Papers and Originals

Controversial Aspects of Rheumatic Heart Disease*

RICHARD W. D. TURNER,† O.B.E., M.A., M.D., F.R.C.P., F.R.C.P.E.D.

Brit. med. J., 1968, 2, 383-390

I have chosen this subject in order to take the opportunity of discussing various controversial aspects of rheumatic heart disease which materially affect recommendations for surgical treatment, with emphasis on what would appear to be some current misconceptions. If a subtitle of "misconceptions" sounds presumptuous at least it reflects the joint experience of a team.

The introduction of cardiac surgery and precise methods of preoperative assessment was a great stimulus to accuracy in diagnosis. It was a chastening experience to find that so much traditional teaching was erroneous, and, in the new context, misleading.

Perhaps I can take as a useful yardstick of current opinion candidates for the Membership examination, particularly in Edinburgh, where many take cardiology as a special subject, because they are usually well read and familiar with what is being taught and written, and balance this against our experience over the past 20 years.

Though I speak as a physician this lecture is largely concerned, directly or indirectly, with surgery; directly because treatment is my main concern and medically there is little new which can be done, and indirectly because it was the advent of cardiac surgery, together with modern investigatory techniques, which has done so much to clarify all aspects of the subject. The surgeon is at least entitled to find what has been predicted by the physician, but in the early days it was apparent that much had to be learned in the hard school of experience.

Perhaps also, as a physician treading Agag-wise with maximal delicacy, I can comment gently where surgeons themselves would hesitate to tread.

Symptoms

Surgical treatment is often not advised or is postponed because symptoms are mild. The usual indication for operation in a patient with mitral stenosis is a history of progressive breathlessness on exertion or there may be other manifestations such as an attack of acute dyspnoea precipitated by tachycardia from any cause, haemoptysis, systemic embolism, or oedema. However, although the history is often short sometimes severe stenosis is present in the complete absence of symptoms. At operation the degree of stenosis is usually severe and the valve sclerotic, a situation which cannot have developed rapidly.

There is a threshold for dyspnoea as for pain which varies considerably between individuals. Physical activity and emotional lability also vary widely and some subconsciously restrict the pace of their activities and thus avoid breathlessness.

Dyspnoea in mitral stenosis is mainly a reflection of left atrial pressure and consequently is also dependent on factors other

than the degree of obstruction, as discussed below. In mitral incompetence and in aortic valvular disease dyspnoea does not develop until there is left ventricular *failure*, which reflects an advanced stage of the rheumatic process.

In order to minimize complications it is important to consider surgical treatment as soon as it is certain that the valvular defect is of serious haemodynamic significance; that is to say, the degree of stenosis or incompetence is causing objective evidence of severity *whether or not symptoms are present*.

Mitral stenosis may be taken as an example because it is the most frequent. Despite the known efficacy of valvotomy today many are still having the operation after the optimal time. In some cases the patient has not been aware of any disability and not consulted her doctor, but in others only symptomatic treatment has been advised without referral to hospital.

Dangers of Delay

In the interim, with delay, there will be progressive changes in the pulmonary circulation, in the lungs, in the right ventricle, and also, if there is cardiac failure, in the liver. There is an ever-present risk of systemic embolism, pulmonary oedema, or pulmonary infarction.

The adverse effects of atrial fibrillation are often stressed, but the symptomless patient in sinus rhythm is in particular peril of disaster from the onset of fibrillation with a rapid ventricular rate.

It may sound platitudinous, but clearly requires emphasis, that the indication for mitral valvotomy is the presence of significant stenosis.

The longer the delay the less likely is a good valvotomy to be achieved with restoration of valve function. It may be possible forcibly to separate the adherent margins of the cusps, which is what is meant by valvotomy (misnamed commissurotomy), but this is not synonymous with a good functional result, so that often left atrial pressure remains raised, at least on exercise.

There is, of course, no evidence that valvotomy decreases the rate of sclerosis, and prophylactic valvotomy does not mean the prevention of later restenosis. It does imply the prevention or delay of secondary changes and complications consequent on obstruction.

A second valvotomy may be inconvenient but the risk is low. In our series of 160 consecutive cases only four patients died and each had important complicating features. In the past 20 years many of our patients have been kept alive and physically active by first, second, and even third valvotomies. More recently, of course, many have had valve replacement.

We are convinced that lives have been prolonged, complications prevented or postponed, and the quality of life improved by this individual approach. We have been much influenced by the disasters which may follow unrecognized valvular disease, delay in referral to hospital, or delayed operation. Any physi-

* Based on the Oliver Sharpey lecture delivered to the Royal College of Physicians of London on 1 December 1967.

† Reader in Medicine, University of Edinburgh; Physician, Western General Hospital, Edinburgh.

cian who has had the opportunity of studying a large number of patients with rheumatic heart disease over a long period must have been impressed with relentless progression in the majority and the high incidence of complications. The relief of obstruction is a sound surgical principle.

Many patients with severe aortic valvular disease reach the advanced stage of left ventricular failure before the condition is recognized owing to absence of previous symptoms and the maintenance of sinus rhythm. By this time not only has gross left ventricular hypertrophy developed but also considerable replacement fibrosis. It is in this group in particular that operation may have to be advised well before the onset of symptoms or serious irreversible changes will have taken place.

It would be possible to give numerous examples of the dangers of unrecognized or untreated valvular defects.

New York Heart Association Classification

In relation to pregnancy in particular it is pertinent to refer to the New York Heart Association classification of disability because it is still widely used, particularly by obstetricians, with the implication that it is a reliable guide to severity of the underlying heart disease. Grade I includes those with cardiac disease but without limitation of physical activity, and grade IV those unable to carry out any activity without discomfort. Grades II and III are intermediate. Clearly this classification refers only to symptoms and in the present context of rheumatic heart disease is no more than another way of saying that the patient is or is not disabled by breathlessness and to what degree.

The introduction of this classification may have served a useful purpose in emphasizing the need during pregnancy for special care of all patients with symptomatic heart disease and in providing a rough-and-ready guide to severity. It has, however, long outlived its usefulness, because it is often misleading and potentially dangerous and should be abandoned. It would be best not to use this classification even in a strictly functional sense because of the implication that symptoms are necessarily related to heart disease and, albeit subconsciously, of a correlation with severity of heart disease.

It is obvious that the *majority* of women who feel fit enough to undertake pregnancy will be in grade I or II, and also that those with symptoms are more likely to have underlying heart disease than those who do not and to receive special medical attention. What is not so obvious or sufficiently appreciated is that the *majority* of *maternal deaths* during pregnancy occur in patients who when first seen were placed in functional grades I and II. In Edinburgh over the past 18 years there have been 18 maternal deaths during pregnancy in patients with rheumatic heart disease. Fifteen were in grade I or II when first seen in an antenatal clinic. Figures from other centres are similar.

The objections to this classification are that it takes account *only* of symptoms and ignores the severity and type of underlying valvular disease, the state of the myocardium and pulmonary circulation, cardiac rhythm, and the presence or absence of other relevant conditions, such as anaemia.

In pregnancy a first and fatal attack of pulmonary oedema in a previously asymptomatic woman may be induced by emotion, exercise, infection, the onset of an arrhythmia, or tachycardia from any cause. In fact, she may pass from grade I to grade IV in a few hours. Likewise a patient with pulmonary oedema may be transferred by surgical treatment from grade IV to grade I and remain well during the remainder of her pregnancy, delivery, and the puerperium. Similarly a patient placed in grade III on account of symptoms may improve to grade I as a result of the correction of anaemia. By contrast, except as a result of surgical treatment, a cardiac grading would not vary from day to day, week to week, or month to month and often only gradually from year to year.

It is no exaggeration to say that for a woman with mitral stenosis grades I and II are potentially the *more dangerous* because those in grades III and IV have obvious disability and are likely to be well cared for either by their practitioner or in hospital and kept under close observation throughout. They are less prone to pulmonary oedema and more likely to present with congestive failure and respond well to treatment.

It is essential that cardiac assessment should never *primarily* be based on symptoms which may be absent, mild, moderate, or severe in any grade based on objective findings. Numerical *cardiac* grading is likewise not recommended because, with so many variable factors, precision would be impossible. Correct management must be decided on an individual basis. Valvotomy in the young pregnant woman may indeed be prophylactic—against death.

Signs: Concept of the “Pliant” Valve

Prediction of Operability

The concept of the “pliant” valve is a diagnostic misconception. The term was introduced to relate certain auscultatory findings to the prospect of a good valvotomy. In the original description Sellors, Bedford, and Somerville (1953) placed first in the indications for operation in patients with mitral stenosis, “severe stenosis of the mitral orifice, the anatomical conformation of which must be suitable for surgical correction,” and stated, “we regard the following clinical signs of mitral stenosis as indicative of a pliant diaphragmatic valve amenable to valvotomy: a snapping apex beat; a snapping first sound (closing snap); and a loud opening snap of clicking quality.” To these others have added a loud rumbling diastolic murmur.

This has been widely interpreted as meaning that it is possible to forecast the “divisibility of the commissures” and to recognize preoperatively the type of valve which will give a good functional result.

The phrase “division of the commissures” is an unsuitable one because division of an anatomical commissure would result in disastrous incompetence. What is meant is separation of the adherent margins of adjacent cusps, and it is more satisfactory and more correct simply to state “complete or partial separation of the cusps” or, more concisely, “complete or partial anterior or posterior valvotomy.”

Certainly a good valvotomy is often attained in patients having auscultatory findings of the type described, but there are too many exceptions for any reliance to be placed as regards operability. *In particular no patient should be turned down for surgery because these qualities are absent.*

The signs of the “pliant diaphragmatic valve” have been observed with adhesion between the cusp margins of such strength that they have resisted all efforts at complete separation even with the dilator and also when the cusp tissue adjacent to the orifice was so sclerosed as to impair movement after valvotomy. They may even be present with a calcified valve. Conversely these signs have been absent in patients with tight mitral stenosis in whom a complete anterior and posterior valvotomy was achieved and the general mobility as a result has permitted freedom from symptoms for many years.

These findings are compatible with the view that the signs of a pliant valve are largely caused by the to-and-fro displacement of the aortic cusp in systole and diastole. In rheumatic disease the part of the mitral valve which at operation seems least affected by sclerosis is usually that of the aortic cusp furthest from the mitral orifice. It can sometimes be felt moving vigorously with the heart's action when the region of the orifice is rigid. However, it is the state of the cusps *at the orifice* and the strength of their fusion which determines whether valvotomy can be performed and to a considerable extent how well the valve will function postoperatively.

These facts require emphasis because it is still not infrequently stated that in a particular patient valvotomy should be advised "provided the valve is suitable." The point I am making is that it is not possible to predict by any means, least of all by auscultation, whether or not a satisfactory valvotomy is likely to be achieved. Even heavy calcification may not preclude a satisfactory valvotomy with maintenance of a good functional result for many years, because it is not the extent but the precise *disposition* of the calcification which is important.

It may also be mentioned in regard to mitral incompetence that for related reasons it is likewise *not* possible to predict by auscultation which valves will be amenable to repair.

Opening Snap

The presence or absence of an opening snap by itself bears no relation to the degree of stenosis. A snap can be heard in the majority of cases, and sometimes more significant than its presence is its absence, which is often due to rigidity, calcification, or dominant mitral incompetence.

Interval between Second Heart Sound and Opening Snap

It is widely accepted that the interval between the second heart sound and the opening snap (2-OS) is a reliable guide to the severity of mitral stenosis. In any large group of patients there is certainly a fairly close relation, the shorter the interval the greater being the degree of stenosis, and after a good valvotomy it may be noted that the interval is wider than before. On the other hand, there are many exceptions to this generalization, and we have concluded that the sign is, in the individual patient, unreliable.

It is only to be expected that when left atrial pressure is raised as the result of mitral obstruction the valve will open sooner than if the pressure is normal. However, there are a number of factors other than the degree of stenosis which influence left atrial pressure. These include the volume of the atrium, the distensibility of its walls, an associated regurgitant jet, and the various factors which influence right ventricular stroke output. In addition the gradient across the valve will of course be influenced by the diastolic pressure in the left ventricle.

It will therefore be appreciated that there are good reasons why, in the individual patient, the interval between the second sound and the opening snap should be an unreliable guide to the severity of stenosis.

Duration of Diastolic Murmur and Severity of Mitral Stenosis

Though in a large group of cases there is a fairly close relation between the duration of the diastolic murmur and severity of mitral stenosis, the longer the murmur the greater being the degree of stenosis, there are so many exceptions that this measurement is of little value in the individual patient.

In severe stenosis with a high pulmonary vascular resistance and consequently low blood flow the murmur may be short or not even heard, though with careful attention to auscultation at the precise site of maximal pulsation in the left lateral position a murmur will usually be audible from time to time.

We have, however, seen numerous examples of a short murmur in patients with tight mitral stenosis but only slight or moderate increase in the pulmonary vascular resistance and also in patients with a long murmur but without severe stenosis. Turbulence is influenced not only by the degree of obstruction, left atrial pressure, and blood flow but by the qualities of the valve cusps. Flow will also be influenced by the presence or

absence of mitral regurgitation. Also audibility is dependent on good conduction from the heart to the chest wall. This may be reduced in patients with emphysema but also in other individuals from the configuration of the chest and possibly the closeness of the heart to the stethoscope in the supine or lateral positions.

Apical Systolic Murmur

Many patients with severe mitral stenosis have also a loud apical systolic murmur and many have been denied valvotomy on this account. Such a murmur may be due to a strong regurgitant jet through a narrow valve, to tricuspid incompetence, or to aortic stenosis. A mitral regurgitant murmur is likely to be loud if the margins of the valve are sclerotic or calcified. In tricuspid incompetence with right ventricular hypertrophy and dilatation the heart may be rotated clockwise, as viewed from below, so that the apex is formed by the right ventricle and the systolic murmur is loudest in this position. In some patients with aortic stenosis the systolic murmur is loud, and sometimes loudest at the apex. It may be possible to confirm by phonocardiography that the murmur has the classical diamond-shaped configuration, but it is by no means always possible to be sure of this by auscultation, particularly if the heart sounds cannot be heard or if there is also mitral incompetence.

If the presence of severe mitral stenosis is indicated on other grounds a systolic murmur from any cause is no contraindication to valvotomy.

As with all murmurs intensity is often a poor guide to the severity of the underlying valvular defect. The majority of patients with severe mitral incompetence have a loud, long apical systolic murmur, heard towards the left axilla and frequently the left lung base. However, some patients with severe incompetence have a relatively quiet murmur or occasionally none, and sometimes, as mentioned above, a loud murmur signifies relatively mild incompetence.

The most useful auscultatory sign of severe incompetence is the addition of an associated third heart sound during the phase of rapid ventricular filling.

Critical Stenosis

The questions are often asked, "What constitutes a critical degree of stenosis?" and "What in terms of centimetres, determines an adequate valvotomy?" but they betray lack of appreciation of the factors involved. The sole indication for surgical treatment is a degree of stenosis sufficient for benefit to follow valvotomy or valve replacement, by reducing a raised left atrial pressure, but this degree of stenosis cannot be defined merely by the size of the orifice.

The determining factor in all cases is the level of left atrial pressure at rest, on exertion, or in special circumstances such as pregnancy or tachycardia from any cause. Left atrial pressure is influenced not only by the severity of stenosis but by the cardiac output, by the capacity and distensibility of the atrium, and by the presence or absence of associated mitral incompetence. Numerous interrelated factors influence the cardiac output, including the blood volume, the pulmonary vascular resistance, the force of right ventricular contraction, and the heart rate. Changes in the volume and elasticity of the left atrium are probably determined by rheumatic myocarditis rather than by the degree of duration of mitral stenosis or incompetence. The force of right ventricular contraction is influenced by rheumatic myocarditis, hypertrophy, replacement fibrosis, the diastolic ventricular volume, nervous and chemical factors, and the venous return.

Severe stenosis is certainly present when the valve will not accept more than the tip of an index finger of average size—that is to say, an orifice less than 1.5 sq. cm. However, the

area of the mitral valve cannot be estimated by the exploring finger with the precision sometimes expressed by surgeons. The orifice may not be rounded but slit-like or irregular, and if sclerotic its estimated size is dependent also on the force with which the finger is inserted. Sometimes it is clear that functional stenosis is considerably greater than that estimated by the surgeon.

Sometimes an orifice which will accept the terminal or even the middle phalanx of the finger constitutes sufficient stenosis, from the functional point of view, to raise left atrial and consequently pulmonary venous pressures to dangerous levels. Though physical exertion can be readily controlled tachycardia induced by emotion cannot be turned off at will, and after the onset of an arrhythmia there may be an unavoidable delay in controlling the ventricular rate.

In pregnancy the physiological increase in circulating blood volume varies widely between individuals and in the same individual in different pregnancies, and likewise cannot always be sufficiently controlled to prevent pulmonary oedema.

Respiratory infections are particularly dangerous and do not always respond promptly to antibiotics because often they are viral in origin.

Pulmonary venous hypertension is always suggested by a complaint of undue breathlessness on exertion or at night or in undue special circumstances, and may be reflected in physical signs or radiographic changes. If there is doubt catheterization should always be carried out and, if necessary, pressure measurements be made during exercise.

Auscultation

Reference may be made to two aspects of nomenclature which are still in current use, although deceiving, and would be better abandoned.

Firstly, as regards the so-called *areas of auscultation*. The facts are that the conventional aortic area does not lie over the aortic valve, the component of the second heart sound heard there is not always that from the aortic valve, an aortic systolic murmur may be loudest at the left sternal border or at the cardiac apex, a systolic murmur best heard in the aortic area may result from mitral incompetence, and an aortic diastolic murmur is rarely, if ever, loudest in the aortic area.

The conventional mitral area is rarely the region where heart sounds or murmurs are loudest in patients with significant mitral stenosis or incompetence, but lies further to the left. A systolic murmur loudest in the conventional mitral area may be due to tricuspid incompetence or aortic stenosis.

When tricuspid murmurs are present in a patient with rheumatic heart disease there is usually considerable cardiac enlargement and often clockwise rotation as viewed from the apex, and consequently they are often best heard in the conventional mitral area or between the apex and the sternum.

Secondly, as regards the use of the term *ejection murmur*. This may lead to errors in diagnosis, partly from misuse, but also because it is often inaccurate as regards conventional implications. This is not the place to discuss the subject in detail, but in summary it may be said that precise timing of murmurs is often not possible because the first, second, or both heart sounds are inaudible in the context in which an ejection murmur occurs, by no means all aortic or pulmonary systolic murmurs are loudest in mid-systole or have a diamond configuration on the phonocardiogram, and not all mitral systolic murmurs or systolic murmurs from a ventricular septal defect are long, not all murmurs which are loudest in mid-systole derive from the aortic or pulmonary valve, and as mentioned above, mid-systolic and pansystolic murmurs are not always loudest in the expected "area."

In every patient it is best to describe the precise characteristics of the abnormal auscultatory findings and draw conclu-

sions from all the available data and not from the application of classification which may or may not be accurate in the particular case.

Myocardial Factor

Varying opinions have been expressed on the relation of cardiac enlargement to valvular defects.

In our experience gross cardiac enlargement or absence of enlargement may be present with uncomplicated severe mitral stenosis, a giant left atrium may be present with pure mitral incompetence, pure stenosis, or any combination of these two valvular defects, and a giant right atrium with or without tricuspid disease or pulmonary hypertension. Enlargement of the right ventricle in patients with mitral disease may be associated with severe pulmonary hypertension, but again is sometimes disproportionate. Enlargement of the left ventricle may be present in some patients with uncomplicated mitral stenosis when no other cause is apparent, in which case the presumptive reason is rheumatic cardiomyopathy. It is particularly noteworthy that severe mitral stenosis may be present in a patient without any cardiac enlargement and even with a heart which is smaller than average as judged by the cardiothoracic ratio, and occasionally without left atrial enlargement, facts which must reflect the absence of rheumatic myocarditis but do not exclude hypertrophy.

Finally, considerable enlargement is occasionally present with a mild valvular defect.

Our multifactorial analyses of clinical, radiographic, electrocardiographic, cardiac catheterization, and angiocardiographic findings have shown that chamber enlargement bears little relation to the degree or duration of valvular defects or to the pressure within. Enlargement is therefore more likely to be mainly due to myocardial damage by the rheumatic process.

Operative Mortality

The question, What is your operative mortality? lacks insight because with every procedure results are largely dependent on the type of patient being accepted for treatment. From the early days mortality from mitral valvotomy in the good-risk group—that is to say, those in sinus rhythm without gross cardiac enlargement, pulmonary hypertension, calcification of the valve, or a history of cardiac failure—has been low. At the other end of the scale—those who are older with atrial fibrillation, large hearts, heavy calcification of the valve, pulmonary hypertension, polyvalvular disease, and a history of congestive failure with secondary changes in the lungs and liver—the mortality is higher.

Reported mortality varies widely, but in large centres where almost all patients with severe stenosis are accepted despite associated adverse factors, however severe, the overall operative mortality over the past 15 years or so has probably been about 5 to 6%, and for closed valvotomy this is probably an irreducible minimum.

In our recent experience the operative mortality for mitral valve replacement in the severest group has been lower than for closed valvotomy.

In assessing the risk in the individual patient numerous factors must be taken into account, but multifactorial analyses have clarified the significance of many features (Kitchin and Turner, 1967).

Another significant aspect is that, even granted equal opportunity and comparable training, it is a fallacy to assume that all surgeons are equal any more than are other craftsmen.

Operative Technique

Sometimes a relatively poor postoperative result is due to an inadequate valvotomy either from the technique, particularly

in the days of early experience, or because the valve was too rigid. In such cases recurrence of symptoms is mainly attributable to the effects of persistent stenosis.

Not only are the skill and experience of the surgeon important but also the method employed. Instrumental dilatation is in most cases superior to and safer than the unaided finger or the knife, and in our experience the transventricular approach is best. One cannot, of course, be too dogmatic, because each surgeon is likely to achieve the best results with the technique with which he is most familiar, but we are not aware of any who has abandoned the transventricular approach after experience has been gained. Since July 1954 all patients in Edinburgh have been treated by the transventricular dilator except for the few in whom a satisfactory valvotomy was unexpectedly achieved during preliminary exploration with the finger. In the majority of cases although finger valvotomy may be attempted there is no great persistence, because it is known that instrumental valvotomy is not only more certain but safer and in particular less likely to result in traumatic mitral incompetence or systemic embolism.

Subvalvular stenosis from fusion of the chordae may be present, and be important to relieve. Occasionally it appears to be the principal or even sole cause of obstruction. The fused chordae are separated by the finger and not by the dilator.

If an adequate valvotomy with restoration of function cannot be achieved replacement of the valve is necessary.

Operative Complications.—The most frequent causes of operative death from valvotomy have been traumatic mitral incompetence, systemic embolism, and circulatory failure, but each of these has become rare. As regards open heart surgery the risk is mainly related to secondary changes in the myocardium, pulmonary circulation, and liver.

Traumatic Mitral Incompetence

In the early years of mitral valvotomy traumatic mitral incompetence was not infrequent, and, as a result, five of our first 400 patients died. In addition some had a relatively unsatisfactory degree of improvement and a few were made worse.

It is commonly supposed that the incidence of important traumatic incompetence has been increased by the introduction of the transventricular dilator, though it would probably be conceded that this technique has made valvotomy possible in patients with sclerotic or calcified valves in whom little could be achieved with a finger or knife. In fact the reported incidence of severe incompetence in some series is high. In Edinburgh since the introduction of the transventricular dilator significant traumatic incompetence has become rare. There has been no operative death from this cause in our last 500 patients, and since open heart surgery became available six years ago there has been no instance in which repair was necessary as an emergency.

Some degree of traumatic incompetence as judged by the production of a systolic murmur or increased intensity of a murmur previously present is not infrequent and has occurred in about 20% of cases. However, the effects of this have rarely been commensurate with the systemic benefit derived from the relief of mitral stenosis nor associated with objective evidence of severity in the form of a third heart sound or of clinical, radiographic, or electrocardiographic signs of left ventricular hypertrophy or enlargement. In a few cases it is probable that traumatic incompetence has been a contributory factor to a relatively unsatisfactory long-term result and a third operation for valve replacement has been carried out some years later.

The late effects of incompetence produced by operation may be difficult to assess because of some degree of persistent stenosis or the development of restenosis or the presence of other valvular defects, and one can only be sure if there is objective

evidence of an effect on the left ventricle not explicable on some other basis. In the course of time it is only to be expected that the effects of such incompetence may contribute to subsequent deterioration.

This low incidence is attributable to the proper use of the transventricular dilator. With the finger technique the force which can be applied is less and without adequate counterforce, and with a knife the incision cannot always be made in the precise direction required.

With the expanding dilator the amount of force available for separating the adherent margins of the cusps is greater so that better splits may be obtained in poorer valves and can be well controlled. One blade provides counterpressure for the other so that there is no dragging on the heart. The state of the valve must be checked after each minimal widening of the dilator, since a slight movement of the blades may cause a remarkably extensive separation of the cusps. When separation of the cusps is complete either anteriorly or posteriorly further use of the dilator may tear a cusp or detach it from the myocardium instead of completing the valvotomy. Therefore in these circumstances the dilator can no longer be used.

Systemic Embolism

Some of the factors which influence the incidence of intracardiac clot and of systemic embolism are known and include in particular atrial fibrillation. The incidence increases with age and is greater in those with large hearts and with heavy calcification of the mitral valve.

It is worth emphasizing that in 20% of cases embolism occurs in those in sinus rhythm.

In the early years systemic embolism was a not infrequent complication of mitral valvotomy. Twelve of our first 500 consecutive patients died on this account and 16 others experienced non-fatal embolism. With increasing experience the incidence of this complication fell and in recent years has been low. In our last 500 patients two have died on this account and two others experienced non-fatal embolism. A number of factors have probably contributed to this.

Great care must be taken to allow an initial strong gush of blood to escape from the auricle before it is compressed with a clamp, and should any clot be seen the escape of blood should be repeated. The mitral valve should be approached through the atrium if clot in the auricle is expected and the finger introduced between atrial wall and organized thrombus with the least possible disturbance. The use of the transventricular dilator permits the minimum disturbance in the atrium and is therefore to be preferred. Although the carotid vessels are always occluded with a vascular clamp if clot is found or suspected or if atrial fibrillation is present or the valve is calcified, we have no evidence that in any patient thrombus has, so to speak, been redirected to some peripheral site other than the brain.

Size of Left Auricle

It has also been claimed that the incidence of embolism is related to the size of the left auricle (atrial appendage). However, in our series there has been no close relation between the size of the auricle, as judged radiographically, and the incidence of embolism. However size is unlikely to be the only or even the most important factor. Auricles vary also in length, calibre, tortuosity, and trabeculation, and in some cases they lie anteriorly and do not project as much on to the cardiac border as in other cases.

We have been unable to find a close relation not only between a past history of systemic embolism and auricular size but also between ablation of the auricle and the incidence of subsequent embolism.

Removal of Auricle

It has often been proposed that removal of the left auricle is an important part of the surgical treatment of mitral stenosis. Before the introduction of valvotomy we did in fact operate on a small group of patients with recurrent embolism for the sole purpose of removal of the auricle.

For the first few years of mitral valvotomy it was our routine practice also to remove the auricle. This was both in order to obtain a specimen for histological study and in the hope of preventing subsequent systemic embolism. However, we formed the impression that there was no clear relation between the size of the auricle and the incidence of systemic embolism, and it was also considered that loose or readily detachable clot was just as likely to come from the atrium. In addition it seemed that the auricle might usefully serve as anchorage for any thrombus present and that clot firmly attached in the trabeculae of the auricle would not easily be displaced. Consequently the practice of appendectomy was abandoned.

From about this time of change in policy the incidence of systemic embolism at operation began to fall and in recent years has remained at a low level. Doubtless these facts are unrelated and the improvement is attributable to greater experience and the introduction of the ventricular approach to the valve by means of a mechanical dilator rather than by way of the auricle and atrium with the finger and greater likelihood of disturbance of thrombus. Nevertheless it may serve as a useful reminder that conclusions cannot safely be drawn from an association of circumstances.

At all events we have concluded that surgical treatment in patients with systemic embolism is warranted only if the degree of stenosis is such that reduction in the degree of obstruction would be of benefit on haemodynamic grounds and that routine removal of the auricle after valvotomy is unnecessary. We have no evidence that it is harmful.

Value of Anticoagulants

As a matter of comparable interest and possibly of greater practical importance reference may be made to the claims that the preoperative administration of anticoagulants and their continuation for a few weeks thereafter will likewise reduce the incidence of systemic embolism.

In our series similar results appear to have been achieved without the use of anticoagulants, which have been given only to the occasional patient who has experienced systemic embolism in the few weeks immediately preceding operation. Though it was possible that anticoagulants might decrease the likelihood of fresh clot being laid down during this period it was obvious that clot disturbed at the time of operation had often been present for a considerable period.

Also, anticoagulants are not without danger, and in the immediate postoperative period are occasionally responsible for haemopericardium.

A review of published work makes it clear that no adequate trials have been carried out. After 25 years the place of anticoagulants in rheumatic heart disease, as in the management of coronary disease, remains uncertain and there are as many proponents as antagonists. The conclusion follows that this form of treatment is probably of little value. Nevertheless if anticoagulants are of value then what is potentially preventable is not being prevented. If it is not true many are having unnecessary hospital attention and blood tests and are running the risk of haemorrhagic and other complications of oral anticoagulant drugs. It is overdue that adequate controlled multi-centre trials should be carried out.

Mitral Valvotomy in Presence of Aortic Valvular Disease

Associated aortic valvular disease has often been taken as a contraindication to mitral valvotomy and many patients have

been denied operative relief on this account. It has apparently been considered that the left ventricle is likely to be embarrassed by a sudden increase in cardiac output following the relief of mitral obstruction with consequent functional aggravation of the aortic disease as reflected in the left ventricle. The facts in our experience are quite otherwise and probably for good reasons.

Some years ago we analysed 500 patients treated by mitral valvotomy with and without associated aortic valvular disease and found no difference in operative mortality nor in the proportion of good results up to six years (Kitchin and Turner, 1967).

In our experience *severe* aortic incompetence has not been present with severe mitral stenosis, and if severe aortic stenosis was also present transventricular aortic valvotomy has been carried out at the same time. From an analysis of those who died as a result of valvotomy or who failed to achieve or maintain a satisfactory postoperative course, in no instance has this been attributable to the concomitant aortic defect. It is only to be expected that with the further passage of time those with associated aortic disease are likely to do less well, but there is no justification on this account for failing to relieve any individual from the adverse effects of severe mitral stenosis.

The only way in which abolition or reduction of mitral stenosis might "aggravate" the aortic disease would be by increasing left ventricular work as a result of too great an increase in cardiac output. Experience indicates that such "aggravation" seldom if ever occurs. The explanation presumably lies in the fact that, as haemodynamic studies have shown, after mitral valvotomy the principal effect is a reduction in left atrial pressure with increasing lung compliance and consequently a fall in the work of breathing, but the cardiac output either rises little, remains the same, or not infrequently actually falls (Donald *et al.*, 1957).

It is important to lay the boggy of associated aortic disease because we have established that this should never in itself be a contraindication to the relief of severe mitral stenosis—a tribute again to the remarkable capacity of the left ventricle to compensate, at least for many years.

Combined Mitral and Aortic Valvotomy

Our first transventricular aortic valvotomy was performed in July 1953 and our first combined aortic and mitral valvotomy six months later, when Andrew Logan carried out the *first ever* mitral valvotomy by the ventricular approach. It was soon established that combined valvotomy was a remarkably safe procedure. There are a number of possible reasons for this.

Firstly, symptoms from associated mitral stenosis may lead to earlier diagnosis and consequently treatment. Next, in rheumatic cases the aortic valve is initially tricuspid with normal commissures, in contrast to a congenital bicuspid valve, and in consequence likely to be relatively amenable to valvotomy. Also in cases of associated mitral disease calcification of the aortic valve is usually relatively mild. This may be related to the higher incidence in females and the reduced blood flow and turbulence to which this valve has been exposed on account of the limiting effect of mitral stenosis on the cardiac output.

It is not of course possible by a blind technique to be certain at the time of operation what has been achieved by the aortic valvotomy, but from preoperative and postoperative assessments of long-term follow-up we were of the opinion, before the introduction of open heart surgery, that this procedure was of benefit and remarkably safe. In the past 15 years 36 patients with combined aortic and mitral stenosis have been treated in this way with no operative deaths, and the long-term results in those followed for 10 years or more have been almost as good as for mitral valvotomy alone.

It is appropriate to emphasize here that the incidence of traumatic mitral incompetence of any severity has been extremely low in Edinburgh, a tribute to the proper use of the transventricular dilator. Because of this satisfactory experience we still sometimes advise closed mitral and aortic valvotomy for patients with severe stenosis of each valve and with relatively unimportant incompetence or, in a few patients, replacement of one valve with valvotomy of the other.

It is still our policy to avoid double valve replacement unless calcification is severe, because of the greater operative risk and reluctance to insert so much foreign material. If necessary the second valve replacement can be done later when better prostheses are likely to be available.

Aortic Valve Surgery

This is not the occasion to discuss aortic valvular stenosis other than of rheumatic origin or the various other forms of obstruction to left ventricular outflow. However, it is necessary to put in perspective the results of closed and open heart surgery for aortic valvular disease.

Earlier closed operation to try to reduce the haemodynamic effects of aortic incompetence were unsatisfactory. At the present time, except in a few cases where repair is possible, treatment is by valve replacement. Aortic stenosis can be treated by valvotomy or valve replacement. Before the days of open heart surgery, and including a few cases since valve replacement was possible, we have experience of 75 patients treated by valvotomy.

Thirty-nine of them had isolated aortic stenosis—that is to say, without mitral disease—and it was considered probable that most had a congenital bicuspid valve with secondary calcareous changes. All had advanced disease with the familiar severe symptoms of angina, syncope, paroxysmal dyspnoea, and congestive failure, and it was known that without surgical treatment the expectation of life was limited to one or two years. In this very severe risk group there were 12 operative deaths in 39 cases, but in survivors the degree of improvement attained with prolongation of life was usually well worth while.

It is against this background of experience, and taking into account that the long-term results of valvotomy are probably going to be relatively poor, that we now advise valve replacement, especially since the operative risk for open heart surgery in this group is considerably lower than for the closed procedure.

In the last two years in Edinburgh, for example, 42 of my patients have had valve replacements, with six deaths.

The situation, however, is more favourable in those with aortic stenosis of presumably rheumatic origin—that is to say, in association with mitral disease.

Restenosis

The reported incidence of restenosis has varied in different series, and this is probably in part related to the closeness of follow-up. In some centres personal interview by a member of the same medical team is carried out on at least an annual basis. In other centres the patient is not asked to report unless there is a recurrence of symptoms, or at least not for a few years. As before a first valvotomy, the history of dyspnoea preceding restenosis may be short, and yet severe obstruction which cannot develop rapidly is found.

It is usually assumed that the principal factor in restenosis is a relatively inadequate first operation, but though in our series of 160 cases there is a trend in this direction the correlation is not strong.

In some patients despite a complete valvotomy with supple cusps restenosis occurs in less than five years, whereas in others, despite an incomplete valvotomy with sclerotic cusps, restenosis

does not occur in 10 years. After a poor valvotomy it may reasonably be considered that persistent stenosis rather than restenosis is the main factor.

As judged by palpation at the time of valvotomy it is often evident that between operations there has been progressive sclerosis and frequently also calcification of the valve. It would seem that this progress in the natural history of rheumatic heart disease after the initial infection, with increasing immobility of the cusps, is an important factor.

The most obvious feature has been that the need for reoperation increases with time from 5% of patients at five years to 70% at 10 years and that sclerosis and calcification tend to be progressive and at least contribute to functional restenosis.

Heavy Calcification of Mitral Valve

The overall incidence of calcification of the mitral valve in our surgical series has been 35%, with heavy calcification in 18%. The incidence is higher in males and increases with age. It was present in 70% of all males and heavy in 50% of those over the age of 30. For obvious reasons calcification militates against a good functional result. Calcification in the line of fusion may prevent separation of the cusps or, if present diffusely through the cusps, may perpetuate the obstruction despite valvotomy. Severe sclerosis without calcification may have similar significance in this respect. Nevertheless a good functional result maintained for many years is often produced by a valvotomy in a heavily calcified valve provided that the calcification is not so disposed as to prevent separation of the cusps or seriously limit their mobility once they have been separated.

From another point of view heavy calcification is a disadvantage because in our experience it is associated with a considerably higher incidence of other adverse effects, including relatively advanced age, atrial fibrillation, enlargement of the heart, a regurgitant jet, aortic valvular disease, a relatively high pulmonary vascular resistance, and intracardiac clot. These factors will also influence operative mortality and long-term results.

The facts are as follows. Firstly, as regards operative mortality, in our first 150 patients with heavy calcification of the valve there were 23 operative deaths. This, however, includes early experience, and in the last 50 cases there were six deaths.

Forty of these patients with heavy calcification were under the age of 50, were in sinus rhythm, and had a cardiothoracic ratio less than 60%, and in this group there were no operative deaths.

Valvotomy, Plication, or Replacement

It is our present policy to advise as a first procedure closed transventricular valvotomy for all patients with pure or dominant stenosis, to treat mitral incompetence where possible by plication, and to treat by replacement those who have been found at a previous valvotomy to have a valve so sclerosed or distorted as to preclude a successful second valvotomy.

We are not convinced that a better or safer operation can be performed under vision than by a standard closed technique in more than a small proportion of cases. Even if it were so it is doubtful if the mere extent of valvotomy determines the duration of subsequent freedom from mitral obstructions; also a valve which may give five years or more of good function may look so unpromising that it is replaced, perhaps to the patient's disadvantage if the stage is set for that procedure. The results of closed valvotomy are usually good and there is no contraindication to a second valvotomy if necessary. The valve may be replaced later at a time when better prostheses are likely to be available.

Summary

Some controversial aspects of rheumatic heart disease are discussed in the light of personal experience in Edinburgh. Symptoms are not always a reliable guide to severity, and the correct time for surgical treatment should be based on an objective assessment. Dangers of delay include progressive damage to the pulmonary circulation, lungs, right ventricle, and liver, and the risks of systemic embolism, pulmonary oedema, and pulmonary infarction.

The New York Heart Association classification of disability is unreliable and a potentially dangerous guide.

The concepts of the pliant valve, critical stenosis, areas of auscultation, and the ejection murmur are criticized.

No relation has been found between the size of the left auricle or atrium and the incidence of embolism. There is reason to doubt the value of anticoagulants.

In relation to mitral valvotomy factors influencing operative mortality, complications, traumatic mitral incompetence, sys-

temic embolism, and restenosis are discussed, and also the influence of calcification and of associated aortic valvular disease.

Reference is also made to the place of open heart surgery.

I am grateful to my colleagues, Andrew Logan, with whom I have been so closely associated since he carried out our first valvotomy in 1950 and later introduced the transventricular approach to the mitral valve and, for many years now, Arthur Kitchin, who as a clinician is also in charge of our laboratory, for innumerable discussions and for their advice on the subject matter of this paper.

REFERENCES

- Donald, K. W., Bishop, J. M., Wade, O. L., and Wormald, P. N. (1957). *Clin. Sci.*, **16**, 325.
Kitchin, A., and Turner, R. (1967). *Brit. Heart J.*, **29**, 137.
Sellors, T. H., Bedford, D. E., and Somerville, W. (1953). *Brit. med. J.*, **2**, 1059.

Folate Status and Requirement in Pregnancy

I. CHANARIN,* M.D., B.SC., D.C.P., M.C.PATH.; DOREEN ROTHMAN,† B.SC., M.R.C.O.G.
AUDREY WARD,† M.B., CH.B., M.R.C.O.G.; JANET PERRY,‡ B.SC.

Brit. med. J., 1968, **2**, 390-394

A number of notable studies on pregnancy anaemia have appeared in the last few years. In particular the studies by Lowenstein's group in Montreal have clarified many of the uncertainties in this field (deLeeuw *et al.*, 1966; Lowenstein *et al.*, 1966a, 1966b). In these, as in almost all studies, evidence of both iron and folate deficiency was common and was associated with a megaloblastic form of haemopoiesis in a high proportion of patients. Thus there is a wide agreement about the desirability of both an iron and a folate supplement in pregnancy so that the physiological need for these is met without undue depletion of maternal stores. These aspects were reviewed in the *British Medical Journal* (1964). There is a difference of opinion, however, about the amount of folate needed each day in pregnancy, and amounts between 50 and 5,000 µg. are prescribed.

The purpose of this study was twofold. Firstly, to study the changes in folate status in pregnancy in the absence of associated iron deficiency, and, secondly, under these circumstances to determine the amount of additional folate required to maintain normal tissue stores of folate throughout pregnancy. Iron deficiency was largely eliminated by giving 1 g. of parenteral iron to all subjects in early pregnancy. Folate status was assessed by assay of the red cell (and serum) folate concentration and the state of haemopoiesis by carrying out a marrow aspiration at the end of pregnancy. Folate intake was assessed by direct assay of daily food collection in 16 subjects. Half the women taking part in the study were given an oral daily folate supplement after the 20th week of pregnancy. This paper reports our observations of the effect of the folate supplement, and, secondly, compares the finding in the group of patients who showed megaloblastic haemopoiesis with the finding in the whole group.

Patients, Materials, and Methods

Two hundred and six women attending the antenatal clinic at St. Mary's Hospital took part in the study. All were less than 16 weeks pregnant at the first attendance, and in order to eliminate iron deficiency all received 1 g. of intravenous iron dextran as four 250-mg. doses at weekly intervals. At the 20th week they were allotted to one of two groups, receiving tablets dispensed in a bottle with a grey or a red label. These were to be taken once daily, and contained either ferrous fumarate 260 mg. or ferrous fumarate 260 mg. and 100 µg. of folic acid, the survey being conducted as a blind trial.

On the first attendance (average 15 weeks) blood was taken for a blood count, serum iron estimation, and folate determination of both serum and red cells. This was repeated at the 30th and 38th weeks of pregnancy and a sternal marrow aspiration was performed in the 37th-38th week. All the marrows were assessed at the end of the survey without any knowledge of the colour of tablet taken or of any of the assay results obtained.

Haematological methods were those set out by Dacie and Lewis (1963). Neutrophil polymorphs having five or more distinct nuclear segments were termed hypersegmented, the normal frequency of such cells being 0 to 3%. Marrows were regarded as showing megaloblastic haemopoiesis when megaloblastic change was present in erythroblasts. Giant metamyelocytes were usually present as well. Iron status was assessed by both serum iron estimation and staining of marrow spreads for iron by Perl's Prussian-blue method.

Red cell and serum folates were determined by microbiological assay with the method of Toepfer *et al.* (1951) and *Lactobacillus casei* as the test organism. One gramme of ascorbate was added to each 500 ml. of medium. For red cell folate assay the blood was diluted tenfold in a 0.1 M phosphate-ascorbate buffer pH 6 (Hansen, 1964). In our hands this method gave red cell folate results one-third lower than that obtained when blood was diluted in an aqueous solution of ascorbate. How-

* Reader in Haematology, St. Mary's Hospital Medical School, London W.2.

† Lecturer in Obstetrics, St. Mary's Hospital Medical School, London W.2.

‡ Technical Officer, M.R.C. Experimental Haematology Research Unit, London W.2.