THROMBOSIS

by

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THE CARDIOVASCULAR STREAM-BED has two arresting physical properties. The endothelial membrane which lines it possesses a high degree of smoothness which must very materially diminish the frictional resistance between the walls of the vessels and their contained blood. Equally obvious, but less frequently commented upon, is the exquisitely stream-lined construction of the complex pathway traversed by the flowing blood. This is planned to reduce obstruction to a minimum and to eliminate swirling, eddying, back-water formation and local stagnation. Any obstruction to the forward flow, especially in vessels in which the normal local velocity is low, carries the risk of stasis and, as blood *in vivo* clots when it ceases to move, we may take it that the preservation of the physical properties of the cardiovascular pathway is a natural safeguard against intravascular coagulation. It is abundantly clear that the smoothness and stream-lining of the vascular bed is frequently threatened in many different ways and it is most probable that some rapidly acting mechanism has been evolved to preserve its physical integrity. Fig. 1 illustrates some of the more simple conditions which, by producing physical abnormalities in the vascular walls, predispose to local stasis. Amongst these are external pressure producing internal bulging; local narrowing of a vessel from spasm, inflammation or degeneration; pathological dilatation of a cardiac chamber or of a blood vessel expanded into an aneurysmal sac; puckering, folding or corrugation from surrounding cicatrisation; valvular sclerosis and rigidity. In each of these instances the site of swirling, eddying or back-water formation is indicated by a small cross in the diagram. Endothelial swelling or roughening needs further consideration. A rough intima obviously produces a series of abnormal elevations and depressions in the surface where the stream is obstructed and slowed down. Small as each of these depressions may be, their total area when there is arteritis or phlebitis may be considerable. If we review these conditions, it is clear that some may be the immediate result of infection and others a remote consequence, but many could arise in the complete absence of frank inflammation in the vascular wall.

Fig. 2 shows the natural method whereby such irregularities are rectified. In each case the smooth stream-lined internal contour of the vessel is restored by the formation of a firmly adherent, homogeneous and hyaline deposit completely free of cells or fibrin. If the stream is rapid, the vessel wide, and the physical abnormality is not extensive, this deposit may in itself offer no appreciable obstruction to the blood-flow; further

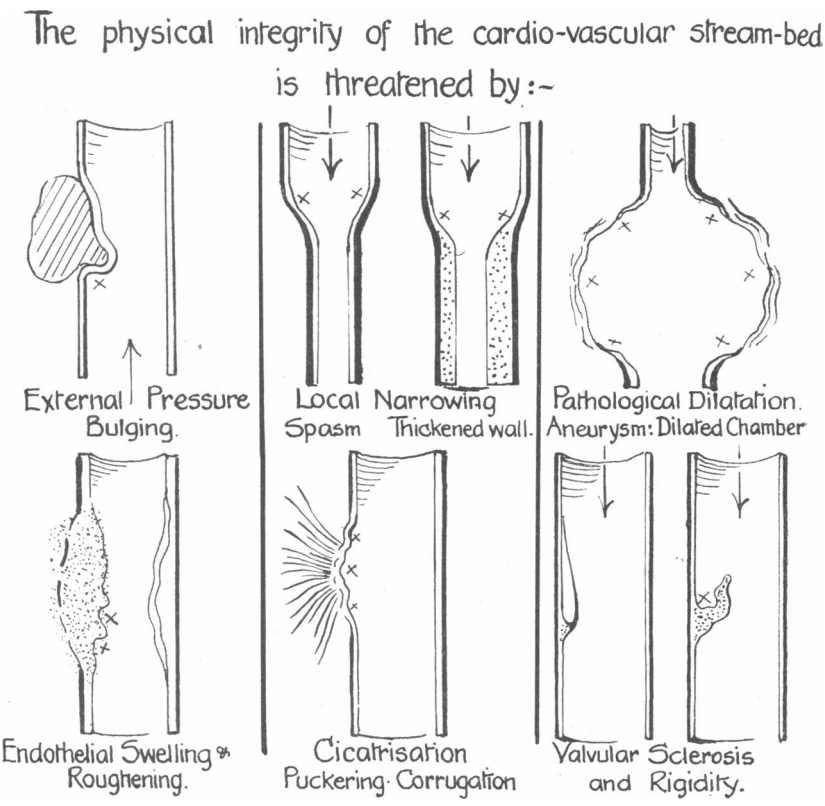

Fig. 1

deposition will cease and, in course of time, the hyaline material will become an integral part of the living vascular wall. There is no need for me to remind you that the formation of this firmly setting *vascular cemen*, which ultimately restores the smoothness and stream-lining of the stream-bed, is the result of the rapid deposition out of the streaming blood of masses of agglutinated blood platelets. The whole process can be watched under experimental conditions and, provided that the mass itself does not offer additional appreciable obstruction, the deposition will stop as soon as its purpose is achieved. It is important to remember that this process, which may with every justification be described as purposeful, may not, and often does not, involve the local deposition of fibrin. I would like to suggest to you, therefore, that the formation of this *vascular cement* is one of the major functions of the blood platelets, that the process is a rapidly acting defence mechanism calculated to restore the physical integrity of the vascular stream-bed, and should be regarded as the primary and essential event in the process of thrombosis.

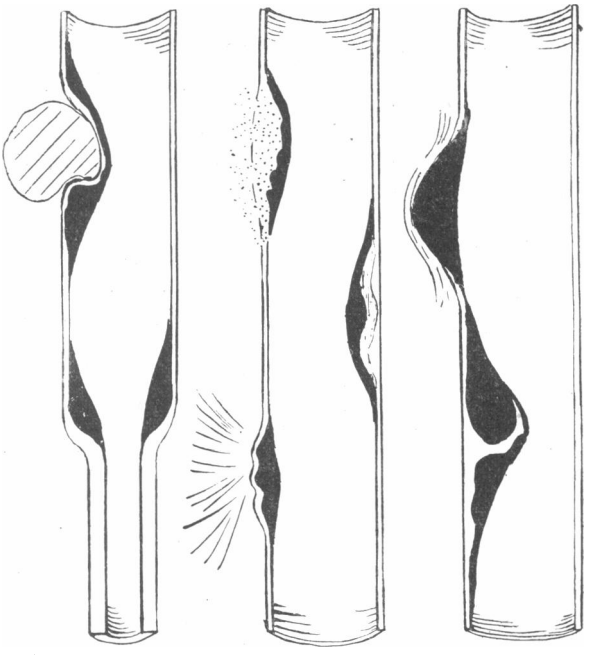

Fig. 2.

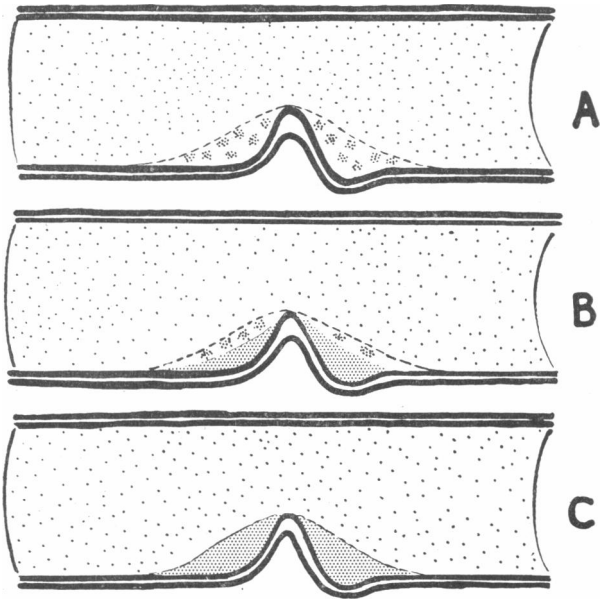

Fig. 3.

Above a critical velocity of flow the blood platelets are evenly distributed in the moving blood. They circulate as discrete particles of negligible weight (see Fig. 3). Below this critical velocity, they exhibit a remarkable tendency to stick to one another, producing large masses in which the outlines of individual platelets are rapidly and completely lost. Being relatively heavy, the masses of hyalinised platelets fall by their own weight, provided that they remain in a stationary or slowly moving stream, and, on reaching the vascular intima, they rapidly become firmly adherent to it and to each other.

The whole process, therefore, depends on this inherent tendency of slowly moving or stationary platelets to stick to one another. Platelet stickiness has been investigated by H. Payling Wright who has devised an ingenious method whereby it can be measured. Two interesting discoveries were made. It was first shown that a significant increase in the number of circulating platelets (i.e., *thrombocytosis*) is accompanied by a corresponding increase in platelet stickiness. As thrombocytosis is due to a discharge of young platelets from the bone marrow, it is quite possible that young platelets are more sticky than old ones. The other discovery was that if the physiological anticoagulant, heparin, is added to the blood or injected into animals, the platelets lose their stickness to such an extent that one wonders if it is to this action that heparin owes its anticoagulant action. You will remember that a significant increase in the number of circulating platelets has often been observed as a result of tissue injury of many kinds under natural and experimental conditions. Thrombocytosis invariably follows the tissue trauma of parturition so that we may regard the sustained discharge of young and abnormally sticky platelets from the bone marrow as a physiological response. It follows simple fracture and surgical operation, and the greater the tissue injury the greater the thrombocytosis. The spleen pulp is exceptionally rich in platelets, and maximum degrees of thrombocytosis follow the operation of splenectomy, probably as a result of the massage of the organ during its surgical removal. It is justifiable to regard post-traumatic thrombocytosis as a purposeful and essentially physiological reaction of the bone marrow but when it reaches a high level as a result of extensive tissue injury it may become a menace. The masses of *platelet cement* deposited upon an abnormal area of intima may then become so large that instead of smoothing out the stream-bed they produce increased obstruction by virtue of their own large size. If this takes place in narrow vessels such as the arterioles, in the high-capacity, low-pressured and slowly-moving peripheral venous blood-stream, in vessels narrowed by spasm or by acute or chronic intrinsic disease in their walls, the margin between obstruction to the flow and obliteration of the lumen becomes greatly reduced. Under these conditions there will be an increasing local concentration in the stagnant area of thrombokinase derived from the accumulating platelets, and a local transformation of fibrinogen to fibrin in the stationary or almost stationary mass of blood. In other words, the very exuberance of the

purposeful mechanism of *platelet cement* formation calculated to restore the normal stream-bed has given rise to fibrin formation which is at once purposeless and progressive, and very frequently completely obliterates the vascular lumen. I would like to suggest to you, therefore, that it will conduce to clear thinking if we regard the process of thrombosis as being solely concerned with the restoration of the physical integrity of the vascular stream-bed, but that it may be *complicated* by such a degree of vascular obstruction that local coagulation becomes inevitable. If you accept these suggestions, it follows that, depending on the diameter of the vessel, there must be a critical degree of vascular obstruction beyond which the defensive and purposeful deposition of platelets (i.e., thrombosis) ceases and the useless, purposeless process of coagulation and vascular occlusion succeeds it.

I would also like further to accentuate the dissimilarity between these processes. Coagulation quite clearly comes into full play as a physiological mechanism when a blood vessel is completely severed. It is a complex physico-chemical reaction whereby a sol, fibrinogen, becomes a gel, fibrin, and can take place just as well *in vitro* as *in vivo*. Thrombosis, on the other hand, can take place in no other environment than the flowing blood-stream of a living animal. It results in the formation of a temporary structure, a thrombus, whose construction is beautifully adapted to its function. It is conditioned by platelet stickiness. It must be very often successful within the limits of our definition and will then be clinically silent. Success is conditioned by the maintenance of a blood flow through the vessel of such force and velocity that *any appreciable local accumulation of thrombokinase from the platelet deposit is rapidly washed away*. We may, therefore, regard post-thrombotic intravascular coagulation as an accident due to the local accumulation in a stationary mass of intravascular blood of thrombokinase in sufficient concentration to initiate coagulation. It strongly tends to be clinically manifest. In some situations its results may be trivial ; in others (e.g., the mesentery of the small bowel), it may be catastrophic ; in others (e.g., the coronary arteries), it is frequently fatal.

In studying the sequence thrombosis intravascular coagulation, the interesting fact emerges that there is an intermediate period before complete vascular occlusion takes place, during which these two diametrically opposed processes are occurring together. This will be clear from an examination of Fig. 4 in which the various stages are set out in diagrammatic form. The sequence is as follows :

1. Deposition of a *primary platelet thrombus.*
2. Formation of a *finely laminated coralline thrombus.*
3. Production of a *coarsely laminated occluding clot*
   followed by
4. Formation of the *consecutive clot*
   and
5. The *propagated clot.*

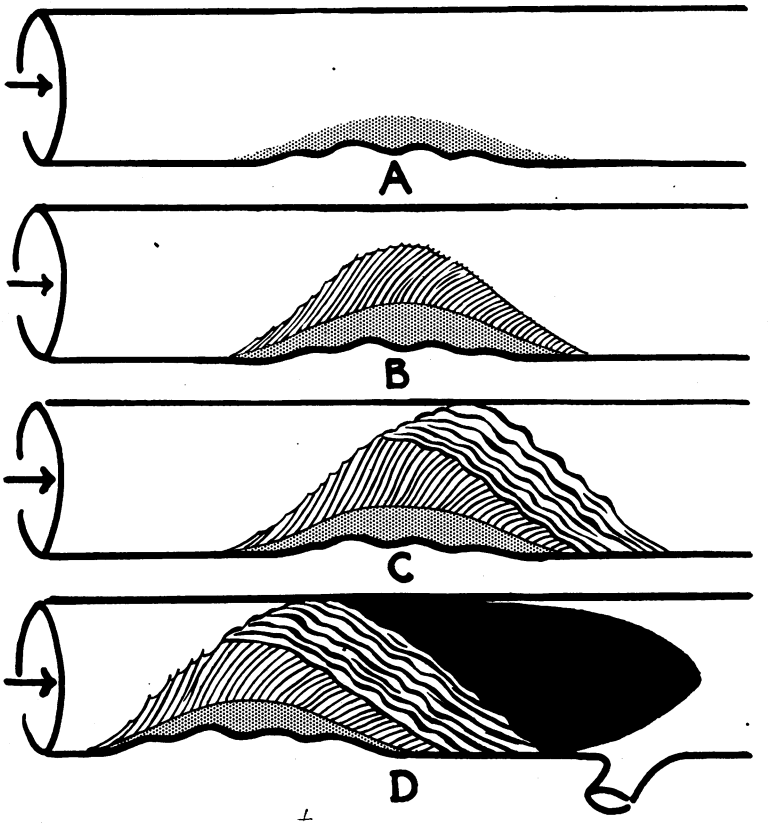

Fig. 4.

Fig. 4A shows the formation of the primary platelet thrombus which Boyd compares with the formation of a snow drift during a snow storm. This thrombus is grey and amorphous, semi-transparent and cement-like. It has a smooth stream-lined surface and rapidly becomes an integral part of the vascular wall. Its formation is the first and essential event in the process of thrombosis. Fig. 4B shows the addition to the platelet thrombus of the *coralline thrombus*. This interesting structure consists of a series of upstanding, corrugated and roughly parallel laminæ, composed of hyalinised platelets which grow across the stream and are bent in the direction of its flow. They anastomose freely with one another and look remarkably like coral (see Fig. 5). The anastomosing laminæ, by acting as powerful cross-struts, materially assist in holding the thrombus together against the momentum of the flowing blood. At this stage the surface of the thrombus is traversed by very fine, closely-set ridges (see Fig. 6), each of which is formed by the edge of a platelet lamina. The

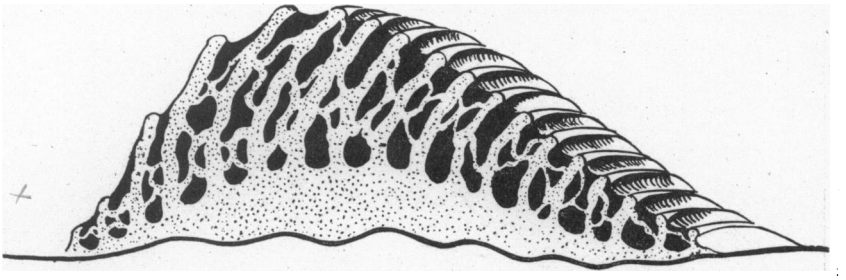

Fig. 5. Diagram showing structure of coralline thrombus.

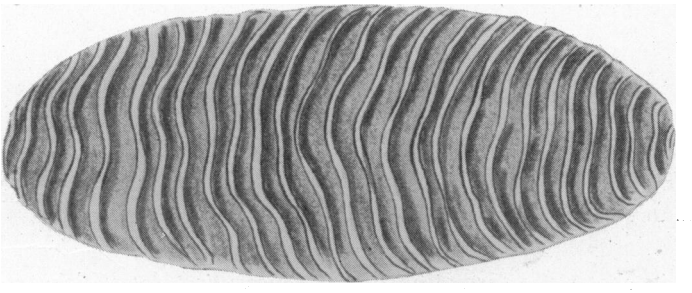

Fig. 6. Surface view of coralline thrombus.

ridges which can only be clearly seen with a hand lens are often known as the " ripple lines " of Zahn and closely resemble the rifling of a gun barrel. As the laminæ grow across the stream many leucocytes are thrown against them and adhere as " flies to a sticky fly-paper " (MacCallum) (see Fig. 7). Stagnant blood plasma accumulates between them and quickly coagulates, the fibrin at first forming delicate festoons which stretch from one lamina to those on either side of it. The structure of the coralline thrombus is clearly adapted to its function but if its growth is progressive, it increasingly obstructs the stream and comes to contain more and more fibrin and trapped red and white cells, whilst its platelet laminæ become increasingly irregular and weaker.

In Fig. 4C the coralline thrombus has produced a significant degree of vascular obstruction ; thrombosis has ceased and a coarsely and irregularly laminated, deep red, *occluding clot* adherent to the thrombus has formed. As long as the blood flows this clot grows by the addition of successive layers of fibrin and red cells. It forms the neck of the occluding mass. *At the moment of occlusion thrombosis ceases altogether.*

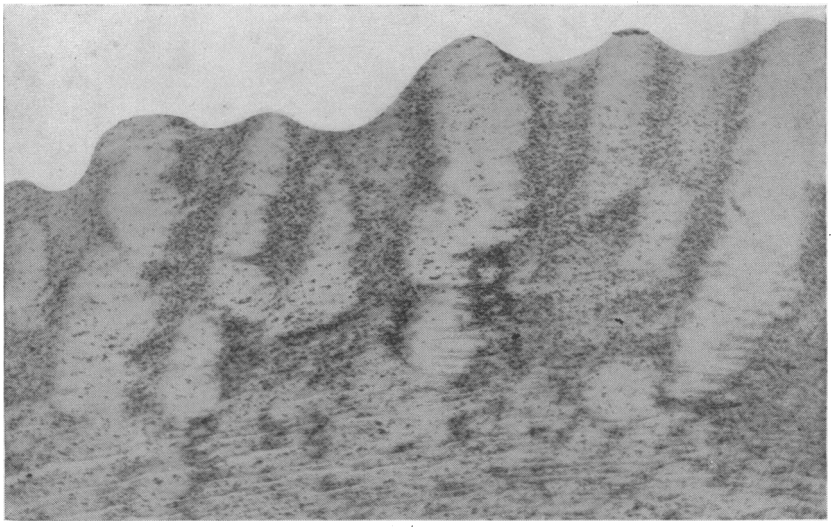

Fig. 7. *Coralline thrombus.* Photomicrograph of vertical section including free surface of a coralline thrombus adherent to the wall of a large artery. Pale platelet laminæ are seen projecting from the surface. Coagulated plasma containing leucocytes lies between them. Many leucocytes are adherent to the platelet laminæ.

Fig. 4D shows the formation of the *consecutive clot*, which extends as far as the next side branch or tributary of the vessel, provided that this vessel is large and the blood flow is not impeded and is sufficiently rapid. If the clot extends for some distance it is said to be *propagated.* Clot propagation may be due to the coagulation of a long stationary column of blood *en masse.* After syneresis has taken place in such a clot it lies floating free in the vessel lumen, anchored to the occluding clot and thrombus proper (see Fig. 8). These long propagated clots lying in the peripheral venous circulation of the lower limbs and sometimes 1½ feet in length may, by becoming dislodged, obstruct the pulmonary circulation. Their formation in the majority of instances is conditioned by failure of one or more of the mechanisms which maintain the velocity of flow in the peripheral venous stream. Another method of clot propagation is seen in situations where the tributary vessels are large and numerous and when the normal velocity of flow is well maintained. The consecutive clot (see Fig. 9) then lies in the direct path of the stream, entering from a large tributary, and rapidly becomes coated by platelet deposit. This may progress until an appreciable degree of obstruction takes place in the side vessel, a coralline thrombus and occluding and consecutive clots are formed up to the next tributary, and the process may be repeated at the entrance of each tributary for a long distance along the course of the vessel. Under these conditions the occluding mass shows a complex

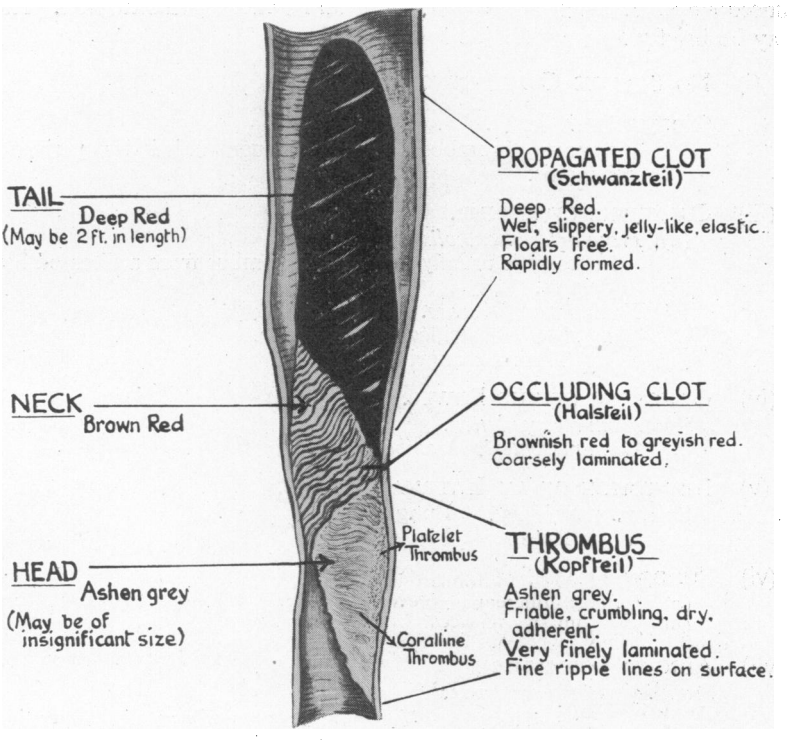

Fig. 8.

pattern of fine and coarse lamination in varying colours and is of necessity firmly adherent and most unlikely to become dislodged and to enter the pulmonary circulation.

We must now consider the basic classification of thrombosis and the variations in the process depending on its site and ætiological background. It will be justifiable to regard as *primary thrombosis* all those varieties, whatever their situation, which are conditioned by a change in the physical characters of the vascular walls. *Secondary or post-embolic thrombosis* can properly be applied when, the vessel being normal, it is partially obstructed by an embolus. In either case, having regard to the marked dissimilarity in outcome, we must divide all varieties into those which are *infective*—clot and thrombus containing living bacteria which may be virulent—and those which are bacterium-free, *bland or non-infective* It is clearly essential, in view of the enormous variation in ætiology and pathogenesis, to classify each type into those occurring in the heart, arteries, veins or capillaries.

Before considering the various anatomical varieties of thrombosis, it may be profitable to remind you of the very great diversity in the clinical

consequences of thrombosis, depending on its cause and situation. These may be briefly summarized as follows:

(i) NO SERIOUS CONSEQUENCE.

(ii) ŒDEMA OF A LIMB.
From venous thrombosis, usually accompanied by perivenous lymphangitis.

(iii) GANGRENE OF A LIMB.
(*a*). *From arterial embolism.*
Embolus is usually a mass of thrombus from a diseased heart valve.
(*b*) *From arterial disease.*
e.g., Medial calcification.
Thrombo-angeitis obliterans.

(iv) GANGRENE OF THE BOWEL.
(*a*) *From strangulation.*
(*b*) *From mesenteric thrombosis.*

(v) INFARCTION OF AN INTERNAL ORGAN.
Spleen. Kidney. Lung.
Brain. Retina. Myocardium.

(vi) SUDDEN DEATH.
(*a*) *From pulmonary embolism.*
(*b*) *From coronary thrombosis.*

(vii) ABSCESS FORMATION.
From infective thrombosis:
(*a*) Local—Thrombo-phlebitis in an area of acute inflammation.
(*b*) General—In both lungs by embolism from thrombo-phlebitis in a peripheral vein.
In many organs by emboli from particles of infected thrombi forming on a heart valve.

It will be clear from this brief and general consideration of the clinical consequences of thrombosis that, apart from the serious effects which may follow acute infective phlebitis, those which follow arterial thrombosis tend to be more serious. On the other hand, there is no doubt that venous thrombosis is far more common than arterial, and this in spite of the fact that, compared with veins, intrinsic disease is more common in arteries. The reasons for this become obvious if we compare the general structure of arteries and veins, and more especially if we analyse the factors which maintain the two circulations. The venous circulation is a capacious, low-pressure and low-velocity system, largely maintained by the stroke volume of the contracting ventricle, by the depth of respiration, by voluntary muscular contraction and by the action of the venous valves. The force of the contraction of the left ventricle has been very greatly dissipated by the time it reaches the peripheral venous circulation and the maintenance of venous flow is very highly susceptible to any diminution in the stroke volume of the left ventricular contraction. There is, under normal conditions, therefore, a narrow margin between flow and stasis

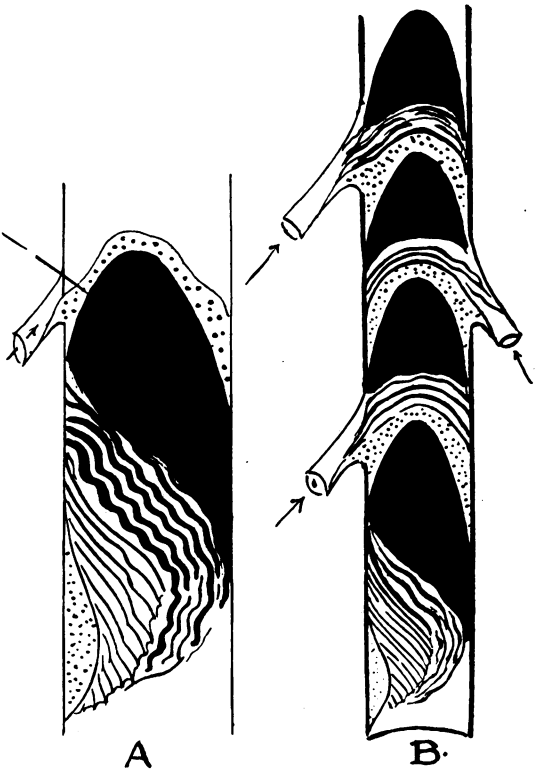

Fig. 9.

in the venous circulation, and any appreciable fall in the minute volume of the heart, in the vigour of the suction-pump action of the sub-atmospheric intra-thoracic pressure, of the force pump action of the diaphragm, the massaging action of the voluntary muscles, or a lowering of the tone of the abdominal muscles, will contract this normally narrow margin still further. Venous thrombosis may therefore be precipitated by structural or functional myocardial disease. Post-operative venous thrombosis is almost entirely confined to patients who have an ageing heart muscle and is a remarkably common complication of congestive failure from any cause and at any age. It often arises on a background of general muscular immobility in ill patients confined to bed from any cause. Shallow breathing accompanying pulmonary disease, pain, shock or sedation will clearly predispose, as will inadequate diaphragmatic contraction from abdominal distension.

In considering the local causes which may be responsible for the greater incidence of thrombosis in veins, we must remember that venous anastomoses are plentiful and the anastomotic vessels are often tortuous; the

intima is provided with valves which, in the lower limbs at least, frequently become incompetent from sclerosis. Vein walls, compared with those of arteries, are weak and thin, the media is composed of loosely woven muscular fasciculi, and the elastic tissue is sparse ; they are easily distended in the erect posture, easily collapsed by pressure, and readily invaded by bacteria, whilst many of them are superficially placed and therefore especially liable to injury and infection. The arteries, on the other hand, form part of a far less capacious, high-pressure and high-velocity system, maintained by the full force of ventricular contraction. They are far less numerous and their anastomoses are much more scanty. They remain open when empty, as they possess considerable tone and elasticity, and the walls are thick and the muscle bundles compact. They are far less distensible, are not commonly invaded by bacteria, and, the large majority being deeply placed, they are well protected from injury and infection.

ARTERIAL THROMBOSIS

Arterial thrombi which result from intrinsic arterial disease form in a high-velocity, turbulent and torrent-like stream, build up very slowly, contain relatively few red cells and little fibrin. They are remarkably firm, dense and dry. In post-embolic arterial thrombosis there is a large element of obstruction from the moment of embolisation ; the thrombus is soft and crumbling and contains much fibrin and many red cells. By far the most common general factor, pre-disposing to primary arterial thrombosis of clinical importance, is reduction in size of the arterial lumen. This may be the result of acute arteritis producing acute swelling of the vessel wall which may be involved from without inwards as the result of trauma or after surgical operation through heavily infected or contaminated tissues such as those of the upper respiratory tract. It is common in the immediate vicinity of ulcerating new growths of the respiratory and gastro-intestinal tracts and occurs with marked regularity in polyarteritis acuta nodosa. In all these conditions, as a result of rapid swelling of all coats of the vessel as the inflammatory process spreads through its walls, there is a preliminary phase of protective thrombosis followed by occlusion by clotting. The infection may then spread into the delicate, recently-formed clot and thrombus, which become disorganized and softened. The result is secondary hæmorrhage. The sequence of events is similar in acute post-embolic thrombosis with a greater likelihood in this condition of the formation of a mycotic aneurysm.

Arterial thrombosis in chronic disease may be similarly due to the intra-mural spread of local infection. Witness the slowly progressive endarteritis in the arteries lying close under the floors of chronic peptic ulcers, and the heavy incidence of thrombosis in them. No less striking are the thick-walled endarteritic vessels lying in the walls of tuberculous cavities in the lung. No clearer example of arterial thrombosis capable of producing serious effects could be quoted than that which so frequently follows the periarteritis and endarteritis which affects the small nutrient

arteries lying in a focus of chronic active syphilitic inflammation. Other conditions varying widely in their causes and consequences, but all characterised by a local reduction of arterial calibre and a strong tendency to be complicated by arterial thrombosis, are atheroma (especially when it affects smaller arteries such as the coronaries), the slow necrosis of arteriolar walls which occurs in malignant hypertension, and arterial lesions of medial calcification, thrombo-angeitis obliterans, temporal arteritis, giant-celled arteritis, and disseminated lupus erythematosus. In many of these diseases, where it is possible to demonstrate a cellular inflammatory reaction in the arterial wall, there is some direct and rather more indirect evidence that the arteritis and thrombosis are in some instances at least the results of bacterial or protein hypersensitiveness. In tertiary syphilis the almost complete absence of living treponemata, combined with progressive tissue destruction, clearly affords some grounds for supposing that the tissue comprising the walls of small arteries and arterioles is prone to become abnormally reactive to minute doses of the antigens of certain infective agents.

VENOUS THROMBOSIS

During the last twenty years there has been an increasing appreciation of the supreme importance of general circulatory and respiratory efficiency in maintaining the peripheral venous flow, and every well-informed clinician now realises how narrow a margin exists in health between movement and stasis in its outlying parts, how dangerously constricted this margin becomes in the bed-ridden patient, and how rapidly a diminution in the vigour of left ventricular contraction will reduce the narrow margin to a level at which peripheral venous thrombosis becomes inevitable. The rate of venous flow in the lower limbs of a healthy young adult can be diminished to a surprising but never a dangerous degree by simple confinement to bed. It falls to an appreciably lower level in those with an ageing myocardium, to a lower level still if the vigour of respiration is diminished, and, if to these handicaps we add general muscular immobility, the stage is set for peripheral venous thrombosis which, I need not remind you, affects the deep veins of the calves in the majority of patients. This process has four fundamental features. It is *quiet*, *deep*, *bland* and *remote*. *Quiet* in that it gives rise to few clinical signs ; *deep* in that it usually affects a venous system embedded in the musculature of the lower limb ; *bland* in that there is no evidence that infection of the vein wall plays any part in its causation ; and *remote* in that it occurs in the distant periphery of the venous circulation and has no anatomical connection with the primary disease which it complicates, nor with the operation site when it is post-operative. It is quite inaccurate and totally misleading to associate this process with phlebitis or thrombo-phlebitis, and it is now customary to describe it as *phlebo-thrombosis*. I would commend this word to you not only because it is accurate but in order that you may assist in forcing it into current usage. It is instructive to compare phlebo-thrombosis

with frank infective thrombo-phlebitis as I have done in the following table :—

	PHLEBO-THROMBOSIS	THROMBO-PHLEBITIS
Root Cause	Venous stasis in the deep veins of the lower limb in bed-ridden patients	Invasion of vein wall by living bacteria or gross damage by chemicals or trauma
Pathological Sequence	(1) Stasis (2) Limited thrombus formation (3) Extensive clotting (4) A poorly anchored propagated clot	(1) Extensive protective thrombosis with firm adhesion over a large area (2) Propagated clot firmly anchored
Physical Signs	Few Phlebo-spasm mild or absent	Outspoken Phlebo-spasm prominent
Predisposing	(1) Age (80 per cent. over 40) (2) Myocardial disease (3) Decubitus and immobility	Conditioned by local infection, especially perivenous lymphangitis
Serious Risks	Massive pulmonary embolism (which has a 10 per cent. mortality) and pulmonary infarction. Infarcts never suppurate	Multiple bilateral pulmonary infarcts from small fragments of disintegrating thrombus. Infarcts are small and often suppurate Massive embolisation—a remote possibility

PULMONARY EMBOLISM FOLLOWING PHLEBO-THROMBOSIS

In the majority of cases this is the result of phlebo-thrombosis in one or more of the deep calf veins, most commonly the peroneal or posterior tibial, less frequently the veins in the sole of the foot or the back of the thigh. The deep femoral is an uncommon site. Estimations of the post-mortem frequency of phlebo-thrombosis of the leg veins, whether complicated by pulmonary embolism or not, are instructive. The following percentage incidences are quoted by Paul White :—

(*a*) 8 to 12 per cent. of all routine post-mortems ;

(*b*) 5 to 10 per cent. of all post-operative deaths ;

(*c*) 0·1 to 0·5 per cent. of all patients operated upon.

Of more general significance are the figures relating to patients suffering from organic heart disease. Phlebo-thrombosis in the lower limbs was present in 30 per cent. of all autopsied cases of mitral stenosis and 48 per cent. of all cases of congestive heart failure. Bearing these figures in mind it is not surprising that, of a large series of cases of fatal pulmonary embolism following phlebo-thrombosis of the leg veins, 60 per cent. of the deaths were in medical cases and 40 per cent. were post-operative.

The primary lesion in post-operative pulmonary embolism is the formation of a true adherent thrombus, usually in one of the deep veins of the calf, followed by the formation of a propagated clot which normally extends well into the thigh. *This lesion is often bilateral.* The total length of

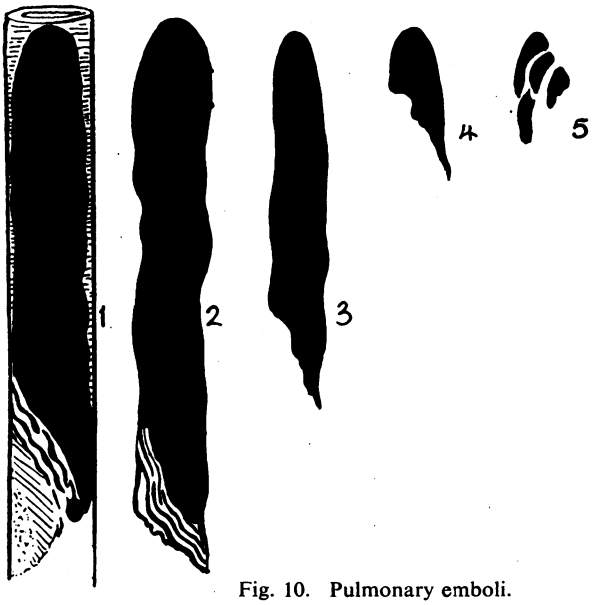

Fig. 10. Pulmonary emboli.

(1) Long length of peripheral vein occluded by thrombus and clot.
(2) Long embolus, composed of propagated clot and laminated clot which, by impaction in pulmonary artery, would prove fatal.
(3) Part of propagated clot which would probably obstruct the main artery to a lung or lobe, and cause massive infarction.
(4) Embolus likely to produce a single smaller infarction.
(5) Multiple small emboli likely to produce multiple small infarcts which may be bilateral.

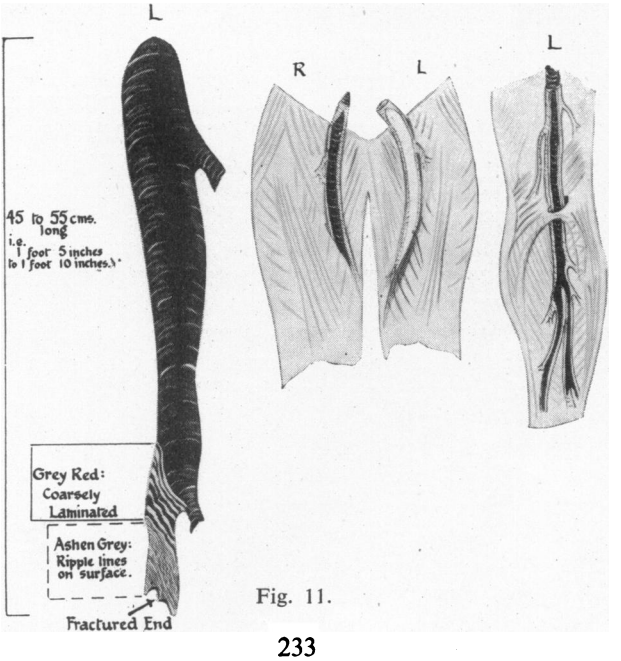

Fig. 11.

the thrombus, occluding clot, and propagated clot, varies from 45 to 55 cms. (1 foot 5 inches to 1 foot 10 inches), and in the majority of instances the embolus is composed of part of the propagated clot or the whole of this structure, together with varying amounts of occluding clot and, in some cases, part of the thrombus itself. The clinical effects will obviously depend upon the size of the mass which breaks away (see Fig. 10). If the embolus is small and of recent formation it may, on reaching the right heart, break up into a series of small fragments which are propelled into the lungs producing relatively small and bilateral sterile pulmonary infarcts. Larger emboli which remain intact may embolise branches of the pulmonary artery of varying size and produce large single infarctions, sometimes involving a whole lobe or a whole lung. Rapidly fatal embolism is the result of impaction of a mass of clot and thrombus in the main pulmonary artery or at its bifurcation. The clot varies in length from 8 to 20 inches or more and is invariably fairly tightly coiled on itself several times. It may show the broken ended casts of tributary vessels and there may be at its lower fractured end a mass of coarsely laminated, deep brownish red occluding clot (see Fig. 11). The main vessels of one lower limb will be found empty, and the thrombus in the right heart, when uncoiled, will fit accurately into them, its lower fractured end fitting the broken end of the clot still lying *in situ* in a vein (see Fig. 11). Examination of the other limb shows a similar state of affairs in a surprisingly high proportion of cases except that, if the patient dies in the first embolic episode, these vessels will still contain thrombus and clot, whereas, if death took place during a second or third episode, it may be clear that pulmonary emboli had been contributed by both lower limbs.

I would, in conclusion, like once more to stress that the key to the understanding of the mechanism of post-thrombotic pulmonary embolism is a full appreciation of the factors which normally maintain the peripheral venous circulation. With regard to the conditions which favour its occurrence you will be interested in the following statement, written in 1945 by the American cardiologist, Paul White :—

" It is an astonishing and disconcerting fact that I and many others had been examining and treating patients for years without realising what we now know, namely, that pulmonary embolism instead of being predominantly a surgical or rather post-operative complication is actually much more commonly a condition occurring in the practice of internal medicine, particularly in heart disease itself."