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Raynaud's disease

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---RAYNAUD'S DISEASE---

by

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------FOREWORD------

It was on just such an occasion as this, some seventy years ago, that Maurice Raynaud published his monograph entitled, "De l'asphyxie locale et de la gangrene symetrique des extremites". This was to fulfil the requisites for his Doctor's Degree in Medicine, and he was just twenty-nine years of age at the time. How well he did the task he set out to do is seen, readily, when we find that the malady he described has borne his name since he described it, in spite of the fact that others had seen it before him--a fact he admitted freely.[38]

Because this disease is so rare it is mentioned only rarely in the didactic work of the medical school of today. However, in view of the rapid advances which have been made so recently in the treatment of Raynaud's Disease the writer undertook this paper, primarily to learn more about the disease himself. If the reader can glean a few nuggets from this review of the pertinent literature, this paper will have served a triple purpose, because, as was written above, this paper is presented after just such an occasion as did Raynaud present his original Thesis.

The writer is frank to admit that he has never seen a case of Raynaud's Disease, but he feels he will be much better qualified to recognize it than he was when he began work on this paper.

I.C.S.

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NOMENCLATURE.

It is evident that this disease bears the name of the man who first wrote a complete description of it. Many men of science have bewailed the fact that a man's name is ever attached to a disease, as well as to a nerve, a syndrome, a process, or anything else scientific. Indeed, it is unfortunate that in attempting to pay tribute to the men who have done so much for the advancement of our knowledge of disease, we have, so often, done this very thing.

When a man's name is attached to a disease it tells you absolutely nothing of the disease. E.V. Allen draws a very nice comparison. He uses for contrast the term "duodenal ulcer". This gives you the meaning of the term clearly. The situation and type of lesion are described, and, as a result, the term means about the same to all who use it. And we certainly must agree with him when he further says, "This does not hold in Raynaud's Disease, in which there is a marked confusion as to the exact connotation of the term".

Some have advocated, further, that the term, "Raynaud's Disease", should be discarded and the term, "Local Syncope of Raynaud", or, "Local Asphyxia of Raynaud", substituted. Or, if all three phases of the disease are present, "The Phenomena of Raynaud", would be satisfactory.[13] The writer can see little improvement over the present name in, "The Phenomena of Raynaud's Disease". It tells little more.

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Again, relative to Raynaud's Disease, Raynaud was well aware of the fact that others had seen the condition which he described in his Thesis. But no one had attempted to make a description or a study of it. It was to this end that Raynaud labored so successfully. Because he described the disease so well, and because he brought the syndrome which constitutes the disease into prominence, the disease bears his name.

HISTORICALLY.

It is known that Schrader in 1629, and Hertius in 1685 had observed the phenomena which now constitute the disease.[24] In 1739, Quesnay wrote of gangrene with obstacles in the vascular system, that is, embolism and thrombosis.[4] But Raynaud, in 1862, wrote, "I propose to demonstrate gangrene which it is impossible to explain by arterial occlusion."[38] This was done in French, his native tongue. The next step historically is Thomas Barlow's translation of Raynaud's original thesis and also the paper Raynaud wrote twelve years later representing further work on the disease. Barlow's translation was done in 1888. Finally, Leo Buerger and von Winiwarter were able to clarify many cases that were called Raynaud's Disease in the male, and thereby place them in another, more correct grouping. Allen states that Marchand clearly described a case of this disease when Raynaud was but

a boy of four years.[5] It was not the good fortune of this writer to have seen that paper. Allen, however, does not hesitate to give great credit to Raynaud for the extraordinary fine work he accomplished--especially in view of his age.

Since Barlow's translation in 1888 practically nothing has been found to add to Raynaud's description of the disease. And peculiarly enough, in spite of those that do not totally agree with Raynaud, his description still stands, with very few notable additions---and just as his description stands, so do his views still predominate, concerning this malady.

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DEFINITION.

By way of definition I can think of no better one than Raynaud's own suggestion as to what his disease really did constitute. Also, in view of the fact that the writer is anxious to adhere closely to the principles that Raynaud himself laid down, then let us see what he has to say about it.[38].

> "I propose to demonstrate that there exists a variety of dry gangrene affecting the extremities which is impossible to explain by a vascular obliteration---a variety characterized especially by a remarkable tendency (There is much quibbling about this word in the literature--the writer) to symmetry, so that it always affects similar parts, the two upper or lower limbs, or the four at the same time; further in certain cases, the nose and the ears; and I hope to prove that this kind of gangrene has its cause in a vice of innervation of the capillary vessels which it remains for me to define".
>
> -----"Pain is almost a constant phenomenon, it may be sufficiently sharp to draw forth cries from the patients; to a painful numbness there succeeds a sensation of burning and shooting which increases on pressure. Meanwhile the cutaneous anaesthesia is complete, and interferes with the prehension

of small objects. There period of reaction is accompanied by irritating tingling sensations, which the patients compare to tingling from cold, or to the stinging of nettles."

"I have never observed in local asphyxia the blue color of the lips which is constant in cyanosis"

"Sometimes the digits become entirely black and insensible; small phlyctenulae appear upon one digit, then on another, always at the extremity. This phlyctenula develops, fills with seropurulent liquid, breaks and leaves the derma naked".

"The pulse never ceases to be perceptible in the arteries of the affected limbs, but it may present remarkable alterations."

"In the more pronounced cases, those in which the asphyxial phenomena predominate, the pallor of the extremities is replaced by a cyanotic color. This colour affects many different shades. Sometimes it is of a bluish white; it seems as though the skin had acquired a greater transparence than natural, so as to allow the subjacent tissues to be perceived; sometimes it is violet or slate-colored, even becoming black, quite comparable to that which a slight blot of ink produces on the skin".

That in a brief way presents the outstanding critera of the malady, from Raynaud's own work.

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ETIOLOGY.

Although there is no definite etiology to this disease, there are many ideas maintained by writers as to what the nature of the contributing features which produce the symptoms and findings should be. Again, reference may be made to Raynaud's work, and then a general branching out from there in order to see what the variety of opinions held at this time by contemporary authors, really is.

Raynaud[38] says that it is due to a "vice of innervation of the capillary vessels which it remains for me to define". Later on he states again--"To attribute these phenomena to a fault of vasomotor innervation, was an interpretation which physiology assuredly authorised".

The immediate cause of the defective circulation is spasm of the digital arteries. And these same vessels are capable of full expansion in milder cases, and nearly so in severe cases, according to Kerr.[29] In discussing the paper which Kerr presented Wm H. Barrow describes the condition as being due to a "Neurovascular diathesis"--maybe resulting from psychic stress. He does not feel that it is purely a local thing, the opinion held by Kerr.

Adson and Brown[4] readily state that the etiology is not known in the idiopathic or primary type--as the name suggests.

Lewis[33,34] and others[50] do not agree with Raynaud in the

contention that the clinical effects characteristic of the disease are due to a primary abnormality of the sympathetic nervous system. Lewis holds that a local fault in the peripheral arterioles is the fundamental cause of the clinical phenomena.

Raynaud[38], Monro 35, Barker[11], Buerger[15], and Barlow[38], have at different times ventured forth with the suggestion that there is a possibility of a hereditary factor. But the work of Buchanan[13] and others seems to rule this out definitely.

It is interesting to know that Unsworth in discussing a paper presented by Texada[47], states in no uncertainty, "This is not a neurological problem".

Syphilis, Malaria, Typhoid Fever, Typhus Fever, Influenza, and other conditions which give rise to toxemia have been more or less, seriously considered as etiological in the past. Now they are considered as only associative

Sexual excesses and excitation have been suggested by Raynaud, but along with exposure, trauma, psychic exertion, sudden fright, and acute infections--all are looked upon in the light of contributing factors, only.

Poulton[36] has known Raynaud's disease to result from poisoning from arsenobenzol. He adds too, that he feels that colic may be explained by similar changes in the walls of the alimentary canal, which sounds highly plausible.

The recent work of Adson[2] and others, which has shown that Raynaud's Disease can be relieved, and in certain cases, cured by sympathetic neurectomy must surely go a long way

towards confirming the opinion that the disease is due to definite changes in the sympathetic nervous system .

In the main however, we are forced to admit that the search for a real tangible cause has been fruitless..

S. Iwai[27] asserts that this disease can be traced through to the presence of an autohemagglutinin--and that the cause is not due to any neurosis of the vasomotor nerves. This substance, he feels, agglutinates the corpuscles which in turn occlude the vessels.

Here is a good place to speculate upon the dictum of Dr. John E. Summers, who believes that all diseases which we do not now have any definite knowledge of the etiology, will sometime be found to be due to a definite infection. And to this end he looks forward to placing carcinoma, angina pectoris, (and I suppose, Raynaud's Disease would have to be included,) and others into that group.

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MORBID ANATOMY:

INCIDENCE;

Raynaud found that it occured most often, between the ages of 18 and 36 years. Morgan[47] set the average age at 26.6 years; Monro[35] found it to be between 28 and 29; Cassires[47] believed the averages showed he had most of his cases between their twenty-first and thirtieth years. Although he reports 22 cases in patients less than five years of age. Henry24 reports a single case of the disease in a woman 77 years old.

As to race, Lee[24] found three cases in negroes. Most of the cases occur in the white race because it is more easily recognized, probably.

Women have the disease more frequently than men. Raynaud's cases were 80% women. Monro said that 63% of his cases were in the female, and Texada[47] believes the ratio is about 6:4 in favor of the female.

On the whole, the disease is rare. Buchanan found[13] that it constituted only about 0.02% of the registrations at the Mayo Clinic. And Johns Hopkins' Hospital found that out of twenty-three-thousand admissions there were ninteen cases diagnosed "Raynaud's Disease".

DURATION:

It is known that the disease may subside of its own accord, yet proof is not forthcoming because the recovered cases are lost before the conclusive period of observation is ended.

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Certainly many mild cases are never diagnosed, and many are even unobserved, simply because they subside or do not progress to the extent that the classical picture is evident.

SYMPTOMATOLOGY: PATHOLOGY:

The circumstances in which attacks appear and disappear have been carefully observed by Kerr[29]. In mild cases there is but slight variation from the normal; but in severe cases the fingers slavishly follow the environmental temperature. These fingers do not react to overcooling as readily as do normal fingers, and are the ones which develop gangrene.

Monro[35] ascertained that nearly ¼ of all the patients he saw with Raynaud's Diasease were reported to have suffered from phenomena related to disturbances of the nervous system. Five per cent had had convulsions at one time or another, and others had had such diseases as congestion of the brain, general paralysis and so forth. The patient may be a regular epileptic, and Raynaud's phenomena are found to have begun about the same time as, or many years after the fits.

Carp[16] believes that there are definite central vascular manifestations represented by vertigo, headache, unconsciousness, aphasia, paralysis, and convulsive seizures. He further agrees that there are definite mental manifestations, also, and here he puts several psychoses and psychoneuroses of various types. In his opinion cerebral symptoms of Raynaud's

disease are far more frequent than is the usual impression. The manifestations may be central, vascular, or mental. And these may precede the obvious clinical syndrome by varying periods of time.

Adson and Brown[4] have divided the group that comes under the classification of Raynaud's Disease into four lesser groups, according to the degree of severity of the symptoms.

1-Normal persons, females, who have frequently, mild degrees pallor in symmetrical single digits, ("dead finger" or cyanosis), usually with moist clammy, cold extremities. These people are asthenic and easily suffer cold. The surface temperature of the extremities fluctuates widely, with environmental temperature. They seldom seek a doctor--this is not a disease.

2-In this group, the color changes are more profound, and frequently paroxysmal with a lesser degree of lowered temperature. Pallor may alternate with or be followed in a short time by more or less chronic states of cyanosis. Symptoms are sometimes severe enough to seek advice from physician. There are symptoms of numbness, occasionally partial anaesthesia during the period of local asphyxia; extreme coldness is present during the stage of syncope with dull aching distress, and cyanosis. With high environmental temperature

the hands become excessively warm and red with a burning sensation.

3-This represents further aggravation. Pallor is still more extensive, it is more painful, and chronic cyanosis or asphyxia intervenes. In this stage temporary recovery is much more difficult. There are color changes with the least change of temperature. Hands and feet are frequently swollen and puffy. Trophic disturbances appear, gangrene at the tips of the digits, symmetrically,

4-A still more sever group--and rarer. Pallor is intense and the condition is more painful, so much so that it may be a marked feature. Gangrene may develop in the entire end of symmetric digits without prolonged antecedent history of vasomotor disturbances.

All these groups fit Raynaud's Classification--there is the Symmetry, the paroxysmal attacks on a functional basis, and in each case pulsations of the vessels are present. However, they feel that the name "Raynaud's Disease" should be used for only groups 3 and four and possibly two. Groups one and two are just exaggerated normals.

Allen[5] believes that Raynaud had intended that there be four points to distinguish the disease; these were to be as follows; the absence of arterial occlusion, the symmetry of

involvement, the minor nature of the gangrene, and the intermittency of changes in color. It is without doubt, due to the failure to observe these cardinal criteria, that has lead to many false diagnoses of Raynaud's Disease. Allen[5] laments the fact that a great many of the cases presented by Raynaud, were not seen by Raynaud himself, Now they have served as models for subsequent authors, without due regard for the fact that they were often representative of other types of disease than that which Raynaud was describing.

In this review of the literature the writer has found very few articles that have considered the disease as a whole. Many writers are anxxious to present some new finding--or present some new phase of the disease, or perhaps, just present a case because of the rarity of the malady. A few men have chosen to present a general consideration of the disease, and to them the writer is grateful for pathological physiology and morbid anatomy. It will be noted the author has refrained from the use of textbooks in this article, because as Alvarez stated to us so recently, "It seems that textbooks are the graveyard for everything that is wrong in medicine". The following then, will represent only what has been written of very recent years about the Pathology of this disease--except, where the writer makes reference to Raynaud's original thesis which he is attempting to use as a guide, more or less.

Probably Texada[47] has written one of the best resumés of Raynaud's Disease during recent years--March 1931.

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The Pathological Physiology:[47]

1-The Stage of Pallor; the capillaries are [redacted] only rarely seen filling--and then only incompletely. They appear as broken segmented vessels--and no blood is seen passing into capillary loops from arterioles. The collecting venules are invisible.

2-The Stage of Cyanosis; blood is admitted into the capillaries both from the arterioles and back flow from venules. Blood enters capillaries in the form of small segments. Capillaries dilated, and increased numbers are visible. In capillary loops the blood is stationary or flows after long intermission.

The same grouping is used by Adson and Brown[4] as above, and the words are almost identical. However, they go one step farther and describe the stage of Recovery, which will be added at this point;[4]

3-Arterioles open and the flow in the capillary loops becomes rapid, and the blood is of a bright red color. Rubor due to large numbers of open capillaries and venules, many of which are dilated to some degree and contain red oxygenated blood agrees with Raynaud.

Young[50] in 1931--summarizes his findings in three brief sentences: (1) There is no evidence in the early mild cases of any essential abnormality of digital arteries. (2) In severe cases (and complicated) there existed

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both abnormality of sympathetic nervous system and a local fault in digital arteries.

(3) That this local fault should be regarded as a complication or late effect of the disease, and not as an etiological factor.

Abbott[1] presented a case of Parkinsonian Disease, in 1927, in which there were bilateral, cold, cyanotic extremities with trophic ulcers at tips of the fingers--and the disease as a whole resembled Raynaud's Disease.

Southey[44] has reported a case of Raynaud's Disease with effusion into both knee joints.

Allen and Brown in February 1932,[8] find that local applications of heat and cold show that the spasm is profoundly influenced by temperature, in response to which the vessels behave abnormally. These observations are opposed to the current view that the spasm is vasomotor in origin; the abnormal element in the reaction to cold is a direct reaction and due to a peculiar condition of the vessel wall locally; it is not the result of a reflex through the vasomotor nerves. The state of the vasomotor nerves naturally influences the tone of the vessels in these patients as it does in normal people, but the pathological element in the vascular spasm is not of nervous origin, as at present it is generally thought to be.

Lewis[34] was one of the first to deny the vasomotor nerves a connection to Raynaud's Disease. The vascular lesion is an imtimal thickening leading to a diminution in the size of the

lumen of the vessel. The vascular defect underlying discoloration of the fingers in this disease (Raynaud's Disease resembling Scleroderma) is of the same nature of Raynaud's Disease of the usual type. The circulatory manifestations of Raynaud's Disease are due to a local vascular defect. In milder forms the defect is expressed as a susceptibility to enter a state of spasm, in the severer forms spasm is re-inforced locally by structural change.[34]

Cassirer was one of the first to notice the change in the bones. They become atrophic, there is a thinning of the cortex with a consequent increase of marrow space and a sharpening of the outline of the canalicular system. On the other hand bones may become completely absorbed without becoming necrotic or forming a sinus[13].

Buchanan[13] studied the blood picture to note any changes that might be found there. In 45 patients the hemoglobin ranged from 45% to 88% with an average of 81%. The red cell count on 34 patients ranged from 2,820,000 to 5,890,000 with an average of 4,810,000. Enumeration of the white cells of the blood in 34 patients showed numbers from 5,600 to 13,400 with an average of 7,800. The pulse was normal in twelve patients, increased in four, and lessened in twenty-six.

Buchanan further finds that in all cases he had studied the urine was normal--and in no case was hemoglobin found therein.

Interesting, though perhaps relevant (perhaps not), Buchanan found that in one case the patient was always well during pregnancy,

and another found menstruation to be suppressed during her attacks of the disease. One noticed excessive menstruation during the attacks, and another was irregular. One patient suffered a transient hemiplegia, and one man found himself sexually impotent. Many observed that when they pricked their fingers during an attack there was no bleeding. One individual suffered eighteen convulsions over a period of two years, and complained also, of migraine. In every case the Wassermann showed complete inhibition and there was no history of Lues.

Since the disease was--and still is--thought of by many as being purely a disease of the extremities, it is well that a general survey of the ramifications of the malady be looked into.

Monro[35] found the upper extremity involved without the lower in 43% of his cases. There was 22% in which both were involved, and 24% in which only the lower extremities were affected. Buchanan[13] found that 56.7% of his cases were bilateral and symmetrical, while 43,3% were asymmetrical. In 19 cases he found lesions all over the body. One had only the tongue involved. One had only the pharynx, and another suffered with only one side of his face. And still another had the disease involving both forearms and lips, which sloughed and healed by cicatrices.

The writer will attempt to review recent literature with regard to what Raynaud called "Local syncope and Local ashphyxia", rather than repeat what Raynaud himself wrote. As was mentioned in the beginning, Raynaud's original description has not suffered by comparison with any of the present work.

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Texada[47] divides the symptomatology and clinical course into three stages: (1) Vasomotor symptoms; (2) Marked trophic disorders; and (3) Gangrene.

Local syncope and local asphyxia are the two divisions of the vasomotor upheaval. Local syncope is characterized by sudden blanching of the skin, and varying in intensity from a cadaveric white to bluish red. The temperature to the part is reduced. There may be both hyperesthesia and thermo-hyperesthesia. Pain may be extremely intense. This may all give way to a benumbed state, or maybe a paraesthesia will replace it. There is a rigidity or clumsiness of the affected part. Cold perspiration is usually present. This is what Buchanan[13], who classifies the stages by colors, calls the "white" stage. He says that it is perfectly compatible with good health. He says the part is "surprisingly white and cold" and has the appearance of death. Osler believed that such a thing was rare other than in Raynaud's Disease.[13]

Local asphyxia usually follows local syncope. Boyer[24] originated the term "local asphyxia", but Raynaud applied it to the stage following syncope. Monro[35] found that in three out of 176 cases there was only local syncope. Buchanan[13] reports that he found this to be true in 15% of all his cases. It was concomitant or with asphyxia in 10% of Monro's cases, and in 42% of Buchanan's cases.

Now, in local asphyxia the color of the skin changes to a violaceous hue, and the adjacent parts present a mottled

appearance. There is a fall in surface temperature. By pressure over the affected part the return of the blood is seen to be sluggish. There is a certain degree of swelling. It may last for minutes, hours, or days--or it may occur simultaneously with syncope in rare cases. Buerger says that asphyxia may precede syncope, and in some cases syncope may be absent entirely. Buchanan[13] terms this as the "blue" stage in contradistinction to his "white" or first stage. He gives a little more detailed description of the colors. It may be bluish white--violet gray, or red with a varying blue. It disappears on pressure with a long interval before it returns. Asphyxia may present a "marbling" effect, blue rings with pale centers.[13] This is the phase that is most inconveniencing, it renders life miserable with pain. It usually is of longer duration than the first stage. It is paroxysmal and recurrent. It may be either symmetric or asymmetric. Often the epidermis will desquamate--and if it persists too long gangrene will result. The attacks finally disappear by a gradual daily decline of the severity of the symptoms.

Buchanan[13] adds another stage that Raynaud did not include. This is his "red" stage or hyperemia. Local hyperemia was probably not observed by Raynaud, believes Buchanan. It occurs only infrequently. It may follow either syncope or asphyxia--and is never alone. The part becomes bright red, and pulsations are palpably increased. There is increased

warmth, and there is a slight increase in moisture. At times there is an unpleasant sensation, accompanying--it is almost a pain, called tingling.

Texada[47] groups his last two stages together under the sub-title "Trophic Disorders and Gangrene". In this stage the symptoms of a sensory nature are extremely marked, according to Raynaud[38]. Others minimize the sensory findings in this stage. Pain may initiate an attack or come on during the asphyctic stage. The pain is always diffuse, and never is only one nerve involved. Small blebs over the affected part usually signal the onset of gangrene. The gangrene may be either the dry or wet state--but more often the dry. There are bony changes demonstrable by x-ray during this stage. These usually consist of atrophy with disappearance of the tips of the terminal phalanges. This may extend as far as the metacarpals or metatarsals. Graves[24] describes this phase carefully. He says a bleb may form at the tip of the fingers and discharge a blackish or serosanguinous content. The resulting ulcer heals by cicatrization. Not infrequently a finger tip may merely become thickened and indurated and later desquamated. More commonly there occur sharply demarcated blackened, symmetrical areas. These remain dry for variable periods of time before sloughing. These areas may be massive, causing a loss of a leg or forearm, or even a whole extremity. Healing by granulation with the formation of a cicatrix which tapers is characteristic. The writer can hardly feel that this is in keeping with what Allen[4] calls "minor gangrene".

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This latter stage of gangrene belongs to Buchanan's[13] "black" grouping. It is called "Spontaneous","Idiopathic", or "Symmetric Gangrene". Here, he calls attention to the fact that the writer emphasized early in this paper--(i.e.) that Raynaud merely said that the gangrene showed a "....tendency to be symmetric". He did not say that it had to be symmetric. Again, Buchanan uses almost the same words Graves did as he tells how the patient may so much as lose a limb, or part of the thigh by this gangrene. He also, brings out the fact that the gangrene may remain in its dry black state for months before sloughing.

Landis is convinced that the slowness with which capillary pressure rises when venous congestion is artificially imposed during spasm, and the rapidity with which it falls at the release of such congestion shows that this spasm is situated on the arterial and not on the venous side of the network.[31]

Usually the first symptom to attract the patient's attention to his own condition is pain. It may be present in one attack and not in another. It may be sharp and paroxysmal and coinciding with syncope or asphyxia. It is almost a constant finding, according to Raynaud[38]. It is increased with pressure. It is not limited to the affected extremity, but radiates to every limb. Analgesia occurs rarely, but infrequently there is a slight diminution in tactile sense. There may be clumsiness in performing ordinary work. The chief difficulty consists in accomplishing small movements, according to Barlow[38].

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Monoplegias, hemiplegias, aphasias, and even paraplegias attend the malady, in rarer cases. It seems reasonable to regard these attacks as due to vascular changes in the brain of the same character as those which occur in the peripheral vessels, believes Graves.[24]

Osler is known to have seen many mental disorders with Raynaud's Disease. Mania, epilepsy, amentia, melancholia, circular insanity and progressive paralysis of the insane have been associated with this disease.[24]

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DIAGNOSIS:

As stated before, Allen[4] finds that, "......there is a very marked confusion as to the exact connotation of the term". Allen and Brown[8] have noted that the concept varies from that held by those who deny the existence of such an entity as Raynaud's Disease, to that held by those who include under the term all vascular disturbances associated with intermittent changes in color of the skin, and all grades of gangrene. The tendency at this time, is to use the term "Raynaud's Disease" or "Raynaud's Syndrome" as a general depository for a heterogeneous group of cases far removed from the condition originally described by Raynaud. A frequent statement found in the literature is....." a typical case of Raynaud's Disease", yet close examination of the report shows no similarity of the case to one of Raynaud's Disease. The problem then resolves itself into the question, "Should the diagnosis be reserved for a carefully defined condition, with characteristics sufficiently common to all cases for the condition to be regarded as a disease, or should its boundaries be so extended as to include the large and more inclusive group of vasospastic disturbances?"

Unfortunately, Raynaud's description of the gangrene does not fit his own cases, and many cases don't today. Too many are due to arterial occlusion. Is this Raynaud's fault?

Allen and Brown[8] feel that it was not Raynaud's intention that the term "symmetrical gangrene" should apply to gangrene

occurring in one extremity weeks or months before involvement of its homologous member of the opposite side. This should be borne in mind when speaking of symmetrical gangrene. He intended the word to connote symmetry--that is simultaneous symmetrical involvement. It is apparent that close adherence to this tenet of simultaneous symmetry, alone, would obviate a large share of the confusion whichnow surrounds the diagnosis of Raynaud's Disease.

Allen and Brown[8] after a careful study of the cases presented by Raynaud in his Thesis to see how well they fulfilled the requirements he laid down, found that only cases number 6,8,9 of the first group, and cases number one and three of the second group fulfilled his syndrome. They eliminated the others on one or more of three premises; excessive gangrene, arterial pulse absent or not noted, or the absence of intermittent color changes.

And so it is that Cassirer (quoted by Allen and Brown), was forced to say, "Those who have reported cases of this kind since Raynaud, have not by any means limited themselves to the characteristics of the affection as given by Raynaud. Cases have been described, especially by English authors which have hardly a single characteristic in common with those originally given by Raynaud; the vascular system was not intact; the gangrene occurred in the course of an infectious disease and spread widely----much more".

Raynaud's Disease is rare in men and children in Allen's

experience, yet it is very commonly reported in the literature. Allen[4] just to demonstrate the confusion that exists, took twenty-five cases from the literature at random--German, English, and American--and studied them from the standpoint of diagnosis. The result was appalling. Remember--all of these cases were diagnosed "Raynaud's Disease". In 18 cases the pulsations were not even noted. (As Allen says, "Such an oversight is analagous to presenting a case of cardiac disease without auscultating the heart, or noting the murmurs and sounds to be heard"). In six cases the pulsations were absent or diminished, and in one case normal. Symmetry was set down in thirteen cases, eleven were asymmetrical, and one was not noted. Gangrene was present in fifteen cases, but exceeded Raynaud's maximum in ten instances. There was cyanosis or pallor in fifteen cases--in nine it was constant, six were intermittent. In one the color changes were only while using a pneumatic tool, one only in the morning, one only when cold, and one spontaneous. Included in the histories of some of these patients we find, "Intermittent claudication", "Superficial phlebitis", and "Absence of Pulsations". Of the twenty-five cases Allen made his diagnosis as follows: Buerger's disease, 16; Arteriosclerosis, 1; Embolus, 1; Vasomotor changes due to use of a rapidly vibrating tool, 1; Congenital heart, 1; multiple cutaneous gangrene, not limited to extremities, with cyanosis of extremities, 1; unknown, but not Raynaud's Disease, 1; and not one single case of Raynaud's Disease. The writer feels that Allen is capable of judging correctly--and in that light

he feels that the profession should blush at such a gross negligence. It most certainly seems that with the criteria so obviously laid down by Raynaud, that there can be little excuse for going as far astray as was done in some of these cases. Raynaud's criteria are so simple--so easy for the examiner to say whether or not he finds the things Raynaud says are necessary--that it should not be necessary to have such errors in diagnosis so complete as 100% in any twenty-five cases picked at random anywhere.

Here are Raynaud's Criteria:

1--Intermittent attacks of discoloration of the extremities.

2--Absence of evidence of organic arterial occlusion.

3--Symmetrical or bilateral distribution.

4-Trophic changes, when present, limited to skin and never gross gangrene.

Secondary:

1--Females 90%.

2--Gangrene in less than 20% cases, and then only minute excavations without symptoms.

Accurate diagnosis in peripheral vascular disease is essential if treatment is to be properly evaluated.[4,8].

The palpable vessels are never pulseless in Raynaud's Disease. The presence of diminished or absent pulsations in palpable vessels, indicates the presence of an organic or occlusive

vascular lesion. All the accessible arteries of the extremities should be carefully palpated as a routine, as occlusion frequently occurs in other extremities and thus furnishes a clue as to the nature of the disease.[7]

Again, Allen and Brown[6], seeking to get better diagnosis of Raynaud's Disease set forth a brief outline of vascular diseases.

- Functional or vasomotor type
  - Local distrib
    - vaso-constrict types
      - 1-Multiple phase color reaction. Raynaud's Disease
      - 2-One phase color reaction--dead finger, acrocyanosis, syncope.
    - vaso-dilator types — Erythromelalgia
  - General distrib.
    - vaso-constrictor type — Primary essential hypertension early stages.
    - vaso-dilator type — Primary essential hypotension.
- Organic type
  - Local distrib.
    - 1-Arterioscl. $\bar{c}$ or $\bar{s}$ thrombosis. Diabet. gang.
    - 2-Thromboangitis obliterans--Buerger's Disease.
    - 3-Simple thrombosis--embolism
    - 4-Aneurysm $\bar{c}$ or $\bar{s}$ thrombosis.
  - General distr.
    - Arteriosclerosis
      - 1-Primary
      - 2-Secondary to hypertension.

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If the typical picture of Raynaud's Syndrome be borne in mind, and the phenomena not underrated, the differential diagnosis should not be difficult. It is the atypical form which may present the trying problem. Thus, the mere presence of cadaveric fingers does not warrant the diagnosis of Raynaud's Disease, nor does the single absence of symptoms, even gangrene, disprove the diagnosis.....Buchanan.[13]

During the past summer the writer found a large chart in the museum of Pathology at St. Mary's Hospital of the Mayo Clinic--and he does not know whom to ascribe the authorship of this chart to, definitely. It seems that it is a very concise and feasible piece of work.

	Buerger's D.	Arterioscl.	Raynaud's Dis	Erythrom.
Pulsation arteries	Pulseless 50% Dimin. 45% N-5%	P-50% N.5% Dim-45%	Normal	Normal
Rubor c dependency	Present	Present	Absent	Absent
Pallor c elevation	Prsent	Present	Absent	Absent
Claudication	Usually	Usually	Absent	Absent
Gangrene	Common	Common	Rare	Never
Rest Pain	Very severe	Mild	Absent	Mild--severe
Type pain	Sharp-sting	Aching	Absent	Burning
Appearance gang. ulcer	Moist-disch.	Usually dry	Small punched out areas+	None.
Superficial phlebitis	30% cases	Absent	Absent	Absent
Age	25-45	55-85	17-35	30-50
Sex	males 99%	males 90%	Females 95%	Females 70%
Race	Hebrews 50%	Any	Any	Any
X-ray arteries	Neg for scl.	Pos. for scl.	Negative	Negative
Color changes exp. to cold	30%	15-20%	Always	Never
Temp. extrem.	Low	Low	Low	High
Edema	Frequent	Infrequent	Absent	Absent

%'s are approximate

+In early stage.

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Rake[37] has called attention to the possibility of confusing Raynaud's Disease with Scleroderma. In a large number of cases both diagnoses are made either contemporaneously or at different stages of the disease, and often it is impossible to be sure with which disease one is dealing. Usually the symptoms and changes commence is a manner slightly atypical of Raynaud's Disease, with circulatory changes in the extremities especially the fingers. Subsequently changes characteristic of scleroderma appear and often dominate the picture, and the diagnosis which origninally has been "Raynaud's Disease" is changed to "Scleroderma". Rake quotes Kaufman[37] saying that the form of scleroderma which is symmetrical and confined for the most part to the extremities (sometimes called sclerodactylia) often begins with symptoms of Raynaud's Disease, and then progresses with atrophy of the bones and mutilation of the fingers.

The implication is apparent---that one is not dealing with true Raynaud's Disease, but only a certain phase of scleroderma in which the changes simulate that condition. So little is known about the pathology of either condition that perhaps little can be done yet to clear that confusion.

The changes in the vessels in scleroderma resemble very closely the changes in the vessels which form a constant, or almost constant, feature in Raynaud's Disease. In Raynaud's Disease it is usually thought that the anatomical changes in the vessels are secondary to vasomotor disturbances,

spasm and the like, which in turn are due to some rather hypothetical nervous lesions. Whatever may be the truth of this surmise, there is no doubt that such an endarteritis serves to connect certain cases of scleroderma with Raynaud's Disease.

The acroparaesthesia of Schultz or Nothnagel resembles Raynaud's Disease, according to Buchanan[13]. They are alike in that suddenly or gradually the fingers or even the hands and arms become cold, numb, white, and painful. Disturbances of tactile sense and a diminished sensibility for needle pricks, touch, temperature, and electrical irritants exists. Both hands are affected though usually unequally. The differentiation from early Raynaud's Disease is impossible unless Raynaud's second phenomenon of asphyxia occurs.[13]

Buchanan[13] agrees with Rake[37] that scleroderma and sclerodactylia are not infrequently associated with Raynaud's Disease. Some think it a complication. When either is present it is impossible to rule out Raynaud's Disease.

It is important to bear in mind that the requisites for a diagnosis of Raynaud's Disease are absence of arterial occlusion, the minor nature of the gangrene, symmetrical involvement, and intermittent changes in color. A considerable number of cases meet all but the first requirement, and those for the present time, must be regarded as vascular lesions of indeterminate nature. It would seem that clarity and better understanding are served if the requirements stated by Raynaud originally are adhered to.[5]

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TREATMENT:

Like a good many other diseases of unknown origin practically everything that could be tried has been attempted in an effort to reach a cure for the malady. For Raynaud's Disease there are many things suggested--and probably right now the one treatment holding the attention of most men interested is sympathetic ganglionectomy. The writer shall first consider some of the other treatments advanced before giving a serious consideration to ganglionectomy.

DuBose[21] found that an improvement in the circulation was most evident after the use of his therapeutic paravertebral alcohol block. "Alcohol block of the rami communicantes is an anatomical section first employed by Swetlow in 1924. And in 1929 it was established as a major therapeutic measure to treat angina pectoris", says DuBose[21]. He recommends it for the treatment of Raynaud's Disease.

Adson, one of advocators of ganglionectomy, also says that some relief is gained by protection from cold. Sometimes a change of occupation or clothing, and some even try migration to a milder climate.[4] Byall means an attempt should be made to remove the exciting factors if they are known. Protective measures surely fail if the case is severe--and on the whole medical treatment has been very disappointing to Adson[4].

Allen and Waller[9] have written about the use of sulfur for the production of fever in these vascular diseases of the extremities. They had hoped to get three features in their

results with sulfur--(1) safety of use in advanced age--(2) production of prolonged fever---(3) absence of disagreeable sequelae. They obtained only the first two. Pain at the site of injection is the only contraindication.

Allen and Waller[9] also discuss the use of Typhoid Vaccine from which they conclude that the pain is alleviated alright, and the vaccine serves admirably for the production of the fever. But the disadvantages are (1) The occurrence of a chill ---(2) the absence of the desireable part of the reaction after repeated injections---(3) untoward effects and ---(4) it is of comparatively short duration.

Texada[47] found that Borak, working under the supposition that Raynaud's Disease is due to increased activity of certain spinal cord centers, has administered Roentgen ray therapy to those portions of the spinal chord which supply the diseased extremities. He got definite therapeutic results in nine cases, six of which were in the second stage, and three in the third.

Buchanan[13] finds that the attacks can be aborted often and even shortened by the application of heat. Galvanic hand and foot baths of ten minutes duration will help. He believes the application of Cushing's elastic band intensifies the pain though it is beneficial. He feels, further, that amyl nitrite and nitroglycerin have not proved themselves of any worth. Various endocrine gland extracts have been vaunted as of exceptional value, but like all conservative measures, these

have fallen into disuse in uncomplicated Raynaud's Disease. Buchanan[13] believes that small areas should be allowed to slough. Large gangrenous areas are best amputated to save time and to free the patient from the pain. He recommends periarterial sympathectomy for those "who are poor risks for ganglionectomy".[13]

Crichlow[17] has been able to get results in Raynaud's Disease by the use of Bier's Hyperemia method. He feels that it brings the circulation of the extremity under ones entire control. Atropine or other drugs, after a short time lose their effect, and we do not get a dilation of the vessels. With the Esmarck bandage it is difficult to get the hyperemia or the pressure wanted because the bandage is applied at such a great distance from the periphery. The patient can easily be taught to use the apparatus (Bier's hyperemic apparatus) himself. The results have been most gratifying to Crichlow--and he believes to the patient in removing his pain, and in stopping the progress of the disease, as well as restoring him to his former health. In discussing Crichlow's paper, Gessner[17] says, "....that the use of anything effective in the treatment of Raynaud's Disease besides amputation is most worthy of consideration".

The intravenous injection of radium emanation in normal saline, with a dose of 2 or 3 millicuries and gradually increased to 15 millicuries prevents the local action of peripheral vasomotor nerves, according to Poulton[36]. He feels that

radium is antagonistic to adrenalin which he suggests, is responsible for the spasm.

Buchanan[13] does not agree with Crichlow. Not one of his cases were benefitted by Bier's hyperemia. He had one whom he was able to relieve with Blaud's pills. Thyroid extract proved of no aid, and the eradication of foci was in vain. Five patients mentioned relief from warmth--and one was helped by cold applications.

Shinkle[42] presents a case of Raynaud's Disease involving the feet, the retina, and the heart wall. The retina afforded him a good opportunity to watch the actual progress in a living artery thru the ophthalmoscope, and to see the good effect of amyl nitrite, in contradiction to Buchanan. This patient was also benefitted by large doses of potassium iodide, used by mouth;and by hypodermic administration of sodium nitrite. Hemoglobinuria and a moderate rise of systolic and diastolic blood pressure accompanied exacerbations of the trouble.

Any part of the palmar arch in patients suffering from Raynaud's disease, can be made to contract down to obliteration by applying cold locally, if Boggan[12] is correct. If a lead box through which water is circulated at 15 degrees C. is applied to the base of the little finger, the result will be that this finger only will turn blue. Now there is no vasomotor reaction involving a path through the central nervous system that is so localized. This local arteriospasm can be overcome by local warmth, but warmth applied at a distance, such as to the upper

arm, does not give relief. A large number of the anatomists and physiologists are agreed that the vasomotor fibers to the hand travel in the ulnar nerve. If this nerve is locally anaesthetized at the elbow, with novocain, attacks can still be induced to occur, although admittedly with difficulty. From this is derived the fact that the sympathetic vasoconstrictor fibres play no part in these attacks directly. He believes that when sympathectomy is done the disease should not recur at all if cured. But it does, he observes.

Poulton[36] has found that the use of Einhorn's duodenal saline treatment has served him well. He gives two pints of saline (0.85%) into the duodenum after a light breakfast. He admits that it is not a cure--but subsequent attacks are light.

It is only within the last decade that the therapeutic effects of removal of the cervico-thoracic (stellate) ganglion on one or both sides has been tested in Raynaud's Disease.[50] Loyal Davis,[19] Kanavel[19], Royle[39,40], Adson[2,3,4], and others have, with varying success carried out the operation.

Adson[4] whom many of us heard in his recent lecture to the surgeons of Omaha and vicinity, is one of the men most enthusiastic about cervical and lumbar ganglionectomy in Raynaud's Disease. In five cases of this vasomotor neurosis of the spastic type with symptoms of Raynaud's Disease, there was a marked and maintained vasodilatation in the feet for

periods as long as three years, following the operation. Vasomotor activity, as measured by the surface temperature, was absent or markedly diminished, with complete relief from the signs and symptoms of the disease.

Cervical sympathetic ganglionectomy by the anterior approach, carried out in two cases of Raynaud's Disease of the hands was unsuccessful in producing vasodilatation or in ameliorating the signs or symptoms. Intrathoracic sympathetic ganglionectomy was successful in two cases of Raynaud's Disease affecting the hands, producing dilating affects on the arteries of the hands comparable to that observed in the feet following lumbar operation. The striking, maintained, and unequivocal therepeutic effects of the lumbar and dorsal sympathetic ganglionectomy in Raynaud's Disease seems to warrant the belief that surgical control in the disease is an accomplished fact. Of the results of transperitoneal lumbar sympathetic ganglionectomy Adson concludes[4]: "Therefore we can say with confidence, that the pain is relieved, abnormal color reactions disappear, feet and legs present a pinkish color, are dryer anddefinitely warmer than before operation, and there is an average sustained increased surface temperature of 12°C."

Bailey agrees, "That periarterial sympathectomy performed on the main artery supplying a limb will quickly alleviate the symptoms of Raynaud's Disease. There is evidence to justify the hope that the relief is permanent". And of this same operation Adson, enthusiastically, states, "Results already

published show that aconsiderable number of cases have shown results so favourable in character as to justify the name of 'cure'. Where cure is only partial, it is due to partial technical defect or to want of completeness in operative procedures carried out." Viewed as a test of efficiency of the procedure employed the results admit of no question. One patient and her friends, at any rate, are so convinced of the benefits received that they are anxious to have the other two limbs dealt with in the same manner.

Dean[20] is convinced that periarterial sympathectomy is of great benefit. He reports a successful case of a male aged 46, suffering from Raynaud's Disease. "On Febraary 8, 1931, under ether, sympathectomy was performed on the left arm with exposure of the brachial artery by a 5" incision. The artery was entirely freed and the adventitious tissue scraped off for about 2½ inches from the whole circumference of the vessel. Then absolute alcohol was applied over the denuded area.. Immediately the artery contracted down to about ¼ its normal diameter and became white, and constricted while at the same time the assisstant reported loss off pulsation at the wrist. The latter continued for twelve hours. When it returned the hand became swollen, red, and warm, with loss of all pain. The same condition prevailed following a similar operation on the right arm; with the same results the second operation being performed March 26, 1931. The patient has complete use of hands and no pain in either hand or arm".

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Adson[4] has a unique method of chosing those eligible for sympathectomy. Not all cases are suitable. He induces a fever by the use of some non-specific protein, or intravenous triple typhoid vaccine. The surface temperature of hand and foot is taken simultaneously with that of the mouth or blood. The temperature rises after a preliminary drop with the chill. The index is calculated thus: The rise in the surface temperature minus the rise by mouth. This figure in degrees centigrade constitutes the change in temperature of the skin that is due largely to the shifting of blood, that comes from vasomotor changes. This increase divided by the number of degrees increase in the temperature of the blood gives a figure which in simple terms indicates that for every degree rise in the temperature of the blood there is in the skin a certain number of degrees' rise which is largely due to vasomotor activity. In Raynaud's Disease indices from 5-14 are not infrequent. In Buerger's Disease with vasospasm indices of 2-6 are high. It is interesting to note that the same index is obtained after sympathectomy, as is obtained with the vaccine. This helps to differentiate cases with pure vasomotor disturbance from organic disease of the arteries. Arteriosclerosis present a very low index, even zero. Hence sympathectomy is useless, in this disease.

Kuntz[30] studying the innervation finds that extirpation of the stellate ganglion or section of the gray rami connecting this ganglion with the brachial plexus is inadequate to insure complete sympathetic denervation of the blood vessels

of the upper extremities in cases in which the inconstant intrathoracic ramus connecting the first and second thoracic nerves is present. In such cases, complete sympathetic denervation of the upper extremity requires extirpation of the stellate ganglion and of the upper portion of the thoracic sympathetic trunk to the level below the communicating rami of the second thoracic nerve, or section of the communicating rami of the second throacic nerve and any peripheral rami arising from the thoracic trunk above this level; in addition to section of the gray rami connecting the stellate and middle cervical ganglia with the brachial plexus.

The writer does not feel that it is worth while to review the techique of the two operations--periarterial sympathectomy, and lumbar or cervical ganglionectomy. If the reader is interested to that extent he would be well repaid to read Adson's article numbered 4 in the bibliography, which is most beautifully illustrated.

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PROGNOSIS:

The prognosis is subject to wide variations. This much is certain--the disease never has been known to be the cause of death. If the case is mild--unchanged for two or three years and progress is not rapid--the prognosis is good, and reassurance is all that is needed, according to Adson[4]. However he feels that the prognosis in the primary type is not good from the standpoint of a spontaneous cure. It may not go to gangrene but it is a source of real disability to the patient. If there is gangrene the prognosis is grave from the standpoint of the preservation of the digits.

In considering the prognosis the most important factor is the rate of progression of the disease during the first two or three years. If no trophic changes by then they usually never occur. There may be long periods of remission without a known cause.

Buchanan[13] says the prognosis as far as the life of an affected part is concerned has been poor in the past and amputations have been frequently performed in order to alleviate the pain. It seems only the severest cases have been observed and hence the gloomy outlook. We are finding that an affected part may remain useful for many years in not a few cases.

The enthusiastic attitudes shown by the men doing active work in Raynaud's Disease, causes the writer to feel highly optimistic for this malady in the future.

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SUMMARY AND CONCLUSION:

The writer has attempted to review the literature and bring it up to date. It remains, that the cause of the disease is not definitely known. The trend of thought now seems to be that the pathology is local rather than central.

It has been shown that little has been added in the way of description to Raynaud's original work.

A plea has been made for more accurate diagnosis--and to this end the criteria laid down by Raynaud have been reviewed and emphatically stated, and restated. All this, because the writer feels that in view of the many treatments advocated it is only fair that the treatment should be given the advantage of a fair diagnosis to begin with.

The treatments that seemed to have proved the most successful have been treated, with the views of the men that use them appended. Where controversy is present it has been presented.

And finally the writer is glad to be able to give a better prognosis than has ever been given before, because of advance in treatment.

It is hoped that the near future will find some one who can definitely lay his finger upon etiology, and say this to the world, and be correct. For then--and probably not until, will the treatment be more perfectly aimed, and probably give more perfect results.

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