Artery causing sudden death.
A. Coiled and jumbled Embolus.

Fig. 38. (Page 110.)
A. Recent Embolus. B. Pulmonary Artery. C. Small branches plugged with emboli.
Fig. 39. (Page 112.)

Microphotograph of embolus in a small branch of Pulmonary Artery.
(H. & E. x28.)

Fig. 40. (Page 112.)

Recurrent Emboli.
A. Old Embolus. B. Recent Embolus.
(By courtesy Dr. J.H. Belt.)
Fig. 41. (Page 113.)
Pulmonary Emboli in small branches
A. Old - organised and canalised.
B. Fairly recent. C. Recent. (H. & E. x 10.)

Fig. 22 (Page 113.)
Organised Embolus.
( H. & E. x 28.)
Fig. 43. (Page 113.)

Trabeculation in Pulmonary Artery.
(By courtesy Dr. J. H. Belt.)

Fig. 44. (Page 117.)
Pulmonary Artery with its branches laid open longitudinally.
Fig. 45. (Page 120.)

Syphilitic Aortitis.
A. Right Coronary Ostium - stenosed, pin point.
B. Left Coronary Ostium.

Fig. 45a. (Page 120.)

Myocardial fibrosis. Section of left ventricle showing fibrosis as a result of ischaemia caused bystenosis of the Coronary Orifices.
**Fig. 46.** (Page 120.)

**Coronary Thrombosis.**

A. Coronary Artery with atheromatous patches.
B. Narrowed part with recent thrombus.

**Fig. 46a.** (Page 120.)

Microphotograph of Coronary Artery with thrombus.

A. Thickened Intima. B. Old thrombus.
C. Recent thrombus.  

( H. & E. x 20.)

**Fig. 46b.**

High power of 46a.  

( H. & E. x 80.)
Fig. 47. (Page 120.)
Pedunculated Thrombi on ulcerated Valves.
A. Pedunculated thrombi. B. Aorta.

Fig. 48. (Page 120.)
Pedunculated thrombus constituting a Coronary Embolus.
A. Embolus in the left Coronary Artery.
B. Right Coronary orifice. C. Aorta.
**Fig. 48a.** (L20.)
Thrombus suspended from Aorta by a thin pedicle.
A. Aorta.  B. Pedunculated thrombus.

**Fig. 49.** (Page 121.)
Thrombus in Ventricle.
A. Fibrous wall.  B. Thrombus.
Early thrombosis in Saphenous Vein at three levels.

A. From area 1. Adhesion at one point.
B. From area 2. Propogated thrombus, free.
C. From area 3. Absence of thrombus.
   (H. & E. x 8.)

Hyaline thrombus with commencing organisation.
   (H. & E. x 12.)
Fig. 53. (Page 122.)

Point of commencement of organisation.
A. Media. B. Thickened Intima.
   (H. & E. x 80.)

Fig. 54. (Page 122.)

Area C, in Fig. 53. High Power.
   (H & E. x 400×)
Fig. 55.
Formation of blood vessels in organising thrombus.
A. Small vasal vessels.
B. Blood space lined by endothelium. Note fibroblasts migrating towards it to strengthen its wall.
C. Small blood space without an endothelial lining. D. Angioblasts. (H. & E. x400.)

Fig. 56. (Page 124.)
Obliteration of vasal vessels in organising thrombus.
A. Four vessels in the process of obliteration. (Verhoeff Elastic stain. x 80.)
Almost complete occlusion of lumen by a fibrosed thrombus.
A. Canals. B. Vasal vessels in the process of obliteration. C. Remains of lumen.
(Weigert's Elastic stain. x 28.)

Almost complete occlusion of vessel. A stage further. Note complete absence of Vasal vessels.
(Weigert's Elastic stain. x 28.)
**Fig. 59. Page 125.**

**Trabeculation.**

A. Trabeculus.  B. Commencing thrombus formation.  
C. Thickened Intima.  D. Internal Elastic layer.  
E. Media in the process of fibrosis.  
F. External Elastic layer.  G. Adventitia.  

(Weigert's Elastic stain. x 112.)

**Fig. 60. (Page 125.)**

A. Trabeculus.  B. Thrombus.  C. Intimal thickening.  
D. Internal Elastic layer.  E. Media.  

(Weigert's Elastic stain. x 60.)
Figs. 61 and 62. (Page 125.)

Lumen of veins separated into compartments by trabeculae. Note haemosiderin pigment—black spots in trabeculae.
( H.&E. x 60. and Weigerts stain x 28.)

Fig. 63. (Page 125.)

Retraction of thrombus from vessel wall and attachment to wall of vein by both ends—constituting a trabeculus A.
( H & E. x 12.)
Fig. 64. (Page 125.)
An old trabeculus separates vein in two compartments.
A. Older thrombus. B. Thrombus more recent.
(Weigert's Elastic stain x 28.)

Fig. 65. (Page 125.)
A. Small trabeculae. B. Recent superadded thrombus.
C. Older thrombus — note lamination.
(H. & E. x 10.)

Fig. 66. (Page 125.)
A. Older thrombus.
B. More recent. — Note looseness in structure.
(Weigert's Elastic stain x 60.)
Fig. 67. (Page 125.)
An old organised thrombus attached to the wall by a pedicle with recent thrombosis round it.
(Weigert's Elastic stain. x 28.)

Fig. 68. (Page 125.)
Femoral Vein showing cicatritial trabeculation, thickening and distortion due to organised thrombus.
(By permission Dr. T.H.Belt.)
Phlebolith Formation.

**Fig. 69.** (Page 125.)
A. Vein. B. Artery. C. Phlebolith in organised thrombus
( H. & E. x 12.)

**Fig. 70.**
Vein from Fig. 69. high power, to show-
A. Thrombus with Phlebolith. ( Weigert's Elastic. x 28.)

**Fig. 71.** (Page 125.)
Calcium deposit in wall of vein.
A. Calcium.
B. Bone formation in calcified artery.
( H. & E. x 28.)