resting; to maintain this attitude the nerve mechanisms must have in them a nucleus which may have been expanded into that elaborate mechanism which serves the needs of orthograde apes.

SCOLIOSIS.

In none of the orthograde forms is such a continuous and urgent demand made on the postural spinal mechanism as is the case in man. In man only is the whole weight of the suprasacral part of the body supported erect on the spine over long intervals. The demand on this neuro-muscular postural mechanism is, I think, even greater in the sitting than in the standing posture, particularly if we sit leaning forwards in writing and reading. Sitting bolt upright is particularly exhausting, more especially for young people in whom growth of vertebrae and of spinal muscles is proceeding apace. The muscles which act on the short levers of the spine yield first, while the muscles which act on the long costal levers can still keep on. We rest these exhausted short spinal muscles by allowing the vertebrae to rotate until the articular processes begin to lock and the transverse processes rest upon the necks of the long costal levers. Herein lies the beginning of lateral curvature or scoliosis. If the habit becomes fixed, then come the deformities of chest, vertebrae, and spine with which orthopaedic surgeons are only too familiar. It is not true, however, to say that our spines are not perfectly adapted to the upright posture; it would be more accurate to say that human spines were not evolved to withstand the monotonous and trying postures entailed by modern education and by many modern industries.

REFERENCES.

¹ T. Wingate Todd: *Anat. Record*, 1913, vol. 24, p. 251. ² See Wingate Todd, loc. cit.; A. Keith: *Journ. of Anat.*, 1932, vol. 37, p. 18.

The Goulstonian Lectures

ON

THE NATURE OF ARTERIO-SCLEROSIS.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON

BY

GEOFFREY EVANS, M.D.CANTAB., F.R.C.P.LOND.,
ASSISTANT DIRECTOR, MEDICAL UNIT, AND ASSISTANT PHYSICIAN,
ST. BARTHOLOMEW'S HOSPITAL.

LECTURE II.—THE INTRINSIC PROCESS IN ARTERIO-SCLEROSIS.*

The histology and distribution of diffuse hyperplastic sclerosis formed the subject of the last lecture. The nature of the process concerned in the development of the lesion is the next aspect of its pathology to be considered. From a theoretical standpoint one or more of four cardinal processes are involved—namely, Involution, Growth, Inflammation, and Degeneration. The subject is a difficult one to present concisely, and if it is dealt with from an abstract point of view its presentation is liable to be either too dogmatic or ambiguous; hence I have chosen a chief advocate for each theory, and will discuss the theory on the basis of the argument and facts brought forward to support it.

PHYSIOLOGICAL PROCESSES.

(a) *The Process of Involution.*

Thoma's¹ view of arterio-sclerosis was based on the observation of the changes that take place in the aorta at birth on the interruption of the placental circulation. He observed an intimal thickening of the aorta between the origin of the ductus arteriosus and the origin of the umbilical arteries, due to cellular proliferation and new formation of connective tissue in the subendothelial layer, and, as Jores showed later, due also to the formation of elastic tissue in this layer. Thoma compared this change to the intimal thickening found in ligatured arteries and in the obliterated hypogastric arteries of infants, and he attributed it to a slowing of the blood stream. He applied this theory to the development of arterio-sclerosis. Thus, in the case of nodular sclerosis, he held that the intimal thickening was secondary to weakening of the media,

as a result of which bulging of the vessel wall occurred, with consequent slowing of the blood stream at the site of bulging. In the case of diffuse arterio-sclerosis not due to initial weakening of the media he presumed a destruction of capillary fields by disease, and argued that as a result of reduction in the size of the vascular bed a slowing of the blood stream occurred in the vessels supplying the affected area. The theory involves the assumption that an artery may fail to adapt its lumen to the amount of blood flowing through it by contraction of the media, and that the necessary narrowing of the lumen is completed by thickening of the intima.

It is generally agreed that as a basic explanation of the development of arterio-sclerosis Thoma's theory does not hold good. Thus, as Fuchs pointed out, there is no evidence of a failure on the part of the aorta to equalize by muscular contraction the size of its lumen to the decreased quantity of blood flowing through it after cessation of the placental circulation. Further, it is inconceivable that in a system such as the cardio-vascular, which adapts itself so rapidly to changes in the distribution and quantity of blood content, a single alteration in these conditions could be responsible for intimal thickening which gradually increases over a period of years. Thoma's premisses were also shown to be incorrect by the fact that the intimal changes in the aorta are not limited to the length of the vessel between the ductus arteriosus and the origin of the umbilical arteries. Jores raised objection to the theory on histological grounds; he emphasized the fact that the intimal thickening in involution is of the connective tissue or regenerative type, whereas in arterio-sclerosis it is of the hyperplastic type—a distinction based on the different form of elastic fibres in the two conditions. Marchand also attacked the theory on histological grounds, and pointed out the absence of fatty degeneration in arterial involution in contrast to its constant presence in arterio-sclerosis. The same fact has come to my notice in studying the changes that take place in involution of the ductus arteriosus and hypogastric arteries of infants. There seemed to be an exception to the rule that fatty degeneration does not occur in arterial involution in the reported presence of fatty degeneration in uterine arteries undergoing normal involution, but, as I have shown elsewhere,² the work which led to this opinion was based on the examination of pathological material, and the fatty change observed in the specimens examined was due to disease elsewhere and was not a part of the process of normal uterine involution.

Though Thoma's theory fails in providing a basic explanation of arterio-sclerosis, it probably holds good in so far as it includes the idea of replacement fibrosis. For instance, in the case of nodular sclerosis, if the primary lesion is in the intima Thoma's theory has no application, but if the initial lesion is in the media it may well be that the intimal proliferation occurring as a secondary event is compensatory. Thoma attempted to prove that the initial change was a weakening of the media by injecting arteries affected by nodular sclerosis with melted wax equivalent to the blood pressure during life, then allowing the wax to set and cutting sections of the artery. He claimed that the nodules disappeared and the lumen of the artery so distended had a normal cylindrical form. These experiments have been repeated by Klotz,³ who used water instead of wax, and cut the vessel frozen; he failed to confirm Thoma's results. Thoma also attempted to demonstrate the primary weakening of the media by injection of the vasa vasorum of the larger vessels, and he showed that a greater penetration of the media by vasa vasorum occurred at certain points where there was no intimal thickening, and since this increase in vessels in the media was found in patches of nodular sclerosis he argued that the new formation of vessels showed a damage to the media as a primary event preceding the intimal proliferation. My own view of the matter is that Thoma's view of arterio-sclerosis holds good to the limited extent that it involves the idea of a replacement fibrosis. To this extent it is in keeping with the inflammatory theory of arterio-sclerosis, and it is of this further value—that it brings out the fact that degenerative changes are a primary event in one form at least of arterio-sclerosis. Yet even when the degenerative changes are primary it cannot be assumed that the intimal proliferation is necessarily of the nature of a replacement fibrosis, since the proliferation may be a direct response to the insult that is simultaneously responsible for the medial degeneration. Thus Thoma's theory is merely an adjunct to any basic explanation of the production of the lesion in arterio-sclerosis.

* Abstract of lecture delivered on March 8th.

(b) The Process of Growth.

Jores's⁴ views on the production of arterio-sclerosis may be discussed in terms of the physiological process "growth." He finds the basic explanation of the lesion in arterio-sclerosis in the intimal changes that normally occur in the aorta in the process of growth, and he expresses the opinion that "an increased functional demand on the vessel wall is a necessary factor for the development of arterio-sclerosis." He also says: "The hypertrophy of certain layers of the vessel wall and their subsequent degeneration is the essential feature of arterio-sclerosis." A distinction is drawn between this process and the process of inflammation in these words:

"In direct contrast to the thesis already advanced I regard the connective tissue thickenings of the intima as secondary events, reactions and compensatory endeavours on the part of the vessel wall, which are on a par with the phenomena of repair after injury and defect, regeneration, and scar formation processes of inflammatory reaction."

He sums up with the words:

"The development of arterio-sclerosis does not depend on these; they arise from quite other causes and do not lead to true arterio-sclerosis."

Jores bases the distinction between the hyperplastic and fibrotic layers of the intima on a study of the changes in structure of the intima of the aorta during the natural process of its growth. In the aorta in the first year of life he describes a layer on the inner side of the media consisting of two lamellae of elastic tissue lying close together; cells of variable form, in the main elongated, lie between these two lamellae. Comparing this with the aorta at the age of 13 years the same layer is seen, and now wider; the two lamellae are stronger and between them lies a fine network of elastic fibrils, while the nuclei previously seen between the two elastic lamellae have, in the majority, an obvious morphological identity with muscle cells. This is the musculo-elastic layer. It increases in thickness with growth, and though there are variations in its development the variation is within narrower limits than is the variation in thickness of the rest of the intima. At the age of 20 years the musculo-elastic layer is increased both in the thickness of its lamellae and by the splitting off of two further layers of elastic tissue from the original inner lamella. The splitting off of elastic tissue layers from the original lamellae in the process of growth of the aorta is directly compared with the same process which Jores describes as occurring in the small arteries in arterio-sclerosis. It is in this comparison of the development of the musculo-elastic layer of the aorta with the development of new lamellae of elastic tissue in small arterio-sclerotic vessels and the parallel development of the changes in the two conditions, the one of growth and the other of disease, that Jores discovers the underlying process in arterio-sclerosis.

There is, however, a difficulty in maintaining the distinction between hyperplastic intimal thickening of arterio-sclerosis and the connective tissue or regenerative thickening in the intima that is found in inflammation of arteries—a difficulty which Jores himself appreciated. The two types of intimal thickening always occur together, except in normal growth of the aorta, and as a matter of fact Jores's hyperplastic layer is often found in pure inflammatory states. [Specimens of syphilitic and tuberculous endarteritis with well formed hyperplastic intimal thickening were shown.]

A more serious criticism of Jores's views is directed against his theory of the formation of elastic tissue. He suggests that the laminae of elastic tissue in the hyperplastic layer of arterio-sclerotic vessels develop by a process of swelling and splitting of the internal elastic lamina, as distinct from the process by which elastic fibres are formed in the connective tissue or regenerative layer of the intima. Since, however, elastic fibres have no nuclei, and presumably no independent activity, the idea that an elastic lamina can grow in thickness, split and throw out thread-like branches into neighbouring tissues, is contrary to the accepted canons of biology. The present view of the formation of elastic tissue is that it is laid down by connective tissue cells or by endothelium, and, like other intercellular material, it is living but inert. Little, however, is known of the conditions that govern its formation and form, and it is an interesting speculation to draw an analogy between the formation of concentric laminae of elastic tissue in the thickened intima of sclerotic vessels and the Liesegang phenomenon,⁵ in which banded precipitates are formed in gelatin solutions. Bradford⁶ has shown the fundamental rôle of adsorption in the formation of these stratified layers,

and though the physico-chemical factors concerned in their formation are not yet accurately known, the influence of the surface area of the precipitated salt, the concentration of the solute and solid, the reaction of the gel and other factors have been closely studied, and may ultimately throw light on the formation of elastic tissue in arterio-sclerosis. It is evident, therefore, that Jores's theory is based on a wrong principle, and I do not think that his observations provide evidence on the proposition that arterio-sclerosis is a result of an increased functional demand made on the vessel wall.

INTRINSIC PATHOLOGICAL PROCESSES.

The two theories of arterio-sclerosis that are more directly based on the pathological processes of inflammation and degeneration remain for consideration. The latter will be taken first, since of the four theories of arterio-sclerosis it is the most generally accepted:

(c) The Process of Degeneration.

Marchand⁷ is chosen to represent this theory, as he has so far made it his own as to suggest the word "athero-sclerosis" in place of "arterio-sclerosis." Thus he states that there can be no doubt that degeneration is the main feature of arterio-sclerosis. He finds that the degeneration begins (*simultaneously with proliferation of the intimal cells*) in the deeper layers of the intima; and that the occurrence of "primary" fatty or atheromatous degeneration is so closely associated with sclerotic processes that the term "arterio-sclerosis" is not sufficiently comprehensive for the whole disease. Thoma's theory of arterio-sclerosis postulated a weakening of the vessel wall with resulting loss in its elasticity and widening of its lumen as the initial fact that determined a slowing of the blood stream. He did not, however, accept the necessity of demonstrable pathological changes in the weakened media, and inclined to the view that the more obvious degenerative changes were secondary to those anatomical changes to which he attached most importance—namely, the involutionary changes previously discussed. Marchand controverts him on this matter, and says that Thoma attached too little importance to the essential degenerative character of the processes involved. The difficulty in fatty degeneration, which the difference in the opinions of Thoma and Marchand illustrates, is as to whether it is primary or secondary; whether in fact, as Virchow pointed out, its appearance is the first sign of disturbance of tissue structure, or whether it only comes after other evidence of disturbance is visible. Marchand's views are endorsed by Andrewes, who has written, under the title of "Arterial Degeneration," "there can be no doubt that the primary histological change is a degenerative one affecting the muscular and elastic tissues."

In the case of diffuse hyperplastic sclerosis the specimens I have shown demonstrate equally beyond doubt that the primary histological change in the arterioles is proliferative and not degenerative. The interpretation of the changes seen in the parent vessels of the arterioles will depend on the significance attached to hyaline substance in their walls. I have adopted the presence of fat as my criterion of degenerative change and do not regard the presence of hyaline substance in the inner layer of the intima in these vessels as critical evidence of degeneration (Lecture I), and in this interpretation I am, I think, supported by Jores. In addition to the reasons already given for this view, it is a striking fact that the anatomical changes progress to marked extent without the appearance of fatty degeneration—in fact, fat is characteristically absent in the intima of these vessels. Hence I maintain that the lesions of diffuse hyperplastic sclerosis are primarily proliferative, and at the same time they share with other forms of arterio-sclerosis the stigma of fatty degeneration in some part of the lesion. This degenerative change is, however, secondary.

These contradictory views as to the nature of the initial lesion of arterio-sclerosis depend on the type of artery and the form of arterio-sclerosis studied, and the stage in the disease process at which the observation is made. Thus, in the case of diffuse hyperplastic sclerosis, it is only by the demonstration of the endothelial proliferation in the earliest phase of the lesion that the priority of proliferation over degeneration has been established. Klotz, on the other hand, has identified a form of arterial lesion occurring in older subjects in which fatty degeneration of the media is the primary event. This type of arterial disease will be referred to later, and in the present connexion it illustrates the fact that all forms of chronic arterial disease do not start in the same way.

(d) *The Process of Inflammation.*

Virchow's opinion⁸ is best stated in his own words:

"In this matter I have no hesitation in completely accepting the old view and in attributing the origin of the so-called atheromatous degeneration to an inflammation of the vessel wall, and I have taken pains to show that this kind of inflammatory disease of the vessel wall is in fact exactly the same as the condition of the heart wall commonly called endocarditis. There is no other difference between these two processes than that endocarditis more often runs an acute course, and endo-arteritis more often runs a chronic course."

This is the view of arterio-sclerosis to which my own observations have led me, with this reservation—that there is at any rate one form of chronic arterial disease that begins as a primary degeneration of the media.⁹ I have no doubt that Virchow's theory holds good for diffuse hyperplastic sclerosis, and before resuming the evidence in support of this theory it is necessary to refer to two objections that have been urged against it.

In the first place it has been urged, particularly by Jores, that the histology of diffuse hyperplastic sclerosis is different from that of lesions which are without doubt inflammatory. The difficulty of this distinction has already been alluded to, and sections of arterial lesions that are without doubt inflammatory and in which the so-called hyperplastic layer is present have been shown. Neither is it possible to make a hard and fast distinction between arterial inflammation and arterio-sclerosis on the absence of fatty degeneration in the former and its presence in the latter, since fatty degeneration may occur at a later stage in these lesions. Warthin⁹ has pointed out the difficulty of distinguishing between syphilis and arterio-sclerosis of the aorta, and says that in the later stages these lesions can only be differentiated by the specific lesion of syphilis that he describes. In short, the comparison of the lesion of diffuse hyperplastic sclerosis with tuberculous and syphilitic endarteritis both controverts Jores's distinction between the two forms of elastic tissue formation and at the same time provides additional evidence for the inflammatory nature of arterio-sclerosis.

In the second place, it has been urged against the inflammatory theory of arterio-sclerosis that the ordinary signs of inflammation are absent; in the early stages of the lesion there is no small cell infiltration and no dilatation of the vasa vasorum. The absence of these changes in the early phases of the lesion is the important matter: their appearance later is characteristic, and due to tissue reaction to products of degeneration and necrosis. Thus Bergel¹⁰ has shown that lymphocytic infiltration results from the presence of fatty degeneration in any tissue, and among other illustrations of this fact he quotes the well known small cell infiltration in arterio-sclerosis. Sir Bernard Spilsbury has drawn my attention to polymorphonuclear infiltration provoked by tissue necrosis. In addition to infiltration with lymphocytes, polymorphonuclear cells, and fibroblasts, there is a permeation of the media and even of the thickened intima with capillaries and occasionally very small arteries in well marked arterio-sclerotic lesions. These inflammatory lesions are secondary, and throw no light on the nature of the initial process.

Many authors, including Virchow and Andrewes, have called attention to the fact that arteries are relatively avascular structures, and this fact is in part responsible for the absence of the usual signs of inflammation. Thus, according to Koelliker,¹¹ all the larger vessels from 1 mm. diameter and over possess nutrient vessels which are distributed predominantly in the adventitia, in which they form a rich round-meshed capillary network, and the general consensus of opinion agrees that the tunica media of only the larger arteries and veins possesses nutrient vessels, and that these are supplied only to its outer layers; in fact, the middle and inner layers of the media and the whole of the intima are avascular structures. Inflammation of the intima may, therefore, be compared with inflammation of the cornea. Senfleben¹² showed that a minimal injury to the cornea causes local destruction of the corneal cells and the appearance of a surrounding zone in which the corneal cells appear enlarged, distinct, and tumefied. The process may continue and advance insensibly to repair without the intervention of leucocytes, the hypertrophying cells of the granular zone eventually undergoing karyokinesis, and thus by multiplication replacing the cells destroyed. A more severe injury provokes the accumulation of wandering tissue cells in its neighbourhood, still without evidence of dilatation of neighbouring vessels, or diapedesis through their walls. The

absence of a primary proliferation of fixed tissue cells in keratitis and the proliferation of endothelial cells in arterio-sclerosis has no other significance than the emphasis it lays on the inflammatory process in diffuse hyperplastic sclerosis. The difference in the lesion in the two conditions may be due to the irritant acting once and for a short time in experimental keratitis, in comparison with its possibly prolonged action in arterio-sclerosis, or it may be due to the fact that whereas the corneal cells lie in an avascular medium, the endothelium, as distinct from the rest of the intima, is in a vascular medium with an abundant oxygen supply.

This distinction between the endothelium and the intima is highly important, and is supported by Grünstein,¹³ who has published one of the best accounts of the normal structure of the larger arteries and their variation with age, and who expresses the opinion that "the endothelium does not belong to the intima, but forms an independent constituent of the arterial wall."

If this is true in fact it becomes obvious that we are dealing with inflammation in a quite peculiar structure when we consider inflammation in an arterial wall. It is a structure which is vascular in its outer layer, avascular in part of its middle and all its inner layer, and it is lined by a layer of cells which belong rather to the blood than to the vessel whose structure it is their function to form, and perhaps in pathological conditions to keep in repair.

The importance of the blood supply in determining the type of tissue changes, whether they are of an inflammatory or degenerative type, has recently been brought out in the study by Mr. A. G. Timbrell Fisher of the pathology of osteoarthritis.¹⁴ He finds that the lesions are degenerative or proliferative according to the proximity of an adequate blood supply: thus in the articular surface of the knee-joint the initial lesion is a degeneration of the intercellular matrix in the central area of the cartilage—an area which is completely avascular—whereas the peripheral lesion is proliferative, due (he thinks) to the presence of an adequate blood supply from the *circulus articulari vasculosus* of William Hunter. These changes are to be compared with degenerative lesions in the depth of the intima in the larger arteries often appearing first in the internal elastic lamina, and with the proliferation of the endothelium already demonstrated in diffuse hyperplastic sclerosis, and perhaps also occurring in nodular sclerosis, as will be shown later when reference is made to the work of Klotz.¹⁵

All that is known about the function of endothelium supports the view that its proliferation in diffuse hyperplastic sclerosis is evidence of the inflammatory nature of the lesion. Thus endothelial cells have been shown to take up bacilli within ten minutes of their inoculation into the circulation.¹⁵ Behring and Mutch¹⁶ have called attention to the great phagocytic powers of the endocardial endothelium. In typhoid fever the endothelial cells of the spleen swell, proliferate, and become separated. There is general agreement that the large mononuclear cells of the blood have their origin from endothelial cells of capillary walls, and Baumgarten has shown that vascular endothelium under mild grades of irritation gives rise to fibroblasts and connective tissue. Adami¹⁶ sums up by saying:

"We have, indeed, to recognize the very active part played by vascular endothelium in inflammation, its pronounced proliferative and phagocytic powers . . . microscopically these cells can be seen to alter during the inflammatory process; they become enlarged and project into the lumen of the smaller vessels, and in my experience this enlargement affects not only the cell bodies but also the nuclei, which at the same time would seem to contain more chromatin and to stain more intensely. In cases of chronic inflammation the enlargement is seen followed by proliferation, notably in the arterioles and capillaries, a process which may lead to the ultimate occlusion of these small vessels."

The actual form of the lesion in diffuse hyperplastic sclerosis is, therefore, strong evidence that the process of inflammation is responsible for its production.

In addition to the four main theories of arterio-sclerosis, which depend on the activity of the unit processes Involution, Growth, Inflammation, and Degeneration, it is suggested vaguely from time to time that the lesion is due to an altered nutrition of the vessel wall. This idea is crystallized by Adami in a few suggestive paragraphs dealing with the subject of productive fibroses, in which he makes the tentative suggestion that intimal proliferation in arterio-sclerosis may depend on stimulation rather than irritation, and that the nature of the stimulant may be an increased strain thrown on the intima by weakening of the underlying media, and in other cases the stimulant is an increased nutrition brought

about by heightened arterial tension. This theory turns rather on causes than processes; in its distinction between stimulation and irritation it has been considered in the review of Jores's theory, and in its reference to primary weakening of the media it comes under Thoma's theory of arterio-sclerosis. Lastly, the lesion in arterio-sclerosis has been compared to keloid, and though he does not make this comparison Ophüls¹⁷ approaches this hypothesis in his reference to the autochthonous development of arterio-sclerosis. If simpler pathological conceptions fail it may be necessary to have recourse to the complicated explanations offered by the terms "productive fibroses," "fibrous diathesis," and "autochthonous development," but in the meantime I am of the opinion that the simple process of inflammation is sufficient explanation of the production of the lesion in diffuse hyperplastic sclerosis, and in the next and last lecture its activity in other forms of arterio-sclerosis will be considered.

REFERENCES.

- ¹ Thoma, R.: *Textbook of General Pathology*, translated by Bruce, 1896; *Virchow's Arch.*, 1886, 104, 209; *Ziegler's Beitr.*, 1891, 10, 433. ² Evans, Geoffrey: *Proc. Roy. Soc. Med.*, 1921, 14, 315. ³ Klotz, Oskar: *Journ. Exper. Med.*, 1906, 8, 322. ⁴ Jores, L.: *Wesen u. Entwicklung d. Arterio-sklerose*, Bonn, 1903. ⁵ Hatschek, E.: *Ldb. Man. Element. Colloid. Chem.*, 1920, 124. ⁶ Bradford, S. C.: *Biochem. Journ.*, 1920, 14, 474. ⁷ Marchand: *Verhandl. des Cong. f. inn. Med.*, 1904, 21, 58. ⁸ Virchow, R.: *Cellular-Pathologie*, fourth edition, 1871, 463. ⁹ Warthin, Aldred Scott: *Harvey Lecture*, 1917. ¹⁰ Bergel, S.: *Die Lymphocytose*, Berlin, 1921. ¹¹ von Ebner: v. Koelliker's *Handb. d. Gewebelehre*, 1902. ¹² Senftleben: *Virchow's Arch.*, 1878, 72, 542. ¹³ Grünstein, N.: *Arch. f. Mikr. Anat.*, 1896, 47, 583. ¹⁴ Fisher, A. G.: *Timbrell: Brit. Journ. Surgery*, 1922, 10, 52. ¹⁵ Adami, Abbott, and Nicholson: *Journ. Exper. Med.*, 1899, 4, 349. ¹⁶ Adami, J. G.: *Allbutt and Rolleston's System of Medicine*, 1911, 1, 726. ¹⁷ Ophüls, W.: *Stanford Univ. Pub. Med. Sci. Series*, 1921, 1, 5; *Journ. Am. r. Med. Assoc.*, 1921, 76, 700. ¹⁸ Klotz, O.: *Journ. Exper. Med.*, 1910, 12, 707.

TREATMENT OF PUERPERAL INFECTIONS.*

BY

B. P. WATSON, M.D., F.R.C.S. EDIN.,
PROFESSOR OF MIDWIFERY AND DISEASES OF WOMEN,
UNIVERSITY OF EDINBURGH.

In obstetrics probably more than in any other branch of medicine old methods of treatment persist long after their efficacy has been disproved by more recent scientific knowledge and experience. In recent years our conception of puerperal infections has undergone a great change, and yet the general body of the profession has not realized it, for we daily see and hear of procedures being carried out which we can only regard as harmful.

The great danger of specialization is that the specialist is apt to lose his perspective and to be so immersed in the details of his own subject as to lose sight of advances being made in other directions, many of which may be of the utmost importance to him. What we have to realize is that the general principles of pathology have a universal application, and that the details of treatment founded upon them should require only slight modification to meet the different anatomical and physiological conditions present in any region of the body.

I do not intend to go fully into the treatment of all the different varieties of puerperal infections. All I wish to do is to ask if that treatment is always in conformity with what we know of pathology and of infections in general, for on this must depend its likelihood of yielding the best results.

Much has been learned in recent years regarding the mode of invasion of infective organisms, and nothing is of more importance from the obstetrical point of view than a realization of the frequency with which infective organisms spread throughout the blood stream from what was at first a purely local focus. The organisms concerned principally in puerperal infections—the streptococci, staphylococci, colon bacilli, pneumococci, and gonococci—very readily gain the blood stream, so that probably a few escape into it from every local focus. In the majority of instances their numbers are so small and the reaction of the blood tissues so great that they do not long survive. Furthermore, a great many organisms hitherto regarded as purely saprophytic have been proved to be capable of living in the tissues and spreading by the circulating blood. In view of these facts we must discard altogether the old classification of puerperal infections into sapraemias and septicaemias. We must regard every case of bacterial invasion of the genital tract as a potential bacteraemia and must direct our treatment accordingly.

When organisms invade a raw surface the lesion is at first quite localized. There is inflammatory reaction with a certain amount of destruction of tissue. Whether the condition remains localized depends on the degree of the reaction, on the number and virulence of the organisms, and on the amount of rest that can be ensured. If spread occurs it may take place by continuity of tissue, sometimes along the surface, often along the lymph channels, or the larger lymph vessels may be invaded and the organisms disseminated in the tissues through which they run, there producing other lesions. Thrombosis of blood vessels may occur and the organisms invade the thrombus, so that it becomes more and more extensive, spreading up the veins towards the heart and to a lesser extent along the arteries. From such a thrombus the organisms may spread into the general blood stream, although this is not necessarily the case. Pieces of thrombi may become detached, and such emboli, laden as they are with the infecting organism, may set up lesions in distant parts without there being any general blood infection. Finally, without any degree of thrombosis and often with a very minute local lesion there may be a massive general dissemination throughout the blood stream—a true bacteraemia.

CAUSE AND SYMPTOMS.

Apply this general knowledge to the particular subject. We know that the majority of infections of the mucous surface of the puerperal uterus remain localized. Reaction is such that the organisms are destroyed. If any escape into the blood stream they are so few in number as not to survive. The patient has an elevation of temperature for a few days, the lochia may be profuse and purulent for a time, but soon everything settles down to normal.

Extension by continuity of tissue results in a spreading inflammation of the mucosa, in an infiltration of the muscular wall of the uterus, or an extension to the tubes, with or without pus formation. If the lymph stream is invaded, a general peritonitis may occur, but more usually there results an inflammatory reaction in the cellular tissue of the broad ligaments with, in my experience, nearly always an involvement of the tubes—the so-called pelvic cellulitis. This may or may not go on to abscess formation, but nearly always remains localized to the pelvis.

Thrombus formation is always present at the placental site, and any organismal invasion of this area is peculiarly liable to cause an extension of it; hence the frequency of septic thrombo-phlebitis of the ovarian and other pelvic veins as a manifestation of puerperal sepsis. Bacterial invasion of the general blood stream I have already referred to.

These are the lesions our general knowledge of infections would lead us to expect, and these are the lesions which we find clinically and in the post-mortem room in cases of puerperal sepsis:

1. A localized surface infection of the mucosa.
2. Spreading infective lesion of the general surface of the mucosa, often with extension to the tubes.
3. Inflammatory infiltration of the uterine wall, sometimes with abscess formation.
4. Inflammatory effusion in the cellular tissue of the broad ligaments with or without pus, and usually accompanied by tubal inflammation with or without pus.
5. General peritonitis.
6. Septic thrombo-phlebitis of the pelvic veins with or without emboli, and with or without bacteraemia.
7. A general bacteraemia.

In any one case there may, of course, be a combination of these conditions. Knowing these to be the possibilities, how ought we to approach the investigation and treatment of the case of a woman confined two or three days previously and presenting febrile symptoms? The first thing to do obviously is to exclude the possibility of the fever being due to any other cause than puerperal sepsis. This involves a careful examination of the heart, lungs, kidneys, breasts, and other organs. Some time ago Dr. W. A. Scott and I made an analysis of all our cases of fever in the puerperium; in 2,096 cases confined in the Burnside Maternity Hospital, Toronto, 476 showed definite puerperal morbidity according to the standard laid down by the British Medical Association. In only 50 of these could we find any definite septic lesion in the pelvis. In 20 the cause of the temperature was extragenital from such conditions as pyelitis, cystitis, pneumonia, miliary tubercle, suppurating ear, etc. In the remaining 406 no definite lesion to account for the temperature could be detected by any of the ordinary methods of examination, including blood cultures. All of these patients made a

* Read at meeting of Edinburgh Obstetrical Society, February, 1923.