show that it does undergo decomposition, though very slowly; it is then one of the least active preparations.

As for the bromhydrate, it is to-day chiefly employed in subcutaneous injections, and I shall return to this salt when I come to speak of the hypodermic use of quinine.

To introduce these salts of quinine into the economy, we can make use of several ways; the stomach, the intestine, the skin, the subcutaneous cellular tissue and the lungs. In giving it by mouth you can administer it in solution, in suspension, in powder or in pills. By very careful experiments Briquet[1] has shown us that the solution is the most prompt and certain of these forms of administration, and the pill form is the worst.

In making your solution[2] you should either prescribe the bisulphate or order enough of sulphuric acid to effect the change into a soluble bisulphate.

[1] Briquet has made comparative trials of solutions, powders and pills containing sulphate of quinine. He endeavored to ascertain by the presence of quinine in the urine the rapidity of absorption, and by the manifestations of encephalic troubles, the action on the nervous system. These are his conclusions:

Complete solution.—1st. There is manifested at the end of from two hours and a half to three hours after the ingestion of the solution of bisulphate of quinine, signs of absorption in two-fifths of the patients who took fifteen centigrammes (2½ grains); in about two-thirds of those who took from 20 to 25 centigrammes (3 to 4 grains), and in three-fourths of those who took from 30 to 35 centigrammes (5 to 6 grains).

2d. There were manifested signs of action on the encephalon in one-fifth of the patients who took fifteen centigrammes (2½ grains); in a little more than one-third of those who took twenty centigrammes (3⅓ grains); in more than two-thirds of those who took 25 centigrammes (4 grains), and in three-fifths of those who took 50 centigrammes (7½ grains).

In the case of the administration of the pulverulent form, these were the results:—1st. There were no signs of absorption at the end of three hours save in one-fifth of the patients who had taken 25 centigrammes (4 grains); in one-sixth of those who had taken 30 centigrammes (5 grains), and in one-fourth of those who had taken 35 centigrammes (6 grains); a degree of absorption which considered *en masse* is not equal to that of 15 centigrammes (2½ grains) of acid sulphate in solution.

2d. There were no signs of physiological action in at least one-third of the patients who had taken 25 centigrammes (4 grains) of neutral sulphate in powder, in one-sixth of those who had taken 30 centigrammes (5 grains), and in a little less than one-third of those who had taken 35 centigrammes (6 grains). This degree of action, taken as a whole, is less than that of 15 centigrammes (2½ grains) of bisulphate in solution.

Administration of quinine in pill form.—1st. With the pill form there did not exist at the end of three hours any signs of absorption of quinine except in a very feeble proportion which might be approximately estimated at one-sixth as many as were markedly affected when the same dose was given in solution.

2d. The signs of absorption observed at the end of two hours were noticed in a larger proportion than in the case of those to whom the quinine salt was given in powder (as 2 to 3) but in less proportion than where the quinine was given in solution (as 4 to 5).

3d. Whatever may have been the dose in the pill form, no physiological action on the nervous system was ever noted, (*a*)

[2] Below are several formulæ for potions of sulphate of quinine :

(*a*) Briquet, Therapeutical Treatise on Cinchona and its Preparations. Paris, 1853.

You can use tartaric or citric acid in making your solution, or you can do as Herard directs, dissolve your quinine in a small wineglassful of brandy or rum.

Unfortunately, all these active preparations have the disadvantage of being exceedingly and persistently bitter to the taste. One of the best means of getting rid of this inconvenience is to give immediately after the draught a little licorice powder. Bear in mind that when you wish to obtain a speedy effect, and utilize the whole of your dose of quinine you must give it in solution. If you choose to give it suspended in some liquid menstruum you cannot do better than administer it in strong coffee, which well disguises the bitterness of the salt. This form, however, is less active than the preceding, as a certain quantity of the sulphate remains adherent to the cup, and a part is transformed into tannate of quinine, a combination, as above stated, ill-fitted for absorption.

The pulverulent mode has been recommended in order to obviate the bitterness of the quinine, which is given in capsules or in pearls. If the administration of the salts of quinine is rendered easier by this means, there are the inconveniences attending it that the therapeutic action is less prompt than with the solutions, and the direct contact of the powder of quinine with the gastric mucous membrane is apt to be attended with a sensation of heat and burning. So whenever you resort to this convenient way of giving quinine, recommend to your patients to drink after each dose a tumblerful of tartaric or citric lemonade, which effects the solution of the quinine.

The pill form, as I have said, is the worst, by reason of the tardy solution of these pills.[3] I advise you, then, if you have occasion to give quinine in pills, to see that they are made with some soluble excipient, as honey or conserve of

GRAMMES.

(1) ℞ Sulphate of Quinine..... .50
Acid tannic..... .60
Distilled water..... 60.00
Syrup of ginger..... 3.00

M. For one dose in malarial fevers.

(2) ℞ Sulphate of Quinine..... .75
Acid tannic..... .10
Acid sulphuric..... gtt. ij.
Distilled water..... 100.00
Syrup of orange..... 40.00

M. The whole would be a full dose.

(3) ℞ Sulphate of Quinine..... 1.00
Acid sulphuric,..... q. s.
Water..... 100.00
Syrup,
Syrup poppies..... ää 20.00

M. The above represents one full anti-malarial dose for an adult.

[3] Formulæ for quinine pills:

℞ Quiniæ sulph..... 1.—
Acid tartaric..... .20
Conserve of red roses..... .10

M. Ft. pil. No. x.

red roses, and not of gum arabic, which is hard to undergo solution in the digestive fluids.

In certain cases, either because the patient has an invincible repugnance to the quinine potions, or because he cannot take the capsules or pills, as in the case of young children, it has been proposed to give the quinine in enemas. Briquet[4] has shown us that the action of the medicine is often more rapid by this method than by the mouth, but much less persistent; you can then order enemata of sulphate of quinine, having care to change the sulphate into bisulphate,[5] but to insure their activity these injections should be kept up, and you know how difficult this is when your patient is a child. So in cases of this kind it has been advised to administer the quinine by lotions and pomades, thus making use of the skin as a channel of introduction. This is a means that will give disappointment, for it has been demonstrated that the skin covered

℞	Quiniæ sulph	.10
	Citric acid, pulv	.20
	Honey	.05
	Starch	q. s.

M. For one pill.

℞	Quiniæ sulph	.60
	Ext. Absinthe	q. s.

M. Ft. in pil. No. vi.

Starke has also proposed to give quinine in pill form with tartaric acid and sugar. The patient should drink freely of tartaric acid lemonade before swallowing these pills.

[4] Briquet, in giving lavements containing one half gramme of quinine to fever patients, has observed:

1. That generally sulphate of quinine given in lavements is absorbed.
2. That this absorption is very prompt, and twice as rapid as by the stomach.
3. But it is too feeble, and insufficient in three-fourths the cases to determine appreciable effects on the encephalon and heart.
4. That finally absorption abruptly and completely ceases in most cases after an hour and a half.

Hence Briquet considers lavements of sulphate of quinine as of only secondary importance, and to be efficacious they must be given at the very moment even when their therapeutic effect is desired.(*a*)

[5] The following is a good formula for a quinine lavement:

℞	Sulph quinine	gr.x.
	Acid sulph	gtt.i.
	Warm water	℥ v.
	Tinct Opii	gtt.x.

M. Quinine is used in suppositories; seven or eight grains being incorporated with sufficient cacoa butter to form a suppository. This method is not to be recommended.

Where this salt cannot be borne by the stomach, or as an adjuvant to its internal administration, it may be rubbed up with lard and a little alcohol, in the form of an ointment, one drachm being incorporated with half an ounce or an ounce of the fatty excipient.

(*a*) Briquet Loc. Cit., p. 338.

with its epithelium does not absorb the salts of quinine, or if it absorbs them, it is in such trifling quantity that no therapeutic result can be obtained.

But if the skin does not absorb, the cellular tissue, on the contrary, lends itself rapidly to the introduction of the salts of quinine, and the hypodermic method finds in the paroxysms of pernicious fever one of its most useful applications. You will see, in fact, as I shall further on point out, that there are cases of paludal intoxication when it is necessary to act with extreme rapidity, and you understand of what utility must be in these cases the subcutaneous injections of quinine, which to promptitude of absorption add a great therapeutic activity. Albertoni and Ciotto,[1] by their brilliant experiments on the channels of elimination of quinine, have shown us that this medicament, when it is introduced by the mouth, passes through the liver, and a certain quantity sojourns there, to be eventually eliminated in the bile; while, when introduced by the hypodermic method, quinine salts pass immediately into the circulation and are eliminated by the urine.

Only, as these salts to be soluble must be acid, it is easy to see that such injections introduced under the skin may determine there local inflammations; therefore, endeavors have been made by Albertoni and Ciotto by the addition of glycerine or tartaric acid,[2] or by seeking more soluble salts of quinine, to render these solutions less irritative. Tanret has recommended the lactate of quinine,[3] of which he dissolves one part in five parts of distilled water. Paul

[1] Pietro Albertoni and Francesco Ciotto have especially studied the channels of elimination of quinine. They have found it in the bile from two to five hours after its ingestion in the stomach. When the salt is introduced in other ways it does not appear in the bile, but in the urine. They have found it in the blood during the first hour after its ingestion. Quinine sojourns long in the blood, and may be found in all the viscera, and in particular in the spleen, liver, and brain.(*a*)

[2] Reynolds has proposed the following solution for hypodermic injection:

		Grammes.
℞	Quin sulph	28.
	Acid sulphuric	q. s.
	Glycerine	24.
	Water q. s. to complete 170 cubic centimeters.	

Each cubic centimeter (syringeful) contains 16.7 centigrammes of sulphate of quinine.

Kobner prefers the hydrochlorate, as in the following solution:

		Grammes.
℞	Hydrochlorate of quinine	1.
	Glycerine	
	Distilled water, ää	2.

M. Dissolve without acid. One cubic centimetre contains 15 centigrammes hydrochlorate of quinine. This solution keeps well in a warm room. Should be injected tepid.

[3] The following is Tanret's formula:

(*a*) Pietro Albertoni et Francesco Ciotto, Sur les voies d'elimination electives de la uinine (Gaz. med. ital., provi Venete, 18 mars 1876, p. 93, et Bull de thér., t. XC, 1876, p. 360).

advises the soluble sulpho-vinate of quinine, unfortunately of little stability. Generally the bromhydrate is the salt employed.

Described by Latour and Boille,[4] this salt was introduced into therapeutics by Gubler, and since then we have seen Soulez, of Romarantin; Dardenne, of the Isle of Mauritius, and Auliffe extol the effects of this salt in the treatment of intermittent fevers. As the bromhydrate contains more quinine than the sulphate, and is more soluble, it is no wonder that it has been utilized for hypodermic injections, and solutions have been made of one part in ten. But in such large doses, it is necessary to add alcohol, which renders this solution somewhat more irritating.

Finally, struck by the rapidity of action of medicaments introduced by the

	Grammes.
℞ Lactate of quinine.....	1.
Distilled water q. s. to complete.....	5.

This solution, which is stable, contains in each cubic centimetre 20 centigrammes of lactate of quinine.

[4] The combination of bromhydric acid and quinine was made in 1870 by Latour and in 1872 by Boille. The formula of neutral bromhydrate of quinine is as follows:

$$C_{48}H_{24}N_2O_4Hbr,2H_2O$$

That of acid bromhydrate is:

$$C_{48}H_{24}N_2O_42Hbr,6H_2O$$

This substance is crystalline, and its solubility is greater than that of sulphate of quinine; one part of bromhydrate being soluble in 5 parts boiling water, or 60 parts cold water; it contains more quinine than the sulphate.

Gubler has employed this salt in subcutaneous injections, using ten per cent. solutions in water slightly dosed with alchol; one gramme of this solution contains one decigramme of the active principle; it suffices to inject two syringefuls, in order to introduce into the organism the equivalent of 30 centigrammes of sulphate of quinine.

Soulez was one of the first to make use of this salt subcutaneously in fever and ague. In his experience in the fevers of Sologne it proved superior to sulphate of quinine. Given one hour before the paroxysm, it prevented its occurrence. Moreover, in the dose of half a gramme to a gramme it produced little of the quinine intoxication. He has recommended this method of subcutaneous introduction: Plunge the needle directly through the skin and inject the solution very slowly, at the same time, with the pulp of the fingers, press over the tract of the injected liquid, and diffuse it as widely as possible through the subcutaneous cellular tissue, then withdraw the needle gradually.

Dardenne, of Mauritius, employs the following formula for hypodermic injections:

	Grammes.
℞ Acid bromhydrate of quinine.....	1.
Dilute sulphuric acid.....gtt. x..	
Distilled water.....	10.

M.

Or the following solution:

	Grammes.
℞ Acid bromhydrate of quinine.....	1.00
Tartaric acid.....	0.50
Distilled water.....	10.00

M.

respiratory passages, Jousset of Bellesme, has practiced intra-tracheal injections of salts of quinine in cases of pernicious fever, and this bold attempt has been crowned with complete success. In a previous chapter I have enumerated these facts and dwelt on the utility of these intra-tracheal injections. I see with pleasure that since the publication of this chapter, the method has won favor: Bergeron has maintained its advantages, and in veterinary practice, where the trachea can be so easily reached, I have seen Cagny and Levi, of Pisa, employ these injections with brilliant success. I believe, then, that in cases of pernicious fever it would be well to always have in mind the possibility of these tracheal injections of the salts of quinine, and not to hesitate to practice them.

I have finished with the modes of administration of the salts of quinine, but before going farther it is well to ask if the introduction of these salts into the economy, apart from the symptoms of local irritation which I have pointed out, has not other inconveniences. You all know that the principal property of quinine salts is to determine a cerebral state known under the name of quinine intoxication; but these salts have also been accused of provoking abortion and hæmaturia.

I will say little about the symptoms which constitute quinine intoxication; the buzzings of the ears, the vertigo, the obscurations of sight, which are the principal symptoms, and which manifest themselves whenever enormous doses are given. Women seem more susceptible than men to this physiological effect, owing to the predominance of the nervous system in females. So great is the susceptibility in some persons that it takes but small doses of quinine to produce these symptoms, and it is difficult in such patients to obtain a therapeutic effect. It may, in fact, be necessary to abandon quinine and employ some other alkaloid of cinchona, cinchonidia, for example, which, in pretty large doses, does not occasion any cerebral trouble.

The question of the influence of quinine in producing hæmaturia[5] has

These injections determine no local accident, except a slight induration. This treatment has given excellent results with marsh fevers of the island of Mauritius.

Auliffe's formula is as follows:

	Grammes.
℞ Bromhydrate of quinine.....	2.
Sulphuric ether,.....	8 cent. cub.
Rectified spirits.....	2.

M. A hypodermic syringe full of the above contains 10 centigrammes of bromhydrate. It is proper to inject as much as a gramme of the salt in cases of pernicious fever.(*a*)

[5] Antoniades, of Athens, was the first, in 1858, to call attention to the hæmaturia which often follows intermittent fevers. Berettas, the same year, attributed these hæmaturias to the use of quinine. Karamitzas, of Athens, while admitting that there are intermittent

(*a*) Gubler, Note sur l'emploi thérapeutique du bromhydrate de quinine (Jour. de thér., No. 13).—Soulez. De l'utilité du bromhydrate de quinine dans le traitement des fièvres palustres (Jour. de thér,, Nos. 21, 24, 1879). Remarques sur les précautions à prendre pour éviter les accidents locaux de injections hypodermiques de sulfate de quinine (Jour. de thér., No. 17, 1876).—Dardenne, Contribution à l'étude du bromhydrate de quinine dans les fièvres d'orlgine paludéenne (Jour. de thér., No. 9, 1877).—Mac Auliffe, Injections éthérées de bromhydrate de quinine (Jour. de thér., No. 21, november, 1880).

been especially agitated by Greek and Italian physicians, and we see Ughetti and Tomaselli maintain that in many cases hæmaturia with bilious fever results from treatment by sulphate of quinine. It is not, indeed, a veritable hæmaturia which is observed in these cases, but rather, as Karamitzas has shown, a hæmoglobinuria, that is to say, that the coloring matter of the blood alone passes out in the urine. For my part, I have little belief in this quinine hæmaturia, for in typhoid fever treated by large doses of sulphate of quinine, you never see hæmaturia or hæmoglobinuria; it is probable then that the malarial condition favors the appearance of these hemorrhages At the same time, I am of opinion that in individuals affected with hæmaturia or hæmoglobinuria, it is well to be chary in the use of sulphate of quinine.

The same reserve should be made when you have to treat pregnant women,[6] affected with intermittent fever. Although the action of sulphate of quinine on the uterine contractions is still a matter of dispute, and to the facts of Monteverdi of Duboué and Warren, who report cases of abortion following large doses of quinine in this disease, we may oppose the observations quite as positive of Thezet, Delmas, Burdel, and D'Alamo, who have shown that pregnant women may with impunity support quinine treatment—it none the less remains demonstrated that in other circumstances quinine may determine

hæmaturic fevers, has shown by precise experiments that quinine does determine hæmaturia, but that in these cases it is not a true hæmaturia, but rather what he calls hæmospherinuria, in which only the coloring matter of the blood is found in the urine, and not the globules.

Moreover, Ughetti and Tomaselli have maintained that the bilious hæmaturia, which sometimes attends malarial fevers, does not result from the marsh poison, but from the toxic action of sulphate of quinine in therapeutic doses.(*a*)

[6] Quinine has long been considered as a congestioning medicament of the uterus, and Tilt and Delioux de Savignac range it among the emmenagogues. It has, moreover, been asserted that it may determine uterine contractions and provoke abortion. Thus it is that Petijean, Monteverdi, Duboué, of Paris, and Warren, have mentioned cases of abortion caused by sulphate of quinine. Thus, too, Cocheran, John Lewis, and Rich consider it a useful medicine in obstetrics to quicken the contractions of the womb. To these positive facts Thizet, Delmas, Alamo, Bardel, etc., have opposed another series of observations, showing that medication by quinine has no danger whatever to the majority of pregnant women. Plantard has collected a great number of cases of pregnancy where treatment by sulphate of quinine was followed by no bad results. Nevertheless, as abortion may supervene, it is well to employ at the same time as the quinine, calmative medicaments, and particularly subcutaneous injections of morphia and sulphate of atropine.

Quite recently, moreover, this oxytoxic action of quinine has been affirmed by Lartigan.(*b*)

(*a*) Ughetti, Intosçicazione Chinica e la febbre biliosa ematurica (lo Sperim., fasc 6, 1878).—Karamitzas, Sur l'hématuric provoquée par la quinine (Bull. de thér., t. XCVII, p. 53, 1879).

(*b*) Plantard, De l'emploi du sulfate de quinine pendant a grossesse (thèe de Paris, 1875).—Duboué (de Pau), De l'action des sels de quinine sur l'utérus (Ann. de gynécol., octobre 1874, p. 286).—Delioux de Savignac, Médicaments obstétricaux (Bull. de thér.. t. LXXXI., p. 298).—Tilt, the Lancet, Feb. 1854, et Bull. de thér., 1851, t. XL.—Monteverdi, Un. méd., 1871 et 1872.—Thézet, Bull. de thér,, 1846, t. XXX.—Rich, Charleston Med. Jour. and Rev., March 1881, et Bull de thér., 1892, t. LXII., p. 180.—Lartigan, the British Med. Journ., 2 June 1883.

abortion, and you should always have this in mind when you have to treat patients in a state of pregnancy.

To point out the principal alkaloids of cinchona bark and show you the superiority of quinine, to indicate the modes of administration and preparation, all this does not suffice to make known in their entirety the numerous medications which have been counselled in the treatment of intermittent fever, and I must now point out the succedanea of cinchona and its derivatives. You already know that the principal motive of researches made to find a substitute for quinine is the high price of the latter; you will not then be astonished at the numerous medicines which have been proposed to take its place, all of which have been proved to be inferior to cinchona. These succedanea have been derived successively from the vegetable kingdom, from the mineral, and even from the animal kingdom, and without giving you a complete list of these medicaments, I will only point out the principal of them.

I shall omit mention of the indigenous plants which have been recommended in intermittent fever,[1] making allusion only to berberis vulgaris so much praised by Piorry, centaury recently experimented with by Bertin, euca-

[1] The barberry (berberis vulgaris) contains in the bark of the root, which is very bitter, two alkaloids: berberine and oxyacanthine; the last is one of the most bitter of substances. An extract has been made from the bark of the root which has been counselled in malarial fevers, and oxyacanthine has been used instead of quinine.

The European centaury (centaurea calcitrapa), which grows everywhere in chalky soils, has been employed by Bertin under the form of alcoholic extract of the root, in intermittent fevers. In the Quotidian form, it suffices to give during two or three days, six pills of three grains each, one pill every two hours, to break up the attack. In the grave forms it is necesary to exceed the quantity of fifteen grains a day. The same medicament is valuable in the larvated fevers. (Bertin, on the Employment of Centaury in Malarial Fevers, Montpellier Medical Journal, February and March, 1876).

Under the name of cedron nuts there exist two products of different origin. The one belongs to the *simaba cedron*, or *quassia cedron*; the other to the valdivia (picrolemma valdivia). The first of these fruits contains a product known as cedrine, which is uncrystallizable and which is injected under the skin in doses of $\frac{1}{80}$ to $\frac{1}{15}$ of a grain. In Columbia the cedron powder is used, mixed with a little brandy, in the dose of eight to fifteen grains a day. This powder of cedron has been used by the Indians from time immemorial.

In 1848, Vauvert, of Mean, vice-Consul of France, at Panama, sent a box of cedron nuts to the Academy of Medicine, but no trials were made; in 1852, however, Reyer demonstrated the febrifuge properties of cedron. Purple, of New York, Posada Arango, of Columbia, employed also with success in malarial fever the powder of cedron nuts. Dujardin-Beaumetz and Restrepo have also obtained good results by this means, while Bardel reports only disappointments.

The fruit of Valdivia contains an alkaloid, discovered by Tanret, and crystallized under the name of valdivine, and which has for formula:

$$C^{36}H^{24}O^{2}{}_{5}HO.$$

This valdivine is eminently toxic; $\frac{1}{80}$ grain killed a hare in eighteen hours; it determines vomiting in man in the dose of $\frac{1}{15}$ grain. In cases of hydrophobia, valdivine causes abatement of the convulsive paroxysm, without, however, accomplishing a cure. (*a*)

(*a*) Restrepo, a Study of Cedron, of Valdivia, and their active principles, Paris, 1881.

lyptus which Gubler and Gimbert introduced into therapeutics, and lastly, cedron, which I have studied along with my pupil, Restrepo.

This experimental investigation showed us, first, that there exist two kinds of cedron; the one belonging to the simaba cedron, the other to a variety of plant whose botanical characteristics Planchon, our colleague at the Academy, has determined, viz: the *picrolemma valdivia*. From the first a neutral non-crystallizable substance has been obtained called cedrine, from the other a crystallizable alkaloid, discovered by Tanret, viz: valdivine. Cedrine alone has an action in intermittent fever, in the dose of four milligrammes ($\frac{1}{15}$ grain) in subcutaneous injections, or under the form of cedron powder as the Indians of Columbia prepare it, and which is given in the dose of one-half gramme to one gramme a day (7½ to 15 grains). The trials which Restrepo has made in Sologne with cedron and cedrine, while showing us the febrifuge properties of this substance, have also proved its inferiority to the salts of quinine.

Eucalyptus has enjoyed a much greater reputation, and it was thought that we had found a real substitute for cinchona, having this singular advantage that the cultivation of this tree, so strange in color and in the shape of its leaves, has the power to destroy the marsh miasm.[1] Hence it is that you may see in the Campagne Romaine the railroad stations in the most unhealthy localities, surrounded with eucalyptus trees. But more rigorous observation of the facts has shown that the preparations of eucalyptus are untrustworthy medicaments

[1] The eucalyptus globulus is a tree of the Myrtaceæ family, which often attains a colossal size. All the parts of the tree and especially the leaves contain an aromatic essence, eucalyptol, which has been analyzed by Clöez.

This tree was introduced into France in 1857 and 1858 by Ramel. It is to-day cultivated in abundance in the Maritime Alps, and in Algeria.

Gubler and Gimbert have studied the physiological action of eucalyptol. It produces excitation in the dose of several drops, and irritation, if the dose is augmented from half a drachm to a drachm.

This tree, which is called fever tree, has been employed from the earliest time by the Aborigines of Australia in the treatment of intermittent fever. More than forty years ago the captain of a schooner from Salvy saw the good effects of the bark and leaves in an epidemic of pernicious fever which broke out among the sailors of the French sloop, La Favorite, at Botany Bay. In Corsica, Regulus Carlotti, of Ajaccio, obtained remarkable results from eucalyptus in the treatment of paludal fevers, and he had similar success in Algeria.

In these cases the tincture of the leaves or the powder is generally used. Gubler gave of this powder from sixty to ninety grains a day. Kirchberg treated nineteen patients by eucalyptus, and all got well without sulphate of quinine. Burdel, of Vierzon, has obtained only incomplete results in the treatment of the malarial fevers of Sologne.

Eucalyptus has still another property, that of destroying on the spot the marsh miasm, and this results either from the rapid absorption of the water by this tree (which is very greedy of water), or from the aromatic emanations which it develops. (*a*)

(*a*) Gubler, l'Eucalyptus et son emploi en thér. [Bull. de thér., 1881, t. LXXXI, p. 145].—Castan, Montpellier méd., 1872, t. XXX, n° 6.—Burdel [de Vierzon], l'Eucalyptus globulus en Sologne [Bull, de thér., t. LXXXV, p. 529].—Gimbert [de Gannes], l'Eucalyptus globulus, 1870, p. 69.—J. Campian, l'Eucalyptus globulus et l'Eucalyptol [thèse de Paris, 1872].—Régulus Carlotti, Mémoire sur l'action thérapeutique et la composition élémentaire de l'écorce et de la feuille de l'eucalyptus, présenté à la Société d'agriculture d'Alger, 1869 — Kirchberger, Observations de fièvres intermittentes traités au moyen de l'eucalyptus globulus [Journ. de méd. de l'Ouest, 1re série, 6e année, t. VI, p. 260].

in the treatment of intermittent fevers, and that it will not do to depend on the cultivation of this tree to effect the disappearance of malaria.

I will say nothing of jaborandi or pilocarpine.[1] Rokitanski and Griswald have indeed recommended this alkaloid in the first period of intermittent fever, but this is an exceptional kind of treatment which is not applicable to the paroxysmal stages of the fever as ordinarily witnessed.

Among the substances not of vegetable origin[2] which have been recommended in the treatment of fever and ague, I will enumerate only picric acid and the picrates, arsenic and the arseniates and the medicaments of the aromatic series.

A dozen years ago, I made some researches on the physiological action of picrate or carbazotate of ammonia, and, while recognizing that this medicament diminished the number of pulsations and produced on the part of the brain a symptomatic aggregate comparable to quinine intoxication, I noted, after Braconnot, Calvert and Mossa, Haspland, Parisel,[3] etc., its febrifuge action; only this action, like that of the succedanea of quinine generally, is uncertain.

[1] Griswald counsels in intermittent fevers subcutaneous injections of one-sixth grain of pilocarpine. These injections, according to him, not only cause the chill to subside, but they often throttle the paroxysm, and when one or two attacks have been cut short the fever does not return. He advises the employment of these injections in pernicious fever. (*a*)

[2] Certain mineral substances have been recommended in intermittent fever, such as chlorate of potassium (febrifuge salt of Sylvius; chloride of sodium, vaunted by Thomas, of New Orleans, Selles, of Mount Desert, and Piorry; chloride of ammonium, extolled by J. Franck, Aran, and Padiolo; tincture of iodine (Seguin, Boinet, and Barilleau, of Poitier); solution of iodide of potassium (Wildebrand and Helsingfors); the sulphites and hyposulphites, by Polli.

[3] Picric or carbazotic acid was discovered in 1788 by Hanssmann. Obtained in 1794 by Welter, by the action of nitric acid on silk, it was prepared in 1834, by Runge, by exposing tar oil to nitric acid. Laurent in 1841 showed that this substance was a derivative of phenic acid [C^{12} H^5 O,HO], in which three molecules of NO^3 are substituted for three atoms of hydrogen; it is called on this account trinitrophenic acid. Certain alkaline carbozotates are very explosive, but the carbazotate of ammonia is not so. It crystallizes in brilliant yellow rectangular plates or six-sided prisms, and is of an intensely bitter taste.

It was Braconnet, of Nancy, who first, in 1830, employed the picrate of potassa as a febrifuge. Calvert and Massa, in 1836, pointed out the antiperiodic properties of picrate of ammonia. In 1862 Aspland again took up the subject and showed that one could derive the same effects from carbazotate of ammonia as from sulphate of quinine in the treatment of the malarial fevers of the Indias.

Parisel, in 1868, quotes the reports of Barot (Son), who obtained a cure in more than sixty cases of fever and ague by frequent three-grain doses of picrate of ammonia. The same success was obtained by Henry, of Tureaux, in the province of Cher, by Chazereau, at Aubigny, by Charles Flain, at Sancerre, and Manoha, at Medeah.

Dujardin-Beaumetz has studied the physiological and therapeutical action of carbazotate of ammonia. This salt causes diminution in the beatings of the heart, and in the dose of one grain brings down the pulse ten beats. In the frog there is produced arrest of the heart with one-sixth grain; in the hare three grains diminish by one-half the pulsations of the heart. When you exceed one grain or a grain and a half a day, you produce a train of symptoms

(*a*) Griswald, Pilocarpine in Intermittent Fever [New York Med. Jour., August, 1880].