

ON
SULPHATE
OF
CINCHONIDIA,
AND OTHER
CHEAP ALKALOIDS
OF
CINCHONA BARKS.

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POWERS & WEIGHTMAN,
MANUFACTURING CHEMISTS,
PHILADELPHIA.

1874.

SULPHATE OF CINCHONIDIA.

The article from which the following selections are made, appeared in the February (1874) number of *THE MEDICAL AND SURGICAL REPORTER*, published in this city. The editor of that journal, Dr. D. G. BRINTON, has kindly permitted us to use it for this circular:—

ON THE USE OF SULPHATE OF CINCHONIDIA IN MALARIAL FEVERS.

BY WHARTON SINKLER, M. D.,

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Orthopædic Hospital.

There is no doubt that one of the greatest blessings conferred upon mankind was the discovery of Peruvian bark; and even had the Jesuits been the cause of greater evils than are accredited to them, they are, nevertheless, entitled to the gratitude of the human race; for it is to them that we owe the introduction of cinchona into the practice of medicine.

Since it was carried into Europe, in the year 1632, its use has extended vastly, and the only difficulty now is to supply the demand for the various alkaloids of the bark. In fact, the crude material itself is becoming difficult to obtain in sufficient quantity. It is for this reason that the cultivation of the cinchona tree has been attempted in countries where it is not indigenous, and the British Government has turned attention to its growth in India, and so far with success. * * * *

During the months of July, August and September of the past year, I had the opportunity of using, in the wards of the Episcopal Hospital, an alkaloid of cinchona bark which has

recently been put into the market by Messrs. Powers & Weightman, manufacturing chemists of this city. This is the Sulphate of Cinchonidia. It is isomeric with cinchonia, and is in long, silky crystals, resembling very much in appearance sulphate of quinia. It is slightly more soluble in cold water, and has a somewhat less bitter taste than the latter salt.

For some years there has been known what was called cinchonidia, but its composition was uncertain. It contained, however, both cinchonidia and quinidia; in some specimens the former was in much the largest proportion, and in others the reverse was the case. This preparation was used with success by Dr. Cullen, in 129 cases of intermittent fever, in 1855 (*Amer. Jour. Med. Sci.*, vol. XXIX, p. 81), and also by the late Prof. Pepper (*Med. Exam.*, vol. X, p. 523), who stated that he believed it to be more efficacious than quinine in malarial fevers.

The article which we are now considering is a pure sulphate of cinchonidine, and can be purchased for between one-third and one-fourth the price of quinine.

The Madras Commission, appointed by the British East Indian Government to test the value of the other alkaloids of cinchona bark than quinine, stated that they found quinidine and cinchonidine of almost equal value with quinine as an antiperiodic. Their report was made in June, 1868, and sums up the result as follows:—

“Most of the medical officers employed in using the alkaloids seem fully impressed with the belief that they are equally or very nearly as efficacious as quinine, and as already shown, the mass of information furnished in the tabular reports proves that the belief is well founded.

“In regard to the relative effects of the three new alkaloids, and with them chemically pure sulphate of quinine, the evidence derived from their use shows that, with the exception of cinchonine, as already stated, they in a remarkable degree so closely resemble each other in therapeutical and physiological action as to render distinctive description of little or no practical utility.”

In the report of the same Commission in October, 1868, Dr. Fogo writes:—

“In small doses all the alkaloids produce the same therapeu-

tic effects, that is as tonics, anti-periodics, and anti-neuralgics. Hypodermically and internally they have proved successful.

"In large doses they are all equally energetic, and produce their effects rapidly. They have been successfully used as anti-periodics and febrifuges.

"We have now three alkaloids in addition to quinine, all of great power. Quinine appears to be the most active and certain in its effects, and from long-established reputation it is not likely to be superseded by any of the other alkaloids, at least not until they become more known. In many constitutional peculiarities, where quinine cannot be borne, these alkaloids will be found good substitutes, and they can all be substituted for each other."

Dr. BENSLEY, of Midnapore, whose therapeutical report treats mainly, and his statistics entirely, of the collective value of the alkaloids, makes the following distinctive remarks of cinchonidine:—

"It is admirably suited to those cases requiring a tonic or febrifuge, in which at the same time there is a great tendency to diarrhoea, or diarrhoea already exists. Among the cases will be found two in which quinine produced irritation of the bowels, but cinchonidine was well borne. None the less valuable is it in consequence of the mildness of its influence on the nervous system, in those cases which, from peculiarity of constitution, are ill able to bear the more powerful alkaloids."

Dr. BENSLEY concludes by saying:—

"I have used cinchonidine extensively in the fevers of children, on account of its mildness, and because it is less liable to produce head and bowel disturbance than other alkaloids. Upwards of thirty of my cases were children varying in age from one to nine years. I have such confidence in it that it is now the only preparation I prescribe for children."

The whole number of cases on which this report was based was 2272.

Dr. JOSEPH DOUGAL, Surgeon in the Madras Army, gives, in the *Edinburg Medical Journal*, for September, 1873, the result of treatment in 108 cases of malarial fevers, mostly of the quotidian type, by these alkaloids. The conclusion he arrives at is, that, next to quinine, quinidine is the most active, that cinchonidine is but little inferior, and cinchonine the least efficacious.

[Both Sulphate of Cinchonia and the Purè Alkaloid have

been used in large quantities, and with great success in this country during the last fifteen years.—P. & W.]

In my own investigations with cinchonidia, I determined simply to compare it with quinine in the treatment of intermittent fever, and therefore administered it in the same dose and manner in which it is customary to give quinia in our Philadelphia Hospitals, in the above mentioned disease. The formula used was:—

R.—Cinchonidiæ sulph.,	gr. iv.	
Acid sulph. aromat.,	ʒiv.	
Aquæ,	ʒ.ʒj	M.

This dose was given every four hours, beginning as early in the day as possible, until grs. xvj had been taken. The same amount was continued until five or six days after the last chill, when the dose was reduced to grs. xij a day. After a day or two more, but six or eight grains a day were given. There were seventeen cases of malarial fevers in which the cinchonidia was tested. Of course this is not a sufficient number upon which, alone, to base any positive conclusions, but the result of the treatment was confirmatory of that of the Indian physicians, and was so eminently satisfactory that I report the cases briefly, in order that other physicians throughout the country may have the opportunity of testing the antiperiodic and tonic properties of cinchonidia.

CASE I. Quotidian.—R. H., æt. 30, sailor, admitted July 17th. Three years ago, and again three weeks ago, he had chills, and was cured each time by quinine. Six days ago, while on board ship near Boston, was taken with a chill, and has had one of an hour's duration each day since. On the day of admission he took cinchonidia, grs. iv, but the chill returned as usual. On the next day he had grains xvj before the hour for the paroxysm, and it did not recur. He continued to take grs. xvj a day, but on the 25th he stated that during the previous night he had had several slight chills. He was discharged July 28th, having had no further return of his disorder. On August 20th the patient was readmitted, having been again exposed to malarial influences and having had two

chills. Was given cinchonidia, grs. xvj a day, until August 29th, when it was reduced to grs. xij. On September 1st it was increased for a day to grs. xvj. Discharged September 22d, having had no return of chills.

CASE II. Tertian.—J. D., laborer, æt. 35, admitted July 22d, 1873. For five days has been suffering from chills, and has taken no medicine. Placed at once on cinchonidia sulph. ; had taken but grs. viij before the hour for expected paroxysm, and had no chill. Was given grs. xvj daily until July 27th, when it was reduced to grs. xij. On the 30th, however, having had a slight chill in the evening, he was given grs. xvj a day for three days. Discharged well, August 4th.

CASE III. Quotidian.—L. M., æt. 30, laborer, admitted July 25th. Has been sick for five weeks ; for the first two with tertian, and for the last three weeks with quotidian intermittent. For some time he has been under treatment at the Out-Patient Department of the Hospital, and has been taking quinine and quinoidine without relief. On admission was put on cinchonidine, and took grs. xij before the hour for the chill, and had no paroxysm that day. Was discharged August 2d, having been nine days under treatment and having had no more chills.

CASE IV.—O. A., æt. 17, admitted August 6th. One year ago had an attack of malarial fever which lasted three months. For five weeks before admission has had chills at irregular intervals, and suffered from periodical headaches. Quinine had been given without success, and his stomach was very irritable. Was ordered liq. potass. arsenit. gtt. vj three times a day, which had the effect of stopping the chills, but in six days the toxic effects of the arsenic were observed and it was suspended. The chills then returned, and he was anæmic and very weak. He was now given cinchonidia, grs. xij daily, until the 22d, when he had a slight chill, and was given grs. xvj daily for four days. Under this treatment the headaches became less violent and occurred at longer intervals, and when discharged, September 6th, they had ceased altogether. The irritability of the stomach disappeared while he was taking the cinchonidia, and he had no return of chills.

CASE V. Quotidian.—G. B., æt. 36, sailor, admitted August 11th. Has had a chill, followed by severe headache, every day since the 3d ult. Has never had malarial fever before. Had cinchonidia, grs. xvj daily, and left the hospital August 18th, having had no chill nor headache while in the institution.

CASE VI. Quotidian.—L. E., æt. 36, laborer, admitted August 20th, having had one chill daily for six days. From the 20th to the 28th was given cinchonidia, grs. xvj a day. From August 28th to September 2d was given grs. xij daily, when the specific treatment was suspended. - The patient was in the hospital until October 6th, for some other ailment, and was then discharged well, having had no symptoms of a malarial nature since his admission.

CASE VII. Quotidian.—R. W., æt. 35, sailor, admitted August 25th. Eight years ago, while in Peru, had ague for four months. Since then he has been free from it until the present attack. Was at sea on August 21st, when he was seized with a chill, and he has had one each day until admission. Was given cinchonidia, grs. xvj daily, until August 29th, when it was reduced to grains xij. When first seen there was marked tenderness over the spleen. He was discharged September 1st, having had no return of chills and the splenic tenderness having subsided.

CASE VIII.—Catharine W., domestic, admitted August 28th. For a week she has had chills at irregular intervals. Was placed upon cinchonidia, grs. xvj daily, for three days, when, there having been no tendency to return of chills, it was reduced to grs. xij a day. On September 6th she had a slight chill in the evening, and the medicine was increased to grs. xvj a day. She was discharged September 16th, having shown no malarial symptoms since the 6th.

CASE IX.—M. L., æt. 23, sailor, admitted August 29th. Has had chills at irregular intervals for five weeks. Had the last paroxysm on the day of admission. Was ordered cinchonidia, grs. xvj a day. On September 4th it was reduced to grs. xij. Discharged well, September 8th.

This patient had been in the hospital from June 13th to July

8th, for intermittent fever, and was given from twelve to sixteen grains of quinine daily. Was discharged well, but in seven days returned with a relapse. Was again treated with quinine, grs. xvj a day, and was discharged July 22d, to return a second time in seven days with another malarial attack.

CASE X. Quotidian.—I. H., æt. 35, sailor, admitted September 9th. One month ago, while lying in the James River, he was taken sick with malarial symptoms. He had no marked chill until September 4th, since when he has had one paroxysm each day. Was given cinchonidia, grs. xvj for five days. For three days he took grs. xij a day, and after that time grs. xvj were administered daily until his discharge, September 27th. No chill after admission.

CASE XI.—W. B., æt. 23, engineer, admitted September 18th. Six weeks ago he had intermittent fever, of the tertian type, for a month. He then had no chill for a week, but had one on each of the two days before admission. Took cinchonidia, grs. xij, the day he came in, and he escaped the expected chill. After this the patient was given grs. xvj daily, and was discharged September 25th, having no recurrence of the chills.

CASE XII. Quotidian.—O. G., æt. 28, sailor, admitted September 20th. Had been with his vessel at Richmond, Va., for some time, but was not taken sick until September 15th, while at Delaware Breakwater. He states that on the 15th he had two chills during the day and two at night, and the paroxysms returned in the same manner until the 18th. He had taken some quinine and had had no chill for twenty-four hours before admission. Was put on cinchonidia, grs. xvj a day, and was discharged September 27th, having had no recurrence of the chills.

CASE XIII. Double quotidian.—J. R., æt. 34, sailor, admitted September 20th. This patient was from the same ship as case xii, and had also taken some quinine before admission, but does not know how much. Had two chills daily on the 17th, 18th and 19th, and one after coming into the hospital, on the 20th. Was given cinchonidia, grs. xvj a day, until his dis-

charge, September 27th. He had no return of chills after treatment was begun.

CASE XIV.—H. S., æt. 26, sailor, admitted September 27th. In June, while lying in his vessel in the Potomac River, near Washington, he contracted intermittent fever. Since then he has had chills at irregular intervals. Sometimes a paroxysm daily for a week, and then none for several days. He has taken quinine from the beginning of the attack, but without relief. His last chill was on September 25th. On admission his spleen was enlarged and tender on pressure. Was ordered cinchonidia, grs. xvj a day. On October 12th the cinchonidia was suspended, as he had had no symptom of a relapse since his admission. When this note was taken, on October 20th, the patient was still in the house, under treatment for bronchitis, but had had no evidence of malarial trouble.

CASE XV. Quotidian.—J. H., æt. 50, weaver, admitted October 2d. Has had a severe chill daily, since September 2d. On October 3d the patient was given cinchonidia, grs. xvj, but had a slight chill about three P. M. On the fourth he was given grs. xx, and escaped the chill. From the 5th to the 7th took grs. xvj daily, and for the next two days grs. viij. On the 9th and 10th was given grs. xx each day. The dose was then reduced to grs. viij a day, and the patient was discharged October 24th, having had no return of the chills.

CASE XVI.—M. N., æt. 24, laborer, admitted October 10th. Has been sick for two weeks with general debility, loss of appetite and strength. On October 6th he had a chill, and one on the 7th, 8th and 10th. Was given cinchonidia in the usual manner, and was discharged November 3d, having had no return of his sickness.

The following case was communicated to me by my friend, Dr. S. R. KNIGHT.

CASE XVII.—Mrs. A. B., has been suffering from quotidian intermittent during the months of July, August, and the early part of September. The treatment has been quinine, grs. xvij a day, in doses of grs. ij every hour before the time for the paroxysm. This treatment acted only as a palliative, for as

soon as it was suspended relapses occurred. About the middle of September the patient had a recurrence of her chills, and Dr. KNIGHT gave her grs. xij of cinchonidia one day, and the next day grs. xvj. By this means the usual paroxysm was prevented. The patient was afterwards put on arsenic and iron, and up to November 8th had not had another chill.

Many of these cases were sailors who had been exposed to intermittent fever in our Southern rivers, and who had become thoroughly saturated with the malarial poison. Of the seventeen cases, nine were of the quotidian type.

In cases 3, 4, 9, 13, 14 and 17, quinine had been administered and had failed to relieve the disorder. In number 17 the quinine had been pushed until its most marked effects were produced, as ringing in the ears and headache; but as soon as the medicine was suspended the chills returned. In all of these cases there was prompt relief from the use of cinchonidia.

In only three cases was there any relapse while the patients were under observation, and they were all kept in the hospital for some days after they seemed entirely well.

In none of these cases did I observe any unpleasant effect from the use of the drug. Unlike quinine, cinchonidia caused no headache, ringing in the ears, or disordered vision, and there was no disturbance of digestion. In fact, in case 4, while the patient had been taking quinine his stomach became disordered, but under the use of cinchonidia the gastric irritation subsided.

In addition to the foregoing, we extract the following from communications which we have received from different parts of the country:—

Messrs. ARTHUR PETER & Co., of Louisville, write:—"Dr. THEODORE S. BELL, Professor of Theory and Practice of Medicine in the Louisville Medical University, as also Dr. J. F. BIRKHEAD, of Shepardsville, both pronounce the Sulphate of Cinchonidia as 'equal in therapeutic effect to Quinia.'"

From Messrs. J. H. ZEILIN & Co., Macon, Ga.:—"We have

disposed of the samples of Sulphate of Cinchonidia sent, and parties are much pleased with them."

Dr. H. D. GARRISON, Chicago:—"Your Sulphate of Cinchonidia has given excellent satisfaction. I propose to advertise it a little on my own account, in the *Chicago Medical Times*, which I publish."

Dr. GUSTAV. T. FOX, Baltimore:—"I have tried it (the Sulphate of Cinchonidia) in several cases of intermittent neuralgia, and am happy to state that it has thus far sustained in full the advantages you claim for it."

Mr. F. T. MAYNARD, druggist, Petaluma, California:—"Our physicians have used the Sulphate of Cinchonidia in several cases, in place of Quinine, and find its effects identical with that alkaloid."

Mr. S. J. HILLMAN, druggist, Indianapolis:—"I have given an impartial trial to the sample of Cinchonidia sent me some time ago, and find it answers all the uses that Quinia is put to. I had a severe attack of chills, which would return constantly in spite of all the Quinia I would take. The Cinchonidia, in two-grain doses four times a day, relieved me."

Dr. F. MARION SHIELDS, Hashaqua, Mississippi:—"I have tested the Sulphate of Cinchonidia on my own son, who has been afflicted with chills for eight months. Please accept my and my wife's many grateful thanks for your cure—never one roaring in the head, as from Quinine."

Mr. J. W. PRICE, druggist, Burlington, Iowa:—"I have called the attention of my patronizing physicians to the Sulphate of Cinchonidia, and have very favorable reports from it, especially where Quinine has been given for a length of time. I think very well of it."

POWERS & WEIGHTMAN.

PHILADELPHIA, March, 1874.

ON THE CHEAP
ALKALOIDS OF THE CINCHONAS.

**SULPHATE OF CINCHONIA, SULPHATE OF QUINIDIA,
AND PURIFIED CHINOIDINE.**

While on the subject of Cinchonidia, we would suggest to our friends not to overlook the other alkaloids of Cinchona—SULPHATE OF CINCHONIA, SULPHATE OF QUINIDIA, and PURIFIED CHINOIDINE, all of which possess febrifuge and anti-periodic powers, in a most decided degree.

The first, SULPHATE OF CINCHONIA, has been largely used in past years, the dose being double that of Sulphate of Quinia.

SULPHATE OF QUINIDIA is well known in some of our Western cities, and for many years past has been regarded as quite equal to Sulphate of Quinia.

PURIFIED CHINOIDINE is a much cheaper preparation, also largely used.

The following paper on the Cheap Alkaloids of the Cinchonas was written by our friend, DANIEL B. SMITH, Esq., of Germantown, for many years President of the Philadelphia College of Pharmacy. It was published in September, 1855; and now that over eighteen years have elapsed, the favorable views therein expressed in regard to the efficacy of Sulphate of Cinchonia and Chinoidine, have been fully corroborated, and there has been a steady increase in the consumption of these articles.

Sulphate of Cinchonia has been largely used in the United States Army; and we beg leave to refer to a paper on the use of this salt by A. PAUL TURNER, M. D., in Hays' *Americal Journal of the Medical Sciences*, April, 1864, page 396.

The Cinchona Barks are, without doubt, the most precious contribution of the New World to the *Materia Medica* of the Old. Their entire control over all the forms of Intermittent Fever was early ascertained, and remains undisputed and unrivaled. Three varieties of the Bark have usually been distinguished in commerce, viz, the Pale or Gray Bark, or the Crown Bark of Loxa; the Yellow or Calisaya Bark; and the Red Bark. For more than a century after the Peruvian Bark

came into use, it was procured almost exclusively from Loxa and the neighboring provinces.

It was this variety, the Pale or Gray Bark, in all probability, the success of which established the reputation of Peruvian Bark as an anti-periodic.

The Yellow or Calisaya Bark appears to have come later into notice, and to have been generally preferred on account of its greater bitterness and stronger taste.

The Red Bark is stronger and more astringent than either of the others. Humboldt says that "in intermittent fevers the *C. Condaminea* (*the Crown Bark of Loxa*) and *C. Lancifolia* (*the Calisaya Bark*) are preferable to the others; while in diseases of the muscles and purulent ulcers *C. Oblongifolia* (*the Red Bark*) is more fitted, and the milder *C. Cordifolia* (*the Gray Huanuco Bark*) is adapted for convalescents."

When Humboldt wrote the above, the trees producing the several commercial varieties of Bark had not been fully identified, but the barks mentioned in the parentheses are those which he believed to be the products of the species named by him.

In this country, the best Red Bark has always been regarded as the bark most to be relied upon in obstinate intermittents.

It was in the year 1803 that Dr. Duncan, of Edinburg, announced the existence of a peculiar proximate principle in Peruvian Bark, which he called Cinchonine. Dr. Gomez, a Portuguese physician, followed up these researches, in the year 1810, and obtained the Cinchonine in a crystalline form, but without suspecting its alkaline nature. In 1806 Vauquelin undertook the chemical examination of the Cinchonas, and isolated the Kinic acid.

Little more was added to our knowledge respecting them, till the brilliant discoveries of Pelletier and Caventou were made known, in 1820.

They began their researches by the examination of the Gray Bark, "*Kina Losas*, *Cinchona Condaminea*, generally regarded," say they, "as the type of the various barks." Repeating the experiments of Dr. Gomez, with their own greater chemical skill, they ascertained the alkaline nature of Cincho-

nia, and most of its properties, prepared its sulphate and many other of its salts, and proved that it existed in the bark combined with Kinie acid.

They next directed their attention to the Yellow Bark, "*Cinchona Cordifolia*," as they call it, and were rewarded by the discovery of the new alkaloid, Quinia, the properties and combinations of which they investigated, but without succeeding in obtaining the alkaloid itself in a crystalline form.

They completed their labors by the analysis of the Red Bark, "*Cinchona Oblongifolia*," in which they discovered both alkaloids to exist.

"If," say they, "we have established that the active principle of the Cinchonas resides in a salifiable base, we can explain how it is that the gray and yellow Cinchonas present shades of difference in their medicinal properties. As to the Red Bark, it is the best of the Cinchonas, since it unites the two principles, and combines them in the greatest proportions."

When subsequent analysis discovered that these alkaloids differed in composition by only an atom of oxygen, the presumption as to their equal curative powers, derived from the fact that they existed separately, one in the pale, and one in the yellow bark, and combined in the red, all which barks were celebrated for their anti-febrile virtues, seemed to amount to certainty.

Perhaps it is not difficult to explain how it happened that one of them, the Quinia, has come into universal use, to the almost total neglect of the other.

These distinguished chemists were naturally anxious to test the virtues of the new alkaloids, and they submitted specimens of the sulphates of both to the principal physicians of Paris for trial.

Their attention was principally directed to the effects of the Sulphate of Quinia, which was attainable more readily and in greater quantities than the Cinchonina, from the barks then in use.

Out of twenty cases reported, fourteen by Dr. Chomel and six by Dr. Double, the Sulphate of Cinchonina was administered only in one, and that of Quinia in all the others. The success

of the latter was so great that it became, from that time, the universal remedy for intermittent fever. The medical profession was satisfied with its powers, and did not care to inquire into the virtues of the Cinchonia. Time and experience have only added to the reputation of the Quinia, and it is unnecessary here to enter into any details respecting its properties. The object of this memoir is to call attention to other preparations from the Cinchonas.

Although the single trial of Dr. Chomel "did not fully realize his expectations," and the further use of Cinchonia was, for the time being, prematurely abandoned, there is no reason to doubt that it is equally efficacious with the Quinia. The patient on whom he tried it "had been suffering with the disease for two months, in the quotidian form, and also had great enlargement of the spleen; at first only six grains of the Cinchonia were administered during the apyrexia, but as this failed to check the disease, on the following day twenty grains were administered, with the effect of completely arresting the paroxysms. Upon reducing the dose, however, it appears that the patient soon relapsed, and was not permanently cured until twenty-four grains were given during the intermission. When we bear in mind that the above case had been of long duration, and was complicated with visceral enlargement, it is by no means surprising that the disease was not checked by small doses of Cinchonia at the first effort, or that it should even have recurred after it had once been arrested by larger doses; for, under similar circumstances, it is well known that the same difficulties will often occur under the use of Quinia, or any other treatment that may be instituted. And yet there is good reason to believe that the partial want of success in this single instance has had much to do in establishing the common opinion that Cinchonia is less energetic than Quinia, and consequently requires to be given in a stronger dose.

A more thorough and impartial trial of this important remedy was, however, made by Dr. Bally, in 1825. He gave the sulphate in twenty-seven cases of intermittent fever; and although only six or eight grains were administered during the

intermissions, he succeeded in promptly checking twenty-five of the cases, sixteen of which were of the tertian and nine of the quotidian type, the average duration of the treatment being only four days. The remaining two cases were quartans, and these were checked quite as promptly as this most obstinate form generally is by Quinia or any other therapeutic agent; in one instance the disease lasted only two days, and in the other it was permanently checked by the end of one week. From these observations, the above-named author concluded that the Sulphate of Cinchonia arrested acute paroxysmal affections with great promptitude, and that but a moderate dose was necessary for this result; he also inferred that it was less irritating, and that it might, therefore, be more generally administered than the same salt of quinia; he was even disposed to ascribe many of the cures usually attributed to this last-named substance to the well-known fact that it was no uncommon thing to adulterate Quinia with Cinchonia. In the *Dictionnaire Universel de Matière Médicale*, par Mérat et De Lens, allusion is made to numerous instances in which the Cinchonia had been successfully used by French and Italian physicians; amongst these may be mentioned Dufour, Petroz, Potier, Mariani, and Bleyne; by all of whom it was fully shown that Cinchonia was at least as efficacious as Quinia. In confirmation of the same views, we also find it stated, in *Christison's Dispensatory*, that "prejudice, together with the unquestionable energy of Quinia as a remedy, has led to the other alkaloid, Cinchonia, being overlooked in practice. The equally strong prepossessions, however, which were long entertained in favor of Crown bark as a febrifuge and stomachic, though it contains but little Quinia, or perhaps none at all, and the proofs which have been given of the great efficacy of the gray, or Huanuco bark, would justify the inference that Cinchonia, too, is eminently active. Accordingly, trials made with it by Dr. Bardsley, in England, as well as various practitioners of credit in France, Germany and Italy, seem to leave little doubt that it is scarcely inferior to Quinia in the treatment of intermittent; and some continental writers even maintain that, while equally energetic, it is likewise even

less likely to disorder the stomach in large doses." In like manner, in the *United States Dispensatory*, Dr. Wood states: "There is little doubt, however, that *Cinchonia* possesses febrifuge properties little, if at all, inferior to those of Quinia; and should the source of the latter begin to fail, the pale bark would come into more extensive use for the preparation of the former." — *On the use of Bebeerine and Cinchonia*, by Dr. Wm. Pepper; *American Journal Med. Sciences*, Jan. 1853. So likewise in *Pereira's Materia Medica and Therapeutics*, a work of the highest authority:—

"If we take into consideration the similarity of chemical properties of *Cinchonia* and Quinia, we are led to suspect analogy of physiological effects. When they were in the first instance submitted to examination, *Cinchonia* and its salts were thought, principally on the evidence of Chomel, to be much inferior in activity to Quinia and its salts. But the subsequent observations of Dufour, Petroz, Potier, Bally, Nieuwenhuiss, Mariani, Bleyne, and others, have appeared to prove that the sulphates of these alkaloids may be substituted for each other. Nay, Bally gives the preference to the Sulphate of *Cinchonia*, on the ground that it is less irritating than the Sulphate of Quinia. That *Cinchonia* is as active as Quinia might have been anticipated, *à priori*, when we recollect that those barks in which *Cinchonia* is the predominant principle were the first which were celebrated as therapeutic agents.

"As *Cinchonia* and its salts are less bitter than Quinia and its salts, we might expect that the former would possess somewhat less medicinal activity than the latter; and this inference is probably correct. Moreover, as *Cinchonia* and its salts have a more nauseous flavor, and are more allied to that of Sulphate of Magnesia, it might naturally be anticipated that large doses of Sulphate of *Cinchonia* would be more apt to create nausea and vomiting than like doses of Sulphate of Quinia; and I have been informed by some medical friends that this is in reality the case. I must confess, however, that I have been unable to verify it. I have extensively used, in hospital practice, Sulphate of *Cinchonia*, in doses not exceeding

ten grains, and have not met with the nausea and vomiting I expected to have met with. In a case of ague I ordered the patient (a young man) to take ten-grain doses of the Sulphates of Quinia, Quinidia, and Cinchonia, on separate successive days, every two hours, before dinner; that is, the Sulphate of Quinia on one day, the Sulphate of Quinidia on the second, and the Sulphate of Cinchonia on the third day. The case was very carefully watched by one of my clinical clerks, but no difference of effect was discernible. No sickness or vomiting took place. I have found the Sulphate of Cinchonia valuable, both as a tonic and febrifuge or antiperiodic."—*Pereira's Mat. Med.* (Philada. 1854), vol. ii, pp. 681-2.

Dr. Pepper, in the memoir already quoted, reports the result of the trials made by him of the Sulphate of Cinchonia at the Pennsylvania Hospital.

In the fifteen cases reported, "the Cinchonia was administered with the most signal success, and fully confirmed the above statements as to its efficacy. In a majority of these the disease had been of many months' duration, and was attended with enlargement of the spleen, and more or less impairment of the general health; yet, notwithstanding these serious difficulties, it was promptly checked at the first effort in eleven of the cases, and in two of these Sulphate of Bebeerine had first been unsuccessfully tried. In only two instances was it necessary to administer the Cinchonia a second time for the arrest of the paroxysms; and of the whole number, as far as it could be ascertained, but two relapsed, and these were promptly and permanently checked by again resorting to the Cinchonia in full doses." * * "Judging from my experience in former seasons, in similar cases, I am fully convinced that the Cinchonia proved quite as efficacious as Quinia, and occasionally, indeed, it appeared to be even more prompt." Dr. Pepper adds "that in several cases of neuralgia and intermittent fever, which have fallen under my observation in private practice, the Cinchonia has succeeded after the failure of the Quinia in similar doses."

*Dr. Kenderdine, the Resident Physician of the Hospital of the Protestant Episcopal Church, in Philadelphia, in a commu-

nication dated 7th October, 1854, and addressed to Powers & Weightman, states that he has used the Sulphate of Cinchonia in over three hundred cases of Malarious Fevers of various types. "In these cases the Sulphate of Cinchonia has been given in the same doses that Sulphate of Quinia would have been, viz, fifteen to eighteen grains, the chills checked, the periodical character of the disease broken up, but the tendency of the disease to return at weekly or bi-weekly periods has been about the same as when the Sulphate of Quinia had been used."

The evidence thus brought together, proves conclusively that the Sulphate of Cinchonia is a remedy for intermittent fever, fully as efficacious as the Sulphate of Quinia. There are probably the same shades of difference in their medical properties as in the gray and yellow barks in which they severally exist, giving the preference sometimes to the one and sometimes to the other.

Yet, if the Sulphate of Quinia answers all the purposes for which the Cinchonas have become celebrated, why need the Cinchonia be used at all? There would perhaps be no sufficient reason for wishing to introduce it, were the expense of administering the two alkaloids the same.

But the barks which are now collected in South America, and which have to be used in the preparation of these alkaloids, yield Cinchonia as well as Quinia, and the small demand for the former causes it to be offered at a lower price, in order to find sale for it.

"Not only," as Dr. Pepper remarks, "is Cinchonia an efficient remedy, but it derives additional importance from the fact that at the present time it can be supplied at far less than half the price of Quinia. The poor are now in a measure debarred from the use of this last-named remedy, owing to its high cost, but this evil could, in a great degree, be obviated by the general introduction of Cinchonia."

In the quotation from Pereira's *Materia Medica*, given above, a third alkaloid of the Cinchonas, the Quinidia, is mentioned. It was discovered and its properties investigated in 1848. It exists in the pale Loxa and Lima Barks, and the gray Huanuco

Barks, along with the other alkaloids. The barks which are now used for the manufacture of Quinia do not contain it in very appreciable quantities, so that whatever may be the case hereafter, its properties are not now a matter of much practical interest.

The composition of the Quinidia closely resembles that of the other cinchonic alkaloids. They are all, probably, oxides of the same organic base.

Cinchonia is almost insoluble in ether and in cold water, and Quinidia is much less soluble in them both than Quinia.

The Sulphate of Cinchonia is soluble in about fifty-four parts of cold water, that of Quinidia in about one hundred and thirty parts, and that of Quinia in about one hundred and forty parts. When a solution of the sulphate of these alkaloids is mixed, first with chlorine water, and then with ammonia, the Sulphate of Quinia becomes of an emerald green color; the Sulphate of Quinidia either remains unchanged or yields a white precipitate, and the Sulphate of Cinchonia becomes purplish, and yields a white precipitate.

The Sulphate of Quinia was first successfully prepared in America in 1823; and Farr & Kunzi, the founders of the present house of Powers & Weightman, soon became its largest manufacturers. They early discovered that, as in the refining of sugar there is always a portion so combined with resinous proximate principles as to be uncrystallized, there remained in this new manufacture, after all the Quinia they could obtain was separated, a viscid dark brown liquid, evidently very rich in the active principle of the Cinchona. They evaporated this liquid to dryness, and John Farr furnished the writer of this memoir with specimens for the purpose of trial by his medical friends. It was first prescribed by Dr. Samuel Emlen, in doses of two grains, with entire success. Drs. Parrish and Wood next tried it with the same result; and from that time "*the Extract of Quinine*," as it was then called among us, came into use, and has ever since been extensively prescribed in

Dispensary practice, as a cheap and perfectly reliable anti-periodic.

This amorphous residue has been the subject of much investigation in Europe. Sertürner announced, in 1829, that he had discovered it to consist chiefly of a new alkaloid which he called Chinoidine, and which he regarded as a more valuable anti-febrile than the Quinia itself.

Professor Liebig more recently obtained samples of this Chinoidine or Quinoidine from several of the best manufacturing chemists of Germany, and after carefully separating the foreign matters which they contained, ascertained its composition to be identical with that of Quinia. He says that the inference from his experiments is irresistible. "Some doubts," says Pereira (1853), "however, still exist as to the real nature of the so-called amorphous Quinia. Roder declares (1848) that it is merely ordinary quinia combined with a resin; while Van Heijningen (1850) resolved the so-called quinoidine into ordinary quinia, cinchonin, and a resinous substance."

In 1846 a series of preparations known as Bullock's "Purified Chinoidine," Bullock's "Amorphous Quinine," Bullock's "Basic Extract of Bark," were patented in England, and were highly recommended. They were obtained from the amorphous residue of the manufacture of Sulphate of Quinia; but the cost of preparation was not compensated by any great superiority over the cheaper purified Chinoidine of our best manufacturers over old "Extract of Quinine."

"The uncrystalline substance derived from Quinoidine bears exactly the same relation to ordinary quinine that uncrystalline sugar (barley-sugar) bears to crystalline (sugar candy). Both yield the same products of decomposition; both have the same atomic weight, and identically the same composition; they differ only in form; in one word, the one is crystalline, the other, *amorphous*.

"I deem this to be an important discovery, when we consider the high price of Quinine, the possibility of a check to the supply of Cinchona bark from the countries producing it, and the amount of the crude Quinoidine which has accumu-

lated since the manufacture of Sulphate of Quinine was commenced. Quinine, indeed, seems to be absolutely indispensable for the treatment of diseases; the progress of civilization in modern times has depended, far more than has been conceived, upon the discovery of a remedy for the fevers which prevail where tillage is imperfect, and in new and unbroken soils.

“This chemical investigation has thrown an interesting light upon the testimonies borne to the efficacy of Quinoidine in the treatment of fever, and the highest encomiums have been passed upon it; but the commercial specimens have differed very much in value; while some have consisted nearly altogether of amorphous Quinine, others have contained only a small percentage.

“It is necessary that the amorphous Quinine should be separated from all admixtures and impurities, and prescribed in its pure state. There can be no doubt but the same substance will produce the same effect on the animal organism, whether exhibited in a crystalline or an amorphous state. The system, as we may say, makes no difference in such a case. As I have already observed, the mystery about Quinoidine is completely solved by the discovery that it usually contains a very large percentage of pure quinine in an amorphous state.

“In a commercial point of view, it is certainly a matter of great importance that we should be able to judge by the mere external appearance of a remedy of its purity, and, consequently, how far we may rely upon its efficacy. This is thought to be the case with the Crystalline Sulphate of Quinine, whilst the non-crystalline form of Quinoidine has probably led to a disregard of the evidence of its usefulness, even more than the fact of its being, as usually sold, an admixture of various substances. But with respect to the mere amorphous form, when the Quinine is separated from all its adhering impurities, it is in the same case with opium, castor, and many more of the most efficient remedies which we possess, particularly with the extracts of our Pharmacopœias. It is necessary to be assured of their purity before we employ them, but their amorphous form does not prevent their use. In many of these cases, indeed, having no direct or ready way of testing them, we rely

solely upon the honorable character of the merchant and dealer; but we have a completely satisfactory test for the purity of amorphous Quinine. Few medicinal agents afford so ready a means of distinguishing them, and detecting admixtures, as the organic alkaloids; but if these tests are not employed, it is as easy to be deceived in purchasing Crystalline Sulphate of Quinine as the amorphous."

There is additional evidence of the value of this latter preparation, in an article "On Quinoidine in the treatment of Intermittent Fever, by J. Da Costa, M. D.," in the *Medical Examiner* for May, 1855.

The Quinoidine used by Dr. Da Costa was from the manufactory of Powers & Weightman. He gives the result of fifty-three cases in which he administered it. He says that the therapeutical effects of Quinoidine, as far as he has observed them, "are very nearly those of the ordinary Sulphate of Quinia. In doses two-thirds larger than those of the latter, he succeeded perfectly in checking intermittent fever; but it was never noted to give rise to the headache, nor the ringing and buzzing in the ears, nor to the sickness at the stomach, which so frequently attend the ministration of the Sulphate of Quinia, or of the other ordinary preparations of bark. It was sometimes given in doses of forty grains, without the slightest inconvenience to the patient resulting from it, and in no case, with the exception of one, did it fail in checking the periodical returns of the paroxysms. In a few instances, indeed, it proved successful where Sulphate of Quinia had been previously administered without result. As a tonic, it seems to present the same advantages as any other of the preparations of bark. Age does not constitute an objection to its use, for it was employed with equal advantage in the very young and the very old."

"Of the fifty-three cases cited, in many of whom the disease was of long standing, the chills were arrested in forty-nine cases by the first administration of the medicine; only four required a repetition of the dose. In ten cases the disease returned, which, although it may seem a large proportion of relapses, was not in reality so, when we consider the well known tendency of

intermittent fever to return, and the fact that, in many of the cases, no medicine, for reasons above stated,* was given after the first arrest of the chill. In conclusion, the writer can state as his honest belief, that Quinoidine possesses anti-periodic qualities which, if not superior, are certainly not inferior to the Sulphate of Quinia or Cinchonia, whilst he thinks it preferable to these, from the absence of bitter taste, from its being less liable to affect the head or stomach of the patient, and from its comparatively low price."

The objection that the amorphous character of the Quinoidine renders it liable to adulteration, applies alike to every amorphous article of the *Materia Medica*. It can only be met by the assertion that establishments of unquestionable integrity, such as our best manufacturing chemists and wholesale and retail druggists, are above all suspicion of willful adulteration; that the packages containing these preparations always bear the name of the manufacturer, and that a fraud would be almost immediately followed by detection and exposure.

*The reason given is that "as patients when relieved are not always willing to return to a public Institution, it was sometimes impossible to persevere with the treatment, and the disease then generally reappeared after the lapse of a week or two."

