Since then there have been discovered quinidine, cinchonidine, quinamine, paricine, aricine, cusconine, pitoyine, etc.[5]

Do not expect of me a description of all these alkaloids. I shall content myself with a brief reference to the principal of them, especially those which may in part take the place of quinine. Cinchona bark, in fact, being of relatively high price, it is apparent that quinine itself must be costly, and you will see, as we proceed, that this question of price has considerable importance in the treatment of intermittent fever, and that it is incumbent on us always to endeavor by a good use of the medicament to obtain the maximum thera-

Among the yellow cinchonas we note: 1, The flat or royal red cinchona calisaya, which is the cinchona calisaya the most diffused and best known—the officinal cinchona; 2, the calisaya of New Granada, of which there are two species, the cinchona lancifolia and the cinchona pitayensis, which give barks of the first order; 3, the cinchona carabaya, employed especially for the manufacture of quinine; 4, the yellow cinchona of the King of Spain (of Loxa); it is furnished by the cinchona condaminea.

Among the red cinchonas are: 1, The bright red; 2, the pale red of Equador, furnished by the cinchona succirubra of Quito, the red cinchona of New Granada or of Mutis; 3, the warty red cinchona furnished by the cinchona Humboldtiana.

The French codex admits three varieties which are obligatory on pharmacists: The gray huanco cinchona (cinchona micrantha), the cinchona calisaya or royal yellow (cinchona calisaya), and the red warty or non-warty cinchona (cinchona nitida, or succirubra.)

With the true cinchonas one often finds mixed certain strange or false cinchonas. The principal are: 1, The new cinchona, furnished by the portlandia grandifolia; 2, the cinchona of Caraibes or Jamaica, furnished by the exostema caribeum; 3, the cinchona piton-cinchona of Martinique, of St. Lucie, or of St. Domingo, produced by the exostema floribun, dum; 4, the cinchona cusco or Arica bark; 5, the cinchona jæn (cinchona ovata); 6, the cinchona pitoxa; 7, the cinchona of Para; 8, the white cinchona of Payta.

[5] The cinchona barks used in medicine come from the trunk, the large, middling sized, or small branches of the tree. They have, therefore, a variable thickness, according to the part from which they are taken, and are flat and thick, or thin and curled. The indians employed during the cinchona bark harvest have received the name of cascarilleros. When they have collected a certain quantity of bark they dry it on the spot. The large pieces, arranged on slabs, are piled up in heaps and dried in the sun; they are kept flat by the pressure of some heavy body put on top of the pile. These barks constitute the flat cinchonas (quinquinas en table, en planches).

The thin fine barks are also exposed to the sun, and curl up to form the quilled cinchonas.

The principal centres of the cinchona crop are: 1, In the republic of Equador, Loxa, and the environs of Chimborazo (cinchona succirubra); 2, in lower Peru, Huanco, Cuzco, Hamalies; 3, in Bolivia; 4, in New Granada, Pitayo, Santa Fe, of Bogota; 5, in Venezuela, Maracaibo.

The principal ports of exportation are: Carthagena, Lima, Valparaiso, Arica, and Buenos Ayres—names that sometimes distinguish the various barks.

The cinchona barks contain: 1, Certain alkaloids, quinine, cinchonia, quinidine, cinchonidine (cinchonidia), quinamine (Hesse), paricine (Winckler), aricine (Pelletier and Corriol), cusconine (Lever Koehn), paytine (Hesse), etc. There are also: 2, Certain acids, quinic cinchotanic, quinovic, etc.; 3, neutral substances, such as quinovine, cinchona red, etc.; 4, a fatty matter; and 5, an essential oil.

According to the experiments of Howard, Fluckiger, and Carles, the alkaloids exist in greatest abundance in the cellular parenchyma (meso-phlœum), and the quinine is found especially in the external portions of the epiphlœum or corky envelope. The cinchonia is

peutic effect with the least quantity. This costliness of quinine explains also both the numerous falsifications of which this alkaloid is the subject, and the unwearied endeavors to find good substitutes for it. It is to be hoped that through the incessant progress of chemistry we shall be able in the future to manufacture quinine by a process of synthesis out of relatively inexpensive sub-

almost equally diffused throughout the three layers. It is possible to increase the secretion and production of quinine by a process which has been put in practice by McIvor, director of the English plantations in Hindostan. Having remarked that the thin barks, protected from the light, are richer in alkaloids than those which are exposed, McIvor conceived the idea of covering the trunk of the trees with moss, and it was found that by this simple method, called mossing, the rendition of quinine might be quadrupled. To this mossing another process has been added, that of peeling. From the trunk of the tree chosen the external layer of the bark is removed and the place covered with moss. After suffering somewhat from the injury the tree recovers, and at the end of a couple of years there is obtained by this operation a new rind, richer in quinine than the first bark.

The most active ingredients of the bark are quinine, then cinchonia, then quinidine and cinchonidia.

Quinine was discovered in 1820 by Pelletier and Caventou. It is crystalline or amorphous. Pure quinine may be obtained from calisaya bark, treated successively by hydrochloric acid, lime and alcohol. It may also be procured from sulphate of quinine by decomposing it by ammonia. In the first instance you obtain brute quinine, a substance of firm consistency, resinous, and formed of a mixture of quinine, cinchonine, fatty and coloring matters. Almost insipid, it is employed in powders, potions, and pills. Trousseau prescribed it to infants of two years and below in the dose of 2½ to 5 grains, rolled into little pellets, and mixed with tapioca or sago.

To extract from sulphate of quinine pure quinine, the Codex recommends the following process: Dissolve 100 grammes sulphate of quinine in 3000 grammes of boiling water. Having effected solution, leave the liquid to cool, and pour in sufficient water of ammonia to entirely decompose the sulphate. The quinine set free is precipitated. It is collected on a filter and washed with warm water to remove ammonia. It presents itself under the form of a white porous friable substance of bitter savor after desiccation. It is soluble in two parts, boiling (absolute) alcohol, in 60 parts ether, in 6 parts chloroform, in 400 parts cold water, and 250 parts warm water. It dissolves also in the fatty oils and in the volatile oils; also in the concentrated mineral acids.

On adding an excess of ammonia to a dilute solution of sulphate of quinine, you obtain crystallized quinine, which retains 3 molecules of water. This melts at 120°C, losing its 3 molecules of water, and forms an oil which, on cooling, takes on the appearance of a resinous mass.

Cinchonine exists in greatest abundance in the gray cinchonas. It crystallizes in large quadrilateral prisms, soluble in 2500 parts of boiling water, 40 parts of chloroform, 30 parts of boiling alcohol, and is fusible at 165°C. It forms with acids salts more soluble in water or alcohol than the salts of quinine. The basic sulphate of cinchonia is chiefly employed, and in much larger dose than sulphate of quinine.

Quinidine, discovered in 1833 by Henry and Delondre, studied especially by Pasteur in 1853, crystallizes in rhombric octahœdra.

Cinchonidia, discovered in 1844 by Winckler, and called in Germany quinidine (name which Winckler gave it), crystallizes in rhombric prisms.

Cinchonidia is soluble in 1680 parts cold water, 19 of alcohol, and 76 of ether. It melts at 206°C.(*a*)

(*a*) Pelletier and Caventou Chemical researches on cinchona. (Jour. de Pharm., t vii., Feb., 1821.) Pasteur on the alkaloids of cinchona. (Paris, 1853.) Prunier on the cinchonas. (Nouveau Dict. de Med., et Chém., 1882.)

stances, or, at least, to transform the less active alkaloids of Peruvian bark into quinine. Among these alkaloids I desire to draw your attention only to cinchonine, cinchonidine, and quinidine.

Since Pelletier and Caventou discovered cinchonine,[1] endeavors have been made to apply this alkaloid—which differs, as you know, from quinine only by an atom less of oxygen—to the treatment of intermittent fever, and Marianini, Girault, Pepper, Wahu, and Hudellet have affirmed that sulphate of cinchonine is equal, if not superior, to sulphate of quinine; nevertheless, Laveran, and especially Moutard Martin, who have made of cinchonine a very interesting therapeutic study, have shown us that sulphate of cinchonine, while rendering considerable service in the treatment of paludal fevers, is yet inferior in potency to sulphate of quinine.[2] This salt, then, merits the name of "quinine of second quality," under which it is sold abroad.

[1] It was Pelletier and Caventou, who first discovered this alkaloid in gray cinchona bark about the year 1821.

Cinchonia differs from quinine by having one atom less of oxygen:

Cinchonia ..... $C_{20}H_{24}N_2O$
Quinine ..... $C_{20}H_{24}N_2O_2$

Cinchonia forms with acids a great number of salts. Heated with potassa, it gives rise to several alkaloids, among them to quinoleine.

Attempts have been made to transform cinchonia into quinine. This has not yet been accomplished, but quinine has been turned into cinchonia.

Cinchonia is not soluble in ether. This enables us to separate it from quinine, which is soluble in this menstruum. Cinchonia is obtained from the mother liquor used for the preparation of sulphate of quinine.

Certain cinchonas contain even more cinchonia than quinine. Thus the C. scorbiculata, which has in 1000 grammes 12 of cinchonia and 4 of quinine. Cinchona cordifolia mutis contains 12 parts in 1000 of the former to 2 or 3 of the latter; while the C. pubescens has 30 per 1000 of cinchonine, and only 3 or 4 of quinine.

[2] Sulphate cinchonia was early applied to the treatment of intermittent fevers. Marianini, Girault, Pepper, Wahu even think it equal or superior to quinine. Briquét shares this opinion.

The military physicians have bestowed much study on the comparative effects of these two alkaloids. Laveran regards cinchonia as much inferior to quinine. Moutard Martin has best summarized the action of the former:

1. Sulph. cinchonia, administered in intermittent fever has incontestable though variable action.

2. Sometimes its effect is rapid, it cuts short the attack like sulphate of quinine; at other times it is slow, whatever may have been the dose administered, and the paroxysms wear themselves out little by little.

3. The dose ought always to be large; at least a third more than that of quinine employed under the same circumstances.

4 To obtain a curative action, you must employ a dose varying, according to individuals, from 10 grains to 15.

5. In this dose it often determines certain physiological effects which it will not be prudent to exceed.

6. The therapeutic action is not in proportion to its physiological action, for it sometimes cures without the patient having felt its effect. In other cases where the physiological action is energetic the therapeutic action is *nil.*

Laborde has put in clear light the physiological difference between quinine and cinchonine, the latter being "more convulsivant" and determining in all animals to which it is administered, an aggregate of symptoms to which he has given the name of cinchonic epilepsy.[3] Cinchonidine (cinchonidia) and quinidine are isomeric respectively with cinchonine and with quinine;[4] long

7. It cannot replace quinine in grave intermittent fevers.

8. It may become a precious adjuvant to quinine; in completing the cure begun by one or two doses of the latter. In this way you may economize quinine, which is much the more expensive.(*a*)

[3] Magendie was the first to study the physiological and toxic action of the salts of cinchonine (cinchonia), and concluded from his experiments that this alkaloid was not toxic. According to Briquet, cinchonine and quinine differ only by the intensity of their effects, sulphate of quinine manifesting a toxic power double that of sulphate of cinchonia. These results have been contradicted by the experiments of Bouchardat, Delondre, and Girault, who have found the toxic power of cinchonia far superior to that of quinine.

Berandi regards sulphate of cinchonia as an excitant. Sée and Bochefontaine, in their recent physiological experiments, have arrived at the same conclusions as Briquet, and consider quinine as more active and more toxic than cinchonia. Both substances, according to them, are convulsivant; cinchonia the most so. Ten grammes of sulphate of quinine injected subcutaneously, would put the life of a man in the same jeopardy as 16 grammes of sulphate of cinchonia.

According to Laborde, what characterizes the toxic action of cinchonia is the production of epileptiform convulsions, described by him under the name of cinchonic epilepsy. These symptoms follow 25 centigrammes in a guinea-pig weighing 250 to 300 grammes, and 75 centigrammes in a dog weighing 12 kilogrammes, after subcutaneous injections. (*b*)

[4] Cinchonidia was first distinctly separated from quinidine by Pasteur. Its formula is as follows:

$$C^{20}\ H^{24}N^{2}\ O^{1}.$$

It is isomeric with cinchonia. This alkaloid seems to predominate in certain barks of cinchona, as Winkler has shown. It is scarcely soluble in water and ether, and combines with acids to form a series of salts; it is laevogyrus (polarization being left-handed). According to Laborde, the physiological and toxic action of cinchonidia is as follows: The animal is taken at first with a trembling similar to that of paralysis agitans, then with an attack of epilepsy resembling that produced by cinchonia.

Chirone and Curci have arrived at like results. They find cinchonidia more active than quinine and its toxic power greater. It produces epileptiform convulsions, which are the more intense the higher the animal is in the zöological scale, and the more developed his brain; it acts more especially on the motor cortical centres and leaves intact the spinal.

Gubler has employed the dibromhydrate of cinchonidia in subcutaneous injections. This salt, obtained by Petit by decomposing sulphate of cinchonidia by barium bromide, is in fine prismatic crystals of feeble yellow color, and having for formula:

(*a*) Laveran, Etude sur l'action comparée du sulfate de quinine, du sulfate de cinchonine et du quinium dans le traitement des fièvres intermittentes d'Afrique (Gaz. méd de Paris, 1856).—Hudellet, Etude comparative des deux sulfates de quinine et de cinchonine dans le traitement des fièvres intermittentes (Ann. thér de Bouchardat, 1856, p. 121).—Corps de santé militaire, Résultats de l'expérimentation faite dans les hôpitaux militaires sur les succédanés de la quinine (Rec. de méd., de chir. et de pharm. militaires, 3e série, t. II, 1859).—Moutard Martin, Mémoire sur la valeur du sulfate de cinchonine dans le traitement des fièvres intermittentes (Mém. de l'Acad. de méd., t. XXIV, 1860.

(*b*) Briquet, Therapeutical Treatise on Cinchonia and its Preparations, Paris, 1853. Bouchardat, Delondre and Girault, Physiological and Therapeutical History of Cinchonia. Magendié, Jour. de Pharm., Vol. VII, p. 138. Sée and Bochefontaine, on the Toxic Power of Quinine and Cinchonine. Compt. Rend. de l'Acad. des Sc., 1883, No. 96, p. 266.

confounded together under the name of commercial quinidine, it is to the brilliant researches of Pasteur on the alkaloids of cinchona that we owe their definite separation. Like cinchonine, they are, from a toxic point of view, convulsivant; from a therapeutic point of view they antagonize morbid periodicity. Cinchonidine especially, according to the observations of Gubler, Wessell, Bouchardat, Coletti, and Bourru, is equal, and even superior to quinine in the

$$C_{40} H_{24} N_2 O_2 HBr. + 4 H^2 O.$$

The solution which Gubler used for hypodermic injections is as follows:
Take of:

Dibromhydrate of cinchonidia .....10 grammes.
Distilled water, q. s., to make 50 cubic centimetres.

Each syringeful containing one cubic centimetre, represents twenty centigrammes of the active principles. These injections have an action (according to Gubler) equal to that of sulphate of quinine.

Palcolo Machiavelli has made use of sulphate of cinchonidia in 851 cases. He claims the same results as are obtained from sulphate of quinine.

Le Judge, of Mauritius, considers sulphate of cinchonidia just as efficacious as sulphate of quinine in the treatment of intermittent fevers; it is well tolerated by the stomach, and produces neither buzzings in the ears nor nervous troubles. Weddell has pointed out the importance of cinchonidia in the treatment of malarial fevers at Madrid and the East Indies. He gives statistics relating to 1145 patients treated by cinchonia, cinchonidia, and quinidine; the therapeutical results were similar with all of them; he maintains, therefore, that it would be well to substitute cinchonidia for quinine.

Coletti has studied the physiological and therapeutical action of cinchonidia. This substance, while producing convulsions, did not, in his experiments, produce veritable epileptic attacks as in the experiments of Laborde and Dupuis. In his estimation, cinchonidia is equal, therapeutically, to quinine.

According to Bourru, who has also made comparative trials with quinine and cinchonidia in malarial fever, the latter produces, generally, favorable results, being unattended with vertigo and other accidents. Out of twenty-seven cases, cinchonidia arrested the attacks in twenty-four. The same dose was given as of quinine. The alkaloid should be given six or seven hours before the probable onset of the paroxysm.

Quinidine was brought to notice for the first time by Henry and Dilondre, in 1833. Pasteur, in his work on the alkaloids of cinchonia, has shown that under the name of quinidine is found in commerce a mixture in variable proportions of cinchonine, of quinine, of cinchonidia, and of quinidine. Quinidine and cinchonidia are very often confounded. This quinidine forms with the acids certain basic and acid salts.

Wunderlich, in 1865, was the first to experiment with quinidine. These trials were resumed in 1878, by Machiavelli. This medicament, in the dose of about a scruple, caused a fall in the temperature equal to that of quinine. Its antipyretic properties in fevers were found equal to those of quinine, only it produced vomiting, which was readily met by opium.

According to Laborde, quinidine produces, like cinchonidia and cinchonia, epileptic attacks in toxic doses; that is to say, in doses of from 20 to 25 centigrammes for a guinea pig weighing from 350 to 400 grammes.

Dougall, at Madras, has experimented comparatively, with quinidine, cinchonidia, and cinchonia. It results from these researches, that quinidine has the first place in order of efficacy, then cinchonidia, then cinchonine. (*a*)

(*a*) Dougall, on the Febrifuge properties of Cinchonia, Quinidine, and Cinchonidia (Edin. Med. Jour., Sept., 1873). Laborde, Thése de Paris, 1883.

treatment of paludal fevers; so interested pharmaceutical firms, in captivating pamphlet monographs, urge on the profession the substitution of cinchonidine for quinine, and this especially by reason of its cheapness.

By the side of these alkaloids I will mention quinoleine (chinoline)[1] and quinoidine (chinoidine). The first has this character, that it has been obtained by way of synthesis, and that this body, which forms a part of the aromatic series, and which furnishes, as you know, kairine, serves as intermediary between the alkaloids of cinchona and the antipyretic medicaments of the group of phenols and oxy-phenols. If we can trust the experiments of Loewy, this quinoline has an anti-periodic action of the most marked kind.

As for quinoidine it is not, properly speaking, a genuine alkaloid, but rather a combination of all the alkaloids which remain in the mother liquid after the preparation of quinine. Burdell, of Vierzon, continuing the experiments of Natorp, at Berlin; of Fraser, in Ohio; of Ossieur and Vanoye, in Flanders, has shown all the advantages which may be derived from quinoidine in the treatment of intermittent fever of the quartan form, especially in the telluric cachexia. Unhappily this substance, which is of low price, presents a varied composition, and it is easily understood that, according to the process of preparation, you obtain different quinoidines.[2]

Having concluded this rapid survey of the alkaloids of cinchona, I hasten to the most important of them, viz., quinine. I have already spoken to you of its physiological action; it remains to consider the question of its absorption and elimination.

Quinine has a local irritant action which is indubitable. The most marked proof of this is the multiple eruptions with which operatives are affected who are occupied in the manufacture of quinine. This irritant action is also

[1] Quinoleine, obtained by Gerhardt by distilling cinchonia with quinine and potassa, is a body analogous to *leucol*, which Runge extracted from coal tar, in 1843. It has been experimented with by Donath. It is given in the same doses as quinine, and is said to produce the same effects. Loewy claims good results from it in intermittent fever. (*a*)

[2] Sertuerner was the first to designate under the name of quinoidine an uncrystallizable and alkaline substance obtained from the mother liquid employed in the preparation of quinine. It is a mixture of quinine, cinchonia, cinchonidia, and quinidia. It has been employed by Natrop, of Berlin, Fraser, of Ohio, Ossieur, in Belgium, etc. Briquet has noted the same action from this substance as from sulphate of quinine.

Burdel employs quinoidine, and considers it superior to quinine in chronic malaria. He gives it pure, or in the form of soluble sulphate; prescribing from eight to fifteen grains to an adult, and continuing the treatment for several weeks in gradually increasing and rather infrequent doses. Administered in this way, Burdel thinks that he finds in quinoidine a more powerful febrifuge than quinine in the treatment of quartan fevers and malarial cachexia. (*b*)

(*a*) Loewy, Wein. Med. Presse, No. 39, 1881. Gerhardt, Revue Scientifique, t. x, p, 186. Runge, Pogg. Ann., t. 31, p. 68.

(*b*) Stertuernerner, Ueber die neuest. Fortschrift in d. Chem. Phys. u. Heilk., t. III, p. 269). Ossieur et Vanoye, De la quinoïdine dans le traitement des fièvre intermittentes (Ann. de la Soc. méd. d'émul. de la Flandre occidentale, mai 1848, et Bull. de thér., t. XXXV, 1848, p. 43). Briquet, Traité thérapeutique du quinquina, 1853, p. 469. Burdel (de Vierzon), Du traitement des fièvres intermittents telluriques par la quinoidine (Un. méd., 30 novembre et 5, 7 et 9 décembre 1878).

manifested on the mucous membranes, and this explains to you the gastric and intestinal disturbance which is produced when we give quinine salts by mouth in too big doses or too prolonged doses. This same local irritant action of the salts of quinine explains also why it is that subcutaneous injection of quinine solutions may be the point of departure of indurations and even suppurations.

When quinine enters the stomach it is dissolved by the acid of the gastric juice, and it is probably in the state of hydrochlorate or of lactate of quinine that this alkaloid is absorbed. At the same time, when quinine salts of the vegetable acids are given, they are changed to carbonates in the blood.[1] Quinine and its salts, after being absorbed, are forthwith eliminated by the various emunctories, and in particular by the kidneys. As Kerner has well shown, this elimination is the more active and more prompt the more soluble the salt of quinine.[2] From this fact we may adduce a very important conclusion, viz., that the activity varies with the solubility of the preparations, and hence we should choose those saline combinations of quinine which are the most soluble.

[1] According to Briquet and Quevenne, the salts of quinine pass unchanged into the blood when their acid is undecomposable; when the acid is decomposable, as is the case with the vegetal acids, it passes into the blood in the state of carbonate. Miahle even thought that quinine must always be set free in the blood by reason of the carbonic acid of that fluid liberating it from its saline combinations, but Delioux, of Savignac, shows this theory to be inadmissible, and that the sulphate of quinine must remain as such in the liquor sanguinis without undergoing any decomposition. (*a*)

[2] The following is the reagent proposed by Bouchardat for the detection of the alkaloids of cinchona in the urine:

℞	Iodine	15 parts.
	Iod. pot.	4 "
	Water	300 "

M.

Briquet's modification of the above, which shows well the precipitate, though less delicate, is as follows:

℞	Iodine	1 part.
	Iod. pot.	4 parts.
	Water	125 "

M.

These liquids give an orange red precipitate of ioduret of iodohydrate of quinine, of cinchonia, etc.

We here give Kerner's table, showing the rapidity of elimination of the various alkaloids of cinchona:

The figures indicate the proportion of quinine eliminated in the urine for 100 parts of the alkaloid contained in the dose employed—

(*a*) Briquet, Therapeutical Treatise on Cinchona, 1853. Delioux of Savignac, Art. Quinine in Dict., Encyclop. des Sciences Med.

These quinine salts are very numerous,[3] as you can judge by the following table, made at my request by Tanret. This table contains the quinine combinations most in usage, classed according to the quantity of base which they contain, for you easily understand that the activity of a quinine salt depends on the one hand on its solubility, and on the other on the quantity of the alkaloid which it possesses, and you see what an elevated rank the chlorhydrate of quinine occupies in comparison with the sulphate.

DATE OF THE EXAMINATION OF THE URINE AFTER TAKING THE MEDICINE.

	15 minutes.	30 minutes.	45 minutes.	1 hour.	3 hours.	6 hours.	12 hours.	24 hours.	36 hours.	48 hours.	50 hours.	62 hours.
Chloride of quinine dissolved in gaseous water	1	4	4	8	15	19	30	12	2	1	0	0
Bisulphate of quinine	0	1	2	6	14	26	19	16	6	2	0	0
Sulphate of quinine	0	0	5	6	13	25	18	15	8	4	1	0
Carbonate of quinine	1	4	4	10	12	22	15	12	10	3	0	0
Acetate of quinine	0	2	5	6	13	27	16	12	8	3	0	0
Citrate of quinine	0	1	4	7	15	29	14	10	7	4	1	0
Tannate of quinine	0	0	0	0	1	2	9	28	14	4	2	2

Instead of employing the test proposed by Bouchardat, Kerner utilizes the fluorescent properties of solutions of quinine in order to determine the most minute quantities of this alkaloid contained in the urine. (*a*)

[3] Quinine is an energetic base, which readily enters into combination and forms crystallizable salts. These salts, less soluble than those of cinchonia, are very bitter. They are incompatible with alkaline hydrates, ammonia, iodureted iodide of potassium, tannin, double iodide of potassium and mercury, etc., which precipitate them from their aqueous solutions. We may divide the quinine salts into three groups:

1. Those perfectly soluble (the bisulphates, chlorhydrates, lactates).
2. Those less soluble (the neutral sulphates, acetates, valerianates).
3. Those little, if at all soluble (the phosphates, ferro-cyanates, arsenites).

The salts the most soluble are also the most active. We shall here specify a few of the most known of these salts:

Sulphate of quinine.—There are two sulphates: the neutral and the acid sulphate. The neutral sulphate crystallizes in prismatic, white, silky needles. Is efflorescent, inodorous, very bitter, little soluble in water (740 parts of cold water and 30 of boiling water being required); almost insoluble in ether, very soluble in glycerine, soluble in 60 parts of cold, absolute alcohol. Solution in water is favored by a drop or two of some strong acid.

The acid sulphate, or bisulphate, crystallizes in rectangular prisms. Is soluble in 11 parts of water at 59° F., making an intensely bitter solution. On account of its high price, various falsifications have been resorted to: 1, salicine, which may be detected by adding concentrated $H^2 SO^4$ to the suspected preparation, in presence of salicine it gives a red coloration; 2, sugar, which blackens under sulphuric acid; 3, stearine; dilute sulphuric acid does not completely dissolve the salt; 4, starch and magnesia; the preparation containing these adulterations would not completely dissolve in alcohol. Recently, sulphate of quinine has been largely adulterated with sulphate of cinchonidia.

(*a*) Briquet, loc. cit. Kerner, Pfluger's Arch. f. die Gesammte Physiologie, 1870.

The sulphate is the salt most employed, at least in France. It is one of the most stable combinations, but which presents the inconvenience of being little soluble when neutral; so whenever you wish to administer the sulphate in potion you must make it into a soluble bi-sulphate. Regnault has, moreover, furnished the most precise indications in regard to the solubility of this salt.[4]

Lactate of quinine crystallizes in flat, silky needles; savor is disagreeable; therapeutic action feeble.

Tartrate of quinine.—There is a neutral tartrate and an acid tartrate; the latter is very soluble and crystallizable.

Acetate of quinine is very soluble in boiling water, though little soluble in cold water. Is much employed in Germany.

Arseniate of quinine.—White, soluble in water and dilute alcohol. Is given in doses of 2, 4, and 6 centigrammes a day.

Iod-hydrate of quinine occurs in white, opaque, lamellated crystals.

Valerianate of quinine.—Octadædral crystals, of bitter taste, slightly soluble in cold water, very soluble in alcohol. Dose, 20 to 50 centigrammes (2 to 9 grains), in intermittent fever.

Tannate of quinine.—An amorphous, yellow-white powder, little soluble in water, more soluble in alcohol. Almost tasteless.

Phosphate of quinine.—Crystallizes in needles. Little soluble in cold water, soluble in alcohol. Dose, 5 to 20 centigrammes. Is employed in Italy.

Citrate of quinine.—Crystallizes in needles. Little soluble. Is employed in Italy. Dose, 20 centigrammes.

Ferro-cyanate of quinine.—Crystallizes in needles. Little soluble in water, soluble in alcohol. Employed in Italy in pill form. Dose, 20 to 40 centigrammes.

PERCENTAGE OF QUININE IN DIFFERENT SALTS OF THE ALKALOID.

	Percentage of Anhydrous Quinine.
Acetate of Quinine $C_{20}H_{24}N_2O_2C_2H_4O_2$	87.34
Hydrate of Quinine (Quinine precipitated and dried) $C_{20}H_{24}N_2O_23H_2O$	85.70
Basic Chlorhydrate of Quinine—the sole chlorhydrate employed, the Neutral Chlorhydrate not being stable—$C_{20}H_{24}N_2O_2,HCl.2H_2O$	81.60
Lactate of Quinine $C_{20}H_{24}N_2O_2C_3H6O_3$	78.26
Basic Bromhydrate of Quinine $C_{20}H_{24}N_2O_2BrHH_2O$	76.60
Valerianite of Quinine $C_{20}H_{24}N_2O_2(C_5H_{10}O_2)$	76.05
Basic Sulphate of Quinine (the ordinary sulphate) $C_{20}H_{24}N_2O_2SO_4H_2,7H_2O$	74.30
Sulpho Vinate of Quinine $C_{20}H_{24}N_2O_2SO_4C_2H_6$	72.
Neutral Bromhydrate of Quinine $C_{20}H_{24}N_2O_2BrH\ 3H^2O$	60.
Neutral Sulphate (or acid sulphate) $C_{20}H_{24}N_2O_2SO_4H_28H_2O$	57.24
Tannate of Quinine $C_{20}H_{24}N_2O_2(C_{14}H_{10}O_9)$	20.60

[4] Regnauld has studied the solubility of sulphate of quinine, and these are the results:

One gramme (15 grains) of sulphate of quinine dissolves in two litres (Oiv) of water at 59° F.; 560 grammes (℥ xix) in the same quantity of water at 212° F.; one gramme is soluble in 1.133 grm., of absolute alcohol at 59° F.; in 1.926 grm., of chloroform at 59° F.; in 22.632 grm., of ether, at 59° F.

One gramme (15 grains) of tannate of quinine demands for its solution 20 litres (5 gallons) of water.

If the sulphate is the most use in France, it is the chlorhydrate which is employed the most in England and in Germany.[1] This salt, in fact, is more soluble than the sulphate, and contains more quinine, so that, according to the rules previously laid down, it would be better to employ the chlorhydrate, and this is a point worthy of remembrance. As for the acetate, which contains so large a quantity of base, it is too unstable a salt for constant use.

In combining salicylic acid with quinine the intent has been to increase the antipyretic power of this medicament,[2] and notwithstanding the very interesting experiments of Maury, of Lyons, and the therapeutic results of Graham Brown and of Antonescu, the usage of this salt is very limited.

Of all the salts of quinine the most stable is the tannate.[3] and it has been claimed that it may even traverse the economy without undergoing decomposition. At the same time the experiments of Kerner and especially of Vulpian

[1] There exist two combinations of quinine with hydrochloric acid: one neutral, which is not stable, and a basic salt, which has the following formula:

$$2\ (C^{20}\ H^{24}\ N^2\ O^2, Hcl) + 3\ H^2\ O.$$

This salt crystallizes in long, silky fibres; it is more soluble in water than the sulphate; it contains also more quinine.

[2] Salicylate of quinine has the following atomic formula:

$$C^{20}H^{24}N^2O^2C^7H^8C^{20}H^{34}N^2O^2C^2H^6O^3.$$

It crystallizes in silky tufts; is soluble in 1430 parts of water at 68° F., and in 100 parts of boiling water. It has been especially studied by Graham Brown (Edin. Med. Journ. Nov. 1876, page 421), who considers it a very active antipyretic medicament.

Maury, of Lyons, has made some interesting experiments with this salt, showing its great antiseptic power.

German Sée has also experimented with this salt in his hospital service in intermittent fevers and typhoid fever, but with indifferent success. Antonescu, however, claims good effects from this salt in malarial fevers.

[3] Tannate of quinine was described for the first time in 1821 by Pelletier and Caventou under the improper title of gallate of quinine. This salt contains 26 per cent. of quinine and 3.50 grm., of the tannate (52½ grains) corresponds to one gramme (fifteen grains) of the sulphate.

Regnauld's process of manufacture (Journ. de Pharm. et de Chim. t. xix, 1879) gives a preparation with the following formula:

$$C^{40}\ H^{24}\ N^4\ 2\ (C^{54}\ H^{22}\ O^{34}).$$

Becker, of Bonn, considers tannate of quinine as a good medicament. He has especially derived benefit from it in whooping cough. Hagenbach also considers tannate of quinine as a good febrifuge. It combats the fever and diarrhœa of typhic patients.

Vulpian has shown that tannate of quinine is absorbed and eliminated. At the same time this medicament has a very feeble action. It is especially beneficial in preventing profuse sweats (Delioux, of Savignac.) It may also be employed in infantile diseases. (*a*)

(*a*) Regnauld, On tannate of quinine, in Jour. de Pharm et de Chem., 1879.—Vulpian, On tannate of quinine (Acad. de Med., 1872).—Delioux, of Savignac, On the employment of tannate of quinine in the treatment of night sweats (Un. Med., 1853.)