

QUINIDINE SULPHATE IN CARDIAC DISEASE

By JOHN HAY

With Plates 10-16

IN October, 1921, Alan N. Drury and C. C. Iliescu published in the *British Medical Journal* their experience of the administration of quinidine sulphate in thirteen cases of fibrillation of the auricle, and stated that the number of cases so treated was well over 100. As an indication of the widespread interest in this matter I have been able to find records of 383 cases reported on by twenty-five observers, the majority of these having appeared since the publication of Drury and Iliescu's paper.

It is not difficult to understand the eagerness with which the problem is being investigated when one remembers that auricular fibrillation is present in over 60 per cent. of the cases of cardiac failure admitted into hospital, that it is often the cause of the acute cardiac collapse in the arterio-sclerotic with hypertension, and that it is not infrequently the explanation of the onset of rapid cardiac distress in patients suffering from mitral disease who, previous to the fibrillation, were endowed with adequate cardiac reserve.

Some experimental work by Eyster and Swarthout¹ on dogs has shown that fibrillation diminished the cardiac output by 40 per cent., and from the clinical evidence it is clear that the inception of fibrillation means a sudden and definite increase in the load which the heart has to bear.

Hearts with a liberal reserve may tolerate this sudden call with equanimity or they may rapidly compensate to meet it, but others with a narrower margin of reserve are overwhelmed, and the result is cardiac failure and a transitional period of stress. Under rest and medicinal treatment the fibrillation may be controlled and a condition of relative comfort produced, but at a lower level of physical effort than before.

Fibrillation being then so common an occurrence and also such a potent factor in the deterioration of a heart case, the appearance of a drug which, it is claimed, has the power to cut short this vicious arrhythmia is of the utmost importance, and it is essential that in so far as it is possible we should investigate its action and determine the indications and contra-indications for its exhibition.

It is possible by means of the electro-cardiograph to follow in detail certain important changes taking place in the heart in response to quinidine. These are definite and significant.

¹ *Archiv. of Int. Med.*, Chicago, 1920, xxv.

1. There is almost invariably a steady decrease in the number of auricular oscillations per minute, i. e. from 450 to 500 down to 250 to 300.
2. Occasionally auricular flutter appears with a 2 : 1 rhythm.
3. There is, as a rule, a steady increase of ventricular rate.
4. The appearance of ectopic beats, ventricular in origin, is common.
5. In about 50 per cent. of the cases the appearance of a normal rhythm.
6. Continuation of treatment with quinidine does not prevent the recurrence of the fibrillation.

My experience of quinidine sulphate is confined to fifteen cases. In twelve of these fibrillation was established and of some standing; in one it appeared towards the end of an attack of acute pneumonia; in another it was paroxysmal, and the remaining patient was suffering from paroxysmal tachycardia.

In six of the twelve established cases quinidine failed. Of these six one patient was so intolerant of the drug that it had to be discontinued after the first dose.

In three of the patients pure flutter developed. In one of the three this gave way to a normal rhythm, in another the flutter persisted after the quinidine was stopped, and in the third fibrillation returned while under treatment.

Of the seven in whom fibrillation was arrested it is too early to speak of the stability of the change, but in two, at least, there have been relapses. In four the improvement has been pronounced and the cardiac reserve has been considerably increased (see cases).

There was one death among the fifteen. This occurred in the patient suffering from paroxysmal tachycardia. It was most disappointing; the paroxysm had been cut short, and the patient appeared to be progressing satisfactorily when suddenly, without warning, she died. Death occurred twenty-four hours after the cessation of the abnormal rhythm and after 2 grm. of quinidine had been taken. No autopsy was permitted.

		Reverted to Normal.	Recovery only Temporary.	Flutter.	Total Failure to obtain Normal Rhythm.
Established fibrillation	(12)	6	2	1	6
Onset during pneumonia	(1)	1			
	(13)	7	2	1	6
Paroxysmal tachycardia	(1)	1	Died 24 hours later.		
Paroxysmal fibrillation	(1)	Ultimately much improved. Quinidine did not prevent recurrence of paroxysms. (See Plate 16, Fig. 8.)			

The usual procedure adopted has been as follows: The patient is kept in bed for a few days free from drugs. He is electro-cardiographed, and it is determined which of the three leads gives the most sharply-defined auricular oscillations, and this lead is utilized for observation. A tentative or experimental dose of 0.2 grm. quinidine sulphate is given, and all being well quinidine is started next day in full doses. An electro-cardiogram is taken twice a day when possible and any change noted in the action of the auricles and ventricles. In our experience the most satisfactory method of dosage is that of 2 grm. of the quinidine sulphate in the twenty-four hours given in capsules by the mouth, in doses

of 0.2 grm. for ten doses—given at 8 a.m., 10 a.m., 12 p.m., 2 p.m., 4 p.m., 6 p.m., 8 p.m., 12 a.m., 3 a.m., and 5 a.m. If necessary, the daily dose is increased to 3 grm. by doubling the dose at 10 a.m., 2 p.m., 6 p.m., 12 a.m., and 5 a.m. In the first few cases the dosage was 0.4 grm. at 8 a.m., 2 p.m., and 8 p.m., and sometimes another dose at 2 a.m.

The ward Sister has instructions that the heart is to be examined before each dose is given and the drug stopped if the action appears to be normal. As Sir Thomas Lewis has pointed out the action of the quinidine passes off rapidly, and it is desirable that there should not be any long delay between any two doses. The first six cases briefly recorded are those in which quinidine failed to procure a normal rhythm.

Case I. A. M., aged 24. Admitted 30.12.21. A case of old-standing valvular disease, rheumatic in origin. Mitral stenosis and regurgitation and slight aortic regurgitation. Marked distress for three years. Responds badly to digitalis. Is liable to attacks of decompensation, engorged liver, oedema, cyanosis, and severe dyspnoea. The preliminary dose of 0.2 grm. caused vomiting, headache, and feeling of considerable discomfort with orthopnoea. The ventricular rate ran up to 190, and the pulse became very feeble. It was not considered advisable to continue with the quinidine.

Case II. W., aged 36. Admitted 23.11.21. Moderate mitral stenosis and regurgitation with slight aortic regurgitation of old standing. Heart moderately enlarged. Presents the typical clinical picture of mitral disease. Dyspnoea on slight effort. Fibrillation probably dates back seventeen months (after the birth of her last child). Known duration since 23.8.21. Quinidine caused no discomfort, and there followed the typical slowing in the auricular oscillations (Plate 10, Fig. 1). A drop from 470 per minute to 300 with little, if any, change in the ventricular rate. Fibrillation persisted. Total quinidine 14 grm.

Case III. P., aged 46. Admitted 23.11.21. Mitral stenosis of old-standing, rheumatic in origin. Heart moderately enlarged; no venous engorgement, always liable to rapid action. This was noticed for years before the fibrillation began. In June, 1920, there were short bouts of flutter. Fibrillation began November, 1920, and has persisted. Quinidine caused considerable distress, palpitation, giddiness, faintness, buzzing in the ears, and headaches.

The initial rate of the auricular oscillations was 480, with a ventricular rate of 150. The auricular oscillations fell to 320, and then, after 2.4 grm. of quinidine, flutter appeared with a 2:1 rhythm and an auricular rate of 240. This gradually increased to 288 next day. After 5.6 grm. fibrillation was resumed with an auricular rate of 405; this again fell, and after 7.6 grm. flutter reappeared. Auricular = 264, ventricular = 132. However, this again was transitory and passed into fibrillation with an auricular rate of 300 and a ventricular rate of 140. The auricular oscillations rapidly ran up to 450 on the cessation of quinidine. Total dosage 12 grm. See Plate 11, Figs. 2 and 3.

Case IV. B., aged 55. Admitted 6.12.21. A tall, pale man with an emphysematous chest, slight enlargement of the heart, no evidence of valvular disease. Blood-pressure not raised. Slight arterio-sclerosis. Fibrillation dates probably from 1917; certainly from August, 1921. The quinidine caused discomfort, chiefly headache and some praecordial pain. Before the administration of the quinidine the oscillations of the auricle were 450. The quinidine reduced the rate to 360. He had in all 12 grm. in doses of 0.4 grm. *ter in die*, but the fibrillation persisted.

Case V. W. J. B., aged 51. Admitted 22.2.22. A case of old-standing mitral disease, with definite enlargement, some limitation of reserve power shown by palpitation and shortness of breath. The aetiology is obscure, but he gives a history of syphilis, and the Wassermann is + +. There is no evidence of hypertension. The fibrillation is probably of some years' duration, but known to be present from June, 1921. There was practically no discomfort during the administration of quinidine. The usual rapid diminution in the number of the oscillations of the auricle took place. After 0.8 gm. they had fallen to 360, after 2.8 gm. to 260 per minute, and they remained at that level while the quinidine was being taken (Plate 12, Fig. 4). The outstanding feature was the steady development of the tendency to premature beats of various types. After 10 gm. the majority of the ventricular contractions were of this nature, and as the ventricular rate had risen from 92 to 138 per minute it was not considered advisable to continue with the quinidine.

Case VI. G. P., aged 36. Admitted 2.3.22. Heart enlarged. Mitral valvular disease. Evidence of very defective cardiac reserve. Marked emphysema. Probable duration of the fibrillation two years. Quinidine was begun on March 4, 1922, and produced some discomfort, slight palpitation and headache, nausea and buzzing in the ears. In all 10.8 gm. were given; 2 gm. daily in 0.2 gm. doses. An electro-cardiogram taken just after quinidine had been started showed a tendency to premature beats (Plate 13, Fig. 5 B). Fibrillation yielded to flutter, and the flutter showed a peculiar variation. At first the ventricular complexes were normal with a 2:1 rhythm; then a period ensued in which the ventricular complexes were similar to those of the premature beats above mentioned (Figs. 5 B and 5 D), and which had occurred before the inception of the flutter. These again suddenly gave place to flutter with normal ventricular complexes (Fig. 5 C). Owing to the discomfort and the refusal to respond the quinidine was discontinued. Later he was put on full doses of Tinct. digitalis without any material change in the rhythm. The injection of strophanthin sufficed to change the flutter into fibrillation with a rapid fall of ventricular rate to 80.

Case VII. D. R., aged 60. Admitted 12.12.21. Heart materially enlarged, but no definite evidence of valvular disease. Complained of praecordial pain and tenderness, and was conscious of the irregularity. Probable duration of fibrillation was five years—possible onset dating back to shell shock and exposure in the Dardanelles. Had been definitely observed since July, 1921. Transition from fibrillation to normal action was unnoticed by the patient. Took place after 1.2 gm. (Plate 14, Fig. 6). The rate of auricular oscillations when first observed was 408, with a ventricular rate of 84. Just previous to the transition the auricular rate was 360 and the ventricular 108. Normal rhythm started at 72.

Case VIII. E. W., aged 43. Admitted 6.2.22. Heart slightly enlarged, but no evidence of valvular disease. No venous engorgement. Some dyspnoea on exertion. Probable duration of fibrillation was twelve months. Tolerated the quinidine well. It caused some acceleration of the ventricular rate. Normal rhythm attained after 4.8 gm. There was marked improvement. He was returned to Pensions Hospital on February 18, 1922, and asked to be discharged to work March 2, 1922.

Case IX. W. A., aged 33. Admitted 18.2.22. Heart somewhat enlarged ($4\frac{3}{4}$ in. to left of mid-line). Suffering from valvular disease of rheumatic origin; aortic regurgitation and mitral regurgitation; no evidence of decompensation. Reserve power good. Probable duration one to two years. Practically no subjective symptoms, and nothing to suggest cardiac failure. Response to quinidine was rapid and satisfactory. Before quinidine, auricular oscillations were 480 per minute and ventricular rate was about 80 to 90. After 0.8 gm.

auricular oscillations were 420 and ventricular rate 72. After 2.8 gm. auricular oscillations had dropped to 330 and ventricular rate had risen to 110. The rhythm became normal after 4.2 gm., with cardiac rate of 90 and marked prolongation of the P. R. interval. No discomfort during administration of quinidine. 22.3.22: Two or three weeks after leaving hospital he noticed his heart suddenly become irregular. Normal for about ten days. Was never much distressed by fibrillation and is not distressed now.

Case X. P. B., aged 42. Admitted 18.2.22. Heart moderately enlarged. No clear evidence of valvular disease, chief complaint being palpitation and shortness of breath of two years' duration. Occasional dizziness and occasional slight prae-cordial pain. *Aetiology indefinite. Wassermann negative.* Duration of fibrillation probably two years. Known to be present from February 4, 1921. Ventricular rate 165 when record taken (Plate 15, Fig. 7). The average ventricular rate in bed was between 90 and 100. This was before the administration of quinidine. *Quinidine method of dosage.* 0.2 gm. in 10 doses every 24 hours at 8 a.m., 10 a.m., 12 p.m., 2 p.m., 4 p.m., 6 p.m., 8 p.m., 12 a.m., 3 a.m., and 5 a.m. to obtain continuity of effect. Only slight discomfort as result of quinidine. Occasional palpitation; steady rise in ventricular rate; slight headache and some buzzing in the ears. At 11.30 p.m. on February 23 he awoke and found his heart 'banging away'; about midnight it suddenly changed its rhythm. In this patient fibrillation changed to flutter after 2.4 gm., and after 2.8 gm. there was a 2:1 rhythm with the auricle beating at 270. After 3.4 gm. the rhythm became normal. This rapid ventricular rate did not appear to distress him materially. Four weeks after the restoration of a normal rhythm he felt better than for two years, and could walk up and down stairs with comfort.

Case XI. H., aged 42. Admitted 2.3.22. Definite enlargement of heart. Evidence of old-standing mitral disease (stenosis). No presystolic bruit. Duration of fibrillation probably eight years. Certainly $4\frac{1}{2}$ years. Heart reverted to normal rhythm after 0.8 gm., and the presystolic murmur and thrill developed. Unfortunately, there were short relapses, during which the presystolic murmur and thrill disappeared.

Case XII. R. E., aged 39. Admitted 2.3.22. Heart enlarged. Apex beat 5th and 6th spaces. V.D.H. of old standing, dating from chorea when 20 years old. For last six years some dyspnoea on exertion. Symptoms worse since pneumonia last October. On admission cardiac reserve very poor. Considerable dyspnoea and palpitation on walking upstairs. 5.3.22: Heart reverted to normal action after 2.4 gm. Only slight symptoms of distress during the administration of quinidine. 10.3.22: The improvement was such that he was able to run up and down stairs without discomfort. 23.3.22: Improvement maintained. Later he reverted to fibrillation and was readmitted, and normal rhythm was restored after 2.4 gm. of quinidine.

Case XIII. Seen with Dr. Macalister and Dr. Murphy. I report this case although it was not possible to check the findings with the electro-cardiograph. Fibrillation occurred towards the latter end of a typical pneumonia in a healthy young adult of about 25. The temperature fell on the 6th day and fibrillation began on the 7th. The ventricular rate ran up to 160 and more beats per minute. Strophanthin intravenously had no effect, and the condition was causing very great anxiety. There was extreme dyspnoea and some cyanosis. Two doses of quinidine sulphate were given in 0.4 gm., which served to break the fibrillation, and recovery was uninterrupted.

Case XIV. A. C., aged 23. Well-nourished woman with slight thyroid enlargement. Liable to typical paroxysms of fibrillation. History indefinite as to date of first attack. Full doses of quinidine did not prevent the recurrence of fibrillation. During the periods of normal rhythm when quinidine was being administered it was found that the junctional tissues were depressed. See Plate 16, Fig. 8.

Later note, June 13, 1922. Through the kindness of the Editor it is possible to add further information concerning the after history of some of the cases recorded, thus bringing them up to date, and to give a very brief record of five additional patients who have been treated with quinidine sulphate.

Case VIII. Normal rhythm maintained.

Case IX. Has reverted to fibrillation.

Case X. Normal rhythm maintained.

Case XI. Refused intramuscular injections of calcium chloride and was discharged. Liable to recurrences of fibrillation.

Case XII. Normal rhythm maintained.

Of the five new cases the fibrillation yielded in each, but Case XV temporarily relapsed after some weeks. In this man a tendency to hydrothorax was materially lessened when the auricle resumed its normal activity.

Case XVIII is an example of the tendency to cerebral embolism on the cessation of fibrillation, a tendency present whether the cessation is spontaneous or induced. In this connexion, showing how easily quinidine may be blamed for untoward happenings, it might be well to record that a man aged 56 was about to be treated with quinidine, when, on the day he was to receive his first dose, he suddenly became blind from embolism of the cerebral artery of the retina in both eyes.

An attempt has been made with the later patients in the series to determine whether the administration of calcium chloride intramuscularly will stabilize the condition of the normal rhythm on the cessation of the fibrillation, but so far no conclusions appear to be justifiable.

Case XV. P. G., aged 51. Admitted 6.4.22. Case of arterio-sclerosis, with hypertension, and evidence of renal inadequacy. Mitral regurgitation present. Possibly syphilitic in origin. Some enlargement of the heart, engorged liver, no oedema. Fluid in the right pleura. 50 oz. withdrawn on April 14. On April 20 (third day of treatment) 36 oz. withdrawn from right chest. No further fluid collected. Probable duration of fibrillation, five years. Certain since April 6, 1922. Tolerated quinidine without discomfort. Complained of headache after 6.4 grm., at which point the rhythm became normal. Discharged May 13 feeling well, carrying his luggage down the stairs without loss of breath. After discharge there was a temporary relapse. On June 13 heart's action normal.

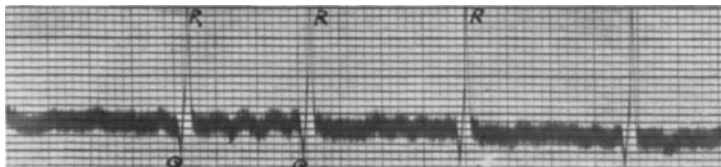
Case XVI. J. M., aged 30. Admitted 24.5.22. Mitral disease of old standing, moderate in degree. No venous engorgement. Heart slightly enlarged. Dyspnoea on exertion and palpitation. *Duration of fibrillation.* Probable seven years. Certain since May, 1922. Exhibition of quinidine caused no discomfort. Return to normal rhythm after 3.2 grm. on May 30. This was accompanied by the appearance of a soft diastolic bruit just internal to the left nipple. Intramuscular injections of calcium chloride, gr. 1 in α xx water, on May 31 and June 1, 2, 6, 9. Discharged 10.6.22. Normal rhythm maintained.

Case XVII. F. B. C., aged 32. Admitted 24.5.22. Mitral stenosis of old standing. Some enlargement. No bruits during fibrillation. Aetiology uncertain. Probable duration of fibrillation, seven years. Certain duration from February 16, 1921. No discomfort from quinidine. Normal rhythm after 1.6 grm. Half an hour after the last dose at 5 a.m. May 30 patient felt dizzy, 'drunk'. This lasted a few minutes, and when he recovered his pulse was found to be regular. With the resumption of normal rhythm a presystolic murmur developed and also a soft systolic murmur over the mitral area. After first tentative dose of 0.2 grm. at noon June 27 the ventricular rate increased from 90 to 115 at 10 p.m., and then dropped to 96 per minute. After the second tentative dose of 0.2 grm. given noon 28th the rate increased from 96 to 136 at 10 p.m., and then dropped to 88 by 10 a.m. Followed by intramuscular injections of calcium chloride, gr. 1 in α xx water, May 30, 31, June 1, 6, 9. Discharged 10.6.22 with normal rhythm.

Case II. *Mrs. W.* Mitral stenosis and regurgitation.
Slight aortic regurgitation.

A : 470. V : 78.

Before quinidine.



A : 312. V : 84.

After 3.6 grm.

26. xi. 21.

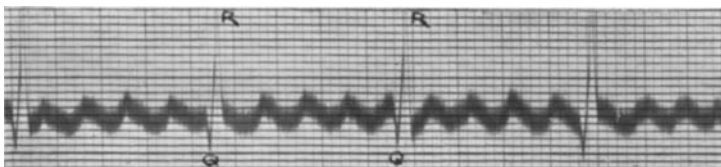


FIG. 1

Normal rhythm was not obtained.

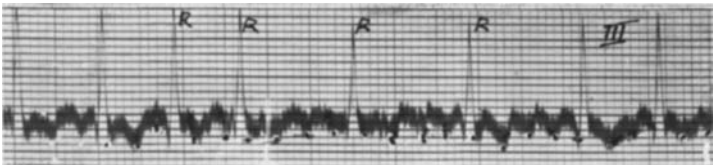
Continued from p. 318 :

Case XVIII. R. R., aged 37. 24.5.22. Double mitral lesion of old standing. Heart enlarged 5 inches to left of mid-line. Aetiology uncertain. Wassermann positive. Cardiac reserve poor. Dyspnoea and dizziness and cardiac pain on exertion. Symptoms began suddenly November, 1914, since when he has never worked. Cannot tolerate digitalis. Quinidine caused discomfort, increase of dyspnoea, and headache. This persisted throughout treatment. Normal rhythm after 3.4 grm., May 30, 1922: No material change in subjective symptoms. June 4: Embolism, cerebral. Sudden, left-sided hemiplegia, hemianaesthesia, conjugate deviation to right, no loss of consciousness, no pyrexia. Still in hospital. Normal rhythm maintained.

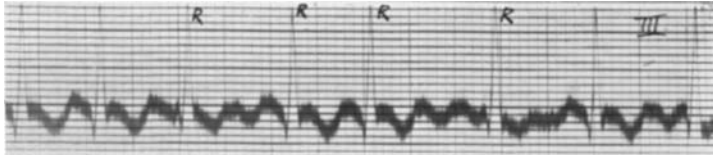
Case XIX. C. H. W., aged 50. No clear evidence of any organic lesion of the heart. Spare, wiry man. There is some palpitation on exertion, shortness of breath, and an unpleasant sensation in the cardiac area. Fibrillation began May 19, 1922, following sprint of $\frac{3}{4}$ mile for a train. Seen on May 22. Heart rate 140, disorderly. Treatment with digitalis steadied and slowed the ventricles. General condition improved, but fibrillation persisted. On June 8, 0.2 grm. quinidine. On June 9, 0.2 grm. quinidine, followed in an hour by resumption of normal rhythm. Occasional ectopic beats auricular in origin. Ventricular action very slow. Normal rhythm maintained.

Case III. Mrs. P. Mitral stenosis.

A : 480. V : 150 Before quinidine. 22. xi. 21.



A : 360. V : 150 After 0.8 gm. 3.30 23. xi. 21.



A : 320. V : 120 After 2.0 gm. 3.30 24. xi. 21.

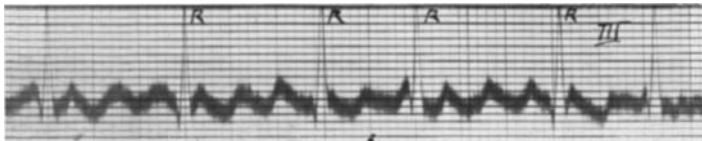
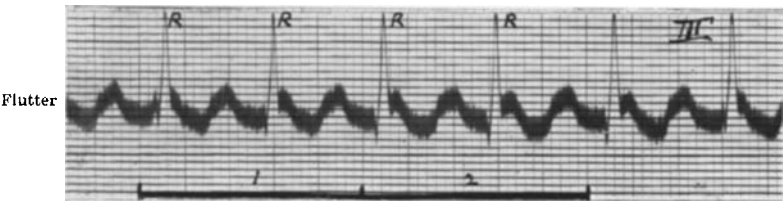
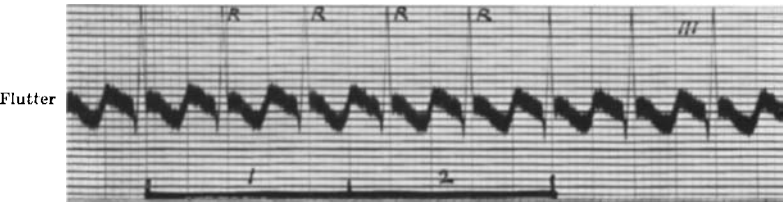


FIG. 2

2:1. 240:120 After 2.4 gm. 10.30 25. xi. 21.



2:1. 288:144 After 5.6 gm. 27. xi. 21.



A : 405. V : 120 After 5.6 gm. 28. xi. 21.

Back to fibrillation

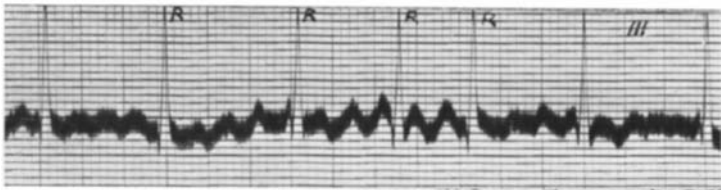
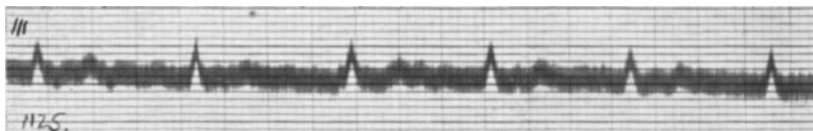


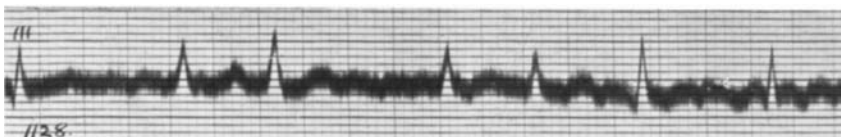
FIG. 3

Case V. *W. J. B., aged 51.* Large heart. Old standing mitral disease. Fibrillation known to be present since *June 1921.*

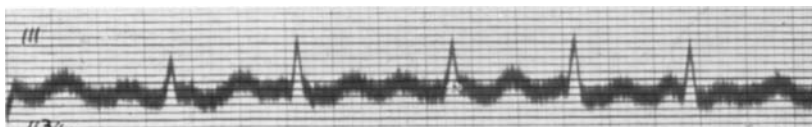
V : 92 After 0·4 grm. 10.30 a.m. 22. ii. 22.



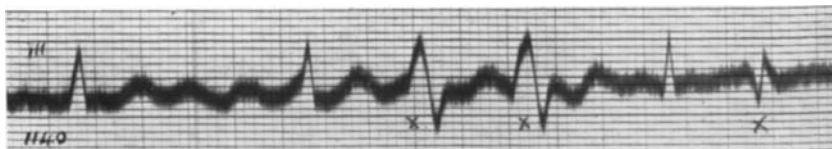
V: 108. A: 360 After 0.8 gm. 2.30 p.m. 22. ii. 22.



V: 100 A: 260 After 2.8 grm. 3 p.m. 23. ii. 22.



After 4.8 grm. 2.30 p.m. 24. ii. 22.



After 7.2 grm. 12-30 p.m. 26. ii, 22.



V : 138 After 0·0 grm. 10.30 a.m. 27. ii. 22.

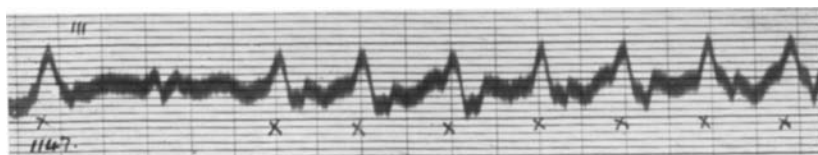


FIG. 4

x x Numerous ectopic beats excited by quinidine.

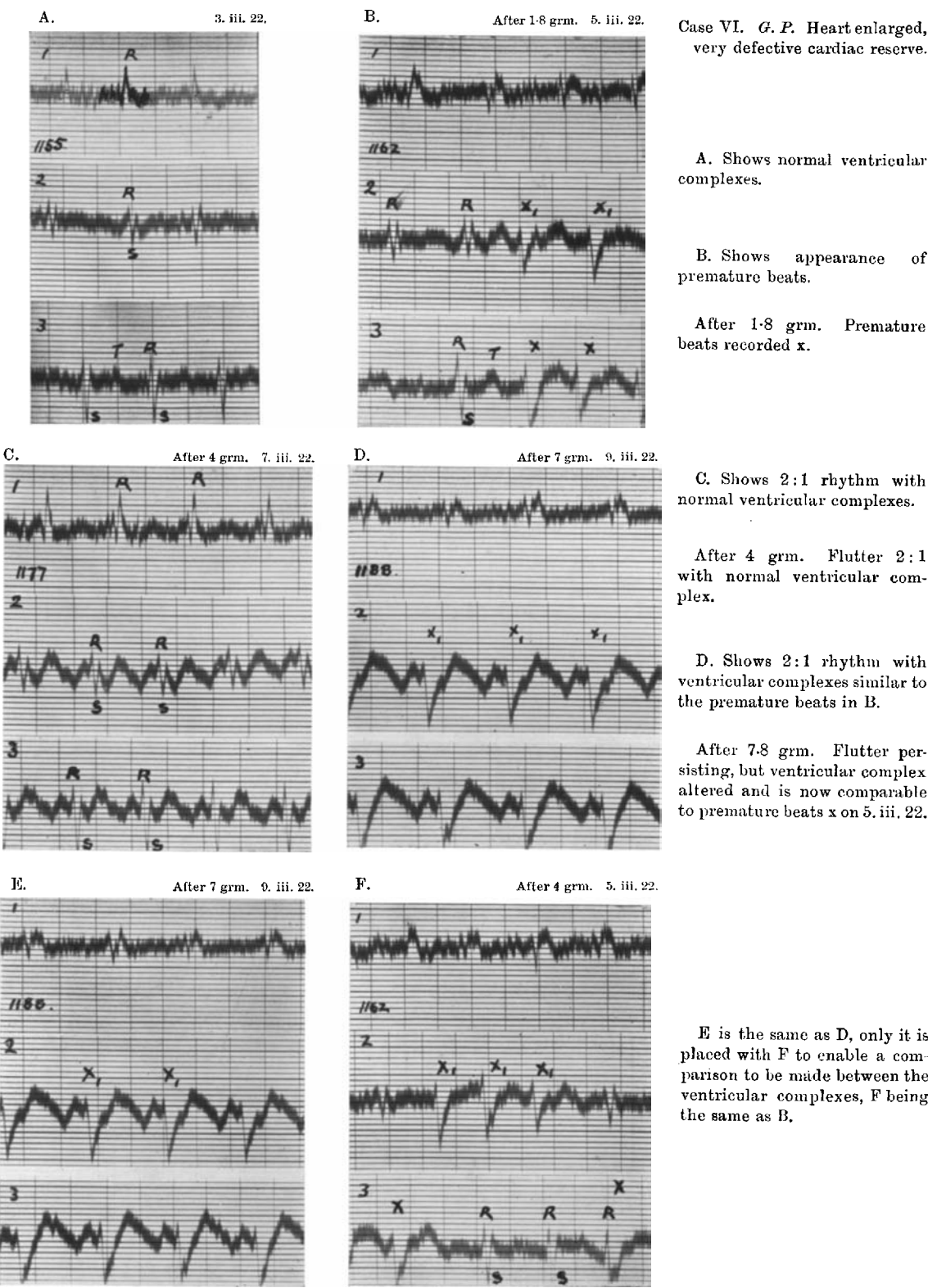
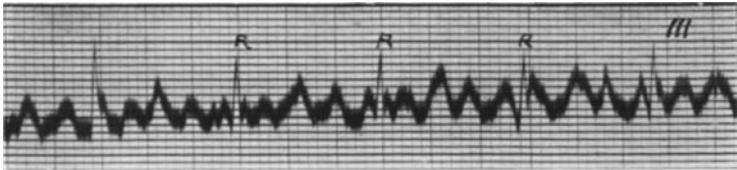


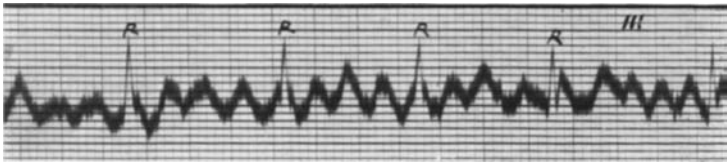
Fig. 5

Case VII. D. R. Heart enlarged, no V.D.H.

A : 408 V : 84 Before quinidine. 9. xii. 21.



A : 360. V : 84. After 3 grm. 12. xii. 21.



Normal 72. After 1.2 grm. 13. xii. 21.

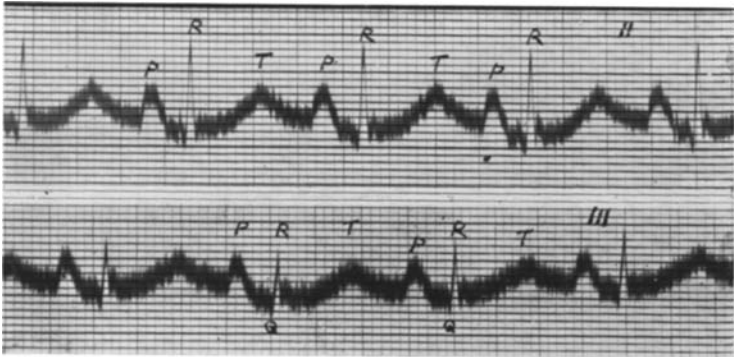
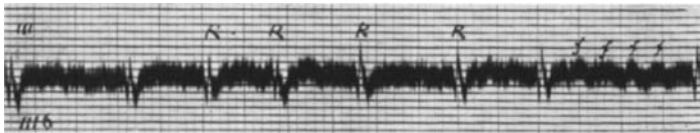


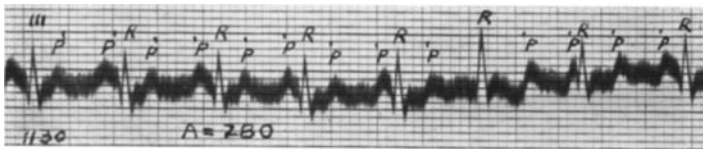
FIG. 6.

Case X. P. B., aged 42. Mod. enlargement, no V.D.H.
Duration of fibrillation probably two years.

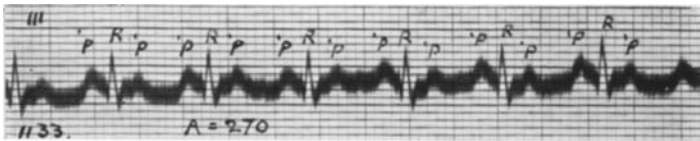
A : 510. V : 165 Before quinidine. 20. ii. 22



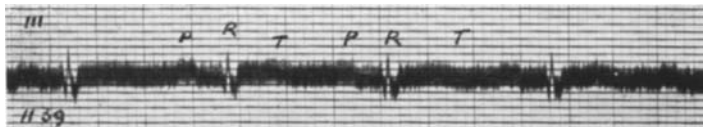
After 24 gm. 10.30 a.m. 23. ii. 22.



2:1 flutter. After 28 gm. 3 p.m. 23. ii. 22.



After 34 gm. 2.30 p.m. 24. ii. 22.



Rate 80: Change to normal via flutter. 25. ii. 22.

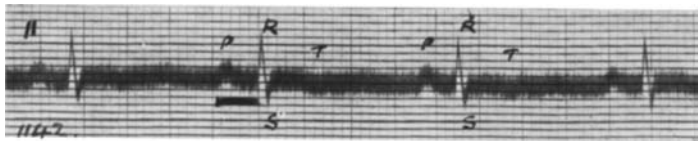


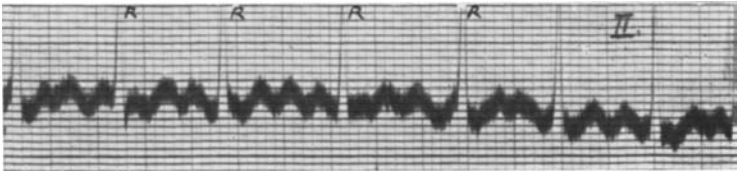
FIG. 7

Case XIV. A. C. No V.D.H.

Shows recurrence of fibrillation during the administration of quinidine sulphate.

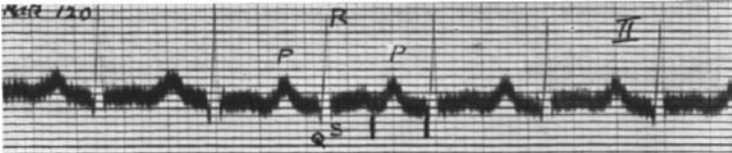
A : 420. V : 140. After 0.4 grm. 23. xi. 21.

Paroxysmal fibrillation

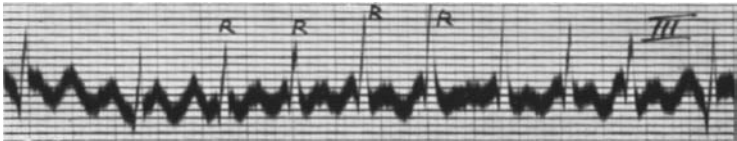


Normal rhythm but depression of conductivity. P R interval prolonged.

After 3.2 grm. 25 and 26. xi. 21.



Reverted. After 6.8 grm. 28. xi. 21.



Fibrillation which
recurred while patient
receiving quinidine

Normal again. After 7.2 grm. 29. xi. 21.

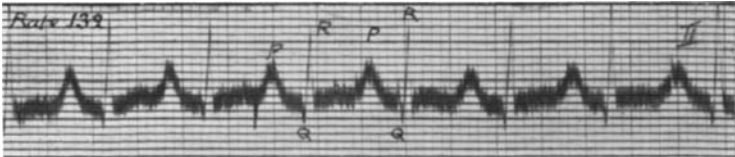


FIG. 8