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Syphilitic aortitis

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SYPHILITIC AORTITIS

SENIOR THESIS
UNIVERSITY OF NEBRASKA
COLLEGE OF MEDICINE
OMAHA NEBRASKA

J. EDW. FELDMAYER
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HISTORY

While the relationship between aneurysm and syphilis was suspected as early as the Sixteenth Century, by Pare, and later by Lancisi (1728) and Morgagni (1761), it was not until 1876 that Francis H. Welch first described accurately the gross and histologic changes which take place in syphilitic aortitis. At that time Welch studied 117 cases of "Fibroid aortitis" in 48 per cent of which syphilis was definitely present.

Years later, (1888), Dohle published a comprehensive report on syphilitic aortitis, and for a time the disease was called Dohle-Hellerschen aortitis. Dohle defined mesoaortitis as a specific inflammation of the adventitia and media which terminates in cicatricial deformity.

Schaudinn and Hoffmann, in 1905, were the first to direct attention to the Treponema pallidum as the specific cause of syphilis. In 1905-1906 Wassermann described the complement-fixation test which bears his name. In 1906 Reuter demonstrated the Treponema pallidum in sections of syphilitic aortae. Rebaudi, and Roch and Eiesner found the same to be true a short time after. Vanzetti reproduced lesions similar to those found in humans by injecting material obtained from the testicles of syphilitic rabbits into the sheaths of the carotid arteries of other rabbits. (1) (2)
ETIOLOGY

Specific--The specific cause of all syphilitic lesions is the Treponema pallidum. This organism is characterized by the geometric regularity of its spirals which are deeply cut and, like a corkscrew, remain sharp when the focus is changed in the dark-field. The organism varies from 3-15 microns in length, and from 0.3-0.4 microns in width. The spirals are about 1 micron apart, so that a spirochaete with eight turns would be about 8 microns long. (3)

The Treponemata are readily killed by drying, exposure to air, sunlight, and various antiseptic agents. Conversely, warmth, moisture and anaerobiosis, as afforded by mucous membranes and macerated cutaneous surfaces offer the greatest opportunity for their propagation and spread. Hence, coitus accounts for the greatest proportion of cases. A further appreciable group arises from the contact of infected mucous membranes in kissing. A portal of entry through abrasions of the skin constitutes another mechanism of infection; but evidence is available in support of the entrance of the Treponema even through the unbroken skin. Finally there comes the large group of congenital syphilitics, wherein transplacental infection is the rule.

Following the invasion by the Treponemata and their early general dissemination through the lymph and blood streams, their lodgment in any given tissue excites a characteristic
reaction. Lymphocytes and the plasma cells appear at each of these points of arrest of the organisms. (4)

**Frequency**—There are wide variations between clinical and pathological estimates of the incidence of involvement of the cardiovascular apparatus in patients with syphilis. From the clinical standpoint, Bruusgaard's (5) figures and those from the Johns Hopkins Hospital by Turner (6) are in essential agreement. Bruusgaard had the opportunity of examining 473 patients with early syphilis who had received no treatment, at long intervals after infection, ranging between 10 and 40 years and averaging about 20 years. Of these patients approximately 10 per cent developed definite clinical evidence of cardiovascular damage. In the material at Johns Hopkins Hospital, Turner's (6) statistical survey of the admission diagnoses of more than 6000 patients with late syphilis showed that exactly 10.1 per cent were suffering from cardiovascular syphilis, 5.3 per cent uncomplicated aortitis, 1.2 per cent aortic aneurysm, 2.7 per cent aortic insufficiency, 0.7 per cent other scattering diagnoses.

These data are in striking contrast to the pathologic information furnished by such observers as Warthin (7) and Langer (8). On the basis of very large necropsy material, these investigators, one in Berlin, the other in Ann Arbor, find that from 70 to 90 per cent of all patients with late syphilis show pathologic evidence of cardiovascular damage, most commonly syphilitic aortitis. The discrepancy between
clinical and pathologic diagnosis is based on the presence of macroscopic or more frequently microscopic lesions in the aortic wall so insignificant as to be below the threshold of physiologic disturbance and hence of clinical recognition.

The pathologic evidence is, however, of great clinical significance in that it indicates that some degree of syphilitic involvement of the aortic wall is an almost universal accompaniment of long-standing syphilitic infection. It should prompt the clinician to painstaking and repeated investigation of the cardiovascular apparatus of every patient with late syphilis.

Age and Stage--In a group of 51 clinical cases and another of 54 necropsies, both at the Massachusetts General Hospital (9) and a series of 24 necropsies at the Boston City Hospital (10) the following data was secured:

The average age in the 78 necropsies was 47.9 years. The lesions were advanced in 53, with an average age of 52.2 years, moderate in 21, with an average age at death of 49.8 years, and minimal in 4, with the average age 37.7 years. The minimal age was 31, 18 and 21 years in the advanced, moderate and slight groups, respectively. But 5 of the 78 necropsy cases achieved the age of 80 years; only two passed the age of seventy. In one of the latter the syphilitic lesions were slight and in the other moderate in degree. In 107 autopsies at the Cleveland City Hospital (11), the youngest patient was twenty-three years old; the oldest, seventy-nine
years. The number of cases in the various decades is as follows:

Decade-- 20-30 30-40 40-50 50-60 60-70 70-80
5 25 32 27 15 3

Thus it is seen that the largest number of cases is in the
decade from 40 to 50 years.

**Latent period of aortitis**—One of the most important
factors in syphilitic aortitis is the appearance of late
lesions without apparent previous lesions with objective and
subjective symptoms. Syphilis is a disease which among other
curious facts offers that of latent periods. It happens,
therefore, that a patient who is apparently cured and has
had no symptoms for years may suffer a new serious attack. In
another instance it may occur that a syphilitic showing no
symptoms and no organic alterations develops an acute case
concomitant with grippe, typhoid fever or rheumatism. (12) (13)

Gougerot (16) recently called attention to the fact that
cases of syphilis acquired many years before, may one day re-
appear in the form of tabes, general paralysis, aortitis, and
that under circumstances it is possible to encounter treponemic
foci in the medulla, the cerebrum and in the aorta.

A syphilitic localization in the aorta is rather often
latent. The forms of aortitis are many in number and associa-
tions. A justifiable distinction in regard to its evolution
is the following: Acute, subacute and chronic. There may be
a latent process for each of the forms.
Hubert (15) studied 300 cases of aortic syphilis, of which 60 appeared 23 years after the infection. The affections which may develop in the secondary stage are varied. From a table compiled in 1927 by D'Almeida (16), it appears that the period of latency is all the way from 5 to 29 years.

However, there is not a long latent period in all cases of syphilitic aortitis. Reid (17) records a case in which a young man infected in June had definite evidence of involvement by August of the same year, and enough signs for positive diagnosis in September. Brooks (18) observed a case in which death resulted from perforation of the aorta just above the valve before the secondary eruption was fully developed.

Shields and Jones (19) also report a case of syphilitic aortitis with aneurysm of the thoracic aorta developing within nine months of the primary lesion, proved at autopsy.
MORBID ANATOMY

Initial lesion—Syphilis shows a distinct disposition to attack the aorta. The inflammatory process generally originates just above the root of the aorta, whence it extends upward through the ascending and downward toward the aortic ring. (1)

The main and most important lesion in nearly all cases of syphilis of the aorta is a supravalvular involvement. Most of the other changes and phases of cardio-vascular syphilis depend upon this lesion. (20)

According to a number of pathologists, Martland (20), McMeans (21), Longcope (22), Maher (23), Scott (24), Warthin (7), Giauni (25), Waite (26), Cecconi (27), and several others, the infecting agent reaches the wall by way of the vasa vasorum in the adventitia and sets up an inflammatory reaction. The earliest lesions are microscopic and occur in the adventitia around the vasa vasorum in the form of a collection of lymphocytes and histiocytes lying probably in the perivascular lymph spaces. Larkin and Leoy (28), go so far as to say that this perivascular cellular infiltration has syphilis as its etiological factor, and further, that it is diagnostic of luetic aortitis. The authors base their opinion on the following facts. Eighteen of forty-two aortae examined presented this picture and seventeen of these gave a positive Wassermann during life. Stained sections may show spirochaetes in these areas, but usually they are found with difficulty.
There follows a secondary invasion of the media with consequent breaking up of elastica and weakening of the vessel wall. The cells of the intima are proliferated and heaped up to form projections from the inner surface of the vessel. In the more extensive lesions the perivascular infiltrations of the adventitia is very pronounced. The media presents very characteristic areas of coagulation necrosis surrounded and partly infiltrated with plasma cells and small round cells. Giant cells may also be encountered.

The lesions develop to a stage at which they can be recognized with the naked eye. It usually begins in the aortic wall just distal to the attachments of the aortic cusps. The earliest patch is often triangular and is situated just above the commissures connected with the aortic cusps forming the sinus of the Valsalva, where the left coronary has its origin. The base of the triangle is usually pointed distally. There is a grey or slightly yellowish elevation with steep sharp edges, smooth on top, or marked by shallow furrows separating trivial secondary elevations.

The process spreads in a horizontal manner, around the root of the aorta distally as far as the mouths of the great vessels springing from the aortic arch, rarely beyond. The orifices of the great vessels of the arch may often be narrowed to a marked degree, and it may diffusely involve the whole aortic arch. Separate processes may develop in the thoracic or abdominal aorta.

At a later stage of the process, the aorta presents a
scarred, distorted wall almost unrecognizable as such, with perhaps complete destruction of all three coats of the artery. Small foci of necrosis surrounded by connective tissue, partly vascularized and infiltrated with varying numbers of plasma cells take the place of the media, and extend in both directions.

Following the initial lesion in the aorta we have involvement of the aortic valves and ostia of the coronary arteries, and aortic aneurysm, Quinn and Meyer (29) report a case which showed at autopsy three aneurysms of the aorta.

**Involvement of the aortic valves**—Extension of the syphilitic gummatous process through the media into the subintimal spaces producing the triangular patches continues in the direction of the attachment of the aortic cusps, usually following the lines of least resistance, which is along side of and between the fan-shaped subintimal spaces, the remnants of those fibers forming originally the aortic cusps. The result is a pushing apart of the cusps at their attachments. Sometimes the attachments of the cusps may be separated by at least one centimeter. Often just a furrow exists between the attachments of the adjacent cusps which are thickened and infiltrated. This widening of the commissures is the earliest sign of aortic regurgitation, and is practically the main factor in its production.

A continuation of the process down the attachments of the cusps takes place and often occurs across their free edges. Fibroblasts lay down collagenous fibers. A hyalinized ball-like edge results. While, of course, considerable round-
cell infiltration of a specific nature is seen in the free edges of the cusps near their attachment, the portions between the free edges are often remarkably clear of such specific changes. The distorted, thickened, rolled, and retracted aortic cusps with the widened commissures produce irreparable damage to the valve.

From trauma of the regurgitant blood stream, subendocardial fibrosis over the interventricular septum below the aortic valve, with production of false bands and cusps often take place.

Hypertrophy of the muscle of the left ventricle due to the regurgitation followed by dilatation is the end state of the aortic valve involvement.

Formation of aneurysm—There are two factors present in the formation of an aneurysm of the aorta: degeneration or destruction of the mesial coat, with consequent weakening of the vessel wall; and strain. (1) As it has been very plainly pointed out we have the first factor present, and due to the physiological pressure within the artery we have added the trauma.

Stokes (2) quotes the following: “Study of the relations between the blood pressures of patients with aneurysm and of those with aortitis alone in our cross-section seemed to throw some light on the development of aneurysm. It is certainly strongly suggested that the production of aneurysmal dilatation in the diseased aorta is not the direct result of the sharp,
repeated pounding of a powerful ventricle producing a high but transient systolic pressure against a weakened vessel wall. On the other hand, the tendency of systolic blood-pressure in both aortitis and aneurysm is to be low, especially low in aneurysm. On the other hand, diastolic pressure, presumably maintained in part by the integrity of the aortic valve, tends to be low in aortitis without aneurysm, and high in aneurysm. It appears, therefore, that the integrity of the valve, by making possible the maintenance of constant, even though lower pressure on the aortic wall, is the more probable factor in deciding whether a diseased aorta will tend to develop aneurysmal dilatation. If aortic valvulitis is the principal feature of the picture, the patient tends to escape aneurysm by the development of regurgitation. He reaps little benefit thereby, however, for he is only precipitated then onto the less kindly lap of myocardial failure from atresia of the coronary orifices and coronary sclerosis."

Involvement of the orifices of the coronary arteries—
As the primary lesion of syphilitic aortitis usually occurs in the portion of the aorta above a base line drawn through the upper limits of the aortic cusps, coronary arteries which are congenitally situated above this line are especially liable to scarring of their ostia, especially by the replacement fibrosis which takes place, while those normally arising in the sinuses often escape encroachment. (30) (31)

It is unusual for the syphilitic coronary disease to be
seen in the artery away from the ostia, and is practically limited to a narrowing, or atresia, of their orifices by the lesion in the aortic wall.

The histo-pathological picture of the very first portion of the coronary arteries is very much like that of the aortic wall. The round-cell infiltration is found in the main arteries. At the ostia this may be very pronounced. The invasion is characteristically located in the adventitial coat, but may invade the media or the subintima. In addition to the acute process, connective tissue replacement may be seen. (23)
SYMPOMS

Syphilitic aortitis often exists in the absence of symptoms. It has been said that the disease is often symptomless until complications such as aortic insufficiency or aneurysm are present. In the out-patient or clinical group at the Massachusetts General Hospital, as reported by Reid (32), substernal pain or shortness of breath was present in all but in about one-quarter of the necropsy cases there were no symptoms of the disease. The latter statement is, of course, the more important, as it is not surprising that the diagnosis in the living patient is usually made in patients exhibiting symptoms which draw attention to the disease.

Pain, shortness of breath, cough, hoarseness and weakness are the more prominent symptoms, as reported by Reid (32). In many cases the symptomatology is simply that of congestive failure of the heart, or broken compensation, if the older term is preferred. (11) In the 107 patients that came to autopsy at the Cleveland City Hospital during the past 10 years the first symptom complained of by the vast majority of patients were those of beginning heart failure—dyspnea on exertion, palpitation and edema of the lower extremities. Precordial and substernal pain or anginal attacks were seldom noted except in those cases of marked narrowing of the coronary arteries. Even in the presence of marked constriction of the coronary mouths, chest pain was not always present. For example, in one instance of complete occlusion of both coron-
aries, pain was not present during the three weeks that the patient was under observation before death.

**Pain**—Any injured organ becomes painful. This is a general law and the aorta does not escape from it. (12) If there are symptoms, pain is prominent. (11) It varies from an ill-defined pain in the chest, or epigastrium, or a sensation of tightness or burning about the upper sternum to the utter torture of severe angina pectoris. It may come in attacks, be associated with exertion or be present almost continuously. In location and radiation the pain sometimes resembles that of angina pectoris.

Pain was present in 28 per cent of the necropsy cases as reported by Reid (32), and conformed to the syndrome of angina pectoris in but 4 per cent. Levine (33) attributed to syphilis but 7 per cent of a series of cases of angina pectoris.

It is known that syphilis of the aorta may involve the orifices of the coronary arteries, and it is sometimes stated that this localization of the aortic lesions may account for the occurrence of anginal pain. Reid (12), however, in his 78 necropsies, found the orifices of the coronaries were narrowed in 10 cases. The right orifice was completely occluded in three instances, the left in one, and both in one. Pain, however, was recorded in but two of the patients, in each of whom the necropsy disclosed a narrowing but not complete occlusion of the orifice of the right coronary vessel. The pain did not conform to the syndrome of angina pectoris. The
relation of the pain to the condition of the coronary arteries, aside from their orifices, was analyzed in the final group of 24 necropsies. In 14 cases the coronaries were normal and in 6 of these pain was present; in one it was described as sensation of pressure; in one, that of angina pectoris, and in the other 4 it was a definite pain which did not conform to the syndrome of angina pectoris. In another 6 cases there was slight or marked coronary lesions, with pain present. It is evident that the condition of the coronary arteries was not the determining factor in the presence of the pain. Further analysis disclosed that the symptom of pain was not related to the degree of syphilitic change in the aorta. In the 78 necropsies there were 18 aneurysms, which gives a percentage of 23. Eleven or over half were without pain. Fourteen of the aneurysms involved the ascending or transverse part of the arch of the aorta. The remaining three were below the diaphragm, one each located in the abdominal aorta, the celiac axis, and the superior mesenteric artery.

**Dyspnea**—This is a common symptom but often is not present until a few weeks or months before death. It appears to be a symptom of congestive failure of the heart and is often associated with edema of the extremities. It was noted in all but 3 of the final group of the 24 necropsies by Reid (32). In 2 of these it was characterized as nocturnal dyspnea. The duration of shortness of breath in these 21 patients before entrance to the hospital was: three months or less in 4; four to eight
months in 6; nine months to two years in 4; five years in 2; and unknown in 5 patients. This discloses that in 10 cases, or nearly half of those affected by shortness of breath, this complaint had been present not more than eight months before their admission to the wards, and death usually followed within one to two months more.

Peete (34) describes a type of paroxysmal dyspnea that should receive special mention for it is often mistaken for allergic asthma, cardiac asthma, and sometimes, bronchial asthma. These attacks most frequently come on at night and may awaken the patient from a sound sleep and terrify those about him. He is suddenly seized with a great difficulty in breathing, becomes cyanotic, there is a heaving of the chest, the patient is cold and clammy, the pulse is very small in volume and very rapid. One usually hears asthmatic and sibilant rales throughout the chest. These attacks are often unaccompanied by pain and are benefited by nitroglycerin and morphine. Adrenalin or the ephedrine compounds usually do not give much relief. Patients may die in these attacks or may completely recover, except for exhaustion, almost as quickly as the attack came on.

Cough--Cough is quite typical when present, but is only seen in a few cases. When present it is a dry, brassy, non-productive hack.
In a series of cases reported by Stokes (2), 106 of which had uncomplicated syphilitic aortitis and 61 of which had aneurysm complicating, the following symptoms were presented:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Uncomplicated</th>
<th>Complicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>44%</td>
<td>33%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>30%</td>
<td>60%</td>
</tr>
<tr>
<td>Palpitation</td>
<td>28%</td>
<td>20%</td>
</tr>
<tr>
<td>Indigestion</td>
<td>20%</td>
<td>17%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>17%</td>
<td>14%</td>
</tr>
<tr>
<td>Cough</td>
<td>15%</td>
<td>23%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td>Edema</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Weakness</td>
<td>8%</td>
<td>10%</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>1%</td>
<td>24%</td>
</tr>
</tbody>
</table>
PHYSICAL SIGNS

The evidence of syphilitic aortitis detected by physical examination varies according to the nature and extent of the lesions present. In many cases, before the condition has become advanced, physical examination discloses no significant abnormal signs. (33)

Nearly all authorities agree that probably the first and most important physical sign is an accentuated second aortic sound, which is ringing and bell-like in quality, or tympanic, as Allbut (35) describes it. Carrera (36) insists a finding in a man between thirty and forty-five years of age, without evidence of arteriosclerosis, hypertension, or rheumatic heart disease, should force one to exclude syphilis by using every available means. He goes on to say that the diagnosis is very difficult, and the disease is rarely recognized in its early stages and if we depend upon a serological diagnosis, some 30 per cent of the cases will go undiagnosed.

Extension of the lesion to the aortic cusps causes a change in the systolic murmur. The murmur is thereby transmitted down the left border of the sternum, and as the cusps become involved, it becomes rough and harsh and transmitted into the vessels of the neck.

According to Reid (32) the diastolic murmur of insufficiency due to syphilitic aortitis begins with the second sound and continues some time after it. In this respect it differs from the only other common murmur occurring in the diastole,
i. e., that of mitral stenosis; the latter never begins until just after the second sound.

Widening of the aorta to percussion, fluoroscopic and roentgenographic examination may or may not be present. A slight hypertension is the rule in well-developed, pure forms of aortic syphilis, the systolic pressure being 135 to 155. At this period there is usually no hypertrophy of the left ventricle detectable.

Stokes (2) gives the following as important consecutive signs of aortitis followed by aortic valvulitis:

1. Accentuated or sharpened aortic second sound. (Tambour second sound).

2. Systolic murmur: maximal at aortic area, transmitted along left margin of sternum.

3. Slight hypertension: systolic blood pressure 135 to 150, with equivalent rise in diastolic pressure.

4. Slight left ventricular hypertrophy: left border out by percussion. Apex to left and down, increased apex impulse and x-ray shadow enlarged.

5. Slight signs of aortic dilatation: broadening of arch. Dulness to right of sternum between second and fourth costal cartilages.

6. Fluoroscopic pulsations of the aorta.

7. Increased intensity and roughening of systolic murmur at aortic area.

8. Diastolic murmur appearing at aortic second, usually blowing. Beginning regurgitation, and transmitted along left
border of heart.

9. Increasing evidence of left ventricular hypertrophy; increasing cardiac dulness and a heaving systolic impulse over precordium.

10. Flint murmur, presystolic at the apex.
11. To and fro murmurs all over precordium.
12. Capillary pulse of lips and fingers.
13. Waterhammer pulse.
15. Difficulty in obtaining diastolic pressure, low diastolic, high pulse pressure.
16. Symptoms of increasing coronary sclerosis, frequent attacks of angina pectoris.
17. Electrocardiographic signs of myocardial disease.
18. Slow death from cardiac dilatation.

Stokes (2) gives the following important consecutive signs in aortitis followed by aneurysm:

1. Accentuated aortic second sound.
2. Precordial dulness at various points about the base of the heart.
3. Dulness posteriorly, but less sharply defined.
4. Absent or impaired breath sound over the dull area.
5. Fluoroscopic pulsation: plate shows dilatation or aneurysmal shadow.
6. Systolic bruit over the dull area.
7. Systolic impulse, upper thorax, palpable or faintly visible.
8. Paralysis of one or both vocal cords, with or without hoarseness.


10. Differences in blood pressures of the two arms.

11. Signs of mediastinitis, fulness of neck veins, flushing, lividity on stooping or lying down, retarded venous return, etc.

12. Inequality of pupils.

13. Conspicuous x-ray signs of tumor.


15. Tracheal tug.

16. Visible tumor, heaving or expansion pulsation.

17. Signs of cardiac failure.

18. Sudden death if rupture.
An editorial (14) in a recent number of The Journal gives the impression that the diagnosis of aortitis is something very recent, and in practice rests on the development of subjective symptoms and the use of the roentgen ray and the Wassermann reaction. Hoover (37) points out that the diagnostic signs of aortitis were clearly described long before the roentgen ray or the Wassermann reaction of the spirochete was known to the medical profession. If inaccurate percussion and palpation and auscultation are employed, then of course the roentgen ray affords the only dependable diagnostic method; but in the hands of an examiner who in a routine manner estimates the size and elasticity of the ascending aorta, just as the character of the arterial pulse is studied, the pre-symptomatic period of aortitis is diagnosed with fully as much accuracy as can be procured by aid of the Roentgen ray and Wassermann reaction.

Elastic, fibrous and muscular tissues form the wall of the aorta. The smooth muscle fiber is, however, the constituent which enables the aortic wall to withstand intrac- aortic pressure. When the muscle fiber deteriorates, the aortic tube is elongated and dilated. It is elongation of the ascending arch and not dilatation which renders the aorta so readily accessible after slight pathologic changes.

The visibility of the aorta to the right of the sternum depends not only on elongation and dilatation of the aorta,
but on the size of the thoracic cage and volume of the lung. As a rule, by the time the aortic pulsation is visible to the right of the sternum, one is dealing with a severe aortic disease, which requires no particular skill in diagnosis and offers little prospect for improvement with the employment of therapy.

Percussion for aortic dulness to the right of the sternum should be done by the direct palpating method. As a matter of routine, the examiner should percuss the intercostal spaces to the right and left of the sternum, beginning at the first intercostal space on the right and continuing downward to the fifth, and percussing downward from the first intercostal space on the left until precordial resistance is encountered, which is usually on the third rib. If the aortic arch projects beyond the sternum at the second interspace, then the examiner will perceive increased resistance and diminished resonance in the second interspace to the right as compared with the second interspace to the left of the sternum; and comparisons should also be made between the resistance to the right of the sternum.

An increase in pulsatory expansion of the aorta during systole may be detected by palpating bimanually. The examiner places his right hand over the second interspace at the right of the sternum, and his left in the interscapular space at the left of the vertebrae. This method of palpation does not employ the tactile sense or vibratory sense of the palpating hand, but the muscular sense of the thoracoscapular muscles.
Further evidence of enlargement of the ascending arch of the aorta is accentuation of the aortic second sound and the palpable diastolic impact perceptible at the second interspace to the right of the sternum. This accentuation means just one thing—increased accessibility of the first portion of the arch of the aorta.

A palpable diastolic impact over the second interspace to the right of the sternum is perceptible in the adult only when there is increased accessibility of the arch. The diastolic impact is due to the arrest of a column of blood within the aortic tube arrested by the closure of the aortic valve. This diastolic impact is best perceived by the part of the hand where vibratory sense is most acute, and that is over the end of the metacarpal bones. If the examiner will place himself at the right side of the patient and palpate the second interspace to the right of the sternum with the ends of the metacarpals, asking the patient to expire so as to render the aorta as accessible as possible, it will be found that only very slight dilatation of the arch of the aorta is required to made a diastolic impact clearly perceptible to the palpating hand.

The early diagnosis of syphilitic aortitis, before the development of aortic regurgitation or aneurysm is a question of fundamental importance in the treatment. (38) With this in mind it occurred to Moore, Danglade and Reisinger that information of value as to the possibility of accurate clinical diagnosis of uncomplicated aortitis might be obtained by an approach
from two angles: (1) a comparison of the clinical with necropsy observations in those patients in whom syphilitic aortitis was discovered at necropsy, whether or not recognized in life, and (2) a survey of the clinical outcome, for evidence of progression to valvular incompetency or aneurysm or, when possible, to the autopsy table, in a series of patients in whom the diagnosis was made during life. They took the first approach. The records of the department of pathology of the Johns Hopkins Hospital from 1910 to 1930 were reviewed. All cases with aortic regurgitation or aortic aneurysm were excluded from consideration, as were likewise certain instances in which the presence of extensive aortic arteriosclerosis rendered doubtful the pathologic diagnosis. After these exclusions there remained 105 cases with definite uncomplicated syphilitic aortitis, in all of which the pathologic diagnosis was made on the basis of grossly visible lesions of syphilis in the aorta, confirmed by microscopic examination. The clinical records of these patients were then studied, in order to determine the frequency with which the diagnosis had been made. The results of this survey are summarized in the following table:

<table>
<thead>
<tr>
<th>Cases</th>
<th>Med. Ser. 63</th>
<th>Surg. Ser. 43</th>
<th>Total 105</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diag.</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>15.2</td>
</tr>
<tr>
<td>Suspected</td>
<td>12</td>
<td>1</td>
<td>13</td>
<td>33.3</td>
</tr>
<tr>
<td>Phys. signs</td>
<td>12</td>
<td>5</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>9</td>
<td>3</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>
In all cases correctly diagnosed or suspected, either the usual symptoms of substernal pain, dyspnea on exertion or paroxysmal nocturnal dyspnea or the classical physical signs of widened retromamubrial dulness, pulsation in the substernal notch, an aortic systolic murmur or an altered tympanitic bell-like quality of the aortic second sound, or both symptoms and signs were present.

From a clinical standpoint, a most difficult differential diagnostic decision is between syphilitic aortitis and hypertension. Both may produce substernal discomfort, dyspnea on exertion, widening of the aorta and a change in the intensity of the aortic second sound. Paroxysmal nocturnal dyspnea is, however, a frequent feature of syphilitic aortitis, especially with aortic regurgitation, but is uncommon in hypertension. Although there is an accentuated second aortic sound in both conditions, Carter and Barker (39), a tympanitic bell-like alteration of its quality is peculiar to and characteristic of syphilitic aortitis. In this group of patients 75 showed a normal blood pressure, 23 showed a systolic pressure between 150 and 200, and was over 300 in 7. The diagnosis of syphilitic aortitis was correctly made more often in the group with hypertension than without. This is probably due to the fact that the hypertension focused attention on the cardiovascular apparatus.

The association of other clinical evidence of syphilis with aortitis was also studied. A Wassermann test of the blood was done in 31 of the 105 patients, and was found to be posi-
tive in 61 or 75.3% and negative in 30 or 24.7%. Of the pa-
tients with negative Wassermann reactions of the blood, two 
showed some other clinical evidence of syphilis, and three 
more gave a definite history of infection.

On only 29 patients of the entire series was there a 
roentgenographic examination carried out. In 25 of these there 
was definite roentgen evidence of dilatation of the aorta. 
There have been numerous studies made on the roentgenologic 
diagnosis of syphilitic aortitis, one of the most recent of 
which Steel (47) concluded that the lesion can be suspected 
when: (1) a diffuse dilatation is present and is associated 
with a normal heart shadow, or (2) when a dense, high aorta 
is present in a young person without previous hypertension.

The following table summarizes the signs and symptoms 
presented by the 115 patients.

<table>
<thead>
<tr>
<th>Cases with</th>
<th>No. showing signs and symptoms</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of circulatory embarrassment</td>
<td>38</td>
<td>44</td>
</tr>
<tr>
<td>Widened retrosternal dulness</td>
<td>39</td>
<td>44</td>
</tr>
<tr>
<td>Accentuated tympanic aortic sound</td>
<td>39</td>
<td>23</td>
</tr>
<tr>
<td>Roentgen evidence of widened aorta</td>
<td>29</td>
<td>25</td>
</tr>
<tr>
<td>Paroxysmal dyspnea</td>
<td>90</td>
<td>7</td>
</tr>
<tr>
<td>Pain</td>
<td>89</td>
<td>16</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>92</td>
<td>24</td>
</tr>
</tbody>
</table>
On this basis, one can tabulate, in order of relative importance, the following diagnostic criteria of uncomplicated syphilitic aortitis:

1. Teleoroentgenographic and fluoroscopic evidence of aortic dilatation.
2. Increased retromanubrial dullness.
3. A history of circulatory embarrassment.
5. Progressive cardiac failure.
7. Paroxysmal dyspnea.

It is believed by the authors that in a patient with known late syphilis, whether or not the Wassermann is positive, the presence of any three of these criteria is strong evidence of the diagnosis of syphilitic aortitis, while the presence of any two of them renders the diagnosis probable. In a patient with a negative Wassermann reaction of the blood, with no history or other physical evidence of syphilis and without obvious disease of the mitral valve, the presence of any four of these symptoms or signs is also clinical justification for the diagnosis.

Carter and Baker (39) express the belief that the diagnosis of syphilitic aortitis is permissible if any five of the following criteria are clinically demonstrable:

1. The history of a relatively abrupt and unexpected onset of symptoms of circulatory embarrassment.
2. The presence of a positive Wassermann reaction.

3. A demonstrable increase in the retromanubrial dulness in the second interspace, and a change in the tonal quality of the aortic second sound. The fluoroscopic evidence of aortic dilatation.

4. An absence of the signs of mitral disease, connoting rheumatic infection.

5. The history of paroxysmal dyspnea, often nocturnal.

6. The history of pain, particularly paroxysmal pain.

7. Progressive cardiac failure.

Danzer points out that the confusion which has existed in the diagnosis is due to two factors: (1) frequent association of the disease with aortic atherosclerosis and (2) the misinterpretation of the Wassermann reaction. In his mind the diagnostic triad of syphilitic aortitis consists of: (1) angina pectoris, (2) negative carotid sinus reflex, (3) a rapid blood sedimentation reaction. (14)
Roentgenology—This is probably the chief laboratory aid in the diagnosis of syphilitic aortitis. The roentgen ray is of very distinct value with pulsation to the right of the sternum and visibility of the aorta in a patient under 50 years of age constitute criteria for the conclusion of aortitis upon fluoroscopy. Of course, an etiologic deduction from such data is presumptive but apparently justified, if the history and the physical examination admit of no other cause. The close study of the retrocardiac space for the aortic changes and encroachment of the heart and aorta especially upon the esophagus may be enhanced by having the patient swallow barium as the observation is made. For permanent records of these changes orthodiagrams and teleroentgenograms are invaluable. (41)

Steel (47), in a study of forty cases of luetic aortitis, observed roentgenologically and proved by autopsy, in no case of which aneurysm was present, came to the conclusion that there are cases of syphilitic aortitis which present definite roentgenological changes and which are indistinguishable from the other common lesions of the aorta, that the lesions can be suspected when (1) a diffuse dilatation is present and is associated with the normal sized heart silhouette, (2) a dense aortic root is present in a young individual without a previous hypertension. It can be safely diagnosed when localized dilatation associated with localized increased pulsation is demonstrable.
Stokes (2) thinks that diagnostic interpretation depends on evidence of altered pulsation and dilatation just above the valve, just above the shadow of the right auricle. Lamb (48) is of the same opinion.

In syphilitic aortitis the aorta is tortuous, the upper part of the shadow appearing more marked to the left. (49)

Wassermann Reaction—In evaluating the worth of the Wassermann reaction one must take into consideration several factors. It is highly important to consider the amount of treatment the patient has previously had and also the technique under which it is carried out. A diagnosis of syphilitic aortitis should not be made therefore on the basis of a single positive blood Wassermann result unless it is supported by other convincing evidence of the disease. Likewise a negative Wassermann result does not rule out syphilis.

Stokes (2) and Lamb (48) place the margin of error of the negative blood Wassermann reaction in syphilitic aortitis as high as 40 per cent.

Stokes (2) in suspected cases with a negative Wassermann advises the provocative procedure of a small dose of neoarsphenamin in an effort to get a positive Wassermann. In twenty-seven such cases he got nine positive reactions and an additional nine simply from a number of repetitions of the test. He thinks that even though it may be inadvisable to give a provocative injection of arsphenamin to patients with suspected aneurysm, for fear of a Herxheimer flare-up of the involved
tissues, it is well worth while to make at least a series of five to seven blood tests.

Electrocardiology—Ingrahm and Maynard (50) in an electrocardiographic study of 37 cases of early luetic aortitis, none of which had a systolic blood pressure of over 140 mm. or had history of any other disease which might affect the heart, found that 70 per cent gave electrocardiograms that fell within normal limits, and 30 per cent showed a left axis deviation, including one with premature ventricular beats as well. Compared with the findings in the series of cases of early syphilis studied by Turner and White (51), the incidence of left axis deviation is much higher. They found only one instance in 50 cases or 2 per cent. Cohn (52) in an investigation of size of the heart in soldiers in 1920 found that of 203 normal soldiers, six showed signs of left ventricular preponderance, an incidence of 3.3 per cent. Proger and Davis (53) have recently studied axis deviation in normal hearts and found 33 per cent to show left axis deviation.

Therefore, when one considers the frequency with which left axis deviation may be found in normal hearts, one must conclude that early syphilitic aortitis causes no changes in electrocardiographic tracings.
TREATMENT

Prophylaxis—It is much easier to prevent the development of cardio-vascular syphilis than it is to cure it after it has appeared. There has been some debate over the question as to whether the adoption of modern methods for the treatment of early syphilis has increased the incidence of cardiovascular syphilis. Moore (40) believes this to be quite untrue. Approximately 90 per cent of all of his own patients with cardiovascular syphilis had never been treated prior to the development of the aortic lesion and he cannot recall having seen a patient who, having received as many as 24 injections of arsphenamine for early syphilis, subsequently developed evidence of cardiovascular damage. From his own clinic he has shown that cardiovascular syphilis may be expected to develop in inverse ratio to the amount of treatment given for early syphilis. In a large series of his patients admitted with primary and secondary syphilis and followed for a considerable number of years, none who had received as much as three courses of arsphenamine plus interim heavy metal, subsequently developed clinically recognizable cardiovascular syphilis; whereas approximately 9 per cent of patients who received less than this amount of treatment were observed to develop aortic lesions.

In a more elaborate study of the results of treatment in 2889 patients with early syphilis carried out by Moore, Danglade and Reisinger (40), much the same observations were noted. All the patients of that group had been treated with arsphenamin, though in some instances with only small amounts of the drug.
Only 30 of them have been observed to develop cardiovascular syphilis. While it is undoubtedly true that with the passage of further time many of the patients of both groups will develop clinical evidence of cardiovascular damage, it nevertheless seems fairly definite that adequate treatment for early syphilis markedly diminishes, if it does not entirely prevent, the appearance of this late lesion.

Equally satisfactory results in the prevention of cardiovascular syphilis may be obtained by the treatment of latent syphilis at any interval after infection. Moore, Banglade and Reisinger (40) have studied the outcome of treatment in 1936 patients with latent syphilis, in none of whom could the diagnosis of cardiovascular syphilis be made before treatment. The condition was later observed to develop in only 31 patients following treatment. Since, reasoning by analogy from pathologic evidence by Bruøsgaard (5), Turner (6), Warthin (7), and Langer (8), subclinical lesions must have been present in the aortae of many of these patients, this result can be interpreted to mean that treatment has prevented its further progress and the development of symptoms or physical signs. It is fair to assume, further, that if this result can be accomplished in late syphilis without apparent cardiovascular involvement. The importance of these points lies in the fact that every patient with outspoken cardiovascular involvement passes through a preliminary stage of clinical latency during which his infection is nevertheless recognizable, and if recognized, may be treated with reasonable assurance that cardio-
vascular syphilis will not develop.

The ideal method of treatment of cardiovascular syphilis, therefore, lies in the hands of the physician who sees the syphilitic patient before the development of clinical evidence of cardiovascular involvement and who applies intensive modern therapy at a time when, although the aortic wall may already have been invaded, tissue involvement in this area is at a minimum.

The aims of treatment in cardiovascular syphilis—The aim of treatment in cardiovascular syphilis is not the radical cure of the syphilitic infection, nor even the restitution of the damaged structures to anatomic integrity. These aims are obviously impossible. One cannot replace dead elastic tissue in the aortic wall, nor make distorted valve leaflets. The best that one can hope for is to bring about healing of the active inflammatory process, and its replacement by connective tissue, to prevent the development of fresh inflammatory lesions in the involved structures; and to compensate so far as possible for the mechanical damage done to the cardiovascular apparatus. From the standpoint of the patient, this is tantamount to saying that the two primary aims of treatment are the relief of distressing symptoms and the prolongation of life past the average duration to be expected had no treatment been given. These aims can often be accomplished by a combination of general medical care and of antisyphilitic treatment. It is no longer justifiable to withhold specific treatment from patients with
cardiovascular syphilis, even when the situation seems hopeless. (40)

The principles of treatment of cardiovascular syphilis—The indications for the management of syphilitic aortitis are modified by the complications which may be present. The state of compensation constitutes the most important criterion for the control of treatment in these patients. If well compensated, the etiologic background is the natural objective in treatment. Since aortitis is a late manifestation of syphilis and usually occurs in the neglected patient, unusual caution is observed in initiating antisyphilitic treatment. Particular care is enjoined in patients where aneurysmal dilatation, serious arrhythmia, anginal attacks and recent decompensation have occurred. (4)

Moore (40) says the essentials on which the formulation of a treatment scheme for patients with cardiovascular syphilis are based may be summarized as follows:—first, a clinical evaluation of the location and extent of the anatomic damage; second, rest; third, restriction of physical activity; fourth, digitalis when necessary for cardiac failure; fifth, specific treatment. In planning specific treatment, five cardinal principles must be kept in mind, all of which are based on the fundamental fact that any scheme of treatment must be one calculated not to do the patient any harm. The first essential is the absolute avoidance of a grave immediate treatment reaction particularly associated with cardiovascular syphilis. It has long been known, as pointed out by Longcope (32), Middleton (41),
Moore, Banglade and Reisinger (42), Reid (43), Wile (44) and O'Leary (45), that the arsphenamines, and especially old arsphenamine itself, when given to a patient with cardiovascular syphilis, may produce during or immediately after treatment, a syncopal reaction with ashy pallor and sudden circulatory failure, the patient dying within a few minutes. This is believed by most authorities to be due to ventricular fibrillation.

As pointed out, this phenomenon is more common after arsphenamine than after any other of the allied products, and the disastrous outcome of immediate death during treatment is in large part responsible for the disrepute into which all treatment efforts in cardiovascular syphilis fell for a period of several years. Moore (40) says the reaction may be in part dependent on the bulk of fluid injected, and in part on the size of the dose administered. It may be largely avoided by the use of the less toxic arsphenamine products, neoarsphenamine and silver arsphenamine or bismarson; all of which are soluble in small amounts of water, and all of which, for caution's sake, should be given in very small doses.

The second principle of treatment is that one must attempt to avoid not only this disastrous reaction of ventricular fibrillation, but also all treatment reactions. It is undesirable to place any added strain on an already over-burdened myocardium; and even so mild a post-treatment upset as a few hours of nausea and vomiting should, if possible, be entirely eliminated.
The third danger to be guarded against is the production of therapeutic shock, the so-called Jarisch-Herxheimer reaction. This flare-up or intensification of a syphilitic lesion a few hours after the first injection of an arsphenamine product becomes of paramount importance when the lesion may be located at the mouth of a coronary artery, or in the wall of an aneurysm. Here the associated sudden local edema may result in coronary occlusion or in aneurysmal rupture, in either case with immediately fatal outcome.

The therapeutic paradox is a fourth element of danger. Attention was drawn to this phenomenon some years ago by Wile (46), who pointed out that in certain patients with cardiovascular syphilis and with previously adequate cardiac compensation, treatment which was followed by the sudden appearance of congestive heart failure. This is probably due to the too rapid healing of syphilitic inflammatory tissue which is replaced by contractile scar, with the result that the patient is pathologically better, but functionally worse, than he was before treatment began.

The last risk which must be considered is that of giving too intensive treatment of any type to a patient who has previously had, or is in the midst of an attack of congestive heart failure. When decompensation is actually present, the first essential is to deal with this mechanical defect by rest, restriction of fluid, and digitalis before attempting more than the absolute minimum of specific treatment.

The fifth principle of treatment is that it should be pro-
longed to an absolute minimum of two years; and that so far as possible, it should be continuous.

Middleton (40) says much of the distrust which arose from the deleterious results on the administration of the arsenicals in the early days of the arsphenamines, could have been averted with the proper preparation of the patients for their use.

Evolution of a method of treatment.—The past twenty years have seen three almost complete revolutions in the attitude of physicians toward the treatment of cardiovascular syphilis. Before the introduction of arsphenamine, it was generally agreed that some benefit could be obtained from the judicious use of mercury alone, mercury with iodides or the iodides alone. Symptomatic improvement occurred often with combination of these treatments and many able clinicians were convinced that, at least in individual cases, life was prolonged.

After the introduction of arsphenamine, and in spite of the original cautions against its use in patients with damaged hearts or aortae, it was almost as universally applied to the treatment of those with late syphilis of all types. The indiscriminate use of a powerful drug was disastrous. It was found that when the drug was given in average therapeutic dosage to ambulant patients, sudden death might occur during the injection. Such reactions were characterized by fainting, ashy grey-green pallor and profuse sweating; the pulse became rapid; the patient gave a few gasps and died. Four such deaths were reported by Moore (54).
Electrocardiographic studies by Reid (55) and by Wilson, Wile, Wishart and Herrmann (56), have an important bearing on the mechanism of this type of reaction. Each of these observers gave arsphenamine in average therapeutic doses, 0.3 to 0.4 gram, to patients with advanced lesions, obtaining electrocardiographic records before and shortly after the injection. Reid observed changes that he interpreted as a prolongation of conduction time and a shortened refractory period of the muscle. He concluded that in a heart which was damaged by syphilis, and which is in a bad metabolic state, these two changes predispose to the occurrence of ectopic ventricular tachycardia or to ventricular fibrillation, the latter of which is suddenly fatal. Wilson and his co-workers likewise noted abnormal rhythm and di-phasic complexes suggesting incomplete bundle branch block, and concluded that the administration of arsphenamine may sometimes be followed by myocardial changes of an undesirable kind.

A second type of disastrous outcome was sudden death within from twenty-four to forty-eight hours after the injection of the drug, due to therapeutic shock. Usually this was due to sudden coronary occlusion or to rupture of an aneurysm. Still a third untoward effect was the sudden appearance of congestive heart failure in patients where cardiac compensation had been adequate before treatment. This is emphasized by Wile (46) as "the therapeutic paradox". He attributed the phenomenon to the rapid healing of syphilitic inflammatory tissue in the aortic wall, valve cusps or myocardium, which is then replaced by contracting scar tissue. This brings about anatomic healing by
leaving the patient functionally worse than before treatment. The early current favorable opinion as to the beneficial effect of treatment with arsphenamine, summarized by Longcope (22), was more than counterbalanced by the ill effects just described.

For a time the pendulum swung back, and it was generally thought that, since the treating of patients with cardiovascular syphilis was far greater than the improvement to be expected, it was better to give no antisyphilitic treatment, or, if any, mercury and potassium iodide only, as in the prearsphenamine era.

The World War was partly responsible for the inauguration of the plan of treatment which is now employed, and which, subject to various modifications, has been independently evolved by many observers, Goldberg (57), Herrmann and Jamison (58), Hines and Carr (59), Horder (60), Schottmuller (61), Stokes (2), and others. Neoarsphenamine became popular during the war years because of its ease of administration. It was found to be less prone to produce minor reactions in average therapeutic doses than arsphenamine and in small doses to be practically free from any after-effects. This led to its trial cautiously in patients with cardio-vascular syphilis, and it was generally found that with proper precautions such patients could tolerate small doses, 0.1 to 0.2 grams, without dangers of sudden death from ventricular fibrillation or from therapeutic shock. The measures taken to avoid the latter disaster, namely, several months of preliminary treatment with mercury and the iodides in order to produce slow rather than rapid resolution of syphilitic inflammatory tissue, were also found to be of value in preventing
the therapeutic paradox. The introduction of bismuth provided another drug free from dangerous after-effects and therapeutically more active than mercury.

From the accumulated experience with the use of these drugs, in combination with the older medical measures, our present-day treatment has been established.

The treatment of uncomplicated syphilitic aortitis—It is always wise, because of the incalculable factor of possible coronary involvement, to begin treatment with a preparatory course of bismuth and potassium iodide for from 2 to 3 months, before any arsphenamine is attempted. In the absence of aortic insufficiency, aneurysm, or congestive heart failure, however, all of the arsphenamines, even old arsphenamine itself, are fairly well tolerated and the dosage may be much larger than when any of these complications are present. It is better to start with a small dose, for example, 50 mgm. of arsphenamine or 100 mgm. (0.1 gram) of neoarsphenamine, and to increase this dosage cautiously until a maximum of 0.3 gram of arsphenamine or 0.6 gram of neoarsphenamine is reached for the average adult patient. Neoarsphenamine is easier to give, is probably safer, and for the purpose for which it is being used, probably equally effective with arsphenamine. It is better to use an arsphenamine and a heavy metal in alternation, rather than simultaneously, in order to ease the strain of antisyphilitic treatment on the patient. We believe, on clinical grounds, that patients do better on continuous treatment without rest
periods than on intermittent treatment with interpolated intervals. Courses of both arsenical and heavy metal drugs tend to be long, i.e., 10 to 12 weekly injections of each. Treatment is prolonged, regardless of serologic progress, for a period of at least 2 years. In most patients, including those who have progressed satisfactorily, we believe it to be wise to keep the patient under the most rigid post-treatment observation for the balance of his lifetime, and occasionally, perhaps once a year, to administer a course of a heavy metal, to be followed by a course of an arsphenamine preparation.

If when the patient is first seen, there is any evidence of congestive heart failure, he must be promptly put to rest in bed and digitalized. If there is no edema, antisyphilitic medication, except for the iodides, should be omitted until compensation has been regained. If edema is present, one of the soluble mercurial salts, succinimide intramuscularly or salyrgan intravenously, may be employed for a few days for its combined diuretic and antisyphilitic effect. As Brooks (18) and also Carter and Baker (10) pointed out, these patients seem to be more refractory to digitalis than those with other forms of cardiac failure, and even in large doses fail to produce any physiologic effect. Rest in bed should be prolonged until well after compensation has been recovered.

Antisyphilitic treatment, usually with intramuscular injection of an insoluble bismuth salt combined with administration of potassium or sodium iodide by mouth, should be started as soon as a fair degree of cardiac reserve has been established.
The dosage of bismuth should be small at first 0.1 grams every four or five days. If this is tolerated for four or five injections without an upset, the dose is increased to 0.2 grams. At the start the treatment insoluble salts should be used because they are not absorbed as quickly as the soluble salts. This type of treatment should be carried out for at least ten to twelve weeks before any of the arsphenamines are given. If by the end of this time there is not complete compensation the drug of choice is bismarsen. This preparation is administered intramuscularly in a dosage of first from 0.05 to 0.1 grams, not oftener then every five days. A course of bismarsen consists of from twelve to twenty injections. If, on the other hand, there are no signs of decompensation after a course of insoluble salt and iodides, than one may carry out the treatment as suggested for early cases without any complications.

During the entire course of treatment the patient must be kept under close observation and be warned against physical strain of any kind. Powdered digitalis, in a dosage of from 0.1 to 0.2 grams daily, should be given to those patients with low cardiac reserve.

Results of treatment--It is difficult to obtain a comparison between the results of older treatment and the treatment of today because most writers on the subject discuss the prognosis and the outcome in syphilitic aortitis without differentiating the clinical material upon which they base their claims. Obviously, the prognosis and the results to be expected from
treatment should be better in the stage of simple aortitis than from those that developed aortic insufficiency or aneurysm, and in the latter two conditions, better before than after the appearance of manifest myocardial failure. Many of the older clinicians advocate one or another method of treatment, or advise against treatment, on the basis of their opinions, failing to detail the facts on which their opinions are based. Others describes the results of treatment in a small number of cases. To draw conclusions from individual instances of apparent therapeutic success or failure, or to consider a few cases only, no matter how carefully studied, is a dangerous procedure. The only fair method of approach to the problem is by the statistical study of a large number of comparable cases.

The results of treatment in patients with uncomplicated syphilitic aortitis—Moore and Metildi (40) have recently studied the outcome in relation to treatment in 115 patients in whom the clinical diagnosis of uncomplicated aortitis had been made. This information for two groups of patients, that is, those who received no or inadequate treatment, less than 12 injections of an arsenical product with interim heavy metal, and those treated adequately, more than 12 injections of an arsphenamine, and in the majority of instances more than a year of continuous treatment. The mortality rate is based on all patients dead from any cause, whether or not related to syphilitic aortitis. In spite of this strict interpretation of mortality there is a clear cut difference in the outcome: 42 percent of those inadequately treated are dead, and 31 percent have
developed aneurysm, aortic insufficiency, or have died as a result of congestive heart failure, as compared with corresponding figures of 14 and 18 percent for the adequately treated group.

It is not surprising that aortic regurgitation may develop in spite of thoroughly adequate treatment (8 of 47 patients in the best treated group). In some instances it is probable that the development of valvular incompetency is actually hastened by treatment. With the healing effect of treatment, inflammatory tissue in a still competent valve may be replaced with scar tissue with the subsequent distortion and the production of mechanical insufficiency. This may be a blessing in disguise rather than disaster, since, as Stokes (2) puts it, a progressive disability has been exchanged for a static one.

It must be emphasized that the observed outcome in this group of cases is further justification for our insistence on the feasibility of diagnosis of uncomplicated aortitis. If a patient in whom this diagnosis has been made later develops an aneurysm, the aortic regurgitation or congestive heart failure, and if in the latter instance, the presence of aortic involvement is proved at necropsy, the original clinical diagnosis must have been correct. In the total 115 patients, these eventualities were observed to occur in 22 percent and death from syphilitic aortitis was probable, though not definitely proved.

The probable outcome in uncomplicated aortitis is
materially worse if the lesion is complicated by hypertension, essential or otherwise. This is shown in the 31 patients which present the picture of hypertension. Among these 31 patients the mortality rate was 32 percent, and incidence of graver forms of aortitis in patients living or dead, 35 percent, as compared with corresponding figures of 19 and 17 percent for 74 patients without hypertension.

Relief from symptoms, especially pain and paroxysmal dyspnea but also other signs of circulatory embarrassment, as a result of treatment is usually so prompt and complete in patients with uncomplicated aortitis as to leave some doubt of the correctness of diagnosis when it does not occur. In the 75 patients treated, 84 percent showed symptomatic relief.

In summarizing these results one then may illustrate the relatively favorable prognosis of uncomplicated aortitis, since 86 of the 115 patients are still living. Among those well treated the average duration of life, dating from the diagnosis of aortitis, is 8 years, and 57 percent of this group are now completely symptom-free, without progress in physical signs.

Cotton (62) in 1926, discussed the ultimate outcome in 107 patients with aortic regurgitation complicating the aortitis, 7 of whom also had aortic aneurysm. Fifty-two of this group were given no antisyphilitic treatment and were used as controls. The remaining 55 were treated with courses of neorarsphenamine and mercury, a course of each drug once a year for five years. Both the untreated and treated were given the same type of
general care, and that they were observed over a five year period. Presumably, at the end of this period, 34 of the 52 untreated patients were still living and 18 were dead, a mortality of 34 percent. Of the 55 treated patients, 41 were still living and 14 dead, a mortality of 25 percent. Thus treatment appeared to offer a 9 percent increased chance of survival for the period of observation. Scott (24) places the average duration of life after the onset of symptoms of aortic regurgitation in untreated patients as from one to two years.

Conybeare (63) reported on the effect of treatment in syphilitic aortitis with aneurysm. His series was small, consisting of only 23 patients, but his data are well presented. Twelve patients, serving as controls, received no antisyphilitic treatment. Of these 4 were living at the time of the report, the average duration of life from the onset of symptoms being 43 months. Eleven patients were treated with varying amounts of neaarsphenamine. Only 3 of these received much treatment, the remaining 8 all being given from one to eight injections of the drug. In spite of this relatively small amount of treatment 7 of the treated patients were still living over an average period of forty months from the onset of symptoms, and 4 of these were symptom-free and able to do hard physical labor. Four were dead in an average period of thirty months. On the basis of these figures, Conybeare was convinced of the value of neaarsphenamine in aortic aneurysm.

Recently, Herrman and Jamison (58) discussed the outcome
of treatment in 100 patients with aortic regurgitation, all of whom had had congestive heart failure before treatment was started. They subdivided their material into small groups and attempted a simultaneous but not interrelated analysis of the effect of varying amounts and types of antisyphilitic treatment and the effect of such various measures to relieve congestive heart failure as large versus small doses of digitalis etc., so it is difficult to draw conclusions from their figures. Disregarding all features of their report except that dealing with antisyphilitic treatment one finds that 40 patients received little or no treatment, of whom 12 were living and 28 dead, a mortality of 70 percent. Fifty-eight patients were given a moderate amount of treatment, one course of neosarsphenamine and one course of mercury. Of these, 26 were living and 32 dead, a mortality of 55 percent. From these figures the authors concluded that antisyphilitic treatment definitely prolongs life, and that, while living, treated patients are usually much more comfortable than those who are untreated.

Probably the best work, in so far as a report of what treatment actually accomplished, was done by Moore, Danglade and Reisinger (54) on a group of patients in which 53 had developed aneurysm and 112 who had developed aortic regurgitation. The patients were divided up into four groups on the basis of the amount of antisyphilitic treatment received. Group one includes those patients who received the equivalent of no antisyphilitic treatment. Group 2 includes patients who received
the equivalent of one course of an arsenical drug, from 6 to 8 injections, or one long course, from 12 to 16 injections of a heavy metal, either bismuth or mercury. In group 3 are patients who received the equivalent of one long course each of an arsenical drug and of a heavy metal, occupying from four to twelve months time. Group 4 includes all patients treated for more than one year. This involved a minimum of two long courses each of an arsphenamine product and of a heavy metal alone.

It is important to note that although the 165 patients studied differed in the amount of antisyphilitic treatment received, they were all treated when necessary by the usual medical regime of rest, diet, digitalis, restriction of activity etc. It is perfectly fair, therefore, to attribute any difference observed in course or ultimate outcome to the difference in amount of antisyphilitic treatment. A summary of their results as quoted in their article is as follows:

Symptomatic relief from antisyphilitic treatment:*  

<table>
<thead>
<tr>
<th>Group</th>
<th>Total No.</th>
<th>Relief</th>
<th>No relief</th>
<th>Total No.</th>
<th>Relief</th>
<th>No relief</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11</td>
<td>3</td>
<td>8</td>
<td>26</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>13</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>12</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>IV</td>
<td>11</td>
<td>10</td>
<td>1</td>
<td>20</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>21</td>
<td>13</td>
<td>71</td>
<td>37</td>
<td>33</td>
</tr>
</tbody>
</table>

* Excluding all who were not treated, those who were symptomless, before treatment, and those in whom reliable data was lacking.
Effect of treatment upon prolongation of life in patients with aneurysm of the aorta:

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Living</th>
<th>Dead</th>
<th>Onset of Symptoms</th>
<th>Start of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>22</td>
<td>2</td>
<td>20</td>
<td>19 mo.</td>
<td>14 mo.</td>
</tr>
<tr>
<td>II</td>
<td>10</td>
<td>2</td>
<td>8</td>
<td>51 mo.</td>
<td>45 mo.</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>67 mo.</td>
<td>43 mo.</td>
</tr>
<tr>
<td>IV</td>
<td>15</td>
<td>9</td>
<td>6</td>
<td>75 mo.</td>
<td>63 mo.</td>
</tr>
</tbody>
</table>

Effect of treatment upon prolongation of life of patients with aortic regurgitation:

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Living</th>
<th>Dead</th>
<th>Onset of Symptoms</th>
<th>Start of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>37</td>
<td>5</td>
<td>52</td>
<td>30 mo.</td>
<td>23 mo.</td>
</tr>
<tr>
<td>II</td>
<td>16</td>
<td>4</td>
<td>12</td>
<td>23 mo.</td>
<td>15 mo.</td>
</tr>
<tr>
<td>III</td>
<td>14</td>
<td>10</td>
<td>4</td>
<td>46 mo.</td>
<td>37 mo.</td>
</tr>
<tr>
<td>IV</td>
<td>25</td>
<td>21</td>
<td>4</td>
<td>64 mo.</td>
<td>53 mo.</td>
</tr>
</tbody>
</table>

Effect of treatment upon prolongation of life in entire group of patients:

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Living</th>
<th>Dead</th>
<th>Onset of Symptoms</th>
<th>Start of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>79</td>
<td>7</td>
<td>72</td>
<td>27 mo.</td>
<td>21 mo.</td>
</tr>
<tr>
<td>II</td>
<td>26</td>
<td>6</td>
<td>20</td>
<td>33 mo.</td>
<td>26 mo.</td>
</tr>
<tr>
<td>III</td>
<td>20</td>
<td>13</td>
<td>7</td>
<td>46 mo.</td>
<td>39 mo.</td>
</tr>
<tr>
<td>IV</td>
<td>40</td>
<td>30</td>
<td>10</td>
<td>68 mo.</td>
<td>57 mo.</td>
</tr>
</tbody>
</table>
In summary of all this data it seems fairly definite that adequate treatment for early syphilis markedly diminishes, if it does not entirely prevent, the appearance of late lesions. Equally satisfactory results in the prevention of aortic lesions may be obtained by the treatment of early syphilis.

It is also evident that even after the development of late cardiovascular lesions that the patient can be relieved of many of their symptoms and in many instances life prolonged.
LIBRIOGRAPHY

5. Brussgaard, as quoted by Moore, J. E. (40).


56. Wilson, F. N., Wile, U. J., Wischert, S. W. and Herrmann, G. R.: Changes in the Electrocardiogram Following the Arsphenamine Treatment of Cardiac and Aortic Syphilis,


