Quinidine as a Cause of Sudden Death

By George W. Thomson, M.D.

Sudden death and arterial embolism are unpredictable hazards of quinidine therapy for atrial fibrillation that act as deterrents to its most effective use. In this paper an attempt is made to determine the incidence of these accidents as reported in the literature. The mechanism of sudden death is also examined. The difficulty of determining the role of quinidine in producing these accidents in seriously ill patients is clarified.

Sudden death and embolism have long been feared as major hazards of quinidine in the treatment of atrial fibrillation. Isolated reports of untoward reactions began to appear shortly after the introduction of the drug by Fray in 1917. Viko, Marvin, and White compiled the first sizable group of cases in 1923 dealing with this problem. In 484 patients, they reported 9 sudden deaths, 6 of which were presumed to be due to embolism. The over-all incidence of embolism, fatal and nonfatal, was 3.1 per cent; the incidence of sudden death was 1.8 per cent. In 1929, Parkinson and Campbell reported on the basis of 554 cases a 4 per cent incidence of sudden death. This latter figure has been generally accepted as the standard risk. In contrast to the emphasis placed on embolism in the earlier report, they noted that “hardly any of these deaths were proved due to emboli, and in most of them necropsy showed no obvious structural disease to account for it [death]”. The most recent statistical data were presented by Askey in 1946. He reported on 839 cases, segregated into patients with and without congestive heart failure. Of 275 patients in failure, the incidence of death during treatment with quinidine was 4.0 per cent; in 564 cases not in failure, the incidence was 1.8 per cent. Although no such separation was made in the preceding reports, congestive heart failure was believed to play an adverse role. More recent authors have suggested that the hazards of embolism have been overemphasized, and that sudden death, though a possibility, is rare. In the face of these conflicting data and impressions, it was believed that a review of more recent experiences was in order.

Review of Reported Experiences, 1947–1954

Accordingly, 611 previously uncollected cases have been reviewed from 1947 to the end of 1954. The data given here are based on the experiences presented in 12 major reports, and are limited by their scope. Patients were generally unselected as to the underlying cause of heart disease, its severity, the presence or absence of congestive heart failure, the duration of atrial fibrillation, or the association of other disease processes. Attention devoted to these details was so infrequent and involved so few cases that little of statistical significance about these variables was revealed.

In this group of 611 cases, 20 deaths occurred during therapy and were variously interpreted by the several authors. In the interests of uniformity all 20 deaths were arbitrarily regarded in this review as being caused by quinidine. The mean fatal incidence was 3.3 per cent. Clearly, in certain cases death could be attributed to other causes, making the adjusted death rate 2.1 per cent. This compares with Askey’s over-all incidence of 2.5 per cent. This adjusted death rate of 2.1 per cent may be regarded as the maximal risk of sudden death from quinidine in this series. Table 1 reveals the wide range of total deaths in proportion to the total number of cases in various hands. The crude death rate varied from 10 per cent in 1 series to no deaths in 2 series. In the largest group of 111 cases, the incidence of death was 0.9 per cent. It was impossible to collect control series of sudden deaths in patients with atrial fibrillation who were not

From the Cardiovascular Service, Lenox Hill Hospital, N. Y.
National Heart Institute Trainee at Lenox Hill Hospital, N. Y., 1953–1954.

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receiving quinidine, partly because of the difficulty in deciding the cause of death. This difficulty also applies to the 20 patients who died suddenly while they were receiving quinidine.

In the majority of the 20 deaths reported, death occurred suddenly; patients were either observed to die suddenly or were found dead unexpectedly (table 1). Almost half of the deaths occurred in rheumatic patients with

### Table 1.—*Deaths During Therapy with Quinidine* (1947–1954)

<table>
<thead>
<tr>
<th>Series</th>
<th>Total Cases</th>
<th>Total Deaths</th>
<th>Clinical and pathologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleischmann⁷</td>
<td>34</td>
<td>1</td>
<td>Rheumatic heart disease. Severe mitral stenosis, developed ventricular tachycardia and ventricular fibrillation during therapy. Necropsy: “No explanation for sudden death.”</td>
</tr>
<tr>
<td>Sokolow⁴</td>
<td>111</td>
<td>1</td>
<td>*Died 30 days after conversion from bilateral lobal pneumonia and advanced nephrosclerosis, verified by necropsy.</td>
</tr>
<tr>
<td>McMillan¹⁰</td>
<td>50</td>
<td>3</td>
<td>Severe hypertensive. Died several days after conversion in uremic frost. No necropsy.</td>
</tr>
<tr>
<td>Belaval¹¹</td>
<td>14</td>
<td>3</td>
<td>Severe congestive heart failure, died suddenly, no necropsy.</td>
</tr>
<tr>
<td>Yount¹²</td>
<td>80</td>
<td>1</td>
<td>Rheumatic heart disease. Died suddenly in bed, half hour after last seen. Necropsy: Mitral stenosis, no pathologically evident cause of death.</td>
</tr>
<tr>
<td>Feigin¹⁴</td>
<td>33</td>
<td>1</td>
<td>Arteriosclerotic heart disease. Died suddenly on maintenance dose. No necropsy.</td>
</tr>
<tr>
<td>Bedard¹⁵</td>
<td>67</td>
<td>7</td>
<td>Arteriosclerotic heart disease. Died suddenly on day of conversion. No necropsy.</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>611</td>
<td>20</td>
</tr>
</tbody>
</table>

Total incidence of death among patients receiving quinidine = 3.3%.
Adjusted incidence where death could be reasonably ascribed to other causes = 2.1%.

* Death from causes other than quinidine therapy.
mitral stenosis. In 10 cases where pathologic examination was permitted, embolism was implicated only once. This patient had rheumatic heart disease and died in pulmonary edema. Necropsy revealed multiple small pulmonary infarcts, fresh and old, and thrombosis of the superior mesenteric artery. In 2 cases without postmortem examination, undoubted cerebral embolism with hemiplegia occurred, followed by death in coma. The infrequency of pathologically verified embolism as a cause for sudden death is provocative. However, in none of the 10 cases necropsied was it specifically stated that examination of the brain was performed; no pathologically evident cause of death could be found, nor could embolism be implicated from evidence of intracardiac thrombi of peripheral emboli in 5 cases. In the remaining 5, the cause of death was determined at necropsy as indicated in table 1. On the other hand, where nonfatal embolism was observed, the brain was the most frequent site, manifested by signs of hemiplegia and aphasia. From the available data, in accord with the experience of Parkinson and Campbell,² we are inclined to comment on how frequently no pathologically evident cause of sudden death could be found. However, valid conclusions regarding the cause of sudden death cannot be drawn from the limited necropsy data available; similarly, the inference of cerebral embolism does not seem warranted in view of these limitations.

Embolic was recognized clinically in 11 patients in a subgroup of 418 where the presence or absence of embolism was specifically noted (table 2). This is a clinical incidence of 2.3 per cent. Despite the notion that embolism most

<table>
<thead>
<tr>
<th>Table 2.—Occurrence of Embolism in Patients Under Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Series</strong></td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>Saland⁵</td>
</tr>
<tr>
<td>Goldman⁶</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Fleischmann⁷</td>
</tr>
<tr>
<td>Sokow &amp;</td>
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<tr>
<td>Edgar¹⁶</td>
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<tr>
<td>Belaval¹¹</td>
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<tr>
<td>Yount¹²</td>
</tr>
<tr>
<td>Goldman¹³</td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Feigin¹⁴</td>
</tr>
<tr>
<td>Bedard¹⁵</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

Over-all incidence of embolism during treatment = 2.3%  
Incidence of clinically defined embolic deaths = 0.4%
frequently occurs on resumption of normal sinus rhythm, when the time of occurrence of embolism was noted in 8 cases, it occurred twice at conversion, twice sometime after conversion, twice during continued fibrillation, and twice on relapse to fibrillation after prior conversion to normal sinus rhythm.

The results of giving quinidine to patients with established fibrillation in whom embolism had previously occurred were interesting. Sir Thomas Lewis\textsuperscript{17} regarded previous embolism as an absolute contraindication to the use of the drug. However, there has been a gradual evolution of a different opinion. By 1944, the National Research Council\textsuperscript{18} listed the history of systemic embolization in paroxysmal or established fibrillation as an indication for treatment with quinidine. Of 230 cases reviewed where the presence or absence of previous embolism was noted, 79 patients had previous embolic accidents. During treatment with quinidine, only 1 of these 79 suffered a second embolization, and this occurred on relapse to fibrillation. He was again converted, and remained symptom-free in sinus rhythm for a follow-up period of 9 months. Embolism however occurred in 6 patients who had no previous episodes. It would appear, therefore, that previous embolism adds a negligible embolic hazard to quinidine therapy.

The frequency of intracardiac thrombi and systemic and pulmonary embolism in the presence of fibrillation has been long appreciated. However, only recently has regularization of rhythm by quinidine as a means of preventing embolism received much attention. Saland and co-workers\textsuperscript{9} selected 15 cases in a group of 24 with an embolic history as an indication for quinidine treatment. They reported good immediate results, although no long term follow-up was available. Yount\textsuperscript{8} reported no further emboli after conversion in 23 patients in whom previous embolism had occurred. Occasional dramatic results with longer follow-up observations have been reported in individual cases with repeated or multiple embolization threatening life. Parkinson and Campbell\textsuperscript{2} mentioned a patient with rheumatic cardiac disease who suffered 3 successive major embolic events and who, after conversion to normal rhythm, remained free of recurrence for 5 years. Sokolow\textsuperscript{19} reported a patient with multiple emboli, who remained symptom-free for 1 year in sinus rhythm. White and Blumgart\textsuperscript{20} converted a 49-year-old rheumatic patient exhibiting recurrent multiple pulmonary emboli with increasing heart failure, who was free of congestion and embolism 5½ years thereafter.

There has been a general impression among recent authors of the protective effect against embolism of sinus rhythm, although more long-term observations are needed.

In the matter of concurrent use of anticoagulants with quinidine, only meager data are available. In a group of 137 patients so treated (table 2), 4 suffered embolism. In a "control" group of 348, 7 embolic accidents occurred. Statistically significant conclusions obviously cannot be drawn.

**Discussion**

It is apparent that the risk of sudden death from quinidine is real, and in some cases it is not susceptible to pathologic explanation. No final conclusions regarding the cause of sudden death can be made because of the limitations of the reported necropsy material. The available data favor some reason other than embolism. Certainly several known factors are operative. The nature and the severity of the underlying heart disease, of associated serious illness such as lobar pneumonia, uremia, and recent severe hemorrhage, and senile debility appear on occasion to affect the result (table 1). Of most concern, however, is the occurrence of sudden death in the relatively well patient. It may be possible to reduce the number of such catastrophes.
An analytic approach to the problem suggests that uncontrolled dosage may be a significant lethal factor (table 3). It is widely recognized that idiosyncrasies manifest by profound circulatory collapse, leading sometimes to a fatal outcome, do occur on small doses of the drug and at low plasma levels. Since dosage is not sharply defined, the total dose and the time over which it is given reflect, among other things, the prevailing local conceptions of the drug’s mode of action and toxicity and the evaluation of the clinical situation. But most important of all appears to be the care exercised in the control of dosage, which amounts to the frequency with which observations of one or another type are made on the patient while he is receiving large doses of the drug. Table 3 indicates that the mortality may be greater where no limits on the amount of the drug are set.

The occurrence of serious ventricular arrhythmias during quinidine therapy has been well documented. Ventricular tachycardia and fibrillation appear to have been noted with greater frequency than cardiac standstill, although the latter has been recognized electrocardiographically as a terminal event on occasions when quinidine has been given intravenously to control ventricular tachycardia. Coma, convulsions, and altered states of consciousness described during the course of aberrant ventricular rhythms are undoubtedly related to the failure to maintain an adequate cardiac output and adequate cerebral blood flow. Seven such fatal reactions were reported following intravenous administration of the drug, and conduction defects such as complete bundle-branch block or intraventricular block appear to add to the hazards. Similarly, ventricular tachycardia has been reported to occur with the use of quinidine in atrial fibrillation associated with complete atrioventricular dissociation.

Also pertinent to the problem is the reported occurrence of events, similar in nature to idiosyncratic reactions to the drug, which may become manifest only with high plasma quinidine levels or large or frequent doses of the drug. A generally unappreciated phenomenon is the apparent effect of quinidine as an excitant and at times depressant of the vital centers of the central nervous system. Acute studies of toxicity in animals indicate that severe depression of respiration occurs with apnea, followed by circulatory collapse. This reaction can be reversed with vasopressor drugs, artificial respiration, and central nervous system stimulants. Comparable reactions have been observed in man.

Kalmanson lists precipitant hypotension as the chief contraindication for continued use of the drug, since it frequently heralds the onset of circulatory collapse. Ferrer and co-workers found significant hypotensive reactions with a single 0.8 Gm. dose of the drug. These were seen in control patients with normal cardiac output and normal right ventricular end-diastolic pressure, so that a myocardial effect could be excluded.

In retrospect, it is of interest that Frey in 1921 in his early reports of toxicity listed cases of respiratory paralysis successfully revived by artificial respiration and central nervous stimulants. One year later, Levy reported 4 cases of sudden collapse with unconsciousness marked by temporary cessation of heart beat and respirations, with recovery. Clarke-Kennedy reported a fatal reaction in 1922 in which “sudden unconsciousness, apnoea, pulselessness, and profound cyanosis” occurred 16 hours after conversion. In a somewhat similar experience in recent years massive intravenous doses of quinidine provoked a sudden collapse with “complete unresponsiveness, cessation of breathing, and heart sounds” with successful revival by neosynephrin, caffeine, and oxygen and eventual complete recovery.

Berman and co-workers in 1953 reported a unique case among 5 cases of severe untoward reactions. This patient developed a convulsive state followed by apnea, cyanosis, and pulselessness after quinidine was given; recovery subsequently occurred. The reaction was unwittingly reproduced by a second dose and led to a fatal outcome. No cerebral embolism or obvious cause of death was demonstrated on postmortem examination. These authors suggest that convulsions, respiratory failure, circulatory collapse, and absent blood pressure represent a syndrome of “quinidine shock.”
### Table 4.—Analysis of Thirty-two Sudden Deaths Reported Before 1947

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Cases</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical data</th>
<th>Manner of death</th>
<th>Necropsy</th>
<th>Evidence of embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viko, Marvin, White</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>None given</td>
<td>Both sudden</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Burwell and Dieusaie</td>
<td>1</td>
<td>22</td>
<td>F</td>
<td>RHD, EH, MS, AI</td>
<td>Sudden</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Kohn and Levine</td>
<td>3</td>
<td>64</td>
<td>M</td>
<td>Chronic myocarditis</td>
<td>Suddenly dyspneic, unconscious, died in bizarre rhythm.</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Parkinson and Campbell</td>
<td>1</td>
<td>57</td>
<td>M</td>
<td>Thyroid adenoma, AF</td>
<td>Sudden</td>
<td>Yes</td>
<td>No emboli found</td>
</tr>
<tr>
<td>Newman and Spiro</td>
<td>1</td>
<td>40</td>
<td>—</td>
<td>RHD, MS</td>
<td>Sudden</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Clarke-Kennedy</td>
<td>1</td>
<td>4</td>
<td>—</td>
<td>RHD, MS, hypertension</td>
<td>Sudden</td>
<td>Yes*</td>
<td>No emboli found</td>
</tr>
<tr>
<td>Smith and Boland</td>
<td>3</td>
<td>45</td>
<td>F</td>
<td>RHD</td>
<td>Ceased talking and died.</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Jamieson</td>
<td>4</td>
<td>29</td>
<td>F</td>
<td>RHD, MS, CHF</td>
<td>Sudden</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Smith and Clarke</td>
<td>1</td>
<td>22</td>
<td>F</td>
<td>RHD, EH, MI</td>
<td>Muscle twitching; rapidly dyspneic, cyanotic, and died.</td>
<td>Yes*</td>
<td>None</td>
</tr>
<tr>
<td>Hay</td>
<td>6</td>
<td>30</td>
<td>F</td>
<td>RHD, MS</td>
<td>Died suddenly</td>
<td>Apparently none</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55</td>
<td>M</td>
<td>No diagnosis</td>
<td>Suddenly apneic, died</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>34</td>
<td>F</td>
<td>No diagnosis</td>
<td>Sudden</td>
<td>Apparently none</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27</td>
<td>M</td>
<td>RHD, EH, MS</td>
<td>Sudden</td>
<td>Yes*</td>
<td>None</td>
</tr>
<tr>
<td>Maynard</td>
<td>1</td>
<td>49</td>
<td>F</td>
<td>AF of unknown cause</td>
<td>Respiratory difficulty, unconscious; heart beat continued, then died.</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Sappington</td>
<td>1</td>
<td>50</td>
<td>M</td>
<td>AF, CHF</td>
<td>Kicking, twitching, became unconscious, died.</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>Levy</td>
<td>1</td>
<td>49</td>
<td>F</td>
<td>AF, EH</td>
<td>Became cyanotic, dyspneic, respirations ceased.</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Berman and Blumenthal</td>
<td>5</td>
<td>80</td>
<td>M</td>
<td>Coronary disease, hypertensive</td>
<td>Died suddenly</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>F</td>
<td>Hypertensive, EH</td>
<td>Sudden</td>
<td>No</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td></td>
<td>67</td>
<td>M</td>
<td>Coronary disease</td>
<td>Sudden</td>
<td>No</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>M</td>
<td>Coronary disease</td>
<td>Found dead</td>
<td>Yes</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>54</td>
<td>M</td>
<td>Hypertensive, CHF</td>
<td>Sudden</td>
<td>Yes</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

* Autopsy failed to show immediate cause of death.

AF = atrial fibrillation; AI = aortic insufficiency; CHF = congestive heart failure; EH = enlarged heart;
HHD = hypertensive heart disease; MD = mitral disease; MI = mitral insufficiency; MS = mitral stenosis,
RHD = rheumatic heart disease; SHD = syphilitic heart disease.

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which may be brief and responsive to artificial respiration and central nervous system stimuli. They speculate that these reactions "in the past interpreted as cerebral emboli, in reality . . . represent this . . . syndrome, occurring shortly after regularization."

Thirty-two cases in the older literature, where sudden death was specifically stated to have occurred, were reviewed with the view to applying these criteria (table 4). Despite the infrequency of detailed description of the mode of exitus, the possibility of sudden central nervous system depression was suggested in 13 cases as manifested by sudden cyanosis and dyspnea, unconsciousness, apnea, groaning, muscle twitching, and convulsions. In the total group, necropsies in 13 failed to show any embolic phenomena; 3 of these had demonstrated signs of sudden central nervous system depression during life. Although it is possible that primary central nervous system depression reflecting an unappreciated toxic action of the drug may have had a role in the production of sudden death, such cerebral phenomena may also have been secondary to the failure to maintain an adequate cardiac output in clinically unrecognized arrhythmias.

As previously noted, the incidence of death is increased by the presence of congestive heart failure. Evidence exists that the toxicity of quinidine is augmented by the presence of congestive failure. Plasma quinidine tends to persist at high levels and the drug is dissipated slowly. Unusually high serum levels and serious toxicity can occur in contrast to what occurs in normal subjects, or in patients with frank hepatic or renal disease. Further, it has been observed that ventricular tachycardia, as a toxic manifestation of quinidine, occurs more frequently in patients with congestive heart failure. The tendency to toxicity with congestive failure is so imminent that some authors have advised that continued administration of the drug to such patients be controlled by frequent determinations of the serum level.

**Summary**

1. The separate risks of sudden death and embolism during therapy with quinidine are appreciable. In 611 recently reported cases (1947-1954) the over-all death rate was 3.3 per cent. In 418 of these patients, the incidence of clinical embolism was 2.3 per cent. Death due clinically certain cerebral embolism occurred in only 2 cases.

2. In 10 fatalities studied at necropsy, embolism was implicated only once. In the majority, no pathologically evident cause of death could be found. Nearly half of the total deaths occurred in patients with rheumatic heart disease and mitral stenosis.

3. Prior embolism appears to carry a negligible risk of repetition during quinidine treatment.

4. Where no arbitrary dosage limit is set, the mortality appears greater.

5. Severe organic heart disease, congestive heart failure, and associated grave illnesses increase the possibility of a fatal reaction.

6. Unappreciated toxic effects of the drug, especially on the central nervous system, appear to play a role in the production of sudden death ("quinidine shock"). It is suggested that these effects might be avoided by a more judicious selection of patients for therapy and meticulous supervision of all patients receiving large doses.

**Acknowledgment**

The author is grateful to Charles E. Kossman, M.D., for his help in the preparation of this paper.

**Summario in Intere lingua**

1. Le duo distintce riscos de morte e de embolismo in therapia a quinidina es appreciabile. In 611 caso reportate inter 1947 e 1954, le mortalitate total esseva 3,3 pro cento. In 418 de iste patientes, le incidentia de embolismo clinic esseva 2,3 pro cento. Morte per embolismo cerebral con certitude clinic occurreva in solmente 2 casos.

2. In 10 mortes studiate necropicamente, embolismo esseva involvite solmente 1 vice. In le majoritate de iste 10 casos, nulle pathologicamente evidente causa de morte esseva constatable. Quasi un mediate del mortes total occurreva in patientes con rheumatic morbo cardiae e con stenosis mitral.

3. Casos con embolismos de occurrentia
previe pare curren un risco negligibile de repetizione durante le trattamento a quinidina.

4. Quando le dosage es sin limites de fixation arbitrar, le mortalitate es apparentemente plus grande.

5. Sever organic morbo cardiac, congestive disfallimento cardiac, e associate morbos de alte severitate augmenta le possibilitate de un reaction mortal.

6. Non-recognoscite effectos toxic del droga, specialmente super le sistema nervous central, ha apparentemente un rolo significative in le causation del morte ("choc a quinidina"). Nos opinha que iste effectos es possiblemente evitabile per un plus meticulose selection del patientes subjicite a iste therapia e per un detaillate survelliantia del patientes qui recipe grande doses del droga.

REFERENCES


From this view of the different parts of the plant, it is sufficiently obvious why I still continue to prefer the leaves.

These should be gathered after the flowering stem has shot up, and about the time that the blossoms are coming forth.

The leaf-stalk and mid-rib of the leaves should be rejected, and the remaining part should be dried, either in the sun-shine, or on a tin pan or pewter dish before a fire.

If well dried, they readily rub down to a beautiful green powder, which weighs something less than one-fifth of the original weight of the leaves. Care must be taken that the leaves be not scorched in drying, and they should not be dried more than what is requisite to allow of their being readily reduced to powder.

I give to adults, from one to three grains of this powder twice a day. In the reduced state in which physicians generally find dropssial patients, four grains a day are sufficient. I sometimes give the powder alone; sometimes unite it with aromatics, and sometimes form it into pills with a sufficient quantity of soap or gum ammoniac.—William Withering. An Account of the Foxglove, and Some of Its Medical Uses. Birmingham, 1785.
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GEORGE W. THOMSON

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