CARDIOVASCULAR SYphilIS
A CLINICAL STUDY OF 578 CASES*

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Review of the Literature

With the perfection of penicillin schedules and improved epidemiological procedures during World War II and the ensuing years, the incidence of early syphilis has reached its lowest level. It is feared that, as interest in early syphilis wanes because of its relative scarcity, interest in late syphilis will also diminish. This would be unfortunate, since there are 2,100,000 persons in the United States with undetected or inadequately treated syphilis (U.S. Publ. Hlth Service, 1953). With the present promiscuous use of penicillin, persons with masked syphilis may develop lesions of late syphilis through inadequate therapy. There seems to be general agreement with the opinion expressed by one group (Diseker and others, 1944) that adequate metal chemotherapy of early and latent syphilis prevented the appearance of cardiovascular lesions, but we feel that though it markedly decreased late syphilitic involvement, it by no means halted progression in all patients.

For the purposes of this study we have classified cardiovascular syphilis into three main categories: aortitis, aneurysm, and aortic insufficiency. Coronary ostial involvement is also considered as it occurs as a complication of these conditions; other less frequently encountered lesions of the cardiovascular system will be considered briefly.

The earliest and most important phase of cardiovascular involvement is uncomplicated aortitis, since it is at this stage that we believe adequate penicillin therapy can prevent further progression of the lesion. One investigator (Howe, 1943) is of the opinion that adequate arsenic and bismuth therapy accomplished this purpose, but others (Hood and Mohr, 1937) felt that such treatment was of little value.

The diagnosis of syphilitic aortitis is not easy, the reported incidence of cardiovascular involvement in patients having latent and late syphilis on a histological basis varies from 40 per cent. (Rosahn, 1946; Peters and others, 1955) to 70 to 90 per cent. (Warthin, 1931), while only 10 per cent. of patients with untreated late syphilis develop clinically manifest cardiovascular lesions (Bruusgaard, 1929). More careful screening of patients with latent and late syphilitic involvement of other systems should result more frequently in the correct diagnosis of cardiovascular involvement.

Opinion varies regarding the presence of diagnostic symptoms in uncomplicated aortitis. Kampaier and others (1942) feel that the condition is completely symptomless, but we are in accord with those who feel that non-radiating substernal pain unrelated to exertion and/or symptoms of diminished cardiac reserve (in the absence of hypertension and valvular disease) is present in some patients with aortitis (Mattman and Moore, 1943). Nor is there any agreement concerning diagnostic physical findings in this condition. An aortic systolic murmur has been considered significant (Maynard, 1942), but we are in agreement with Moore and others (1943) that an accentuated aortic second sound of characteristic tambour quality, in a patient without hypertension or arteriosclerosis, is the only significant physical finding. Lucia and Sears (1946) say that uncomplicated aortitis cannot be diagnosed with any degree of certainty on the basis of physical findings.

Kemp and Cochems (1937) noted x-ray evidence of aortic dilatation in 59 per cent. of a group of patients with clinically evident syphilitic aortitis utilizing routine postero-anterior views. After comparison of the postero-anterior chest films of large numbers of syphilitic and non-syphilitic patients, using the technique of aortic measurement of Vaquez and Bordet (1920), they concluded that there was no difference between the degree of aortic widening due to hypertension, arteriosclerosis, and the ageing process in syphilitic patients without clinically evident cardiovascular involvement, and
that in non-syphilitic patients. Similar findings were reported by Boharas and others (1942). Moore (1949) has stated that aortic measurements are of little value unless marked distortion is present, and the routine use of fluoroscopy, anterior oblique films, or röntgen kymography has been recommended for diagnostic purposes. The left anterior oblique view is particularly valuable in delineating the ascending aorta. Calcific deposits in the aorta were felt by Blumenthal and others (1944) to be due more frequently to hypertension and arteriosclerosis than to syphilis. Leighton (1948) and Jackman and Lubert (1945) thought that linear calcification, particularly in the ascending aorta, was pathogenetic of syphilitic aortic involvement. Though this was not usually an early sign of involvement, it was valuable in the differential diagnosis of aortic insufficiency. We feel that the importance of this finding as a diagnostic aid has not received enough emphasis in practice. The technique of angiocardiography described by Robb and Steinberg (1938) has been helpful in the early recognition of cardiovascular syphilis (Dotter and Steinberg, 1949). This procedure permits visualization of the first portion of the aorta, which is usually obscured by the heart shadow in routine x-ray studies, but unfortunately does not lend itself to application in an out-patient clinic.

Cole and Bohning (1944) and Berk (1941) were unable to demonstrate any specific electrocardiographic changes in uncomplicated aortitis.

Spread of the syphilitic process proximally with resultant weakening of the media produces dilatation of the aortic root and, consequently, dilatation of the aortic ring. This dilatation is the basis for regurgitation in the earliest stage of aortic valvular insufficiency. An interesting case of this type has been found at autopsy (Massachusetts, 1941). At this stage the aortic second sound may be discernible, followed by a short, very faint diastolic murmur. Involvement of the valve resulting in deformity of the cusps and widening of the valve commissures is a later development. Extension of the elastic fibres of the media proximal to the attachment of the cusps has been observed in some patients (Wilens, 1940). This variation seemed to have a definite bearing upon the degree of regurgitation.

The commonest symptoms in aortic insufficiency, when present, are exertional dyspnoea and paroxysmal nocturnal dyspnoea. Precordial pain is usually evidence of coronary ostial involvement (Bruenn and others, 1936), though aortic insufficiency with a lowered diastolic blood pressure may result in diminished coronary circulation and anginal symp-

toms with essentially normal ostia. There may be little, if any, correlation of ECG changes and precordial pain (Blackford and Smith, 1938). Aortic insufficiency may exist in an asymptomatic phase for a variable period (McDermott and others, 1942).

The murmur of aortic insufficiency has been described (White, 1944) as a blowing diastolic aortic murmur, decrescendo in nature. Auscultation is facilitated by the use of a diaphragm stethoscope, with the patient leaning forward in a sitting position and holding his breath after full expiration. Maximal intensity may be over the left sternal border in the third and fourth intercostal spaces or over the right lower sternal margin, depending upon the position of the heart. Transmission of the murmur may be to the apex, left axilla, or neck. Rarely, the murmur may have a musical or “dovecote” quality and may be of such intensity as to be heard without a stethoscope some distance from the patient. Such was the case in two of our patients. The pathological basis of this murmur may be a ruptured or perforated aortic cusp (Wilbur, 1941) or merely retroversion of a valve leaflet (Bellet and others, 1939).

A presystolic apical murmur (Austin Flint) has frequently been reported in patients with aortic insufficiency (Nicol, 1950), but Luisada (1944) felt that true Austin Flint murmurs were uncommon.

The more prominent peripheral findings of advanced aortic regurgitation are the water-hammer or “Corrigan” pulse and a capillary pulse detected in the nail bed or mucous membrane of the lips. Duroziez’s sign is frequently encountered. Peripheral signs may be entirely lacking in the early stages and in patients with a normal pulse pressure.

X-ray evidence of left ventricular hypertrophy was demonstrated in 93 per cent. of a group of patients with aortic insufficiency due to syphilis (Nichols, 1940); however, this finding may be minimal or absent in early cases and in those without peripheral signs. The diagnostic importance of linear calcification in the ascending aorta has been mentioned previously. Left axis deviation is a common electrocardiographic finding. The T-wave and S-T segment changes, so frequently seen in advanced aortic insufficiency, have usually been attributed to myocardial hypertrophy rather than to coronary involvement (Parsonnet and Bernstein, 1943).

The differential diagnosis of aortic insufficiency may be a difficult matter; this problem arises in distinguishing syphilitic from rheumatic lesions. Bacterial endocarditis, congenital cardiac lesions, arteriosclerosis, and calcific disease of the aortic valve must also be ruled out.
The importance of a careful history cannot be overemphasized. A history of murmur present since childhood may sometimes be obtained, and frequently a history typical of rheumatic fever or symptoms suggestive of the so-called "rheumatic state". Rheumatic heart disease usually becomes clinically evident earlier in life (20 to 35 years of age). Rheumatic aortic involvement commonly produces a stenotic lesion in addition to insufficiency and, quite often, mitral stenosis co-exists. Radiological examination in these patients may reveal left auricular enlargement. As a rule, x-ray and fluoroscopic examinations fail to reveal dilatation of the aorta in lesions of rheumatic origin. Auricular fibrillation has been reported as very unusual in syphilitic heart disease (Comeau, 1942), although contradictory findings substantiated at autopsy have been presented (Plice and Pfister, 1949), and the conclusion has been drawn that auricular fibrillation is almost as common in syphilitic heart disease as in other cardiac conditions. Bacterial endocarditis complicating aortic insufficiency strengthens the probability of a rheumatic aetiology, though this complication is rarely noted in syphilitic aortic valvulitis (Braunstein and Townsend, 1940). In addition, cases of combined syphilitic and rheumatic valvular disease have been reported by Plice and Edinburg (1942) and by Lisa and others (1942). The serologic test for syphilis (STS) is usually negative in rheumatic heart disease. It must be emphasized, however, that a negative STS does not rule out the diagnosis of syphilitic heart disease. Beckh (1943) found 4 per cent. of a group with proven syphilitic heart disease to be sero-negative, and Kampmeier (1938) found a positive STS or history of previous treatment in only 86 per cent. of a large group of patients with aortic aneurysm.

Varying degrees of arteriosclerosis are often associated with syphilitic involvement in older patients, though valvular insufficiency due to arteriosclerosis is a rare occurrence (Epstein, 1938). Seven per cent. of a group of patients with syphilitic aortic insufficiency also exhibited at autopsy aortic stenosis due to calcification of the aortic valves (Woodruff, 1948).

Involvement of the coronary arteries may occur at any stage of cardiovascular syphilis, but is most commonly associated with aortic insufficiency (Burch and Winsor, 1942). The syphilitic process is usually limited to the coronary ostia, but a case has been reported by Strassmann and Goldstein (1942) which, at autopsy, showed involvement of the entire length of the coronary artery. Coronary involvement is a finding more frequent in those cases with an anomalous origin of the coronary arteries distal to the aortic ring (von Glahn, 1923). Marked narrowing of the ostia usually produces myocardial fibrosis occasionally resulting in myocardial infarction (Fisch and Rosenbaum, 1950; Norris, 1937). Cole and Bohning (1944) described three cases with the typical electrocardiographic findings of anterior infarction. Bundle branch block has been considered as indicative of coronary obstruction (Sprague, 1942), though this finding may result from myocardial hypertrophy with essentially normal coronaries (Rasmussen and Moe, 1948). Myocardial infarction secondary to thrombosis or embolism on a syphilitic basis may occur (Pratt-Thomas, 1943; Volk and others, 1950).

The most frequent site of syphilitic aneurysm is the ascending aorta, the occurrence being progressively less frequent in the more distal portions. Signs and symptoms, when present, are primarily due to aneurysmal pressure on adjacent structures. Dysphagia results from compression of the oesophagus, while involvement of the recurrent laryngeal nerve may give rise to hoarseness, aphonia, or a typical brassy cough. Compression of the trachea or a bronchus may produce stridor, and, if bronchial compression is marked, it can produce atelectasis. Horner's syndrome has occasionally been due to aneurysmal pressure on the superior thoracic sympathetic chain. The classic picture of the superior vena cava syndrome secondary to an aortic aneurysm is a possibility (Hinshaw and Rutledge, 1942) and aneurysmal compression of the pulmonary artery has been known to cause embarrassment of the pulmonary circulation (Brill and Jones, 1946). Bone pain is due to erosion of the ribs and sternum or the vertebral column. Neurological signs, such as cord bladder, can result from aneurysmal compression of the spinal cord (Shimkin, 1939).

An aneurysm of the ascending aorta may produce dullness to percussion to the right of the sternum. Visible pulsation in the right second and third interspaces is sometimes apparent. Large aneurysms in this region produce a prominence of the right anterior chest wall. Aneurysm of the arch may present as a pulsatile mass in the suprasternal notch, and tracheal tug can be elicited in some cases. Rarely, an aneurysm in this region may impinge on the great vessels arising from the arch, causing diminished pulsation in the neck or a discrepancy of the pulse or blood pressure in the arms (Maynard, 1942). Aneurysm of the descending thoracic and abdominal aorta are as a rule devoid of signs and symptoms.

Thrombus formation in the aneurysmal sac accompanied by fibrosis and deposition of calcium
in the wall of the sac greatly improves the outlook. When these events fail to occur, the possibility of aneurysmal rupture is always present. The sac may rupture into a bronchus (Massachusetts, 1941), pulmonary artery (Scott, 1924), superior vena cava (Armstrong and others, 1949), the pleura or pericardium (Goldstein, 1949), or rarely into the right ventricle (Harris and Schattenberg, 1944), with bizarre terminal physical findings.

The reported frequency of syphilitic aneurysm of the abdominal aorta varies from 9 per cent. (Mills and Horton, 1938) to 74 per cent. (Scott, 1944) in pathological studies to determine the aetiology of abdominal aneurysms. Scott concluded that aneurysms above the origin of the renal artery were most often syphilitic. In approximately 34 per cent. of the syphilitic group an aneurysm of the thoracic aorta was also present, and an additional 18 per cent. also had aortic regurgitation.

While it is well to be aware of the signs and symptoms attributable to aortic aneurysms, it should be emphasized that in many instances this condition is entirely symptomless and diagnosis depends solely upon adequate radiological examination.

Rarely encountered conditions of the cardiovascular system due to syphilis include involvement of the pulmonary arteries (Boyd and McGavack, 1939), the great vessels arising from the arch of the aorta (Barker, 1949), the hepatic artery (Malloy and Jason, 1942), and the renal artery (Price and Skelton, 1948). Additional findings are those of aneurysm of the heart (Cookson, 1929), as well as of the sinuses of Valsalva (Chipps, 1941; Ostrum and others, 1938) and the coronary arteries (O'Neill and Laipply, 1949; Snyder and Hunter, 1934).

Syphilitic myocarditis is considered rare (Saphir, 1942), but others think that this condition should be considered in the differential diagnosis of any syphilitic patient who develops moderate decompensation or other unexplained cardiac symptoms (Rasmussen and Moe, 1948; Magill, 1935). A case of interventricular block of short duration which developed under observation and disappeared after antisyphilitic therapy (Nolan and Pedigo, 1946) lends support to the latter idea. Another rare finding, guma of the myocardium, should be suspected in cases where radiological examination reveals unexplained shadows at the cardiac margins (Sohval, 1935).

The general feeling is that uncomplicated syphilitic aortitis without coronary ostial involvement carries a good prognosis. In one series of 105 patients diagnosed at autopsy, only 24 had died of causes related in any way to syphilis, and only ten of these died as a probable direct result of aortic involvement (Moore, 1949). On the other hand, prognosis in aortic insufficiency and aneurysm is said to be poor after the onset of symptoms (average 1½ years) and especially so after the appearance of congestive failure (Montgomery and others, 1952). In one group, however, the asymptomatic phase of syphilitic aortic insufficiency ranged from 2 to 10 years (average 6) and survival after the onset of symptoms was 2 to 14 years (average 5 to 6) (Reader and others, 1947). Survival after the appearance of symptoms in patients with untreated aneurysm in another series was 1 to 3 years (average 19 months) (Moore and others, 1943).

The reported results obtained by adequate treatment of cardiovascular syphilis vary; some feel treatment to be of little or no value in prolonging life and halting progression of the disease process (Kampmeier and Combs, 1940), while others believe such therapy to be definitely beneficial (Jensen, 1942; Barnett and Small, 1950).

In a series of recent publications (Padget and others, 1950; Densen and others, 1952; Webster and others, 1953), the problem of therapy evaluation in cardiovascular syphilis has been analysed exhaustively with respect to the medical, statistical, and methodological problems involved; the weaknesses inherent in most of the past attempts to evaluate therapy are pointed out, and the prerequisites for a valid analysis of penicillin therapy in cardiovascular syphilis are demonstrated.

In spite of the lack of statistically sound analyses, in practice, in the United States, penicillin has been increasingly used as the specific drug in all types of cardiovascular syphilis. The experience of various groups (Stokes and others, 1951; Sinclair and Webster, 1954; Eisenberg and Brandfonbrener, 1953a, b; Edeiken and others, 1953) is reflected in the general recommendation of penicillin (U.S. Publ. Hlth Service, 1953; Curtis and others, 1951).

The possibility of adverse reactions, such as those of Herxheimer (Butterly and Fishman, 1952; Diefenbach, 1949; Whorton and Denham, 1951) and the "therapeutic paradox" (Mohr and Hahn, 1952; Porter, 1948), necessitated caution in the use of penicillin, but these untoward reactions rarely have been encountered in patients with cardiovascular syphilis (Tucker and Farmer, 1947; Edeiken and others, 1949, 1950; Russek and others, 1946, 1949; Flaum and Thomas, 1949; Sinclair and Webster, 1951).

Clinical Study

Against this background of previous experience, our experiences with the treatment of cardiovascular
syphilis in the venereal disease control program of the Chicago Board of Health are here reported.

The series comprises 578 patients in whom cardiovascular syphilis was diagnosed before 1947. A breakdown of the series by particular diagnosis and outcome is given in Table I. A patient who could not be located was listed as unknown only after a thorough check of both city and State files had failed to place him as dead. All patients used for comparison had a follow-up of 5 years or more, and those living but not observed are included only in the consideration of longevity.

The majority of these patients were referred to the cardiovascular section because of some abnormality discovered on routine physical examination in the general venereal disease clinic. The cardiovascular examination consisted of:

1. Complete cardiac history and physical examination
2. Radiological examination, originally consisting of routine postero-anterior x-ray, supplemented by fluoroscopy in a small percentage of patients and, more recently, by right and left anterior oblique views
3. Electrocardiography: until 1947 this consisted of the three standard leads and CF₁; it now includes the three standard leads, V₁-V₆, and the AV leads.

The majority of patients living and observed were examined approximately every 6 months, and repeat x-rays and electrocardiographs were taken at yearly intervals as nearly as possible. Some in this group, however, lapsed from observation and may have had only an initial examination, with a repeat in the past year.

Most patients after diagnosis of cardiovascular involvement received prolonged bismuth therapy. Bismuth (150 mg.) was administered bismuth weekly for a 10-week period and repeated at least once and, often, two or three times yearly. Some of the group received arsenical therapy, and, in more recent years, penicillin has been administered to a few patients.

The diagnosis of uncomplicated syphilitic aortitis was based on the presence of at least two of the following criteria:

1. Typically accentuated tambour-like aortic second sound, either with or without an associated soft systolic aortic murmur
2. History of chest pain, usually dull substernal pain unrelated to exertion, or symptoms of diminished cardiac reserve in the absence of hypertension, arteriosclerosis, or other clinically evident cause
3. X-ray evidence of widening of the supracleavicular shadow
4. Positive STS, history of a previously positive STS, and/or previous antisyphilitic therapy

Syphilitic aortic regurgitation was diagnosed on the basis of the typical aortic diastolic murmur in patients with a negative history of rheumatic disease and in the absence of radiological findings suggesting a co-existent mitral valvular lesion.

Syphilitic aortic aneurysm was diagnosed on the basis of radiological findings.

Comparisons were made of the influence upon prognosis of a number of variables.

The influence of race, sex, and age at diagnosis can be seen in Table II (opposite).

**Race.**—In the group with aortitis, prognosis was significantly poorer for the white males. At final evaluation 5 years or more after original diagnosis, 36-1 per cent. were living and 63-9 per cent. were dead among the white males, as compared with 62-9 per cent. living and 37-1 per cent. dead among the Negro males. In the group with aortic regurgitation and/or aneurysm, prognosis was slightly poorer for white males; 21-3 per cent. living and 78-7 per cent. dead, as against 29-3 per cent. living
and 70-7 per cent. dead among the Negro males. Since these differences among patients with more severe cardiovascular involvement are not statistically significant, the findings do not suggest to us a peculiar racial susceptibility.

**Sex.**—In both diagnostic groups, those with syphilitic aortitis and those with aortic regurgitation and/or aneurysm, the prognosis for females was significantly better than that for males in both races. These findings concerning sex may reflect the deleterious effect of heavy manual labour upon prognosis among patients with cardiovascular syphilis.

**Age.**—With the exception of Negro males, the prognosis was better for persons under 50 years of age at time of diagnosis in each race-sex group in both diagnostic categories. However, since none of these differences by age proved to be statistically significant, the higher death rate among older patients probably only reflects the normally higher death rate in an ageing population.

No particular difference is noted in the prognosis of those receiving adequate or inadequate treatment in either diagnostic category (Table III). The larger percentage of patients living among those treated with penicillin is based on a comparatively small number of patients. Furthermore, because of the comparatively short period before 1947 during which penicillin was available for the treatment of syphilitic cardiovascular disease, the final disposition was made in many cases shortly after the 5-year minimum follow-up period, which, in the penicillin group, would weight the outcome in favour of those living at final evaluation.

The status of the serologic test for syphilis at time of diagnosis does not appear to influence the prognosis in either diagnostic category (Table IV, overleaf). No significant differences could be demonstrated in the syphilitic aortitis group between the 64-5 per cent. living of sero-positive cases and the 76-9 per cent. living of sero-negative cases. Similarly, the 32-5 per cent. living of those who were sero-positive when diagnosed with aortic regurgitation and/or aneurysm is not significantly different from the 22-2 per cent. living of sero-negative cases. Of the 228 cases who were sero-positive at the time of diagnosis with syphilitic aortitis, 110 (48-2 per cent.) had attained sero-negativity at final evaluation, and of the 160 cases who were sero-positive at the
TABLE IV
RESULTS OF PATIENTS HAVING CARDIOVASCULAR SYPHILIS BY ORIGINAL DIAGNOSIS AND SEROLOGICAL STATUS AT TIME OF DIAGNOSIS

<table>
<thead>
<tr>
<th>Original Diagnosis</th>
<th>Serological Status</th>
<th>Total Cases</th>
<th>Living and Observed</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Per cent.</td>
<td>Number</td>
</tr>
<tr>
<td>Syphilitic Aortitis</td>
<td>Positive</td>
<td>228</td>
<td>147</td>
<td>64.5</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>13</td>
<td>10</td>
<td>76.9</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>19</td>
<td>5</td>
<td>26.3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>260</td>
<td>162</td>
<td>62.3</td>
</tr>
<tr>
<td>Aortic Regurgitation and/or Aneurysm</td>
<td>Positive</td>
<td>160</td>
<td>52</td>
<td>32.5</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>9</td>
<td>2</td>
<td>22.2</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>172</td>
<td>54</td>
<td>31.4</td>
</tr>
</tbody>
</table>

Time of diagnosis with aortic regurgitation and/or aneurysm 64 (40 per cent.) were sero-negative at final evaluation.

Among those originally diagnosed with syphilitic aortitis, 39 were diagnosed with cardiovascular progression either before or at final disposition. Table V shows that twelve out of 25 of the cases living and observed at final disposition had progressed from aortitis to aortic regurgitation and/or aneurysm more than 7 years after the original diagnosis, and that nineteen of this group had progressed more than 5 years after the original diagnosis. Patients in whom uncomplicated aortitis has been present for a long time may still develop aortic insufficiency or aneurysm after therapy since damage to the media and aortic valves may have occurred before the causative agent could be eradicated.

X-ray and electrocardiographic findings by diagnosis are presented in Table VI. The x-ray findings re-emphasize the ascending aorta as the site of predilection for syphilitic infection of the

| TABLE V |
| INTERVAL BETWEEN ORIGINAL DIAGNOSIS OF SYPHILITIC AORTITIS AND PROGRESSION TO AORTIC REGURGITATION AND/OR ANEURYSM BY FINAL DISPOSITION |

TABLE VI
X-RAY AND ELECTROCARDIOGRAPHIC FINDINGS IN CARDIOVASCULAR SYPHILIS

<table>
<thead>
<tr>
<th>Findings</th>
<th>Aortitis</th>
<th>Aortic Regurgitation and/or Aneurysm</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Living and Observed</td>
<td>Dead</td>
<td>Living and Observed</td>
</tr>
</tbody>
</table>

The X-ray and electrocardiographic findings by diagnosis are presented in Table VI. The x-ray findings re-emphasize the ascending aorta as the site of predilection for syphilitic infection of the
**CARDIOVASCULAR SYphilis**

**Table VII**

**INTERVAL BETWEEN PRIMARY SYphilis INFECTION AND CARDIOVASCULAR DIAGNOSIS**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Disposal</th>
<th>Interval (yrs)</th>
<th>Interval of Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10 or less</td>
<td>11 to 19</td>
</tr>
<tr>
<td>Syphilitic Aortitis</td>
<td>Living and Observed</td>
<td>Number Cumulative percentage</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Dead</td>
<td>Number Cumulative percentage</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>Number Cumulative percentage</td>
<td>16</td>
<td>17-8</td>
</tr>
<tr>
<td>Aortic Regurgitation and/or Aneurysm</td>
<td>Living and Observed</td>
<td>Number Cumulative percentage</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dead</td>
<td>Number Cumulative percentage</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>Number Cumulative percentage</td>
<td>3</td>
<td>4-2</td>
</tr>
</tbody>
</table>

**Table VIII**

**COMPARISON OF PRECORDIAL PAIN, T-WAVE AND/OR QRS CHANGES, AND CARDIAC DECOMPENSATION BY DISPOSAL**

<table>
<thead>
<tr>
<th>Signs or Symptoms</th>
<th>Disposal</th>
<th>Interval between Onset and Disposal for Patients with Cardiovascular Syphilis (yrs)</th>
<th>Total Number of Patients with Specified Signs or Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 or less</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Precordial Pain</td>
<td>Living and Observed</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dead</td>
<td>Number Cumulative percentage</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>. . . .</td>
<td>. . . . . . . . . .</td>
<td>22</td>
</tr>
<tr>
<td>T-Wave and/or QRS Changes</td>
<td>Living and Observed</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Dead</td>
<td>Number Cumulative percentage</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>. . . .</td>
<td>. . . . . . . . . .</td>
<td>49</td>
</tr>
<tr>
<td>Cardiac Decompensation</td>
<td>Living and Observed</td>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Dead</td>
<td>Number Cumulative percentage</td>
<td>44</td>
</tr>
<tr>
<td>Total</td>
<td>. . . .</td>
<td>. . . . . . . . . .</td>
<td>46</td>
</tr>
</tbody>
</table>

Total number in group: Living and Observed, 216; Dead, 216.

Of the ninety patients with aortitis in whom the primary infection was reported, 49 (54-4 per cent.) showed cardiovascular involvement less than 20 years after the infection. Aortic regurgitation and/or aneurysm was diagnosed less than 20 years after infection in thirty (41-7 per cent.) of the 72 patients in whom the time of infection was known (Table VII). The fact that so many of those with known intervals of infection in both diagnostic categories showed cardiovascular involvement less than 20 years after infection (48-8 per cent.) indicates that this condition should be searched for in younger patients than is usually the practice.

Table VIII shows for the whole series the duration before final result (observation or death) of three factors: precardial pain, T-wave and/or QRS changes, and cardiac decompensation. This information was collected chiefly for the purpose of estimating the duration of these factors before death, and the cumulative percentages have been computed only for those known to have died. Precordial pain was present in 93 (21-5 per cent.) of the 432 patients in the series and to date 62 of these patients have died. Death occurred within 1 year of onset of symptoms for 22-6 per cent., within 2 years for 37-1 per cent., and within 4 years for 64-5 per cent. In the majority of patients this symptom was more probably due to syphilitic involvement of the coronary ostia. T-wave and/or QRS changes were noted in 170 (39-4 per cent.) of this group; of the 88 who died after these changes were noted, 10-2 per cent. died within 1 year, 48-9 per cent. within 2 years, and 79-5 per cent. within...
4 years. Cardiac decompensation occurred in 74 (17-1 per cent.) of the patients and 59 of these have died; death occurred within 1 year after onset of this symptom in 74-6 per cent., within 2 years in 84-7 per cent., and within 4 years in 94-9 per cent. These three factors may therefore be said to have definite prognostic implications.

An additional finding which indicates the need for careful screening of neurosyphilitic patients is that 73 (41 per cent.) of 178 patients in whom a cerebrospinal fluid examination was made were found to be positive.

The period of survival after diagnosis can be seen in Table IX (opposite). The group of patients with aortic regurgitation and/or aneurysm lived longer than is generally expected in such cases. This discrepancy is no doubt due primarily to the fact that the majority were asymptomatic when the original diagnosis of cardiovascular involvement was made, and that after the diagnosis of cardiovascular syphilis they were instructed to avoid heavy manual labour and undue physical exertion.

Life expectancy at various age levels for this group of patients with syphilitic heart disease and for the general population of the United States is compared in Table X (opposite). It is common knowledge that syphilitic aneurysm or aortavalvular insufficiency shortens the expectation of life, (Shafer and others, 1954a, b). Rosahn (1952) has stated that every form of syphilitic infection is associated with a reduction in life expectancy. In our group the decrease would seem to be mainly due to syphilitic cardiovascular involvement, but we must keep in mind the low socio-economic status of these patients, which may also have exerted an adverse effect on longevity.

Bismuth alone or in combination with arsenical therapy did not seem to be very effective in halting the progression of the disease or in prolonging life, but the results obtained in the small number of penicillin-treated patients suggest that this form of therapy may have been more effective. In our experience with penicillin we have noted many patients who experienced a marked diminution of symptoms as well as improvement in the general feeling of well-being. We have not seen a case of fatal Herxheimer reaction in our cardiac clinic. There were a few patients in whom an aortic diastolic murmur developed within a year after penicillin therapy, but most probably this deterioration would have occurred without penicillin therapy. We feel that pre-treatment with bismuth is unnecessary. Penicillin in amounts of 6,000,000 units or more, over a 2- to 3-week period, has proved to be adequate treatment. Decompensation or evidence of severe coronary involvement is an indication for hospitalization with adequate medical supervision, in addition to antisypophilic therapy.

Discussion

The diagnosis of early uncomplicated aortitis is sometimes difficult, especially in the presence of hypertension or arteriosclerosis, but with increased awareness of the physical and laboratory findings it may now be made more frequently than was previously thought possible. At the slightest suspicion of syphilitic involvement, it seems important to treat the case accordingly, rather than to wait for developing valvarular insufficiency, aneurysm formation, or post-mortem examination to prove the suspicion correct. This was proved by the fact that 40 to 60 per cent. of patients with untreated or inadequately treated syphilis showed evidence of cardiovascular syphilis at autopsy in the Tuskegee group (Peters and others, 1955).

It is of utmost importance to diagnose and treat these patients early and adequately in order to halt the progressive damage due to the syphilitic process. If the disease process in the aorta is halted before marked damage has been done to the elastic fibres of the media, before valvular damage has occurred, or before marked narrowing of the coronary ostia is present, the patient's expectation of life should be unaffected. Treatment will be of some value at any stage, though the later in the course of disease the therapy is administered the less helpful it will be. The presence of one complication of syphilitic aortitis offers no assurance that further complications will not occur if treatment is delayed or inadequate. We feel that adequate penicillin therapy will halt further progression, particularly the development of coronary involvement, and markedly improve prognosis.

Summary

The findings presented in this study of 578 patients diagnosed before 1947 as having cardiovascular syphilis are listed below:

(1) Treatment with bismuth, alone or in combination with arsenicals, after the diagnosis of cardiovascular syphilis had no apparent effect in prolonging life or preventing the development of further cardiovascular complications.

(2) Prognosis was poorer for males than females, and for white males in particular.

(3) Progression was more frequent among males than females and among patients with aortitis who were over 50 years of age at the time of diagnosis.


## Table IX

**INTERVAL BETWEEN ORIGINAL DIAGNOSIS AND DISPOSAL OF CARDIOVASCULAR SYPHILIS PATIENTS**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Disposal</th>
<th>Interval (yrs)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less than 1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Aortic Regurgitation</td>
<td>Living Observed</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Not Observed</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Aortic Aneurysm</td>
<td>Living Observed</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Not Observed</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Aortic and Aneurysm</td>
<td>Living Observed</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Not Observed</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>22</td>
<td>13</td>
</tr>
</tbody>
</table>

## Table X

**LIFE EXPECTANCY OF SURVIVORS AT BEGINNING OF EACH AGE PERIOD. COMPARISON OF CARDIOVASCULAR SYPHILIS PATIENTS WITH GENERAL POPULATION**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Diagnosis</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to 34</td>
<td>Cardiovascular Syphilis</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Syphilitic Aortitis</td>
<td>25.92</td>
</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>26.07</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>38.18</td>
</tr>
<tr>
<td>35 to 39</td>
<td>Cardiovascular Syphilis</td>
<td>20.92</td>
</tr>
<tr>
<td></td>
<td>Syphilitic Aortitis</td>
<td>20.71</td>
</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>21.07</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>33.61</td>
</tr>
<tr>
<td>40 to 44</td>
<td>Cardiovascular Syphilis</td>
<td>16.35</td>
</tr>
<tr>
<td></td>
<td>Syphilitic Aortitis</td>
<td>16.75</td>
</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>16.07</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>29.20</td>
</tr>
<tr>
<td>45 to 49</td>
<td>Cardiovascular Syphilis</td>
<td>12.84</td>
</tr>
<tr>
<td></td>
<td>Syphilitic Aortitis</td>
<td>13.61</td>
</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>12.31</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>25.00</td>
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<tr>
<td>50 to 54</td>
<td>Cardiovascular Syphilis</td>
<td>9.12</td>
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<td></td>
<td>Syphilitic Aortitis</td>
<td>10.31</td>
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<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
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</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>21.08</td>
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<tr>
<td>55 to 59</td>
<td>Cardiovascular Syphilis</td>
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</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>5.53</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>17.40</td>
</tr>
<tr>
<td>60 to 64</td>
<td>Cardiovascular Syphilis</td>
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<td></td>
<td>Syphilitic Aortitis</td>
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</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>5.53</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>14.23</td>
</tr>
<tr>
<td>65 to 69</td>
<td>Cardiovascular Syphilis</td>
<td>1.92</td>
</tr>
<tr>
<td></td>
<td>Syphilitic Aortitis</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>Aortic Regurgitation and Aneurysm</td>
<td>1.89</td>
</tr>
<tr>
<td></td>
<td>General Population†</td>
<td>11.36</td>
</tr>
</tbody>
</table>

(4) Syphilitic cardiovascular disease should be searched for in younger patients than hitherto.

(5) The high incidence of co-existent involvement of the cardiovascular and central nervous systems is demonstrated.

(6) The prognostic value of three factors (precordial pain, T-wave and/or QRS changes, and cardiac decompensation) is suggested.

(7) The incidence of hypertension and sero-reversal, and the x-ray and electrocardiographic findings are presented.

(8) Uncomplicated syphilitic aortitis, if untreated or inadequately treated, shortens the expectation of life.

(9) The results obtained after 5 or more years' observation after penicillin treatment of a small group of patients indicate that penicillin is the drug of choice in this condition.

The authors wish to express their appreciation to the Epidemiology Staff of the Municipal Social Hygiene Clinic, Chicago, for their aid in locating the patients who had lapsed from observation and to the following groups for their cooperation: Chicago Department of Welfare; Bureau of Vital Statistics of the City of Chicago and the State of Illinois; Medical Record Library of Cook County Hospital; and the personnel of the Research Section, Venereal Disease Control Program, Chicago.

REFERENCES
CARDIOVASCULAR SYPHILIS