The exacting routine of repeated applications of gentian violet, silver nitrate, and tannic acid solutions to produce a dry smooth coagulum is well justified by results.

We are indebted to Major H. G. Hobson, R.A.M.C., for permission to record these cases, for much help in carrying out their treatment, and for advice and many hints in recording them.

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HEPARIN IN SUBACUTE BACTERIAL ENDOCARDITIS

BY

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The therapeutic results of the treatment of subacute bacterial endocarditis with heparin and sulphonamide as recorded in American journals (Kelson and White, 1939; Friedman, Hamburger, and Katz, 1939) are noteworthy, and justify the report of a case treated in this way. The American reports must be mentioned, but space does not permit of their discussion. They do not give an account of the bacteriological investigation and controls done in every case, and thus leave their claim to diagnosis and complete cure often open to doubt. For this reason frequent bacteriological tests were performed and recorded in the investigation of the present case.

Case Report

A girl aged 19 was admitted to Dr. Steevens' Hospital for observation. She suffered from recurrent rheumatic swellings of the joints and an old-standing mitral lesion of the heart. Her present complaints were a swollen and painful left ankle and hip, great weakness, and sweating. On physical examination she appeared normally developed, and among the abnormal findings were painful periarticular swellings of the left ankle and hip, increased heat over these joints, and some degree of limitation of lateral rotation and flexion of the hip-joint. The heart was moderately enlarged and a loud systolic murmur was present in the mitral area. During the first three weeks the patient was under observation she ran an intermittent moderate temperature, which reached 101° F. on numerous occasions. She was listless, and often delirious at night. The urine contained some albumin, a few leucocytes, and a large number of red blood cells. The blood showed a moderate degree of secondary anaemia. The blood culture was positive after thirty-six hours, the organism being *Strep. viridans*. During the following week the patient's condition deteriorated; the albuminuria became more severe, and a chain of petechial spots broke out around the neck. A blood-agar plate made with 1 ml. of her blood grew 220 colonies of the organism.

Treatment consisted of the following therapeutic agents: (1) sulphapyridine (M & B 693) was given to combat the bacteraemia; (2) heparin (the preparation liquemine of Roche Products Ltd.) was given as the anti-coagulant and probably fibrolytic agent; (3) vitamin C was administered freely to aid fibrous repair as recommended by Kelson and White.

The sulphapyridine was given orally powdered in milk, and occasionally, when vomiting was too severe, by injection. The concentration of the drug in the blood was estimated daily by Werner's (1939) method. The heparin powder was made up in 350-mg. lots and autoclaved in 1 litre of saline or glucose saline. After a priming injection of 40 mg. in 5 ml. of saline the heparin was given by continuous intravenous drip—15 to 18 drops per minute, running for nine days in succession.

An efficient control over such a slow and prolonged drip was easily obtained by the use of the rotary-pump transfusion apparatus. The effect of the drug was watched by the estimation of the clotting time by Lee and White's method (four tubes); the prothrombin time was also estimated. Vitamin C was administered in 200-mg. doses four-hourly until there was a free urinary overflow of the vitamin. A maintenance dose of 100 mg. daily was then given.

The analytical data are shown in the accompanying table.

Day of Active Treatment	Heparin (ml. in 24 hrs.)	Sulpha-pyridine (gm. in 24 hrs.)	Total Sulpha-pyridine of Blood (mg. per 100 c.cm.)	Clotting Time (minutes)	Prothrombin Time (minutes)
1st		3		7	12
2nd		3		8	10
3rd		2.5		8	10
4th	510	5.5		70	10
5th	775	3	6.0	105	12
6th	550	5.5		110	
7th	700	6	7.2	115	14
8th	500	6	9.6	130	12
9th	700	6	8.0	100	12
10th	800	6			
11th	600	6			
12th	300	6		10	

The effect of the treatment was dramatic—the heparin acted promptly, increasing the clotting time from seven minutes to over one hour. The patient came out of the listless condition, began to take interest, and even sat up in bed reading a novel. No new petechiae formed and the old ones disappeared altogether; a large subcutaneous node on the right temple also disappeared. Towards the end of the period of treatment the albumin in the urine had become much more scanty. The temperature was around normal levels during the administration of the sulphapyridine. This drug was badly tolerated at the beginning; it was discontinued on the twelfth day of treatment, when the blood count revealed a moderate leucopenia with a very toxic appearance of the white cells. All blood cultures made during the administration of sulphapyridine remained negative. Eight days after the sulphapyridine was discontinued the patient broke out in a diffuse papulo-macular rash accompanied by a sharp peak of temperature up to 104° F. The rash was quickly followed by desquamation. A blood-agar plate made with 1 ml. of the patient's blood on that day gave rise to over 400 colonies of *Strep. viridans*. In the following week petechiae came out in repeated fresh crops. Osler's nodes appeared on the palms of the hands. The patient fell back into the same state as before treatment was started and gradually became worse. She lived for almost three months after treatment had been stopped.

The post-mortem picture confirmed the clinical diagnosis. There was an old-standing endocarditis of the left auricle and of the cusps of the mitral valve, parts of which were completely destroyed and replaced by granulations. Large infarcts were present in the spleen and kidneys.

Conclusion

Heparin proved to be a powerful anti-coagulant. It exhibited its action in a concentration of 350 mg. per litre, whereas a concentration of 250 mg. per litre remained without effect. The combined treatment with heparin and sulphapyridine was only of very transient value. This does not, however, disprove the theoretical value of its application, considering the few occasions it has been used.

We are indebted to Messrs. Roche Products Ltd. for generously making available to us without charge a sufficient supply of heparin for use in this case.

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