Cardiovascular syphilis was suspected in one patient who had been treated for secondary syphilis, and in three whose disease was inherited.

Criteria for the establishment of the diagnosis of syphilis are discussed. The great majority of syphilitic patients present undoubted serological evidence of the disease. Time alone will establish the value of the treponemal immobilization test in the remainder.

Difficulties attending the diagnosis of cardiovascular syphilis are briefly mentioned.

Necropsy results in 27 cases confirmed our diagnosis in all but one instance.

REFERENCES

- Cochems, K. D., and Kemp, J. E. (1937). *Amer. J. Syph.*, **21**, 282.
 Cole, H. N., Usilton, L. J., Moore, J. E., O'Leary, P. A., Stokes, J. H., Wile, U. J., Parran, T., and Vonderlehr, R. A. (1936). *Vener. dis. Inform.*, **17**, 91.
 Dressler, M., and Silverman, M. (1943). *Ann. intern. Med.*, **19**, 224.
 Hubert, G. (1919). *Dtsch. Arch. klin. Med.*, **128**, 317.
 Jackman, J., and Lubert, M. (1945). *Amer. J. Roentgenol.*, **53**, 432.
 Kampmeier, R. H. (1944). *Essentials of Syphilology*, p. 300. Blackwell Scientific Publ., Oxford.
 Kerley, P., and Shanks, S. C. (1951). *Text Book of X-ray Diagnosis*, 2nd ed., 2, 129. Lewis, London.
 McDermott, W., Tompsett, R. R., and Webster, B. (1942). *Amer. J. med. Sci.*, **203**, 202.
 Maynard, E. P., Curran, J. A., Rosen, I. T., Williamson, C. G., and Lings, C. (1935). *Arch. intern. Med.*, **55**, 873.
 New York Heart Association (1942). *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*, 4th ed., p. 9. Little, New York.
 Stokes, J. H., Cole, H. N., Moore, J. E., O'Leary, P. A., Wile, U. J., Parran, Thos. jun., Vonderlehr, R. A., and Usilton, Lida J. (1934). *Vener. dis. Inform.*, **15**, 149. Quoted by H. N. Cole *et al.*, *J. Amer. med. Ass.*, 1937, **108**, 1861.
 Turner, T. B. (1930). *Bull Johns Hopk. Hosp.*, **46**, 159.

OUTCOME OF UNCOMPLICATED SYPHILITIC AORTITIS

BY

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There have not been many clinical studies of uncomplicated syphilitic aortitis, and on account of the exceptional difficulties of making the diagnosis few are satisfactory.

Some authors, impressed with the frequency of aortitis as a chance finding at necropsy when it had never caused symptoms during life, have claimed that asymptomatic aortitis carries a normal life-span (Heller, 1927; Schlesinger, 1932; Moore, 1941). Among others who have confined their attention to the disease when it is detectable in life opinion is more varied but still comparatively favourable. Moore (1941) suggested that such patients might expect to live for 10 to 20 years after diagnosis. Kalz and Scott (1955) have recently claimed that the expectation of life is never diminished by uncomplicated aortitis, but O'Brien *et al.* (1955) find that it is shortened by at least 10 years.

All the work on this subject has been done in Germany or America, and no one has attempted to study the problem in this country. It therefore seemed of interest to examine the outcome of uncomplicated aortitis in a group of patients attending a British clinic.

Material and Methods

This paper is based upon the experience of 61 patients with uncomplicated syphilitic aortitis seen for the first time before the end of 1951. They were found during the routine cardiological examination of 1,330 syphilitic patients at a special joint clinic established in 1947 at the Newcastle

General Hospital by Professor Sir William Hume in collaboration with Dr. W. V. Macfarlane, Director of the Department for Venereal Diseases, and Dr. W. G. A. Swan, physician in charge of the Cardiovascular Department (Macfarlane, Swan, and Irvine, 1956).

All patients had a history of syphilis, or signs of the disease in other systems, or positive serological evidence in the blood or C.S.F. The disease was of the acquired type in every case save one, in which it was congenital.

All patients were examined clinically, fluoroscopically, and electrocardiographically, and those suspected of having aortitis were re-examined at approximately annual intervals. All living patients in the group were reviewed in 1954 with the exception of two who reported themselves well but refused to attend for examination. No patient was untraced.

Age and Sex.—There were 37 males and 24 females. The ages ranged from 36 to 73, with an average for the whole group of 56 years (males 58, females 53).

Duration of Infection.—Twenty-four of the men were aware of the probable time at which they acquired their syphilis. In these the average duration of infection before the discovery of the aortic lesion was 27 years (13 to 37 years).

Early Treatment.—Ten of the patients had received some treatment at the time of their initial infection. This varied from a single injection of arsenic in one case to 18 months' treatment and surveillance in another. Only two patients seemed to have received more than one course of arsenic.

Diagnostic Criteria

The essential criterion for diagnosis consisted in fluoroscopic evidence of a dilated aorta detected on more than one occasion and in the absence of aortic incompetence. Hypertensive patients were excluded unless the ascending aorta was calcified (two cases) or unless they subsequently developed aortic incompetence, in which case a diagnosis of uncomplicated aortitis was made retrospectively (two cases). The ascending aorta was calcified in seven patients. There is no reliable measurement of the diameter of the aorta apart from angiocardiology, which was not attempted in the present series. The diagnosis rests on a personal impression, formed at fluoroscopy, that the aorta, particularly in its ascending part, is wider than it should be at any given age. Suspicious cases have been re-examined repeatedly, and consistency has been achieved by the fact that all the fluoroscopy has been performed by one observer, Dr. W. G. A. Swan.

Clinical Features

Forty-seven patients were free of any symptoms referable to the cardiovascular system. Among the remaining 14, breathlessness on effort occurred in 11, angina of effort in 4, other sorts of chest pain in 3, and palpitation in 2. There can be no certainty that any of these symptoms were really due to disease of the aorta, for many patients were at an age when some degree of breathlessness is normal, and they all come from a population in which chronic bronchitis and emphysema are extremely common. Moreover, in those with angina it is probable that this symptom was due to concomitant coronary atheroma rather than to coronary ostial stenosis, and this was proved to be so in one case examined at necropsy. No patient complained of paroxysmal dyspnoea.

In 27 patients there were no abnormal physical signs. In 26 there was a basal systolic murmur and in 23 the second sound was increased. In 15 these signs occurred together.

Survival after Diagnosis

In 1954, 51 of the patients were still alive and 10 were dead. The survivors had been under observation for at least three years, extending to 14 years in one patient, who happened to have been thoroughly examined ten years before the inception of the regular clinic for cardiovascular syphilis. The mean observation period was 5.1 years.

In Fig. 1 the survival of these patients is compared with the expected survival of the general population of the same average age and sex distribution (Registrar-General, 1936). The graph shows that there is no significant difference between the two groups.

FIG. 1.—Uncomplicated aortitis. Survival after diagnosis compared with general population.

Progression

Eighteen patients (30%) showed some mark of progression in the aortic lesion; 15 developed aortic incompetence, which was slight in every case but one. In a further case a transitory early diastolic murmur appeared and was heard for two successive years but not subsequently. This was the only example in which the development of aortic incompetence appeared to be temporary. In two more cases the aortic valve remained competent, but the aorta became more dilated, reaching aneurysmal proportions in one. In 13 cases (12 with aortic incompetence and one without) this progression was not accompanied by the appearance of symptoms when these had previously been absent or by an increase in any disability already present. In these the advance of the disease could not have been detected except by repeated clinical and fluoroscopic examination. There were five further cases in which progression was accompanied by an increase in disability, breathlessness appearing in three and angina of effort in two.

All the patients initially had normal electrocardiograms, but in 6 of the 18 cases showing progression the tracing became abnormal. Of five who developed aortic incompetence the pattern of left ventricular strain appeared in three (two of these were hypertensives and in the other the aortic incompetence was gross); in two others with previous

FIG. 2.—Uncomplicated aortitis. Progression after diagnosis.

angina the patterns of cardiac infarction appeared. One without incompetence, whose aorta became further dilated, also acquired right bundle branch block.

In only two cases was the development of aortic incompetence accompanied by cardiac enlargement.

Time of Progression.—The time at which progression occurred after the original discovery of the aortic lesion is shown in Fig. 2. It is apparent that progression occurred at a fairly constant rate. The average interval before progression was 3.4 years from diagnosis.

Causes of Death.—Progression did not carry any immediate risk to life and only one patient who developed aortic incompetence died of it, and then not for 14 years after the original diagnosis of uncomplicated aortitis. Deaths from causes other than cardiovascular syphilis occurred in nine cases, none of which had shown progression. The cause was a cerebrovascular accident in four; in the other five the causes were liver failure, biliary peritonitis, tuberculous meningitis, carcinoma of the tongue, and pneumonia. Post-mortem evidence is available in only two cases. In both, the clinical suspicion of syphilitic aortitis was confirmed macroscopically and microscopically.

Individual Prognostic Factors

In an effort to study individual factors affecting prognosis the 18 patients whose disease progressed have been compared with the 34 who showed no change. The nine patients who died from other causes without showing progression have been ignored.

Age.—The average age of those who showed progression was 56 years at the time of the first cardiovascular examination. In those remaining unchanged it was 58. The difference is not great enough to suggest that increasing age is a factor tending to favour progression.

Sex.—Twelve males and six females showed progression. In those showing no change the sexes were equally divided—17 males and 17 females. The apparently greater risk of deterioration in males does not reach the level of statistical significance.

Occupation.—The male patients were classified into three occupational groups—light (that is, clerical, sedentary, or supervisory workers), medium (that is, drivers, electricians, fitters, etc.), and heavy (that is, miners, sailors, heavy labourers, etc.). Among those who progressed one was in light work—an insurance agent—six were in medium grades of work, and five in heavy. Of those who showed no change three were in light work, seven in intermediate jobs, and 15 in heavy. These figures do not suggest that occupation has any influence upon progression.

Duration of Infection.—In 8 of the 12 males who showed progression the probable duration of infection was known, and it averaged 27 years. In those who showed no change the figure was identical. There is thus no evidence to support the view that progression is more likely in those whose infection is of longer standing.

Symptoms.—Of the initially asymptomatic cases 10 progressed and 31 showed no change. Of the patients who had symptoms when first seen eight progressed and only three remained unchanged. This would certainly seem to suggest that the presence of symptoms is an adverse prognostic factor; but the point is valid only if it is certain that the symptoms are due to the aortic lesion and not to some intercurrent disease. Such certainty is not a feature of the present series.

Physical Signs.—Of 33 patients with an aortic systolic murmur or an increased second sound 13 progressed and 20 showed no change. Of those without these signs 5 progressed and 14 showed no change. These differences are insignificant, as were analyses of each sign separately.

Radiological Signs.—The degree of aortic dilatation was regarded as slight in 41 cases and more pronounced in 11 others. Of these 11, five deteriorated and six were unchanged. Among the remainder, 13 deteriorated and 28

showed no change. This rather suggests that cases with more advanced degrees of aortic dilatation carry a worse prognosis (a fact which is certainly true if the dilatation amounts to an aneurysm), but these figures do not prove statistically that this is so.

Serology.—The titre of the initial quantitative Wassermann reaction has been studied in relation to the outcome. Among 29 cases in which the Wassermann was strongly positive when the aortic lesion was diagnosed 11 progressed and 18 showed no change. Among those in which the initial Wassermann reaction was doubtful or negative 9 progressed and 14 showed no change. These figures do not suggest that the strength of the initial Wassermann reaction is a factor of prognostic importance. A similar analysis of the change in Wassermann titre in response to treatment failed to show any correlation with the chance of progression.

Treatment

Thirty patients received 15 mega units or more of penicillin. Of the 22 who did not, 15 received some penicillin, usually up to a maximum of 10.7 mega units (average, 9 mega units) while the other seven received arsenic or bismuth only. Symptomatic and asymptomatic cases showed a roughly even distribution between the two groups. Of those who received at least 15 mega units of penicillin, 11 progressed and 19 showed no change. Of the remainder, 7 progressed and 15 remained unchanged. There is thus no material difference between the two groups to suggest that those who received the larger amounts of penicillin did any better than the rest, or that those who received little or no penicillin did any worse than the others.

Discussion

This study shows that there is no appreciable threat to life from uncomplicated aortitis, at least for the first seven years after its discovery, and the only patient to die of cardiovascular syphilis survived for 14 years after his aortic lesion was first detected. These results are in accord with the relatively favourable prognosis given by Moore (1941) and by Kalz and Scott (1955).

Progression to aortic incompetence or to further dilatation of the aorta occurred in just under a third of the patients after an average period of 3.4 years, and the risk of progression appeared to be fairly constant over the first seven years. These figures show a much higher risk of progression than those of any series published hitherto. Thus Hubert (1931) reported that only 11 out of 200 patients developed more serious forms of the disease during six to eleven years' observation. Moore and Metildi (1933) found progression in 19.1% of a group of 115 patients observed for two to eight years. Their figure includes a few cases of syphilitic "myocarditis" whose significance is uncertain. The Co-operative Clinical Group (Cole *et al.*, 1936) found progression in only 8.6% of 267 cases observed for five to fifteen years. Maynard (1942) reported a progression rate of 9.5% in a small series but failed to make clear the length of time over which these changes were observed. Finally, Rich and Webster (1952) noted progression in 15% of 93 patients observed for an average of 6.6 years. They found that progression occurred after an average interval of three and a half years—a figure almost identical with that observed in the present series. Their cases may have been a little less strictly selected than the ones in the present study; for it is not claimed that all of them had radiological evidence of a dilated aorta, and the remainder were diagnosed on the strength of a basal systolic murmur or an accentuated second sound.

The number of progressions noted among the patients under review is thus at least 50% higher than any other comparable series and more than twice as high as the majority. There would seem to be two possible reasons. One is that the patients in the present series were inadequately treated in comparison with those of other authors.

This is unlikely, for two-thirds of these patients received at least 10 mega units of penicillin, which was not available during any previous investigation except that of Rich and Webster.

The alternative explanation may lie in the strictness of the diagnostic standards that have been employed. When comparison is made with other published series reporting the results of routine cardiological examination among patients with syphilis it becomes clear that this is the only one in which fluoroscopic evidence of aortic dilatation has been made the essential criterion for the diagnosis of uncomplicated aortitis. This criterion naturally makes great demands upon the unsupported clinical impression of the observer. There is, however, evidence that it has been critically used, because fewer cases were accepted as examples of uncomplicated aortitis than in any previous comparable series (Macfarlane, Swan, and Irvine, 1956).

The failure to find any prognostic factors of importance is disappointing but not unexpected, since no previous series has had any more success in this part of the investigation.

Summary

In the course of the routine cardiological examination of 1,330 syphilitic patients 61 were detected with probable uncomplicated aortitis.

The diagnosis was made in the presence of a dilated ascending aorta, recognized at fluoroscopy. In seven cases the ascending aorta was also calcified.

These patients were observed at repeated intervals for periods of 3 to 14 years, with an average of 5.1 years.

For the first seven years after diagnosis the expectation of life in these patients was normal, but one died eventually of aortic incompetence after 14 years.

Progression to aortic incompetence or to further dilatation of the aorta occurred at a fairly constant rate and affected about a third of the patients after an average interval of three and a half years from diagnosis.

No factors of undisputable prognostic importance were discovered, but there was some evidence to show that those with symptoms at the time of diagnosis and those with the greater degrees of aortic dilatation did worse than the others.

No appreciable prognostic effect could be attached to age, sex, occupation, the duration of infection, the presence of an aortic systolic murmur or accentuated second sound, the titre of the serum Wassermann reaction, or the amount of antisyphilitic treatment.

The significance of these findings is discussed.

I am indebted to Dr. W. G. A. Swan and Dr. W. V. Macfarlane for the opportunity to study this subject, and for helpful criticism and advice in the preparation of this paper, which is based on part of a thesis for the degree of M.D. in the University of Cambridge.

REFERENCES

- Cole, H. N., Usilton, L. J., Moore, J. E., O'Leary, P. A., Stokes, J. H., Wile, U. J., Parran, T., and Vonderlehr, R. H. (1936). *Vener. Dis. Inform.*, 17, 91.
- Heller, J. (1927). *Dtsch. med. Wschr.*, 53, 1176.
- Hubert, G. (1931). *Z. Kreisforsch.*, 23, 387.
- Kalz, F., and Scott, A. I. (1955). *Canad. med. Ass. J.*, 72, 274.
- Macfarlane, W. V., Swan, W. G. A., and Irvine, R. E. (1956). *British Medical Journal*, 1, 827.
- Maynard, E. P. (1942). *Bull. N.Y. Acad. Med.*, 18, 383.
- Moore, J. E. (1941). *The Modern Treatment of Syphilis*, 2nd ed., p. 280. London.
- and Metildi, P. E. (1933). *Arch. intern. Med.*, 52, 978.
- O'Brien, J. F., Smith, C. A., and Fisher, M. A. (1955). *Brit. J. vener. Dis.*, 31, 74.
- Registrar-General (1936). *Decennial Supplement*, 1931, p. 48.
- Rich, C., and Webster, B. (1952). *Amer. Heart J.*, 43, 321.
- Schlesinger, H. (1932). *Ergebn. ges. Med.*, 17, 331.