THROMBO-ANGIITIS OBLITERANS IN ASSOCIATION WITH SYPHILIS.

(With Special Plate.)

BY

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As comparatively few cases of thrombo-angiitis obliterans have been reported in this country we desire to record the following instance. As will be seen, the symptoms were characterized by pain, coldness of feet, ischaemia, intermittent claudication and erythromelalgia, evidence of trophic disturbances shown by ulceration of leg and gangrene of toe, and, at a later date, extension of the disease to the other limb.

The patient, who is of British nationality, is a tailor's cutter, aged 59. Previous to this illness he was always healthy, and he gave no history of syphilis. The first symptoms were noticed nine or ten years before he came under observation, when he suffered from paroxysmal pains in the calf of the left leg; at first they came on after standing for some hours at his work, and were relieved on resting. Superficial ulcers developed on the anterior aspect of the lower third of both legs a few years later. For the past two years the pain had increased in severity; it was intense after walking, and was situated in the lower third of the left leg and foot. Resting gave relief, but the pain recurred on walking a short distance, say a hundred yards. These symptoms of intermittent claudication were associated with a sense of numbness or coldness, especially when the weather was cold and wet, and the foot became blanched and cold to touch. This transitory anaemia rapidly passed off on resting. The family history revealed nothing noteworthy. The patient is married; his wife and two children are alive and well. The latter show no evidence of congenital syphilis.

On admission to the Royal Victoria Infirmary, Newcastle-on-Tyne, on May 18th, 1925, an oval ulcer, measuring 1 in. by 3/4 in., posterior to the internal malleolus of the left foot was present; the skin edges were smooth, and its base was granulating, but covered with purulent exudate. The ulcer was superficial, and did not extend deeper than the subcutaneous tissue. The skin in the vicinity was pigmented, and showed numerous depigmented scars of previous ulceration. A similar appearance of healed scars was present in the right leg; the left great toe showed a condition of moist gangrene, limited to the toe.

The lower third of the left leg and foot were colder to touch than the rest of the leg, and on allowing the leg to hang down an erythematous blush developed rapidly over the inner border and dorsum of the foot, extending up to the ankle, thus giving the foot the appearance of typical erythromelalgia. The foot was most comfortable when elevated and kept cool. No alteration in sensation was detected, and no loss of motor power. No pulsation could be felt in either anterior or posterior tibial arteries, and only faint pulsation over the popliteal artery. Later on no pulsation could be felt in this vessel. The blood gave a strong positive Wassermann reaction, and the urine contained no sugar. A radiograph taken on May 23rd, 1925, revealed nothing of note in either leg. No evidence of tuberculosis was found in the lungs or elsewhere in the body.

The patient was transferred to the surgical side of the hospital, and on June 23rd Mr. Pybus amputated the leg about a hand's breadth above the knee-joint. There was little bleeding from the stump, and recovery was uninterrupted. The lumen of the femoral artery appeared to be practically occluded.

When seen again nearly six months later (December 14th, 1925) pulsation was present in the left femoral artery, and the right foot had rather an erythematous blush over the dorsum and inner aspect, extending to the ankle; pulsation, however, was still present in the anterior and posterior tibial arteries. The patient complained of coldness of the foot, especially on standing, but not of pain. These symptoms appeared to point to an extension of the condition to the right leg. The arms had never been affected. Blood examination on this day revealed nothing noteworthy.

Red cells	...	...	4,535,000 per c.mm.
Haemoglobin	...	...	90 per cent.
Colour index	...	...	1
White cells	...	...	5,800 per c.mm.
Blood platelets	...	...	363,000 (that is, 100 to 1,250 red cells)

No increase in the fragility of the red cells was present.

Differential count (250 cells counted):

Polymorphonuclears	...	54.8 per cent.
Lymphocytes	...	37.2 "
Large mononuclears and transitionals	...	6.8 "
Eosinophils	...	0.8 "
Basophils	...	0.4 "

No abnormality was found in the white or red cells in stained films. No nucleated red cells were seen.

Naked-eye Appearance of Amputated Limb.

Much difficulty was experienced in the dissection of the main vessels owing to the great degree of chronic inflammatory thickening in their vicinity, which caused the venae comites and nerves to be matted together. They appeared like fibrous cords in places. The popliteal artery was occluded by a greyish *ante-mortem* thrombus. The vein was markedly thickened but not thrombosed. Both anterior and posterior tibial arteries were completely thrombosed. The thrombus, especially towards the middle of these vessels, appeared to be organized. One of the venae comites of the anterior tibial artery contained some *ante-mortem* clot, but those of the posterior tibial did not. All the veins were thickened, and the surrounding structures were bound together by fibrous tissue, possibly from an associated periarteritis. The clot in the anterior tibial artery extended down to the commencement of the dorsalis pedis artery, the lumen of which was patent.

Histological Appearances of the Blood Vessels.

The affected peripheral vessels—the popliteal and anterior and posterior tibial arteries—showed completely organized thrombi in their lumina, some of which were partially recanalized. Marked histological changes occurred in all the coats.

The Popliteal Artery.—The vasa vasorum showed endarteritis obliterans (Fig. 1), and around them was distinct infiltration of cells of lymphocytic type, including definite plasma cells. The tissues in the immediate vicinity showed fibrous overgrowth. In the media a degree of fibrosis with interruption of the continuity of the muscle and elastic fibres, dilatation of vasa vasorum, and some lymphocytic infiltration was present. The internal elastic lamina was reduplicated in places, and interrupted by small thin-walled vessels passing into the clot. The intima was merged into clot by the process of organization. The thrombus, which occupied the whole lumen, was densely fibrous and completely organized. Between the fibres were deposited yellowish granules of altered blood pigment, and some of the newly formed capillaries had developed into quite large channels.

The Anterior Tibial Artery.—Sections were examined from the upper, middle, and lower ends of this vessel, and from one of its branches. The changes were more advanced in the upper end (Fig. 2), and were similar to those described in the popliteal artery. The wall of the vessel, however, showed much more fibrous thickening, and the vasa vasorum were more dilated. The periarteritis was more prominent. In the middle and lower ends, in addition to the appearances previously described, the adventitia showed a greater degree of cellular infiltration, and throughout the media were foci of epithelioid cells with pale vesicular nuclei and abundant protoplasm, and numerous multinucleated giant cells, with nuclei arranged around their peripheral parts (Fig. 3). These were external to the internal elastic laminae (Fig. 4). A marked degree of lymphocytic infiltration, especially around the vasa vasorum and at the margins of the foci, was present. The thrombus presented the same features as are described above, but just above the ankle-joint in a few places some small calcareous deposits were seen. There was also one large dilated vessel in the clot; its wall, however, was composed only of endothelial cells.

The branch of the anterior tibial artery showed a similar appearance to that described above, but no giant cells were seen. The thrombus appeared to have receded from the wall and permitted canalization to take place; some red blood corpuscles were present in its lumen.

No thrombus was present in the lumen of the anterior tibial artery at its junction with the dorsalis pedis artery. The adventitia only showed a slight degree of periarteritis; the vasa vasorum in media were distended, and only a slight degree of fibrosis was present; lymphocytic infiltration was not marked; the intima showed distinct fibrous thickening.

Sections taken from two separate parts of the posterior tibial artery, one higher up in the course of the vessel than the other, showed the lumen to be more or less closed by an organized thrombus, in the centre of which was present a new channel. The changes in the vessel wall were pronounced. The adventitia showed marked periarteritis with endarteritis obliterans of the vasa vasorum, lymphocytic accumulations, and occasional focal areas of epithelioid cells and scanty giant cells. The tissues in the vicinity were greatly fibrosed. While lymphocytic infiltration was present in the media, no giant cells were seen. The vasa vasorum were greatly dilated, and the muscle and elastic fibres much atrophied and replaced by fibrous tissue. The internal elastic lamina shows reduplication in places. The intima merged into thrombus, but appeared thickened by fibrous overgrowth. The thrombus had been completely organized by a cellular granulation tissue, and there was a large central opening present, which may possibly be due to recanalization, as in one of the sections it appeared to extend to the intima. This canalization extended almost the whole length of the vessel (Fig. 5). One of the branches showed marked intimal proliferation almost obliterating the lumen, and another branch was occluded by an organized thrombus similar to that previously described.

Sections from all the arteries, particularly where giant cell foci were present, were stained for tubercle bacilli, but, notwithstanding an exhaustive search, none could be detected. Other sections were stained by Levaditi's method for the detection of *Spirochæta pallida*, but none were discovered.

Histological Appearances of the Veins.

The veins all showed some fibrous thickening of their walls, especially internal to the internal elastic lamina (Fig. 6). Lymphocytic infiltration and endarteritis obliterans of the vasa vasorum were not marked. The popliteal vein and venae comites of the posterior tibial artery were not thrombosed, but one of the venae comites of the anterior tibial artery contained a thrombus composed of fibrin, leucocytes, and red blood corpuscles, which showed early organization at one point.

Histological Appearances of the Nerves.

Both the anterior and posterior tibial nerves were the seat of perineural fibrous thickening, and the fibrosis extended between the various nerve bundles and between individual nerve fibres which appeared atrophied. In places fat could be demonstrated in the nerve fibres.

While the symptoms and appearances described in this case are identical with thrombo-angiitis obliterans occurring in the young subject, syphilis apparently plays no part as an etiological factor in that disease, and no spirochaetes have been demonstrated (Buerger).¹ In Perla's² series of 41 cases 36 gave a negative Wassermann reaction. The term "thrombo-angiitis obliterans" was first employed in 1908 by Buerger, who gave a detailed description of the disease from an examination of 38 cases, but it has been described under various names—such as pre-senile gangrene, non-syphilitic obliterative endarteritis of the Jews, obliterative endarteritis of the young, and endophlebitis and endarteritis, etc., by many of the earlier writers. Russian, Polish, and Rumanian Jews, it is said, are most generally affected. Perla found 41 cases, all Jews, out of 10,000 cases in the records of the Montefiore Hospital, New York, but states that no conclusion can be drawn from this, as 95 per cent. of all the patients there are Jews. Other authors have reported cases among Turks, Chinese, Koreans, and Japanese. The average age of onset is about 30 years, and all the recorded cases have been males; 10 of Perla's cases were tailors. Buerger found the left leg the first to be affected, but Perla the right leg in the largest number of his cases. All the limbs, however, may be affected. Perla described a case occurring in the aorta and coronary arteries as well as in the peripheral vessels of both legs. The disease in all cases originates in the smaller vessels, such as the dorsalis pedis artery, and ascends to the vessels above. The capillaries of the extremity remain free. Professor C. F. M. Saint of Capetown University informs us that he has seen a considerable number of these cases in South Africa in recent years; in certain cases the disease involved both upper and lower extremities.

The histological appearances of the present case show a condition of thrombo-angiitis obliterans with an associated phlebo-sclerosis or phlebo-thrombo-sclerosis, which would appear, in view of the positive Wassermann reaction and the exclusion of other causes, to be of syphilitic nature. Tuberculosis is reasonably excluded from the absence of tuberculous lesions elsewhere. There was no evidence of a generalized miliary tuberculosis or of a tuberculous lesion in the immediate neighbourhood from which direct infiltration could arise. As has already been stated, no tubercle bacilli were detected in the lesions. Such extensive giant cell formation as was present in our case is uncommon in the smaller arteries in syphilis. Buerger described giant cell formation as occurring in the intima, internal to the elastic lamina, and also in the thrombus, and regarded these cells as probably phagocytes assisting in the process of organization. No giant cells were present in any of Perla's cases. It is possible that some of Buerger's cases were of syphilitic origin, as no Wassermann tests were performed, the disease having been excluded on the ground that no spirochaetes were found.

The condition is distinguished from gangrene due to injury, with resulting thrombosis, and thermal gangrene following prolonged exposure to extreme cold, by the fact that these develop in forty-eight hours. The absence of sugar in the urine excludes diabetic gangrene. In arterio-sclerotic endarteritis obliterans the vasomotor phenomena, blanching and hyperaemia, are infrequent, and gangrene supervenes early and progresses more rapidly. Again, physical manifestations of impaired circulation are few prior to the onset of gangrene. Raynaud's disease is distinguished by its sudden onset with local syncope or regional ischaemia, involving the fingers, more rarely the toes and other parts; by short duration of sensory and vascular manifestations; their intermittent character and absence of arterial occlusion between the attacks.

The changes in the vessel walls in the present case would account for the thrombus formation with all the other related symptoms, gangrene, etc., and the sclerosis of the nerves for the atrophic disturbances. The feature of such cases is the slow progressive thrombus formation, with

periods of remission of symptoms and the comparatively late onset of gangrene.

We have difficulty in accepting Buerger's view of a primary thrombosis with secondary change in the vessel wall. It seems more probable that the toxic agent which has caused the condition set up the changes in the vessel wall primarily and that the thrombosis occurred secondarily. No doubt when existing thrombosis has altered the current of blood in an artery abnormal eddies may precipitate thrombosis in other parts of the vessel where there may be no obvious disease in its walls.

The thrombosis in the present case would appear to have originated in the popliteal artery and to have spread progressively downwards to the anterior and posterior tibial arteries, rather than to have ascended from below.

Perla agrees that luetic endarteritis, leading to occlusion of the peripheral arteries of the extremities, while rare, can only be distinguished from thrombo-angiitis obliterans by the presence of other evidences of syphilis.

REFERENCES.

¹ Buerger: *Amer. Journ. Med. Sci.*, 1908, 136, pp. 567-580. ² Perla: *Surg., Gynecol. and Obstet.*, 1925, xlii, p. 21.

LIPIODOL IN PULMONARY DIAGNOSIS: ITS USES AND LIMITATIONS.

(With Special Plate.)

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LIPIODOL, a compound of iodine and oil (poppy seed) introduced as a diagnostic aid by J. Forestier, is non-irritant to the tissues of the body and opaque to the x rays*; when injected into the bronchial tree it will flow to the utmost limit of the ramifications and fill the alveoli, rendering both opaque and clear cut. It might be thought, therefore, that by its use bronchiectatic and emphysematous dilatation would be seen, lung cavities demarcated, the position of lung abscesses determined, the site of a broncho-pleural fistula demonstrated, and the existence of a foreign body in the bronchus or a tumour shown; that we should be able to distinguish between an abscess, an old empyema cavity with a fistulous opening into the lung, and bronchiectasis—a problem which not infrequently confronts us; we might also expect to diagnose with greater ease conditions which are notoriously difficult in the early stages—such, for example, as new growths—and be able to assess the significance of the constant clicking basal râles that from time to time puzzle us. How far this expectation has been realized we shall endeavour to show by the cases described below. We have injected lipiodol in over fifty cases at the City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, and it will be seen that while in some instances information of great value was obtained, in others no help was given; or the information obtained was sometimes of a negative character, by which is meant that the examination with lipiodol having excluded bronchiectasis we are driven to search for other conditions which give rise to a similar clinical syndrome.

Methods of Injection.

Several routes for injecting the lipiodol have been used by different workers: (1) through the crico-thyroid membrane; (2) through the trachea below the isthmus of the thyroid gland; (3) the bronchoscopic route; and (4) the transglottic, by means of a laryngeal syringe; a rubber tube extension is sometimes employed, or a weighted catheter which can be passed into the right or left bronchus at will. We have used the first method almost exclusively.

* See BRITISH MEDICAL JOURNAL, 1923, vol. ii, p. 214.

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FIG. 1.—Popliteal artery, showing occlusion of lumen by an organized thrombus. The adventitia shows endarteritis obliterans of vasa vasorum with some lymphocytic infiltration and fibrous overgrowth of tissues in vicinity. A degree of fibrosis with dilatation of vasa vasorum and extension of thin-walled vessels into thrombus is present in media. The thrombus is densely fibrous and completely organized, and between the fibres are deposited yellowish granules of altered blood pigment. ($\times 15$.)

FIG. 2.—Anterior tibial artery, upper end, showing similar condition to that described in the popliteal artery. ($\times 6$.)

FIG. 3.—Anterior tibial artery, middle and lower ends, showing a condition similar to that in the popliteal artery. In addition marked lymphocytic infiltration of media and foci of epithelioid and giant cells are present. The vessel wall is situated above and the organized thrombus below. ($\times 45$.)

FIG. 4.—Wall of anterior tibial artery, showing the giant cells situated external to internal elastic lamina, which is folded in places. The vessel wall is situated above and the thrombus below. ($\times 60$.)

FIG. 5.—Posterior tibial artery, stained methyl violet. The same features as in other sections are present, but the thrombus shows a large central channel which extends to the intima at one area. The internal elastic lamina is folded. ($\times 20$.)

FIG. 6.—Popliteal vein, showing marked fibrosis of wall, especially of intima. ($\times 60$.)