Abarbanel (1945) has pointed out, the process of ageing can become manifest in various organs at varying times, and just because the testis may be one of the last to succumb does not mean that it has now become the site of a pathological process while a similar state in the ovary is merely physiological.

Summary

It is considered that the male climacteric is a definite clinical entity, for the following reasons: (1) Similar symptoms occasionally occur in post-pubertal castrates and eunuchoids and are improved by androgen therapy. (2) The 17-ketosteroid secretion, while by no means diagnostic of testicular insufficiency, tends to be low. (3) Some of the symptoms can be explained by lack of the anabolic action of testosterone. (4) The urinary excretion of gonadotrophin is raised—indicative of testicular, but not necessarily of androgen, insufficiency. (5) The testicular histology may show structural changes. (6) The symptoms are improved with androgen therapy, but relapse when an inert substance is substituted. (7) Arguments similar to those advanced against the concept of a male climacteric could be raised against the existence of a female climacteric, which, however, has never been questioned.

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Can better use of the domiciliary services provided by local authorities help to relieve the pressure on the hospitals? This was one of the questions put by the Minister of Health, Mr. IAIN MACLEOD, when he addressed the annual meeting of the County Councils' Association in London on May 26. Mr. Macleod made a plea not only for closer co-operation between those responsible for the operation of the health and welfare services and the general practitioners, but also for the fullest opportunity to be given for voluntary effort to make this contribution, especially in helping to solve the growing problem of the care of old people. "We know," he said, "that it is possible to relieve the hospitals of some part at least of the burden now falling on them if better and perhaps more intelligent use can be made of the services provided by the local health authorities. It is not only a question of cost. There are many types of patient who, provided always that there is no clinical reason to the contrary, are better cared for in their own homes than in hospital. This applies particularly to many children and old people, and to the majority of maternity cases, and it is even more true that the vast majority of healthy old people and children are far better if they can be enabled to continue living in their own homes and families and to receive there proper care and supervision." The home nursing of sickness, he continued, was entirely dependent on a sufficient number of home nurses and home helps. Local health authorities should carefully watch to make sure that there were enough of them in their areas. He would also like to see local health authorities consulting general practitioners in their areas, through either executive councils or local medical committees, to find out to what extent doctors felt themselves compelled, owing to the shortage of home nurses and home helps, to refer patients to hospital who might otherwise have stayed at home.

ISONIAZID IN TREATMENT OF BONE AND JOINT TUBERCULOSIS

A REVIEW OF 20 CASES

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The Medical Research Council's (1952) interim report on the use of isoniazid (isonicotinic acid hydrazide) alone in 173 patients with pulmonary tuberculosis and of streptomycin combined with *p*-aminosalicylic acid (P.A.S.) in 158 others, concluded that, "judging wholly from short-term results," isoniazid is "a very effective drug" in that condition. It therefore seemed necessary to us to make an immediate study of its short-term effects in bone and joint tuberculosis in circumstances in which the drug would be used as the sole chemotherapeutic substance in the patients under consideration. There have already been reports on the use of the drug with and after streptomycin in bone and joint disease, and especially in "advanced" cases with sinuses and other complications, but we are not aware of any reports of its planned use alone in reasonably early uncomplicated cases.

To study such effects means denying our patients the known and very real benefits of streptomycin, and to obtain many suitable cases of bone and joint disease takes a long time. We therefore planned a small short-term study, designed purely as a pilot experiment, to tell us whether or not anything unexpected would occur in the course of the disease under treatment with this drug alone. We decided that six months was as long as we might deny streptomycin to our patients, and, though this is a very short time in the evolution of skeletal disease, we regarded it as probably adequate for a pilot investigation. All we sought was the answer to one simple question, Does anything unusual occur in the early evolution of the disease under the influence of isoniazid?

The Investigation

To give the drug every chance we selected "good" cases, not failures after other measures. Our 20 patients all had short histories of hitherto untreated new tuberculous lesions of bones and joints. We carefully excluded any case which could have been a recrudescence of an old lesion, and any patient who had had previous chemotherapy. The details of the patients are summarized in the Table. All 20 were admitted to the Robert Jones and Agnes Hunt Orthopaedic Hospital. In all save six spinal cases the diagnosis was or had been proved by biopsy or by recovery of the bacillus by aspiration of abscesses and recovery of *M. tuberculosis* therefrom, and in one of these six, all of which were clinically and radiologically typical, we accepted the presence of a proved active tuberculous lesion elsewhere in the body as adequate evidence that the spinal lesion was in fact tuberculous. The patients' ages ranged from 5 to 45 years. Ten were aged 20 or under. There were 13 males and 7 females. The sites of the lesions were: lumbar spine, 6; hip, 5;

Summary of Cases

Case No.	Sex and Age	Site of Lesion	Type of Lesion	Treatment		Iso- niazid (mg./ day)	Other Treatment Given	Weight			X-ray Appearances		General Response to Treatment	E.S.R. (mm./hr.)		White-cell Count		Comments
				Began	Ended			Before Treat- ment	After 3 Months	After 6 Months	Before Treat- ment	After 6 Months		Before Treat- ment	After 6 Mths	Before Treat- ment	After 6 Mths	
1	F 20	L. knee	Synovial (proved by biopsy)	31/5/52	1/12/52	250	Thomas splint and plaster gutters	112 lb. (50.9 kg.)	126 lb. (57.3 kg.)	128 lb. (58 kg.)	Visible synovial thickening. Some diffuse porosis. No destruction. Joint space normal	Unchanged	Good	29	12	9,000	8,000	
2	F 37	Lumbo-sacral angle	Bony (not proved)	31/5/52	1/12/52	250	Frame fixation	122 lb. (55.5 kg.)	125 lb. (56.9 kg.)	133 lb. (60.5 kg.)	Uniform destruction of contiguous margins of L5 and S1; loss of disk space. No abscess visible	No further destruction. Some evidence of healing	"	18	18	15,000	8,000	
3	M 18	Dorsal spine (D8-9)	" "	31/5/52	1/12/52	200	"	77 lb. (35 kg.)	84½ lb. (38.2 kg.)	92½ lb. (41.9 kg.)	Narrower disk D8-9. Small area of destruction lower margin D8. Small peri-spinal abscess shadow	No further destruction. No further loss in disk space. Lesion "hardening", a little further destruction of body of L5	"	55	40	9,000	7,000	Tuberculous pleural effusion remained unchanged
4	M 25	Lumbar spine (L4-5)	Bony (proved by culture of psoas abscess)	31/5/52	1/12/52	300	"	124 lb. (56.4 kg.)	138 lb. (62.8 kg.)	144 lb. (65.5 kg.)	Narrower disk space L4-5. Slight collapse of body of L4. Erosion of anterior part of upper margin of body of L5. Diffuse porosis	A little further destruction of body of L5	"	50	48	8,000	5,000	Psoas abscess present at onset continued to fill, and an abscess developed on the other side after 3 months' treatment
5	M 12	L. hip	Synovial (proved by biopsy of iliac glands)	31/5/52	1/12/52	200	"	88 lb. (40 kg.)	103 lb. (47 kg.)	113 lb. (51.4 kg.)	Narrowing of joint space. Diffuse porosis	Some loss of joint space and increased porosis	Moderate	16	4	9,000	5,500	
6	M 11	L. hip	Bony (proved by iliac gland biopsy. Later by culture of pus from hip)	6/6/52	7/12/52	150	"	59½ lb. (27 kg.)	70 lb. (32 kg.)	81 lb. (36.8 kg.)	Narrowing of joint space. Erosion of acetabulum with small sequestrum. Porosis of head	Further destruction of acetabular roof. Sequestration	Good	34	34	6,500	11,000	Developed abscess over hip after 3 months' treatment; it continued to fill, and pointed through an aspiration. Sinus persists. Organism <i>insensitive</i> to isoniazid after 5 months. Originally sensitive. General and local condition immediately improved on streptomycin after 6 months isoniazid
7	F 13	R. knee	Synovial (proved by biopsy)	6/6/52	7/12/52	200	Thomas and plaster gutter splints	94 lb. (43 kg.)	114 lb. (51.9 kg.)	132 lb. (60 kg.)	Diffuse porosis. No loss of joint space. No soft-tissue thickening on x-ray	Unchanged	Very good	10	3	10,000	5,000	
8	F 23	L. sacro-iliac	Bony (proved by culture of gluteal abscess)	13/6/52	14/12/52	250	Frame fixation	107 lb. (48.6 kg.)	110 lb. (50 kg.)	107 lb. (48.6 kg.)	Widening and porosis of left sacro-iliac joint	Porosis much less. Appearances of healing. Improved	" "	55	27	8,000	5,500	Left gluteal abscess originally present was aspirated once and has <i>not</i> refilled. (Developed alopecia, thought <i>not</i> due to isoniazid)
9	M 20	L. knee	Bony (proved by aspiration of knee and culture)	13/6/52	14/12/52	300	Thomas and plaster gutter splints	138 lb. (62.7 kg.)	150 lb. (68.2 kg.)	182 lb. (82.7 kg.)	Loss of joint space. Erosion of articular surfaces of tibia, femur, and patella	No further destruction. Lesion "hardening" with much clearer definition	Good	19	4	9,000	5,000	Thick pus was aspirated from the knee-joint before treatment began
10	M 24	Dorsal spine (D9-10 and D11-12)	Bony (not proved)	27/6/52	26/12/52	300	Frame fixation	131 lb. (59.5 kg.)	137 lb. (62.1 kg.)	135 lb. (61.3 kg.)	Loss of disk space D9-10 and D11-12. Collapse of bodies of D9-10-11-12, with erosion of anterior margins. Paravertebral abscess	Slight collapse of D9 body with further destruction on right side	Moderate	10	4	7,000	8,000	
11	F 14	L. hip	Synovial (proved by iliac gland biopsy)	25/7/52	29/1/53	150	"	70 lb. (31.8 kg.)	81 lb. (36.8 kg.)	87 lb. (39.5 kg.)	Narrowing of joint space. Diffuse porosis	Slightly narrower joint space, but no destruction. Considerable porosis	Good	12	4	6,000	9,000	
12	M 45	L. hip	Bony (proved by culture of abscess pus)	1/8/52	3/2/53	300	"	131 lb. (59.5 kg.)	115 lb. (52.3 kg.)	146 lb. (66.3 kg.)	Loss of joint space. Erosion of head. Tendency to subluxation. Gross osteoporosis	No further erosion or tendency to subluxate. Evidence of healing. Improved	"	47	44	6,000	8,000	Abscess developed in thigh during last month of isoniazid therapy

Summary of Cases—continued

Case No.	Sex and Age	Site of Lesion	Type of Lesion	Treatment		Isoniazid (mg./day)	Other Treatment Given	Weight			X-ray Appearances		General Response to Treatment	E.S.R. (mm./hr.)		White-cell Count		Comments
				Began	Ended			Before Treatment	After 3 Months	After 6 Months	Before Treatment	After 6 Months		Before Treatment	After 6 Months	Before Treatment	After 6 Months	
13	M 15	Lumbar spine (L3-4)	Bony (not proved)	15/8/52	14/2/53	250	Frame fixation	126 lb. (57.2 kg.)	140 lb. (63.6 kg.)	150 lb. (68.2 kg.)	Narrowing of disk space L3-4. Erosion of both bodies anteriorly	Some collapse of bodies. Hardening of lesion. Improved	Good	21	14	5,000	6,000	Psoas abscess at commencement of treatment. Discharging sinus after 2 weeks and continued to discharge for 3 months
14	M 24	Lumbar spine (L4-5)	Bony (proved by culture from abscess)	15/8/52	14/2/53	350	"	150 lb. (68.2 kg.)	161 lb. (73.2 kg.)	170 lb. (77.3 kg.)	Narrowing of disk space L4-5. Erosion of anterior margin of bodies L4-5	Evidence of healing. Improved	"	12	5	6,000	7,000	
15	F 16	L. knee	Synovial (proved by biopsy)	22/8/52	26/2/53	300	Thomas and plaster gutter splints	127 lb. (57.8 kg.)	126 lb. (57.3 kg.)	146 lb. (66.4 kg.)	Diffuse porosis. No loss of joint space	No change	Poor initially. Then good	23	38	6,000	6,500	
16	M 5	R. hip	Synovial (proved by biopsy of hip)	13/9/52	14/3/53	100	Frame fixation	39 lb. (17.7 kg.)	28 lb. (12.7 kg.)	42 lb. (19 kg.)	Loss of joint space. Diffuse porosis	"	Poor initially. Then moderate	32	5	8,500	9,000	
17	F 40	Lumbo-sacral angle	Bony (proved by bacteriology of lumbar abscess)	13/9/52	14/3/53	350	"	160 lb. (72.7 kg.)	158 lb. (71.8 kg.)	164 lb. (74.5 kg.)	Destruction of lower margin of L5. Loss of L5-S1 disk space	Lesion "hardening" well. No further destruction. Improved	Poor	30	18	5,000	5,000	Large lumbar abscess opened and drained after 3 months. Healed one month later. General condition much improved on streptomycin after 6 months' course of isoniazid
18	M 34	Lower dorsal spine (D11-12)	Bony (not proved)	22/8/52	26/2/53	250	"	118 lb. (53.6 kg.)	126 lb. (57.3 kg.)	108 lb. (49.1 kg.)	Narrowing of disk space D11-12. Erosion of anterior border D12	"Hardening" of lesion. Some collapse. Evidence of healing change.	Moderate	38	27	7,000	7,500	
19	M 26	1. L. sterno-clavicular joint 2. L. ankle joints	1. Bony (proved by culture of pus) 2. Synovial (not proved)	26/9/52	28/3/53	300	Bed rest and plaster cast below left knee	142 lb. (64.5 kg.)	154 lb. (70 kg.)	158 lb. (71.8 kg.)	1. Some widening of joint space. No bony erosion. 2. Generalized porosis	1. No change. 2. Porosis of ankle disappeared. No destruction	Good	11	2	6,000	7,000	Abscess over sterno-clavicular joint aspirated at onset. No recurrence
20	M 24	Lumbar spine (L1-2)	Bony (not proved)	19/9/52	20/3/53	350	Frame fixation	160 lb. (68.6 kg.)	172 lb. (78.2 kg.)	206 lb. (93.6 kg.)	Narrower disk space L1-2. Erosion of anterior margins of these bodies. Slight collapse of body of L1	Some further narrowing of disk space. Hardening of lesion. Improved	"	34	5	10,000	8,000	

knee, 4; dorsal spine, 3; sacro-iliac joint, 1; sterno-clavicular joint and ankle, 1. One dorsal spine lesion was accompanied by a tuberculous empyema. Three lumbar spinal lesions had produced palpable abscesses, and there was an abscess over the affected sterno-clavicular joint. No other complications were present when treatment was begun.

As soon as treatment was started the patients were immobilized and the affected bones and joints splinted exactly according to the time-honoured practice of the hospital. A full open-air regime was established, but the patients received no other anti-tuberculosis drugs and no operations were performed apart from biopsy and aspirations of abscesses.

Dosage of Isoniazid.—All patients received 5 mg. of isoniazid per kg. of body weight per day, in two divided doses regularly at 12-hour intervals. The various weights of the patients meant that the doses given ranged from 100 to 350 mg. per day. In most of the patients the body weight changed appreciably during treatment, but we did not adapt the dose to this change. The drug used was "tubomel," kindly supplied by Bengers Laboratories, Limited. For the first two months of treatment the concentration of the drug in the serum was checked at weekly intervals in 10 cases, the estimations being made by Messrs. Bengers. As it was found that the dose was constantly giving a level of between 1.15 and 2.3 mg. of isoniazid per ml. of blood plasma, the estimations were stopped after the first two months. This concentration was regarded as adequate. The drug was given continuously for six months in all cases.

Criteria Studied.—The course of the 20 cases was studied with regard to general health and well-being, body weight, local clinical condition, progress of the lesion as revealed by x-ray films, E.S.R., and sensitivity of the organisms in those patients in whom repeated study of this aspect was permissible. The patients were weighed and x-rayed at the beginning of treatment, after three months, and after six months. The E.S.R. (Wintrobe) and full blood counts were estimated at monthly intervals. Regular routine urine analysis and clinical examination completed the study. A careful watch was kept for toxic effects. It was not possible to establish a control series. It takes years to find a group of identical cases of bone and joint tuberculosis, and for the purposes of this purely pilot survey we thought controls unnecessary as well as unobtainable.

Results

Effect on General Health.—It is, of course, manifestly impossible to analyse the results obtained in 20 patients as one would those of a much larger series, but there is no doubt that an immediate and striking improvement

occurred in the general condition of 17. Many of these patients had been pale and miserable on admission. They immediately developed a sense of well-being, with an increase in appetite and a striking improvement in appearance. The three exceptions (Cases 15, 16, and 17) ultimately improved in the same way, though to a lesser degree, but their early response was disappointing. Neither a good response nor a poor one in those respects, however, gave any indication of what was happening to the local tuberculous lesion. In the 17 patients who looked so much better so soon, this improved in nine, remained apparently unchanged in five, and was actually worse in three. In the three patients who made a disappointing general response the local lesion improved in one and was apparently stationary in the other two.

Weight.—Fifteen patients, not all of whom had apparently improved in health, gained weight steadily and at the end of six months were anything from 11 to 46 lb. (5 to 21 kg.) heavier. Two (Cases 16 and 17) lost weight in the first three months and then recovered it, and ultimately exceeded their starting weights. One (Case 8) gained 3 lb. (1.4 kg.) in the first three months and then lost just as much in the second. Another (Case 18) gained 8 lb. (3.6 kg.) and then lost 18 lb. (8.2 kg.). One (Case 10) gained 6 lb. (2.7 kg.) in the first period and lost 2 lb. (0.9 kg.) in the second. Again, however, there was no apparent correlation between the gain in weight and the progress of the lesion itself. Gains of 18 and 21 lb. (8.2 and 9.5 kg.) went with local deterioration, and a net loss of 9 lb. (4 kg.) with improvement.

Abscesses and Sinuses.—Two of the four abscesses which were palpable when treatment started resolved after aspiration during the course of treatment. The third required incision: the wound was sutured after evacuation of the pus; it healed well. The fourth, originally palpable in one flank, increased in size so as to become palpable in both flanks, although the patient (Case 4) gained 20 lb. (9 kg.). One patient (Case 6) developed an abscess, which became a sinus during treatment despite a gain of 21 lb. (9.5 kg.) in six months and a good general response. Another patient (Case 12) developed an abscess three weeks after the drug was stopped, at which time his disease (a hip lesion) appeared to be much improved clinically and radiographically.

Changes in X-ray Appearances.—It is, of course, well-nigh impossible to judge, except very broadly, the progress of a tuberculous lesion in its early stages, as shown by x-ray films. Allowing, however, for this difficulty, we feel satisfied in saying that the films in 10 cases showed appreciable improvement. In seven there was no demonstrable change, and in three (Cases 4, 6, and 10) bone destruction advanced despite treatment. Case 6 is of sufficient interest to be described in detail (see below).

E.S.R.—This gave no indication of response. In most cases there was a slow fall over the six months, and in only one (Case 15) was the rate higher after that period.

Insensitivity.—Five patients had abscesses. The pus from one was sterile. Two others cleared up too rapidly for pus to be recovered more than once. In the fourth the organism was never grown in culture but produced tuberculosis in the guinea-pig (Case 4); and in the fifth (Case 6) relative insensitivity was demonstrated after five months' treatment. The abscess over the hip of a boy of 11 appeared after three months' treatment. After three and a half months the organism was sensitive to concentrations of 0.2 mg. per ml. after two weeks' incubation at 37° C., but after five months it was insensitive to 1 mg. per ml. and was inhibited only at a strength of 5 mg. per ml.

Toxic Effects.—One patient (Case 14) developed a rash after four months' treatment. Treatment was not stopped, and the rash disappeared in a week. Another's hair fell out (Case 8). We were unable to convince ourselves that these were toxic effects of the drug, and certainly no others were seen. The white-cell count fell in 9 cases, but never below 5,000 per c.mm. In 10 cases it actually rose.

Case Report

The patient was a boy of 11. Pain in the left hip and a limp had been first noticed in March, 1952. The diagnosis of tuberculosis of the hip had been proved by iliac-gland biopsy in another hospital and the patient was transferred to our care in June, 1952.

On admission he was a pale, thin boy, weighing 59½ lb. (27 kg.). His left hip showed a flexion-abduction deformity, with a good deal of soft-tissue thickening around and in front of the trochanter, and marked pain and spasm on attempts at movement. No abscess was palpable. The biopsy scar in the left iliac fossa was well healed.

A radiograph of the hip showed narrowing of the joint space, porosis of the head of the femur, and a little erosion of the roof of the acetabulum. His E.S.R. was 36 mm. in the first hour (Wintrobe).

The child was splinted on a Robert Jones abduction frame, nursed in the open air, and given 150 mg. of isoniazid daily. After three months his general appearance was much improved, he had gained 11 lb. (5 kg.), but a radiograph of the hip showed further destruction of the acetabular roof, with sequestration. Four months after the beginning of treatment an abscess became apparent and 30 ml. of thick pus was aspirated. *M. tuberculosis* was recovered from this pus, the organism being found to be sensitive to isoniazid at a concentration of 0.2 mg. per ml.

The blood concentration of isoniazid during the first two months of treatment had shown that the dose given was producing a concentration of 1.3 mg. per ml. but, despite the fact that a sensitive organism was receiving an apparently adequate dose of the drug, the disease continued.

The abscess was aspirated five times during the next two months and, despite all precautions, a sinus appeared in December, 1952. In November, 1952, the sensitivity of the bacillus had been reduced so that it was now sensitive only to a concentration of 5 mg. per ml. This concentration was not being obtained.

Gain in weight continued; so did destruction of bone, as shown by the radiograph. After six months isoniazid was discontinued and streptomycin with P.A.S. was given. The E.S.R. rapidly fell to 16 mm. in one hour, the next radiograph showed arrest of the bone destruction, and the sinus began to dry up. By June, 1953, the sinus was healed, the hip lesion quiescent, and the patient's general condition very good.

Comment.—This case is quoted in detail particularly because it illustrates our firm impression that isoniazid alone did not appear to make very much difference, at least during the six months in which it was being given. Even in the cases which improved we felt quite convinced that that improvement was no greater than we would have expected in the days when treatment would have consisted of fixation in the open air without chemotherapy. We were never convinced that the improvement was as great as would have occurred had streptomycin been given instead of isoniazid.

General Conclusions

We do not want to attach too much importance to this small experiment, which we regard as nothing more than a guide to future work, but our impression from these 20 patients is that isoniazid alone is no magical cure for early uncomplicated skeletal tuberculosis; and after six months of its use we felt we could no longer withhold the more certain benefits of streptomycin from our patients. Our original question was, Can anything remarkable be expected from this new drug in six months in circumstances as near ideal as possible? The answer in this series of cases was "No."

Summary

Twenty patients with early uncomplicated tuberculous lesions of bone and joint were treated with recumbency, splintage, an open-air regime, and isoniazid, 5 mg. per

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.

REFERENCE

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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.