kg. per day, for six months. Neither streptomycin nor *p*-aminosalicylic acid, nor any other drug, was used during this period. There was an almost regular improvement in general health, a gain in weight was usual, but the local tuberculous lesions fared no better and no worse than we would have expected had no drug been used.

We wish to record our gratitude to the members of the consultant staff of the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, who transferred to our care patients whom we thought suitable for this therapeutic trial; and also to Bengers Laboratories Ltd., for supplies of the drug and for the performance of most of the chemical tests and tests of sensitivity.

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MASSIVE LEFT ATRIUM AND MITRAL VALVOTOMY

BY

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The frequency with which massive (aneurysmal) dilatation of the left atrium in rheumatic mitral valve disease is associated with predominant mitral incompetence (Parsonnet *et al.*, 1946; Daly and Franks, 1949) has been a factor against attempting mitral valvotomy in such cases (Baker *et al.*, 1952). The case reported here is of interest in that the physical signs were purely those of mitral stenosis, which was confirmed at and relieved by a subsequent valvotomy.

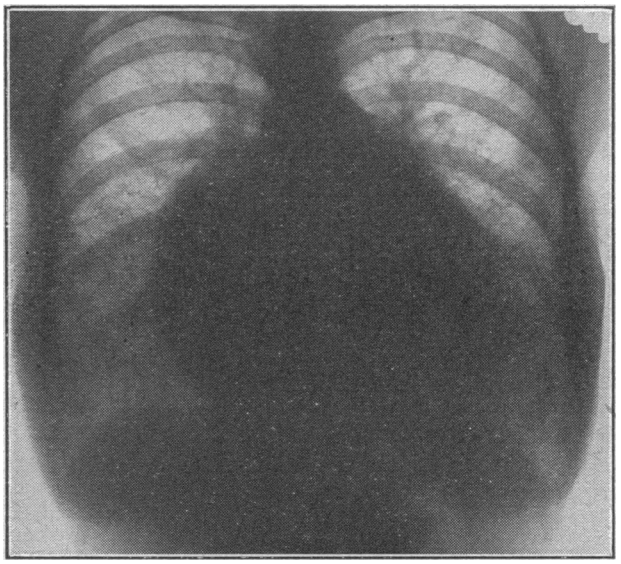
Case Report

The patient, a nulliparous housewife aged 33, gave no history of rheumatic fever. Her heart lesion was first discovered at a National Service medical examination at the age of 23. By the age of 26 she had begun to be aware of dyspnoea on exertion and to have recurrent attacks of winter bronchitis. Her effort tolerance steadily decreased; from the age of 30 onwards she rarely left her second-floor flat because of inability to walk upstairs or more than 50 yards on the level. She used extra pillows at night, but had had no nocturnal attacks of dyspnoea. There had been no haemoptyses, nor congestive cardiac failure with oedema. She had atrial fibrillation, which was presumed to have been present for some years, for she had had a cerebral embolism at the age of 28 and had been on digitalis since the age of 25.

On examination she was very thin, with a pronounced mitral facies, and was dyspnoeic talking at rest. The pulse was of moderate volume, and the blood pressure was 125/80. The jugular venous pressure was not raised and showed no abnormal pulsation. The apex was in the fifth space outside the mid-clavicular line and was tapping in character. There was a widespread systolic heave to the left of the sternum. The first heart sound was loud and abrupt; the second sound was increased in the pulmonary area, with first-degree splitting; there was a very loud mitral opening snap, and a long rumbling grade 3 mitral diastolic murmur at the apex. Systolic murmur was not heard. She had impaired resonance to percussion over the right lower chest posteriorly. There was no hepatic enlargement or pulsation.

Radioscopy of the chest showed a large dense heart shadow, mainly due to gross enlargement of the left atrium (see Fig.). No pulsation of the atrium was apparent in either the anterior or the oblique views. The pulmonary arteries were considerably enlarged; the aortic knuckle could not be clearly distinguished; and no calcification of the valve cusps was detected. The electrocardiogram (multiple unipolar leads) showed atrial fibrillation and considerable right ventricular preponderance.

At cardiac catheterization the following observations were made at rest:—Pressures (in mm. Hg to mid-point of chest): right atrium, mean 4; pulmonary artery, 52/26, mean 34; pulmonary capillary, 23/18, mean 20. Cardiac output,



Radiograph of the chest. Radioscopy showed that the right border of the heart in this view is formed by the left atrium, which owing to its size and density obscured the outline of the right atrium.

2.4 litres a minute. Cardiac index, 1.7 litres/sq.m./min. Blood oxygen saturation: pulmonary artery, 59%; brachial artery, 96%. Blood oxygen combining power, 17.7 ml./100 ml. Calculated pulmonary arteriolar resistance, 560 dynes/sec./cm.$^{-5}$

As her disability was considerable and her physical signs were those of mitral stenosis, mitral valvotomy was carried out by Mr. R. C. Brock on January 21, 1954. The pressure in the pulmonary artery was 48/27, mean 34 mm. Hg; and in the left atrium was 25/19, mean 21 mm. Hg. The enormous size of the atrium was confirmed. A large amount of old and recent thrombus was encountered in the appendage and in the body of the atrium, much of which was washed out by permitting free bleeding. It was regarded as impracticable to attempt to remove all clot from the atrium. Embolism of the carotid vessels was guarded against by occluding them by tapes while the valve and deeper parts of the atrium were explored. To the examining finger the valve orifice appeared to be about 4 mm. in diameter; the edges were fibrous, but no calcium was felt in the cusps; no regurgitation could be detected. Complete separation at both commissures was effected by means of a valvotome. The chordae tendineae were fibrous and fused, but the cusps opened completely at the medial commissure and partly at the lateral commissure. The resulting valve orifice was large and there was a little regurgitation.

Three weeks after the operation she was able to walk up three flights of stairs; at the time of writing her exercise tolerance was still improving.

Comment

The case of massive left atrium reported by Parsonnet *et al.* (1946) showed gross rheumatic mitral incompetence at necropsy. A review of the reported rheumatic cases suggested that this association was invariable, and they concluded that mitral incompetence was a causal factor in the production of massive left atrium, and that mitral stenosis was not. Similarly, Daly and Franks (1949) found clinical evidence of mitral incompetence in all their 15 cases of massive left atrium.

It is generally agreed that the severe fibrosis and loss of muscle fibres seen in the atrial wall in this condition are evidence of particularly severe local damage from the original rheumatic process, and that this is the prime causal factor of the extreme dilatation. Observation that the pressures in the left atrium are as high in mitral stenosis as in mitral incompetence (Venner and Holling, 1953) suggested that mitral incompetence need not be a concomitant factor, and it was of particular interest to observe this patient, in whom the physical signs were clearly those of mitral stenosis and in whom the left atrial pressure (at operation) was only moderately increased.

The diagnosis of mitral incompetence is difficult, and many of the accepted physical signs are unreliable, especially when there is also stenosis—although it seems to be general experience that where the physical signs are purely those of mitral stenosis alone (tapping apex beat, slapping first heart sound, mitral opening snap, rumbling apical mid-diastolic murmur), incompetence of an important degree is not found at operation. The case reported here offers a further illustration of this point and also shows that massive dilatation of the left atrium is not unequivocal evidence of mitral incompetence. In rheumatic heart disease both massive left atrium and gross mitral incompetence appear to result from a particularly severe rheumatic injury and their observed association probably depends on this fact alone.

I wish to thank Dr. C. G. Baker and Mr. R. C. Brock for encouragement to prepare this report.

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INTRA-ARTERIAL THERAPY IN OCCLUSIVE VASCULAR DISEASE

BY

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Degenerative arterial disease of the lower limbs produces intermittent claudication, ischaemic necrosis, or both. At the present time it is not possible to reverse this degenerative process. Consequently, treatment aims at the opening up of a collateral circulation and the abolition of sympathetic tone. Since occlusive vascular disease affects all the vessels in some degree, the best that can be hoped for is the maximal dilatation of all the arteries in the limb. In order to obtain the greatest local effect without a general vasodilatation, injection of drugs direct into the femoral artery has been advocated. Trying a series of drugs, Edwards *et al.* (1952) found papaverine and tolazoline (benzyl-imidazoline, or "priscol") to be most effective in their action, and reported some success in the treatment of these cases.

Selection and Technique

The present investigation was deliberately kept on an entirely clinical basis, as the object was to assess the value of these two drugs as a routine method of treatment in a busy peripheral vascular clinic. No attempt was made to measure the effects instrumentally by temperature change, oscillometer, or claudicometer. It was thought that if such therapy was to be of practical value it must produce symptomatic improvement. With this in mind the following procedure was adopted. Any patient arriving at the peripheral vascular clinic suffering from intermittent claudication or ischaemic necrosis due to occlusive vascular disease was, without selection, started on a course of injections. The first 20 were given papaverine and the next 20 tolazoline. Both legs were treated when both were the subject of complaint. The course consisted of one injection a week into each artery for six consecutive weeks. The amounts used were papaverine 40 mg. in 20 ml. of saline and tolazoline 100 mg. in 20 ml. A 20-ml. syringe fitted with a No. 17 B.W.G. needle which had been ground down to a short bevel was used and the injections were made into the femoral artery immediately below Poupart's ligament. After a little practice no difficulty was experienced in the introduction, the injection being made against the flow of the blood. No local analgesic was used, and the patients were allowed to travel home shortly after the treatment. No untoward happenings occurred.

The sex and age groups of patients in the series are shown in Table I.

TABLE I.—*Sex and Age Groups of Patients*

Drug	Male	Female	Age Range			70+
			40–49	50–59	60–69	
Papaverine ..	18	2	2	8	7	3
Tolazoline ..	16	4	2	9	8	1

Results

Immediate Effect.—On making the injection most patients showed a rapid response with a local flush. This was most pronounced in the thigh, and almost always demonstrated the territory of the superficial external pudendal artery by a flush over the pubes. However, the extent down the limb varied, as did the patient's impression of warmth. In some it went as far as the knee; in others it included the whole limb. With tolazoline a general vasodilatation rapidly followed, and often shivering. The local flush was quite transient, lasting between 10 and 30 minutes. After this the patient felt quite normal. These injections were made by four different workers.

Assessment of the result was made by seeing the patient two weeks after finishing the course and again a month later. In the case of intermittent claudication he was asked how far he could now walk, and he was allowed to compare this with some definite distance he had to walk during the day. His own estimate had already been recorded before starting treatment. Usually it was possible to find how far he walked without pain first thing in the morning—for example, on going to work. In assessing these results alleged improvements or deteriorations of a few yards were neglected—bearing in mind the stated object of the inquiry. Again four persons were engaged in the assessing. In ischaemic necrosis the healing was taken as the criterion, local treatment being confined to a dry dressing and crêpe bandage.

TABLE II.—*Response in Intermittent Claudication*

Drug	No. of Cases	Immediate Flush to Toes	Final Improvement
Papaverine ..	15	9	0
Tolazoline ..	13	7	2
Total ..	28	16	2

TABLE III.—*Response in Ischaemic Necrosis*

Drug	No. of Cases	Immediate Flush to Toes	Final Improvement
Papaverine ..	5	5	5
Tolazoline ..	7	5	4
Total	12	10	9

Tables II and III summarize the results in intermittent claudication and ischaemic necrosis respectively.