

tinal motility in older children may also be applied to certain conditions in infancy. Dr LeWald mentioned pylorospasm in infants. When there is pylorospasm, there is in all probability also enterospasm. It is commonly accepted that the whole thing is probably due to overactivity of the vagus, which explains the good effects obtained with atropin. The condition should really be called pyloro-enterospasm. In such cases, once the vomiting has been overcome, and with it the starvation and constipation, the food is hurried through the intestines; and thus, once the pylorus has been passed, the intestines empty with considerable rapidity. These infants undoubtedly require more food than normal infants do.

DR. ALFRED L. KASTNER, Milwaukee: In regard to older children with poor appetites, I see no other conclusion to arrive at than that the three-hour feeding interval is a common cause. The school child eats at 7 a. m., comes into school and has a glass of milk at 10 o'clock and then has lunch at 12. Now, in children who are properly nourished, why impose such an extra load? It is true the child needs the extra food, but is he able to handle it in three-hour intervals?

DR. LOUIS W. SAUER, Evanston, Ill.: I am sorry not to have made observations on older children with poor appetites during illness, fever and infections. Of course, it is a well-known fact that infants in hot weather secrete less free hydrochloric acid than on cold days. I agree that it is not a good thing to give these children milk between meals. Children who will not eat breakfast should not be expected to drink milk between breakfast and the noon lunch. I am not speaking of the child with good appetite who is underweight. I am sorry not to have mentioned the work of Drs. LeWald and Kerley. Dr. Kerley, a year ago, pointed out that one of the pronounced effects of delayed emptying time is loss of appetite and that a child will not be hungry with a portion of a previous meal in the stomach. In one of his cases, the stomach was not empty for thirteen hours. If such a child eats breakfast at 8 a. m., and something is still in the stomach six hours after that, it will not eat a hearty lunch. In regard to Dr. Foote's question—sixteen out of twenty-one were of the asthenic habitus. The significance of habitus is greatly neglected in pediatrics. Many children who are frequently ill belong to the "slender" type. The stomach is normally below the umbilicus. Roentgenologists show that normal stomachs of this type may have an emptying time not of four but of six hours. For that reason they set up six hours as the normal emptying time. Normal persons of this type may have a long emptying time. Children who come into this group are not children who have food dislikes. With regard to the treatment, we made the children "free to gain," fed them on foods rich in vitamins (lettuce sandwiches, carrots, spinach and, at times, cod liver oil), and tried to get them to take a quart of milk a day, giving 8 or 10 ounces at each meal. If we found the hydrochloric acid low, we gave 1 dram of essence of pepsin with 3 drops of dilute hydrochloric acid with each meal. The two children without free hydrochloric acid are interesting in that neither of them showed free hydrochloric acid in spite of the administration of 3 drops of the dilute hydrochloric acid for a period of several months.

**Preparation of Chaulmoogra Oil Derivatives.**—The working details of methods used at the University of Hawaii for the preparation of certain derivatives of chaulmoogra oil are described by Dean and Wrenshall in *Public Health Reports*, June 9, 1922. The chaulmoogra oil used is obtained through dealers, and varies greatly in quality, some lots being clear and liquid at laboratory temperature, other lots being dark, muddy looking oils with large quantities of precipitated material. The differences in appearance seem to have no correlation with differences in rotation of polarized light, which is the distinguishing characteristic of these oils. The valuable oils show specific rotations around plus 50 degrees. The first step in the preparation of derivatives for therapeutic use is to break up the glycerids into glycerol and the sodium soaps of the fatty acids by saponifying the oil with sodium hydroxid under pressure. These crude mixed fatty acids are then treated in different ways, the details of which are given as noted, and the following products obtained: (1) mixed ethyl esters, (2) ethyl hydnocarpate, (3) ethyl chaulmoograte, and (4) ethyl dihydrochaulmoograte.

## THE QUINIDIN TREATMENT OF AURICULAR FIBRILLATION \*

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Since the report by one of us (W. W. H.<sup>1</sup>) in December, 1921, of eight cases of auricular fibrillation in which quinidin sulphate was administered, we have observed and treated ten additional cases. In this paper we shall present (1) a further study of the cases previously reported; (2) the details of treatment and observation in ten new cases, and (3) the results and conclusions obtained from our experience with these eighteen cases in connection with a critical survey of the literature up to the present time.

In spite of lack of complete knowledge of the pharmacology of quinidin, its indications and contraindications in practice, and the occasional reports of serious untoward effects (paralyses, embolism and death), interest in its therapeutic use continues to grow. Reports and studies in quinidin therapy have appeared so fast during the past year, especially during the past six months, that it is well-nigh impossible to keep up with the constantly growing literature on the subject. One gets the universal impression that, in spite of the accidents referred to above, it is rapidly establishing a place for itself in modern cardiac therapy. Appreciating that our knowledge of the drug is as yet most incomplete, it must be borne in mind that its use in auricular fibrillation dates back only four years, since Frey's<sup>2</sup> work in 1918. It is interesting in this connection to reflect, as Jackson, Friedlander and Lawrence<sup>3</sup> have recently pointed out, that "Witherington introduced digitalis in 1783, while the year 1922 finds us still willing to learn more than we at present know about the foxglove."

Before presenting our own cases, it may be worth while to review very briefly the subject itself and its present status. Auricular fibrillation, the most frequent serious irregularity of the human heart, may be converted, in approximately 50 per cent. of the cases, to a normal cardiac mechanism by the administration of quinidin, one of the four better known alkaloids of cinchona bark, a stereo-isomer of quinin. In a recent compilation of the literature by Oppenheimer,<sup>4</sup> in a total of 461 reported cases, 53 per cent. of the patients were restored to a sinus rhythm. Of our series of eighteen cases, eleven patients (61 per cent.<sup>5</sup>) have secured, for a time at least, a normal rhythm, and in five (27 per cent.) it has lasted three months or more. The introduction of quinidin in the therapy of auricular fibrillation dates from Wenkebach's<sup>6</sup> accidental dis-

\* From the Medical Services and Electrocardiographic Laboratory, Michael Reese Hospital.

\* Read before the Section on Practice of Medicine at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Hamburger, W. W.: Effects of the Administration of Quinidin Sulphate in Auricular Fibrillation, *J. A. M. A.* **77**: 1797 (Dec. 3) 1921.

2. Frey, W.: Ueber Vorhofflimmern beim Menschen und seine Bezeitigung durch Chinidin, *Berl. klin. Wchnschr.* **55**: 417, 1918; Weitere Erfahrungen mit Chinidin bei absol. Irregularität, *Ebenda* **55**: 849, 1918.

3. Jackson, Friedlander and Lawrence: *J. Lab. & Clin. Med.* **7**: 311 (March) 1922.

4. Oppenheimer: Paper read before the American Society for Clinical Investigation, Washington, D. C., May 1, 1922.

5. Our slightly better percentage is due to the fact that eight of our cases were of the acute or paroxysmal variety and that, from a larger experience, more effective dosage and treatment were possible.

6. Wenkebach: *Die unregelmässige Herzthätigkeit und ihre klinische Bedeutung*, Leipzig, Engelmann, 1914.

covery of the use of quinin in 1914 and Frey's work in 1918, at which time he showed the greater suitability of quinidin. Since this time a large number of papers have been contributed on this subject and have served to throw considerable light on the exact mechanism, indications and contraindications, dangers, mode of action and selection of cases.

#### CASES PREVIOUSLY REPORTED

Our first eight cases, reported last year, have been kept under observation, and the patients have reported back from time to time for examination and treatment.

TABLE 1.—CASES PREVIOUSLY REPORTED

Case*	Diagnosis	Duration of Auricular Fibrillation	Quinidin, Gm.	Duration of Sinus Rhythm
A. Cases in Which Normal Cardiac Mechanism Was Restored				
1. I. B. ♀	Mitral stenosis; chronic A. F.	3-4 years	1.8	11 months
2. M. B. ♂	Gen. arteriosclerosis; diabetes mellitus; chronic A. F.	Unknown	1.8	14 days
3. J. M. ♂	Mitral stenosis; chronic A. F.	2 years	3.2	6 days
4. J. K. ♂	Hyperthyroidism; acute A. F.; M. B. R. 50.4+	Paroxysmal	1.4	10 days
B. Cases in Which Auricular Fibrillation Persisted				
5. I. G. ♂	Postinfec. myocarditis; chronic A. F.; adv. heart failure	2 months	3.7	
6. S. ♂	Chronic myocarditis; chronic A. F.; adv. heart failure	2 years	2.0	
7. M. P. ♂	Postpneu. myo. and end.; mitral sten. and insuff.; adv. heart failure; chronic A. F.	3½ years	10.6	
8. M. ♂	Chronic inter. nephritis; adv. heart failure; chronic A. F.	1½ years	24.4	

\* For sex, ♂ indicates male and ♀ female.

Table 1 shows in brief the details of these cases. As stated in our original paper, only four of these eight patients (50 per cent.) secured a normal cardiac mechanism, and only one of the four has maintained a normal rhythm for any considerable period (eleven months). The remaining three, in spite of various dosages and combinations of quinidin and digitalis, have experienced frequent returns of fibrillation so that, finally, quinidinization was discontinued, as no permanent benefit could be secured. Patient 2 has died, eight months after treatment, from increasing intoxication from his diabetic gangrene. Patient 4, with hyperthyroidism (metabolic rate 51.8+) is at present undergoing roentgen-ray treatment for his thyroid hyperfunction with the expectation that, when this is controlled, quinidin therapy will be more effective.

The four cases that failed to respond to quinidin were all cases of advanced heart failure and have continued to pursue a progressively downward course. One patient has died; the remaining three are seriously handicapped in their cardiac reserve and in their ability to carry on sustained activity.

Summarizing our experience with our first group of cases after an interval of one year, it must be stated that the results are not particularly gratifying, as only 50 per cent. of the total number of cases responded, and in only 25 per cent. of these, or 12.5 per cent. of the whole, has there been a permanent result. Patient 1, whose sinus rhythm has persisted eleven months, underwent in March a gynecologic plastic operation necessitating a general ether anesthetic, lasting one

hour, with no evidence of return of fibrillation. It may be recalled that this patient, at the time of the restoration of normal rhythm, showed a disappearance of right heart preponderance with coincident relief of clinical signs of heart failure.

#### NEW CASES

The new cases which we have to report comprise ten. Seven of these (Tables 2 and 3) responded to quinidinization with the establishment of a normal rhythm; three cases were not responsive. Of the seven responsive cases, three have maintained a normal rhythm for three months or more; the remaining four have had one or more recurrences of fibrillation. Three may be classified as acute auricular fibrillation undergoing their first attack of irregularity, and three as recurrent paroxysmal fibrillation. The contributory causes that were probably important etiologically were: acute respiratory infection, paratyphoid fever, pneumonia, menopause, hypertension, toxic goiter and generalized arteriosclerosis. The duration of the fibrillation varied from a few hours to several weeks. The amount of quinidin necessary to control varied from 0.2 to 3.8 gm.; the total amount of quinidin administered to any one patient was 23.2 gm. While it is well known that the paroxysmal type of fibrillation often ceases of its own accord, these cases were so controlled that it appeared likely that the restoration of sinus rhythm was brought about as a result of

TABLE 2.—NEW CASES, IN WHICH NORMAL CARDIAC MECHANISM WAS RESTORED

Case	Diagnosis	Duration Auricular Fibrillation	Quinidin Necessary for Sinus Rhythm	Total Quinidin, Gm.	Duration Sinus Rhythm
9 W. S. ♂	Acute A. F. occurring 5th day; acute grip infection	1 parox. attack lasting 12 hrs.	0.4 gm.	0.6	3 months
10 M. L. ♀	Recurrent parox. A. F.; menopause; hypertension	Variable: few min. to several hours	Variable: from 0.2 gm. to 1.2 gm.	5.6	Variable: 1st attack 1 year, 2-4 months
11 M. F. ♂	Recurrent parox. A. F.; hyperthyroid; M. B. R. 72.2+	Variable: from several hrs. to 2 wks.	Variable: from 1.2 gm. to 2.0 gm.	8.4	Var.: sev. hrs. to 3 wks.; earlier attacks, sev. months to sev. years
12 H. R. ♂	Recurrent parox. A. F.; post-infec. myo.	Variable: from 1-4 days	0.2 gm.	4.0	Variable one to sev. years
13 M. C. ♂	Acute A. F.; gen. arterioscl.; chr. myocarditis; begin. heart failure	3 weeks	3.8 gm.	23.2	7 days
14 B. W. ♂	Acute A. F.; post-pneum., myo. and endocarditis; mitral sten.	24 hrs.	1.2 gm.	10.2	3 months
15 B. C. ♀	Chr. A. F.; mitral sten. and regur. adv. recur. heart fail.—8 yrs.	4 yrs.	1.0 gm.	7.4	24-48 hrs.; 7 days during contin. adm.; prompt relapse after discontinuing

quinidin administration. It is probable, too, that the drug materially shortened the paroxysm of irregularity, for in one and the same case, in which for various reasons certain attacks were allowed to continue untreated, the giving of quinidin was promptly followed with a restoration of normal cardiac mechanism. Four of these seven cases were private cases under careful and repeated observation and control and, with the patients' intelligent cooperation and insight into their own problems, they themselves were convinced of the controlling action of quinidin. One of them, a physician, administered the capsules to himself and controlled the paroxysms of irregularity largely at his own discretion.

There is little to be said regarding the three cases of auricular fibrillation which failed to respond to quinidin. In contrast with the nonresponsive cases of the first series, none of them were cases of advanced heart failure, although one was classified as moderately advanced and the others early heart failure. In one case, quinidin was discontinued after a dosage of 8.4 gm., covering a period of eight days, because of complaints of spots before the eyes, dizziness and ringing in the ears. In a second case, after 12 gm. had been given, quinidin was discontinued because of the production of a bradycardia varying between 40 and 52 apex beats a minute. One or two other of our patients have experienced a similar bradycardia. Curves of this patient showed a continuance of the high auricular rate with the very slow ventricular, suggesting that in large amounts over a prolonged period, quinidin does affect the auriculoventricular bundle, producing a rather high degree of partial heart block. The effect of quinidin direct on the heart muscle and on the vagus must also be considered in this connection. These patients, in spite of showing evidence of heart

TABLE 3.—NEW CASES IN WHICH AURICULAR FIBRILLATION PERSISTED

Case	Diagnosis	Duration of A. F.	Quinidin
16. S. E. ♀	Chronic A. F.; chr. myocar. and interst. neph.; mod. adv. heart failure	1-2 years	1st. ser. 10.2 gm. 2d. ser. 7.0 gm. Total 17.2 gm.
17. D. S. ♂	Chronic A. F.; early heart fail.; chr. myocard.	2-3 years	24.6 gm.
18. T. ♂	Recurrent parox. A. F.	Recurrent 7 years	12.0 gm.

failure, were all cases of relatively long fibrillation, so that we conclude that this factor is probably of greatest constancy in the nonresponsive cases.

Rather than present the details of these cases, we shall discuss certain of the more important and obscure problems in connection with a critical survey of the literature up to the present time. We shall discuss these in this order: (1) favorable cases and indications for quinidin therapy; (2) unfavorable cases and contraindications; (3) dosage and method of administration; (4) digitalis; (5) subjective symptoms, clinical value, effects on compensation and decompensation; (6) toxic effects, accidents occurring during administration, respiratory paralysis, skin lesions; (7) effect on auricular and ventricular rate, vagus, venous, arterial and pulmonary pressure, peripheral vessels; (8) changes in P-R interval, QRS complex, T wave, heart block.

#### FAVORABLE CASES AND INDICATIONS FOR QUINIDIN

It is generally agreed that patients with fibrillation of short duration and with relatively good heart muscle, with no signs of decompensation, are most favorable for the administration of quinidin. Bock<sup>7</sup> and Cheinisse<sup>8</sup> believe that it is particularly valuable in patients with hyperarterial tension and with peripheral arteriosclerosis. Wolferth's<sup>9</sup> case of hyperthyroidism showed the most striking improvement. Pardee<sup>10</sup> inclines to patients with relatively good heart muscle and fair compensation. Our best results have

been obtained in the acute and paroxysmal varieties, although our instance of restored sinus rhythm of longest duration occurred in a chronic case in which fibrillation had been present for three or four years. Our two hyperthyroid cases responded easily to small amounts of the drug, but quickly relapsed to fibrillation, although one of them could be controlled for weeks at a time with daily small amounts of quinidin (Fig. 1). We are hopeful that reducing the hyperthyroidism by roentgen-ray treatment will result in a more permanent cure. Our experience with patients with peripheral arteriosclerosis is that, while they respond promptly, they relapse equally so, and permanent results are difficult to obtain.

#### UNFAVORABLE CASES AND CONTRAINDICATIONS

The literature is fairly in agreement in the fact that the most unfavorable cases are those of long duration with moderately advanced or advanced heart failure. Our experience is in accord with this, although there are many exceptions to it. Ellis and Clark-Kennedy<sup>11</sup> believe that those which do not respond to digitalis will not respond to quinidin. Smith<sup>12</sup> believes that patients with large hearts are unfavorable. Jackson, Friedlander and Lawrence, from results with experimental aconite poisoning, suggest that there may be two types of fibrillation, the early aconite poisoned animals responding, the late not. White<sup>13</sup> believes heart failure and long duration are unfavorable cases. Bock and Cheinisse speak of acute and recurrent endocarditis as contraindications. Thomas Lewis<sup>14</sup> warns against patients in whom there is any history or findings of previous embolism and patients with advanced heart failure as evidenced by an engorged, tender liver and dilated veins of the neck. While we have been fortunate in experiencing no serious mishaps, we share in general the statements of the foregoing observers. However, it is certainly difficult to predict whether a given case will be successful or not, although, in general, we now feel fairly safe in stating that the case with a single acute attack or a recurrence can usually be controlled promptly with quinidin.

#### DOSAGE AND METHOD OF ADMINISTRATION

All observers are using practically the same amounts of quinidin, varying from 0.2 to 0.4 or 0.6 gm., three or four times a day. Lewis recently spoke of using as a test dose 0.8 gm., the largest amount of which we know. In general, we are using frequent small doses, and find that they are as advantageous as the larger amounts. In a few recent cases we have omitted the preliminary idiosyncrasy dose, starting with 0.2 gm. every two hours with careful, frequent examinations of the patient, and find that many attacks can be controlled immediately in from two to twelve hours by this method. If such dosage is ineffectual, after a three or four day attempt, we increase the amount to 0.4 gm. every two hours. In our last cases we have been accustomed, after the establishment of sinus rhythm, to continue giving 0.2 gm. once or twice a day for a considerable period, decreasing only gradually, believing, with Eyster and Fahr,<sup>15</sup> that, since in most

11. Ellis, A. W. M., and Clark-Kennedy, A. E.: *Lancet* 2: 894 (Oct. 29) 1921.

12. Smith, F. M.: *Quinidin in Cardiac Irregularities*, J. A. M. A. 78: 877 (March 25) 1922.

13. White, P. D.: *Boston M. & S. J.*, Dec. 17, 1921.

14. Lewis, Thomas: Paper read before the Institute of Medicine, Chicago, May 10, 1922.

15. Eyster, J. A. E., and Fahr, G. E.: *Quinidin in Auricular Fibrillation*, *Arch. Int. Med.* 29: 59 (Jan.) 1922.

7. Bock: *Med. Klin.* 17: 1052 (Aug. 28) 1921.

8. Cheinisse: *Presse méd.* 29: 748 (Sept. 17) 1921.

9. Wolferth, C. C.: *Am. J. M. Sc.* 162: 812 (Dec.) 1921.

10. Pardee: *Discussion*, *New York Acad. of Med.*, Nov. 17, 1921.

cases the conditions tending to produce auricular fibrillation are still present even after a normal rhythm is restored, subsequent administrations of the drug are necessary to avoid recurrence. If stoppage of the drug is followed in a short time by a relapse, we start a second series of quinidin administration, continuing it practically indefinitely, meanwhile making every possible attempt to diagnose and treat the probable underlying causative disease. It is remarkable how long and uneventfully patients can take small amounts of quinidin. Several of our patients are continuing now in their second and third month taking one or two capsules (0.2 gm.) a day without apparent harm.

#### DIGITALIS

The rôle of digitalis has been and continues to be a much discussed one. Pardee believes there is no effect either way from its administration. Wolferth had an interesting experience in which the administration of digitalis was effective in restoring a sinus rhythm temporarily; later, quinidin was not successful. Robert Levy<sup>16</sup> believes that digitalis is not essential to successful treatment. Fred Smith feels that it is contraindicated, as both digitalis and quinidin may produce heart block. White concludes that digitalized cases are more likely to respond, but that it is better not to give the two together. Lewis believes that there is little difference in the auricular response, although possibly the undigitalized cases may be a shade more likely to respond than the digitalized; but he strongly feels that digitalis effects are desirable, especially in the rapid type of fibrillation, and shows graphically in one and the same patient the relative slowing of the ventricular rate in the digitalized cases. We have had three interesting experiences. To one patient, in whom, in spite of evident decompensation (cyanosis and orthopnea) digitalis was certainly indicated, we gave quinidin first without digitalis, and a prompt restoration of sinus rhythm occurred, with a simultaneous disappearance of signs of heart failure. The second case, reported last year, showed without digitalis and with small amounts of quinidin a clearing up of early heart failure and disappearance of evidences of right heart embarrassment (right preponderance). In the third case, an exophthalmic goiter patient with an extremely rapid type of fibrillation, we had great difficulty in maintaining, without digitalis, a normal rhythm for more than a few hours until a time when he was completely digitalized, after which the same or even smaller amounts of quinidin were successful in holding his heart regular for three weeks. As a result of these experiences, our practice at present is to give quinidin at once in a properly selected case without preliminary digitalization, in spite of a moderately rapid heart and signs of early or moderately advanced heart failure. If, on securing a normal rhythm, the ventricular rate remains over 100, or if the signs of heart failure have not disappeared entirely, or if the restoration of a regular pulse is of short duration with frequent and early tendencies to relapse, we then digitalize the patient in the usual way.

#### SUBJECTIVE SYMPTOMS; CLINICAL VALUE; EFFECTS ON COMPENSATION AND DECOMPENSATION

The symptoms mentioned most frequently in the literature as due to the administration of quinidin are palpitation, weakness and dizziness, dyspnea, oppression and tachycardia. A few have noticed epigastric

distress, ringing in the ears, headache, nausea, hemoptysis and hot flashes. Some of these complaints have been voiced by our patients; others have noticed no subjective effects of any sort.

From the standpoint of the effect on subjective complaints, that is, the value of the treatment from the patient's standpoint, the literature contains such statements as "no striking change"; "no more than ordinary rest and diet"; "relief experienced in slow type of fibrillation"; "relief from palpitation"; "general improvement." Lewis makes the interesting observation that, although several of his patients showed no immediate improvement and experienced no immediate change with restoration of normal rhythm, they experienced later improvement in strength, in general well-being and in ability to carry on. In our experience, the private cases have experienced decidedly more personal satisfaction from the change than the ward cases, not only patients with exophthalmic goiter but also those with acute fibrillation following infection; they are extremely grateful when the irregularity has been stopped. Our easy-going, phlegmatic patients noticed little if any change; our nervous, apprehensive, frightened ones were intensely frightened during the attack and strikingly relieved when it was over, and insisted on having their capsules near them day and night. One patient with goiter, whose attacks often come at night, puts his capsules at his bedside and helps himself when his attacks rouse him from his sleep.

Several men have reported that quinidin caused decompensation in a previously well-compensated fibrillating heart; or, at least, with the restoration of sinus rhythm by quinidin, decompensation occurred. We have fortunately had no such experience.

#### TOXIC EFFECTS; ACCIDENTS OCCURRING DURING QUINIDIN THERAPY (EMBOLISM); RESPIRATORY PARALYSIS; SKIN LESIONS

Wilson and Herrmann<sup>17</sup> group the accidents occurring under quinidin therapy under six headings: (1) increased cardiac failure; (2) apparent respiratory paralysis; (3) embolism; (4) failure of the sinus node to resume function; (5) depressed intraventricular conduction; (6) increased ventricular rate. Embolism is, of course, the most serious, has resulted in several sudden deaths, and has caused infarcts in the kidney, lung, spleen and brain. It has caused transitory paralyses.

We have been fortunate up to the present time in having no embolic cases, at least none that we recognized. We have had several scarlatiniform rashes, dizziness and ringing in the ears, spots before the eyes, and sudden rise of temperature to 101.6 with severe headache, diarrhea and abdominal pain. Such results as these are frequent findings throughout the literature. The less serious findings are undoubtedly cause for immediate discontinuance of the drug. We fully agree with Sir Thomas Lewis that any evidence of embolism is an absolute contraindication. It is striking that several clinics report a much greater number of these accidents than others. In this connection, it might be recalled that embolism is not an infrequent occurrence in fibrillation without quinidin; witness the reports of paralysis, infarcts, hemoptysis, etc., in the older literature.

17. Wilson, F. N., and Herrmann, G. R.: Cerebral Embolism Following Arrest of Auricular Fibrillation by Quinidin, *J. A. M. A.* 78: 865 (March 25) 1922.

16. Levy, Robert: *Proc. Soc. Exper. Biol. & Med.* 19: 88, 1922.

EFFECT ON AURICULAR AND VENTRICULAR RATE,  
VAGUS, VENOUS, ARTERIAL AND PULMONARY  
PRESSURE, AND PERIPHERAL VESSELS

Acceleration of the ventricular rate (ventricular tachycardia) is a frequent experience in patients undergoing quinidin treatment. Drury and Iliescu,<sup>18</sup> by using sternal leads, have shown clearly the progressive depression of auricular rate, falling sharply from a single dose and only very gradually resuming its original rate. We have taken sternal leads in connection with the regular leads in a number of cases, and have estimated the auricular rate (Fig. 3). Table 4 shows the typical result of such estimation, showing

TABLE 4.—REGULAR AND STERNAL LEADS, CASE 11

Date	Hour	Leads	Auricular Rate	Ventricular Rate	Rhythm
3/7/22	8 p.m.	Regular before quinidin	461 (approx.)	171	Irreg. (fibrillation)
3/8/22	8 a.m.	0.2 gm. Q.			
	10 a.m.	0.2 gm. Q.			
	11 a.m.	Sternal	428 (approx.)	141	Irreg. (fibrillation)
	12 noon	0.2 gm. Q.			
	1:40 p.m.	Sternal	260	130	Reg. (flutter)
	2 p.m.	0.2 gm. Q.			
	3 p.m.	Regular	260	130	Reg. (flutter)
	4 p.m.	0.2 gm. Q.			
	5:30 p.m.	Regular	240	120	Reg. (flutter)
	6:00 p.m.	0.2 gm. Q.			
3/9/22	8:00 a.m.	0.2 gm. Q.			
	9:45 a.m.	Regular	100	100	Normal (S. R.)
	4:30 p.m.	Regular	75	75	Normal (S. R.)

the gradual depression of an original auricular rate of 460 during fibrillation to 260 during flutter, and finally to 75 with the restoration of sinus rhythm. In contrast to Lewis' findings, the ventricular rate in this case likewise progressively decreased, as it has in one or two other cases, resulting finally in a fairly high grade bradycardia. This rapid early irregularity is usually followed by a rapid regular rhythm (auricular flutter), the "Transition rhythm" of Eyster and Fahr. The rate estimations in three cases, given in Table 5, show the initial ventricular, the transition rhythm and the final sinus rhythm rates.

TABLE 5.—RATE ESTIMATIONS IN THREE CASES

Initial Ventricular Rate	Rate of Transitory Rhythm	Sinus Rhythm Rate
111	130	65
85	133	73
94	107	75

In regard to the effect on the vagus, White believed that quinidin has a paralyzing effect, while Jackson, Friedlander and Lawrence believe that the vagus endings are not paralyzed and that the inhibitory action, if anything, is increased. Lewis, Drury, Iliescu and Wedd<sup>19</sup> conclude that it causes a partial, rarely complete paralysis of the vagus. From our experiences we have no evidence as to the vagus effect unless the acceleration of ventricular action under quinidin can be offered as evidence of such action. Eyster and Fahr found the venous pressure increased as a result of the drug. Cohn<sup>20</sup> found a fall in arterial blood pressure, and the Cincinnati workers describe a general fall in the systemic blood pressure. Dilatation of pul-

monary arterioles and capillaries resulting in a fall in pulmonary pressure has been described, as well as dilatation of peripheral vessels from direct action on the capillaries.

CHANGES IN P-R INTERVAL; QRS COMPLEX;  
T WAVE; HEART BLOCK

Levy found the P-R interval lengthened in one patient. White found it slightly lengthened. Wolferth believes that it increases above the normal with the restoration of sinus rhythm, but that this is not necessarily due to quinidin. We have found no constant effect, but have one strikingly prolonged interval in an unfavorable case. Several observers have noted a lengthening in the QRS complex, with the production of transient intraventricular block and changes in R and S. Several of our cases have shown slight pro-

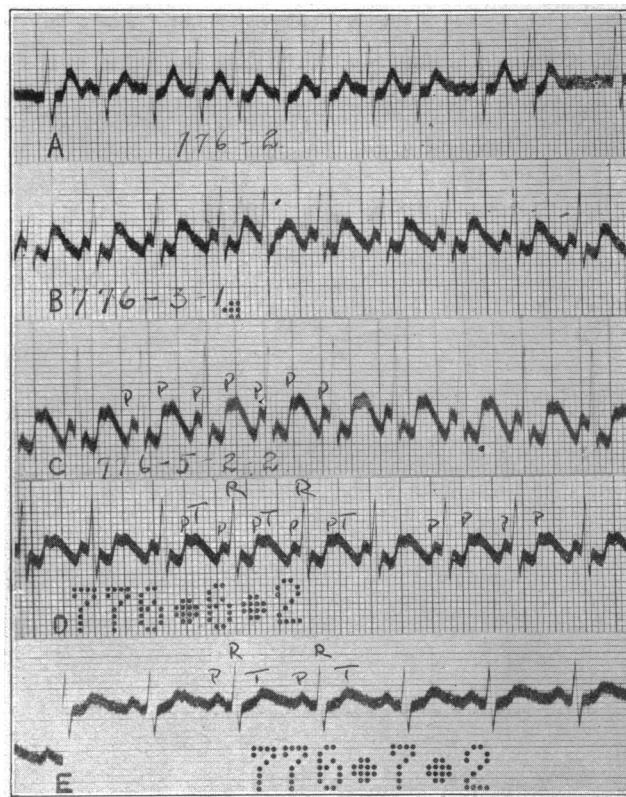


Fig. 1 (Case 11, man, aged 54).—Recurrent paroxysmal auricular fibrillation; change from auricular fibrillation to flutter and to sinus rhythm with slowing of auricular and ventricular rates; exophthalmic goiter. A, March 7, 1922, 8 p. m.: auricular rate, approximately 461; ventricular rate, 171; fibrillation; no quinidin. B, March 8, 11 a. m.: approximate auricular rate, 286; ventricular rate, 150; fibrillation; 0.4 gm. quinidin. C, March 8, 3 p. m.: auricular rate, 260; ventricular rate, 130; flutter; 0.8 gm. quinidin. D, March 8, 5:30 p. m.: auricular rate, 240; ventricular rate, 120; flutter; 1 gm. quinidin. E, March 9, 9:45 a. m.: auricular rate, 100; ventricular rate, 100; sinus rhythm; 1.4 gm. quinidin.

longation and notchings in the initial complexes, and in two cases inversion of T. The latter is in accord with several observers in this country. White records one case of complete heart block. Lewis concludes that it depresses auriculoventricular conduction as part of the uniform influence of the drug on the rate of conduction in all three tissues—auricle, ventricle and junctional tissues.

## SUMMARY

It is difficult to reach final conclusions regarding the exact rôle of quinidin in auricular fibrillation. This

18. Drury, A. N., and Iliescu, C. C.: Brit. M. J. 2: 511 (Oct. 1) 1921.

19. Lewis, Thomas; Drury, A. N.; Iliescu, C. C., and Wedd, A. M.: Heart 9: 55 (Dec. 14) 1921.

20. Cohn, Alfred: Discussion, N. Y. Acad. of Med., Nov. 17, 1921.

difficulty arises from several sources, because (1) of our comparatively short acquaintance with the phenomenon; (2) our lack of knowledge concerning the exact mechanism and underlying cause of fibrillation itself, and (3) the new experiences and findings from each fresh case undergoing treatment.

Stating first our general impression, in spite of our relatively few cases of permanently established sinus rhythm (27 per cent.), we feel that quinidin is establishing a permanent place for itself in cardiac therapy and that no case of auricular fibrillation should be treated at the present time without at least thoughtful consideration of its therapeutic possibilities. Starting, then, from this general favorable impression, which are the cases that are most likely to respond, either permanently or temporarily? Judging by our experience up to the present time, we feel that patients with acute fibrillation or recurrent paroxysmal fibrillation are those most likely to react favorably and promptly to

advanced heart failure (engorged tender liver, pulsating veins of the neck, dropsy, etc.). In these the response is often remarkable. These cases suggest that the cyanosis, dyspnea and palpitation are due to the mechanical effects of the rapidly beating ventricle, and not to ventricular muscle failure.

We come now to the fourth group, the unfavorable cases or those in which quinidin is absolutely contraindicated. They may be listed briefly as those patients suffering with moderately advanced or advanced heart failure, signs or history of embolism, acute or sub-acute endocarditis, auriculoventricular or intra-ventricular block, angina pectoris, coronary disease, idiosyncrasies for quin and its derivatives, or prolonged chronic fibrillation. In these patients, the results of quinidinization are not sufficiently striking to justify the potential risk involved.

The drug should not be given without a careful history and complete examination of the patient. If possible, a preliminary electrocardiogram should be made, for without it there must always exist some uncertainty as to the exact type of irregularity or the presence of additional irregularities (extrasystoles), the relative balance of the right and left heart, and the integrity of the ventricular muscle (disturbance in ventricular conduction). The patient should be put at complete rest in bed, given a preliminary idiosyncrasy test of 0.2 gm., and then starting the following day the same amount every two hours with continuous observation and control, including the electrocardiogram if possible. Digitalis should be given later if the ventricular rate remains high, if heart failure persists, or if frequent relapses to fibrillation occur.

#### CONCLUSIONS

1. Quinidin sulphate has been administered to eighteen patients suffering with auricular fibrillation. In eleven (61 per cent.) a normal cardiac mechanism has been established, which, in five (27 per cent.), has persisted three months or more. One patient has maintained a sinus rhythm uninterruptedly for eleven months.

2. Cases of acute fibrillation or recurrent paroxysmal fibrillation are most amenable to quinidin treatment. In these patients the duration and frequency of the paroxysm can be promptly controlled without undue risk.

3. The following is offered tentatively as a means of selecting cases of auricular fibrillation in the order of their decreasing suitability for quinidin treatment: (a) patients with acute fibrillation or recurrent paroxysmal fibrillation; (b) patients with fibrillation of short duration without history or findings of heart failure or embolism; (c) patients with signs and symptoms of early or apparent heart failure, but without evidence of advanced heart failure.

4. In patients with moderately advanced or advanced heart failure, and history or findings of embolism, endocarditis, heart block, angina pectoris, coronary disease, quinidin idiosyncrasy or prolonged chronic fibrillation, quinidin is contraindicated.

5. Equally good results are obtained with small amounts of quinidin (0.2 gm.) given frequently (every two hours), to be continued in most cases once or twice daily after restoration of sinus rhythm.

6. Quinidin may usually be given at once without preliminary digitalization. If, after restoration of

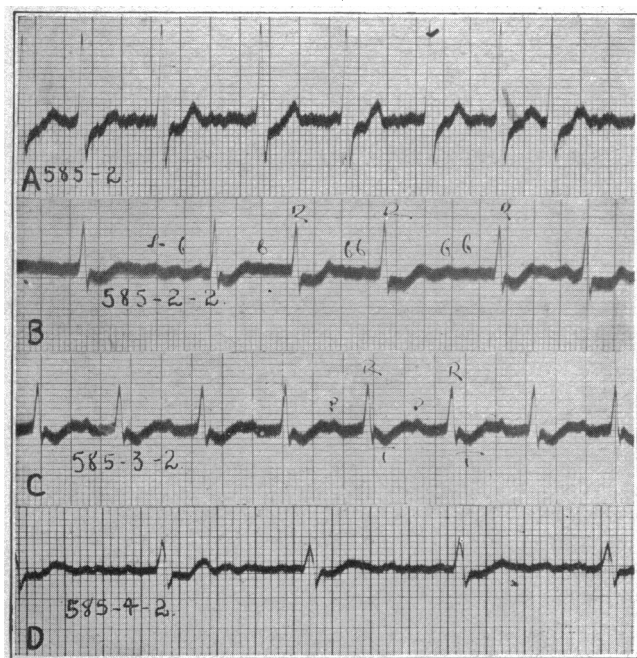


Fig. 2 (Case 15, woman, aged 50).—Chronic auricular fibrillation; mitral stenosis; regurgitation; advanced recurring heart failure. Quinidin response brief; early relapse to fibrillation; prolonged P-R: example of contraindication. Following 0.2 gm., temperature, 101.6 F. Died suddenly one week later. A, Aug. 19, 1921: rate, 94; no quinidin. B, August 23: rate, 75; no quinidin. C, September 2: rate, 107; 2.6 gm. quinidin. D, Feb. 8, 1922: rate, 79; total quinidin, 7.4 gm.

quinidin. While in these patients fibrillation often ceases spontaneously, administration of the drug controls the paroxysms more promptly and without danger. The duration of the response is more likely to be permanent in acute self-limited illnesses (acute respiratory infections, pneumonia) than in cases of hyperthyroidism, generalized arteriosclerosis, etc.

The next most favorable type of case is the patient with fibrillation of relatively short duration without signs of heart failure or evidence of embolism, in whom the administration, so far as we know, is unattended with serious consequences.

The third group, in which the outlook for response is probably as good as the second, but in which the possibilities of danger are somewhat greater, comprises those patients with signs and symptoms suggestive of beginning or early heart failure (cyanosis, dyspnea, palpitation and tachycardia), but without the signs of

normal rhythm, the ventricular rate remains high, signs of heart failure continue, or frequent relapses to fibrillation occur, digitalis should be subsequently administered.

#### ABSTRACT OF DISCUSSION

DR. FRED M. SMITH, Chicago: Every one has been impressed by the remarkable action of quinidin in auricular fibrillation. The beneficial effects of this drug in this disorder are not, however, as promising as it was thought they might be. It is apparently generally agreed that quinidin will ultimately be established as a valuable drug in the treatment of certain cardiac disorders. So far the results seem to be much better in instances of auricular fibrillation of short duration in which the heart is well compensated. A few fatalities have been attributed to the administration of quinidin. In most instances, cardiac failure or emboli have been responsible for the unexpected results. Lewis recommends that patients be well digitalized prior to the administration of quinidin. His reason for this is to ward off the possibility of embolic accidents. At present, it would thus seem that the dangers incident to this method of treatment would not permit its being recommended to the general practice. Observations would seem to indicate that quinidin may, perhaps, be of value in the treatment of premature contractions. It is commonly known that the premature beat may be a very disturbing condition to the patient and often not influenced by the measures that have been employed in the past. In several instances, we have obtained very satisfactory results with quinidin in persons who did not respond to other forms of medication. I well recall one patient who came to the clinic because of an irregular action of the heart that had occurred daily for an interval of more than five months. His general condition was very poor. He was unable to continue his work. He had lost 20 pounds (9 kg.) in weight, was unable to sleep and had a poor appetite. He was instructed to take 3 grains of quinidin three times a day. The irregularity was eliminated. He began to sleep, regained his appetite and in one week gained 10 pounds (4.5 kg.) in weight. At present his weight has increased more than 25 pounds (11.3 kg.), he is back at his former work and feels better than he has in months.

DR. JOHN WYCKOFF, New York: Dr. Hamburger said that quinidin was not indicated in cases of severe, long standing decompensation. I agree, but I think there are two reasons why it is contraindicated: first, as Dr. Hamburger has said, because in this type of case quinidin is most dangerous; although it is interesting to note that in the twenty-four cases of auricular fibrillation which I have observed the only death occurred in a patient who had no symptoms of heart failure at the time he received quinidin; and, second, because the clinical improvement after quinidin is very much less than that which we obtain after digitalization. It has been our practice to place patients with auricular fibrillation with heart failure into two groups. In one group, we gave digitalis first; and after we had obtained full digitalis effect, we gave quinidin. In the other groups, we gave quinidin first, followed later by digitalis. Patients were given a preliminary rest period of seven days with limited fluid intake, so that these factors could be eliminated as a cause of improvement. They were ordered rest for a week, and then given quinidin. Though some of these patients resumed sinus rhythm, none of them showed further clinical improvement. The other group were given quinidin first. Those who returned to normal rhythm usually showed some slight clinical improvement. After seven days' continued rest with the normal rhythm, these patients were digitalized, and every one of them showed marked further improvement. For example, one patient with a ventricular rate of 160, with signs of advanced heart failure, after receiving quinidin, resumed a normal rhythm with a ventricular rate of 90. The only clinical improvement was that palpitation disappeared. The patient was given a further rest for one week. During this time, dyspnea and orthopnea persisted and there was no loss of weight. He was then digitalized with an immediate clearing up of his symptoms. He passed 4 liters of urine in the first twenty-four hours and

lost 15 (6.8 kg.) pounds weight in the first forty-eight hours. This, I believe, shows that quinidin cannot take the place of digitalis in this type of case.

DR. ARTHUR E. STRAUSS, St. Louis: Quinidin has certainly come to be experimented with, even if it has not come to stay. The use of quinidin is still in an experimental stage. As with all drugs, it must undergo a period of study and our final analysis must depend on this study. Dr. Hamburger has emphasized that quinidin apparently is most effective in the cases of transitory auricular fibrillation. In that connection, I think it important to say that we are not certain that all so-called chronic fibrillations do not begin first as periods of transient fibrillation. Certainly, if one takes careful histories, one will often see cases develop as transient fibrillation; and it is not infrequent to see such cases develop later into the chronic forms. If quinidin is valuable in the temporary fibrillation, it is valuable in the chronic fibrillations at the onset. Dr. Hamburger has stated that it is often

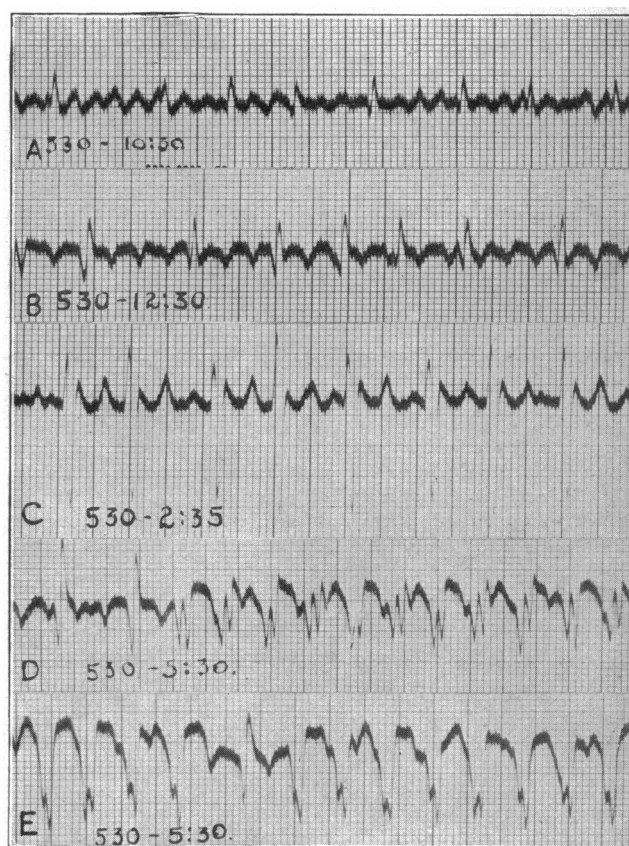


Fig. 3 (Case 5).—Sternal lead curves, showing effect of quinidin on auricular and ventricular rate; Nov. 28, 1922: A, 10:30 a. m., no quinidin; auricular rate, 424; ventricular rate, 124. B, 12:30 p. m., after 0.1 gm., auricular rate, 382; ventricular rate, 150. C, 2:35 p. m., after 0.2 gm., auricular rate, 363; ventricular rate, 124. D, 5:30 p. m., after 4 gm., auricular rate, 375; ventricular rate, 230.

necessary to continue the administration of quinidin. We are not yet certain of the effects of the long-continued use of quinidin. We have seen quinidin used in malaria for long periods of time, and in the majority of cases we have noted no harmful effects. However, in a number of my cases of fibrillation in which quinidin has been used for long periods the patients have complained of weakness when they had no symptoms of idiosyncrasy to quinidin. Therefore, there is some doubt as to how long quinidin can be continued. It must further be emphasized that there are some dangers incident to the administration of quinidin. Therefore, it must be used only after due consideration and with the idea that it should be as carefully controlled as are all experiments. One final word, as to the reason we should not use quinidin in the decompensation of fibrillation is almost invariably beneficial. We know that quinidin is beneficial in restoring normal rhythm

in no more than 60 per cent. of cases on the average. That alone is sufficient reason for using digitalis in the decompensated fibrillators, rather than quinidin.

DR. ALEXANDER LAMBERT, New York: I have tried quinidin in thirty cases. In one patient, the fibrillation stopped and the rate fell to normal. In all the others, with careful electrocardiographic control, there was no effect.

DR. L. F. BISHOP, New York: Dr. Hamburger has probably made the best observations and written the best literature on quinidin. So that, in discussing his paper, I do not wish to add to the experimental side of it, but rather to give my own impressions founded on a rather unusual group of patients. For a number of years, I have been using the electrocardiograph in private practice, and I have instructed my patients to come to the office when they have palpitation and have a picture taken of the heart beat. Thus, I have accumulated a number of examples of temporary fibrillation which did not recur again for a long time or did not recur at all. It seems to me that a very important element in appraising the value of quinidin is a knowledge of the natural history of fibrillation. I believe that nearly every example of fibrillation, except in the very advanced broken-down heart, begin in this way. The vast number of fibrillators commence by short attacks which become more frequent and last longer. It is almost a joke on medical science that the best example of therapeutic effect should be disturbed by the introduction of a new treatment. There is no treatment in all medicine as brilliant as the treatment of fibrillation of the auricle with digitalis, and I would say as a matter of experience that the patients do not feel any better when they are treated by quinidin than when they are treated by digitalis. In other words, the chronic fibrillator carries fibrillation comfortably if he takes enough digitalis or if he develops heart block which balances the fibrillation. I have seen persons who have continued very well with fibrillation for fifteen years or more. There is no doubt that there often exist clots in the paralyzed auricle in fibrillation, and it is certainly dangerous to restore the contraction of that auricle if it is going to throw out an embolus which may kill the patient. I do not believe that quinidin is a valuable general heart tonic, and I believe that men in general practice will do well if for the present they leave the use of quinidin to men who are experimenting with it in hospitals. I think it is unwise to use it in ambulatory patients in private practice.

DR. WALTER W. HAMBURGER, Chicago: I agree with Dr. Bishop in the main. I think his warning in the advanced cases should be emphasized. The real danger is, of course, embolism. If there is any sign or history of embolism, quinidin should not be given. One of my patients is a surgeon who has had paroxysmal attacks of fibrillation for fifteen years. He gets attacks once a year or so, sometimes while operating; once while swimming, and the last time while working in his garden. The attack last year lasted about a week and was associated with severe anginal pains. He was worried about it and was quite ill. After a week's rest in bed, the fibrillation stopped of its own accord, and he has had no attack until a week ago. I immediately gave him 3 grains (0.2 gm.) of quinidin and another dose in two hours. Within three hours this attack was over; and he is confident the drug shortened the attack. Likewise in the paroxysmal attacks of exophthalmic goiter, quinidin undoubtedly controls the attacks. It should not be given to ambulatory patients, and it should not be given as a routine until we know much more about it than we do at the present time. Embolism occurs in fibrillation without quinidin and sometimes without the establishment of a normal rhythm.

**Purpose of Operation for Epilepsy.**—In operating on epileptics, and in choosing cases for operation, we should like to have a clear idea of the purpose of the operation, based on some reasonable conception of that relationship. The surgeon who merely removes a disk of bone from the cranium of an epileptic patient places himself on a level with the practitioner of the stone age, the marks of whose handiwork on the skulls, probably of the epileptic or the insane, are to be seen in museums of ethnology.—Percy Sargent, *Brain* 44:314, 1921.

## THE CAUSE AND RELIEF OF ACUTE INTESTINAL OBSTRUCTION \*

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ROCHESTER, MINN.

Ileus is one of the most serious conditions that confront the medical attendant, since if it is not relieved death is inevitable. In order to lower the death rate in such conditions, much depends on early diagnosis, judgment and promptness of action. Relief is by no means possible in all cases; for instance, there is necessarily a high mortality in cases of mesenteric embolism and thrombosis. Therefore, the discussion of the subject of acute intestinal obstruction, from time to time, is of value, not so much for the older practitioners as for those who have more recently entered the profession, so that they may acquire knowledge without encountering the tragedies which fixed the memory of such conditions in the minds of those long in practice.

Cases of acute intestinal obstruction may be regarded as falling naturally into four groups: (1) apparent obstruction, really intestinal stasis, a reflex symptom occurring with slight abdominal distention, the pulse and temperature changes being such as are caused by the primary lesion, which is often renal; (2) the obvious hernia; (3) acute obstruction from an intra-abdominal lesion, and (4) postoperative obstruction.

The obvious hernias, inguinal, femoral, umbilical and ventral, which formerly caused a considerable proportion of obstructions through strangulation, have now largely been taken from this group, as even laymen appreciate the safety of modern surgery over that of a few decades ago. Hernia repaired at an elective period prevents the high percentage of strangulations formerly seen, when a reasonable fear of surgery led to prolonged taxis which often aided in the development of gangrene. The wasted opportunity, added to the seriousness of preantiseptic surgery, gave a high mortality which resulted in making acceptable this vicious circle of delay. Gangrene, or wet death of tissue, especially abdominal, and when sepsis is possible, furnishes toxins which are most difficult to counteract without the removal of the destroyed tissue or without adequate drainage.

Obstructions within the abdomen are those which cause the greatest apprehension, as there are added difficulties of diagnosis, some of which have been overcome by fluoroscopic observation or roentgenograms revealing obstructions after the opaque material has been given by mouth or by rectum. Volvulus from the twist of an extra long mesentery, usually of the sigmoid, produces not only obstruction but also the toxins of tissue death. Various forms of internal hernia, beneath bands, through congenital or unnatural mesenteric openings or through the diaphragm, usually cause degrees of partial, chronic, rather than acute, obstruction, which, however, may suddenly supervene. A second form of toxin concerning which much has been written is still under discussion. It is observed in obstructions high in the jejunum, blocking the duodenum, and, although the exact cause of retention is not always known, the condition is recognized. Such an obstruction around the duodenojejunal juncture, with paresis and dilatation of the duodenum, may cause

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