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Peripheral Vascular Disease

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C O U R T E S Y O F C I T I Z E N S A I D S O C I E T Y

I. ABSTRACT

PERIPHERAL VASCULAR DISEASE

R. W. Koucky.

Previous discussion

At a previous staff meeting (Bull. IV: 254-265, (Mar. 9) '33), vascular diseases of the extremities were discussed. The summary of the abstract presented at that time is as follows:

Thromboangiitis obliterans is a disease of unknown etiology. Tobacco apparently plays a causative part (drug?, toxin?, allergy?). A large percentage of the cases occur among Hebrews. The disease almost invariably involves males of young adult age. Infections, particularly focal lesions, are present in most cases but their significance is difficult to determine.

The pathology is essentially one of a proliferating occlusion of the lumen accompanied by an inflammatory reaction in the wall. About 60% of the cases involve the lower extremities, about 2% involve the upper and about 38% involve both. About 98% of the cases are bilateral in the late stages.

The classical symptoms are claudication, pain in the extremities, postural changes (i.e., cyanosis on dependency, pallor on elevation) and atrophic changes. About 80% of cases have been treated for months or years under various diagnoses such as flat feet, rheumatism, neuritis, varicose veins, etc.

The differential diagnosis includes arteriosclerosis, thromboangiitis obliterans and various neurogenic or neuropathic forms of spasm. The supportive medical measures are: frequent washing, use of oil on the skin, carefully chosen shoes, supervised care of the nails and corns, warm climate, warm environment, warm clothes, discontinuation of the use of tobacco and alcohol, dry heat, contrast bath, postural exercises and nonspecific foreign protein. Under this type of treatment, about 56% of patients are improved and the incidence from amputation drops from 25% to 14%.

Sympathectomy is of value in this group since skin tests show that spasm is associated with the occlusion. In a series of 100 sympathectomies, approximately 80% obtained satisfactory improvement.

Raynaud's disease is a neurosis with enormous exaggeration of the vasomotor reflexes. The disease occurs in very young individuals, mostly between the years 17 to 35. It is a disease of females (95%). There is no particular racial distribution.

The characteristic findings are a syncope and asphyxia of localized portions of the extremities characterized by color changes, coldness and numbness. Trophic disorders are limited to small, punched-out ulcers.

Sympathectomy gives satisfactory relief in from 60 to 85% depending upon the severity of the disease.

Dr. A. W. Adson attended this meeting and gave an informal and interesting discussion. He particularly emphasized his impression that there was a close correlation between organic occlusion of vessels and spasm both in the obliterative angiitis and the Raynaud's disease. He stated that it was his impression that if the spastic element could be controlled the obliterated process would be stopped or the severity of the disease would be diminished.

Recent Literature

In the literature of the past three years, most of the writings dealt with one or both of two phases of this problem: (1) the importance of supportive medical measures and (2) estimation of the relative amount of anatomical occlusion and spastic contraction of the vessels.

Diagnostic methods:

Skin temperature: The most widely used method of estimating the vasomotor

response has been the elevation of skin temperature following the induction of systemic fever by such substances as typhoid vaccine. Roughly, the principle involved in this method is as follows: (1) At average room temperature, the skin of the extremities involved by peripheral vascular disease is unusually cold. (2) Normally, in the presence of fever, the skin temperature rises two or more times the rise in oral temperature. (3) When fever is induced and the skin of the suspected area does not show this rise in temperature, it is assumed that there is an occluding disease of the vessels. (4) When in the presence of fever, the temperature of the suspected area rises as in normal individuals, it is assumed that the vascular defect is on a spastic basis.

The use of artificially produced fever has been a satisfactory procedure but it involves hospitalization of patient and in some individuals the induction of fever involves a certain amount of risk.

Attempts have been made to obtain this same reflex rise of skin temperature by methods which do not have the objectionable features of typhoid injection. Coller and Maddock have obtained the same vasomotor response in the extremities by wrapping the patient in blankets for one hour. The temperatures are read while the patient is under covers. The method is simple and offers no distress or risk to the patient. The correlations between the skin temperatures obtained by this method and by means of typhoid inoculation are claimed to be identical.

Landis and Gibbon have advocated a similar simple method. These authors state that immersion of the arms in warm water will cause a vasomotor response in all of the other extremities. They place the arm in a bath in which the temperature is 43 to 45° for a period of 35 minutes. The temperature of the skin of the legs is read immediately and the rise in the temperature is observed. Normally, the skin temperature of the legs rises to 32° (normal response) within 35 minutes and usually within 15 minutes. In cases of occlusion of the vessels, the response is delayed or fails to reach the normal height. Fourteen cases of obliterative disease and seven cases of spastic disease were checked with results obtained by other methods and the correlation was essentially the same.

Morton and Scott obtained the skin temperature reflexes after local anesthesia of the nerves to the area.

Cutaneous histamine reaction

One-tenth cubic centimeter of histamine acid phosphate is injected intradermally and normally a zone of vasodilation occurs around the wheel, the so-called arterial flare. This flare is due to a vasodilation of the arterials and its absence indicates: (1) not enough pressure in the skin vessels to fill up these dilated arterials, (2) arterial spasm not overcome by histamine, (3) degeneration of cutaneous nerve. This reaction has its greatest value in determining the proximal level in which circulation is embarrassed and it indicates the improvement or standstill of the circulatory status during the course of treatment.

Oscillometric study

The oscillometer records show definitely the patency of the larger vessels. The shape and height of the curve determined at various levels of the extremity determine the narrowing or occlusion of the main trunk. The oscillometer does not determine the extent of collateral circulation. The pulsations are obtained only from the large trunk.

Arteriography

Arteriography has been developed to accurately visualize the arterial system of the extremities. Several solutions have been tried, one which is most widely used is thorotrast. The technique can be developed only through actual experience with the method. The crucial feature mentioned by all writers is the exact timing of the exposure after the

injection. The thorotrast passes quickly through the arteries, through the capillaries into the veins and is rapidly dispersed. By accurate time of the exposure, visualization may be made of the larger arteries, capillaries or the veins. This method of studying has added very much to our knowledge of the pathology and the compensatory mechanism of these diseases. Thromboangiitis obliterans shows an irregularity in the outline of the lumen with a reduction in caliber that goes on until occlusion is complete. The distal vessels are involved first and the disease progresses in the proximal direction. In arteriosclerosis, the irregularity of the lumen corresponds to the sclerotic or atheromatous plaques in the vessels. Their location is irregular and generally the larger sized vessels are involved most. Frequently, the involvement is greatest in the proximal portion of the extremities. When calcification is visible in an ordinary roentgenogram, the vessel is frequently completely occluded. The development of collateral circulation in itself is evidence of arterial disease. It is most marked whenever there has occurred a complete occlusion of a major artery. Its extent is dependent upon the duration and completeness of the occlusion. Some authors feel that the examination should be limited to questions of extent and location of aneurysm and emboli. Other authors feel that the method has possibilities both in extending our knowledge of peripheral vascular diseases in general and has application in estimating the type of treatment to be carried out.

Drugs

Various vasodilator drugs have been used, such as theobromin, anylnitrate and acetylcholine. These drugs have not been proven to be very satisfactory because the relief of spasm is not complete or regular.

Differentiation of Organic and Spastic Vascular Occlusion

The development of these various diagnostic methods has been stimulated entirely by the desire to estimate the relative amount of spastic and organic occlusion of the vessels. There apparently now is a consensus of opinion that all the various vascular diseases are accompanied by spasm even when definite occlusive characteristics are present. Even in arteriosclerosis and diabetes, the spastic element has been found. In thromboangiitis obliterans, the degree of spasm, particularly in the early cases, is considerable. On the other hand, spastic conditions such as Raynaud's disease may be accompanied by organic occlusion.

Treatment

Sympathectomy: In the literature of the past two years, very little has been given regarding the end-results of sympathectomies. The operative procedure is recognized as a great advance in the treatment of this type of disease. The available statistics on results from operative procedures have already been discussed in the meeting of 1933.

Medical method: There is no doubt of the emphasis placed in the recent literature upon the medical care of vascular diseases of extremities. One author has suggested that the wave of enthusiasm over sympathectomy has caused us to forget the various medical forms of treatment. He urges the revival of these as necessary prophylactic and supportive measures. These procedures, as advocated now, differ very little from those previously discussed (1933). Emphasis is again placed upon protection from cold and trauma, upon posture, contrast baths and heat. The use of artificial fever has apparently been established. In patients in whom the use of typhoid vaccine might be accompanied by some risk, injections of sterile milk have been advocated. Two per cent suspension of sulphur in olive oil, intramuscularly, has been suggested by several authors. An initial dose of 1 cc. gradually increased to 10 cc. is used. The difficulty with this method is the severe pain produced at the site of injection. The desired fever lasts on the average of about 50 hours. The use of vasodilator drugs has been generally unsatisfactory. Some clinics report encouraging results from the use

of acetylchlorine hydrochloride. In other series of cases, the authors state that less than 50% of the patients showed a measurable effect.

A substance released on the market under the title "Tissue Extract 568" by Sharp and Dohme has been developed. This is an extract of the pancreas which is insulin-free. The severity and frequency of claudication have been said to be diminished by the use of this preparation. There are no systemic reactions and only a slight temporary pain at the site of the injection.

Pavaex, a term introduced by Herrmann and Reid, is an abbreviation for "passive vascular exercise." The idea of passively increasing the blood flow through an extremity dates back to Murray in 1812. This has been repeatedly rediscovered since this time: Planny - 1832, Gunod - 1834, Bluck - 1887, Clapp - 1905, Sinkowitz and Gottliev - 1917, and Braeucker - 1930. In 1932, Herrmann and Reid popularized the method which is now commonly known as "Pavaex." The apparatus consists of a box or boot enclosing the extremity attached to a suction apparatus so that rhythmic alterations of the pressure about the extremity may be varied from any amount of negative pressure to any desired amount of positive pressure and at any rate of alteration. Some 12,000 Pavaex treatments have been given by the authors to date. The pressure changes which have given the most satisfaction have been 80 mm. mercury negative pressure and 20 mm. mercury positive pressure. It is felt that more positive pressure is undesirable because of the possibility of spontaneous thrombosis in the vessels. The leg is elevated several inches above the level of the patient so that gravity aids in the return of the blood. The treatment is given for one to two hours or even more at one sitting and repeated as often as convenient. Apparently, there is no limit to the time of length of the treatment as far as discomfort or untoward effects. The result by this method, as given by Herrmann and Reid, shows that 16% of the entire group necessitated amputation, 40% were improved, 44% more completely relieved. There was a very definite difference in end-results depending upon the type of involvement. In the group in which the predominant involvement was of a main artery in the nature of an acute or subacute thrombus or embolus, the most satisfactory results were obtained. No amputations were necessary and 100% were relieved of their symptoms. In the second group, there are included unselected cases of arteriosclerotic obliteration of the vessels. There were 46 patients in this group and 9% went on to amputation, 48% were improved and 43% were relieved of all symptoms. In the third group which consisted of arteriosclerotic obliteration of the small blood vessels of the feet, the results were poor; 42% of this group went on to amputation of one form or another, 42% were relieved and only 16% were cured. It is assumed that the forceful suction of blood into the extremity maintains the flow through the partially obliterated vessels and at the same time hastens the development of the collateral circulation.

Shipley and Yeager have adopted the method of Herrmann and Reid and have applied it not only to arteriosclerotic disease but also to thromboangiitis obliterans, frost-bite gangrene, ununited fractures, delayed union and arthritis. These authors are pleased with the results they have obtained.

Summary

1. The literature on peripheral vascular diseases during the past three years deals chiefly with the importance of supportive medical measures and with diagnostic methods to determine the relative amount of occlusion and spastic contraction of the vessel.

2. The use of typhoid vaccine to induce fever is still the most accepted method of obtaining skin temperature readings on the suspected area.

3. Since many of the patients with this type of disease are old and many have cardiac involvement, the use of typhoid vaccine is sometimes dangerous. Attempts have been made to develop methods without this objectional feature.

4. Coller and Maddock wrap their patients in heavy blankets for one hour and read the temperature while the patient is under the covers. The correlation between this method and that obtained by the use of typhoid inoculation is claimed to be identical.

5. Landis and Gibbon state that immersion of the arms in water of a temperature of 43 to 45° for a period of 35 minutes will induce the vasomotor response in all of the other extremities. With this method, the skin temperature of the leg rises to a normal of 32° within 35 minutes and usually within 15 minutes. In case of occlusion of the vessels, the temperature fails to rise to this level.

6. For a number of years, Morton and Scott have suggested the use of local anesthesia on the nerve to the area. They claim that all of these methods are measures of the amount of vasodilation that will occur following sympathectomy. When no surgery is contemplated, these tests show the degree to which dilation of the vessels may occur and they can be used as a guide to indicate the progress of the treatment.

7. The cutaneous histamine reaction consists of a intradermal injection of .1 cc. of histamine acid phosphate. Normally, a zone of vasodilation (reddening) occurs around the wheal. When this is absent, either the arteries to the zone are obstructed so that no blood can get through or they are closed by arterial spasm or finally they may be, on rare occasions, a degeneration of the cutaneous nerve. This test is used to determine the proximal level at which circulation is intact. It may also be used to determine the improvement during treatment.

8. Oscillometer records are used to determine the patency of the larger vessels. Curves taken at various levels along the extremity indicate the position of the occlusion. These tracings do not give an estimate of the degree of collateral circulation.

9. In recent years, arteriography has been rapidly developed. Important additions have been made to our knowledge of the pathology and the compensatory changes in this type of disease. Thromboangiitis obliterans shows irregularity in the outline of the lumen with reduction in caliber up to complete occlusion. The distal vessels are involved first and the disease progresses proximally. In arteriosclerosis the irregularity of the lumen corresponds to atheromatous or sclerotic plaques within the vessel. Generally, the larger sized vessels are involved first but the distribution of the plaques is very irregular. The extent and location of the collateral circulation can be visualized. It has been shown that the greatest collateral circulation develops when occlusion has occurred in the major artery. While someauthors think that arteriography is of value, only in locating aneurysms and emboli, others believe that the method will extend our knowledge of the disease in general and may have application in outlining the method of treatment.

10. Various vasodilator drugs (acetylbromin, anylnitrate, acetylcholine) have not proven to be satisfactory either for diagnostic or therapeutic relief of spasm.

11. All of these diagnostic methods are aimed at estimating the relative amount of spasm and organic occlusion in the vessels. There is a consensus of opinion that even those diseases which are primarily spastic in nature may be eventually accompanied by occlusion and that the occlusive diseases are likewise accompanied by spasm.

12. The recent literature does not deal to any extent with end-result of this infection. As one author states the wave of enthusiasm over sympathectomy has caused us to forget the various forms of medical treatment. He urges the revival of these as necessary prophylactic and supportive measures.

13. These procedures as advocated now differ very little from those previously discussed. The use of artificial fever still holds an important place. In those cases in which the typhoid vaccine

seems to involve some degree of risk, injections of sterile milk have been substituted or injections of a 2% suspension of sulphur in olive oil, intramuscularly, have been given. The dose of the latter begins with 1 cc. and gradually is increased to 10 cc. The difficulty is that there is severe pain produced at the site of injection. The fever which results lasts on the average of about 50 hours. Vasodilatory drugs, as described above, have been unsuccessful.

14. An extract of the pancreas (insulin-free) has been released on the market under the title "Tissue Extract - #568" (Sharp and Dohme). The severity in frequency of claudication is said to be diminished by this preparation.

15. Passive vascular exercise, "Pavaex," is an old idea which has been repeatedly rediscovered since 1812. In 1932, Hermann and Reid have again presented the idea and have popularized it.

16. The apparatus consists of a box or boot attached to a suction apparatus so that rhythmic alterations of pressure about the extremities may be obtained. They recommend 80 mm. of mercury negative pressure and 20 mm. of mercury positive pressure. A more positive pressure is undesirable because of the possibility of spontaneous thrombosis. The leg is elevated several inches so that gravity aids in the return of the blood. The frequency or length of the treatment apparently is governed only by the convenience to the patient. Prolongation apparently does not result in discomfort.

17. The authors claim by this method to have reduced the number of amputations to 16% and state that 40% of the patients were improved, and 44% were completely relieved.

18. There is a very marked difference in the results however depending upon where the occlusion has taken place. In acute or subacute occlusion of the large vessels, approximately 100% were relieved of their symptoms. In the routine unselected group of arteriosclerosis, 9% went to amputation, 48% were improved and 43% were relieved of all symptoms. In the group in which the obliteration took place in the small vessels of the foot, the results were poor: 42% went on to amputation, 42% were relieved and only 16% were cured.

19. It is assumed that the forceful suction of blood in the extremities maintains the flow through the partially obliterated vessels and at the same time hastens the development of collateral circulation.

20. Other authors have applied the same method not only to arteriosclerotic disease but also to thromboangiitis obliterans, frost-bite gangrene, ununited fracture, delayed union and arthritis.

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II. LABORATORIES

The volume of laboratory work has increased a great deal in the past few years. The extent of this increase has not been generally known by the staff and is entirely unknown to the internes and younger fellows because of their shorter residence.

The following table shows this increase:

Year	Number
July '29 to July '30	40,053
" '30 " " '31	45,713
" '31 " " '32	53,433
" '32 " " '33	65,117
" '33 " " '34	67,011

(67% increase)

While the volume of work has been increasing, economic stress has necessitated diminishing the number of trained laboratory technicians in the general laboratory from 3 to 2 girls. The number of students supervised by these girls has increased from:

Year	Seniors	Juniors	Total
29-30	13	15	28
30-31	15	18	33
31-32	15	22	37
32-33	24	37	61
33-34	28	47	75

The general laboratory has carried the increased load under these circumstances as best as it can. Many services to which the staff has been accustomed have had to be dropped. This curtailment of services must continue until a balance between facilities and volume of work has been reached.

Misunderstanding and discord arise from time to time because of these discontinued services.

A review of some of these may clarify the situation:

1. Requests dealing with individual research projects cannot be accepted by the hospital laboratories for the time being.

2. The number of chemical procedures per day is limited. Some of these (glucose-tolerance tests) must be scheduled ahead. Not infrequently the work is so heavy that the schedule is filled for days ahead.

3. All chemistries must be in the laboratory by 9 o'clock. All subsequent chemistries requested must be emergencies and arrangements must be made with Miss Gillig.

4. Basal metabolism rates and electrocardiograms are scheduled ahead. The schedule for the subsequent day is closed by 4 P.M.

5. The various divisions of services are given a certain allotment of BMR's. The excess cannot be taken care of and it becomes essential for the physicians to request examinations on only those cases in which the tests are of most value.

6. To reduce the amount of time devoted to charting and eliminate the reduplication of work, the laboratory sheets are sent to the laboratory directly from "admissions." They reach the ward only after the admission laboratory work has been completed. During this interval, the laboratory sheet cannot be expected on the chart.

7. Follow-up laboratory studies are done by the clerks or internes. These reports on the chart do not have the signature of the laboratory. The laboratory cannot at present handle these follow-up studies. When, however, circumstances arise in which a check upon the clerk's findings is indicated, the laboratory will do such tests providing they are notified.

Example: "John Jones
Catheterized urine

Dr. A."

A specimen with such a request shall be placed in the student laboratory.

"John Jones
Catheterized urine
To Main Laboratory

Dr. A."

Such a specimen will be examined by the main laboratory.

8. Keep the laboratory available for those tests which are actually important. Do not burden it with matters of casual interest -- for instance, cell count on thick, yellow pus; examination of pus for leukemic cells; differential cell counts on urine, etc.

9. The laboratory closes at 4:30 P.M. The night laboratory service is for emergencies. In order to keep it available for emergencies, routine work must wait until the following day. Please remember that emergency laboratory work is trying and difficult -- be human. Consider carefully the technician's question: "Do you have to have this done tonight?" Remember that your emergency probably is no more important than the one with which the technician is occupied at the time.

10. Finally, and above all, bring your suggestions, troubles, criticisms and the errors which you observe or suspect to the laboratory. Through such cooperation, we can give better service.

III. WANTED

Physician -- Cass Lake, Minnesota - One other physician in town -- Excellent chance for good man.

See Dr. O'Brien for further details.

IV. MOVIES

Title: Casting for Luck

Released by: The Fox Motion Picture Corporation

V. OUR GUEST TODAY

Edgar V. Allen, Assistant Professor of Medicine, Mayo Foundation, Rochester, Minnesota.

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Next week's topic -- PNEUMONIA