**RAYNAUD'S DISEASE, ERYTHROMELALGIA, AND THE ALLIED
CONDITIONS IN THEIR RELATION TO VASCULAR
DISEASE OF THE EXTREMITIES.¹**

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At a meeting of the Association of American Physicians, in 1901, I called attention to the intimate relation existing between certain vasomotor neuroses and trophoneuroses, and vascular disease of the extremities. At that time it seemed to me to be important to prove that Raynaud's disease and erythromelalgia are not independent morbid entities, but symptom groups, pure and simple, that might in rare instances be associated with central nervous disease, but are far more often the expression of disease of the peripheral bloodvessels. It was conceded then, as it is conceded now, that these vasomotor and trophic affections may be due to some occult (say trophic) influence, but in the end it was the interference with the peripheral blood supply that was the direct cause of the clinical symptoms. The majority of writers had recognized that Raynaud's disease might be associated with central nervous disease, but if more often dependent upon disorder of the bloodvessels.

One of the ablest of recent authors on this subject, H. Strauss,² writing in 1905, proposes to substitute for the term *Raynaud's disease* the designation *Angiospastic gangrene*. According to this author, the gangrene is rarely symmetrical, and is the result of malnutrition due to ischemia or spastic cyanosis. Raynaud's disease, far from being a trophoneurosis, is, according to Strauss, a pure angioneurosis occurring either as an independent form of disease or in association with some central nervous affection. In this view I heartily concur.

In the interpretation of erythromelalgia there has been a great diversity of opinion. Efforts had been made to attribute it to changes in the posterior gray matter of the spinal cord (Eulenburg,³ Auerbach,⁴ and others), as though the dignity of the disease demanded such an explanation. I do not deny that such may be the case, but a large experience has taught me that the cases associated with spinal symptoms of any sort are few and far between. By degrees, the views advanced chiefly by American writers (Weir Mitchell,⁵

¹ Read in connection with the following paper by Dr. L. Ruerger, at the meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

² Archiv f. Psychiatr., etc., vol. xxxix, p. 109.

³ Neurol. Centr., 1893, p. 637; Deutsch. med. Woch., 1893, p. 1325.

⁴ Deutsch. Zeit. f. Nerven., 1897, vol. ii, p. 143.

⁵ Philadelphia Med. Times, 1872; also Mitchell and Spiller, AMER. JOUR. MED. SCI., January, 1899; also Clinical Lecture on Nervous Diseases, Philadelphia, 1897.

Sachs and Wiener,⁶ Hamilton,⁷ Barker,⁸ and others) have obtained general credence. The spinal origin of erythromelalgia is now defended less warmly, and the question to be decided is whether or not these various forms of vasomotor and trophic disturbances, including the acrocyanosis chronica, with or without gangrene (Barker), are invariably of purely vasomotor origin, and whether, even when associated with symptoms of an undoubted spinal character (tapes, etc.), they are not due to the accompanying peripheral vascular disturbance rather than to spinal disease.

The continued study of this subject has been fairly forced upon me by the unusually large number of cases of this description that I have seen in the surgical and the neurological services of Mount Sinai Hospital, while some of the most interesting forms have been observed in private practice among patients of all creeds and classes. So far as the hospital cases are concerned, it is probable that malnutrition, premature arteriosclerosis, and the peculiar occupations (tailoring, sewing-machine work—all of them involving, as can readily be understood, a retardation of the venous circulation) are responsible for the frequent occurrence of these special disorders. My dermatological friend, Dr. Lustgarten, is firmly convinced that a large majority of these cases are due to syphilitic disease. While it may be true that a very large number of the hospital patients whom we have seen have had constitutional syphilis, I must state emphatically that in such cases as I have observed, and in which I have made a thorough inquiry and examination to prove or disprove the presence of constitutional syphilis, I have in rare instances only been able to satisfy myself on this point. Moreover, yielding to Dr. Lustgarten's opinions, I have given deep sublimate injections, in many of the cases without satisfactory results, although Dr. Lustgarten reports verbally to me that he has seen a number of the cases get well after antisyphilitic treatment. Many of these disorders are subject to spontaneous improvement, and the majority of the incipient cases do fairly well on rest alone. I am under the strong impression that rest in bed, with the foot elevated, and the application of heat, by favoring the return circulation of the blood, do more to improve the clinical conditions than any severe or thorough antisyphilitic treatment could accomplish.

Ample opportunity has been afforded us not only for the clinical study of all these conditions, but for an exhaustive analysis of the underlying morbid states. These studies in pathology have been carried on by Dr. Buerger.⁹ He will not need me to stand sponsor for his conclusions, interesting as they will prove to be to those concerned with the clinical aspects of various acroneuroses. The important point is that the studies have revealed in these disorders a

⁶ Philadelphia Med. Jour., June 29, 1901; also Mt. Sinai Hosp. Rep. for 1898.

⁷ Jour. of Nerv. and Men. Dis., vol. xxxi, No. 4, p. 21.

⁸ Ibid., 1907, p. 653.

⁹ See the following paper.

striking interference with the peripheral blood-supply, thus fully corroborating and amplifying the findings of Wiener and myself in these diseases, as published seven years ago. So far as we have been able to determine up to the present time, the anatomical changes are very much the same in the various clinical groups. Whether or not special anatomical conditions may at some day be assigned as a basis for special clinical types will have to be left to future consideration. According to Dr. Buerger's studies, the morbid changes are the same whether the cases be designated clinically as erythromelalgia, Raynaud's disease, or acrocyanosis.

If we were to adhere rigidly to the descriptions of the disease as originally presented by Raynaud, or to the description of erythromelalgia as given by Weir Mitchell, we should no doubt be compelled to exclude some of the cases herein referred to. While it is not wise to depart too widely from the type as described by its discoverer, we must make allowance for variations that occur from a type and for the broadening studies of later years. Thus, as Strauss mentions, if we insisted on a symmetrical distribution of gangrene in Raynaud's disease, we should often be compelled to make a different diagnosis in cases in which all other symptoms point to the existence of this affection; and similarly, as I pointed out some years ago, it will not do to eliminate from the category of erythromelalgia all cases in which wet or dry gangrene occurs at some stage of the disease, although Weir Mitchell insisted that this absence of gangrene was one of the points of differential diagnosis between erythromelalgia and Raynaud's disease. I am confident that Dr. Mitchell himself will yield this point, since there are many cases of undoubted erythromelalgia in which gangrene has developed.

The special value of these clinical studies has been not merely in calling attention to the various forms of vasomotor and troponeuroses, occurring in the upper and lower extremities, but the study of them has helped to rivet attention upon the disorders resulting from deficient blood supply of the extremities, and, among other things, the examination of the pulsation of the dorsal artery of the foot has become almost as important a part of the general physical examination as is the routine examination of the radial pulse.

In summarizing clinically the experiences of recent years, I wish to emphasize a number of points; in submitting clinical proof, I have, so far as possible, endeavored to utilize some of the histories of patients in whom the amputation of diseased portions of the extremities has given Dr. Buerger the opportunity to make his excellent pathological studies.¹⁰ The points especially to be emphasized are these:

1. Erythromelalgia and Raynaud's disease are often associated with one another; a sharp line of demarcation between the two

¹⁰ I have purposely avoided giving the histories of text-book cases.

cannot always be maintained; and the types blend into one another so readily that the exact labelling of a case is often a matter of great difficulty.

2. The clinical symptoms at one part of the disease correspond closely to the erythromelalgic type, and at a later stage to the Raynaud type.

3. Erythromelalgia is relatively frequently associated with gangrene, generally dry gangrene.

4. There are cases which, in their incipiency, present typical symptoms of Raynaud's disease, and as they progress might very well be designated cases of spontaneous gangrene due to obliterating endarteritis (or angiothrombosis—Buerger). In the following cases these various points are well illustrated:

CASE I.—S. R., a cigarmaker, aged fifty-seven years, was admitted to the hospital, January 28, 1907. Both his parents died of Bright's disease. He had been a very hard worker, but was well enough until three years ago when his foot became very sensitive to cold. About a month prior to his admission the patient felt pain radiating down the back of right thigh and leg. When the feet were dependent they became livid and cold. After a brief stay in the hospital he was much improved and requested his discharge. He was readmitted June 28, 1907. At this time his left leg was more affected than the right. Both feet were tender on slightest pressure. When they hung over the edge of the bed they became erythematous from the soles to the upper level of the malleoli. The veins stood out prominently in contrast with the vivid red of the skin. If the feet remained in the dependent position, they became cyanosed up to the knees, and erythematous spots of irregular outline appeared over both knees. No pulsation could be felt over either dorsal pedal artery. The left fifth toe was in a state of dry gangrene. After much hesitation on the part of the surgeons, amputation above the left knee-joint was performed. The patient developed delirium three days later, which was followed by coma and death. There was no evidence at any time either of diabetes or of central nervous disease. No autopsy was granted; but Dr. Buerger examined the amputated limb, which yielded typical changes in the bloodvessels.

CASE II.—A. P., laborer, aged forty-nine years, was admitted to the hospital April 5, 1907. Eight years ago he had a burning pain in the fourth and fifth fingers of the right hand which extended up to the shoulder. After six months the pains ceased. One year ago he began to notice a burning sensation over the dorsum of both feet in walking; the feet always felt cold. On examination we found slight cedema of both legs; the toes of both feet were blue; on the outer aspect of the left foot were two ulcers. When the feet were in dependent position the toes became violaceous in color and excessively painful. After a few weeks the big toe of the left foot presented a small dark spot, which gradually developed into an increasing area

of gangrene for which amputation was performed by Dr. Lilienthal about a month later. The amputated limb was examined by Dr. Buerger. The patient made a good recovery.

In this case most of the symptoms were those of the Raynaud type; although in general appearance and behavior there was a distinct resemblance to the limbs as seen in some conditions of erythromelalgia. The histological findings were in all respects like those of our first case.

CASE III.—H. R., a travelling salesman, aged thirty-five years, was seen in consultation September 25, 1907. He denied syphilis, but had been a hard worker since the age of thirteen years. Five years ago he felt severe pain in the big toe of the left foot. After two weeks the nail of this toe came off, and a large ulcer developed on the outer surface of the foot. This ulcer healed; at the same site another ulcer had formed; during the last six weeks the ulcer had grown much larger. This patient got relief when the foot hung downward; while he was in bed the foot was numb and painful. During the examination it was noted that the entire left foot was swollen, red, and extremely painful; the patient was comfortable only when his knees were crossed and when he clasped the foot firmly in his hands. There was a large ulcer of the big toe of the left foot with exposure of the bone. All the other toes were intensely livid. The pulse could not be felt over the dorsal, the popliteal, or the iliac arteries. The pulses in the right lower extremity were equally deficient, except that the right iliac pulse could be felt. There was no evidence of nephritis or of diabetes. Amputation was advised. Such a case as this might well be designated as one of spontaneous gangrene, although the resemblance to erythromelalgia was undeniable. The evidences of widespread arterial disease, the greater pain in the recumbent position, and the early ulceration are of especial interest.

CASE IV.—J. L., a clothing presser, aged forty-seven years, was seen by me at the hospital (Dr. Lilienthal's service) in November, 1906. The only facts of importance in his history were that he had worked as a foreman in a Russian forest fourteen hours per day, and that his hands and feet had been frozen frequently. He was a heavy smoker and a moderate drinker; there was no evidence of syphilis. His present illness dates back about eight years, when he began to complain of drawing pains in both calves. This was worse after standing for any length of time, and especially on walking. Later on, pain set in in the soles of both feet ("flat-foot pains"). About five years ago he began to complain of cold feet; said his feet were bluish in color after standing, and that there were drawing pains in toes of left foot. The second toe of left foot was amputated about five years ago on account of progressive sloughing. Three years ago the second toe of the right foot underwent dry gangrene; three months ago the fifth toe of the right foot met a similar fate. Six months ago

he began to complain of drawing pains in both hands, and noticed a bluish discoloration. The tip of the middle finger of the left hand began to turn black two months prior to my examination. At this time the records showed: A peculiar pinkish coloring of all the finger tips; the tip of the middle finger of the left hand is painful; a small portion of the pulp of the right middle finger has sloughed away. The grasp is good, sensation normal in both upper extremities, and both radial pulses are of fair quality. When the hands are held high above the head the finger tips become much paler, and it takes a long time for the pinkish color to return after the hands have been lowered. In the lower extremities the ravages of the disease are particularly noticeable. The second and third phalanges of the second toe of right foot have fallen off; the middle toe has been amputated; the tip of the right little toe is black and gangrenous; other toes are blue. The tip of the last phalanx of the left large toe is missing. The second toe has been amputated. Pain is not increased when feet are in a dependent position, except that there are pains occasionally in the heels. All reflexes and sensation are normal; pulsation cannot be felt either in the dorsal arteries of the feet or in the posterior tibial arteries. In spite of the inroads made by the disease, after a stay of one month in the hospital, under general tonic and stimulating treatment, the patient was discharged "improved." It is worth noticing as etiological factors, in this typical instance of Raynaud's disease, the exposure to cold, the excessive use of tobacco, and the long hours of work. The process was relatively destructive, but remained limited to the finger tips and toes.

5. I wish to call attention to the occasional association of Raynaud's disease with chronic rheumatism, and to its occurrence in cases of cerebral endarteritis. It is almost superfluous to point out the relation in these cases between the defective blood supply of the extremities and the cardiac and vascular disease accompanying these disorders. The following case may be cited to illustrate this point:

CASE V.—Mrs. M. F., aged fifty-seven years, was seen April 23, 1900. She has had chronic articular rheumatism, and has presented all the symptoms of mitral stenosis, with occasional deficient compensation. At the time of my examination the patient was much troubled by attacks of pain in the upper extremities, the finger tips becoming blanched and the nails turning blue, without any acute heart disturbance to account for such changes. Such attacks would last for several hours and would then disappear. On one occasion a note was entered on my records: "Fingers swollen, glossy, livid, and nails very blue." From May 20 on, for a period of about one month, the hands were invariably blue in the dependent position, the fingers glossy and painful. After treatment by the use of hot baths for the hands, massage, and nitroglycerin, the condition was much improved. This same patient had an attack of left hemiplegia five years previously. I have not seen the patient for

several years, but understand that up to the time of her death, a few months ago, the vasomotor disturbances in the upper extremities did not recur.

6. Special attention should be directed to the association of intermittent claudication with symptoms of the Raynaud type, an association which was theoretically conceived a number of years ago both by Erh and myself, but which I have seen demonstrated in only a few instances. Erh proved conclusively that intermittent claudication is due to interference with the peripheral blood supply, and in my first paper on erythromelalgia I stated that from the viewpoint of pathology, "intermittent claudication may be contrasted with erythromelalgia (motor paralytic symptoms with sensory and vasomotor disturbances, both due to peripheral nerve disease following upon obliterating endarteritis)." If Dr. Buerger's views are correct, we shall have to substitute "thrombo-angiitis" for "obliterating endarteritis."

CASE VI.—Mr. E. R., aged fifty-five years, was seen by me in consultation with Dr. Joerg, of Brooklyn. Patient has the appearance of a man in good health. He states distinctly that until seven years ago he was able to climb high mountains, but found in the last four years that his right calf was painful after walking, and has had calf-spasms for many years. About a year ago he noticed the same pain in the left leg. The pain begins in the dorsum of the foot and travels up the leg as far as the knee. After lying in bed for one hour the pain disappears. During the past few months he feels completely exhausted after walking for about fifteen minutes. After the lapse of this period the legs give way, and he has a feeling of being almost completely paralyzed. After a few hours' rest he feels that he would be able to walk miles, but whenever he has walked ten or fifteen minutes the power of the legs seems to give out. On examination it was found that both feet were blue, particularly the left; toe nails blue; his hands were also livid. He has periods in which the fingers are absolutely white and numb, and he has to rub them very vigorously. Of late he has noticed the same in the toes. He has considerable pain during these periods, both in the fingers and toes. The left knee-jerk is slightly livelier than the right, but there is no ankle clonus on either side, a very slight Babinski occasionally on the left. No dorsal pulse can be felt, and no popliteal. He has a general arteriosclerosis.

There can be no doubt that in this case there is a distinct intermittent claudication, though not as advanced or as complete as in some other cases, and with this is joined distinct evidence of disturbances in peripheral circulation, both in the hands and the feet, resembling in every way the symptoms of Raynaud's disease. The association of these two groups of symptoms points indubitably to the fact that the changes in the bloodvessels of the upper and lower extremities are responsible for both groups of symptoms.