THE RESTORATION OF THE NORMAL CARDIAC MECHANISM IN CASES OF AURICULAR FIBRILLATION BY MEANS OF QUINIDINE SULPHATE.

BY

ALAN N. DRURY AND C. C. ILIESCU,*

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.

For many years quinine has been used in conjunction with other drugs for its supposed beneficial action in cardiac cases; but it was not until 1914 that Wenckebach¹ brought forward evidence of a definite action in its power to terminate paroxysms of auricular fibrillation by restoring the normal rhythm. Prompted by this work Frey² used various alkaloids of the quinine group separately on cases of chronic fibrillation and found that quinine, and especially the alkaloid quinidine, was effective in restoring normal rhythm. This remarkable work of Frey's has been amplified by many other Continental workers, and by Levy³ in America, and the number of cases so treated is now well over 100. The return of the normal cardiac mechanism has not been found to be invariable by any workers, the percentages of successful cases varying up to 66 per cent. in the most successful series, the average varying round 50 per cent. of the cases treated. According to past records the duration of the normal rhythm has varied from a few days up to many months.

The cases herein reported, thirteen in number, all army pensioners, have been under continuous observation for varying periods of time. The known duration of the auricular fibrillation is stated from the dates at which they first came under observation, and from which time, the fibrillation is known to have been a constant condition, and has been treated by digitalis or strophanthus therapy.† The supposed duration is based upon the patients' statements of their symptoms.

The method of treatment adopted has been, in the main, that used by previous workers, although certain variations of dosage have been tried, for reasons which will be stated later. The cases, after being cleared of digitalis or strophanthus, have all received one or two preliminary doses of 0.2 gram of quinidine sulphate by the mouth for the purpose of excluding the presence of quinidine intolerance; after which the quinidine sulphate treatment, given in gelatine capsules by the mouth, has been commenced.

The cases have been recorded electrocardiographically both before and during the quinidine treatment. The method of leading direct from the chest was adopted, as it has been shown that this method gives a much more accurate representation of the auricular movement than do limb leads.¹ The records have been taken every two hours—at 10 a.m., 12 noon, 2 p.m., 4 p.m., and 6 p.m. By this method a record of the auricular oscillations and ventricular movement is obtained and the rates of these are counted.‡

Unsuccessful Cases.

CASE I.

A. H., aged 38. No signs of congestion. Heart slightly enlarged. Developed mitral stenosis. Etiology indeterminate. History of frequent attacks of tonsillitis. Probable onset three and a half years ago. Known duration, 5 months.

Quinidine sulphate. Total dosage, 7.8 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 10 a.m., 12 noon, 4 p.m.—0.4 gram.
Third day ... 4 a.m., 8 a.m., 12 noon—0.4 gram;
4 p.m.—0.6 gram.
Fourth day ... 4 a.m., 8 a.m.—0.4 gram; 12 noon,
4 p.m.—0.6 gram.
Fifth day ... 4 a.m., 8 a.m., 12 noon, 4 p.m.—0.4 gram.

The auricular rate per minute fell from 400 progressively till the end of third day, when it reached 235; on fourth and fifth day there was a slight rise, remaining around 275. Ventricular rate per minute rose from 80 to 126 at end of first day, after which it was variable, being generally about 80. Eighteen

* Working on behalf of the Medical Research Council.

† One exception, Case VI, owing to whose usual low ventricular rate treatment was not indicated.

‡ The auricular rates are the average of a series of oscillation counts, and the ventricular rates an average of counts on the same records.

hours after drug stopped both at original level. Patient complained frequently of short attacks of palpitation.

After seven days, during which the patient received no treatment, quinidine sulphate again given. Total dosage, 2.1 grams, given as follows:

First day ... 9 a.m., 10 a.m., 11 a.m., 12 noon, 1 p.m.,
2 p.m., 3 p.m.—0.3 gram.

Auricular rate per minute fell from 425 to 240. Ventricular rate per minute rose from 75 to 118. Sixteen hours after quinidine stopped, both auricular and ventricular rates at original levels. Patient complained of severe headache towards the end of treatment.

CASE II.

T. F. B., aged 28. No signs of congestion. Heart definitely enlarged, but not greatly. Mitral stenosis. Etiology indeterminate. Probable onset of fibrillation five years ago. Known duration eight months.

Quinidine sulphate. Total dosage 11.8 grams, given as follows:

First day ... 10 a.m., 1 p.m., 4 p.m.—0.4 gram.
Second day ... 8 a.m., 12 noon, 4 p.m., 12 midnight—0.4 gm.
Third day ... 8 a.m., 12 noon, 4 p.m., 12 midnight—0.4 gm.
Fourth day ... 4 a.m., 8 a.m., 12 noon, 4 p.m., 8 p.m.,
12 midnight—0.4 gram.
Fifth day ... 4 a.m., 8 a.m.—0.4 gram; 12 noon, 4 p.m.—
0.6 gram; 8 p.m., 12 midnight—0.4 gram.
Sixth day ... 4 a.m., 0.4 gram; 8 a.m., 12 noon, 4 p.m.—
0.6 gram.

Auricular rate per minute fell from 575 to 350 on the first day, remaining at that level on the second and third with tendency to rise; on the sixth day it had fallen to 325. Ventricular rate per minute rose on the first day from 85 to 120, remained around 90 for three days, and fell on the fifth and sixth to 80; sixteen hours after withdrawal of quinidine both auricular and ventricular rates at original levels.

Patient had no symptoms during treatment. After thirty-six hours with no treatment, quinidine sulphate again given. Total dosage 2.1 grams given as follows:

First day ... 9 a.m., 10 a.m., 11 a.m., 12 noon, 1 p.m.,
2 p.m., 3 p.m.—0.3 gram.

Auricular rate per minute fell from 550 to 375. Ventricular rate per minute rose from 75 to 130. Sixteen hours later both at original levels. Patient complained of headache towards end of treatment.

CASE III.

J. M., aged 24. No signs of congestion. Heart considerably enlarged. Developed mitral stenosis. Etiology indeterminate. Probable onset five years ago. Known duration twelve months. Quinidine sulphate. Total dosage 8.2 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 10 a.m., 12 noon, 4 p.m., 10 p.m.—0.4 gram.
Third day ... 8 a.m., 12 noon, 4 p.m., 10 p.m.—0.4 gram.
Fourth day ... 8 a.m., 0.4 gram; 12 noon, 4 p.m.—0.6 gram;
10 p.m., 0.4 gram.
Fifth day ... 8 a.m., 0.6 gram; 10 a.m., 12 noon,
2 p.m.—0.4 gram.

Auricular rate per minute fell from 400 to 260 on the first day. On the second fell from 350 to 265, and progressively on the third, fourth, and fifth, when it was 180. The ventricular rate per minute rose from 70 to 110 on the first day, returning to 72 at beginning of the second day, rising to 115, remaining around 100 for remainder of treatment. Sixteen hours after treatment stopped, both rates at original levels. Patient had no symptoms except occasional short attacks of palpitation. After seven days, during which the patient had no treatment, quinidine sulphate was again given—9.8 grams. First five days' dosage as above; on sixth day, 4 a.m., 8 a.m., 0.4 gram; 11 a.m., 0.8 gram. (Coincident with this the patient was given liq. atropinae, 0.2 per cent. solution, 10 minims per diem.) The auricular rate and ventricular rate were very similar in degree and distribution to first quinidine treatment, but auricular rate did not fall below 200. Twenty-four hours after treatment, both at original levels. Patient complained of dryness of the mouth, but otherwise had no symptoms.

CASE IV.

T. G., aged 46. No signs of congestion. Heart slightly enlarged. Systolic murmur at apex, no diastolic heard. Etiology indeterminate. Probable onset four and a half years ago. Known duration fifteen months. Quinidine sulphate. Total dosage 1.6 grams.

First day ... 8 a.m., 0.4 gram; 10 a.m., 0.2 gram;
12 noon, 0.4 gram; 2 p.m., 0.2 gram;
4 p.m., 0.4 gram.

Auricular rate per minute fell from 425 to 330 at 6 p.m. Ventricular rate per minute rose from 80 to 120 at 6 p.m. At 6.15 p.m. had a syncopal and epileptiform attack, ventricular rate after recovery being very slow and rising gradually. Attack preceded by feeling of sickness and accompanied by diarrhoea. Auricular rate after attack 268, ventricular rate 56. Patient gave a history of similar attacks previously. Twenty-four hours later both rates at original levels.

CASE V.

F. M., aged 22 years. No signs of congestion. Heart definitely but not considerably enlarged. Mitral stenosis. Etiology

FIG. 1.—Direct chest lead records (sternal lead) from Case XII, showing retardation of auricular rate, with accompanying change in character of the records.

indeterminate. Probable onset indeterminate. Known duration ten months.

Quinidine sulphate. Total dosage 3.6 grams, given as follows:

First day ... 8 a.m., 4 p.m.—0.4 gram.
Second day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Third day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Fourth day ... 8 a.m.—0.4 gram.

Auricular rate per minute fell on first day from 475 to 400, rising to 460 at the beginning of the second, and falling progressively to 300 at the end of the third day. At 8.45 on the fourth day pure flutter at 220 appeared, falling at 12 noon to 200, and rising quickly again to 220; during the day it rose to 260, and remained about that rate; pure flutter continuing. Ventricular rate rose very little from 80 the first three days; on the fourth day, when pure flutter appeared, the ventricle responded 2:1 at 110; when auricular rate fell to 200, ventricle responded 1:1, for about one hour at 200, but as the auricular rate rose 2:1 response returned; during the next twenty-four hours patient had several short periods of 1:1 response, when digitalis therapy was commenced, and fibrillation returned after three days of this treatment.

CASE VI.

H. H., aged 39 years. No signs of congestion. Heart, moderate enlargement. Mitral stenosis. Etiology, acute rheumatism. Probable onset three and a half years ago. Known duration seventeen months.

Quinidine sulphate. Total dosage 4.4 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Third day ... 8 a.m., 4 p.m.—0.4 gram; 12 noon—0.2 gram.
Fourth day ... 8 a.m., 4 p.m.—0.4 gram; 12 noon—0.2 gram.

Auricular rate per minute fell on first day from 450 to 275, and remained at that level till the third day, when slight rise, followed by a fall to 275, produced on this and succeeding days by interposition of smaller doses at 12 noon. Ventricular rate per minute rose on the first day from 52 to 78, varied between 78 and 60 on succeeding days. Twenty-four hours after drug stopped, both at original rate.

CASE VII.

R. L., aged 40 years. No signs of congestion. Heart slightly enlarged. Valves nil. Etiology indeterminate. Probable onset four and a half years ago. Known duration fifteen months.

Quinidine sulphate. Total dosage 15.2 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 8 a.m., 12 noon, 4 p.m., 10 p.m.—0.4 gram.
Third day ... 8 a.m., 12 noon, 4 p.m., 8 p.m.—0.4 gram.
Fourth day ... 8 a.m., 12 noon, 4 p.m., 8 p.m., 12 mid-night—0.4 gram.
Fifth day ... 4 a.m., 8 a.m., 12 noon, 4 p.m., 10 p.m.—0.4 gram.
Sixth day ... 8 a.m., 4 p.m., 10 p.m.—0.4 gram.
Seventh day ... 8 a.m., 4 p.m., 10 p.m.—0.4 gram.
Eighth day ... 4 a.m., 8 a.m., 4 p.m.—0.4 gram.
Ninth day ... 8 a.m.—0.4 gram; 12 noon, 4 p.m.—0.2 gm.
Tenth day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Eleventh day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.

Auricular rate per minute fell slowly but progressively, from 450 to 250 on the fourth day, after this the rate remained around 270 till the seventh day, when it rose to 350, and remained at that level till the ninth day when it again progressively fell to 260 on the eleventh day. Ventricular rate per minute rose slowly but progressively from 70 to 110 on the third day, remaining around 90, with several short periods of high rate about 120, till the eleventh day. Twenty-four hours later both at original level. Patient complained of several short attacks of palpitation.

Successful Cases.

CASE VIII.

W. C. S., aged 46. No signs of congestion. Heart slightly enlarged. Valves, no murmurs heard. Etiology indeterminate. Wassermann positive. Liver enlarged and hard. Probable onset four years ago. Known duration nine months.

Quinidine sulphate. Total dosage 2 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 8 a.m., 12 noon—0.4 gram; 2 p.m., normal rhythm.

Auricular rate per minute fell from 476 to 340 on first day, remaining at that level till two hours before normal rhythm appeared. Ventricular rates per minute rose from 70 to 100 on the first day, remaining about 80 on the second day till normal rhythm appeared at 67 per minute. The patient complained of no symptoms during treatment.

CASE IX.

F. J., aged 50. No signs of congestion. Heart definitely but not considerably enlarged. Valves nil. Etiology indeterminate. Wassermann negative. Probable onset, five years ago. Known duration seven months. Quinidine sulphate. Total dosage 4 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 10 a.m., 12 noon, 4 p.m., 8 p.m.—0.4 gram.
Third day ... 4 a.m., 8 a.m., 12 noon—0.4 gram; 2 p.m., normal rhythm.

Auricular rate per minute fell progressively from 400 to 300, two hours before normal rhythm appeared. Ventricular rate per minute rose from 120 to 135 on the first day, keeping around 120 till normal rhythm appeared at 69 per minute. The patient complained of no symptoms during treatment.

CASE X.

E. N., aged 31. No signs of congestion. Heart not enlarged. Valves nil. Etiology indeterminate (brothers acute rheumatism). Probable onset four years ago. Known duration thirteen months.

Quinidine sulphate. Total dosage 6.6 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.
Second day ... 10 a.m., 12 noon, 4 p.m., 8 p.m., 12 mid-night—0.4 gram.
Third day ... 4 a.m., 8 a.m., 12 noon, 4 p.m., 8 p.m., 12 mid-night—0.4 gram.
Fourth day ... 4 a.m., 0.4 gram; 8 a.m., 0.6 gram; 11.30, normal rhythm.

Auricular rate per minute fell from 540 to 450 on the first day, rising to 525 at beginning of the second and falling to 440 and

FIG. 2.—Limb lead (lead III) records of Case XII. (a) Before treatment. (b) After appearance of normal rhythm.

progressively falling to 350 one hour before normal rhythm appeared. Ventricular rate per minute showed slight rise on the first day from 80 to 100, falling to original level at beginning of the second and rising again and maintaining itself around 90 till normal rhythm appeared at 65 per minute. The patient had no symptoms during treatment.

CASE XI.

H. A., aged 27. No signs of congestion. Heart considerably enlarged. Developed mitral stenosis. Etiology, chorea. Probable onset unknown. Known duration fifteen months.

Quinidine sulphate. Total dosage 4.4 grams, given as follows:

First day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.

Second day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.

Third day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram;

10 p.m.—0.4 gram.

Fourth day ... 8 a.m.—0.4 gram; 10 a.m., normal rhythm.

Auricular rate per minute fell progressively from 420 to 280 at the end of the second day, showed tendency to rise on the third, and at the end was 350. Sixteen hours later normal rhythm. Ventricular rate per minute rose from 70 to 115 on first day, maintaining itself around 90 till normal rhythm appeared at 70 per minute. Patient had no symptoms during treatment.

CASE XII.

W. W., aged 25. No signs of congestion. Heart considerably enlarged. Developed mitral stenosis. Slight aortic regurgitation. Etiology indeterminate; frequent attacks of tonsillitis. Probable onset two months ago. Known duration four weeks.

Quinidine sulphate. Total dosage 2.8 grams.

First day ... 10 a.m., 1 p.m., 4.30 p.m.—0.4 gram.

Second day ... 8 a.m., 12 noon, 4 p.m.—0.4 gram.

Third day ... 8 a.m.—0.4 gram; 10 a.m., normal rhythm.

Auricular rate per minute fell from 425 to 250 at the end of the second day. Sixteen hours later normal rhythm. Ventricular rate per minute rose from 70 to 105 on the first day, maintaining itself around 90 till normal rhythm appeared at 70 per minute.

CASE XIII.

A. J. P., aged 43. No signs of congestion. Heart moderately enlarged. Valves, mitral stenosis. Etiology indeterminate. Probable onset five years ago. Known duration, twenty months.

Quinidine sulphate. Total dosage 0.8 gram, given as follows:

First day ... 8 a.m., 12 noon—0.4 gram; 4 p.m., normal rhythm.

Auricular rate per minute fell from 450 to 275. Two hours later normal rhythm. Ventricular rate per minute rose from 60 to 85, when normal rhythm appeared at 60 per minute.

The cardiac signs and general symptomatology of the patient before and after successful treatment, and also the duration of the normal rhythm, will be dealt with at a later date.

As can be seen from the foregoing results, the first reaction of the auricular rate is similar in all patients, whether the normal mechanism is finally restored or not; the auricular rate is retarded. Commencing from the figure around the average rate of 450 per minute, the auricular rate falls and has reached a rate of 200 per minute in some of the cases studied; and as the rate falls the character of the records changes. The periods of no oscillation which are found in the direct chest lead records of cases prior to treatment become less frequent, to the point of disappearance, and the oscillations become more regular, both in time and form, and at the low rates the maximum variation between the longest and shortest cycles is about 0.05 second.

The records change from those of fibrillation, passing imperceptibly into those of impure flutter, the impurity of

which becomes less and less, but not as a rule attaining the purity of auricular flutter as this is usually seen clinically. A series of such curves taken from Case XII (Fig. 1) illustrates this point. In unsuccessful cases when the drug is withdrawn the impure flutter passing again gradually into fibrillation is shown. Only exceptionally is auricular flutter developed in its pure form (see Case v), and in this case the flutter did not pass again into impure flutter, but continued to flutter after the drug was stopped. The curves of the calculated rates are not smooth during the period of treatment, and there are indications that about two hours after the giving of a dose of the drug the maximum effect is obtained, and thenceforward the auricular rate shows a slight rise. The factor becomes of importance in some cases, as, owing to the lapse of time between the last dose of one day and the first dose of the next, there appears to be opportunity for the auricular effect to vanish, and the condition may be on the second day comparable to that prior to treatment. Through and through, however, the doses suggested by previous workers—that is, 0.4 gram three times a day—are sufficient to ensure a progressive retardation of auricular rate for the first few days, during which time the majority of successfully treated cases have re-established the normal mechanism. The alteration in method of dosage mentioned above has been adopted in some cases in order to maintain a progressive retardation of auricular rate, but such retardation, though continued, does not necessarily ensure the restoration of the normal rhythm in cases which do not respond to treatment in the first few days. It has not been considered advisable to attempt to drive the auricular rate below 200 per minute. There appears to be a definite relation between the auricular rate and the ventricular rate, for as the former falls the latter rises, and vice versa; and although it appears in the later stages of treatment that this relationship is disturbed by the presence of other factors, it has been considered advisable to keep to this limit to avoid the appearance of a 1:1 response of the ventricle and its consequent high rate of beating. That the retardation of the auricle is produced by quinidine sulphate is well shown by the fact that upon withdrawing it in cases where the auricular rate has been retarded, the rate mounts, and in twelve to eighteen hours has reached the level prior to treatment. The ventricular rates, similarly ascertained, show certain features in all cases; during the first day the ventricular rate rises, for example, from 70 often up to 120 or more; after this considerable variation is seen, the rate ranging from the last figures to figures which, though lower, are for the most part in excess of that prior to treatment. Upon withdrawing the quinidine sulphate, the ventricular rate falls to its original level.

Thirteen cases of auricular fibrillation have been treated with quinidine sulphate, and in six cases the normal rhythm has been re-established, while in the remaining seven cases, although similar changes have been produced in the retardation of the auricular rate the movement persisted without break, and the rate returned, upon withdrawal of the drug, to its original level.

The percentage success obtained is of the same order as that obtained by several other workers, and the successful and unsuccessful cases, as previous workers have shown,

do not fall into any special clinical group, either with regard to otiology, cardiac enlargement, valvular involvement, or duration of the malady. Both successful and unsuccessful cases form heterogeneous groups.

The drug, quinidine sulphate, has a very remarkable action upon the auricle, and this action is of a potent nature. For this reason alone the method of direct leads from the chest is of importance, for it gives a record of the effect of the drug upon the auricle itself; the effect on the auricle will vary considerably owing to the factors of absorption, individual tolerance, etc., and the direct leads enable the drug to be controlled.

REFERENCES.

- ¹ Drury, A. N. and Iliescu, C. C.: *Heart*, 1921, viii, 171. ² Frey, W.: *Berl. klin. Woch.*, 1918, lv, 417 and 849. ³ Levy, R. L.: *Journ. Amer. Med. Assoc.*, 1921, lxxvi, 289. ⁴ Wenckebach, K. F.: *Die unregelmässige Herzthätigkeit und ihre klinische Bedeutung*, 1914, 125 and 128. Full references will be found in the above articles.

THE MANNER IN WHICH QUINIDINE SULPHATE ACTS IN AURICULAR FIBRILLATION.*

BY

THOMAS LEWIS, A. N. DRURY, C. C. ILIESCU,
AND A. M. WEDD,

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.

THE action of quinidine sulphate upon the fibrillating auricle, an action but recently discovered, is perhaps one of the most remarkable and dramatic which is now known to therapeutics. The essential feature of the reaction is an invariable and conspicuous reduction of the rate at which the auricle beats; in patients in whom treatment is successful this progressive slowing of the auricular action is abruptly disturbed, the disordered action ceases, and the normal action is at once resumed.

To understand how these changes are brought about is of obvious importance; but this problem cannot be solved unless we are able first to understand the mechanism of fibrillation itself. Several views of the reaction of the fibrillating auricle to quinidine have been published, but as these all assume that fibrillation of the auricle is caused by rapid impulses, arising at one or more irritable centres in the muscle of the auricle, and to which the auricle responds in a confused manner, the explanations founded upon such an assumption remain inadequate. These theories of auricular fibrillation, until recently widely held, have undergone extensive revision, and are now scarcely acceptable.

Recently a series of papers² has been published from this laboratory, in which it has been shown that in auricular fibrillation a circus movement exists in the auricle; that a single wave is propagated and revolves perpetually upon a re-entrant path. The circus movement is repeated in the average 450 times a minute, and it is this circulating wave which, in its revolution, alone controls the beating of the auricle. The auricle is no longer controlled by discrete impulses arising at a single point on the auricular muscle, each impulse originating a corresponding discrete wave of contraction in the auricle which dies away and is renewed, but by a never-ending wave which passes over and over again through the same muscular channels. To understand the action of quinidine it is necessary to understand the factors which control this circus movement. They have been stated previously, and are: (a) the length of the path followed; (b) the duration of the refractory period at any given point; and (c) the speed at which the wave is conducted.

Circus movement in the auricle is only possible (1) if a circular path of sufficient length is available; (2) if the refractory period is sufficiently short; and (3) if the speed at which the wave moves through the muscle is sufficiently slow. Otherwise the crest of the advancing wave in re-entering muscle through which it has already passed will discover this muscle to be still refractory and will be unable to proceed. The wave in travelling leaves muscle behind it which is for some time incapable of response; time must elapse to permit recovery before the new or

re-entrant wave can again pass. Quick recovery (a short refractory period) clearly favours re-entry; so does a long path, and so does a slow rate of travel, for the two last conditions both delay the arrival of the re-entrant wave.

Now experiment has shown us that in auricular fibrillation the gap between the crest of the advancing wave and its wake is very small; on the circular path, the wave is always advancing through muscle which has but just recovered its excitability; the presence of some gap is all-essential, upon its existence the continued movement absolutely depends. It has been stated that if we could find a remedy which would close this gap, either in flutter or in fibrillation, the circus movements to which these abnormal movements of the auricle depend, would at once cease. The first of such remedies has been discovered in quinidine.

Hoffmann¹ in observing the effects of quinidine experimentally found that it reduces the excitability of the auricular muscle; that is true, but it was not made clear by his experiments how this reduction happens, neither is a reduced excitability in itself a sufficient explanation of the remarkable effects of quinidine on the fibrillating auricle. In recent experiments, a full report of which will be published elsewhere, we have found that the most striking action of quinidine upon the auricle is a lengthening of the refractory period; the lengthening which occurs, when doses comparable to those used clinically are employed, amounts to 50 per cent. or more. The reason why quinidine brings fibrillation of the auricle to an end seems to us therefore not to be in doubt. It prolongs the refractory period of the auricle and delays the recovery of the tissue, thus rendering the gap between the crest and the wake of the circulating wave shorter and eventually abolishing it altogether; when the last event happens the abnormal action of the auricle ceases and the normal impulses are thus enabled once again to resume control.

Though we do not doubt that this is the explanation of the successful treatment, the problem is not quite so simple as it may at first seem; for quinidine has not only this action upon the refractory period, it has further actions. The most important of them from our present standpoint is an effect on the rate of conduction; it slows conduction in the auricle. Now slowing of conduction favours re-entry; it prolongs the gap. Thus quinidine exerts two effects which, so far as circus movement is concerned, are opposed to each other; on the one hand, by prolonging the refractory period it tends to shorten the gap; on the other hand, by slowing conduction it tends to lengthen the gap. It is only in those cases where the first effect predominates over the second that the gap will close and the circus movement will terminate. In patients suffering from chronic auricular fibrillation the first effect appears to predominate in approximately 50 per cent. of the cases, for in this percentage auricular fibrillation is abolished; in those patients (the remaining 50 per cent.) in whom this desired end-result is not obtained, it would seem as if the second effect predominates, or that the opposed effects are exerted equally. It is to be noted that in patients in whom fibrillation is not abolished there is nevertheless slowing and usually very profound slowing of the auricle, the rate falling from its original rate of 400, 500, or 600 per minute to 300, 250, or even 200 per minute; such slowing would be the anticipated effect of depressed conduction in the auricle, and it is probable that it is to be ascribed to this cause, in the main, at all events.*

The theory of fibrillation which we support—namely, its dependence upon circus movement—is one which, in the light of our recent experiments upon quinidine, is fully competent to explain the remarkable action of this drug upon the disorderly action of the auricle under consideration. We publish this note at the present time to draw attention to our view of the manner in which quinidine acts, believing that treatment by means of quinidine, which is now engaging the attention of many workers, is best controlled when its action is interpreted in the way which we suggest, and that further progress in this method of treatment, already highly successful, promises to come

* Another factor—namely, lengthening of the path, the wave seeking a new and longer path of re-entry as it finds the old one closed—possibly contributes; but we do not at present regard it as the main factor. It is also to be noted that quinidine very probably affects what we have termed the partial refractory period, and some evidence in this direction has been obtained. But these factors, at present regarded as minor ones, are as yet unripe for discussion.

* Being a preliminary account of work undertaken for the Medical Research Council.