Results

The tablet test could regularly detect a protein concentration of 0.005 g. per 100 ml. of urine : at 0.0025 g. per 100 ml. detection of proteinuria was inconstant. It was equally sensitive to the different proteins tested, and throughout the pH and specific gravity ranges which were examined. The tablets appeared to be stable, and tablets which had been stored at room temperature for three months were as effective as at the time the bottle of tablets was first opened. The solution test was also sensitive to 0.005 g. per 100 ml. and usually to 0.0025 g. per 100 ml., and the boiling test was regularly sensitive to 0.0025 g. per 100 ml. while inconstant results were obtained at 0.001 g. per 100 ml.; both these tests were also unaffected by the nature of the protein and the pH or specific gravity of the urine.

The ingenious internal indicator of the tablet test enables successful correction of the pH of alkaline urines. The urines of pH 7 sometimes needed two tablets, and the urines of pH 8 needed two or three tablets. (The solution test adds the equivalent of four tablets when properly performed, and the problem of excessive alkalinity of the urine therefore very rarely arises.) However, minimal turbidity was more difficult to detect in the resulting deeply coloured yellow solution.

Both the tablet test and the solution test gave a positive reaction with Bence Jones protein and a negative reaction with urates in solution.

The radio-opaque substances do not precipitate on boiling. They give a pseudo-positive reaction (deposit of crystals) with the solution test, and a negative reaction with the tablet test (one or two tablets). This is a quantitative and not a qualitative difference, because when four tablets were added to 4 ml. of urine containing these substances precipitation immediately developed.

Fifty consecutive urines, received in the department for routine examination, were tested for protein in parallel by the solution test and tablet test. (Fifteen urines required two tablets, and two urines required three tablets.) Twelve of these contained protein in varying concentration, and identical positive results were given by the solution test and the tablet test.

Discussion

Two previous reports (Bryan, 1956; Whittet, 1956) have briefly described the altest without critically examining its properties.

Possible users of the tablet test are general practitioners who have to test occasional specimens of urine in their patient's home or in their consulting-room, or nurses, students, or laboratory technicians who have to test larger numbers of urine specimens on frequent occasions.

The tablet test can be recommended for general practitioners. It is sufficiently sensitive for all clinical purposes. It is simpler and much more convenient than the boiling test, though it is less sensitive than this test. The great convenience to the practitioner of having to carry a bottle of small tablets rather than a bottle of acid liquid reagent outweighs, in our view, the slight disadvantages of the tablet test when compared with the solution test.

However, for frequent use in a laboratory or side room we consider that the tablet test does not replace the salicylsulphonic acid solution test. Although the tablets are inexpensive, the salicylsulphonic acid solution (which is also stable) can be prepared in bulk by a hospital at less than half the price of the tablets. The tablet test is slightly slower, because of the time necessary to dissolve the tablets and disperse the froth which otherwise interferes with the reading. The tablet test does not seem to be quite as sensitive, probably because the colour of the indicator makes it less easy to read; this could probably largely be remedied by reducing the quantity of bromocresol green. When the solution test is done, using the proper technique, enough salicylsulphonic acid is added to counteract all but the grossest alkalinity.

We must deplore the manufacturer's name for the tablet, altest, because it perpetuates the "albuminuria" fallacy.

Summary

A new manufactured tablet (altest) has been compared with the boiling test and the salicylsulphonic acid solution test. It can detect a concentration of 0.005 g. of protein per 100 ml. of urine throughout the physiological range of urine pH and specific gravity, and the results of the tablet test are generally comparable to those of the salicylsulphonic acid solution test, but are slightly less sensitive than the results of the boiling test.

The tablets contain an indicator which shows when additional tablets need be added to ensure acidity of the solution. The advantages and disadvantages of the new test are discussed.

We thank the Ames Company (London) Limited for supplies of altest, and the department of radiology, Royal Free Hospital, for the urine specimens containing the contrast media.

REFERENCES

- Bryan, G. (1956). *Brit. overseas Pharm.*, **109**, 120.
Harrison, G. A. (1947). *Chemical Methods in Clinical Medicine*, 3rd ed. Churchill, London.
Whittet, T. D. (1956). *Pharm. J.*, **177**, 19.

Medical Memorandum

Marfan's Syndrome

A small number of patients with Marfan's syndrome (Marfan, 1896) have come to necropsy (Reynolds, 1950; Moses, 1951; Marvel and Genovese, 1951; Whittaker and Sheehan, 1954; McKusick, 1955). A further case, in which Marfan's syndrome was associated with a patent ductus arteriosus and aortic aneurysm from cystic medionecrosis of the aortic wall, is here reported.

CASE REPORT

A married woman aged 32 was admitted to hospital on December 22, 1954. At 18 months of age she had nephritis and an enlarged heart. When 5 years old she was said to have valvular heart disease. She was dyspnoeic as a child, and later had winter bronchitis. From the age of 18 she had oedema of the ankles. Since 1950 she had had attacks of gripping pain in the left chest which radiated into the left arm and occurred both at rest and on exercise. In 1952 she collapsed with a sudden attack of pain in the back and fullness in the chest. After recovery she was breathless on slight exertion and had persistent ankle oedema and attacks of palpitation. For the last six months she had nocturnal dyspnoea accompanied by sweating and palpitations and a gripping retrosternal pain radiating into the left arm. Two weeks before admission a pleuritic pain developed in the middle and lower thoracic regions of the back with dyspnoea, cough, and increased ankle swelling. These improved slightly with digitalis and rest, but her condition again deteriorated.

Examination showed her to be thin, orthopnoeic, and cyanosed. She had arachnodactyly; height 68½ in. (1.74 m.); palate highly arched. No changes in eyes, and no other skeletal deformities. She was in congestive heart failure; pulse regular, rapid, and collapsing; blood pressure 140/40 mm. Hg; femoral pulses palpable. Bed shook with each heart-beat; visible arterial pulsation in neck. Cardiac impulse moved anterior chest wall. Apex beat in 9th left intercostal space in posterior axillary line. Systolic pulsation felt over most of praecordium. In left axilla between 5th and 9th intercostal spaces a loud rumbling diastolic murmur and a blowing pansystolic murmur heard. Below left clavicle, in pulmonary area, and down left sternal

edge, soft diastolic and blowing systolic murmurs heard. Pulmonary second sound accentuated. Spleen not felt; no ascites.

Radiography showed a huge heart with a dilated ascending aorta; lung fields were mottled, suggesting left-sided failure. Electrocardiography showed right and left ventricular enlargement. There was moderate anaemia (Hb 67%). Wassermann reaction negative.

This patient was thought to have Marfan's syndrome with a heart lesion. Aortic regurgitation and patent ductus arteriosus were considered. A diastolic and systolic murmur heard below the left clavicle favoured the latter diagnosis. Marfan's syndrome is, however, more commonly associated with aortic regurgitation and dilatation of the ascending aorta (Reynolds, 1950).

For the first two days her condition improved. She was digitalized and given a course of soluble penicillin. Two days later there was a sudden onset of dyspnoea, cyanosis, and coma; the pulse was rapid and feeble until she died a few minutes later.

POST-MORTEM FINDINGS

Anatomical Diagnosis: Massive haemopericardium. Patent ductus arteriosus with aneurysm of the aorta associated with cystic medionecrosis. The aneurysm had ruptured. Marfan's syndrome. **Internal Examination:** There was brown induration of both lungs, and mucopus was present throughout the bronchial tree. The oesophageal and gastric mucosae, spleen, and pancreas were congested. There was early cardiac cirrhosis in an enlarged liver.

Cardiovascular System.—The heart was greatly enlarged. The pericardial sac was distended by about 850 ml. of blood. Both ventricles were hypertrophied and dilated. The left auricle was normal in size and thickness, but running on its anterior surface, in a linear fashion, was an irregular area of calcified scarring, partly raised above the surface. The mitral valve showed slight nodularity along the free margins, which were fibrotic and not calcified. There was dilatation of the aortic ring and regurgitation, but the aortic cusps were normal. The pulmonary artery was greatly dilated, its greatest circumference 10.5 cm. The ductus arteriosus was widely patent and had a diameter of 0.8 cm.; it opened into the aorta at the usual site just distal to the origin of the left subclavian artery. The ascending aorta and arch were grossly dilated and thinned as far as the ductus arteriosus, mainly involving the right lateral wall. The external site of rupture of the aorta was posterior, at the uppermost part of the pericardial sac, and at this point communicated with the lumen at the top end of a long vertical split of the media which extended down the left posterior part of the aortic wall as far as the left anterior sinus of Valsalva, just missing the left coronary orifice. There was a separate transverse crack involving the intima on the posterior wall of the aorta and measuring 4 cm. The whole internal surface of the dilated part of the aorta was roughened, resembling tissue-paper scarring from previous intimal ruptures which had become covered by fresh endothelium. The aorta below the ductus appeared normal in calibre and showed atheroma. The other parts of the heart were normal.

HISTOLOGY

The thickened intima of the aorta showed fibrosis and hyaline change with some fragmentation and loss of elastic tissue. In the media there was marked fragmentation of elastic tissue. Between the elastic fibres were spaces, some empty, but others containing material which stained positively with mucicarmine. There was patchy atrophy of medial smooth muscle with partial replacement by fibrous tissue, and very marked hyaline thickening of the adventitia, which contained numerous dilated vessels.

These changes resemble those described by Erdheim (1929) as idiopathic cystic medionecrosis. The area of calcification and scarring in the left auricle showed a rather acellular hyaline thickening of the endocardium. There was much less elastic tissue than normal, and this change was asso-

ciated with marked fragmentation. Deposits of calcium salts were present in the hyaline area. This appearance has previously been described in the left auricle in cases of Marfan's syndrome (Baer *et al.*, 1943).

COMMENT

The dilatation of the ascending aorta with cystic medionecrosis of the aortic wall is considered to be characteristic of Marfan's syndrome. Erdheim (1929) described the following histological changes in the ascending aorta: (1) rarefaction of the media with disarrangement of the elastic tissue; (2) absence of a definite internal and external elastic lamina; (3) atrophy of the muscle with irregular branching of the fibres, separated by cystic spaces; (4) small blood vessels starting in the adventitia and penetrating into the media; and (5) slight thickening of the intima.

As in this case, death from rupture of the weakened and dilated ascending aorta is common in Marfan's syndrome. The history and necropsy findings suggest that there had been a previous small rupture of the aortic wall.

Patent ductus arteriosus associated with arachnodactyly is sometimes said to have been described by Apert (1938). He describes the heart lesion as "une bécane du trou de Botol," which has been wrongly translated as "a patent ductus arteriosus." He was, however, referring to a patent foramen Botalli or patent foramen ovale. Later in his paper Apert mentions a similar patient (Parkes-Weber, 1933) who had a patent foramen ovale.

More recently (McKusick, 1955) reference has been made to the association of patent ductus arteriosus and Marfan's syndrome. The present case demonstrates the skeletal changes of Marfan's syndrome and the characteristic aortic lesions accompanying a patent ductus arteriosus. Records of three other aneurysms of the ascending aorta with patent ductus arteriosus that have come to necropsy have been found (Caylor, 1918; Hubeny, 1920; Hall, 1926). In the patients of Caylor and of Hall the histology of the ascending aorta resembles that described by Erdheim as cystic medionecrosis, which is closely associated with Marfan's syndrome. In Hubeny's patient the aneurysm of the ascending aorta was considered to have had a syphilitic origin. In these cases there is no mention of the other changes in Marfan's syndrome, but they may represent *formes frustes*.

I would like to thank Dr. Maxwell Telling for permission to publish this case, and Dr. I. M. P. Dawson for the post-mortem report.

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REFERENCES

- Apert, E. (1938). *Nourrisson*, 26, 1.
Baer, R. W., Taussig, H. B., and Oppenheimer, E. H. (1943). *Bull. Johns Hopk. Hosp.*, 72, 309.
Caylor, H. D. (1918). *Trans. Chicago path. Soc.*, 10, 296.
Erdheim, J. (1929). *Virchows Arch. path. Anat.*, 273, 454.
Hall, E. M. (1926). *Arch. Path. (Chicago)*, 2, 41.
Hubeny, M. J. (1920). *Amer. J. Roentgenol.*, 7, 23.
McKusick, V. A. (1955). *Circulation (N.Y.)*, 11, 326.
Marfan, A. B. (1896). *Bull. Soc. méd. Hôp. Paris*, 13, 220.
Marvel, R. J., and Genovese, P. D. (1951). *Amer. Heart J.*, 42, 814.
Moses, M. F. (1951). *British Medical Journal*, 2, 81.
Parkes-Weber, F. (1933). *Lancet*, 2, 1472.
Reynolds, G. (1950). *Guy's Hosp. Rep.*, 99, 178.
Whittaker, S. R. F., and Sheehan, J. D. (1954). *Lancet*, 2, 791.

The third All-India Conference on Family Planning was held in Calcutta from January 5 to 10. The urgency of India's population problem was summed up by the Governor of West Bengal, SRIMATI PADMAJA NAIDU, when he opened a family planning exhibition, as follows: "If this mistake of increasing our population is not effectively checked, all our schemes of the second Five-year Plan for national development will prove to be pitifully inadequate." Among the subjects discussed at the conference were the shortage of family planning clinics and suitably trained staff for them; the use of group discussion to familiarize husbands and wives with the work of the clinics; marriage guidance; the use of metaxylhydroquinone as an oral contraceptive; and the Government's contraceptive-testing centre in Bombay.