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GENERAL STAFF MEETING
MINNESOTA GENERAL HOSPITAL
UNIVERSITY OF MINNESOTA

CONTENTS

PUBLICATION FINANCED BY CITIZENS AID SOCIETY

MEETING

Date: March 2, 1933

Place: Interne's Lounge, 6th Floor, West Building

Time: 12:15 to 1:20

Program: Purpura Hemorrhagica

Present: 98

Discussion: Leo G. Rigler
Irvine McQuarrie
Henry L. Ulrich
Cecil J. Watson
H. A. Reimann
J. R. Paine
R. W. Koucky

THEME: L.G.R.: Film of heart at entrance shows heart which can be interpreted as within normal limits so far as size, even shape is concerned, or congenital heart. At this time peculiar shadow in mediastinum was not interpreted. These lung films are not very good so far as heart is concerned, but present an interesting picture of the condition which she had in her lungs following operation. Whole series taken. Following the operation (less than 24 hours afterward) you see marked density in central portion of both lungs. This came on rapidly after operation. With the history of possible purpura suggested intrapulmonary hemorrhage.

Followed her at daily intervals with films, some show little change, others do not. Next day looked as if it was beginning to resolve which would support original idea. Next day began to extend. Note distinct involvement of lower lung appearing like pneumonia. Four days after operation looked more like ordinary pneumonia. Left side stationery. Process chiefly posterior, involving upper lobe, also lower (portion of) lobe. Last film shortly before exitus shows process extending and involving upper and lower lobes. My own interpretation was that it started as hemorrhage and pneumonia followed. Mass in mediastinum is somewhat the same as it was before operation, but a little more exaggerated because patient is lying on her back.

I. McQ.: Most interesting, unusual case to us. Not a true thrombocytopenic purpura. Findings of purpuric spots and low platelet count present. The family picture (low platelet counts) made it different from group where one finds no history of family changes. Pneumonia differed from any we have seen. No ovaries makes one think of possible endocrine abnormality back of bleeding. No reason worrying about it but case stimulates study of general physiology, not satisfied with only morphological study of blood.

The heart looked like fetal endocarditis. As soon as I see an aortic valve like this it points against rheumatic heart disease. The story of child's having a diagnosis 5 years before by man who studied heart disease - who told mother that child would not live whole life makes me feel that it had been present for some time.

H. L. U.: This is congenital defect of aortic valve. Congenital valves liable to infection all the time. Cannot correlate cyanosis with aortic lesion, doesn't go at all. History is wrong? I would think this is congenital defect with moderate secondary infectious process.

General Discussion: I think one reason they are finding less correlation of platelets and bleeding is that we are now getting more accurate platelet counts than formerly. Classification still holds water, still an essential type. I am sorry that Frank's discussion was not mentioned. He found no change in leucocytes in essential disease. He points out infectious group which is secondary. Ought to be checked.

Most people who live 10 years or so have focal infection. I do not like the idea of bringing focal infection into the discussion. Some Swedes recently discovered a change in the blood picture in focal infection, shift of leucocytes, etc. Tried in this country but not found reliable. Another thing Frank emphasized is that this disease is precipitous disease and may

not recur. Another point, hemophilia first described in America, described about 110 years ago by Philadelphia physician.

C. J. W.: I think that as Dr. Ulrich has pointed out one of the most illuminating articles on hemorrhagic disease is that by Frank. Frank has shown that the megakaryocytes in the bone marrow are deficient in essential thrombocytopenia, azure granulation is often lacking, and they do not split off platelets in the normal way. The familial nature of the case reported today is very interesting. Several similar cases were reported by A. F. Hess. These were restudied by Frank who would not accept them as instances of thrombocytopenia because the platelets were not low enough, being in all instances more than 80,000. For that reason I do not think Frank would accept this case as an instance of essential thrombocytopenia.

This brings up the question of spontaneous tendency to bleed which is often seen, mostly in women, without any definite platelet reduction but with fairly definite evidence of capillary inferiority as evidenced by the positive capillary resistance test. Infection in such cases usually tends to make the tendency more pronounced. I have brought this patient, Mrs. G., here today at Dr. O'Brien's request. I think she illustrates this type of constitutional capillary inferiority. She has had a tendency to bleed most of her life, particularly nose bleeds which were often severe and of spontaneous type. She had never noticed skin petechiae. These were first seen in the hospital. As you see the capillary resistance test is strongly positive. The platelets vary between 125,000 to 130,000. Her daughter also has a tendency to bleed but she has not yet been studied. I think that the capillary deficiency factor must be emphasized as a probable cause of bleeding in many cases which are reported under the name thrombocytopenia.

H. A. R.: Dr. Fishbein two years ago showed us his hands after he carried suitcase and produced purpuric spots. It seems as if most important thing, deficiency is in capillaries. Platelets can be secondary. In this discussion we see an atypical pneumonia classified as "lobar" pneumonia. Before many years we will have to abandon terms of lobar, broncho, etc. and substitute etiological types. This "lobar" pneumonia did not conform in onset, as it was apparently gradual without chill. Dr. Rigler points out it was atypical from his standpoint. Until we are able to tell cause we will not get far in treatment. Last week, another paper appeared in American Medical Association Journal stressing this point and results of treatment. It is difficult to change terminology because of common use is well established. Until we do that we will make no progress in the treatment or prevention of pneumonia.

J. R. P.: When I was a student in Massachusetts General, spring of 1931, Dr. Churchill was interested in trying to remove pulmonary embolis. He trained special assistants and nurses. They practiced in their off hours on autopsy specimens until they perfected a technique by which they could get in and out in 5 or 6 minutes. When I was on service as clerk patient developed pulmonary embolism. He was an Italian, very large, and I do not remember what he was operated upon for in the first place. About two days after he got up he had one. Dr. Churchill and his corp of surgeons which he had trained were put on waiting shifts. One would go out and eat, while other would watch. Watched for 36 hours. Finally definitely sure he was going to die. Word got out and within 10 or 15 minutes 60 or 70 people assembled to see operation. There was good deal of blood lost. Dr. Churchill got one plug out. Just closing up skin when patient died. Only two cases of this kind reported in the United States, neither lived.

R. W. K.: Correction on page 241: All of the subheadings belong under Symptomatic Purpura, none belong under Essential.

Comment: Not all purpura is on a thrombocytopenic basis. Vascular element plays large role. Platelet count to be significant must be

50,000 or below (following Frank). In this way surgeons have a ready means of determining cases suitable for splenectomy. Apparently essential purpura still exists. The role of splenectomy can never be definitely determined because of the variable course of the disease.

II. ABSTRACTS:

PERIPHERAL VASCULAR DISEASES
With Special Reference to
THROMBO-ANGIITIS OBLITERANS
(Buerger's disease), RAYNAUD'S
DISEASE, AND HYPERTENSION.

Abstr. - Ritchie.

Ref.:

1. Allen, E. V., Brown, G. E.: Raynaud's Disease, J.A.M.A. 99: 18, 1472, (Oct. 29), 1932.

2. Mayo, W. J., Adson, A. W.: Raynaud's Disease, Thrombo-angiitis obliterans and scleroderma, Ann. Surg.: 771-783, (Oct.) '32 (reprint).

3. Brown, G. E.: Erythromelalgia and other disturbances. Am.J.Med.Sc. 186, 468, (Apr.) '32.

4. Brown, G. E., Allen, E. V., Mahorner, H. R.: Thrombo-angiitis obliterans. W. B. Saunders Co. 1928.

5. Rake, G. E. Pathology and pathogenesis of Scleroderma: John's Hopkins Hosp. Bull., XLVIII, 212, (Apr.) '31.

6. Raynaud, M.: Selected monographs, New Sydenham Society CXXI, 1888.

7. Buerger, L.: Circulatory disturbances of the extremities, W. B. Saunders Co., 1924.

8. Allen, E. V., Brown, G. E.: Raynaud's disease, Am.J.Med.Sc., 183: 187 (Feb.)'32.

9. Adson, A. E., Brown, G. E.: Thrombo-angiitis obliterans, J.A.M.A. 99:529 (Aug.13) '32.

10. Scott, W. J. M., Morton, J. J.: Principles of treatment in common arterial disease. J.A.M.A. 99:982, (Sept.17), '32.

11. Dumas, A. G., Evans, E. T.: Thrombo-angiitis obliterans. Minn. Med. 15: 320, (May) '32.

12. Barker, N. W.: Results of treatment of thrombo-angiitis obliterans by foreign protein. J.A.M.A. 97: 841, (Sept.19) '32.

13. Robertson, D. E.: Treatment of Vascular diseases of extremities. J. Bone and Joint Surg., 14: 57, (Jan.) '32.

14. Chapman, D. G.: Diagnosis and treatment of vascular disease of extremities. Virg. Med. Month. 59:288 (Aug.) '32.

15. Simpson, S. L., Brown, G. E., Adson, A. W.: Raynaud's disease. Arch. Neurol. & Psych. 26: 687, (Oct.) '31.

Classification of a case of peripheral vascular disease is often difficult not only because absolute criteria for diagnosis is usually not familiar to physicians but also because diseases present such bizarre forms clinically and what is even more confusing is that there are so many different terms used to represent same condition.

Brown, Allen and Mahorner (4) present good working classification of vascular disease.

- Functional or vasomotor types
  - Local distribution
    - Vasoconstricting types
      1. Multiple phase color reaction: Raynaud's disease.
      2. One phase color reaction: acrocyanosis, dead finger, local syncope.
    - Vasodilating types: Erythromelalgia.
  - General distribution
    - Vasoconstricting types: Primary or essential hypertension, early stages.
    - Vasodilating types: Primary or essential hypotension.
- Organic types
  - Local distribution
    1. Arteriosclerosis, with or without thrombosis: diabetic gangrene.
    2. Thrombo-angiitis obliterans.
    3. Simple thrombosis or embolism
    4. Arteritis of known infectious origin (rheumatic, syphilitic, etc.)
    5. Aneurysm with or without thrombosis.
  - General distribution
    - Arteriosclerosis.
      1. Primary.
      2. Secondary types due to hypertension, lead, etc.

Our interest today is mainly in Raynaud's disease and thrombo-angiitis obliterans (Buerger's disease).

Thrombo-angiitis obliterans.
(Buerger's disease)

Of all peripheral vascular diseases this has most varied nomenclature. According to Jablon's (for ref., see 4) it has been known as dysbasia angiosclerotica, erythromelalgia, intermittent claudication, juvenile and presenile gangrene, spontaneous gangrene, acrocyanosis, Russian, Jewish and Yiddish disease, and Scleroderma as well as a host of other terms, including endarteritis obliterans. Buerger (1908) named disease thrombo-angiitis obliterans since then a widely accepted term. It is a clinical and pathological entity.

Etiology:

Many factors suggested--none fulfill requirements of direct casual agent.

Brown, Allen and Mahorner summarize as follows:

1. Tobacco - difficult to evaluate but subjects with disease show higher incidence of smokers and they use larger amounts of tobacco.

Recently Robertson (D.E.) saw a patient who had had 6 amputations of fingers, toes and one leg who suddenly became free of symptoms when he stopped smoking, a habit to which he was heavily addicted. After 10 years freedom from symptoms, he again used tobacco for one month. Symptoms promptly returned and disappeared with discontinuance of tobacco. Smoking denied in 1% of Buerger's cases (7).

2. Race - Many authors report its exclusive occurrence in Hebrews, but other races are involved.

In Brown, Allen and Mahorner's group, 50% occurred among Hebrews, many times higher than percentage of race registering at Mayo Clinic. But now we find decreasing incidence among Jewish patients and increasing incidence among Gentiles.

In Buerger's study, 4 cases out of 500 did not belong to the Hebrew race.

3. Sex - Disease almost exclusive in male.

Buerger - 99 males, 1 female.
Brown, et al - 300 males, 0 females.
Had one case in female simulating disease but pathological proof missing.

4. Infection - practically all observers who have made careful clinical and pathological studies of thrombo-angiitis obliterans have been impressed with inflammatory appearance of the lesions (4).

75% of 88 cases in which teeth were examined showed significant periapical infection.
20% of cases had tonsils removed, of the 80% who did not, the tonsils were of varying size, most of them containing plugs or fluid pus.
52% of 46 cases in which prostate was examined, prostatitis was found.
Only 3 patients of entire group were free of demonstrable infection in tonsils, teeth or prostate.

Summarizing, authors state that while absolute proof is lacking, there is much evidence that an infection or bacterial toxic substance is etiological factor.

Note: In view of tide against focal infection? and no controls, is this so significant?

5. Occupation - No etiological factor.

6. Age - 150 cases (Mayo Clinic): 15-20 - 1; 20-25 - 6; 25-30 - 18; 30-35 - 31; 35-40 - 33; 40-45 - 31; 45-50 - 31 ; 50-55 - 14; 55-60 - 3; 60-65 - 2; youngest patient 17, oldest 64.

Buerger's cases ranged from 17 to 56. Average age 32 years.

Many other conditions such as lowered sugar tolerance, shortened coagulation time, glandular dysfunction, etc. have been suggested but probably have no significance.

Extent of Lesions:

In Adson's 240 cases, disease involved lower extremities in 60%. Affected upper alone in 2% and both upper and lower in 38%. Also observed that disease would sooner or later become bilateral. Disease was bilateral in 98% of cases (2).

Pathology: (9), (7), (4).

1. Gross: Depends on stage of process in which they are examined. Usually affects larger vessels, more often of lower extremity. Arteries are occluded more often than accompanying veins. First change is thickening of the wall, then occlusion of vessel with a soft, red thrombus in the lumen. Thrombus organizes and is traversed by many small vessels. The adventitia and perivascular tissue becomes markedly indurated and artery, vein and nerve in end stage are bound firmly together.

Microscopic:

Earliest changes (arteries and veins alike), are appearance of lymphocytes in adventitia and thickening of intima. Nuclei of endothelial cells become larger, increase in number. Often there is increase in elastic tissue of the intima. Then thrombosis and occlusion of the vessel take place. There is some evidence that acute inflammation is engrafted upon the chronic process at time of thrombosis. Finally, marked fibrosis even of adventitia occurs. Other changes are indefinite and inconstant. Often increase in connective tissue with some lymphocytic infection.

In later stages, canalization and partial reestablishment of the arterial circulation may occur.

Clinical Course and Diagnosis: (4), (7).

Approximately 75% of cases follow fairly uniform clinical course.

Stage I. Intermittent claudication, due to anemia. Symptomatic manifestation of abnormal fatigue or pain following exercise. At first an indefinite pain in sole of foot, ankle or toe, unilateral or bilateral, followed by sudden pain (intermittent claudication). May be associated with pallor, coldness, numbness and tingling.

Intermittent claudication may pro-

ed by weeks, months or years, with the ther symptoms such as rubor, cyanosis, oldness, trophic disturbances, etc.

Important to recognize symptoms of intermittent claudication. (Symptoms variable.) Described as cramping sensation. In smaller percentage of cases, other signs such as cold feet, sudden arterial occlusion, vasomotor disturbances, recurrent superficial phlebitis, or indolent ulcers following trauma are first signs of disease. A tentative diagnosis of thrombo-angiitis obliterans is made in all cases of idiopathic recurrent superficial phlebitis in adult males.

Stage II. Postural changes - rubor with dependency, pallor with elevation. Usually after, but sometimes before, the first attack of intermittent claudication a peculiar blush of the affected area is noted in dependent position. According to Buerger, this may be called erythromyelia but perhaps rubor is a better term as the former is confusing when discussing the definite clinical entity of erythromyelia (discussed later).

Pallor on elevation is same stage of disease. Return of rubor is usually partially in inverse ratio to the amount of arterial occlusion.

Stage III. Trophic changes - manifested by non-healing abrasions from trauma, ulceration of digits or development of gangrene. Usually, but not always appear after pains of intermittent claudication and postural changes have occurred.

Clinical types:

1. Slow progression - most common type. Coldness of feet is first symptom followed by excessive fatigue, etc. Entire process lasts 4 to 8 years.

2. Absence of progression. - Symptoms of vascular insufficiency (fatigue and pain) progress slowly then remain stationary. Disability minimal in spite of symptoms which have been present 8 to 12 years.

3. Circulatory compensation - may originally belong to 1st or 2nd group. Patients may with care have good function in extremities.

4. Acute fulminating claudication appears suddenly, progresses rapidly. Amputation necessary. Edema and lymphangitis present around the gangrenous area. Process may be complete from 1 month to 3 years.

5. Extensive gangrene without rest pain. Rare.

6. Venous involvement only - not unusual. 1st sign - recurrent superficial phlebitis. Deep phlebitis present.

7. Normal pulsations in palpable arteries. Confusing from diagnostic point of view. Usually acute arterial occlusion in one or more toes followed by color changes. Suggestive of Raynaud's disease. Diagnosis dependent on age, sex, nationality, superficial phlebitis, type of pain, signs of arterial obliteration.

8. Vasomotor disturbance simulating Raynaud's disease. Must remember that 30% of organic arterial diseases have vasomotor disturbance.

9. Association of arteriosclerosis. Many cases impossible to differentiate from clinical standpoint.

10. Absence of trophic changes.

11. Severe rest pain (pain without exercise) without trophic changes. Occurs rarely.

Diagnosis:

Most common error in early diagnosis is ascribing pain to flat foot. Roughly, 80% of Brown's and Allen's cases were treated for months or years with various types of arch supports, shoes, etc.

In cases of Dumas and Evans (11), earlier diagnoses were: pes planus 19, circulatory disturbances 8, metatarsalgia 8, rheumatism 7, Raynaud's disease 6, neuritis 5, trench feet 5, varicose veins 3, luetic endarteritis 3, myositis, 1, acro-cyanosis 1, tuberculous bone 1.

For clinical diagnosis of thrombo-angiitis obliterans, we must depend on (11):

1. Sex - male predilection.
2. Early involvement of lower extremities.
3. Early symptoms of claudication or pain.
4. Migrating phlebitis.
5. Pulseless vessels.
6. Pallor on elevation.
7. Rubor in dependent position.
8. Slow process, chronic course, keeping in mind that some cases have a spontaneous arrest.
9. Absence of simultaneous symmetrical involvement.

Differential Diagnosis: important. (4)(11).

Prime requisite in clinical differentiation of vascular diseases is determining whether disease is primarily organic vascular disease or neuropathic or neurogenic.

This is accomplished readily in from 90-95% of cases by palpation of arteries and study of symptoms (4).

A. Organic vascular disease:

1. Arteriosclerosis - is other common organic disease. The differential features are (4):

	Thrombo-angiitis obliterans	Arterio-sclerosis
Race	50% Hebrews	All
Rest pain	Severe	Mild
Superficial phlebitis	30% of cases	Absent
Age	25-45 (mostly)	55-85 (mostly).
Sex	99% males	90% males.
X-ray	Usually negative	Usually positive for sclerosis.
Edema	Frequent	Absent

Other symptoms of claudication, color changes, etc. are practically same.

2. Diabetic gangrene - other signs of diabetes.

3. Aneurysm - other signs.

4. Embolic or thrombosis - usually acute, unilateral following cardiac condition, infections, etc.

5. Peripheral nerve changes are differentiated by presence of motor paralysis, loss of sensation, etc.

B. Neurogenic or Neuropathic.

1. Raynaud's - discussed later (4)

	Thrombo-angiitis obliterans	Raynaud's
Pulsation of arteries	Pulseless 50% Diminished 45% Normal 5%	Normal
Rubor in dependency	Present	Absent
Pallor in elevation	Present	Absent
Claudication	Usually present	Absent
Gangrenous ulcers	Moist, inflamed	Small punched out areas in early stages.
Superficial phlebitis	30%	Absent
Age	25-45 (mostly)	17-35 (mostly)
Sex	99% males	95% females
Race	50% Hebrews	All
Edema	Frequent	Absent

It must be remembered that in about 30% of organic type of disturbance (Buerger's arteriosclerosis, etc) there are vasomotor disturbances simulating Raynaud's secondary to organic lesions. Diagnosis usually made clear by presence of occlusion in one or more of main arteries.

2. Erythromyelalgia - discussed later. Differentiated from thrombo-angiitis by normal pulsation, dry gangrene, burning pain, females 70%, high temperature of extremities.

3. Other neuropathic - conditions such as angio-neurotic edema, multiple neurotic gangrene of skin, scleroedema, etc. are easily differentiated by symptoms and signs.

Treatment:

Last five years has showed a great change. Previously "high and early amputation" was resorted to as only method.

Brown and Allen - group their cases -

1. Extensive gangrene (with or without pain) - amputation.
2. Mild trophic changes with severe rest pain - medical measures for relief, lumbar sympathectomy in suitable cases.
3. Mild trophic changes without rest pain - medical and physical measure to increase circulation, lumbar ganglionectomy in suitable cases.
4. Severe rest pain without trophic disturbance - same as 2.
5. Cases without rest pain or trophic changes. Prophylactic and medical measures.

Medical measures used are electric baths, intravenous injection of sodium citrate, Ringer's solution, roentgen rays to lumbar spine, subcutaneous injection of insulin units x, every day. Some are in discard, others are still used.

Principles of medical treatment: Brown et al, Allen, Scott. (4),(12),(10),(9).

1. Prophlaxis.

a. Care of extremities is important. Frequent cleansing, use of oils to keep skin soft, care of shoes, woolen hose, careful trimming of nails and corns, warm climate if possible, sedentary occupation in warm place if possible, diminished use of tobacco, etc.

2. Cautious employment of warm dry heat.

3. Contrast baths.

4. Postural exercise.
(Last 3 tend to improve circulation).

5. Nonspecific foreign protein treatment.

Used by Goodman and Gottesman in 1923.

Increase (12) in flow of blood, even if temporary is of primary importance. Vasodilation, with increased flow of blood through extremity occurs during febrile reaction. Many agents used (e.g., foreign protein) to produce this such as B. typhosus, B. paratyphosus, A. and B. vaccine and typhoid H antigen. Result is vasodilation in collateral and non-occluded arteries.

Now given to 300 patients with thrombo-angiitis at Mayo Clinic. In 150 cases, at least 3 injections given. In the others, only 1 or 2 injections were given (usually as a test for vasodilation - see later). Approximmately 2% failed to have a satisfactory febrile response.

Results in 150 cases:

Marked improvement	49%
Slight to moderate or slow improvement	27%
No improvement	6%
Progression - amputation	18%

Most of failures were in group where there was claudication only or in cases with extensive gangrene. Best results in cases in which there is rest pain, with or without ulcers or limited gangrene.

Other measures used coincidently-such as contrast baths, etc.

Adson and Brown (9) state that in this type of treatment 56% of patients are markedly improved. Incidence of amputation of leg or hand which was 25% in cases of inadequate treatment reduced to 14%.

6. Sympathetic ganglionectomy (9).

In a carefully selected group of patients, excellent results have been obtained. Obvious that vasodilation cannot be produced in an arteriosclerotic or occluded artery and surgical intervention is useless unless there is obvious evidence of vasospasm in remaining non-occluded arteries.

Brown suggested recording temperature of skin before and during induced fever to determine amount of vasospasm. Temperature of mouth and skin can be compared with corresponding temperature of normal with spasm, with readings taken during height of fever.

Fever produced by intravenous administration of a foreign protein - triple typhoid vaccine.

In normal persons, mouth temperature average increase 2° C whereas temperature of skin over digits increase 4 to 6° C. indicating the peripheral arteries have been opened by inhibition of vasomotor.

In cases which have a vasospastic disorder increase is greater as initial temperature of skin is lower than that of normal persons in same room.

In general, there may be little if any difference in skin temperature as the vessels are unable to relax. Thus, in thrombo-angiitis, it is possible to determine whetherthere exists an element of vasomotcr spasm of the collateral and unoccluded arteries. Therefore, tests serve as index and unless rise in skin temperature of the digits is two or more times greater than rise of oral temperature, the condition is considered inoperable. Another test of spasm and occlusion by nerve block and regional and spinal anesthesia, presented by Scott and Morton. In occlusive arterial disease without spasm, here is no increase in blood flow but if there is vasospastic element the condition is improved.

Results:

100 consecutive cases, 89 bilateral lumbar sympathetic ganglionectomies and trunk dissections, 15 bilateral cervicothoracic ganglionectomies with resection of upper portion of thoracic trunk.

During earlier years, approximately 1 in 7 were sympathectomized. In last 2 years, 1 in 3 are advised to have sympathectomy.

87 patients markedly improved following sympathectomy. (Average 80% relief).

76 patients received useful extremity.

7 patients still complained of symptoms of neuritis.

7 periarterial sympathectomies, anastomosis of femoral artery and vein, injection of nerve with alcohol, suprarenalectomy, etc. have all been found inadequate.

Raynaud's Disease (Allen and Brown)

Raynaud described condition in 1862.

Practitioners still have great deal of difficulty in recognizing and differentiating it from thrombo-angiitis obliterans mainly because the minimal requisites for diagnosis are not generally known.

Minimal requirements laid down by Raynaud's are:

1. Intermittent attacks of change of color of acral parts.
2. Symmetrical or bilateral involvement.
3. Absence of clinical evidence of occlusive lesions of peripheral arteries.
4. Gangrene or trophic changes, if present, limited in large degree to skin.

To these, Brown and Allen (8) have added 2 more:

5. The disease must have been present for a minimal period of two years.
6. There must be no evidence of a disease to which it could be secondary.

Pathogenesis:

Raynaud felt that it was to be considered as "a neurosis characterized by an enormous exaggeration of the excito-motor energy of the gray parts of the cord which control the vasomotor innervation."

Lewis (for ref., see (8)), (1929) states that there is no abnormal vasomotor impulse but a local fault of the vessels.

Simpson, Brown and Adson uphold Raynaud's view (15).

According to Buerger, there is no satisfactory data on the pathology of Raynaud's disease.

Etiology:

Age:	Morgan	26 yr. average
	Monro	29 yr. average
	Cassirer	168 cases show greatest majority between 21 and 40 years.

Allen, Brown state 3rd decade is predominantly age at which symptoms begin. Predilection of disease for younger people is linked with nervous instability of patients of these ages.

Frequency:

Monro	1 in 3000 patients
Cassirer	5 in 7000 patients

Nationality:

149 patients. Brown and Allen conclude nationality plays no role.

Body type, marital status, blood pressure, anemia, occupation, menstruation seem to have had little to do with etiology in Brown and Allen series.

According to Buerger, cold seems to influence development and frequent occurrence in wash women is noted.

Clinical Course (8), (7):

1. Local syncope - sudden blanching, coldness, etc., numbness present.

2. Local asphyxia - color of skin changes to bluish, purplish, violaceous hue.

Syncope and asphyxia may occur together in same extremity.

Involvement - (Brown and Allen's study of 147 cases). In 47% involvement of hands and feet present, and in an equal number hands were alone involved.

Involvement of nose, cheeks, ears and chin are found but uncommonly.

3. May follow course of slow or rapid progress, or process may remain stationary or recede.

In some cases progressive complications may develop (scleroderma, arthritis, recurrent infections) in from 1 to 15 years.

4. Trophic disorders often develop. Usually superficial. Monro's statistics show gangrene developed in 43% of upper extremities; in 24%, only lower; and, in 22%, both upper and lower (for ref., see 7).

In Allen's and Brown's cases (135) 41% came to Mayo Clinic more than 5 years after onset of symptoms and remainder came within 1 to 4 years.

Diagnosis:

"Mild vasospastic phenomena such as cold, moist hands and feet, or symmetric pallor of one or more digits without pain, numbness or trophic changes can scarcely be interpreted as Raynaud's disease, although in such cases the physiopathological state is identical to that in Raynaud's disease. Diagnosis of Raynaud's disease is reviewed for cases in which there is symmetric pallor followed by cyanosis, in which it is difficult to induce recovery and in which patients complain of numbness and aching pains during the stages of pallor" (2). As in thromboangiitis obliterans, the differential diagnosis is sometimes difficult but if the six requirements are found the diagnosis is more evident.

The most difficult differential

diagnosis are in regard to:

1. Thrombo-angiitis obliterans - discussed.

2. Erythrom-elalgia - discussed.

3. Scleroderma - disease of vascular spasm in which spasm is more or less continuous and produces constant reduction of supply of blood to extremities. Changes in scleroderma similate those that arise from plaster cast that is too tight, namely cyanosis, swelling, pain, atrophy, contracture, deformities and disuse. (2). Mayo and Adson report a group of cases in which sympathetic ganglionectomy was done.

Divided into 3 groups:

1. Primary scleroderma with vasomotor phenomena developing late in disease. Of this group, vasomotor phenomena were improved, skin temperature increased, the skin became more flexible and ulcers healed.

2. Scleroderma and vasomotor disturbances developed simultaneously. Results were same as in group 1 except for greater increase in function.

3. Vasomotor disturbances preceded development of scleroderma. Results averaged 45% recoveries in cervico-thoracic sympathectomy and 85% in lumbar sympathectomies.

Cause:

Etiology unknown. Recently (1931) Rake described changes of great interest in lower cervical sympathetic ganglion in typical cases. There were fewer ganglion cells than normal. Some showed striking changes, were enlarged, pale and showed marked loss of finer structure. They appeared "blown up".

Scleroderma and Raynaud's confused as scleroderma often begun in manner suggestive of slightly atypical Raynaud's disease - then changes characteristic of scleroderma appear and diagnosis is changed. Undoubtedly, closely related diseases.

Treatment:

Milder cases rarely require special treatment and may be controlled by improving social and economic states (2).

Wearing warm clothing, care of extremities, etc. important.

Bier's passive hyperemia often effective.

Severer cases, after medical treatment has failed, are treated by surgical procedures to relieve vasomotor spasm.

Results of Mayo - and Adson

a. Cervico-thoracic sympathectomy (39 cases)

Case		Average % of color changes relief	Average % of pain relief	Average % of ulcers healing	With recurrent Signs	With incomplete Sympathectomy
1. Uncomplicated.	11	85	85	No Ulcer	None	None
2. With Ulcers	3	60	60	100	1	1
3. With ulcers or gangrene with scleroderma and arthritis	25	85	75	85	4	4

Erythromelalgia - one rarest condition in clinical medicine. Mayo Clinic statistics show approximately one in every 200 cases of peripheral vascular disease and yearly incidence is 1 to 40,000 cases to total number of patients registered.

Weir Nutehill first described disease in 1872.

Characteristics:

1. Bialteral or symmetric at-

tacks of burning pain in hands or feet.

2. Attacks initiated or aggravated by standing, exercise or expesure to heat.

3. Relief obtained by exposure to cold and elevation.

4. During the attacks the affected parts were flushed and congested and exhibited increased local heat.

5. Condition was refractory to treatment. Brown has ceased to consider this as an essential characteristic.

Pathological basis not established.

Different from redness and pain of feet often found in thrombo-angiitis obliterans, localized arteriosclerosis, in gout, cellulitis and certain cases of Raynaud's.

Treatment unsatisfactory. Brown has 2 cases responding well to locally applied radium.

Impressions:

1. Diagnosis of peripheral vascular disease difficult because many physicians are not familiar with absolute criteria for diagnosis of each group. Terminology confusing and bazarre clinical forms not uncommon.

2. Classification into functional or organic, local or general distribution, vaso-constricting or dilating types.

3. Thrombo-angiitis obliterans (Buerger's disease) has most varied nomenclature.

4. Cause is not definite. Associated factors are tobacco, race, sex, infection, and age.

5. Lower extremities usually involved with tendency to become bilateral.

6. Gross and microscopic features are infection plus thrombosis. Apparently 75% of cases follow fairly uniform clinical course.

7. Most common error in diagnosis is ascribing pain to flat feet.

8. Differential diagnosis from arteriosclerosis and Raynaud's disease must be made.

9. During past five years early and high amputation is no longer resorted to as only method. Care of feet, dry heat, exercise, non-specific foreign protein treatment, ganglionectomy are used.

10. Foreign protein injection is of great value in diagnosis. Through it can measure degree of possible vasodilation of the vessels of involved extremity.

11. To four original requirements laid down by Raynaud, two more have been added by Brown and Allen: i.e., the disease must have been present for at least two years and there must be no disease to which it could be secondary.

12. The cause is not known, although nervous instability and the age group seem to be predisposing factors.

13. The course is local syncope or asphyxia, slow or rapid progress, and trophic disorders. It must be distinguished from thromboangiitis obliterans, erythromelalgia, and scleroderma.

14. Scleroderma apparently shows changes in the gnaglia. More severe cases are treated by sympathectomy.

15. Scleroderma and Raynaud's disease confused in early stages.

16. Erythromelalgia is rare condition. First described in 1872 and rather refractory to treatment.

III. CASE REPORT

CHRONIC ARTHRITIS, RAYNAUD'S DISEASE.

Case is white male, 44 years old, admitted to Minnesota General Hospital 9/8/32, discharged 10/10/32. Readmitted 11/21/32.

Operations - Arthritis
1-26-32 - Always fairly well except for bilateral hernia (herniotomy), 1910, and cholecystectomy 1928. At this time had exacerbation of pain in left hip joint which had been present to some extent for about year. During this year had gradual development of pain in all joints. Was admitted to a hospital in Duluth for 3 weeks for intravenous therapy. Remained at home for 3 weeks and became progressively worse.

Pallor and cyanosis of hands and feet
2-26-32 - Attack of bilateral pallor followed by cyanosis of hands. Admitted to hospital for 5 months. No attacks of sudden pain, pain described as "rheumatism in joints". Coldness of both hands and feet. Attacks of pallor and cyanosis were more frequent when exposed to cold weather. During hospitalization some improvement in arthritic condition. Referred to the Minnesota General Hospitals.

Physical examination
9-8-32 - Admitted to Minnesota General Hospital. Physical Examination: well-developed, well-nourished white male in no pain. Head: right pupil slightly larger than left. Lungs clear on percussion and auscultation. Heart normal size and shape. No murmurs. B.P. 120/75. Pulse regular - rate 78. Abdomen slight tenderness on deep palpation of abdomen. Old healed operation scars.

Extremities
Tenderness of all joints. Color of upper extremities appears normal but there is some coldness of hands. Lower extremities show marked pallor below level of ankles. Toes on both feet are very pale and both are cold to touch. Thought that left foot was colder than right.
Laboratory: Urine - neg. Hb. 80%. Blood Wassermann negative. X-ray examination of hands, knees and the lumbar spine reveal chronic hypertrophic arthritis of lumbar spine and atrophic arthritis of interphalangeal joints.

Reaction
9-16-32 - 40 million triple typhoid vaccine given. Chill lasting 30 minutes with temperature to 100.4. Greater increase than normal in skin temperature of extremities indicating vasospastic condition. More evident in lower extremities than in upper. Some relief from pain but it was still present. Pain was constant and did not resemble pain of intermittent claudication.

Operation
9-23-32 - Bilateral lumbar sympathectomy done.
9-25-32 - Extremities are warm and red and apparently there is a very good result.
9-28-32 - Complains of rheumatic pains in right leg. No objective change in color of leg.
10-6-32 - Up. Legs feel warm and are red in color. Complains of pain in hip and back. Discharged.

Arthritic pain
10-15-32 - Had severe pain in all joints. Admitted to St. Louis County hospital from which he was transferred to Minnesota General Hospitals.
11-21-32 - Physical examination essentially same as previous admission except for extremities. Tenderness in all joints with some swelling of joints of hands. No redness or cyanosis and hands are warm, feet warm and of good color. Vessels all palpable and pulsations appear normal.

Operations
12-20-32 - Left cervical sympathetic ganglionectomy done. The left hand became warm and evidently good result.
1-12-33 - Attack of pallor and cyanosis of right hand.
2-19-33 - Right cervical sympathectomy done.
2-25-33 - Hands and feet both warm. Up and feels fairly comfortable. Pulsations of all vessels are palpable.

Pain
3-7-33 - Complains of pain in both legs. Pain constant and particularly evident at night. Feet are warm. Dorsalis pedis vessels palpable on both sides. Faint cyanosis in dependent position and slight blanching on elevation. Skin over right toe is scaly and color around base of nail of big toe is rather dark red in color.

Clinical impression of case is arthritis complicated by Raynaud's disease. Operations have relieved

to great extent vascular disease but joint difficulty is not changed. Operations done primarily for vascular disturbance.

Note: that our case does not correspond to two requirements laid down by Brown and Allen: i.e., not present two years, associated disease present.

IV. ABSTRACT

A COMPARISON OF BLOOD PRESSURE IN MEN AND WOMEN. (A Statistical Study of 5,540 individuals).

1. High Blood Pressure:

The invention of the sphygmomanometer has been cursed and praised. Uncomplicated hypertension has no characteristic clinical symptoms (?) so that the discovery of an elevated pressure is often "news". The sign is present under such variable conditions that few physicians (at least in the beginning) had sufficient experience to give their patients good advice or treatment. Pathologists confused it with gross arteriosclerosis--clinicians followed -- textbooks still do.

Efforts to treat it are too often a peculiar combination of therapy (?) for arteriosclerosis, proprietary house advice, unscientific dieting (red vs. white meats, etc.) and pulling teeth. Lay dinner table chatter still suffers with discussion of "my wonder doctor who reduced my pressure 6 points in just 3 days". The last word has not yet been said but these are a few facts at our disposal.

Hypertension is primary and secondary (an associated condition) but is there any real difference in the "mechanism" of the two types? "Essential" stresses the necessity of the change, physicists think of it as a problem in friction (viscosity), physiologists stress the increased work the heart must do, and the stress and strain on the arteries, pathologists and clinicians know what the increased work "may" do to the heart and vessels. Gross arteriosclerosis cannot produce a pressure over 140 mm. Hg (upper limit of normal), microscopic arteriosclerosis is not always present.

Like the islands of Langerhan's in diabetes, sometimes we see changes (sclerosis), sometimes we do not. Vessels about the size of those seen in the eygrounds and pre-glomerular zones (all agreed) and the muscles (some agree) are the seat of the trouble. By comparison with a city water system, the difficulty is the faucet valves, not the mains or leads into homes or business places. Not even "Time" could get away with the normal blood pressure age + 100. We still believe that adult pressures above 140-150 are abnormal, in younger subjects still lower figures.

We still do not know how common the condition is in "normal" people of all ages, why only some elevated pressures are associated with hypertrophy of left ventricle, accentuation (?) of sclerotic changes in larger (small) vessels and other complications, what influence our advice and treatment really has on the condition. Is the pressure we record the "real" pressure 24 hours a day, etc., are there sex differences (biological-environmental)? We know it as a hospital problem but how about the physician's office. Because of marked individual variations, it is an ideal subject for group statistical study. Such a survey has been made by one of our staff members on patients in the Admission Division and Medical Clinic of the Out-Patient Department and will now be reviewed.

Ref.: Wetherby, M.,
Ann. Int. Med. VI:754-770 (Dec.) '32.

"A study was made of the routine blood pressure reading of all individuals admitted to the medical division of the out-patient department of the University of Minnesota Hospital. Records cover 3 year period from December 1926 to December 1929. There are in this series 5,540 individuals, 3,258 women and 2,282 men. The readings have been classified by decades for systolic and diastolic pressures, and a comparative study has been made of blood pressures in men and women.

Group:

"The patients admitted to the out-patient department are largely from the lower and lower middle classes. The patients are both from the city and country and are largely laborers, farmers, housewives, and working women. Many had no medical complaint but were examined as a routine procedure. These patients are ambulant and many have minor complaints or have physical examinations as a routine procedure preliminary to tonsillectomy or hospital employment. A very small percentage come in because of symptoms suggesting hypertension. All patients admitted to the medical clinic were included and routine blood pressures taken as a part of each patient's study. The only cases excluded from the list were the clear-cut cases of glomerulonephritis and aortic insufficiency. It has been interesting to notice the infrequency with which a diagnosis of true nephritis has been made. Consideration has not been given to obesity, although it is well recognized that the overweight individuals tend to have a higher pressure."

Men

Age Group Years	No. of Cases
15-19	135
20-29	477
30-39	495
40-49	437
50-59	365
60-69	247
70 and over	126

Women

Age Group Years	No. of Cases
15-19	285
20-29	731
30-39	786
40-49	636
50-59	513
60-69	241
70 and over	66

Technic:

"The blood pressure in all instances was taken with mercury manometers and by the auscultatory method. The diastolic pressure has been considered as the fourth phase. Most of the readings were taken in the sitting position. Patients had been sitting from thirty minutes to two hours prior to the examination and the blood pressure was taken after the history and hear the end of the examination. In this way the factor of physical exertion was eliminated and the element of excitement reduced to a minimum."

The Percentage of Cases Above Certain Blood Pressure Levels for Men and Women in the Total Out-Patient Group

Percentage Over	15-19 Yrs. Men	15-19 Yrs. Women	20-29 Yrs. Men	20-29 Yrs. Women	30-39 Yrs. Men	30-39 Yrs. Women	40-49 Yrs. Men	40-49 Yrs. Women	50-59 Yrs. Men	50-59 Yrs. Women	60-69 Yrs. Men	60-69 Yrs. Women	70 & Over Men	70 & Over Women
Systolic Blood Pressure														
140 mm.	5	6	10	8	15	18	23	56	40	65	57	76	72	89
150 mm.	1	1	3	3	5	10	12	41	26	51	43	67	62	79
160 mm.	.7	.3	1	1	3	6	7	32	19	38	34	56	47	68
180 mm.			.2	.4	1	3	3	22	9	19	15	34	29	42
200 mm.					.4	1	2	15	5	10	8	14	10	24
Diastolic Blood Pressure														
90 mm.	5	7	16	16	25	24	30	40	38	51	46	63	47	70
100 mm.	2	1	2	2	5	6	8	17	17	24	27	34	31	45

Lability:

"Caution must be taken in discussing to what extent the difference between men and women, so clearly brought out by the analysis, represents a preponderance of chronic hypertension or only a greater lability of the systolic pressure among women. That the labile character of normal and abnormal blood pressures alike constitutes the chief limitation of the significance of single as well as of serial blood pressure readings is by now well recognized. If a greater blood pressure lability among women is the explanation for the difference brought out in this study, then it becomes necessary to introduce a new assumption, namely, the development of such an increased lability among women above the age of 29, since no trace of such a sex difference can be noticed in the two age groups below 30, where not only the mean pressure but also the standard deviations are the same for both sexes."

Milder:

"There exist certain indications that chronic hypertension in its course and outcome behaves as a milder disease among women than among men. In the out-patient service of the University Hospital where there is little difference between the number of men and women above the age of 50, there are a number of women with marked elevation of pressures, but very few men who have been followed over a period of several years. Blackford, Bowers and Baker, in a follow-up study of patients with systolic pressures of 175 mm. Hg or more found 65% to be women, while their general group did not show any such sex preponderance. Their patients were followed from five and a half to eleven years and showed during this time a mortality of 70% for men and 39% for the women. The average length of life, after the diagnosis had been made, was longer for the women than for the men. Riesman likewise comments upon the relatively benign nature of hypertension in women."

Correlation:

"It is a matter of importance to correlate with the findings of this study the results obtained from autopsies. We are fortunate to be able to compare with our blood pressure studies the detailed report by Bell and Clawson, based upon a large autopsy material from the same community as our patients. Bell and Clawson used hypertrophy of the heart (in the absence of valvular lesions or chronic glomerulonephritis) as the chief diagnostic sign. Thus, it is clear that only such elevated

blood pressures as were sustained over a sufficiently high level to produce a marked hypertrophy of the heart, were included in the study of Bell and Clawson. In their total material of 4,578 autopsies on individuals between 21 and 80 years of age they found 420 cases of chronic hypertension. Among these they found the corrected ratio of men to women to be 1.4:1. For the whole hypertension group the causes of death are given as follows: myocardial failure, 45 per cent; cerebral accident, 19 per cent; coronary sclerosis, 16 per cent; renal failure, 9 per cent; miscellaneous, 11 per cent. In the group of coronary sclerosis the ratio of men to women was as 2.7:1. Eliminating the cases of coronary sclerosis, the ratio for the remainder becomes 1.1:1. In the study of Bell and Clawson about 15 per cent of the individuals who died at an age above 50 were afflicted with hypertension.

Conclusions:

1. Statistical analysis shows an increase in mean value of systolic and diastolic blood pressure with age, the most marked rise occurring a decade earlier for women than for men. The relative variation increases over the age period but has a tendency to rise abruptly and remain relatively constant between rises. These rises also occur one decade earlier for women than for men.

2. Absolute variation is greater for women than for men. There is a statistical significant difference in mean value for men and women after 30 to 40 years of age.

3. A statistically significant difference is also shown in incidence of blood pressure of higher groups for women in comparison with men. The averages for men and women in the higher groups do not show a significant difference.

4. The clinical significance of blood pressure of equal degree must be considered independently in men and women. A given elevated blood pressure is more apt to be benign in nature and if of pathological consequence to run a longer course in women than in men. Hypertension as a cause of death is as frequent in men as in women even though the incidence of blood pressure at higher levels is significantly greater in women. In the older age groups this difference is partially explained by the shorter course of the condition in men.

V. WELCOME

Alfred Washington Adson, of the Graduate School of the University of Minnesota (Mayo Foundation), is our guest today. An excellent surgeon, a good doctor, an original thinker, he has contributed to international scientific progress in his field. February 23rd, 1933, he was invited to give the third annual Walter M. Brickner Lecture at the Hospital for Joint Diseases, New York City, on "The Physiological Effect of Sympathectomy in Treatment of Peripheral Vascular Diseases, Hirschsprung's Disease and Cord Bladder." This and many other honors have come to him but through it all he remains the same affable, human fellow who is respected by his associates and recognized by his younger colleagues as an outstanding teacher and good fellow. We had the pleasure of his presence at Staff Meeting last year and trust that his trips will be an annual event. We welcome you today, Dr. Adson, and thank you for your courtesy in coming to our meeting. We hope that you will discuss our problems freely and give us the benefit of your remarkable experience.