have previously criticized the lowness of the reticulocyte responses in some of the cases.³

It appears probable that the manufacture of these products has not been sufficiently standardized or controlled, so that batches of inactive material have been released for use before clinical trials have been carried out—an extremely serious matter where the life of a patient may be concerned. This may account for the occasional reports in the medical literature of cases of true pernicious anaemia "resistant to hog's stomach preparations."

Obviously, rigid clinical control of all material supplied to patients is essential if the safety of a large number of those under medical treatment is to be assured.

I have to thank the honorary physicians of the Manchester Royal Infirmary for allowing access to such patients as were under their care, and the following who have assisted in the blood investigations: Miss A. Bodoano, M.B., Ch.B., Miss M. Johnson, M.B., Ch.B., Miss M. Rickards, B.Sc., Miss B. Porter, B.Sc., and Mr. A. Huntington, M.Sc.

Acknowledgement is also made to the Medical Research Council for assistance in connexion with this work.

REFERENCES

- ¹ Wilkinson, J. F.: *British Medical Journal*, 1930, i, 236; 1931, i, 85.
² Idem: *Proc. Roy. Soc. Med.*, 1931, xxiv, 948.
³ Idem: *Klin. Woch.*, 1931, x, 791.

A NOTE ON AORTIC VALVULAR DISEASE

WITH REFERENCE TO ETIOLOGY AND PROGNOSIS

BY

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Disease of the aortic valves is generally due to rheumatism or syphilis; but the relative importance of these two conditions is very differently estimated. In some series most of the cases have been considered syphilitic, while in others nearly all under the age of 40 have been said to be rheumatic. In the following series of nearly 300 consecutive cases the cause was rheumatic in more than one-half, and syphilitic in about a quarter. Out of every six cases with disease of the aortic valves, acute rheumatism accounted for four, syphilis for one, while atheroma and all other causes were responsible for one or less.

The etiology is summarized below.

TABLE I.—*Etiology in All Cases of Aortic Valvular Disease*

	Acute Rheumatism	Syphilis	Atheroma	Other Causes
Guy's Hospital ...	100	29	9	12
Heart Hospital ...	100	26	11	9
Total ...	200	55	20	21

When rheumatic patients with marked mitral stenosis were excluded, out of every four patients with aortic disease, acute rheumatism was responsible for two, syphilis for one, and all other causes for one or less. Advanced atheroma was present in half of the cases which were not either rheumatic or syphilitic, and was probably the causal factor. Of the twenty-one cases due to "other causes," which will not be further discussed, primary infective endocarditis was responsible for six, and in most of the remainder the cause was unknown. The etiology was adjudged rheumatic when there was (1) a clear rheumatic history (177 cases), or (2) mitral

stenosis, even without this (23 cases). When there was mitral stenosis (confirmed by x rays), only routine inquiries were made for a history of syphilis, and the Wassermann reaction was frequently not done. In the absence of mitral stenosis, careful inquiries for any history of syphilis, and a Wassermann reaction and x -ray examination of the aorta, were included. Patients were placed in the atheromatous group when radioscopy suggested such changes in the aorta in those who could not be included in the two previous groups, or when there were advanced arterio-sclerotic changes in the brachial, radial, or retinal arteries.

Table II shows the different types of valvular disease in the rheumatic group. Of each six cases, roughly

TABLE II.—*Type of Rheumatic Valvular Disease*

	Males	Females	Total
Aortic stenosis and incompetence* ...	24	10	34
Aortic incompetence alone ...	27	15	42
Aortic stenosis and } with mitral stenosis ... {	9	26	35
Aortic incompetence } ... {	37	52	89
Total ...	97	103	200

* Five cases with aortic stenosis had no evidence of aortic incompetence while they were under observation.

speaking, three had aortic incompetence and mitral stenosis, the fourth had aortic stenosis as well, and the fifth and sixth were clinically without mitral disease, one having aortic incompetence alone and the other aortic stenosis and incompetence.

AGE AND SEX INCIDENCE

There were equal numbers of men and women in the rheumatic group, but they were differently distributed. In those without mitral stenosis there were twice as many men as women; in those with mitral stenosis the proportions were two men to three women. In the syphilitic group there were three men to one woman. In the atheromatous group there were seventeen men and only three women. Of those with syphilis nearly 80 per cent. were between 40 and 60, there being no sex difference in the ages; in the atheromatous more than 90 per cent. were over 50. On the other hand, 90 per cent. of the rheumatic cases were between 10 and 50.

The etiology is well shown in Fig. 1; nearly all the

FIG. 1.—Age incidence of three main types of aortic disease.

Note.—Below 40, rheumatism is responsible for nearly all cases; from 40 to 50, it is still a more common cause than syphilis; from 50 to 65, syphilis is the most common cause; after 65, atheromatous changes.

cases under 40 were rheumatic, while after 50 syphilis was the responsible factor twice as frequently as rheumatism, atheroma occupying an intermediate position. With the rheumatic cases the incidence was more evenly spread from 10 to 45, but there was a group of men with aortic stenosis between 45 and 55.

Fig. 2 contrasts rheumatic aortic incompetence with rheumatic aortic stenosis *and* incompetence. Both curves have a similar shape, and make it quite certain that aortic stenosis does not represent a much later stage of

FIG. 2.—Age incidence of rheumatic aortic stenosis, nearly always with incompetence, and incompetence without stenosis.

Note.—Stenosis and incompetence irrespective of mitral stenosis curves are of similar type, that for stenosis being displaced some five years to the right.

rheumatic disease than aortic incompetence. The curve for stenosis is displaced about five years to the right, and this period may represent the usual time taken for stenosis to develop.

BLOOD PRESSURE

In aortic regurgitation due to syphilis, the average diastolic pressure was 60, and the average pulse pressure over 100, varying between 70 and 110 in two-thirds of the cases. In the rheumatic cases the diastolic and pulse pressures were about equal, and represented half the systolic pressure—that is, about 140/70 instead of 120/80. Pure aortic stenosis was rare, and, as would be expected, its pulse pressure was low (it averaged 40), but when there was aortic incompetence the signs of stenosis made little difference to the blood pressure. Evidently rheumatic aortic stenosis does not usually progress far enough to prevent free regurgitation, and often an obvious water-hammer pulse was present, with signs of stenosis and incompetence.

In the atheromatous group, on the other hand, the average pulse pressure was just over 50 when there was aortic stenosis, but 80 when there was aortic incompetence. In a few patients the stenosis had progressed far enough to lead to a very low pulse pressure. The average diastolic pressure was 90, higher than in either of the other groups. In three elderly patients there was independent hyperpiesia.

ELECTROCARDIOGRAPHIC CHANGES

The close association of fibrillation and mitral stenosis is well known. It also holds good where there is also aortic incompetence, and was present in 30 per cent. of these cases. The presence of mitral stenosis was more important than a history of rheumatism, but with rheumatic aortic disease alone fibrillation was still found in 8 per cent. Extrasystoles occurred frequently in about 15 per cent. Paroxysmal tachycardia was noted in four cases. Complete heart block was present in one of the rheumatic group and in one of the others. Two non-rheumatic and five rheumatic patients had right bundle-branch block. Most of the latter had aortic stenosis, and only one had mitral stenosis; all but one were men, with an average age of 44. In addition, three younger patients with rheumatic aortic incompetence had prolonged PR intervals without dropped beats (0.3, 0.24, and 0.22 seconds). In the rheumatic cases with mitral stenosis and aortic incompetence there was little of note as regards preponderance of either ventricle, 23 per cent. showing left, 12 per cent. right, and 65 per cent. being normal. Where there was pure aortic disease (especially when it

was syphilitic) 54 per cent. showed left, and only 2 per cent. right ventricular preponderance, 44 per cent. being normal.

In nearly one-third the T waves were inverted in leads I or II. Where there was mitral stenosis and aortic incompetence, 10 per cent. showed inversion of T in lead I (and sometimes in lead II), and 5 per cent. showed inversion of T in leads II and III, the remainder being normal. The results were very different when aortic disease occurred alone, for 36 per cent. of these showed inversion of T I (sometimes in lead II also, and only a few inversion of the T waves in all leads). Again, 7 per cent. showed inversion of T in leads II and III, and again there was not much difference between the various etiological groups. Among the rheumatic and syphilitic patients curves of unusually high voltage were not uncommon, no curves of low voltage being found. Among the atheromatous patients there were several examples of both these varieties.

PROGNOSIS

This series does not bear out the view that aortic stenosis is an unimportant lesion in elderly patients, for in the atheromatous group, where it was common, 30 per cent. have died while under observation. In the syphilitic group 26 per cent. have died, and even in the rheumatic group 16 per cent. have died, but eight of these died from acute rheumatic carditis and four from infective endocarditis. The other rheumatic patients died from congestive heart failure, generally secondary to fibrillation; and there were no sudden deaths. On the other hand, in the atheromatous and syphilitic groups twelve had congestive failure with normal rhythm, four died absolutely suddenly without preliminary failure, and two died from acute pulmonary oedema. As most of the rheumatic patients are still alive at an average age of 35 years, this only gives one side of the picture. Their aortic disease had developed, on the average, about fifteen years before, at a time when they had rheumatic fever—that is, most of them had already lived for twenty years, and many were still in good health. Admittedly this is an average which gives little guidance in the individual case, because the prognosis depends so much on the condition of the heart muscle. In some of the rheumatic patients the evidence was more complete—for example, a doctor had been told as a student that he had aortic incompetence, was later rejected for life insurance for the same reason, but had successfully carried on his practice, almost without symptoms, until he was 62. Altogether there were more than twenty of the older patients who knew that their hearts had been affected at an average age of 16 years, but were alive and often in good health thirty years later.

In the other groups it was not possible to find patients in whom the disease had lasted so long, but their natural expectation of life was much less, as they were older when the condition developed—for example, in the syphilitic group the average was 49, and in the atheromatous group 61 years. Where it was definitely known, infection with syphilis had occurred, on an average, twenty-five years previously, but during the greater part of this period there would certainly have been no evidence of regurgitation. Five patients with syphilitic aortic incompetence were in relatively good health after six to eight years, but experience of this series agrees with that of many other observers that a large number of such patients die within two years of developing symptoms. This is a very striking contrast to the average expectation of more than twenty years in the rheumatic cases. In the past much of the gloomy prognosis attaching to disease of the aortic valves has depended on the failure to differ-

entiate the rheumatic and syphilitic cases. It is very rarely that this distinction cannot be made with certainty, though sometimes it may be more difficult to differentiate the atheromatous and syphilitic cases. One reason for this contrast is the association of syphilitic aortic incompetence with angina pectoris. In both groups of non-rheumatic patients this was a common finding; frequently, indeed, it was a main presenting symptom, and occurred in 40 per cent. In those with syphilis, nocturnal angina was not uncommon, and often the pain lasted for longer than the usual angina of effort. On the other hand, angina occurred in less than 5 per cent. of the rheumatic patients. These were mostly men with an average age of 45, and all but one had aortic stenosis.

SUMMARY

In a series of cases with disease of the aortic valves, the condition was due to rheumatism in 200, to syphilis in 55, to atheroma in 20, and to all other causes in 21 cases.

Out of every six rheumatic cases, roughly, three had aortic incompetence and mitral stenosis, one had both with aortic stenosis as well, one had aortic stenosis and incompetence, and one had aortic incompetence alone. When there was no mitral disease there were two men for each woman; when there was mitral disease there were two men for every three women. They came under first observation at all ages, least commonly before 10 or after 50. There was so little difference between the ages of those with and those without aortic stenosis that its presence must depend on the severity and nature of the attack rather than on the length of time that had elapsed. Pure

aortic stenosis was rarely found, and, as far as could be judged from the pulse pressure, the stenosis was relatively unimportant compared with the regurgitation, even where the signs were well marked.

Among the syphilitic cases there were three men for each woman, nearly four-fifths being between 40 and 60. Aortic stenosis was rarely or never present, and the average pulse pressure was much greater than in the rheumatic cases (110 instead of 70).

Nearly all the atheromatous cases were men, between 50 and 80. Aortic stenosis was more important and more frequently present, the signs of regurgitation being often absent.

Auricular fibrillation was present in 30 per cent. of those who had also mitral stenosis, in 8 per cent. of the rheumatic cases without mitral stenosis, and only rarely in the non-rheumatic group.

Left ventricular preponderance was found in about half the electrocardiograms of those with pure aortic disease, normal limits being found in the remainder. The T waves were inverted, most often in lead I, in about one-quarter of the rheumatic cases and in about half the others.

The prognosis was enormously better in the rheumatic group. The average duration of life after the development of aortic incompetence was probably twenty years, excluding those who died quickly from active rheumatic carditis. In the syphilitic group, on the other hand, it was not much more than two years after the development of symptoms, few patients living for eight years.

We wish to thank Dr. Parkinson, and the physicians of Guy's Hospital, for allowing us to refer to patients under their care.

A SIMPLE TECHNIQUE FOR PHOTOGRAPHY OF PATHOLOGICAL SPECIMENS

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The importance of photography as a means of recording morbid anatomical specimens is increasingly recognized. The photograph is accurate, impressive, and easily interpreted; a good photograph with a few words of description gives a better idea of a specimen than does a whole page of descriptive matter alone; moreover, photographs are readily comparable one with another. The only difficulty is to obtain sufficiently good photographs. Technique is the essence of photography, and the busy pathologist or physician has little time to acquire it, while the professional photographer is severely handicapped by his ignorance of what is required. In these circumstances the following description of a simple technique is perhaps opportune. The essence of the method is standardization and the elimination as far as possible of the necessity for technical skill.

Apparatus

Camera.—Any camera capable of taking close-ups and with an aperture stopping down to $f/45$ will suffice; we use a Kodak x -ray reducing camera, and find it quite satisfactory. The stand should be adjustable for height and be capable of inverting the camera in order to take pictures directly downwards.

Illumination.—This is standardized by using a wooden box $20 \times 20 \times 15$ inches. In the place of a lid a wooden shelf $4\frac{1}{2}$ inches wide is fitted round the top of the box on the inside; this should slope downwards at an angle of 60 degrees from the horizontal, leaving an opening 11 inches square in the centre. This "roof" rests on the edges of the four

sides and is instantly removable. In each of the four upper corners of the box a 100-watt frosted bulb is fitted, so placed as to be invisible from above when the "roof" is in position. The four bulbs are wired in series, and the box fitted with a switch and a wall plug; each bulb may be independently controlled by its own switch, but this is unnecessary. In one side of the box a door of "lift-out" type, 14×8 inches, is provided. The sides of the box and the under side of the "roof" are painted white, the floor being a dull neutral colour; the upper surface of the "roof" is painted matt black.

The remainder of the apparatus consists of a straight-sided glass bowl 10×4 inches, a circle of ebonite of slightly smaller diameter than the bowl, and four wooden blocks each $1 \times 2 \times 4$ inches.

Preparation of Specimens

To prevent spoiling the picture by glistening of the "high lights" the object is photographed under water, and for this reason specimens are best fixed by Kaiserling's method before being photographed. This obviates the risk of blood staining the water, and the specimen is unharmed by its immersion should it be required for permanent preservation later. The specimen is immersed in Kaiserling's solution "A" as soon as possible after death, and left for a week or more. A thick bed of cotton-wool is always used to ensure that the specimen is not distorted by its own weight, and it is sometimes a good plan to pin a specimen on a piece of board in roughly the position in which it is desired to photograph it. Membranous structures such as heart valves, cyst walls, or fascial bands are carefully coaxed into the required position by packing with cotton-wool, while brains are suspended in the solution by a string passed beneath the basilar artery. The solution requires to be changed after the first twenty-four hours.

After fixation any packing, etc., is removed, and the specimen placed in water. In the great majority of cases it sinks unevenly or not at all, some unimportant portion obtrudes itself into prominence, and many unsuspected fatty and fascial tags float upwards to spoil the outline. The