Quinine and antiperiodics in their therapeutic relations : including an abstract of Briquet's work on cinchona, and a notice of Indian febrifuges / by John Macpherson.

QUININE AND ANTIPERIODICS

IN

THEIR THERAPEUTIC RELATIONS,

INCLUDING AN ABSTRACT OF BRIQUET'S WORK ON CINCHONA, AND A NOTICE OF INDIAN FEBRIFUGES.

BY

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To KENNETH MACKINNON, Esq., M. D.,

Apothecary to the H. E. I. Company.

My Dear MacKinnon,

I inscribe these pages to you, not merely because you are a warm personal friend, or because their contents have a special reference to the department over which you preside.

I offer them to you also, as a steady advocate of the reforms so much wanted in our Service, and as a zealous cultivator of Medical Science for its own sake.

Your's very sincerely,

John Macpherson.

March 1, 1856.

INTRODUCTION.

THE following compilation, which appeared originally in the pages of the *Indian Annals*, is now published in a separate shape, in the hope that it may be found useful by junior practitioners. I know that I should have been very glad, on my first arrival in this country of fever, to have been able to obtain the sort of information, which is here brought together. Much of it was imperfectly ascertained fifteen years ago, and, I believe, is not now to be found in any single work on Materia Medica, certainly not in any English one.

These pages may, further perhaps, be serviceable to medical officers in charge of dispensaries, and at out-of-the-way stations, where large supplies of quinine are not available, perhaps even to non-professional men in the Mofussil, where every man is often obliged to be his own, and more specially his servants' doctor, whose ordinary fevers he may readily cure by an emetic, followed by a few doses of a febrifuge.

Possibly, also, what I have written may contribute to re-call public attention to the use of the febrifuges of this country, which, with some recent exceptions, have, of late years, been so strangely neglected.

In truth, the great enemy of other febrifuges is Quinine. It is so superior to others, that it saves much trouble to use it in preference.

The great test of the power of a febrifuge medicine in the tropics, is its proving useful in other forms of fever besides the simple intermittent ones, and it is in this respect that most of them show their inferiority to Quinine. They have not, indeed, yet had a fair trial; but as far as our knowledge, up to the present date, allows us to go, it is perhaps not too much to say, that the Berberis and Warburg's Fever Drops, (the latter of which has not been proved to contain any febrifuge except Quinine) are the only two antiperiodic medicines, which have been found distinctly useful in remittents.

Entertaining these views of the superiority of Cinchona, I am one of the last who would advise a sparing use of its most important alkaloid, Quinine, or recommend to Government any false economy in its supply. But it cannot be denied that in many instances a great deal more Quinine is given than is at all required, and the slighter forms of fever can be treated quite satisfactorily without its aid.

I have no hesitation in saying that the Presidency of Bengal alone might be saved an annual expenditure of certainly £3,000, by the following measures: first, using the country substitutes wherever it is expedient to do so, and secondly, (this would be the far more important measure,) by large quantities of Sulphate of Cinchonine and of Bullock's

Amorphous Solution of Quinine, of the efficacy of which there is not the slightest doubt, and which are about half the price of Sulphate of Quinine, being sent out by the India house authorities to this country.

This must be done boldly and on a large scale; petty experiments, like a recent one, of sending a hundred ounces of unbleached Sulphate of Quinine, which after all is only about 1 rupee the oz. cheaper than the ordinary Sulphate, can be of no avail.

The saving that might be in this way effected, would afford ample funds for experiments in the importation of Cinchona plants into this country, experiments which should be persevered in, until they are successful, and would also supply means for the care of the plantations, until the trees should be old enough to yield bark fit for Medicinal purposes.

On the desirableness of our being rendered independent of other countries for the supply of Cinchona, it is unnecessary to enlarge, as it is admitted on all hands.

It need scarcely be said, that these pages are not intended to give any account of fevers or of their treatment, but as it might possibly be inferred from some expressions in them, that it is meant to recommend Quinine to the exclusion of other remedies, it may be right to say, that I had no intention of conveying such an impression—for he who does not know how to employ other medicines, does not, I think, understand how to make the best use of Quinine.

It is indeed to be regretted that up to this date we have no complete systematic work on the diseases of

India,* and especially that there is none, not excepting Dr. MacKinnon's valuable work, which can be placed in the hands of a beginner, as fully representing the present amount of our knowledge of tropical fevers and of their treatment.

A whole flood of light has of late years been thrown on the subject by the researches of the French,† mainly in Algiers, but also in some more southern countries. The analogies which their works afford, give us the means of generalizing on a wider basis than has been hitherto possible—and show us how the fevers of Algiers and Brazil are in their essence the same as those of India, just as we long ago had reason to believe that those of Java and of the African coast were so. I say that they are the same in their essence, for I think it useless to consider the question of absolute identity, excepting in some specific diseases, when I can not say that the fevers of Calcutta are identical in successive years, or even at the different seasons of the same year.

Not venturing to enter at present on the consideration of the general subject of fever, I have merely thrown together the accompanying table, which will, I think, be found to include in one or other of its divisions every fever that has been observed in India. Eruptive fevers are merely included to make it complete.

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* Much is however expected from the forthcoming works of Mr. J. R. Martin, and of Drs. Morehead, and Bird of Bombay.

† For instance Faure Raymond, Morea; Armand, Jacquot, Beylot, Italy; Thevenot, Africa; Segond, Cayenne; Sigaud, Brazil; Maillot, Boudin, Cambay, Haspel, Armand, Jacquot, Algiers.

As the object is a practical one, I have made the classification with reference to the most important point in treatment, the degree of remission or of intermission present. For, notwithstanding that Quinine has been found useful to a certain extent in the continued fevers of Europe, its value in them cannot for a moment be compared to its value in the intermittent, remittent and pseudo-continued fevers of the tropics : and I was unwilling that the classification should rest on the uncertain basis of Malaria and Marsh Miasma, for who will say positively, that the Ardent fever of the Hot weather is the result of Malaria alone, and generally, I would ask, how much is known accurately of the effects of Malaria, or how much of the action of the various Thermo-Electro-Hygrometric influences at work around us, to which so little attention has been hitherto paid, but the study of which on an extended basis, will no doubt ultimately throw much light on points which are for the present inexplicable ?

I do not wish to lay down anything in this table dogmatically. I hope rather that it will invite discussion of the subject, and elicit the views of those who have had larger experience of fevers in the very various climates of our eastern possessions, than I can boast of.

Fevers having Remittence, or Intermittence.	Intermittent—	Endemic, seldom epidemic.	All these may put on a typhoid character, but Remittents, much more frequently than Intermittents.	Any of these, but especially the Intermittent and Remittent Fevers, may suddenly assume the pernicious type, when they are commonly known as Pucka, or Jungle Fevers.
	a. Quotidian, ...			Chief complications may be of
	b. Tertian, ...			Head or Nervous system generally, as Comatose Apoplectic, or even Convulsive fever.
	c. Quartan, ...			Stomach and S. Intestines—
	d. Varieties of the above, ...			Doth in enterite or choleroid or algide form.
	Remittent—	Endemic, but liable to become epidemic.		Large Intestines—Dysenteric fever.
	a. Simple, ...			Liver—Hepatic fever.
	b. Bilious, ...			Spleen—Splenic fever.
	May simulate yellow fever, ...			Lungs—Pneumonia.
	c. Gastro-enteric, ...			Cutaneous System generally, Ephidrosis, as Malwa sweating fever.
	May simulate true typhoid, ...			Blood—Hæmorrhagic fever.
	d. Exanthematous, ...			
	May simulate scarlatina, ...			
	Pseudo—continued—			
	a. Ardent, ...			
	b. Congestive, ...			
	May simulate typhus, ...			
	c. Jail fever, ...			
	May simulate typhus, ...			
Fevers with doubtful Remittence.	Typhus of Hills—	All, with the exception of Eruptive and Ephemeral Fevers, which are scarcely so, are Endemic, but liable to become epidemic.		
	a. Peshawur Valley, *b.* Himalayas, ...			
	Bubonic Typhus—			
	a. Pali Plague, *b.* Mahamurree, ...			
	Ephemeral Fever, ...			
Eruptive Fevers.	Variola, ...			
	Varicella, ...			
	Rubeola, ...			

The preceeding table shows that, in my opinion, the great majority of Indian fevers come under the category of the fièvres d'accès or fièvres à quinquina of the French, and that therefore there can be but few of them, in which Quinine and antiperiodics are not indicated in one or other stage.

I exclude entirely from the table, Typhus and Typhoid fever. No fevers that I have seen in the tropics, commence like them. The fevers that come nearest Typhus, and that may possibly be true Typhus, occur in the Himalayas, and the valleys about Peshawur, which are far north of the tropics, and the mere presence of inflammation of Peyer's patches in a Remittent fever, which has occasionally been observed, does not necessarily constitute it a case of Typhoid. Nor does the fact of what are called Typhoid symptoms occurring in the later stages of many fevers, mark such cases as true Typhus.

In like manner I believe that Yellow fever has never been seen in India. Cases do occur in which there is much yellow suffusion, with a certain amount of black vomit, and such cases I have myself seen in Calcutta. It is also very remarkable, that in both the Burmese wars a fever was observed at Prome, which greatly resembled the Yellow fever of the West Indies, (and this would also to a certain degree correspond with what is known of the geography of yellow fever, that it only occurs on coasts or runs up the valleys of rivers) ; but notwithstanding such exceptional cases, and that Heymann seems to be convinced that true Yellow fever (as well as as Typhus)

occurs both endemically and epidemically in some of the Dutch islands in the Eastern Seas, yet it is beyond doubt, that Yellow fever does not occur in the East Indies, in the same way as it does in the West, and on the shores of some of the more southern parts of Europe.

Then, again, as to the Pali Plague and the Maha Murree, it is quite certain that neither of them have been imported into India. The question therefore is rather of similarity than of identity, and I should be inclined to look on the Maha Murree as a form of plague very similar to, but not identical with, that of Egypt, (like the endemic plague of Wallachia,) rather than call it the true Plague, of which, by the way, I am not certain, that it is generally known, that, it is nearly fourteen years since any cases have been observed in the Levant.

With respect to Eruptive fevers, I shall merely remark, that there does not appear to be sufficient evidence to show that true Scarlatina has yet shown itself in India.

It only remains for me to say, that the essential object of these pages is to indicate briefly the practical value of the individual articles. No attempt has been made to give an account of their chemical and natural-historical properties, and except in the case of Quinine and Arsenic, little has been said of their physiological action.

It would have been impossible for me, to quote all the authorities for the numerous facts, which have been noticed, without cumbering my pages with an

unnecessary array of references; in place of doing which, I have to specify my particular obligations to that rich store-house of therapeutic knowledge, the volumes of Bouchardat's Annuaire, to Oesterlen's Hand-buch der Arzneimittel Lehre, who in his comparative estimate of the value of different remedies, evinces a degree of practical shrewdness, for which we do not usually give our German brethren credit. Mr. Waring's Manual of Therapeutics, a monument of judicious industry, has also been of much use.

The great work of Pereira has furnished comparatively little material. There remain to be mentioned, Trousseau and Pidoux's Therapeutique—Craigie's Practice of Physic—Dr. G. B. Wood's Practice of Medicine, and Baumgärtner's Krankheit's Lehre. For Indian Febrifuges I am chiefly indebted to Dr. W. B. O'Shaughnessy's Bengal Dispensatory, and Dr. Cleghorn of Madras, has given me some useful hints on the subject.

March 1, 1856.

CONTENTS.

ON QUININE AND ANTIPERIODICS.

Action of antiperiodics in Fever.—The object of the following pages is to bring together the most recent information respecting the application of antiperiodic remedies to the treatment of tropical diseases.

Of these maladies by far the most common is fever, the one in which they exercise their specific influence in the most marked way, and their action in it may be considered as typical of their action in other diseases. It would be out of place here, in a mere compilation, to propound any theory of fever or of the action of antiperiodics, as my object is strictly practical.

Still it may be well to say "in limine" that the theory, which accounts for the action of antiperiodics best, and which accords most with the present state of our knowledge on the subject, is the following.

The intermittent element (be that what it may) appears to act primarily by an impression on the nervous system, whether cerebrospinal or ganglionic, disturbing in the first place its functional action, and producing along with disturbance of the process of calorification, various disorders of the circulating apparatus, with a tendency of the blood to fluidity, or at least with an entire absence of the plastic element.

In the following pages the general phrase fever must be used often without specifying its particular form. "The fevers of hot countries," says M. Littré, "are only separated by shades; they are marked by a common character, and that essential character is the possibility of interchange between the intermittent, remittent and continued forms. It is marked in the fevers of Bengal, in the fevers of Algiers, in those of Greece, and is as plainly to be recognized in the fevers described by Hippocrates, as in those seen by the French expedition to the Morea in 1825."

This common element of intermittence or of remittence depends most probably on the primary disturbance of the nervous system, and therefore antiperiodic remedies are such as address themselves to that system, or, what have been commonly esteemed, neurosthenics and tonics, and to this class almost all such remedies are usually referred. To say that they have a specific action on the effects of malaria or marsh poison, (some have named them antimiasmatics,) is to assume that they act on a poison, the existence of which is still hypothetical, and which must be as multifarious and Proteus-like in its nature, as the infinite variety of effects that are ascribed to it.

If we assume the existence of miasma, we must still confess that we do not know what constitutes it, on which organ of the system it acts, or in what way antiperiodics neutralise it. And as the more recent applications of cinchona show what power that drug possesses, over many diseases never supposed to be of miasmatic origin, it becomes daily less necessary to insist on the malaria hypothesis.

Since the introduction of bark, or if I may be allowed the expression, still more since its re-introduction by the discovery of quinine in 1820, the proper use of antiperiodic remedies has become by far the most important point in tropical practice. We begin indeed almost to wonder how the worst fevers were ever successfully treated without the aid of those remedies. We know that Alexander the Great died of the common remittent of Babylon, and that Oliver Cromwell died of the ague, both probably merely for want of a few doses of cinchona, although bark was known in London in the days of the latter, but not given to him.

Cinchona.—Though many antiperiodic remedies have come into note, and many have been carefully studied of late years, still cinchona maintains its supremacy, and reigns with none like or second to it. It is the medicine "par excellence," the true "vade mecum" of the tropical physician, for none of its substitutes have been found to aid him materially except in intermittents.

Lavish as these praises are, there are few I imagine who will be inclined to dispute their justice, and the following table, which shows the reduction of mortality by fever, which has been steady and progressive during the last quarter of a century, will suffice to acquit me of extravagance.

The mortality of cases of fever of all descriptions among

all the European Troops in Bengal, has been as follows—for periods of four years since 1830:

1st period,	.....	3·06
2nd „	.....	2·52
3rd „	.....	2·40
4th „	.....	2·32
5th „	.....	2·07 and for

the individual years since then,

1850-51,	.....	1·24
51-52,	.....	1·01
52-53,	.....	0·99
53-54,	.....	0·76

Thus since quinine has been more extensively used, there has been a steady diminution of mortality—and whereas in the year 1830,—3·66, was an average percentage of mortality to cases treated, about 1 per cent. may now be counted the average, and this too not on the small scale—but in a body of at least 18,000 men, scattered throughout the different climates of the Bengal Presidency—from Peshawur to Pegu. In European troops in Madras also, among whom the mortality from fever has of late years been smaller than among the same class in Bengal, the mortality has within the last 10 years diminished about one-third.

Nor have the results among Sepoys been dissimilar.

The mortality among them also corresponds to a certain extent. It has been slowly decreasing, as will be seen from the annexed percentages of mortality:

1846-7,	.....	0·99
47-8,	.....	0·81
48-9,	.....	0·89
49-50,	.....	0·81
50-51,	.....	0·89
51-52,	.....	0·69
52-53,	.....	0·73

As however the mortality among them from fever has never been high, as they were never treated actively, as it is called, like Europeans, their fevers indeed not often requiring it, the change in their treatment has been less, and the effects of it are not so striking.*

* I am indebted to the courtesy of the Medical Board for the mortality of recent years, both among European and Native Troops. The figures for the earlier periods are from the Medical Board's Report published in 1851. Those for Madras are also from the published Returns.

The French in Algiers have had similar results, and believe that they have also made another important discovery, that though quinine conjoined with general bleeding was an improvement on the former practice, yet the full benefit of the quinine treatment was not obtained, till general bleeding was all but abandoned.*

As these results are mainly attributable to the use of cinchona and its salts, these substances will demand the chief share of our attention; nor is this to be regretted, as their uses were not fully known or taught in the English schools in former days, and although they are better known now, yet their use in tropical medicine cannot be dwelt on at length in the ordinary course of lectures in an English school.

Much also of the crude and empirical practice which has been of late years common in Bengal—is attributable to an imperfect acquaintance with the therapeutic history of Bark.

Therapeutic History of Cinchona.—A detailed history of the use of cinchona bark ought to be both curious and instructive. It would show that all the questions, that have arisen during the last 20 or 25 years respecting the quinine treatment, had been frequently discussed before. It would, however, necessarily include the whole subject of the treatment of fever, and I can here only glance at a few chief points.

Is Cinchona to be given before, during, or after the paroxysm?

1. The first method introduced into Europe, was that of giving the cinchona immediately before the expected paroxysm. Sydenham (in 1679) says, that its bad success 20 years before in London had brought bark into disrepute: nevertheless it remained the common practice in Rome, and it is recommended by Torti in 1758. This view was strongly taken up by Cullen. It has, however, not had many supporters either under the cinchona or the quinine treatment. "Immediately before" is too close on the paroxysm to give the medicine fair-play, although I have sometimes found it keep off or reduce the force of the paroxysm.

2. Talbor (1672), Sydenham (1679), Morton, (1694) considered that we should give cinchona immediately after the paroxysm, and go on with repeated doses every four hours until the next expected one. Bretonneau of Tours in modern times after studying the subject carefully, arrived at this result—"Begin giving the cinchona as far off from the expected paroxysm as you can." This seems to have been the

* L'Algerie Medicale.

commonest practice in the treatment of tropical fevers during the greater part of last century. With very few exceptions authors since that period have preferred giving cinchona in the remissions.

Since the discovery of quinine, and especially during the last 20 years, (quinine does not seem to have reached India till 1825,) practitioners have most commonly given it on the principles of Sydenham indicated above, *i. e.* commencing immediately after the remission.

The most important result that seems to follow, from this nearly universal consent of authors, as to the expediency of giving bark at the end of the paroxysm, is, that the system is at that particular time most susceptible of the action of the remedy, and the tendency of the latest practice is to show, that the best time for giving full doses is just when the sweating stage is going off.

3. Torti in 1756 appears to be the first who suggested in pernicious fevers the necessity of the use of cinchona during the paroxysms, although Sydenham, and still more Morton, had some inklings of this method. He laid down that it was to be given, whenever there was the least tendency to remission. Bretonneau, following up his views, laid it down, that cinchona was to be given in the middle of the paroxysm, the moment the pernicious nature of the fever was suspected.

Although Lind (1763) gave cinchona in immense quantities and without much reference to remissions, probably Clarke (1770 to 1780) may be regarded as the strongest advocate in the tropics of the necessity of immediately giving the bark even during the paroxysms. He found many followers, and as late as 1816 the Madras Committee* state, that in certain cases they give the bark, though no very distinct remission may appear. But during the prevalence if not the preponderance of other modes of treatment,† bark does not seem to have been often given in the paroxysms.

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* Medical Report on an Epidemic Fever.

† It has been supposed by some that the use of bark was at one time entirely superseded by calomel and blood-letting, but this is an over-statement of the case.

Towards the close of last century, and during the first quarter of the present, calomel and at a later period general blood-letting, had in the tropics, and especially in the East Indies, in some degree supplanted cinchona—still it never was abandoned—the very sensible report of the Madras Committee on a fever in the South of India, printed in 1816, relies chiefly on the treatment by bark. "There are a description of medical men in this country," they say,

Soon, though not immediately after the discovery of quinine, practitioners began to avail themselves of its virtues at an early period. Dr. Binns in 1832 in the West Indies was among the first of them.* Dr. Elliotson is one of the earliest English writers to recommend the early use of quinine in remittents.

M. Maillot may be considered as perhaps first who administered it in paroxysms—he was followed by a large party of the French army Surgeons in Algiers. The Americans followed in their steps in 1839, and by 1845-6 it had become a very common mode of practice in the new world. But the Americans seem on the whole to have practised it with less discrimination than the French.

In India the first distinct notice of the administration of quinine without reference to paroxysms, is by Dr. Corbyn in 1833, who steadily gave it in 7 or 8 gr. doses every four hours throughout all stages of a fever, then epidemic in Calcutta. In 1842, at the Madras General Hospital, quinine was given in 5 gr. doses every hour, on the least tendency to remission, however slight, with no bad consequences, even after it had been continued throughout the greater part of the exacerbation. Quinine was frequently given in this way in Madras, especially in the jungle fevers of Goomsur, and occasionally in Bengal,† when a great impulse to this mode of treatment was given by the appearance of Mr. Hare's pamphlet (November 1847,) which follows very much the line of argument of Dr. Upshur, of Norfolk U. S.,‡ and by the events, including the experiment at the General Hospital, Calcutta, that arose out of it.

Other questions were, in what doses are we to give cinchona and at what intervals?

1. Talbor, Sydenham and Morton gave small doses

" who suppose that in hot climates bark given for intermittent fever has the effect of bringing on abdominal obstructions, if calomel is not at the same time daily administered. To this opinion we cannot subscribe. It is an irritating and debilitating medicine, &c." Dr. R. Williams writes of a period a little later. "Bleeding and mercury, either separately or conjointly, having been proved to be insufficient, crude bark was very generally used between the tropics in the cure of remittent fever, sometimes throughout the disease, sometimes in the intervals." Dr. James Johnson's book, which gave a fresh, impulse to the calomel and still more to the blood-letting system, though it did not originate either, was published in 1813; but writing apparently in 1821 he says, "The treatment founded by Lind, Clark and Balfour continues to produce incalculable mischief."

* Lancet, 1846.

† Bengal Dysentery, by J. Macpherson, M. D., Calcutta, 1850, p.p. 57 to 68.

‡ Philadelphia Examiner, 1846.

repeated several times a day. This has on the whole been the commonest treatment—both when bark and when quinine were used, but has latterly been yielding to the system of larger doses.

2. Torti recommended a single large dose, and Bretonneau followed him in this. This has occasionally been followed under the quinine practice, but cannot on the whole be counted common in India until within the last few years. This method has been adopted by some both in Europe and in India, chiefly in intermittents, Pfeufer, Eittner, Meyer and others in Europe, giving a single dose of 10 grs. on a day free from fever, Dr. Holmes, in America, Dr. A. C. Macrae,* Dr. C. Mackinnon, and others in India,† giving a large dose of 20 to 30 gr. at the end of the paroxysm.

3. But if a large dose was considered by some to be most efficacious in stopping a paroxysm, most were of opinion that it is safer to continue giving smaller doses for some time after it. Sydenham, Torti and Bretonneau are agreed on this head, although the two latter advise larger doses than the first. About 1830 Dr. Elliotson was in the habit of giving one large dose in ague immediately after the fit to suspend the disease, and of repeating a few smaller ones. Under the quinine treatment the continuance of small doses, whether one large dose has been given or not, appears to be common in India. An instance of this is afforded, where Dr. Murchison, in a recent excellent paper on the diseases of Pegu‡, follows Dr. Elliotson's recommendation in his treatment of intermittents. Dr. Murchison indeed says that small doses were scarcely required after the single large one, but I have no doubt it is wiser to give them.

4. Torti may be considered as the first who gave very large or heroic doses in Europe; in this he was followed by Bretonneau. Lind, Clarke, and Hunter, all appear to have given very large doses of bark in the tropics.

After quinine was introduced, the first who seem to have given very large doses, were perhaps Bally and Maillot and their successors in Algiers; the physicians of the Paris Hospitals in 1843, Italian and American practitioners much about the same date.

In India, the use of very large doses has not been very common till of late years. Mr. Eyre, however, often gave one scruple and one scruple and a half doses in Goomsur in

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* Indian Register, 1848. † Indian Annals, 1853.
‡ Edinburgh Medical and Surgical Journal, 1855.

1835, and others occasionally pursued the same practice. The tendency of late years has been to give high doses, and this may be said to have reached its height, ("3 to 6 or even more scruples in the 24 hours in all cases of fever of malarious origin,") on the publication, in 1851, of the Bengal Medical Board's Report on Mr. Hare, who had advanced greatly on the more cautious 5 gr. doses, which he gave in 1847.*

The history of the use of large doses of quinine and of bark seems to point to the fact, that those who have exhibited them in the paroxysms have given the largest doses, from which it is perhaps a fair inference, that the doses given have been so large, because during the paroxysm the system is least susceptible of the action of the medicine. There seems also to be much to prove, that the use of a few large doses is more economical than that of many small ones.

The preceding sketch may give some though a very imperfect idea of the conflicting opinions that have prevailed respecting the use of cinchona and its salts, and the various modes of administering them, to which they have given rise. My object has been to condense, and thus I have been obliged to omit much.

There can be no doubt, that the last 20 years have witnessed a great change in the practice of medicine, whether caused or not by a corresponding change in the character of disease; that in all parts of the world antiphlogistic treatment has become less common, while a tonic and stimulant one has taken its place. At the present time this reaction may be considered to be at its height, and in it quinine plays the most important part, and on this account, though somewhat foreign to the specific object of these pages, a notice is given of its employment in a few other diseases besides fever.

Quinine has naturally had its advocates and its opponents, and it is not surprising that neither of them have been wanting in India. We have had its parsimonious use on the one hand, and its lavish expenditure on the other—a few oz. in a native regiment, or 22 lbs. in a European one, within the year.

Briquet's Work.—It is not too much to hope that Briquet's work,† the result of 11 years continuous experiment and observation, (some portions of which were published

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* Mr. Hare's Hints. Delhi, no date.

† Traité Thérapeutique du Quinquina et des ses préparations—Paris, 1853.

in 1848,) may lead to a more judicious and rational employment of quinine. While it offers a plausible explanation, to say the least, of many of the results which practical men in the tropics had arrived at, it determines more precisely than has ever hitherto been done, the comparative value of the various preparations, and salts of cinchona, and will tend to put a stop to the endless preparation of new salts from it. His views respecting its physiological action deserve, from their novelty and ingenuity, our most earnest attention, even if not in every respect our unqualified assent. Briquet is a warm but not indiscriminate advocate of the quinine treatment.

I now proceed to offer the following translation or abstract of Briquet's work from Bouchardat's Annual of 1854, adding a few notes which are marked thus[ ]. I regret that I have not yet seen the original, but no one could abridge it so well as Bouchardat.

PART I.

ACTION OF CINCHONA ON THE PRINCIPAL ORGANS AND PRINCIPAL FLUIDS OF THE ECONOMY.

A knowledge of the physiological action of quinine must afford the best means of arriving at an accurate knowledge of its therapeutic action.

Quinine being the most active of the constituents of cinchona, and that which best represents its action, and the sulphate of quinine being the most employed, and the most active of its salts, we shall commence by studying its effects on the various organs.

Action on Circulation.—Cinchona having always been considered a stimulant medicine, it was inferred as a matter of course that it must increase the activity of the circulation, and quinine since its discovery has been viewed in the same light, but experience is far from confirming the generally received opinion.

Sulphate of quinine modifies the circulation in three principal ways, by reducing the frequency of the heart's pulsations, by diminishing their force, and by its action on the blood itself.

First Modification.

Retardation of the Pulse.—1.—*On those in health.*—It has been observed by Giacomini, who experimented on himself

for 47 days, by taking every night from 45 grs. to 1ʒ of quinine, and whose pulse each time was reduced from 3 to 12 beats in the minute; by Revigli of Turin also on himself, and with the same results; by Guersant who, under the circumstances, has seen the pulse lowered 8 or 10 beats; and again by Dr. Favier on himself, who declares that by taking 12 grs. a day, at the end of two days he had a diminution of three, afterwards of ten pulsations; that with 48 grs. his pulse became insensible, and the heart gave 40 to 45 pulsations in the minute. Finally in some cases, where quinine was taken in poisonous doses by persons who were not sick, there was prolonged syncope, and the pulse had in a manner disappeared for several hours.

Duval and Beraudi are the only observers who have recorded an increase of the frequency of the pulse, but as they merely gave one dose of 15 grs. during a single day and at one dose, it is pretty certain that this increased frequency, which was only temporary, was caused by the sudden introduction of an active substance into the economy.

2.—*On Man in disease.*—In 190 cases of rheumatism treated by Briquet with sulphate of quinine, in doses generally from 15 grs. to 38 grs., and more rarely 45 grs. to 1ʒ per day, the lowering of the pulse was almost instantaneous; it took place during the first day of treatment in 120 of them, on the second day it was found in 144, and on the third in 155. The reduction was 7 to 18 beats the first day, 12 to 22 the second, 13 to 26 the third.

It was the more marked, the larger the dose of quinine had been. With doses of from 1ʒ to 1ʒ and 15 grs., it was on an average, 25 beats on the third day: with doses of 1ʒ 24 beats, with 45 grs. 20, with 30 grs. about 17, and with 15 grs. per day, about 4.

The lowering of the pulse was always proportionate to its preceding frequency. In patients whose pulse was at 60, the diminution varied from 12 to 3 beats. In those in whom it fluctuated between 70 and 100, it varied from 24 to 8, and in those whose pulse was over 100, it was as much as from 42 to 32 beats. The results of M.M. Blache and Briquet were analogous in 42 cases of typhoid fever, and this effect of quinine in lowering the pulse has been observed by all physicians who have used it in larger doses than 15 grs. M.M. Bally, Baudelocque, Jadelot, Kapeler, Guersant, Louis, &c. &c., have borne testimony to this fact. [Professor Van Buren*

* Medical Examiner, 1846.

in 1843 remarked that he had in two instances found 20 gr. doses act as a nervous and arterial sedative, reducing the pulse to the natural standard. Bence Jones* has recently verified these statements, finding that when he gave 100 grs. in the 24 hours, there was a marked reduction of the pulse. Dr. Barclay† also, of St. George's Hospital, noted the reduction of the pulse, and the general prostration produced by the exhibition of large doses in continued fever.]

Without choosing to deny so palpable a fact as this lowering of the pulse, some have ascribed it to the general amelioration of the patient's condition produced by the quinine, and not to any direct action on the heart. But on the other hand it cannot be supposed, in the very first days of its administration, to have ameliorated the condition of as many as 197 out of 232 patients: besides in eight fatal cases of typhoid, there was during the first few days of treatment the same reduction of pulse, as there was in those who recovered.

It was plainly observed, that whenever any inflammatory affection supervened during the course of the rheumatic or of the typhoid fever, or when any complication of either of these maladies arose, the quinine lost its power, and the pulse regained its frequency.

A good many observers have recorded that in inflammations of the serous or mucous membranes, quinine has caused a temporary reduction of the pulse, but this less generally than in the cases first alluded to, and they have also sometimes found, that the inflammation being more powerful than the quinine, the fever has continued unabated, and has even been increased.

We may conclude from the preceding facts:—

1. That sulphate of quinine in large doses reduces the frequency of the circulation.

2. That this influence is somewhat persistent, and often lasts for some days after the quinine is discontinued.

3. That it is exactly proportionate to the quantity of the salt given in the 24 hours (15 grs. appearing to be the limit, under which it does not produce an appreciable effect) and to the preceding frequency of the pulse.

4. That this lowering influence may be modified by circumstances.

5. That the action of the quinine is immediate and direct, and in no degree secondary to other influences.

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* Medical Times, 1855.
† Medical Times, 1853.

Second Modification.

Reduction of strength of Pulse.—At the same time that the pulse becomes slower, we observe in those who take more than 15 grs. of quinine, that the force of the pulse diminishes in a quite appreciable degree, and that the pulsations become small, feeble and soft.

This sinking of the pulse may go on to syncope, in cases where the dose of the salt has been excessive, as in some cases of poisoning.

All physicians who have used quinine have made this remark, and M. LeGroux, Physician to the Hôtel-Dieu, has especially insisted on this point, but as this observation is one that to a certain extent depends on the tact of the individual who makes it, and as it may therefore be in some degree open to doubt, it was deemed advisable to make the experiment on the lower animals.

Experiment showed, that if from 15 grs. to a scruple and a half of quinine, dissolved in about 100 times as much water, were injected into the jugular vein on the left side, the force of the pulse immediately diminished, as proved by one of Poiseuille's Hæmodynamometers applied to the carotid, and in proportion to the quantity of the salt used. If the injection of 30 grs. is made at intervals of from 5 to 6 minutes, the force of the pulse is diminished at once, but then recovers itself for a few instants, without however regaining its previous standard, and losing a little, each time the injection is repeated. If, on the contrary, the injection of 30 grs. is made at once, the force of the pulse gradually diminishes, and the pulse is indeed gone by the time the injection is completed, for the animal is dead and the heart has ceased to beat. There has been actual syncope, the heart is found to have lost its contractility, it is no longer excitable, it is distended, its right cavities are filled with dark blood, while the left are full of scarlet; in fact the heart has so quickly ceased to act, that the cavities of the left side have not had time to empty themselves; the heart has been as it were struck dead. It has been further proved, if the experiment is not pushed to causing the death of the animal, that the diminished force of the arteries may last for 24 to 48 hours. This last result corresponds with what has been observed in disease. The diminution of the force of the pulse, may vary according to the quantity of the salt injected, from an eighth to a third or even half of the ordinary force.

The diminution of the force of the pulse takes place not only when the salt is injected into the veins, but also when the experiment has been varied, and it has been injected into the aorta, into the stomach, and even into the cellular tissue. But in these cases it does not manifest itself till half an hour or an hour after; the diminution is slightly less than when the injection has been practised in the veins, but it is just as lasting.

In sick people sulphate of quinine given in doses less than 15 grs. does not produce any lowering of the force of the pulse, and its effect on the circulation is scarcely at all observable; if it is given in fractional doses, it excites the circulation a little; also if it be administered by the stomach in large doses, whether at one time, or at intervals not very wide apart, the circulation is still excited; in fact we must expect that during the first hours of the administration of the salt in large doses, whatever precautions are adopted, there will be a slight increased frequency of pulse and elevation of the temperature of the surface, and slight flushing of the face. But these effects are only transient, and give way to the sedative action, when the sulphate of quinine develops its true powers. [This explains why the action of quinine has been so often considered as exciting. Van Buren* as early as 1843 thought that small doses increased the febrile symptoms, while larger were sedative.]

Third Modification.

Alteration of composition of Blood.—It has been always believed that cinchona acts in some way on the blood. In former times physicians thought, in accordance with their speculative notions, that the Peruvian bark thickened the blood and coagulated the humors, and on this they grounded their opposition to it; of late years the converse has been the case, and the idea has been taken up, that sulphate of quinine makes the blood fluid, depriving it of its power of coagulation. This hypothesis, though it has seduced many sensible men, is only an error resting on a few facts imperfectly observed. The fact of the liquefaction of the blood is incorrect; in all animals that die suddenly from the effects of quinine, the blood is very solid, and firmly coagulated; nothing can be more striking than what we observe in the heart of an animal, who has been suddenly killed by an injection

* Loc. cit.

of quinine through the veins. We find, if the animal is allowed to get a little cold, an immense black, very hard coagulum, filling the right cavities of the heart, and a scarlet coagulum, equally large and hard, filling the left cavities. Dogs have been repeatedly bled before and after taking large doses of quinine, and after these doses, whether followed by death or not, the blood has always been found coagulated. Chemical analysis has indeed shown, that there has always been a greater proportion of fibrine after than before the action of quinine.

There is only liquefaction of the blood, when the animals, after being exposed for 2 or 3 days to the toxic action of the drug, have got lean, almost motionless and cold, nearly without pulse and respiration, and then the liquefaction, which is only observed after death, is the result of slow asphyxia.

As regards the theory which attributes the toxic action of quinine to the liquefaction of the blood, it is at once upset, by the experiment of the animal dying of syncope, at the very moment of the salt being injected.

In fine, the blood of animals and of sick people, who have taken large doses of quinine for some time, has been analysed and has constantly given the following results. An augmentation of the fibrine by more than one half on an average—a slight diminution of the globules, a still slighter diminution of the salts and the albumen, and an increase by a few hundredth parts of the proportion of water. [On this head perhaps more than on any other Briquet differs from the common opinion. As long as it was thought that large doses of quinine increased the fluidity of the blood, it was difficult to explain their beneficial effects in fever patients, who were believed to be already suffering from a too fluid state of blood.]

To what cause is the depression of the circulation attributable?—1. An action common to all deleterious substances; but experiments show that the injection of Hydrocyanic Acid, Strychnia &c., which produces sudden death, causes it by increasing the action of the heart, and augmenting the pressure of the blood on the arteries.

2. An indirect action exercised on the heart by the brain; but injections of quinine made into the carotids or the ascending aorta have always caused extreme agitation, a marked excitement, and an increase of the force and of the rapidity of the heart's contractions.

3rd. A direct action on the heart. To demonstrate the existence of this cause, all that is wanted is to make the

following experiment. A dog is killed quickly, his heart uncovered, and a solution of 1ʒ of sulphate of quinine is immediately injected into the aorta. On the very instant we see the energetic contractions of the different parts of the heart cease quite suddenly, or diminish very perceptibly, and end in stopping entirely, when the fluid of the injection has reached it. Injection of cold water, of acidulated water or of solutions of extract of nux vomica, will again reanimate the contractions.

There cannot, therefore, be any longer a question, that quinine has the property of destroying directly, by the simple effort of contact, the contractility of the heart—and we may consequently infer, that in the sick the retarding and weakening of the pulse depend on the passage into the heart, of blood more or less charged with the salts of quinine.

It necessarily follows, that when by too large doses of quinine the power of the heart is almost annihilated, a stasis of blood must take place in the capillary and venous circulation, causing fulness of the capillaries and injection of the large venous trunks, followed by passive injection of all the tissues. [Mr. Hare's theory of the use of large doses in fever is this. "Fevers destroy life by an accumulation of blood in the veins of the brain and abdominal viscera, and quinine has the power of stopping these accumulations."]

Action on the nervous system.—Action on the encephalon, the spinal column, and its dependencies. All that was known of the action of cinchona on the brain, was confined to a few phenomena of cerebral exaltation, passing delirium, and hardness of hearing. [This scarcely represents the amount of our knowledge either in Europe, America or India in 1853.]

The following observations have been made on an animal, into whose jugular a solution of 24 to 30 grs., or into whose stomach a solution of 1ʒ was injected in the space of a quarter of an hour. The moment the injection is made, if it has been made into veins, or 20 minutes after, if it has been made into the stomach, the animal resembles a subject in a state of drunkenness: he cannot see, his pupils are so dilated, that the iris can be no longer recognised, he does not hear, whatever noise is made near him: he scarcely feels blows or pinching, he is in a state of agitation, tries to run away, totters, falls on his side, or drags himself about quickly enough on his belly, with his paws apart: then after a few moments the agitation ceases, the animal falls on the

ground, and no longer tries to raise himself—he remains squatted without stirring: then commences the sedative action of the drug. The immobility continues, the respiration gets slower, the pulse becomes small and feeble, the skin gets cold, and after 12, 24 or 30 hours of this condition the animal dies. At the autopsy, no change is found, beyond more or less distinct injection of the capillaries, repletion of the large veins, and sometimes the blood not coagulated in the heart. If the dog has been bled during life, even 24 hours before the intoxication, the blood always coagulates perfectly. If the injection is made by the carotids, or by the arch of the aorta, the phenomena are a little different, the animal is agitated, his eye is lively, trembling, restless: he tries to fly by tottering or dragging himself on the ground, he may be seized with convulsions: his circulation and respiration are both accelerated; in short we see traces of the excitement caused by the direct contact of the quinine with the brain. The period of excitement is of shorter duration, and is quickly succeeded by the sedative effects. At the autopsy we sometimes find, if the animal has lived for some days, traces of acute meningitis and encephalitis.

Experiments therefore show that the first or the period of excitement is most marked, when the injection is made by the carotids, that it is less, when it is made by the ascending aorta—less when made by the the veins, and finally least of all when made by the stomach. They also show that this first period is the more intense and lasting, in proportion as the sulphate of quinine has been administered in quickly repeated doses; that it is the weaker and the less lasting, the longer the intervals at which the doses have been given, and this without reference to the exact quantity of the salt injected.

From whence the following important practical corollaries may be deduced :—

1. That the obstacle to the employment of quinine in large doses, is its primary action on the encephalon.

2. That this action is the more marked, the more suddenly the quinine is brought in contact with the brain, and thence the necessity, when we operate with small quantities of the salt, not to divide the doses too much, if we wish to produce a decided impression on the nervous system. We must then strike a blow. Thence also the danger, when we operate with strong doses, of giving the salt in too large quantity at once, or in too quickly repeated doses.

If we pass from these experiments on animals to sick men, we find a series of results perfectly analogous.

By examining them in detail, we shall be able to watch their course, their modifications and their nature, and to deduce most useful inferences for therapeutics.

Effects of large doses on man.—Suppose we administer to a patient with rheumatism 15 to 30 grains of quinine in about 100 times as much water, to be taken, a spoonful every hour.

At the end of an hour or two, we shall find vertigo, a slight uneasiness of the head, then succeed singing in the ears, slight deafness, some sparks of light, increased sensibility of sight; the figure becomes animated, the cheeks get flushed, the eye becomes more lively, the skin is hot, and the pulse gains a little in hardness and in frequency; this sort of paroxysm lasts an hour or two, then the agitation goes off, the patient falls asleep, and every thing is quiet.

If the dose is very large, as in cases of poisoning, such as 10 ʒs. taken in two days, or 5 ℥s. in ten, which has occurred, then, after some symptoms of excitement, the patients sink into a state of entire prostration; they move no longer, and are seized with a sort of general paralysis; they continue to understand, but they do not see, the pupil being extremely dilated and insensible to light; they go on to lose their hearing, they become almost unconscious of being touched, and insensible to heat or cold; the pulse is very small, slow and almost gone, the respiration is short, and the air only penetrates into the larger bronchiæ, and the skin is cold and discoloured; life may be prolonged for some days in this state. The following are some instances in which enormous doses have been taken. M. Guersent says, a lady was compelled by her mad husband to take 631 grs. within a few days. She lost sight, hearing, voice, and animal heat, but did not die. A mad physician took near 7 ozs. in 10 or 12 days, and died of prostration. Bence Jones,* from what he has seen of the effects of 100 grs. in 24 hours, is surprised that the patient did not die much sooner. M. Giacomini took 185 grs. by mistake, and fell into a state of syncope, from which however he recovered.

There are of course many intervening degrees between the two conditions of slight excitement, and entire prostration that have been just described; the doses mentioned by Briquet appear to me much larger, than are often required for toxic effects; any thing over 1ʒ to 1½ʒ daily *may* prove dangerous to life, though it is not likely to do so:

* Loc. Cit.

but the quantity will vary in each individual case, according as it is given in divided doses, and its effects watched.]

If we study more in detail each of the effects produced, we find—

1. *Headache.*—This is most usually a heaviness, an uneasiness, a confusion in the head; sometimes there are pulsations, or a feeling of tension, or like that caused by a tight band; in some rare cases, there is acute pain. Often it is attended with slight epistaxis. These headaches are generally transient and never of any importance. [No one should think of omitting to give quinine where it is necessary, on account of the patient's assuring him that his head cannot bear it, a very common thing]. They generally go off quickly of themselves; a few leeches behind the ears and cold water to the head will quickly relieve them, if they are excessive.

2. *Disturbance of hearing.*—At first there is buzzing or hissing; after a time the ear is disagreeably affected by sounds; they appear dry and hard, next the hearing becomes imperfect, and at last complete deafness supervenes. These effects are very common and are very easily produced. They are transient and yield easily; nevertheless in some cases of African intermittents, where the use of quinine has been very long continued, the deafness has remained complete and incurable. At the autopsy of subjects [as might be expected] no material lesions of the auditory nerve have been discovered. Such cases are to be treated by leeches to the mastoid process, cold applications, strychnia and galvanism. [Permanent injury to the hearing is not infrequent in India, and has been observed in the Deaf and Dumb Institution in Paris.* I have in several instances known officers attribute partial deafness of from 3 months to 2 years' standing, to quinine, and have frequently treated patients in hospital for it. Mr. Hare† has sometimes seen it last partially for a week. Prof. Van Buren‡ has seen intractable tinnitus aurium of 11 months' standing from small doses.]

3. *Vision.*—Affections of this sense are very common, and usually are limited to the presence of flashes of light. Sometimes the eye feels the light painful, and cannot fix itself on objects without being tired. In other more rare cases objects appear dim, smaller than natural, or double, and at last amaurosis may come on, with dilatation of the pupil.

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* Trousseau and Pidoux, Therapeutique.
† Indian Annals vol. I., ‡ Loc. Cit.

This condition is only seen in a complete and persistent state after quinine intoxication, and it leaves no material lesion in the encephalon. Commonly these affections of vision are unimportant, unless the doses are pushed very far. They are to be treated like the deafness. [Mr. Hare* has seen amaurosis last three days. Dr. Spilsbury† has seen excessive intolerance of light, exciting the suspicion of meningitis. In some cases which have occurred of amaurosis, the recovery seems never to have been complete. Van Buren‡ has seen an incurable case of amblyopia. Several cases of vision permanently impaired are detailed by Dr. McLean.§]

4. *Giddiness and Tremor.*—At first patients feel giddiness and shakiness when they sit up. Next they stagger and cannot go straight, when they wish to walk. This effect is constantly and very rapidly produced, and what is remarkable about it, is the length of its duration. Thus after treatment by sulphate of quinine with large doses, when the patient gets up for the first time, he is confused and staggers. The face gets flushed or pale, the eyes are confused, nausea supervenes, with tremor of the limbs, then there is a sort of syncope with slight convulsive movements; all this is relieved by the horizontal position, and a few drops of cold water. ["A dizzy stupid feeling, which seems to me very like delirium tremens."]‖

5. *Delirium.*—This has been called "ivresse quinique," because it is similar to the affection produced by spirits; commonly it is a sort of calm reverie, but sometimes it is an agitated delirium, with signs of cerebral and vascular excitement. This very rare, and by no means alarming effect, notwithstanding the exaggerated importance that has been given to it, ceases of itself after a few hours. It never lasts; acids, and at most a blood-letting cure it. [I am somewhat at a loss to know whether to allude under this head or under the preceding one to certain cases of tremor and delirium, which occurred in the General Hospital in 1849-50, and concerning the nature of which there was difference of opinion, the symptoms resembling, in some respects, those of ordinary delirium tremens, being on the one side ascribed to previous excess in drinking, of which there was not always proof, on the other, to the toxic influence of quinine. I presume that there now can be no longer any doubt as to the nature of

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* Loc. Cit. † Tran. Medical and Physical Society, Calcutta.
‡ Loc. Cit. § Illinois Journal, December 2, 1846.
‖ Mr. Hare's Hints.

a fatal case, in which there was entire deafness; this last symptom could be attributed to quinine alone. What Mr. Scriven* describes as a doubtful case of typhoid fever which was treated with large doses of quinine, &c., and terminated fatally, in which the patient "felt stupid from quinine, was deaf and staggered when he attempted to walk," was probably complicated with delirium tremens, for he "was suspicious, fancying some one was under his bed, that some one was coming to take his life, and so forth," most characteristic symptoms of that disease. He was bled twice, had leeches, quinine one scruple three times a day, and once a fourth scruple in the evening.

Uncomplicated ivresse quinique does not seem to be attended with terror. The following are some symptoms mentioned in a doubtful case transferred to my ward, which recovered. "Says his head is swimming;" next day "Restless all night, and has not slept, but lies quiet in bed. Pulse slow and weak, talks incoherently, little tremor."]

6. *Convulsions.*—This serious affection is excessively rare, and is only produced by rash administration of quinine. Briquet has never seen it, but authors mention examples of it; generally the convulsions have been only transient, but in some cases they have been the accompaniments of meningitis. Their treatment is antiphlogistics and opium in large doses.

[According to American authorities and Dr. Baldwin† convulsions have been not infrequent among children. Baumgärtner‡—has seen two cases in adults. There was a fatal case of epilepsy in the experimental ward of the General Hospital, but I am not acquainted with the details of the case.]

7. *Acute Meningitis.*—This effect is the most serious of all: but it is never produced by the simple employment of quinine—it has only been observed in cases of acute rheumatism. In that disease, treat it is as we like, cases of meningitis occur every now and then. It is therefore difficult to determine exactly what share the employment of quinine may have had in the production of this accident. Nevertheless, although there has been much exaggeration on the subject, it is rational to suppose that the salt, administered unskilfully, or in cases of extreme susceptibility of the brain, may have brought on inflammation of the

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* Medical Times, 1853. † Ranking's Abstract, vol. VII.
‡ Krankheit's Lehre.

meninges. [This refers to the fatal cases of rheumatism in Paris about the year 1843.]

8. *General collapse or typhoid condition.*—When only in a slight degree, and analogous to the condition of a patient with typhus of average intensity, the collapse is not serious, and it generally only occurs when high doses of quinine have been employed for some days successively. It has only been seen to produce grave effects or death, when the medicine has been given in poisonous doses. In such cases, there is almost entire absence of volition, of intelligence, and of motion, the senses are dulled, the skin is cold, the voice gone, the circulation and respiration are almost at an end, and at the autopsy nothing is to be found in the nervous centres, unless perhaps injection of the large vessels of the pia mater. [This was the case in an instance in which I was present at the post mortem.] The treatment is by excitants, stimulants, strychnia and galvanism.

9. *Paralysis of the extremities.*—This extremely rare accident has been sometimes observed, but it is only admitted as an effect, from the analogy which it bears to the results of experiments on animals.

Of the unpleasant effects just described, some, such as the heaviness of the head, the giddiness, the ringing in the ears, the slight disturbance of vision, are the ordinary and almost constant accompaniments of doses of 15 grs. and upwards. They begin to show themselves almost as soon as 3 or 4 grs. of the salt have been taken: they last as long as the salt continues to be taken, and endure after it, for about a period equal to that during which the salt has been used. These disturbances of the encephalon serve to mark the moment when the salt begins to act, and constitute the best proof of its action. Thus in cases of bad fever, it is necessary to produce those cerebral effects, to be sure of the action of the salt on the nervous system. Finally their duration shows that the action of the salt must have commenced, a considerable time before the doses of it were discontinued.

The other disturbances of the encephalon are really more or less accidental, and usually due to maladministration of the medicine in one dose, or in doses too closely repeated. However large the quantity of quinine given may be, it will never cause any trouble, if it is administered in fractions, and at sufficiently divided intervals, and if we have carefully explored the susceptibility of the patient's encephalon. [The dangers of the head affections appear to me to to be some

what understated, especially their production during the months of intense heat in India, and where the administration of large doses must be confided to subordinates, not always trustworthy. Mr. Hare, who has experimented more largely with quinine than most Indian practitioners, thus expresses himself.—"My orders to my apothecary were to give scruple doses to every patient with symptoms of fever, and they often thus got 40 grs., before I saw them. Numbers of small-pox patients were treated as the rest, with large doses of quinine, sometimes for 36 hours, before I could detect that disease. Almost all these cases terminated fatally. The same injurious effects of quinine were remarked also in delirium tremens cases and the febrile symptoms consequent on a debauch."* Were these latter cases of delirium tremens, or of ivresse quinique, or a compound of the two?

However this may be, the fact, as stated by Mr. Hare, is correct, that there was immense mortality among cases of small-pox treated with about 3 scruples of quinine daily. This is curious, as quinine in smaller doses has been recommended in bad forms of small-pox. I find M. Armand in Algiers† treating small-pox by mistake with quinine. He thinks its use was advantageous, but then his doses were smaller; 15 grs. the first day, and on each of the two succeeding ones, 7 or 8 grs. I made the same mistake in small-pox in 1844, and gave several 4 gr. doses without any bad result.]

In man therefore, as in the experiments on the lower animals, sulphate of quinine produces effects on the encephalon, of which two periods may be recognised, the first that of excitement, which we ought to know how to reduce, because it is the inconvenience attending the employment of the medicine, and the second a period of sedative action, which latter is what we wish to obtain. In man, as in animals, the too sudden effect on the brain of a large quantity of quinine produces excitement, while its gradual and continued introduction proves sedative.

Action on organs of respiration.—Quinine produces but few effects on the respiration: the principal of these are a slight præcordial anxiety, and in a few rare cases a transient dyspnœa, somewhat analogous to the effect produced on animals by cutting the pneumogastric nerve.

In toxic cases the respiration becomes slow, feeble, and

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* Indian Annals, vol. I. † L'Algerie Medicale, 1854.

almost disappears. On autopsy the lungs are sometimes found with passive congestion, but without any inflammatory lesion.

Action on digestive organs.—Cinchona bark having always been considered liable to irritate the mucous membranes of the digestive passages, and excite inflammation in them, irritating properties were naturally attributed to its salts; but this also is a mistake.

The sulphate of quinine leaves in the mouth a very disagreeable taste of bitterness, which we try to palliate by acids, by coffee, or by carbonate of magnesia: in animals no appreciable traces of irritation have been found in the digestive passages after large doses of quinine. In man the salt excites the appetite and favours digestion. When there is no fever and the digestive tube is in its normal state, we may, without inconvenience and without producing anything resembling inflammatory action, bear for several days high doses of quinine. But if there is fever present, or any inflammation of the digestive tube, whenever we pass 15 to 30 grs. we may produce inflammation, which would be of no importance if attended to in time, but which might eventually become serious, if we were to persist in giving quinine in spite of the signs of inflammation. Nevertheless it is not to be supposed that the stomach bears quinine with difficulty, for we have often seen cases of rheumatism take doses of from 45 grs. up to 1ʒ. for several days successively, without any sign of gastric irritation. The dread of severe gastritis or gastralgia is a delusion. Diarrhœa as a consequence of the use of quinine is the exception, while constipation is the usual effect. This constipation may be so obstinate, that we see patients taking 30 grs. of quinine daily, remain without any action of the bowels for eight or ten days, probably from torpor of the muscular fibres of the rectum. [The whole of this is important in its bearing on dysentery. I quite think the irritating effect of quinine on the alimentary canal has been greatly exaggerated; in the fatal case of quinine poisoning, which I examined, the coats of the stomach and small intestines were quite healthy.]

On Liver.—As sulphate of quinine does not readily excite the stomach to inflammation, it is clear that we need not expect to find any sympathetic affection of the liver after its use; and such is the case; scarcely any particular effect is known to be produced on this organ: we only know that in animals analysis discovers a great deal of quinine in the blood of the liver; this accords with the results of Orfila's

researches. [This may seem to favor Headland's view* that all bitters operate by their effect on the liver. It appears to be an undoubted fact, although some think otherwise, and one of great importance in tropical practice, that quinine has never been found to act injuriously on the liver; its general action has appeared to me useful in liver abscess, both before and after its bursting. Van Buren never observed any effect on the liver.]

On Spleen.—The case is very different with the spleen. Experiments made on the lower animals by M. Pagès, have proved that immediately after the introduction of 15 grs. of sulphate of quinine, the spleen, previously uncovered, changes its volume very apparently. [Dr. Smith, of Madras,† has also proved this general diminution of the size of the spleen; it is less when the medicine is given by the stomach, than when it is injected into the veins.] M. Piorry asserts that in fever patients with enlarged spleen, a diminution of the volume of that organ may be demonstrated with the plessimeter, a few seconds after the introduction into the stomach of an alcoholic solution of 15 to 30 grs. of quinine. But this is generally considered to be a fallacy. However, although most physicians do not admit the reality of this sudden shrinking of the organ, all agree that it gradually diminishes in size during the cure of intermittent fever, and all agree that no medicine produces this result so effectually as quinine. [This is true enough of recent enlargement of the spleen, but if it be old, and the organ indurated, quinine will often fail; other remedies, such as iodide of iron, &c., local applications, generous diet and change of climate are required. One of the early objections to the use of quinine was, that it was believed to cause enlargement of the spleen; and Piorry thought enlargement of the spleen was the cause of fever, thus putting the cart before the horse.]

Genito-Urinary Organs.—The quinine that is absorbed, is eliminated by the urine, and that fluid rendered more exciting, becomes a source of topical irritation to all the parts of the urinary passages with which it comes in contact. Thus in animals who die under the somewhat prolonged use of quinine, ecchymosed patches are found in the bladder.

In cases of gonorrhœal rheumatism quinine, by exciting the urethra, augments the discharge, and makes the rheumatism

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* Action of Medicines, 2nd edition.

† Medical Reports, Madras, 1850.

more active. In other patients pains at the hypogastrium are observed, and, though rarely, retention of urine, still more rarely cystitis, hæmaturia and dysuria. However these effects do sometimes occur. Use has been made of these effects of quinine to excite fresh irritation, with the view of checking chronic inflammations of the urinary passages, especially in chronic catarrhs of the bladder and in old gonorrhœas.

In women quinine produces frequently hæmaturia—and sometimes menorrhagia, and in some occasions it has brought back the menstrual flux which had been stopped. Many have thought that quinine in large doses may produce abortion, but more extended observation has shown that it has no power of making the uterine organs contract. [These effects on the genito-urinary organs appear to have been the least observed in India; its use in amenorrhœa is, I believe not infrequent in Calcutta, and is often successful. Dr. Cochrane* recently expresses a dread of quinine producing abortion—this can only be in heroic doses. However M. P. Jean in 1846, said that 15 grs. often caused abortion.]

On the Skin.—In some patients who have taken quinine for a considerable time, the appearance of exanthematic and psydracious vesicles has been observed. Applied upon the healthy skin, sulphate of quinine does not produce any important irritation: but when the skin is ulcerated, the case is very different; in powder or in solution, the salt produces in the parts with which it comes in contact, pain and inflammation, causes the formation of false membranes, and if its application is continued, may produce gangrene.

[*Some additional effects.*—M. Chevallier states that workmen employed in the manufacture of quinine are subject to a somewhat obstinate exanthema, and to a sort of quinine fever. But these facts have been but imperfectly observed.†

It may be correct to add to the effects of quinine on the skin, that with its sedative action it often produces profuse perspiration. It has been accused of causing alopecia, but on no good grounds.

Perhaps elevation of the temperature of the skin and increased calorification may be considered constant effects of small doses, while depression of temperature follows large ones; but Parkes‡ does not think the influence of quinine in

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* Charleston Medical Journal.
† Annales D'Hygiene, &c. vol. III. p. 5.
‡ Medical Times, 1855.

febrile heat very marked; in large doses it has been found to reduce the temperature about 2 degrees for a time, but it afterwards rises.

I cannot but wonder that in these days, when so much attention has been paid to chronic poisoning, a chronic quinine poisoning has not been described, as well as an acute one. I have seen derangement of the digestion, impaired vision, and a whole train of nervous symptoms and general irritability, apparently follow its continued abuse, but it is difficult to distinguish the effects of continued febrile attacks, from those induced by the quinine which has been used in their treatment.]

Such is a general review of the effects which sulphate of quinine produces on the principal organs of the economy.

Cinchonine.—The other active principle of cinchona has been found after numerous experiments on animals and long observation on man, to produce, in its state of sulphate, effects precisely analogous to those of quinine: it causes exactly the same cerebral disturbances, and the same degrees of them, a period of excitement and of sedative action respectively: its contact with the digestive tube is neither more nor less irritating than that of quinine, it acts on the spleen, it produces slight hæmorrhages and passes into the urine, exactly like quinine: only its power is less by about one-third. It produces just the same effects on the urinary passages and on the uterine surfaces, only in a smaller degree.

Experience had long ago proved, that, to stop intermittent fever, doses of cinchonine were required to be one-third larger than the doses of quinine, and this has been proved over again. It is absolutely certain that cinchonine is as good a febrifuge as quinine. The great advantage of employing it, is, that it costs infinitely less than quinine, that pharmaceutists would be able to make use of the cinchona barks that are rich in cinchonine and poor in quinine, and there would not thus be such urgent necessity for finding substitutes for that medicine. [It is impossible to exaggerate the importance of these facts, when owing to its price the poorer classes are so often precluded the use of quinine, and when its expenditure has become a serious item in the expenses of all armies. Four years ago the supply for the French army cost 400,000 francs. The Crimea expedition must have greatly increased the expenditure. Dr. K. MacKinnon tells me that the expenditure of quinine in Bengal last year was lb. 773, cost Rs. 72,391-11-9. Cinchonine is at least half as cheap as quinine, and the kinds of bark that are

in cinchonine are poor in quinine, and *vice versâ*—so that there would be a great saving of bark that is now wasted. The varieties of bark that first gave Peruvian bark its renown in Europe, were those that are richest in cinchonine.

Nearly all are agreed that cinchonine is a perfect substitute for quinine, nay some prefer it. Dr. Pepper* reports most favourably on some experiments he made with it in the Pennsylvania hospital: he almost prefers it to quinine, and found it succeed in some cases where that salt had failed. On the whole he cannot discover any difference in the antiperiodic effects of sulphate of cinchonine and sulphate of quinine—but perhaps the action of the first is rather the speediest. M. Forget has indeed reported unfavourably on cinchonine, but Dr. Hudellet of Bourg, in 503 cases found no inferiority to quinine. This was the result in Holland also with Basting, and Pereira and most authors consider cinchonine very little inferior.

We therefore have here a remedy of almost equal power with quinine, not nearly so bitter, and more than half as cheap—not a remedy such as salicine or bebeerine, of which the large doses that are necessary, prevent their being used with any economy as substitutes for quinine. The substitution of cinchonine for quinine would be a great saving to the Government of India, for the quantities imported are becoming very large. Dr. Murchison† ascertained that during the three years, 1851-52-53, there were sent to the three Presidencies, 3,804 lbs. of quinine, and 5,050 ounces of amorphus quinine besides 12000 lbs. of Bark, and this quantity is increasing.

Cinchonine is, I think, preferable to amorphus quinine, because its action and chemical composition have both been more completely ascertained, and it is quite as cheap.

With reference also to attempts to introduce the cinchona tree, into other countries, as the E. Indies or Algiers, it is well to know that it is not very important, whether the species is rich in quinine or in cinchonine.

Adulterations of sulphate of quinine with cinchonine, said to be frequent, become comparatively unimportant.]

Quinic Acid.—The quinic acid is in such small quantity in the cinchona, that it is evident that it can have little to say to its valuable properties, and as the substance is scarce and chiefly a matter of curiosity, Briquet has not investigated its properties.

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* Ranking's Abstract, vol. 20. † Op Cit.

Soft Extract of Cinchona.—The soft extract of cinchona made by decoction, which is much employed, has been experimented with. It is a compound, in which quinine and cinchonine combined with tannin and extractive matters, are presented in an almost insoluble shape. It was proved that in healthy animals and on sick men its action on the circulation and on the nervous system was the same as that of the salts of quinine: it appeared at first to produce less cerebral excitement, but this was the result of its want of power, not of any peculiar virtue. Its action on the nervous system and on the heart, and its febrifuge powers are to those of sulphate, as 1 to 4. It is indeed practically in this proportion that the extract has been used in medicine. This preparation may often be employed in enemata, and as a measure of economy.

Dry Extract of Cinchona.—The dry extract of cinchona, made by maceration in water, which contains only the more soluble parts of the bark, which water will extract, contains very little quinine or cinchonine. It consists chiefly of gum, tannin, coloring and extractive matters: it does not in any degree lower the action of the heart, on the contrary it somewhat increases the force of the arteries; it has absolutely no action on the encephalon. It can therefore be only regarded as a moderate tonic, representing the tonic properties of bark.

The wines, syrups and decoctions of cinchona, and the powder of that substance not being adapted for accurate experiments, have not been studied experimentally—but their therapeutic effects may be guessed, from what has been said above.

PART II.

MODE OF THE ABSORPTION AND ELIMINATION OF CINCHONA.

Absorption and Elimination.—The problem of the vital actions of this substance is now as easy of solution, with the aid of these new views, as it was difficult before. To solve it we must consider separately the two following orders of facts:—

1. Whenever the sulphate of quinine developes its action on our organs, phenomena are produced, which are described under the name of cerebral disturbances, so that the development of that very perceptible, and constant disturbance, where the sulphate of quinine is given in sufficient dose, indicates the point when its action commences.

2. As soon as the quinine is absorbed, it appears in the urine; it is recognised there by means of the deutiodide of potass in solution, which is a sufficiently strong test to produce an abundant precipitate of the colour of powder of cinchona, in a solution of 100th part of a grain of sulphate of quinine in an ounce and a half, of water, and it is always found there in a quantity exactly proportioned to that which has been taken. [Mr. Herapath has discovered a still more minute test by getting crystals of sulphate of iodo-quinine.]

With these two modes of research, we can determine with exactness the moment when the absorption of the salt takes place, the instant when its action begins to be felt in the different organs, the duration of that action, the period that the quinine remains in the economy, and the moment when the absorbed salt is eliminated.

1. The absorption of sulphate of quinine takes place very rapidly; thus by the aid of our test, we find it in the urine in one or two hours, after 15 grs. have been taken in a single dose, and in six or eight hours after a dose of from three-fourths to a grain and a half. It must be admitted, that the salt must have remained some time in the blood before passing away in the urine.

We conclude from the above, that to produce sufficient absorption, where prompt action is required, it is necessary to give doses of at least 15 grs., and that on the other hand we are sure that even with small doses, the absorption has taken place in a few hours, and that consequently the cinchona, which it was supposed was absorbed only at the end of 12 or 15 hours, is so at the end of half an hour or more with large doses, and at the end of 4 or 5 with small ones.

2. This fact not being quite sufficient, it would be desirable to ascertain the precise moment of the action on the organs.

But the cerebral disturbances show themselves about an hour after a few doses of 8 grains, and at the end of a quarter of an hour after the same of 14 grs. The absorption must take place rapidly, for $\frac{1}{4}$ of an hour or $\frac{1}{2}$ an hour, are enough for the cerebral disturbances to have reached their maximum.

It would be extremely useful to know the duration of the action on the organs, but that could be easily learnt by observing the duration of the cerebral phenomena.

We observe that after the ingestion at once of six grs. of sulphate of quinine, the cerebral phenomena last for 2 or 3 hours, that after the ingestion of 15 grains at once, they last

for 3 or 5 hours, and that after 15 grains have been taken in several doses during 12 hours, they do not go off for 8 or 10 hours, and that after 45 to 60 grs. have been taken, they last one or two days.

We may therefore conclude, that the action of a dose of from 30 to 45 grs. may last for 36 to 48 hours; and experience shows that a dose sufficient to keep off one paroxysm of tertian fever, retains sufficient hold on the economy, to keep the next one off also.

The sulphate of quinine therefore penetrates very rapidly into the blood, and distributes itself from it to all the organs: chemistry has always found it there, when it has sought for it—but experience shows that it does not remain there long, and that no given dose remains there longer than 48 hours. The salt does not combine in any way, and does not unite, at least in any appreciable way, with the tissues, for at the end of 24 hours there is no trace of it after a dose of from 2½ to 4 grs., of 40 hours, after a dose of 30 grs., and at the end of 2 days and a half, after as large and as prolonged doses as can be given.

The urine is the chief channel of elimination, for it is found in it, almost as soon as it has been taken by the mouth, and its presence can always be detected as long as the salt continues to be taken, and in quantity proportional to that which has been swallowed. In fine the urine bears trace of it for 24 to 48 hours after it has ceased to be taken.

Quinine has been found in the serous fluid of dropsical patients who have been taking it. It has been said to have been found in the tears, as well as in the milk of nurses. But the quantity that has been detected in the latter fluid, is so infinitely minute, that it need not be taken into consideration in our treatment of infants at the breast.

The action of quinine on the various organs is modified by the following circumstances:—

1. The young of animals and infants bear quinine in doses almost equal to those of adults, without any observable cerebral affections. [This is contrary to the received opinion, for small doses, (eight grains given in two doses at an interval of three hours to a child of six, Baldwin*) are said to have produced narcotism in children. I confess that I have never seen any disagreeable effects follow the free use of two grain doses in very young children].

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* Southern Journal, 1848.

2. Women, on the contrary, do not bear quinine so well as men. They absorb more rapidly by one-fourth. The salt acts on them on an average abont one-fifth more powerfully than on men. [This is practically known to every one].

3. Strong and large subjects bear three or four times larger doses than subjects who are weak, delicate or sickly. [This would explain why large doses may be given much more freely in military, than in ordinary civil practice; also why, during the experiment at the General Hospital of 1849-50, what the French call Quinic accidents, occurred chiefly in the general, not in the regimental ward.]

4. A sanguine, an athletic, or lymphatic temperament admits of large doses being tolerated. On the contrary thin, nervous, and irritable subjects, and those in whom the nervous system predominates, can only tolerate much smaller doses. The first class of subjects is apt to have the sedative action of the salt on the circulation too strongly marked, the other class to experience accidents on the part of the encephalon.

5. A febrile condition makes the depressing influence of the salt on the heart be less felt, and it predisposes to head affections. A non-febrile condition, on the other hand, allows the largest doses to be given without accidents.

6. Blood-letting produces some peculiar effects. 1. Practised before the ingestion of the salt, it renders subjects more susceptible of its action. [It was no doubt on this principle that Maillot, in addition to his large doses, recommended bleeding in 1836, though he afterwards abandoned it, Mr. Hare "believes that moderate blood-letting greatly assists the absorption of quinine into the blood."] 2. Practised after the ingestion of the salt in cases where it has produced toxic effects, blood-letting is useful, if those effects are such as are dependant on cerebral excitement, but it is hurtful, if they are the phenomena of prostration and of syncope that are present.

7. Excitants, such as alcohol, wine, coffee, &c., taken before and during the administration of sulphate of quinine, tend powerfully to neutralize its effects. They have a sort of opposite action to that of this salt; but if any of the accidents accompanied with too great depression have taken place, then excitants become necessary. ["Mr. Hare says* a few glasses of Sherry will almost entirely remove the dizziness caused by a large dose of quinine."]

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* Hints, &c.

8. The salts of morphia administered along with the quinine produce a double effect. They moderate considerably the exciting effects of the primary action of the quinine, and they augment the sedative effects of the secondary one. [I believe many practitioners in India are in the habit of adding small quantities of laudanum to quinine, with undoubted advantage, a practice which has descended to us from the bark treatment.

The use of antimonials along with quinine is a more doubtful practice. The addition of a moderate saline purgative to a dose of quinine, does not appear to interfere with its action. Little is known with any accuracy of the effects of quinine when united to other antiperiodics, and such unions have often led to an imperfect appreciation of the effect of each medicine separately.]

Tannin instantly arrests the absorption of quinine by decomposing the sulphate at once, and forming a new salt with it, which is completely insoluble and consequently inert.

All the preceding results are common to quinine and cinchonine: these two alkaloids always act exactly in the same way.

It is plain that the operation on the economy of the coloring matters, of the tannates, of the gums, and extractive matters of cinchona, is not subject to the preceding laws: they are simply ordinary tonics, which, like other ones, have no medicinal powers that can be compared with the true action of quinine.

PART III.

APPLICATION OF THE PROPERTIES OF THE ALCALIS OF CINCHONA TO THERAPEUTICS.

Application to Therapeutics.—From all the preceding researches, it follows that the alcalis, quinine or cinchonine, administered in portions or in doses not exceeding 3 or 4 grains, may be considered as at most slight stimulants, but that in larger doses their mode of action changes, and this change is the more decided, the stronger the dose is.

Thus from quantities of 15 grs. of the bisulphate of quinine and above it,—[Van Buren said 15 to 25 grs.] we at first observe a slight degree of excitement of the heart and of the encephalon, with congestion of the pia mater; these effects do not last long, and constitute the first period of action. But a second period soon supervenes, in which the sedative action predominates:—1. In the heart, where it may proceed to the absolute extinction of its pulsations. 2. In the

brain, where it produces giddiness enough to make the patient fall : the disturbance of the sight may go on to amaurosis ; that of the sense of hearing, to deafness ; that of smell, till odours are imperceptible ; that of the mouth, till tastes can be no longer distinguished ; and the general disturbance of sensibility till the sense of touch is destroyed ; the disturbance of the trisplanchnic nerve, to the arrest of respiration, and prevention of the production of heat ; in fine to disturbance of the spinal column and paralysis of the limbs. [This sedative action of quinine was announced by Briquet in 1848. It was not even then absolutely novel, for Dr. Mojor, 1830, Professor Van Buren, 1843, Italian Physicians, 1844, and Favier, 1848, had all arrived more or less at the same conclusion.]

At the same time that the alcalies of cinchona have such powerful sedative action, such complete command over the nervous force, these substances, by the way of molecular absorption, are irritants to the surface on which they are applied, for they excite in a very evident, though not dangerous degree the surfaces with which they come in contact, as we have seen above.

In fine, these alcalies given for some time in high doses, increase the quantity of fibrine of the blood in a marked degree as well as that of the water, diminishing at the same time a little the proportion of the globules, the salts and albumen.

This double action of the salts of cinchona is common to them with chloroform, the ethers, hydrocyanic acid, &c., all of them substances very stupifying by absorption, and very irritating by contact. [It is curious that several such substances have been used in intermittents.]

The alcalies of cinchona lower the power of the nervous system, at the same time that, by contact they act as excitants. This lowering action is so great that, like hydrocyanic acid, they may destroy the nervous power entirely.

This mode of action explains very clearly the various applications of cinchona in therapeutics.

Action on Intermittent Affections.—The most delicate point, and one of which it has never been possible to give a satisfactory explanation, is its influence over intermittent diseases. But it is precisely by studying its effect in those cases, that we can arrive at the most important results respecting its therapeutic action.

Intermittent affections are very numerous and varied, comprehending fevers, inflammations, hæmorrhages, neuroses

neuralgias, all maladies, which have only two things in common—1. Their intermittence, that is to say, having intervals separated by complete apyrexia.—2. The fact of their being strangled, or, as it were, knocked on the head by cinchona. It is therefore the intermittence that cinchona attacks.

We know that intermittent affections may be caused in very different ways, by paludal miasma, sudden transition from heat to cold, by moral emotions, by irritations of any part of the nervous system, by alteration of the blood, inflammations of certain mucous surfaces, by diseases or simple tumefaction of the spleen, &c.

It is impossible to admit, that cinchona, given as it is in all intermittent affections, can have the power of acting on all these so varied causes, in such a way as to destroy all of them at once. It therefore follows, that its action must be on the effects of these causes, and further that it must act on the effect, which is common to them all: but on analysis we find that they have no effect common to them, except the action of the nervous system, which is set a-going by an access of fever.

An access of fever is an act of the whole economy, a sort of pathological action, in which more or fewer of the organs, which are connected together by the nervous system, concur. Further this synergic function is always excited by a lesion of part of the nervous system: for example by the lesion of the urethra by catheterism, which may have provoked an access of intermittent fever. In this case there is a communication between the part irritated and the common nervous centre. From this nervous centre will be sent along the different portions of the nervous system, influences, under which will take place the various vital actions constituting the three stages of ague.

We can find no bond of union in these intermittent diseases, except this intervention of the nervous system, which is necessary to constitute the various successive acts of the intermittent access, and indeed without the intervention of which it is impossible to conceive its formation.

Cinchona precisely possesses the power of preventing this intervention of the nervous system. It is an agent which breaks through the meshes of the net work employed by the nervous agent to excite the fever.

This interruption can only be effected in three manners: —1st by augmenting, by virtue of its tonic influence, the resistance of the economy to disturbing causes: but cinchona is the only true antiperiodic, yet there are a thousand sub-

stances as tonic or more tonic than it, and yet which have no antiperiodic virtues. 2nd, by a disturbing cause, by exciting an organic disturbance strong enough to prevent the pathological action in question from taking place. But it is evident to every unprejudiced mind, that 3½ to 5 grs. of sulphate of quinine, which are enough to stop a fever, do not actually produce any disturbance sufficient to interfere with so marked a pathological action as the production of a fit of fever. 3rd, lastly, by a sort of stupefaction, disabling the nervous system from being able to put together all the synergic actions which constitute a febrile access.

It is precisely in this last way that the alcaloids of cinchona appear to act, for they are stupefacients, anæsthetics par excellence. [It may be considered as a triumph of chemical sagacity that Liebig long before the narcotic effects of quinine were known, prognosticated that in its action it must be similar to morphia. Led away by the strong resemblance which Liebig has shown to exist between the taurine of the bile and quinine, Headland* suggests that quinine may exercise its action by taking the place of taurine, and finds the bond of union in tropical diseases in the liver, and therefore thinks that quinine and bitters cure by their action on that organ. It may be remarked however, that gentian, quassia and other bitters in large quantities ars known to act very distinctly on the nervous system.] We have seen that they can destroy the nervous power in all parts of the nervous system. These alcalis act like arsenic, opium, chloroform, hydrocyanic acid and all the best known febrifuges. But all these substances have very strong depressing or anæsthetic action on the nervous system.

This theory, founded on many considerations, of which only a short summary can be here given, conducts in the most satisfactory manner to the rational treatment of fevers.

Rational Treatment of Fevers.—It shows,—1st. That by adding to sulphate of quinine, an opiate preparation, which increases its lowering effects, we increase the power of the febrifuge.—2nd. That to produce the greatest possible lowering effect with a given dose of quinine, the doses should not be too far apart, for fear of the action of the medicine not being continuous.—3rd. That again it does not do to give the medicine only once, lest its effect be too transient.—4th. That the sulphate of quinine should be given solely during the apyrexia, because that is the only time when the

* The Action of Medicines, 2nd Ed. 1855.

nervous system can be stupified, so that at the hour when the access should come on, the system in its lowered state may not be able to conduct and direct the synergic acts, which are necessary to the production of a febrile access. If we give the sulphate of quinine, so that its action will be produced during the cold stage, we run the risk of killing as it were, by the stupefaction it may produce, the nervous system, of preventing its being able to bring about reaction, that is the febrile heat, and possibly of killing the patient in the cold stage. If, on the other hand, the quinine is given so as to act during the second stage, its action would be null, as the over-excited economy would resist its sedative operation. Besides, as the sulphate of quinine acts by preventing the access, and it is evident that when the period of heat has arrived, the access has taken place—its vocation is by that time as it were gone, and it then can have no effect except on the next access: the effect therefore would be feeble, as the quinine would be presented to the nervous system, exactly at the moment least favorable to its sedative action.—5th. The more powerful the cause of the intermittent malady is, that is to say, the stronger the access is, the larger does the dose require to be, and this explains the necessity of doses of from 30 grs. to 1 ʒ. in the course of the day in the simple or the pernicious intermittents of hot countries.—6th. That the more the accesses of the intermittent are periodical, the easier it is to cure them, because we can give the quinine exactly at the suitable time: whereas when the accesses are irregular and non-periodic, we often fail, from not knowing the exact time when to give the quinine. In such cases we often only succeed by making the accesses regular, which has been done with success in cases of epilepsy and of hysteria.—7th. That the more the intermittent disease is compounded of a great many acts linked together, the more the access requires regular synergic action, the more easily can this complex whole be upset, and the disease cut short. On the contrary the more simple the intermittent malady is, and the successive fever acts of which it consists, the more difficult it is to disturb and cure it. Thus an intermittent fever, consisting of very composite acts, is very easily cured by a few small doses of quinine, while a neuralgia, consisting of comparatively simple actions, is difficult of cure, and may yield only to high doses.—8th. That the cinchona is only a palliative, the action of which is limited to the prevention of the access, to placing the nervous system out of a condition for a certain time to respond to the morbid causes which act on it; but it has not the slightest action against the causes themselves: thus in a fever

caused by marsh exhalation, or in a neuralgia caused by any irritation, the cinchona has no action on the miasma, nor on the primary cause of the neuralgia, and yet it cures. In this way the patient, if he remains in contact with the miasma, will get his fever back, as soon as the stupifying influence of the quinine has gone by, &c. [This is unfavorable to a very common and old notion, that the use of quinine is a prophylactic against fever. I have no faith in 2 or 3 grs. of quinine taken every morning, doing more than acting as a tonic, or giving the patient confidence. However, practical men in the navy seem satisfied of their usefulness, and it may be as well to employ them.]—9th. That in its simple palliative action, quinine has no power over the alterations which accompany intermittent diseases (the affections of the spleen excepted,) and that these accompanying affections must be treated separately.—10th. That the cinchona is only in reality curative in intermittents, of which the cause is transient, or has been removed, or is not a very powerful one. It results from this important consideration, that if the intermittent affection is fully and permanently cured, and there is any accompanying persistent organic affection, that organic alteration cannot have been the cause of the intermittent attack.

For instance, suppose there is tumefaction of the spleen, after a fever has been cured. If this co-existing affection is really the cause of the intermittent fever, the latter is only checked for the time; it will re-appear a little sooner or later. Or suppose the hectic fever of phthisical patients; it is easy enough to stop a daily paroxysm with quinine, but it usually soon re-appears.

Cinchona, or more properly its alcaloids, are the certain specifics for intermittent diseases, and it is always right to employ them, using at the same time such subsidiary remedies as may be necessary.

It follows from the above, that our great object in ague is to give quinine so that the maximum of its action may be at the time of the expected paroxysm.

Remittent Fevers.—According to the preceding principles, cinchona ought to be employed in remittent just as well as in intermittent diseases, because the manifestations of both depend on the intervention of the nervous system.

The only difficulty consists in being able to distinguish true from pseudo-remittents: that is to say those in which cinchona should be given, and in which it acts as a specific, and those in which it should not be given, and in which its action is uncertain.

The first class consists of the remittent fevers of marshy places and of hot countries. In them there is no doubt, and it has been proved by the best observers, that quinine is a real specific. [It is, however, by no means equally so in all. The more remittent the fever is, the more useful it is.] The case of the second class of remittents of temperate climates, is more doubtful; you must there watch the disease, and give the quinine accordingly as you may or may not be able to recognise any remitting action. If you observe that there are exacerbations, it necessarily follows that there must be some degree of remission.

As remittents are always the product of a more powerful agent than that which causes intermittent fevers, it is evident that cinchona must be given in the former in much larger doses than in the latter. [I have thought it most convenient to give under the head of *dose*, the opinions of various authors on this point.]

The third class comprehends febrile actions the result of the absorption of pus or of tubercular matters, &c.; you may in these cases by high doses produce at least temporary benefit from quinine, which as it were, depresses the tone of the nervous system, so as to make it insensible to the action of pus.

From this an important practical rule may be deduced. In intermittent maladies for which quinine is exhibited, small doses are enough to prevent returns. In maladies on the contrary for which quinine has no natural suitableness, the doses must be greatly increased to prevent relapses, and after a time a period will arrive when its power ceases.

A fourth class, considered by M. Briquet, consists of certain inflammatory diseases with remissions, such as erysipelas or phlebitis—he considers them to be a series of inflammations preceded by febrile attacks and rigors, and these attacks may be as it were strangled by large doses of quinine. But we cannot follow M. Briquet into these details, or into subjects not connected directly with tropical medicine, beyond giving some of his results in a few important diseases.

Encephalitis.—Experience has proved that sulphate of quinine in high doses has frequently stopped the development of encephalitis, and has cut short idiopathic convulsions.

This fact is constant and has been frequently observed: it is explained by the stupifying action, which quinine in large doses exercises on the brain. Thus when at the commencement of these attacks, and while fever has not yet set in, the brain is stupified and deadened by quinine, it is unable to

become a centre of action, and inflammation and convulsions are alike put an end to.

Observation having superabundantly proved that the sulphate in large doses is a sedative and a narcotic, Briquet has often used it with these objects, and he has often found it succeed, when other narcotics had failed. [In the form of fever with violent head symptoms, which often mask the fever itself, and which has been variously described as meningitis and gastro-encephalitis, generally considered a variety of remittent fever, a disease of extreme fatality, M. Lagrave says, that whereas under repeated blood-letting 21 out of 22 cases proved fatal, in 19 cases in which quinine was administered in doses of from 8 to 24 grains, there were 13 recoveries, and M. Armand* thus sums up. "It is admitted that ether inhalations by themselves produce good effects, that opium by itself sometimes cures, that sulphate of quinine by itself has furnished still more cures, and that a union of these three remedies boldly employed will probably prove as successful, as the antiphlogistic plan has been the reverse." These cases occurring chiefly in barracks and among conscripts, have a good many points of analogy, though they are not identical, with the Indian "apoplexy of the hot winds," a disease requiring further investigation.

The injurious effects which we have seen attributed by Mr. Hare to the use of large doses in delirium tremens, would, according to these views, be a proof of that disease not being the result of meningitis or of encephalitis, as some have supposed. Their injurious effect is probably owing to their too sedative effect on a brain already suffering from debility.]

Typhoid Fever.—Briquet and Blaque have treated sixty cases with quinine, giving about 1 3. daily, in hourly divided doses for twelve hours. The general result of their experience is, that this mode of treatment is only adapted for certain definite forms of the disease; perhaps certain epidemics, or under any particular circumstances, such as the presence of cholera, which may prevent the adoption of other modes of treatment. The use of quinine should not be continued for more than eight days.

The most apparent effects are those produced on the circulation and the animal heat, and on the derangements caused by the disturbance of the encephalon.

Thus the fever is undoubtedly influenced by it as respects the pulse, which in a few days may be reduced 20 to 40

* L'Algerie Medicale.

beats in the minute, and as respects the temperature of the skin, which from a dry feverish heat, may be restored to a normal condition.

We may also, by quinine, anticipate as it were the visceral congestions and inflammations, which are apt to arise from the continuance of the febrile state.

The prostration, the headache, the giddiness, the delirium and all the phenomena of cerebral congestion are ordinarily dissipated in a few days; and the patients in their improved state resemble persons awaking from profound sleep.

The irritant action of quinine on the mucous membrane of the stomach is very slight, and can scarcely ever produce bad effects, except when there are evident signs of inflammation of the upper part of the digestive tube.

[Views similar to these respecting the effect of quinine on complications of remittent forms of fever had been arrived at long ago, in fact they were a necessary consequence of the quinine treatment. M. Faure*20 years ago—describing fevers with symptoms of pleurisy and pneumonia, says—"If I had persisted in treating them with general or local sanguineous evacuations, I should without doubt have hastened the death of patients, whom sulphate of quinine would have saved with absolute certainty." In 1846 with reference to the employment of sulphate of quinine in the form of meningitis just alluded to, M. Lagrave writes.—"It sometimes makes the headache disappear rapidly, along with the delirium and the pains in the spine." Dr. Bartlett, of Philadelphia, in 1847, in his work on fevers, having the experience of the preceding seven years before him, says that the readiest way of relieving the local congestions is to cure the disease on which these congestions depend, and this is to be accomplished by the anti-periodic action of cinchona. Mr. Hare, 1847, has the merit of being the first in Bengal to insist on this point, when he asserted the principle, that "if quinine be given freely it will prevent the congestions and complications which end in death." This in theory: but practically during the experiment at the General Hospital, he lost four cases by pneumonia.]

The cases best adapted for the treatment are, when the typhoid fever is accompanied with very distinct and marked remissions, as in such cases the disease is commonly easily arrested by giving it during the remissions. This treat-

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* Quoted in L'Algerie Medicale.

ment also is suitable, when the fever runs very high, and the temperature of the skin is much raised, when the disease is accompanied with marked cerebral phenomena, delirium and agitation, and in ataxic forms.* [This is far more precise than the vague advocacy of quinine as a specific in continued or typhus fever, which is at present so common in Europe. It may be remarked, that what is now termed typhoid fever, and characterised by ulceration of Peyer's patches, is the form of fevers of high latitudes, which comes nearest to the remittents of the tropics. Mr. Scriven† found these patches diseased in some fever cases in Pegu. This was also often the case in an epidemic in Calcutta in 1848. I found them altered at that time in several cases in the General Hospital, where I may add, my treatment with very little quinine was singularly unsuccessful. Mr. Scriven, however, found his quinine treatment equally disappointing. I have not omitted the section on rheumatism, as it gives a detailed description of the effects of the drug.]

Acute Articular Rheumatism.—M. Briquet has treated 250 patients with sulphate of quinine; a few had somewhat more than 13. daily, others from 30 to 45 grains, and the greater number 15 to 30 grains daily.

The sulphate of quinine was given in solution, a spoonful every hour during twelve hours of the day; as adjuvants, simple drinks and opiate cataplasms were used.

The pains had disappeared in the first ten days of treatment in 100 patients. There were only 30 patients who had any pain at the end of 20 days. In only one case did the malady run into the chronic stage.

In the curable cases, the average duration of the pains was 10 days from the commencement of the treatment. The appetite generally returned early.

The effects on the pulse have been already detailed.

In the patients who took the largest quantity of the salt, the stay in hospital was about seventeen days.

In those who took a medium quantity, 24 days, in those who took least, 26 days.

The average period during which the quinine was given, was 6 to 8 days.

The articular pains yielded after one day in 37 patients, at the end of two in 73, and at the end of five in 36.

Consequently 146 patients were greatly improved at the end of three days. In the others the amendment took

* Op. Cit. † Medical Times, 1853.

place on the fourth, the fifth and the ninth day, and in a very few on the tenth and twentieth.

The convalescence was generally the more rapid, as the patients had not been worn out or pulled down by the treatment.

In fine, sulphate of quinine acts in rheumatism not only by moderating the circulation, but through its depressing effect on the nervous system by preventing the metastases which characterise this erratic complaint. It is best suited for anæmic patients, in whom the disease attacks several joints successively.

[Notwithstanding these very favourable accounts, we must not forget, that in the hands of Bence Jones* and others, it has not been successful, and that it was the imprudent use of quinine in rheumatism that led to the sudden deaths, which gave the salt in high doses a bad name. Grisolle† thinks that relapses are more frequent under this than under any other mode of treatment. As Briquet attributes the advantage of the quinine to its narcotising effect, surely similar results may be obtained more safely with opium. A few trials I made of 20 grs. daily in rheumatism, were disappointing. Dr. Heymann‡ records great success in Java with doses of from 30 to 90 grains in the 24 hours, but only in the acute articular form.

Dysentery.—It has been long supposed by many, that this malady, the treatment of which is in so chaotic a state, is, like fever, dependent on malaria, and consequently is a remittent and intermittent disease. In fact Sydenham described a dysenteria febricosa and an intermittens. Mr. Hare has of late years in Bengal,§ following in the steps of various modern authors, called attention to some forms of dysentery which he considers to be malarious; but M. Armand‖ goes much further, and believes that every case of dysentery, if carefully watched, will be found to be remittent or intermittent; the natural corollary from this is, that cinchona, as it cures fever, must cure dysentery also.

Now with respect to dysentery, as it occurs in Bengal, and more particularly in Calcutta, the apyrexia in most cases is very remarkable. I have never seen intermittent dysentery, and not very frequently fever associated with it,

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* Medical Times, 1855. † Pathologie Interne.
‡ Krankheiten der Tropen länder, 1855.
§ Report of Medical Board, 1851. ‖ Op. cit.

although I have occasionally. Cambay* and Haspel, two of the most practical men that have written on the diseases of Algiers, agree that they have never seen intermittent dysentery, though they have seen it complicated with fever.

With respect to the use of quinine, Cambay says, that he has cured the fever with it, without curing the dysentery, and states generally that, at least in Oran, the province where he has chiefly practised, quinine is not sufficient to cut short dysentery. This is my own experience; I have repeatedly treated dysentery with 15 grain doses of quinine, producing violent quinization, without arresting the fatal termination of the disease. This was also the general experience at Lahore, Dinapore and in Burmah,† where quinine came to be freely used in consequence of Mr. Hare's strong recommendation of it, especially in the hæmorrhagic form. Those who have found it useful, as Mr. Cameron in Ceylon, have used it in comparatively small doses, and combined with other medicines. Mr. Hare in his last report on the subject,‡ still believes in the efficacy of heroic doses of quinine in hæmorrhagic, apparently not in all forms of dysentery; but he appears to be singular in India in confiding in it alone, and even he considers the use of large enemata a necessary adjunct. M. Armand also, its greatest advocate in Algiers, who seems to think all dysentery febrile, does not trust to quinine alone without adjuvants, as he would in treating fever; he gives about 15 grains daily. M. Armand lays no claim to originality, as he says the same views were propounded by M. Raymond Faure 20 years ago.

Perhaps the most sensible view of the case is that taken by M. Catteloup,§—"Many think that sulphate of quinine should be reserved for those cases only which are complicated with remittent or intermittent accesses, or when it has succeeded fevers.—But it is not only as an antiperiodic, that this salt deserves an important place in the treatment of certain dysenteries; given also in small doses as a tonic, it counteracts adynamic symptoms and accelerates the cure. Other preparations of cinchona, when the patient is sick of sulphate of quinine, are useful in strengthening the stomach, after the local symptoms of dysentery have disappeared." I agree to all this, which

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* De la Dysenterie, &c., 1847.
† Reports to the Medical Board to which I have had access.
‡ Indian Annals, vol. I.
§ Recherches sur la Dysenterie, 1851.

has long been ordinary Indian practice. We have seen already how groundless the dread of irritation of the intestinal canal usually is. Where fever is present, it is by all means worth while to try the effects of quinine, especially when combined with opium.

Cholera.—On the idea of the malarious origin of this disease, or from a supposed analogy to the cold stage of fever exaggerated, or to the fievre algide of the French, quinine has been sometimes employed, generally in large doses. It has however never been used unaided by other remedies. Dr. C. Bell, in Persia, and Dr. James Bird, of Bombay, have recommended it. It was tried at home during the last epidemic; and an American author, Dr. Sargent, gives a favourable account of its use.* Some observers in Burmah, as Mr. Taylor, of H. M. 80th,† and Dr. G. Mackay,‡ of the Madras Sappers, think they have found it more useful than most remedies. I have seen a few experiments made with it, but without any great success.

Many look on it as a prophylactic, and Sémanes§ recommends its employment as a preventive, in the form of a lavement of 15 to 30 grains of quinine in a quart of strong decoction of yellow bark. With reference to its supposed prophylactic power, it is worth while to mention, that a case was being treated for diarrhœa in the experimental Ward of the General Hospital, with scruple doses of quinine, when on the second day symptoms of cholera, which proved fatal, came on. This patient had taken at least five doses, of one scruple each, in solution by the mouth.]

PART IV.

PHARMACOLOGY.

This comprehends—1st. The determination of the therapeutic value of each of the principal substances that enter into the constitution of cinchona, [the more important alkaloids are quinine, cinchonine and quinidine; they resemble each other so much, that it is conjectured that some day means will be found of converting them into each other,] and

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* Ranking, vol. 20. † Indian Annals, vol. I.
‡ East India Magazine, 1854.
§ Bouchardat's Annuaire, 1854.

of each of the more important preparations of the bark.—2nd. The doses in which each of them ought to be given to produce their sedative effects, and the manner in which they should be given.—3rd. The absorbing power of the various surfaces of the economy to which they may be applied.—4th. The value of the various pharmaceutical forms in which they are administered.

By the help of the processes to be indicated, nothing is easier than to determine the degree of activity of these substances, and to know the proportion in which they are absorbed.

The degree of absorption and action of bisulphate of quinine will serve as a starting point.

Amorphous Quinine.—Insoluble, insipid, soft as wax, has been prepared by Trousseau, for the use of infants. In the solid state it is absorbed exactly like sulphate of quinine in pills, that is five times less actively than the bisulphate in solution, and its action on the encephalic nervous system is too weak for its employment in treatment with high doses.

In suspension in a fluid its taste is bitter enough to be very disagreeable. The degree of its absorption and action is analogous to that of sulphate of quinine in suspension, *i. e.* one-half less than of the bisulphate in solution.

Thus amorphous quinine administered in comfits or in honey, which is the only practically useful way of giving it, is equivalent to the bisulphate given in pills, and as it is taken in this shape by children without any aversion, it may be given to them, but for any other purpose it offers no advantages.

Amorphous Cinchonine is inferior by one-third to amorphous quinine, so there is no use in employing it.

Pure Quinine is more bitter than the preceding alcaloids, and quite as insoluble. Its degree of action and of absorption is equal to that of the bibasic sulphate in the shape of powder. This proximate principle can be of no use, and has never been employed.

The preceding substances are little used: the principal articles of quinine treatment are the salts of quinine and of cinchonine, which we next examine.

1.—*The bisulphate of Quinine or acid sulphate* is not found prepared in pharmacy: it is made extemporaneously by adding a few drops of sulphuric acid to the aqueous solution of the bibasic sulphate. This salt is very bitter and always liquid. It is the typical preparation for absorption and action on the organs: it is the standard by which we com-

pare all others, and the one to be preferred to all. M. Piorry supposed that the action of the sulphuric acid on the bibasic sulphate might render this salt more dangerous to the economy, and proposed a solution in alcohol. But in the first place the quantity of the additional acid is very trifling, for little more than one grain of sulphuric acid is found combined with 15 grs. of the sulphate, and it is difficult to suppose that a quantity of acid that could barely acidulate a glass of lemonade, can be injurious. Besides the action of alcohol, as we have remarked above, is antagonistic to that of quinine. In short the alcoholic preparation of quinine is useless, and not without inconveniences. [Yet many foreign pharmacopæias contain alcoholic tinctures, which are considered more efficacious than simple quinine.]

The bibasic sulphate of Quinine, or the neutral salt of commerce, is less acid and less soluble than the preceding. We can only dissolve a small quantity of it in an ordinary draught. It can only be given in suspension in a fluid, or in powder on a piece of bread. When it is administered in a partially soluble state, its power as respects absorption and action on the economy is about one-half that of the bisulphate dissolved. M. LeGroux is in the practice of giving this salt in powder, and immediately after giving a cup of very acid lemonade. In this way the salt is sure to be dissolved in the stomach, when its action will be the same as that of the bisulphate. It is therefore a good way of giving quinine, for we escape the bitter taste.

The bitter taste of these two sulphates being very disagreeable, M. Desvouves has proposed to disguise them by giving the sulphate of quinine in coffee. This addition is only useful with the sulphates, when in suspension. With the neutral sulphate in suspension, the bitter taste is almost entirely destroyed: but there is also a precipitate formed of tannate and gallate of quinine more insoluble than the neutral sulphate, and the combination loses more than one-half its power of absorption and action. With the acid bisulphate in solution, the coffee, however strong the decoction may be, modifies the taste but very slightly, and a precipitate of tannate is also formed. Thus the composition loses a good deal of its power, and there is no use in employing coffee except in the difficult-to-be-managed patients, who will not submit to M. LeGroux's way of taking the bibasic sulphate. [Perhaps Tincture of Orange Peel is the best adjunct.]

A hydrochlorate, a nitrate, a carbonate, a citrate and acetate of Quinine have all been proposed. These salts are all

soluble, some a little less than the bisulphate, some more so. They are bitter like the sulphate, and contain various quantities of quinine. Thus the bisulphate being 1, they are in the following proportions—citrate ·90, nitrate ·88, acetate ·85, hydrochlorate ·82.

None of these salts has any particular action derived from its constituent acid. Thus there is no use in their employment, as they are all like the bisulphate, which is more powerful than any of them.

[*Citrate of Iron and Quinine* also soluble, may be excepted from this remark; it is a most useful tonic in many cases, though not used as an antiperiodic, and its cheapness, only 48*s* per lb., is a recommendation.]

Phosphate of Quinine, recommended by Harless of Bonn, is less soluble than the preceding salts, and consequently less energetic in its action. This explains why, its effects had been described as milder. It is quite useless in medicine. If we find the action of a given dose of the bisulphate too intense, we must diminish its dose, and then we shall have all the advantage of a less soluble salt!

Ferrocyanate of Quinine has been greatly lauded in Italy—it was natural to suppose that the union of a powerful narcotic like hydrocyanic acid with quinine, would add to the narcotic effect of the latter—but unfortunately this insipid salt is insoluble in water, and it cannot be dissolved except by the aid of an acid. If it be added, the hydrocyanic acid is disengaged, and we have only the primary salt remaining. Thus this compound can only be given in powder, and however large the dose may be that we give, it has no appreciable effect on the economy, and it is not absorbed, for it is not found in the urine—[yet this salt is said to be much employed in Italy in pernicious intermittents.]

It seemed equally probable, that the combination of two powerful febrifuges, arsenic and quinine, would yield advantageous results.

The *arseniate of Quinine* is insoluble, and can only be given in powder or suspended in a vehicle. At doses of 1½ grs. or a little more, it does not produce any appreciable effect on the nervous system, and it is not absorbed. Given in somewhat larger doses it causes colics, diarrhœa and signs of gastro-intestinal irritation, which must be attributed to the arsenious acid, and which prevents fuller experiments being made with higher doses. [Boudin* found arseniate of qui-

* Archives Medicales, 1846.

nine to have no superiority over an equal quantity of arsenious acid; this is what was to be expected, as the quantity of quinine that can be thus administered is so small.]

The *Arsenite of Quinine* came out with more favourable impressions, because it is arsenic acid that is employed as a febrifuge; but this salt is insoluble in water, and can only be kept dissolved by means of alcohol: even then at doses of 1½ to 2 grs. it produces none of the effects of quinine, and at larger doses it irritates the intestinal canal like the preceding preparation.

The arseniates and arsenites may therefore be at once rejected.

Some special reasons have given a certain degree of favour to the following preparations.

Valerianate of Quinine prepared by Louis Bonaparte, is a very bitter and very soluble salt, which appears to be one-third less active than the bisulphate—it is little used as a febrifuge. The properties of valerianic acid cannot be said yet to have been investigated, and no precise experiments have been made with it, but in neuralgia and nervous affections, this salt would seem to demand a preference.

It is not long since tannate of quinine has been presented, as a salt that corrected the too active properties of sulphate of quinine, and which, adding the properties of tannin to those of quinine, should be febrifuge.

Tannate of Quinine is an amorphous compound, very little soluble, scarcely bitter, and only containing 20 parts of Tannin to 100 of Quinine. The addition of tannin to quinine has the effect of rendering the latter very slightly soluble, and consequently inactive—it is only when given in very large doses that it produces some slight effects on the nervous system—it is very incompletely absorbed. Its power is about one-fourth of that of bisulphate of quinine. Thus this salt is so weak, that it is of no use in medicine except in large doses; as to medication in small doses, for such purposes it is quite useless. Tannate of quinine is opposed to the common sense of therapeutics.

M. Bartella, with the idea of modifying the effect of quinine, has proposed a union of tartaric acid with the bibasic sulphate of quinine, forming thus *sulpho-tartrate of quinine*, which he regards as a better febrifuge than the sulphate. As sulphate of quinine is commonly given in pills, in which shape it is least easily absorbed—new soluble preparations are apt to be compared with its action in this shape, and sulpho-tartrate is undoubtedly more soluble than the bibasic

sulphate. But when compared with the bisulphate it is found to be less powerful, and this so much so, that Bouchardat has proposed the substitution of a few grains of tartaric acid for the sulphuric acid always added to the bibasic sulphate, with the express view of modifying its too great activity. Tartarate of quinine is a salt useless in medicine. [Yet M. Bartella* is very confident that equal parts of sulphate of quinine and tartaric acid make a particularly efficient preparation.]

Nevertheless it has been imagined that organic acids would act more mildly on the mucous surfaces than mineral ones, and M.M. Conte and Bonaparte, have composed a *Lactate of Quinine.* This salt is very soluble, and is somewhat less bitter than the sulphates—but it has been very little used, because its effects and its bitterness are much the same as those of the sulphates; it may however, be useful when the stomach does not bear the sulphate well. [M. Paura of Naples has recently introduced an *Iodide of Quinine* supposed to be adapted to scrofulous cases, dose 8 to 16 grs. This salt was prepared some years ago by Dr. A. T. Thomson, but was again forgotten.]

Sulphate of Cinchonine—Cinchonine may form with the various acids salts like those of quinine, but the sulphate is the only one used. This salt is very soluble and moderately bitter—it is exactly the same in its effects as quinine, only it must be given in a quantity one-third greater. It is very much cheaper.

Quinoidine constitutes the substance left behind in the mother waters from which quinine has been extracted: it is a complex substance, containing quinine, cinchonine and extractive matters in variable quantities. Its physiological action is the same as that of quinine: but it produces a good deal of irritation of the digestive canal, so that more than 15 grs. of quinoidine cannot be given within the 24 hours. It is absorbed like quinine—but it has no advantage except its inferior power, which adapts it for lavements. [Some say that quinoidine is only amorphous quinine.

Amorphous solution of Quinine.—This preparation of Mr. Bullock's, made from quinoidine, by treating it with ether, professes to contain 1 gr. of amorphous sulphate of quinine in 5 drops, a 5ʒ. bottle representing 1ʒ. of the amorphous salt. Cost of it in India 7*s.* 8*d.*

It has been good deal used in Bengal, as a substitute for

* Bouchardat's Annuaire, 1854.

quinine, and with success, but I am not aware that any accurate experiments have been made with it. We have seen above, that Briquet considers amorphous quinine inferior in power to cinchonine, and there are doubts whether what has been prepared under the English patent is quite pure, and uniform in its composition.]

Quinidine.—The third alkaloid of cinchona, is according to M. Henry, merely a slight chemical modification of quinine, which is otherwise of no therapeutic interest. [Dr. Pereira states that he used it and found it a good febrifuge, Dr. Pepper* and others have made some successful experiments with it in America.]

Cinchonicine.—A fourth alkaloid is merely an isomeric modification of cinchonine. A salt of this has been formed with tartaric acid; because it is very insoluble, it is consequently weak in its action. The idea is absurd.

Soft extract of Cinchona.—A compound containing quinine and cinchonine, according to the sorts of bark from which it has been made—a number of coloring matters, tannin, gallic acid, &c.

Its power, as compared with sulphate of quinine, is about one-fourth; the soft extract must evidently vary much, and is a doubtful medicine, only fit for lavements.

Dry extract of Cinchona.—This contains little alkaloid, and coloring and extractive matters predominate—it has none of the narcotic effects of cinchona, and is a simple tonic. The wines, syrups, decoctions, &c., of bark vary according to their composition—their general operation may be easily guessed from the above—but it is impossible to make accurate experiments with them. These are the chief articles derived from the cinchona that are of interest.

[*Warburg's fever drops*, an undoubted antiperiodic, contains quinine in an aloetic tincture. It produces, but in a modified degree, the head symptoms of quinine, and also invariably a profuse perspiration, the cause of which is not known. In its diaphoretic properties the medicine has some analogy with the *rasout* of India, the *Berberis Lycium*—to be mentioned hereafter. It is curious to find that the old tincture, of alöes and rhubarb was once used in India† as a febrifuge. The exact constituents of Warburg's drops are not known. There is little doubt that they contain besides the quinine and aloes some opium. It is also believed by many, and

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* Ranking's Abstract, vols. 20, 21.
† Madras Report, 1816.

stated by Royle, that they contain Bebeerine. Etzelt and Pach, give the following as their probable composition.

Alöes.....		
Angelica.	....	ā ā. ʒi.
Zedoary Root,..		
Camphor.		
Saffron,.....	.....	ā ā. gr. v.
Alcohol,.....		℥ iij.

Digest, and add to the filtered liquor, quinine ʒss.

This nostrum has been recently favourably reported on by various Bengal officers, and in the Austrian pharmacopœia a formula for fever tincture has been adopted, closely resembling the above, with the addition of a little opium. I have tried it in two or three bad cases with uncertain results, and doubt whether it is more efficacious than quinine. Officers going into the jungles without medical aid have very great faith in this preparation. My friend Mr. H. Baillie, now of Hooghly, used it very extensively in the obstinate fevers of Hidgelee, especially in remittents. He found it most useful before complications arose; he generally prefaced its use by a purgative. Its immediate effects are, the production of a feeling of heat at the epigastrium, followed within an hour by profuse perspiration, and a perceptible reduction of the pulse and lessening of the fever. He thinks the effects more immediate and more certain than those of quinine, and also more lasting. Its high price precludes its extensive use. Besides that the employment of all secret remedies is undesirable, its cost is 8*s*. the bottle, containing about 6 ʒ, and at least one bottle must be expended in a fever case. At one time it was procurable in the Calcutta Bazars at 1 or 2 Rupees per bottle.]

We have next to examine the various ways of administering these products of cinchona.

Administration by the mouth.—1. *In the form of a complete solution in a fluid.*—We can administer in this shape all the soluble salts of quinine and of cinchonine. The most used of all is the bisulphate of quinine, that is to say, the solution of the bibasic sulphate with the addition of a few drops of sulphuric acid. This is the most powerful preparation of cinchona that we possess. With a dose of whatever strength dissolved in about 5℥s, of water, we have a medicine which is absorbed almost instantaneously, and acts at once on all the organs of the economy. Thus out of 14 times that patients had taken 3 grs. bisulphate of quinine once, it was

found seven times in the urine at the end of 2 or 3 hours, and four times there were appreciable head symptoms.

This form offers the greatest safety in giving quinine in high doses, because while giving it in divided doses, we can discontinue the action of the medicine whenever we please. Thus the complete aqueous solution is the most suitable form of administering the medicine, because it adds rapidity of action to its energy and its safe employment. Its only drawback is its bitterness. [This is the most common mode of giving it in India. M. Ducros in 1846 thought that a lotion of sulphate of quinine applied to the fauces and velum was very speedy and efficacious in its action, but nothing more seems to have been heard of this.]

Imperfect solution in a fluid.—We may in this shape administer pure amorphous quinine, quinine, quinidine and the slightly soluble salts, such as the bibasic sulphate, &c. There is little bitter taste. The solution is commonly made in water. This mode of administration is half as powerful in its effects, as that of the bisulphate in its complete solution. Its absorption is also about one-half as slow. Its bitterness is almost destroyed by coffee, but then if taken in it, it loses again about half its power, and is only about one-half as powerful as the solution of the bisulphate.

Form of Powder.—This is employed with the object of escaping the bitterness; ordinarily the bibasic sulphate is taken. This form is inferior to the bisulphate in solution by more than one-half, and it remains a shorter time in the tissues. M. LeGroux's proposal, as given above, is suited to those who have an extreme repugnance to the bitterness. Nevertheless, as it leaves a door open to irregularity, it cannot be considered so good as taking the bisulphate in solution.

Form of Pills.—This is the most used in France, and the very worst of all. All the salts of quinine may be administered in this shape. A pill is a sort of plaster that may remain long applied to any given point of the stomach, and which softens there more or less gradually. Its absorption is very slow, and whatever may be the dose, no physiological effects are observable. Its absorption is five or six times more weak than that of the solution.

Medication by the Rectum.—Lavements.—Usually sulphate of quinine administered in this way is absorbed. This absorption takes place very fast, and twice as rapidly as by the stomach. But absorbed in this way, its action is feeble, it has little energy, and never produces any persistent cerebral

disturbance. It ceases to act at the end of one or two hours. Thus its effects are weak and transient.

Medication by the Skin.—In whichever way he tried it, by plasters, cataplasms, stoups, ointments, liniments, frictions, M. Briquet was never able to prove absorption by this channel. Thus it is a mode of the medicine's operation that cannot be counted on. But the endermic mode was very different; in it the absorption and physiological action were active and constant. Only this mode of administering it must not be pushed too far, because the sulphate of quinine irritates and cauterises the denuded surface.

It only remains to point out the doses in which quinine is to be given, and the bisulphate must be taken as the type to which to refer the other pharmaceutic preparations of cinchona.

Quinine treatment is of two sorts, that by large, and that by ordinary doses.

Treatment by large doses is by no means a modern method. It was tried with bark as long ago as 1750. It was carried by the most celebrated physicians to quantities of cinchona representing 45 grs., 1℥, and 1½ ℥, and even 2½ ℥. On the faith of a paper [by Melier] presented to the Academy of Medicine, of no real value, and written with very imperfect knowledge of the subject, great alarm was excited at those immense doses: but Giacomini has taken for 47 days successively 45 grs. to 1℥, simply in an experimental point of view. Piorry declares he has given, more than 1,5000 times, quinine in doses from 15 to 45 grs. daily. Some people have taken as much as 10 to 30 scruples, before feeling any dangerous effects. The experiments on animals which have been invoked to prove the danger of large doses, are imperfectly-conducted experiments which prove nothing. [Although M. Briquet appears to make too light of the disasters that certainly have occurred, yet he elsewhere admits that large doses produce such disturbance of the economy, that they should not be given except when essentially necessary.]

In short the danger of quinine is not in the dose; it lies much more, in the manner of administering it, and in the nature of the maladies for which it is exhibited. Thus the accidents which have taken place, have been, when quinine was given in immense single doses, or in diseases such as acute rheumatism, phlebitis, &c., in which they often originate in the ordinary course of the disease, and may be provoked by the neglect of common caution.

The large doses may be given under the following conditions:—1. The degree of susceptibility of the patient should be observed; this bears reference to two points; 1st, to his debility, which is readily detected, and which gives the risk of syncope; 2nd, to his irritability, which disposes to cerebral accidents, against which we should be on our guard. In all patients of much susceptibility, of a nervous temperament, inclined to cerebral congestions, easily affected by moral impressions, by medicines, or by fermented liquors, quinine should be given with extreme caution in high doses, or not even given at all. [How different is this from the Bengal Report, which assures us of "the perfect safety of exhibiting quinine in large or scruple doses repeated three, four, and six times or oftener in the 24 hours, in fevers of all types the product of malaria"]

2. The nature of the disease must be made out. In diseases with debility and extreme prostration, syncope is to be dreaded. In acute inflammatory diseases, especially erratic ones like erysipelas and rheumatism, and in convalescence from severe diseases, we have to dread accidents to the head.

When quinine is given in large doses, the bisulphate of quinine in solution is always employed, given in portions of 1½ grs., every hour or every two hours during 12 hours of the 24 only. In this way the absorption of the salt taking place instantaneously, its action is prompt, and if we find the cerebral effects developed too powerful, we can at once stop the medicine, and thus prevent accidents. [This requires some care on the part of the physician, and more competent assistants than can always be counted on in India; if a native doctor is allowed any discretion, in administering quinine during a fever, he is generally afraid to go on giving it.]

In cases of intoxication by mistake, or by maladministration, tannin should be given at once, suspended in a vehicle not too bulky; after that, if there is much prostration, stimulants must be used; if, on the contrary, there be excitement, antiphlogistic measures, blood-letting, soothing baths and finally opium must be had recourse to.

The diseases, in which we may be compelled to give quinine in high doses, are the intermittents of hot countries, the bad intermittents of cold ones, the pernicious intermittents and bad remittents, and the pseudo-continued fever of Africa and America, neuralgias, pyrexias, yellow fever, the plague, typhoid fever, puerperal maladies, phlebitis, rheumatism, acute affections of the encephalon, &c.

We should always in such cases employ the bisulphate of quinine, in solution in a sugared vehicle.

In the intermittents and remittents of Africa, the doses vary from 30 grs. to 1ʒ. in the day. [As Briquet has, I believe, never been out of France, it may be well to let some practical writers, most of them great advocates of quinine, speak for themselves.

Haspel* says, "common slight fevers are easily cured by 15 grs. of quinine daily; if the fever is bad, 30 to 45 grs. may be required, or at least is usually enough in the 24 hours; but it may be necessary to increase this to 1ʒ, or to 1ʒ and 15 grs. I have never seen any toxic effects or even grave accidents, when the medicine was properly exhibited; still we are not to depart from the caution, which the use of every heroic remedy requires. Real clinical observation seems to show, that there is not much risk, if the dose does not exceed 30 to 45 grains daily, and is not too long continued." Armand says, "Give quinine *citius et largâ manu.* Never less than 15 grs. by the mouth in the 24 hours in urgent cases, we have rarely to go beyond 24 to 30 grs. in that period. By the second or third dose we are almost sure to have mastered the most formidable access of fever. We must not wait for well-marked intermissions. This mode offers security, celerity and economy of the medicine, and we save and support the strength of the patient. As much as possible seize the moment of remission to give the anti-periodic, but in urgent cases, the sooner the better." Almost all the latest French writers are entirely opposed to general bleeding, and even to local. Some of them say also that emetics must be used with extreme caution.

Heymann in Java† gives larger doses. "In slighter cases of intermittents 12 to 15 grs. divided in 4 to 6 doses, given in the apyrexia, were enough to keep off the fever. In intermittent fever with apoplectic tendency, no time is to be lost. You must not attend much to intermissions or remissions, the sooner the patient gets 30 to 40 grs. of quinine the better. It is advisable to give it in divided doses of 4 or 5 grs., one dose every hour." But he uses leeches and various other remedies, and when there was difficulty in the patients swallowing, he gave 10 to 12 grs. of sulphate of quinine with 2 to 3 oz. of water in an injection. In remittents he gives quinine, as much as 30 or 40 grs. in

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* Maladies D'Algérie.

† Krankheiten in den Tropen ländern, 1855.

the remission, but if there be no remission, he thinks musk in large doses. of 30 to 50 grs. in the 24 hours, the most efficacious treatment.

Or hear Dr. G. B. Wood* in America. Of intermittent fevers, he says, "From 12 to 24 grains should be given between the paroxysms, but the amount required is very different in different individuals. It is seldom that less than 12 grains in each intermission can be depended on. Some physicians are in the habit of prescribing very large quantities of the sulphate in all cases indiscriminately. From 30 to 60 or even 100 grains have been given in the twenty-four hours. These amounts may be required in certain malignant cases, but seldom or never in the disease as it usually occurs. I do not remember to have found more than 24 grains in that period of time necessary. On the whole I prefer the plan of administering the medicine in small doses frequently repeated, one or two grains every hour or two; opium probably adds to the anti-periodic power of quinine." Again on remittent fevers.—"I am entirely confident that I have seen lives saved by the quinine treatment, that must have been inevitably lost under any other. So far as my observation goes, from 18 to 24 grains during the remission, are sufficient to give before the expected paroxysm, in any case not falling under the denomination of malignant fever. In it sulphate of quinine may be advantageously employed, even in the paroxysm before reaction. It is indicated for its effect on the nervous centres, and is all important with reference to the next paroxysm. From 30 to 60 grains of this salt should be given from the commencement of one paroxysm to that of the next."

Another American author, Dr. Drake, says, "In simple intermittents, the best plan is to give quinine in a 5 to 10 grain dose shortly before the paroxysm. In malignant intermittents," he thinks "quinine during the paroxysm unsatisfactory, given in intermissions all important; about one scruple is enough, but if the case be threatening, it is to be given freely." "In simple remittent," he says, "long preparatory treatment before giving quinine is abandoned. Use free and early venesection, and perhaps a purgative, then give 10 grains of quinine with 1 or 2 of opium or 10 grains of calomel added. In malignant remittent, first get a remission by bleeding, or an emetic of lobelia inflata, then give

* Practice of Medicine, 3rd edition, 1852.

the quinine." A writer in the Southern American Journal in 1853 says: "Full doses of quinine and opium given in the midst of the cold or shivering stage of remittent fever, will be found both safe and efficacious in the large majority of cases—dose 20 to 25 grains of quinine, with 2 to 4 grains of opium."

Dr. Dundas in his Sketches of Brazil, says.—"In the treatment of intermittent of whatever type, if the tongue be loaded, an emetic of tartarised antimony should be at once exhibited, after which 10 or 12 grains of quinine are to be given about two hours before the expected access, and repeated after the interval of an hour. If, in spite of this, the fit supervenes, 3 grain doses are to be given every three hours after it has subsided, until within three hours of the next expected paroxysm, when the large dose is to be repeated. In the treatment of bilious remittent, he commences at once with 10 or 12 grains of quinine every two hours, whatever the patient's condition may be, giving 15 grains of calomel with the first dose. When an intermission occurs, which it is said to do generally after the third dose of quinine, the case is to be treated as one of intermittent."

These extracts I hope represent fairly the most modern practice in other tropical countries. There is great variety in the quantity of quinine exhibited, but even the largest of these quantities, it will be observed, falls short of what has of late years been recommended to the profession in India, and it is almost always given in divided doses.

The official report, as has been observed above, has given a great impulse to the use of quinine in India; but I do not know that any account of the effects of heroic doses, except that embodied in its pages, has been published, (and the directions for its use in different forms of fever are sadly wanting in precision,) at all events, any requiring further notice than I have already given them, except that of Dr. C. Mackinnon, who found the most effectual mode of treating obstinate intermittents to be, by giving one 30 grain dose, while the sweating stage was going off, or just after it. This fact is based on pretty extended observation.

The general tendency in Bengal at present seems to be, to give quinine in large doses, with little discrimination as to the sort of fever for which it is administered.

My practice at the General Hospital used to be in the case of an ordinary intermittent, to give two or three 4 gr. doses at 12, 8 and 4 hours before the expected paroxysm (I prefer 4 gr. doses to smaller ones) or an 8 gr. dose

or two 12 to 6 hours before it. This or not more than 16 to 20 grs. is commonly enough to prevent a return. In remittents where general blood-letting was never used, but leeching, and salines, and but little calomel, were employed, 4 gr. doses three or four times a day, when there is any tendency to a remission, or in 8 gr. doses if you are at all anxious about your patient, are very generally enough. The quinine may be continued during the paroxysm, but its efficacy is not then, in my opinion, one-fourth what it is during remissions.

But, to an intelligent practitioner, there should be no uniform treatment of Fevers. In different seasons they require different quantities of quinine. The more ardent fever may often be treated successfully without any. In military practice in the field, and where bad jungle fever is met with, it no doubt is often necessary to give quinine in larger doses, to obtain its full sedative action, and even during the paroxysms, especially where you dread that there may be no remission; but in ordinary cases it appears to me to be a mere waste of a valuable medicine to give it during the paroxysms, or in heroic doses at all.

In two Wards at the General Hospital open at the same time, quinine was given in nearly the proportion of 1 to 5, in about 80 and 130 fever cases respectively, for nearly a year. As far as could be ascertained, the smallest mortality was, where the smallest quantity was given, being at most only one-half that of the other. This statement I make on my own authority from the Hospital records, as such a comparison was not made in the official report. But the experiment was so loosely conducted, that I do not look on this fact as one of any great importance, and the accuracy of this statement, as of nearly every other one connected with the experiment, may be disputed.]

In the remittents of our climate the dose is from 15 to 30 grs. daily; we have already given the doses for rheumatism and some other affections.

In general we do not commence with larger doses than 15 to 30 grs. daily, and we increase the quantity gradually, unless the case is urgent, to 45 grs. or 1ʒ in the 24 hours.

In urgent cases the dose must be taken in 6 or 8 hours, in other cases it may be divided during 12 or 16 hours, and taken as much as possible during the apyrexia or the remission. In general, when there is time to spare, the more the doses are divided, the more will the injurious effects of the medicine be avoided.

Treatment with ordinary doses.—This does not require any particular precaution, as it never produces very grave accidents.

Its most common employment is as a febrifuge, and in Paris a simple intermittent fever, or one complicated with hypertrophied spleen, can always be at once arrested by the following potion:

Bisulph. of Quin.,.....	gr. ivss.
Acet. of Morphia,.....	1-9th gr.
Water, ...	$3\frac{3}{}$.
Syrup of Orange flowers,	$4\frac{3}{}$.

[This is a near approach in English measures to the French. Throughout I have spoken of a gramme as 15 grs., though strictly speaking it is 15·4 grs.]

This potion is to be administered as follows: It is to be taken in five doses, 1-5th every hour, the first dose to be given 15 hours, the last 11 hours before the expected paroxysm.

The determination of the dose, the addition of the morphia, the division of the doses, their administration at fixed times, have nothing arbitrary in them. They are the result of many experiments. It is evident that the potion should be taken on an empty stomach. The above formulæ may be regarded as a sort of type, by which to regulate the use of the various substitutes for quinine.

It is clear: 1st,—that the more marshy or hot the countries are, the higher must be the dose of quinine. 2nd,—the more distant from each other the paroxysms are, the larger must be the dose, for instance, in a quartan 6 or 8 grs. will be wanted instead of $4\frac{1}{2}$.

Cinchonine may be employed in preference to quinine on account of its cheapness, but the dose must be one-third larger.

When sulphate of quinine is given for continued diseases, the dose ought to be given during one-half of the day, the patient being left to himself the rest. The length of time that it may have to be given varies; it may be only wanted for a few days. In acute rheumatism and typhoid fever, quinine is scarcely ever given for more than 6 or 8 days; patients in febrile diseases cannot bear 45 grs. to $1\frac{3}{}$ daily, for a longer time; in non-febrile diseases, they may be continued longer.

In the intermittent fevers of temperate climates, the sulphate of quinine need only be taken every second day, and then every third or fourth for 6 or 8 days. In general four or five doses are enough to arrest the fever completely.

[Celle, a writer on tropical hygiene, states that in hot and dry climates, smaller doses of quinine will answer, than in hot and moist ones. I have not met the remark elsewhere, and this difference does not seem to have been observed in the Upper and Lower Provinces of the Bengal Presidency. Some have supposed that there is a greater tolerance of large doses in tropical than in temperate climates. But the doses given in Paris have been so large, that they afford no countenance to this notion. It may be laid down as a general fact, that natives do not require so large doses as Europeans.

The continued use of Quinine produces tolerance of it, and those who have taken much, generally require larger doses than others, but a great deal depends on the way of administering it. Patients, who are in the habit of taking spoonsful of this medicine for ague without effect, may nevertheless be cured by the judicious use of a few doses.]

OTHER VEGETABLE ANTIPERIODICS.

Leaving Cinchona and Briquet's guidance behind us, we enter on a sea of doubt and difficulty, when we come to examine the endless variety of substances that have been deemed antiperiodic. "Many of these," says an eminent American authority, "have been introduced to the profession with the highest commendations: and not a few of them have ranked in the partial estimate of their recommenders, as equal if not superior to the Peruvian bark. Few of them however have stood the test of trial."

The readiness, indeed, with which the profession is apt to accept the virtues of new remedies, an account of which would form a curious chapter in the history of human credulity, shows that the educated and well informed, are often as ready to be self-deceived as the untutored wild man.

There is this excuse for them however in the case of febrifuges, that they are probably misled by two circumstances—first that, especially in temperate climates, where these remedies have been chiefly tested, many intermittent fevers, (some say more than one-third,) will disappear of themselves, or under any mode of treatment; secondly, that such fevers may be cured by psychical impressions alone.

Thus amulets and charms are undoubtedly used at the present day with success to cure fever among civilized people, just as exorcismal medicine will drive away the fever of the savage. A Paris Savant, Raspail, will cure an ague by placing a bit of camphor on the pit of the stomach, or a Red Indian Medicine man clothed in his mystery garb will dance round the patient, till the fever is frightened away. Faith in such cases is the secret of the physician's success.

When these things are taken into account, it becomes less surprising to find at the present day, such a substance as vegetable charcoal gravely propounded as a cure for ague, and its usefulness supported by the result of many experiments, (Drs. Calaguo, Calvert, Shortt, and lately, 1853, M. Serres.)

Perhaps the acme in this direction has been reached, when gelatine (Seguin), and phosphate of lime (Mr. Blacklock, Madras), are brought forward as antiperiodics, and their claims seriously investigated, for their employment requires perhaps even more faith than the older remedy of cobwebs.*

* Charcoal and cobweb are both discussed at full length in Craigie's Practice of Physic, vol. I., where there is a good account of febrifuges.

Are we then really much more intelligent than the South American Indians, whose pajés or doctors according to Von Martius employ among their strange preparations, the hair and the ashes of the bones of animals, the very gelatine and phosphate of lime of our white wise men?

As it would be impossible without writing a history of half the articles of the Materia Medica, to give an account of all the vegetable substances that have been used as antiperiodics, I shall merely attempt to give a list of the chief of them, dwelling at greater length only on such as appear most important.

I shall be guided in the selection chiefly by three considerations—1st, whether the substances have really been in great repute, and recommended by men of eminence—2nd, whether they have been lately brought forward as substitutes for quinine—3rd, by their being Indian febrifuges, and fit for Dispensary practice in this country.

The classification adopted is not supposed to be the best that could be made, and is open to objections, but seems a practically useful one. The great majority of the substances are bitters or astringents, or astringent bitters, with a few acrids, antispasmodics, and narcotics. The botanical names given are the best known, if not always the most modern ones.

A whole host of febrifuges used in Hindu medicine, as ginger, cummin, coriander, mustard, hellebore, &c., have been necessarily omitted, and I cannot afford room for any notice of chicory, taraxacum, achillea, serpentaria, calamus aromaticus, costus spicatus, valerian, hops, turpentine, geum urbanum, solanum dulcamara, cubebs and copaiba, petroleum? and various other articles, which have enjoyed repute as febrifuges, for longer or shorter periods.

Table of Chief Vegetable Antiperiodics.

Hindostanee Name.	English Name.	Botanical Name.	Natural Family.	Active Principal.	Remarks.	Part Used.
		I. Pure Bitters.				
	Quassia, ...	Simaruba Excelsa, ...	Simarubeæ, ...	Quassein, ...	Recommended by Lysons and many others,...	Wood.
	Cedron Nut, ...	Simaba Cedron, ...	,,	...	Recently brought into notice in the West Indies, ...	Nut.
		Nima Quassioides, ...	,,	...	Foot of Himalayas, extending to near snow, not abundant, long used for killing insects, latterly for fever, by M. Marcadieu, ...	Wood.
Knrroo, ...	Gentian Root,...	Gentiana Lutea, ...	Gentianeæ, ...	Gentianin, ...	Employed by Cullen, and popular in Europe,...	Root.
Cheretta, ...	... ...	,, Kurroo, ...	,,	,,	Grows in the lower Himalayas, ...	Ditto.
		Ophelia Cheretta, ...	,,	... ...	Long familiar in India, ...	Plant.
		,, Elegans, ...	,,	... ...	Species common in some districts, as Pulnay Hills, Vizagapatam, ...	Ditto.
	... ...	,, Angustifolia, ...	,,	... ...	....	Ditto.
Puharee ditto, ...	... ...	Exacum Bicolor, ...	,,	... ...	Neilgherries, Mangalore, ...	Ditto.
Country Creyat, ...	... ...	——— Tetragonum, ...	,,	... ...	....	Ditto.
Ooda Cheretta, ...	... ...	Cicendia Hyssopifolia, ...	,,	... ...	Common in parts of Southern India, ...	Ditto.
Chota Cheretta, ...	... ...	Chironia Centauroides, ...	,,	... ...	Found in some parts of India, ...	Leaves.
Nye, ...	Centaury, ...	Erythræa Centaurium, ...	,,	... ...	Very popular in Europe, preferred by French workmen in Algiers to Quinine, ...	Plant.
	Holly, ...	Ilex Aquifolia, ...	Aquifoliaceæ, ...	Ilicin, ...	Brought into notice by Rousseau, found useless by Chomel, ...	Bark and leaves.
Kreyat Root, ...	... ...	Andrographis Paniculata, ...	Acanthaceæ, ...	... ...	Long a popular febrifuge and stomachic in India. The basis of a well-known French mixture called "Drogue Amere," ...	Root.
Kutkaringa, ...	Bonduc Nut, ...	Guilandina Bonducella, ...	Cæsalpineæ, ...	... ...	Common febrifuge in Bengal and many parts of India, ...	Nut.
Mishmee Teeta, ...	... ...	Coptis Teeta, ...	Ranunculaceæ, ...	... ...	Sylhet and towards Assam. Thought by Mr. Twinning and Dr. O'Shaughnessy to be one of the best bitter tonics. ...	Root.

Hindostanee Name.	English Name.	Botanical Name.	Natural Family.	Active Principle.	Remarks.	Part used.
		II. Mucilaginous Bitters.				
	Columbo, ...	Cocculus Palmatus, ...	Menispermeæ,...	Calumbin, ...	....	Root.
Guluncha, ...	... ...	,, Cordifolius, ...	,,	... ...	A common febrifuge in India.	
		,, Crispus, ...	,,	... ...	In great repute as a febrifuge among the Malays, ...	Root and stems
	Elephant Tree,..	Adansonia Digitata, ...	Malvaceæ, ...	... ...	Imported and thrives in Bengal, lately brought forward as a febrifuge by Duchassaing, used by planters of Guadaloupe, ...	Bark and leaves.
	Iceland Moss, ...	Cetraria Islandica, ...	Lichenes, ...	Cetrarin, ...	Recommended by Herberger and others, ...	Whole plant.
		III. Aromatic Bitters.				
	Cascarilla, ...	Croton Pseudo China, ...	Euphorbiaceæ,...	Cascarillin, ...	Hecker and Stahl were two of its greatest advocates, ...	Bark.
	Augustura bark,	Galipea Officinalis,... ...	Rutaceæ, ...	Augusturabitter,	Meyer and Brand have recommended it. By many thought to come next to Cinchona, ...	Ditto.
	Worm Wood, ...	Artemisia Absinthium, ...	Compositæ, ...	Absinthin, ...	Employed by Richter and others, ...	Plant, flower and seeds.
	Chamomile, ...	Anthemis Nobilis, ...	,,	... ...	Used by Boerhave, Hoffman and Munro, ...	Flowers.
	Leopard's Bane,	Arnica Montana, ...	,,	Arnicin, ...	Noticed by Graumann, in great repute with homœopathists, ...	Flowers & plant.
	Tulip Tree, ...	Liriodendron, Tulipiferum,...	Magnoliaceæ, ...	Liriodendrin, ...	Brought into note by Hildenbrand, grows in United States, ...	Bark.
Pehjuree, ...	... ...	Thalictrum Foliolosum, ...	Anemoneæ, ...	... ...	Mussoorie and Himalayas. Dr. W. O'Shaughnessy says "It promises to succeed well as a febrifuge of some power, and a tonic aperient of peculiar value. It deserves extensive trial:" which does not appear to have been given it, ...	Root.

Hindostanee Name.	English Name.	Botanical Name.	Natural Family.	Active Principle.	Remarks.	Part Used.
		IV. Bitters containing Alkaloids or Tannin.				
	Bark, ...	Cinchona Condamimea, &c., many species, ...	Rubiaceæ, ...	Quinine, Cinchonine, Aricine, Quinidine,	....	Bark.
Pundaroo, ...	... ...	Hymenodictyon Excelsum, ...	,,	... ...	Grows in the mountainous parts of the Circars, as in Goomsoor. This tree demands further examination, as coming very near the true Cinchonas. Dr. O'Shaughnessy could not discover an alkaloid. The bark is used a little by Natives as an astringent. I am told that Europeans have found it febrifuge,	Ditto.
	False Barks, ...	Exostemas chiefly, ...	,,	... ...	South America, ...	Ditto.
	Coffee, ...	Coffea Arabica, ...	,,	Caffein, ...	....	Berry.
		Coutarea Speciosa. ...	,,	Cinchonine, ...	Bark of French Guiana, said by some to contain the principle of Warburg's drops, ...	Bark.
	Carolina Pink,...	Pinkneya Pubescens, ...	,,	... ...	Used in Carolina as a substitute for bark, ...	Ditto.
	Greenheart, ...	Nectandra Rodiœi, ...	Laurineæ, ...	Bebeerin, ...	Native of Guiana, ...	Ditto.
	Willow, ...	Salix Helix, &c., ...	Amentaceæ, ...	Salicine, ...	Common in all cold countries and long a popular remedy in Europe, ...	Ditto.
	Barbery, ...	Berberies Vulgaris, ...	Berberideæ, ...	Berberine, ...	Common in Europe, ...	Bark of root.
Rasout, ...	Extract of B., ...	,, Lycium, ...	,,	... ...	Lower Himalayas, ...	Ditto.
		,, Asiatica, ...	,,	... ...	,, ...	Ditto.
		,, Aristata, &c. ...	,,	... ...	,, ...	Ditto.
	Apple Tree, ...	Pyrus Malus, &c., ...	Pomaceæ, ...	Phloridzine, ...	....	Ditto.
	Amn. Dog Wood,	Cornus Florida, ...	Corneæ, ...	Cornin, ...	Used in America, ...	Bark.
	Horn Bean, ...	Cratœgus Aria ...	Rosaceæ, ...	Pyrarine & Cratægin,	....	Ditto.
	Mock Privet, ...	Phillyria Media, ...	Oleaceæ, ...	Phillyrin, ...	....	Ditto.
		Solanum Pseudo China, ...	Solaneæ, ...	... ...	Employed in Brazil, ...	Plant.
Koorchee, ...	Conessi bark, ...	Wrightia Antidysenterica, ...	Apocyneæ, ...	... ...	Used in Bengal in dysentry, possibly febrifuge,	Bark and seeds.
Neem, ...	... ...	Azadirachta Indica, ...	Meliaceæ, ...	... ...	Used in all parts of India for poultices, extremely bitter, ...	Bark and leaves.
	Cailcedra bark,	Khaya Senagalensis, ...	,,	Cailcedrin, ...	....	Bark.

Hindostanee Name.	English Name.	Botanical Name.	Natural Family.	Active Principle.	Remarks.	Part Used.
	Mahogany, ...	Swietenia Mahagoni, ...	Meliaceæ, ...	... ...	....	Bark.
Rohun Bark, ...	... ...	Soymida Febrifuga, ...	,, ...	... ...	....	Ditto.
Toon Wood, ...	... ...	Cedrela Toona, ...	,, ...	... ...	....	Ditto.
		V. Astringents with Tannin.				
Majoo Phul, ...	Gallnuts, ...	Quercus Infectoria, ...	Amentaceæ, ...	... ...	By Cullun in Decoction of Gentian, in India by Timmins in Cheretta.	
	Oak bark, ...	,, Robur, &c., ...	,,	... ...	Recommended by Cullen, ...	Bark.
	Wallnut bark, ...	Juglans Regia, ...	,,	... ...	....	Ditto.
	Elm bark, ...	Ulmus Campestris, ...	,,	Ulmin, ...	....	Ditto.
	Horse Chestnut,	Æsculus Hippocastanus, ...	Hippocastaneæ,	Æsculin, ...	Brought into notice by Zanichelli, in 1783, ...	Ditto.
Babul, ...	... ...	Acacia Arabica, ...	Leguminosæ, ...	... ...	Common in all parts of India, ...	Ditto.
Anar, ...	Pomegranate, ...	Punica Granatum, ...	Granateæ, ...	... ...	Used by Rehman, ...	Ditto of roots and of fruit.
	Rhatany Root,...	Krameria Triandra, ...	Gramerianeæ, ...	... ...	....	Root.
	Olive, ...	Olea Europæa, ...	Oleaceæ, ...	... ...	....	Leaves and bark.
	Tormentil, ...	Potentilla Tormentilla, ...	Rosaceæ, ...	... ...	Common in Northern Europe, used by Cullun,	Root.
		VI. Acrids.				
Kaka Toddole, ...	... ...	Todalia Aculeata, ...	Xanthoxylaceæ, .	... ...	....	All parts, especially the roots.
Gul Marich, ...	Black Pepper, ...	Piper Nigrum, ...	Piperaceæ, ...	Piperin, ...	Lauded by Gordini and Bertini, ...	The berry and roots.
	Long ditto, ...	—— Longun, ...	,, ...	... ...	....	Capsule.
Lal Marich, ...	Capsicum, ...	Capsicum Annum, ...	Solaneæ, ...	... ...	Used by Bergius and Copland, ...	
		Thevetia Neriifolia, ...	Apocyneæ, ...	... ...	Common ornamental shrub in Calcutta : 2 grains of its bark has been affirmed "to be equal to an ordinary dose of cinchona." Has this been tested? the juice is acrid, ...	Bark.
Satween or Sheltan,.	... ...	Alstonia Scholaris, ...	,,	... ...	Concan.	
	Parsley, ...	Apium Petroselinum, ...	Umbelliferæ, ...	Apiol, ...	....	Seed.

Hindostanee Name.	English Name.	Botanical Name.	Natural Family.	Active Principle.	Remarks.	Part Used.
		VII. Narcotics and Acro-narcotics.				
	Opium, ...	Papaver Somniferum, ...	Papaveraceæ, —	Morphia, &c.. ...	....	Juice of capsule.
	Belladonna, ...	Atropa Belladonna, ...	Solaneæ, —	Atrophine, ...	Recommended by Hufeland and Erdman. ...	Roots and plant
		Physalis Alkekenji, ...	,,	Physalin, ...	....	Berries.
Kuchli, ...	Nux Vomica or False Augustura bark, ...	Strychnos Nux Vomica, ...	Apocyneæ, ...	Strychnine and Brucine,	Used by Aaskow, Horn and Cullen, ...	Bark.
		——— Pseudoquina, ...	,,	... ...	Employed in Brazil, ...	Ditto.
Atees, ...	... ...	Aconitum Heterophyllum, ...	Ranunculaceæ,...	... ...	....	Root.
	Wool's bane, —	,, Napellus, ...	,,	Aconitine, ...	Used for fever in Europe, in great repute for it with homœopathists.	
		VIII. Balsam and Resins.				
	Colophane, —	Pinus Abies, &c., ...	Coniferiæ.			
Hera Bal, ...	Gum Myrrh, —	Balsamodendron Myrrha, ...	Terebinthaceæ, .	... ...	Used by Griffith Heberden, &c., in Europe, by Dr. Kirk, in India, especially in the low fever of natives in Jails, ...	Gum.
Looban, ...	Benzoin, —	Styrax Benzoin, ...	Styraceæ, —	Benzoic acid, ...	Found useful by Thielmann, along with black pepper, ...	Ditto.
Caphoor, ...	Camphor. —	Laurus Camphora, ...	Lauraceæ.			

I. Pure Bitters.—In all parts of the world bitter substances appear to be regarded by the common people as febrifuges. The beautiful Menyanthes Trifoliata and the Tormentil, are as popular in northern regions, as Chiretta and its various substitutes in tropical ones. Such remedies were in great repute in regular practice before the discovery of Quinine. Although however, they act as tonics and improvers of digestion, and are admirable adjuvants of the true antiperiodics, it is doubtful whether they possess any strictly antiperiodic virtues of themselves. In this respect they bear very much the same relation to true febrifuges, as Salicine does to Quinine. Most of them are enumerated in the table, and, as a further account of some of them is given in the notice of Indian antiperiodics—it is only necessary to mention here a new one, the Cedron nut.

The *Cedron nut* furnished by Simaba Cedron, belonging to the family of Simarubeæ, is common through central America, at new Grenada, and especially in the districts near Corta Rica, where it is very cheap.

It has been quite recently introduced into practice. The powder of the dried almond, which is extremely bitter, is the, part administered: each almond weighs from 60 to 90 grs. the powder is given in doses of 4 to 14 grs.

M. Berton has himself taken it without experiencing any inconvenience, and is assured that it often succeeds in fever where Quinine fails. In America and Jamaica Dr. Purple and Dr. Magrath have tried it successfully in intermittent fever, and the latter says, without any benefit in remittent. Dr. Purple considers that it possesses marked tonic and antiperiodic properties, and is less likely than quinine to "produce encephalic or neuropathic phenomena."

It is however to be remembered that M. Lebert has reported to the Academy of Medicine unfavourably on Cedron as a febrifuge: its properties certainly demand a fuller investigation, especially as no complete analysis of it appears yet to have been made. The Cedron reminds one a good deal of the Bonduc nut, which is a native of West as well as East Indies.

II. Mucilaginous Bitters—Must rank in the same category as the last, but some of them would appear to be more active than the preceding. The chief of these, the Goluncha, belonging to this class, will be subsequently noticed. I am not inclined to expect much from the Baobab, and Cetrarin appears already to be forgotten.

III. Aromatic Bitters.—These too were formerly in high repute, but have latterly fallen into disuse as febrifuges.

India does not appear to be particularly rich in them. It is curious that the species of Galipea yielding Angustura bark, is more esteemed by the natives of the Cinchona countries than the true bark. Dr. Hancock gave very strong evidence in its favour.

IV. Bitters containing Alkaloids or Tannin.—To this class belong the most important antiperiodics, and the most valuable of them all, Quinine, has been examined above in detail. It remains to notice the other less important ones, many of which are found to belong to the list of Indian febrifuges.

I am told that no Indian tree comes so near the Cinchonas in its botanical affinities, as the Hymenodictyon Excelsum. As one of its chief habitats is the pestilential jungles of Goomsur, this would be an exemplification, if its virtues were found to be really considerable, of a favorite notion with some, that along with the bane, nature always supplies the antidote.

Bebeerine.—An alkaloid obtained from the bark of the Nectandria Rodiœi or Greenheart tree, which grows in British Guiana. Its qualities were mentioned by Bancroft, in 1769. Rodie announced its use in intermittents in 1834, and indicated the existence of the alkaloid. In 1843, Dr. McLagan made some additional experiments, and brought it into notice.

The bark cannot be said to be used in practice; the form in which the Bebeerine is used, is Bebeerinæ Sulphas. Its preparation is essentially the same as that of Quinine of the Ed. Ph. It occurs in brownish yellow thin glistening scales, which form a yellow powder, have a persistent bitter taste, are soluble in alcohol, sparingly so in water. Its solution is facilitated by a few drops of Sulphuric Acid.

It increases the appetite and improves the tone of the system—raises the pulse a little, occasionally exciting it somewhat, but its effects do not appear to have been very minutely determined. Becquerel says it has no action on the stomach or nervous system.

It has been brought forward in medicine as a subtitute for Cinchona. Dr. McLagan and Dr. Stratton have found it very efficacious in intermittents, but others have not been so successful.

I can scarcely speak of Bebeerine from personal experience, but my friend Dr. Dickson of the Artillery, to whose opinion I would attach much weight, informs me that he found Bebeerine given in equal doses to those of Qui-

nine, quite as good an antiperiodic as that medicine, in Artillery men returned from Pegu with fever. He gave it in repeated small doses.

I think nevertheless that its use would have by this time become more general in the tropics, (various writers as Drs. Anderson, Falconer, &c., in India, having reported favorably,) if its febrifuge powers had been such as they were at one time supposed to be. It was stated to be particularly serviceable in cases of cerebral disturbance, where Quinine might do harm, but we now know that such cases are rare.

It is usually stated, that the dose of Bebeerine must be at least double that of Quinine, and as the price is half that of Quinine, or 6*s*. 7½*d*. per oz., as imported into India, there can be no economy in its use, unless it can be manufactured at a much lower rate.

It is generally believed that Bebeerine is an important constituent of Warburg's Drops; this is stated by Royle, but I am not aware on what authority, unless that of Dr. McLagan.

On the whole Bebeerine is probably an antiperiodic of some efficacy, and a useful tonic; it may be considered the next vegetable febrifuge in value after Quinine, that is brought to India, and its powers both in remittents and intermittents ought certainly to be further tested.

The dose is, 1 to 3 grs. as a tonic, 5 to 20 grs. as a febrifuge. It may be given with Sulphuric Acid, or in substance with conserve of roses.

Salicine.—Willow bark, long a favorite with the common people in the North of Europe in various diseases, was brought forward about a hundred years ago, as a cure for intermittents, and when its active principle Salicine was discovered by Fontana, in 1825, it was hoped that a substitute for Quinine had been found.

Salicine is found in all the willow barks, but perhaps most abundantly in the Salix Helix; when pure, it forms minute rectangular scales, is very bitter and somewhat aromatic, is soluble in about 20 parts of water, soluble in alcohol but not in æther.

Its effects do not appear to have been originally very minutely studied, and it was only said generally that they resembled those of Quinine, and that in passing through the economy it was oxidised, and might be readily detected in the urine by a persalt of iron. Dr. Blom considered that Salicine had a peculiar tonic action on the mucous surfaces. But Briquet has examined it along with the vari-

ous salts of Cinchona, and ascertained that it produces no appreciable effect on the heart or the brain, the urinary passages or the kidneys.

He is therefore inclined to place the febrifuge powers of this substance as compared with Quinine, very low. Delioux too says, that Salicine has been of more use in adulterating Quinine, than in curing fevers.

It has been considered a powerful febrifuge in doses of 6 grs. and upwards. Buchner says 12 grs. in divided doses will generally stop an ague, and many cases of its efficacy are recorded by Dr. Pleischl of Prague. Dr. Blom has used it in intermittent, remittent and other fevers with success; Chomel found it useless. I cannot find any published record of its use in India, and I believe that at present it is not much employed. Dr. Dickson tells me, that he found Salicine quite inert, in the cases in which Bebeerine succeeded. It is said to succeed very often in temperate climates, but not so frequently as Quinine, and like Bebeerine to have the advantage of not causing cerebral congestion.

Its price, 4*s.* 5*d.* per oz., however renders its use in no way economical as a substitute for Quinine.

In truth I apprehend, that though Salicine has been found a tolerably effective febrifuge in the fevers of northern countries, it is comparatively powerless in those of the tropics, but it is a most valuable tonic in convalescence, and in throwing off the sequelæ of fever. It will be found a good corroborant and restorer of the digestion, when the stomach and the nervous system have been disordered by successive attacks of fever, and constant use of Quinine. In this sense it will be found a valuable substitute for that medicine.

The dose is from 6 to 30 grs.; it may be given in powder mixed with sugar, or dissolved in some aromatic water.

Phloridzin.—A crystalline indifferent substance, found in the bark of the root of the apple tree and of many other fruit trees. It is slightly bitter, with difficulty soluble in cold water, easily in hot water, alcohol or æther.

It has been tried by Koninck and others in intermittent fever, but has less power than Salicine.

Both those substances have been experimented with on a large scale at Rochefort, and their efficacy in fevers of any violence has been found to be problematical or doubtful.

The does is grs. x to xx.

Berberine.—A crystalline indifferent substance, procured by Buchner from the bark of the root of the Berberis Vul-

garis; it is very bitter, yellow, not easily soluble in water, more readily in spirits of wine. In Europe it has not been much used, and chiefly as a tonic in indigestion, in doses of i to iij grs.; it has been given up to 10 grs.

As the Rasout of India no doubt owes its properties to this alkaloid, it deserves to be more fully experimented with, as we shall subsequently see.

Cailcedra Bark—or Senegal Cinchona. It contains a bitter extractive matter called Cailcedrin. E. Caventou ascribes valuable properties to it, and Chomel made some experiments with it in ague in Paris, with some degree of success.

Oxyacanthin—Is a crystallisable substance, procurable from the root of the Barbery and white Thorn. It has been used much as Bebeerine.

Phillyrin—In the shape of sulphate was recommended in doses of 15 to 20 grs. in ague, by Jachelli and Dorvault, the young leaves and sprouts to be used also in powder, one oz. of them in the apyrexia. But there is no reason to think more highly of this than of the many similar salts.

Coffee and Caffein.—The Coffee plant belonging to the family of Rubiaceæ, attention was naturally called to its properties, and it has been considered that both Coffee and Caffein are febrifuges of considerable power. The action of Caffein has not been very accurately studied, although various salts of it have been prepared by Van der Corput and Hannon, but there is reason to believe that it acts powerfully on the nervous system.

Delioux gives the following account of the results of his experiments with Coffee.

He has used it extensively, and found it one of the best febrifuges. He never could procure Caffein in sufficient quantity to experiment with it, and therefore he cannot say whether it is to this alkaloid that Coffee owes its virtues. Roasted Coffee is far from possessing febrifuge powers equal to those of the raw berry. He therefore did not use the common infusion but a decoction, which he employed in the two following ways:

1.—A concentrated decoction of 1½ oz. of Coffee in a pint of water, boiled down to one-third or even two-thirds.

2.—In weaker decoction or tisane, ¾ of an oz. Coffee ordinarily being enough for two pints of water, 1-8th of which is lost by boiling.

To make these preparations, it is necessary to bruise the berry, that the water may more readily dissolve the soluble parts, and after letting it boil long enough, to pass it through

a seive. When the filtered fluid is sweetened, we have a drink by no means disagreeable to the taste.

The concentrated decoction is given in the apyrexia, a few hours before the expected access. It may be enough to cut short the fever, if it be a slight one, and especially if not of paludal origin, but it may succeed even in the most serious cases, for example when paludal fevers run on, and are not influenced by Quinine.

The weak decoction is given in the same way, but it is generally taken with less regularity by the patients, and is more likely to fail.

But if many will doubt Coffee being really a powerful antiperiodic, no one can deny its power of supporting the action of Quinine, and in this respect it is of high value. Patients have often found the use of Quinine along with the tisane as a daily drink very efficacious. Delioux says that frequently in cases of very obstinate fever from marsh miasm, where no benefit was derived from the use of Cinchona or Coffee separately, their conjoint use was attended with the happiest results.

The decoction of unroasted Coffee did not appear to excite the nervous system and produce insomnolence, like that of roasted, and this is an additional argument in favour of its employment.

V. Astringent Bitters—and substances containing much tannin, have long been used in Europe as febrifuges. The chief of them are enumerated in the table.

Gall nuts were tried extensively in powder with infusion of cheretta, some years ago in the dispensaries of Bengal, but the general result was unfavorable, conveying the impression that the mixture was not equal to the common country febrifuges.

Pure *Tannin* has been found by M. Chausant and others, and lately by Delioux, to have very manifest antiperiodic powers: the mean dose is 15 grs. during the intermission. M. Delioux goes so far as to say "But if in the treatment of intermittents, it is convenient to have at hand a remedy equal to Quinine, what an advantage is it to have a remedy far superior to it in another respect, the suppression of periodical nocturnal sweats."

As Dr. C. Hennig* found in one instance, that the injection into the left jugular vein of 7 grs. of tannin in half an oz. of water, was followed by decrease of the size of the spleen,

* Archiv für Physiolog. Heilkunde. vol. xii.

which became hard and wrinkled, its effects in spleen disease deserve to be studied.

Tannin has been used in combination with Quinine, and some think tannate of Quinine an efficacions salt. Briquet's opinion of it has been already given, and, if plain Quinine is not administered, surely it would be better to give some of the natural combinations of tannin and the alkaloids, that is the alcoholic extracts of bark, than this artificial one.

Olive.—The bark and leaves of the Olive tree have long been popular febrifuges, and Pallas thought he had discovered a vegetable principle which he called Vauqueline: but the fruit has been of late studied with care, and the result is, that it contains no alkaloid, and that the extract of the green fruit is probably inert. The bark and leaves cannot be considered of much value, although I observe that some experiments have been made with them in the Hospitals of the Army of the Crimea, and with a certain amount of apparent success.

VI. Some Acrid Pungent Medicines, a great portion of them tropical, have been employed as febrifuges. The theory of their action is, that by persistent local irritation, and the increased activity of the stomach and intestinal canal, and secondarily of the whole abdominal ganglionic system, consequent thereon, they help to restore the disturbed balance of the nervous system. One of these substances, pepper, may serve as a type of all, and is discussed among the Indian febrifuges.

A new substance, on which the French have stumbled in their recent attempts to find a substitute for Quinine, demands here a notice. The regular and systematic investigation of the subject which they have adopted, demands our high admiration, although no great practical success has hitherto attended their efforts. Cubebs and Copaiba, and other articles which it is unnecessary to enumerate, have been among the substances experimented on.

Apiol.—The active principle of the seeds of parsley was three or four years ago introduced to notice as a febrifuge, and extensively tried, with the general result that it was a dicided though not a powerful antiperiodic. The most recent and complete account of this substance is that furnished by M. M. Joret and Homolle to the Societé de Pharmacie, which I shall follow.

Apiol appears as a yellowish oily fluid of a peculiar special odour, somewhat like that of the seed; it has a very strong

acrid taste. It is soluble in alcohol of certain strengths, and in ether and chloroform of all.

Apiol in doses up to 15 drops causes a slight degree of cerebral excitement, analogous to that produced by Coffee. It produces a feeling of strength and comfort, along with a little heat at the epigastrium. When the dose is increased to 20 or 30 drops, we observe the phenomena of real intoxication, deafness, giddiness, noises in the ears, pain in the forehead, in short, symptoms very much resembling those which are the consequence of large doses of Quinine; this is extremely remarkable: exceptionally nausea, colic and diarrhœa have been produced.

In using Apiol as a febrifuge (when they incidentally discovered that it was also a very certain emmenagogue), M. M. Joret and Homolle mainly followed Bretonneau's principles of administering Quinine: 1.—To give Quinine in a single dose in sufficient quantity to produce a decided effect. 2.—To avoid giving it in fractional doses, as, like wine, it loses its effects, if given in divided portions. 3.—To continue giving diminishing doses of Quinine for some time after the fever has been stopped. 4.—To double the dose, when there are serious symptoms.

They also followed another result of Bretonneau's experience, and which may be considered an axiom in Indian Medicine, that it is wise to purge and vomit your patient, as a preliminary measure in ordinary intermittent.

They have administered the Medicine in two forms, first, in gelatine capsules, and secondly, in a syrup. Commonly in quotidian fevers they administer every day, five or six hours before the expected access, 4 capsules or 1 ℈ to adults, 2 or 3 capsules to young people, and one capsule to small children, but the last take the syrup more easily. In tertians they give the same dose, and in quartans they double it, and give it for two successive days. However many capsules may be required, it is better to take them all at once, than at intervals.

The results of this mode of administration in 1849 may be thus stated—out of 37 agues in France 35 were cured, 2 resisted the use of Apiol: they were both tertians. The mean quantity required to effect a cure was for quotidians over 15 grs., for tertians near 30, for quartans near 60 grs. The quotidians and tertians were commonly stopped by the first dose, the quartans required a second.

The results of a second set of experiments in 1851-52, at Rochefort, Bourg, Auray and Paris, were nearly similar, and

the aggregate of the two sets of experiments established an average of 86 cures in 100 cases, in temperate climates.

It was desirable to compare these results with those to be obtained in more Southern climates, and accordingly other sets of experiments were made at Ajaccio, Perpignan, Rome and Martinique. There the results were not so favourable, and the cures scarcely exceeded 50 in the 100, and thus the average of cures in all climates is reduced to 60 in the 100.

From this M. M. Joret and Homolle draw the very legitimate conclusion, that Apiol, although it cannot be used with the same advantage as Quinine to check the fevers of hot countries, yet may be very well substituted for it in the treatment of those of temperate ones.

Besides having the emmenagogue effect already alluded to, they have found Apiol especially useful in intermittent neuralgias, and in checking the noctural sweats of phthisical patients.

On the whole they consider the discovery of a substitute for Quinine in so common and abundant a plant as Parsley, one of very considerable importance ; that Apiol combines all the characteristics of a good medicine, energetic action, fixed composition, innocuousness and inliability to alter.

It will be curious to watch the history of this singular substance, which appears to be very interesting in a chemical as well as in a therapeutic point of view. It will surely not share the fate of the many medicines, whose use endures for a day, and which are then forgotten.

VII. Narcotics and Acro-narcotics—Appear beyond all doubt to be endowed with a certain amount of febrifuge power—most probably owing to their anæsthetic action on the nervous system, rendering the frame insusceptible of the peculiar periodic action, which induces a fit of ague. Under this head come, Nux Vomica and barks containing any amount of strychnia, which were at one time more used both in temperate and in tropical climates than now, also Aconite to this day employed in Continental Europe occasionally, Opium too, which has almost fallen into disuse as a febrifuge, and perhaps Physalis Alkekengi, though it does not appear that its active principle Physalin is more than a simple bitter.

Physalin.—The Physalis Alkekengi, having some repute as a febrifuge, M. M. Dessaignes and Chautard analysed it, and succeeded in procuring a bitter substance, which they have called Physaline, forming a light white powder, with a very slight shade of yellow, leaving in the mouth after a

time a very marked taste of bitterness. This substance does not seem to have been used medicinally, nor has its value, if any, been ascertained.

Were it otherwise, it might be well to examine Physalis Flexuosa, the *Isgandha* of this country, used in native medicine as stimulant and diaphoretic.

Opium.—No general account need be given of Opium or of its effects. Before the discovery of Cinchona, it was counted one of the most powerful febrifuges, and given either plain or with bark, or an aromatic tonic, it has since then been found very useful.

Paracelsus, Horstius, Ettmüller, &c., gave it a little before the paroxysm. Berryat, who last century revived its use, gave about an hour before the access, 6 to 8 drops of Sydenham's laudanum to children of 3 to 5 years, 10 to 12 drops, to those of from 10 to 12, and 18 to 30 to adults.

Its action has been thus explained. "It first excites the ganglionic system, increasing its action on the vascular apparatus, and especially augments the activity of the nerves and vessels on the periphery of the body, causing fulness of the pulse, and heat and some turgor of the skin. By this increased peripheral action, the ganglionic system is somewhat relieved, and thus a portion of the real cause of the affection is removed, and this effect is still more strongly produced, when the Opium is given according to the old fashion with Wormwood or bark. If now the cold stage comes on, it occurs when the Opium has already begun to exercise its secondary operation. It then manifests its power of controlling cramps; the shivering and the heat also are less, and the equilibrium of the nervous system is restored, without so strong a reaction as usual of the vascular system being produced. Opium therefore both acts on the causes of the disease, and moderates the violence of the attack."

The Madras Report mentions benefit from a full dose of laudanum about an hour before the attack.

Dr. MacDougal in Chittagong (about 1826) says "it was my constant endeavour to prevent or shorten the paroxysm by giving free doses of laudanum with compound spirits of lavender, and often with the happiest effect," and Mr. Waring of the Madras Service, a very judicious observer, has recently often seen Opium administered in a full dose, of ℥xl at the commencement, or even during the presence of the cold stage, act like a charm in cutting it short, and though it did not appear to shorten the subsequent hot stage, yet seem in many cases to mitigate its severity.

This practice of Mr. Waring's resembles rather that of Lind, Houlston and Odier of Geneva, than the one first described. They did not give the medicine till half an hour after the commencement of the hot fit, when it generally afforded immediate relief. Lind found that an opiate liniment rubbed on the spine of children on the approach of the cold stage, often prevented the paroxysm, which makes one wonder at his not, like Blane, administering the Opium earlier by the mouth.

Gausland thinks that the treatment by Opium, when given in the hot stage, has a tendency to make the fever more obstinate.

"It is a curious fact," further says Baumgärtner, "that sometimes in comatose intermittent, Opium may be administered with advantage, and even remove the comatose state. But it has only this effect, when the cerebral action is as it were suppressed by the violence of the cold stage, and we must be very careful not to give Opium in cases, where such a comatose condition depends on over fullness of the vessels, when its use would very likely induce apoplexy. We thus see how useful and also how dangerous Opium may be in bad intermittents: it is not to be given in common cases of that kind, but it may in certain given cases be the means of saving the patient." The use of Opium under such circumstances is one of the most difficult questions a physician has to decide on. Opium is not used in such cases in Bengal, or indeed much in any fevers, but its power of preventing the paroxysm as well as of moderating it, according to the period at which it is given, is undoubted, and might be oftener brought into play.

We have seen above, that Opium is often found to be a most useful adjuvant to Quinine, and I have no doubt that it will again be used in the treatment of fever, for there seems to be no good reason for its having fallen into such entire disuse. In fact it has begun to be employed again. Dr. K. MacKinnon has some sensible remarks on this subject, in his excellent work on Indian Medicine, of which a new edition is hoped for. Several Indian observers of late years record its use. Dr. Kirk says that Opium greatly assists the use of Quinine. Surgeon Jas. Stewart, of H. M. 18th, in Pegu, found the combination with morphia particularly useful.

In an economic point of view, it is very important to know, that by adding a little Opium or Morphia, the dose of Quinine may be reduced. M. Briquet is not singular in this opinion in Europe. M. Hannon and others think

as he does, and it is scarcely necessary to repeat that from the earliest introduction of bark, laudanum was frequently used in conjunction with it, by Sydenham and others.

VIII. Balsams and Resins.—I have classed somewhat vaguely under this head, a few substances, about which, as they have never been in any very great repute as antiperiodics, it is not necessary to say a great deal.

Myrrh has long been in repute in low fevers in Europe, and occasionally in agues. Dr. Kirk has found it very useful in the typhoid state which is frequently the second stage of paroxysmal fever in this country, and also in the low adynamic fever of jails. He has also hazarded the conjecture that myrrh is an element of Warburg's Fever Drops, but apparently without any sufficient foundation.

Camphor has been much used in all low fevers, and about eight years ago, Dr. Bararch, a Military Surgeon, announced that he cured the bad intermittents of Wallachia with it, giving 1½. gr. pills every two hours for six or eight hours before the expected paroxysm. The advantages were—1. Relapses not so common as under Quinine—2. Its use is not attended by any of the disagreeable effects of Quinine—3. It is much cheaper. I do not however know that this internal use of camphor, has found more imitators than the external employment of it, which has been practised by some.

Benzoin has been little used as a febrifuge; Dr. Thielmann a few years ago recorded that he had cured fevers by a mixture of benzoin, mustard and black pepper given before the paroxysm.

Of these substances, only one more, the product of modern French ingenuity, requires further notice.

Colophane.—This is a resinous powder, procured in a peculiar way by treating Pine Resin with nitric acid. Its febrifuge properties have been attested by 55 cases from distinguished practitioners, but Military Surgeons at Ajaccio, Rome and Rochefort, think very slightly of its powers, and it is not a substance likely ever to become of any importance in medicine.

INDIAN VEGETABLE ANTIPERIODICS.

When we turn to consider the Indian febrifuges, which are neither few nor unimportant, we are immediately struck with the fact, that nothing has of late years been done in the

investigation of their properties, that with the labours of Dr. W. B. O'Shaughnessy, which terminated in 1842, all systematic examination of them has completely come to an end, and that in endeavouring to give a sketch of what we know of them, I shall have to refer to the state of our knowledge as it was 14 years ago. I can scarcely find a new fact to add. While the French have been exercising their utmost ingenuity in a much poorer field, to find a substitute for Quinine, we have absolutely done nothing.*

This has been the case in Bengal at all events.

A few circulars have indeed been now and then addressed to the Service by the Medical Board, asking their opinion respecting the value of certain native febrifuges, but I believe that they have never elicited any thing of importance.

Have we now no longer any Chemists among us, to complete the analysis of such substances?—have we no one who will engage in a regular practical investigation of their Medical properties, such as can only be conducted by those who have large hospitals at their command? The subject is by no means unimportant, or unworthy of the attention of Government, even in an economic point of view.

I hope indeed, that the attention which has lately been directed in the North-West to *atees* and *rusut*, may be construed as a sign, that the profession is beginning to awake to the importance of the subject.

I have treated of Indian vegetable antiperiodics separately from other ones, because I think it will be a convenience to many in this country, to have our chief Indian antiperiodics brought before them in one connected view.

Narcotine, called *Anarcotine* by Dr. W. O'Shaughnessy.—This substance may be treated of as an Indian antiperiodic, for there is no evidence of its possessing such powers in Europe.

The power of Opium to act successfully as an antiperiodic being established as a fact up to a certain point, as we have just seen, and Dr. Roots and Mr. Jetson having had some reason to suppose narcotine antiperiodic, Dr. W. O'Shaughnessy naturally enquired to what extent this property was likely to be available in India, and arrived at a most favorable estimate of the virtues of the alkaloid.

This substance, which occurs in needle-shaped crystals of pearly lustre, of intensely bitter taste, was experimented on by him, with the result of his satisfying himself that, as an

* Mr. Piddington is understood to have devoted a good deal of attention to this important subject, especially to a search for alkaloids in native febrifuges, but the results of his more recent researches have not been yet made known.

antiperiodic, it was scarcely second to Quinine! A great many practitioners in Bengal, for instance Dr. D. Stewart, Mr. H. Chapman, Mr. W. A. Green, gave the sanction of their names to this substance being effectual in curing intermittent fever—but we must recollect, that almost every febrifuge that has been submitted to the profession, has in the first instance been favorably reported on. As it is agreed on all hands that it is powerless in remittent fever, I fear that this substance must be added to the long list of feebly antiperiodic remedies, which have for a time been in fashion. Certain it is that Narcotine has quite fallen out of use. I believe that no one now has any faith in it. The Medical Board's Report of 1851 when treating of substitutes for Quinine, does not even allude to it.

Its advantages were supposed to be, that it did not produce narcotism or constipation, or the disagreeable head symptoms usually produced by Quinine, and it was considered to be particularly useful in ague complicated with dysentery. Mr. A. Grant also, who used it extensively at Bhagulpore in cases of intermittent fever and of neuralgia with excellent effect, tells me that he thought it peculiarly adapted for irritable and excitable anæmic patients, who could not bear Quinine.

All these advantages appear to me to result simply from the inertness of the substance. Dr. G. B. Wood says that he has never been able to divest his mind of the belief, that, as prepared in India, it must have contained morphia. Bally gave 129 grs. in one dose without exciting any obvious effect. Dr. Roots gave it in gradually increased doses up to a scruple without the least injury.

Those who have used Narcotine are very positive as to its diaphoretic effects, and probably we are warranted in considering it a diaphoretic with slight tonic powers.

On the whole I apprehend that there can be little doubt that it should be struck out of the list of antiperiodics. This is very much to be regretted, as its cost, 4 annas per oz., would have made it available to all—that is, if, as Dr. W. O'Shaughnessy imagined, Narcotine could be extracted from Opium, without detriment to the qualities and commercial value of that article, a point I believe very doubtful.

Dr. O'Shaughnessy says—"In 20 grs. doses in acidulated water it is powerfully antiperiodic, in 1 gr. dose thrice daily a valuable tonic."

Berberis Lycium.—From this and other species, common in the lower ranges of the Himalayas, is prepared Rusut,

an extract of bark and wood: there are several sorts of varying quality: the best are of a deep yellow colour, totally soluble in water, and made from the bark of the root.*

The commonest use of the Rusut is as a local application in ophthalmia, and as such it was probably long in repute in Europe, as the ancient λγκιον Ινδικον, for Celsus gives Lycium as an ingredient of half his eye prescriptions. But it is also undoubtedly a powerful febrifuge, in which many have confidence, and besides being tried extensively at the Medical College Hospital by Dr. W. O'Shaughnessy, it has been much used in Rohilcund, by Drs. Kirk, Stiven and Hay, and by Medical Officers before them: it acts especially as a diaphoretic, and in this respect its effects have often been compared to those of Warburg's Drops, for they are both certain diaphoretics. Its use however is not attended with the intense degree of discomfort, which in the first instance follows the administration of the Drops. Part of the efficacy of Rusut is no doubt owing to the presence of Berberin, which has been experimented with in Europe—however without any very striking effects. This alkaloid has not been used in India. But, though its preparation be troublesome, it should be made in considerable quantity from the Rusut, and have a fair trial given it.

Rusut, according to O'Shaughnessy, is best given as a febrifuge in half drachm doses diffused through water, and repeated thrice or still more frequently daily. It occasions a feeling of agreeable warmth at the epigastrium, increases appetite, promotes digestion, &c., and acts as a gentle but very certain aperient. He has found it most useful in

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* No fewer than 11 articles of Ibn Baytar's list of Arabian medicines are referred to the head of Berberis, in Dr. Sontheimer's translation.* The article λογχιτις, the name of the shrub producing the λγκιον Ινδικον according to Dioscorides, occurs twice in the list, but without any reference to Lycium, which is twice mentioned by the names of Lúqyún and Qasid.

Dioscorides says of the λογχιτις that "its leaves and shoots steeped in vinegar are said to cure phlegmasies of the spleen and icterus, and to be emmenagogue," not "prevent menstruation" as Dr. F. Adams seems to have rendered it. Also that "two spoonsful of the seeds are purgative, and useful in poisoning." He also says elsewhere that another λογχιτις, the τραχεια, or rough, is useful in spleen. Lib. 3, Cap. 162.

The dried seeds or berries of barberry are to this day used as refrigerants on the continent—and seem to have been much used in Egypt. Prosper Alpinus, who appears to have been the first to suggest that the λγκιον of Europe was the product of the Berberis Cretica, mentions them with high favour, and states that he was cured of a pestilential fever with bilious diarrhœa in Egypt by their use.

* Transact. Med. and Physl. Society, vol. ix.

curing ague, but it has been employed with success in remittent fevers in the Upper Provinces.

Rusut is used extensively at some dispensaries in the North-West, and many in that part of India think it second to Quinine only. The substance well deserves further investigation, especially as it appears to exercise a beneficial power over remittents, as well as intermittents, (the great test of the value of a febrifuge,) and I believe that the Medical Board not long ago took measures, with the view of having its powers more fully tested, by the preparation on the large scale of the tincture, probably its best form for exhibition. As far as I can learn, the experiment has been in the main a successful one, and Rusut is the most promising of our Indian febrifuges.

Tincture of Barberry is prepared from 8 oz. powdered bark to one pint of alcohol: its dose is ʒii. to ℥ss.: the dose of the extract is 20 to 30 grs. daily.

Soymida or *Swietenia Febrifuga.*—Very abundant in Nagpore and Southern India. *Rohun* bark is an undoubted febrifuge: In the bazars in Bengal, Nux Vomica bark is often sold for it, and from this, Mr. Piddington, who has shown much zeal in examining native febrifuges, procured a salt, which Dr. O'Shaughnessy found to be one of Brucine. Dr. O'Shaughnessy has never succeeded in obtaining an alkaloid from the true Rohun, which it may be observed is of a dull red colour, with rough grey epidermis, and yields a red powder.

The value of this bark as a febrifuge has been attested by Roxburgh, Duncan, Breton and Spilsbury.

Dr. O'Shaughnessy does not think so highly of this bark as others do, not considering it much superior to that of its congener, Mahogany. He counts it useful where astringent tonics are applicable, but of very questionable efficacy as a true antiperiodic; he thinks it may succeed where other astringent tonics will do so.

From the reports of dispensaries I am inclined to have a somewhat higher opinion of this medicine, and believe that it is of considerable use, though by no means equal to the Berberis. If the statement of the Madras Report be accurate, its virtues may be more powerful than is supposed. The Reporters say—"We have from our own experience found that when taken beyond the quantity of 5 or 6 drachms in the course of the day, it produces vertigo and other head symptoms." This is confirmed by Dr. Spilsbury, who says large doses were found to produce vertigo.

The ordinary dose is about a drachm three times daily.

Cedrela Toona.—Bark of Toon-wood tree, which has a wide range throughout India; though tolerably useful with Kutkulinga, it is of no great value, and is merely mentioned here, as it is often given along with that nut.

Cocculus (Tinospora) Cordifolius. Goluncha.—Creeper—especially on neem trees, whence called also *nim gilo ka sath*: roots and stem are intensely bitter.

The native name of the extract is *Palo*, that of the decoction is *Pachana.*

Mr. Piddington found that the bitterness varied, according to the season when the plant was gathered.

No later analysis has been made of Goluncha than that of Mr. Piddington,* whose experiments indicated starch, mucilage, extractive and a crystalline substance.

Dr. Hardie† of Oodypore and Dr. Stewart‡ of Calcutta used the extract with success in several cases of intermittent fever. Dr. H. H. Goodeve§ considered extract of Goluncha if not equal to Quinine as a febrifuge, at least as good as the common Cinchona bark, and much better than Chyretta. Dr. O'Shaughnessy, though he thought it tonic, could not ascribe any very distinct febrifuge effects. Some of the dispensaries in the North-West report very favorably of this substance.

There are however no good recent accounts of it, and the substance certainly demands further examination, as also does Cocculus Crispus, the Menispermum Verrucosum of Roxburgh, to which Mr. Piddington called attention in 1829.

The extract is undoubtedly a useful tonic, and its decoction has a great reputation among native practitioners in old intermittents, when the dose is about 1½ oz. thrice daily.

A tincture is prepared from the stems 8 oz., spirits O. ij. The dose of it is 2 ʒ to ʒss. That of the extract is 1 ʒ to ʒijj. daily.

Guilandina Bonduc, Kutkulinga—East and West Indies, commoner in Bengal than Madras.

The kernels are very bitter. Mr. Piddington has detected in the nuts, oil, starch, sugar, and resin: further analysis is desirable.

This substance is the commonest antiperiodic supplied in the list of Bazar medicines to hospitals in Bengal, and it is undoubtedly one of considerable utility, especially in con-

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* Transact. Med. and Phy. Soc., Calcutta, vol. 4.
† Loc. Cit. ‡ Loc. Cit. § Op. Cit., vol. 5.

valescence from fever. I cannot speak of its qualities from any accurate observation, although like others I have used it a good deal among sepoys and jail prisoners with apparent benefit. Mr. Waring thinks but poorly of it. But many think differently, and Sub-Assistant Surgeon Bholanath Doss of Ajmere, says "a few doses of it with black pepper were sufficient to put a stop to the paroxysm. He sometimes gave 12 to 15 grs. three times during the day, at other times he gave 8 grs. every hour, leaving it off an hour before the expected paroxysm. If it does not stop the paroxysm the first time, it seldom fails the second."

The common way of exhibiting this substance is to give, of the nut finely powdered, and of black pepper, each, 6 to 20 grs. three times daily.

Ophelia Cheretta.—This common and abundant plant in the bazar, supplied chiefly by the lower ranges of the Himalayas, with its many excellent substitutes which have been enumerated in the Table, may be regarded as a type of the simple bitters, so many of which have been employed in Europe as febrifuges. For such purposes it is employed in India, and it will do whatever a simple bitter can in stopping intermittents. This is of course not very much, at least in the tropics, notwithstanding the opinions of physicians of a past age, for instance Boerhave, who had great faith in Gentian, and even of some modern ones, if the fever be of any violence.

Cheretta however is an extremely useful tonic, and of much service in convalescence from fever. It is one of the few articles of the Indian Materia Medica, which is in every respect an adequate substitute for the corresponding European article; and there is no occasion for any Gentian being imported into India, although Twining, with the fondness for particular remedies which is engendered by exclusive modes of practice, imagined that Extract of Cheretta had not the peculiar virtues which he attributed to Gentian in dysentery, virtues which I have never been able to discover.

Cheretta is a useful vehicle for other remedies, and not long ago infusion of Cheretta with powder of gall-nuts, was tried as a remedy in dispensary practice with indifferent success. Probably Cheretta by itself would have been quite as efficacious.

I need scarcely add that Cheretta is given in Infusion and Tincture like Gentian.

Azadirachta Indica.—*Neem* tree—very common in India. Every part of this tree, especially the bark, is bitter. The

bark is also astringent; the leaves are very bitter and nauseous; from the ripe pericarp of the fruit a bitter fixed oil is expressed. Mr. Piddington believes that he has obtained the bitter principle in a crystallised form. But the properties of this tree are imperfectly determined.

The bark is considered by native practitioners as among their most valuable tonics, and is given with aromatics in fever. Dr. White of Bombay used the bark as a febrifuge, and almost with the same success as Cinchona. The Madras Report considers it superior to Rohun bark.

Jadubchunder Sett of Bareilly has recently found extract of neem bark very useful in the treatment of ague. It is certainly a substance well adapted for use in Dispensaries.

It has been given both in decoction and in extract.

Piper Nigrum and *Piper longum*—black pepper and long pepper.—These substances appear to have been used as febrifuges in the east from the earliest periods. The powder and the root of long pepper have been much employed in Hindu medicine.

Both Celsus and Dioscorides recommended the use of pepper, and it has always remained a popular remedy, although Van Swieten and Murray endeavoured to discourage its use, by saying that it produced inflammation, and in more modern times Barbier says that in some instances it has produced death by the aggravation of a pre-existing gastritis.

Its great acridity is recognised when we apply it to the mouth: swallowed, it stimulates the stomach and produces a feeling of warmth in that viscus: in small doses it aids digestion, in large it has caused inflammation of the stomach. On the vascular and secreting system it acts as a stimulant.

It is used as a popular remedy in many parts of Europe for ague, and is commonly taken infused in ardent spirits. I have heard of its being considered a great remedy for spleen at some Indigo Factories. It would seem that the local stimulus and thence resulting increased activity of the stomach and intestines and the whole ganglionic system, help to restore the disordered balance of the latter.

Apparently there is no doubt that slight cases of fever are cured by it.

The dose is 5 to 15 grains, three or four times a day.

Piperine.—A crystalline neutral principle was discovered in pepper by Oersted, and brought into notice by Meli, an Italian physician. Its effects resemble those of strong pepper, and Dr. Hartle never found it affect the sensorium.

Baumgärtner says, he has used it carefully, and thinks that as an as antiperiodic it comes next Quinine. Dr. Gutteeit of Orell says that in some cases it seems to fail. He thinks Arsenic the best febrifuge, next Quinine, next Piperine. Dr. Hartle of Trinidad found Piperine eradicate intermittents, when Quinine had failed. Dr. Blome also bears witness to its efficacy.

Soubeiran, however, found it fail—and in Calcutta Dr. O'Shaughnessy says that it never succeeded. These discrepancies show that the subject requires further investigation. There is a strong *a priori* presumption that Piperine should be of considerable value—its extremely irritating property is its drawback.

Meli gave a whole scruple of this substance in 8 or 10 pills at once before the paroxysm—and continued the use of it some days. Dr. Baumgärtner found repeated 2 gr. doses efficacious. Dr. Hartle states that in all cases of long standing he began, as soon as the sweating stage was established, by giving gr. iij. of Piperine every hour until gr. xviii had been taken, and on the following day, when the intermission was complete, he gave the same quantity every three hours. In other cases he recommends grs. xxxvi. to be given in the 24 hours.

Toddalia aculeata.—A common bush on the Coromandel coast. All the parts are very pungent, especially the roots when fresh cut. The fresh leaves are eaten raw for pains in the bowels; the ripe berries are fully as hot as black pepper, and have nearly the same kind of pungency.

The fresh bark of the root is administered by the Telinga physicians, for the cure of the remittent, called Hill fever. Roxburgh conceived that this tree possessed very valuable stimulant properties, and Dr. O'Shaughnessy is of the same opinion, though he does not appear to have ever made any experiments with it. In fact nothing has been added to what Roxburgh knew, although some specimens of the bark were sent to Europe in 1818. Its properties are worthy of further investigation.

Aconitum Heterophyllum.—The root of this plant has been long known in Indian medicine as a tonic, and aphrodisiac. Mr. Heming, Sub-Assistant Surgeon of Orai, has lately brought to the notice of the authorities, a substance passing under the name of Atees, which he has found to be an invaluable febrifuge, superior in many cases in his partial estimation to Quinine.

I first saw this substance in the form of a fine white pow-

der with an intensely bitter taste, and from which a very bitter extract may be prepared. I have since seen the root from which it is procured; it is fusiform, and occurs in single pieces, with one extremity broken off; the largest I have seen is not more than an inch in length; the roots are grey outside, and white internally, with a very bitter taste. I believe they have not yet been thoroughly analysed.

The true Atees is the root of Aconitum Heterophyllum, which only grows in the Himalayas, and Dr. T. Thomson tells me that the root sent here by Mr. Heming agrees with Dr. Royle's description of that plant; but Captain Lowther says that Atees grows chiefly in the Deccan, especially in Guzerat, whence it is conveyed to Indore. It is procurable there with difficulty for 9 rupees the seer.*

The true Atees is intensely bitter, slightly astringent, and with abundant farina, which is free from any noxious quality. There is a spurious substance resembling it, but by no means of the same efficacy, which Dr. W. O'Shaughnessy says he has reason to believe is the dried tuber of the Asparagus Sarmentosus.

It is to be hoped that the question of the value of the substance used by Mr. Heming, and the locality from which it is derived, will be soon determined. He deserves much credit for the zeal with which he has prosecuted the subject.

The dose may be considered about 1 scruple three times daily; Mr. Heming has given 30 grains as often, without any bad effect. I may mention that I have cured a few cases of slight fever in the College Hospital with 2 grs. of Atees three times daily; but it is questionable whether the cure was not attributable to the purgative or emetic given in the first place.

Coptis Teeta.—The roots of this plant are brought in by the Mishmees, an Assam tribe, whence its name. According to the Bengal Dispensatory, "The roots are nearly cylindrical and uneven, more or less curved, greyish brown outside, internally bright yellow, varying in thickness from the size of a crow-quill to double that diameter. The taste is intensely and purely bitter, very lasting, with a very slight aroma." I have seen it neatly packed in small bags.

As to chemical constitution it is only stated, that it contains neither tannic nor gallic acid, but abounds in a yellow bitter principle soluble in alcohol and water.

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* Proceedings of Agri-Horticultural Society, Englishman.

Besides being found a powerful tonic both in the General Hospital and the Medical College, some 15 years ago, I am told that many Medical Officers in Assam have great faith in it, and have used it as a substitute for Quinine both in remittent fever and in common agues. I would instance Dr. Shurlock and the late Dr. Johnston Long, who himself proved a victim to fever, shortly after he gave me an account of his experience of this substance. Why is it not more used?

The dose is about 15 grs. of the powder—or it may be given in decoction, infusion or extract.

Alstonia Scholaris—Appears to be abundant in the Concan: and Dr. Gibson of Bombay has found it useful as a febrifuge; he published an account of its qualities about two years ago in the Pharmaceutic Journal, to which I have not been able to obtain access. I think he gave it in tincture.

Wrightia (Conemorpha) Antidysenterica.—The bark of this tree, which was once introduced in the London Ph. as Conessi bark, and was greatly lauded more than a century ago by Geoffroy, known also as *Codaga* and as *Koorchee*, has long been a popular remedy on the Malabar and Coromandel Coasts, and also in Bengal in dysentery, and from a somewhat extensive trial which I have made of it in that disease, of which I hope to be able to publish the results, it appears to be a remedy of no mean value.

It has however been also known on the Malabar Coast and among the Portuguese there as a febrifuge, under the name of *corte de palla.* Dr. Cleghorn informs me that several Medical Officers in the Northern Circars have been administering it of late.

I have no knowledge of its febrifuge virtues, which I doubt, but it seems to have fallen into disuse from carelessness in selecting the bark, and it may deserve a further trial.

An infusion of the seeds called *indirjau* has been called febrifuge, but is only demulcent.

The most common and convenient way of administering *koorchee*, is to give 1½ to 2 oz. of decoction three times daily.

Gunti Paringee.—This root, which does not appear in the list of febrifuges, because it has not been ascertained to what plant it belongs, has been brought to my notice by Dr. Cleghorn. It is mentioned by Ainslie, and little more is to the present date known of it, than what has been said by him.

It continues to be used in Southern India by native practitioners as a febrifuge. Ainslie says—"It is a small, knobby, somewhat warm and slightly bitterish tasted root, which I understand the natives prescribe in fevers and

catarrhs; from the word Paringhee, I am inclined to think that it is brought from some foreign country." From its low price, Dr. Cleghorn would suppose this to be improbable, and he is not without hopes of soon ascertaining to what plant it belongs. Of its absolute antiperiodic qualities nothing seems to be known with accuracy.

INORGANIC ANTIPERIODICS.

The great advantage of these substances is their cheapness and abundance. I can only notice the most important of them. As Cinchona occupied the greatest share of our attention among the products of the vegetable world that have been deemed antiperiodic, so shall we find Arsenic to be far the most important of those derived from the mineral kingdom. It will therefore be examined at greater length than the others.

Arsenic—Is one of the oldest articles of the Materia medica—and has been employed from the earliest ages in China and Hindostan. Its white oxide, *Suffeed Sumbhul*, has long been used in India for the cure of intermittents. Although Dioscorides and Pliny, Celsus and Galen used this substance, in which they were followed by the Arabian physicians Rhazes, Serapion and Avicenna, none of these appear to have employed it in fever, and it was not till the end of the 17th and commencement of the 18th century, that the treatment of intermittents by arsenical preparations became known in European practice.

On its first introduction it had its enemies as it has now. It was termed "certissimum at nequissimum." The first regular treatise on the application of Arsenic to cure fevers was by Professor Slevogt, in 1700—who considered it superior to Quinine, especially in respect of its preventing relapses, which to this day is one great alleged advantage of its use.

Frick, Keil, D. Munro and others confirmed his report, and the two Plecitzes gave a fresh impulse to its use, by the accounts of its successful employment published by them in Vienna in 1783.

Fowler and Pearson soon after made the medicine popular in England, where it was known as the tasteless Ague drop. Frere of Birmingham cured upwards of 1,000 workmen. Willan knew no medicine so efficacious. Brera in Italy, Barton in America, Foderé and others in France, attested

its virtues. It was also used in the tropics. The Madras reporters say: "Arsenic which for some years has been in vogue in England, has been occasionally prescribed." They did not however like the practice, although they said that it had in some instances stopped the disease, where other remedies had failed.

The use of Arsenic however again lost ground in Europe, though never discontinued in the tropics, mainly owing to the discovery of Quinine, and Boudin (1842) had many prejudices and much opposition to contend with, when he endeavoured to re-introduce its use. From that date up to the present time, a constant warfare has been kept up, between the supporters and the enemies of the arsenical treatment.

Effects of Arsenic.—1. All preparations of Arsenic may be considered poisonous—but the degree of this quality depends much, on the readiness with which it is absorbed. There is no doubt that horses and sheep have borne doses of several drachms without sustaining injury, and that in some continental districts it is mixed with the food of cattle with the view of fattening them; nay there seems to be reason to believe that it is true that the inhabitants of some parts of Styria, and possibly of India, take it as a tonic and a fattener, and it is to be borne in mind, that Arsenic has of late been discovered in many mineral waters.

2. In very small doses as of 1-20th to 1-10th of a grain daily, Arsenic may be taken for some time without any marked effects being observed. Sometimes there is a feeling of increased warmth in the stomach, and the appetite appears to increase. But sooner or later, thirst, indigestion, and slight burning in the stomach, come on, along with dryness, burning and itching of the larynx and throat, sometimes with salivation. At last come entire loss of appetite and slight fever. The skin becomes dry and hot, the pulse more frequent. The eyelids are sometimes swollen and very itchy, while some complain of stiffness of their hands and feet. All these symptoms may gradually increase but with intermissions. The nose, lips, eyelids and even the eyebrows swell. The patient becomes morose and sleepless, and has a feeling of indescribable anxiety.

3. These effects may increase, all the preceding symptoms be aggravated, and in addition various eruptions appear, sometimes abscesses or ulcers, and the hair and nails come off. The patient falls away—the nervous system is disordered. There are trembling, giddiness, cramps, restlessness along with

excessive feeling of weariness, apathy and heaviness. The patient dies at last, but with his consciousness unimpaired.

4. In larger doses (gr. 1 to 5) the effects are more rapid and violent, and we have acute arsenical poisoning. These effects vary much according to the temperament of the person poisoned, the quantity of the poison, its form, whether in powder or in solution—and according as the stomach may be full or empty, when it is taken.

a. The gastro-enteric form comes on most rapidly, especially when the poison has been taken in solution. The symptoms are, a burning feeling in the throat and stomach, with vomiting, afterwards meteorism and diarrhœa with violent colic and straining, often with strangury and small frequent pulse, voice scarcely audible, skin cold and covered with perspiration. To these succeed convulsive movements and cramps of the extremities, and even Trismus and fainting. The patient dies usually after a few hours, sometimes a few days or later, from the effects on the intestinal canal and the whole economy.

b. Sometimes the cerebro-spinal symptoms predominate. The stomach and intestinal canal appear but slightly affected. There are symptoms of a deep impression on the nervous system, great weakness of the muscles, fainting, delirium, convulsions, insensibility, paralysis and sudden death. These symptoms occur chiefly after the ingestion of large quantities, and have been thus described by Grisolle. "The patients are as if struck down by lightning. Their figures and bodies cold and cyanotic, resemble those of cholera cases, the dyspnœa is extreme, and death occurs in a few hours, with sinking and syncope. Should the patient recover, partial paralysis, sometimes permanent, is the result; at other times there are bad sloughing ulcers especially on the legs."

In cases of poisoning and of its use generally, it may be most easily detected in the urine, spleen, and liver.

Theory of its use in Fever.—If notwithstanding M. Briquet's ingenious explanation of the action of Quinine, its operation as a specific cannot yet be entirely solved, much more is this the case with Arsenic, and with Briquet's theory of its operation. We really know nothing more of its action, than the fact that it does stop fever. We have seen that in small or medicinal doses its palpable action on the economy is slight, and that it is only in certain toxic cases that it produces a great effect on the nervous system.

Nevertheless some have supposed, that its irritating effect on the stomach reacts on the ganglionic system, and thus on the fever. One of the last who has experimented with it, Jacquot, thinks it sedative—for in one of his patients the pulse fell to 50,* and Briquet's theory of its action is, that it acts on the nervous system, depresses the action of the heart, stopping the production of animal heat and the functions of life. Billing says, "it acts on the liver as much as mercury."

Uses.—I cannot do better than quote M. Boudin, "I am assured," he says, "by successive trials, which have been repeated with similar results by many physicians at Marseilles, that arsenious acid, properly prepared, preserves in the somewhat microscopical doses of the hundredth of a grain all its medicinal properties in marsh fevers. Further I have obtained from 1-100th of a grain of this remedy the removal of fevers contracted in Algeria and Senegal, which had resisted all previous measures, including Quinine and change of climate. I have been able in a great number of cases to cure with very small doses of arsenious acid fevers of all types, contracted in latitudes the most various, often complicated with enlargements of the abdominal viscera."

A substance like Arsenic cannot be used with impunity without care. Boudin lays down the following rules: —

1*st Rule.*—To begin with an emetic of Ipecacuanha and Antimony, if there be any disorder of stomach or even loss of appetite. After the fever is stopped, return to the emetic if necessary, that you may get the stomach into a proper state to take abundant nourishment.

2*nd Rule.*—To give the arsenious acid in fractional doses, the last to be administered at least 2 hours before the expected access—to proportion the dose to the special character of the fever, which varies according to individual places and seasons. To profit in the early part of the treatment, by raising the dose of arsenious acid, by giving every quarter of an hour about 1-20th of a grain.

According as the tolerance diminishes, to lessen the dose and give it only in fractions, and if there be cause, to administer the medicine wholly or partially by the rectum. From ½ grain up to 1½ grains are tolerated by the rectum, after the stomach has ceased to tolerate the 1-10th of a grain. The medicine to be taken on the day of apyrexia, as well as during the day of access.

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* Melanges Medico-Litteraires.

To continue it for a time proportional to the duration of the malady, and its resistance or otherwise to former modes of treatment. In first attacks of fever, to continue it for at least eight days after the entire cessation of the access; in cases of old and obstinate fevers, to prolong its use for 30 or 40 days, and even longer periods, if necessary.

3*rd Rule.*—To use as substantial and abundant nourishment as possible, having no limit but the power of digestion—to prefer roast beef and mutton, to abstain as much as possible from drinking much water, and to use a generous wine in proportion to the degree of fever or debility.

Boudin reports that this treatment is particularly successful, and he and Massellot both think relapses less frequent than under other modes, and they assign as reasons for the treatment not being popular—

1.—That the various modifying effects of climate have not been sufficiently considered by others.

2.—That it has not been given in suitable doses.

3.—That there has been a general prejudice against it as a poison.

However practitioners in more southern countries, and many in France, like M. Gintrac, have some forcible reasons to adduce against M. Boudin.

They say that these favorable results have been obtained in the climate of France, not in that of Algiers or even of Rome. It may be true enough, that the patients were cured while they were taking these doses—but when we consider the minute doses given, is it not rather to the improvement in climate and diet, that the recovery is to be attributed? In short, might not these cases have recovered without any medicine at all, seeing that under the expectant system about $\frac{1}{3}$rd of all cases recover?

Then again there is no evidence of arsenic being of use in the remittent and pernicious fevers of southern countries. In them would any one trust to it who has got Quinine at his command? Although indeed Masselot says that in a bad fever he would use both.

It may be true that Quinine is dear, but to use the French pun of Armand, is not Arsenic as *veneneuse* as it is *venal*?*

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* Triller's tirade against Arsenic is so amusing, that I give an extract. "Nihilominus tamen nonnulli, etiam ex medicis ipsis, eo nefandae temeritatis impune processerunt, ut contra febres, praesertim intermittentes, inaudita fere audacia, ceu ultimum Medicorum et ægrotorum refugium, (nisi rectius effugium ex hac vitâ) commendarent hunc truculentissimum vitae ac salutis humanae insidiatorem."—Thesaurus Medicamentorum, 1764.

This objection seems now to be less insisted on—and it is generally admitted, that both the immediate irritation from doses of Arsenic, and its bad effects on the constitution have been overstated. The following are some instances of its tolerance:

Cazenave gave a girl for an obstinate eczema Pearson's solution, for a period of three years, and she continued in excellent health. Professor Carosi inquired into the history of 130 patients, whom he had treated in former years for intermittent with arseniate of potass and soda, and he found that at the end of 20 years, no fewer than 100 of them were alive. In Bahia, when there was a want of Cinchona, Arsenious Acid was used as a substitute in intermittent fevers, without reference to age, sex, or condition—sometimes to the extent of 2 grains in a single dose, without any troublesome result.* It is even stated, that two patients took 85 grains each of Arsenious Acid within the short period of six weeks, without any perceptible effect saving increase of appetite.

As we also know that Arsenic is found in the urine, the dread of its cumulative effects appears to be exaggerated.

In some patients however there seems really to be a great intolerance of Arsenic, though I confess I have not myself seen it, although I often give it, especially in skin diseases, in moderate doses—up to 15 drops of Fowler's solution three times daily.

The following is a summary of the results that have of late years attended its use:—

Boudin cured 2,947 patients, 2,000 of whom had been previously treated with Quinine. A committee at Marseilles reported favorably on his treatment, and the patients were kept in hospital for 15 days after they were well, in case of a relapse. In Marseilles, Montpellier, some Parisian Hospitals, and in Tunis, the results were equally successful, as also with Masselot at Versailles. Since 1846, the date of M. Masselot's memoir, the use of arsenical preparations has greatly increased in France. It has been taken up by Maillot, one of the great advocates of Quinine.

It is however very unpopular with the Army Surgeons in Algiers and in Italy—and this probably because we have such an admirable remedy in Quinine.

I may say that in the East Indies many have confidence in Arsenic, in intermittents. Dr. MacDougal† "frequently

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* Sigaud Statist. de Med. du Brazil.

† Transact. Med. and Phy. Soc.

prescribed 12 to 15 drops three times a day in Cheretta, with safety and advantage."

Dr. H. H. Goodeve* in 1833 "found it sometimes very beneficial in obstinate cases." I have myself cured obstinate fevers with it in Arracan and Calcutta which had resisted Quinine, and I have found the common fevers in the College Hospital yield readily to Cheretta and Arsenic. Mr. Hare† thinks well of it, and "has good reason to believe that it gives immunity from future attacks," counting it a more powerful antidote to marsh poison even than Quinine.

Boudin says it has been used with success in Brazil, also by Hutin in some cases in Algiers.

Dr. Guttceitt of Orell and others attest its virtues in Southern Germany; he has found it fail seldomer than Quinine.

On the other hand, Oesterlen has found it generally ineffectual in the endemic fever of Livonia, and Armand, Cordier, and Jacquot, and most French Army Surgeons, dissuade from its use in Algiers and Rome, and deny that it prevents relapses.

Most authors state the treatment to be most successful in cachectic patients, and as a tonic, but even this is disputed too.

Perhaps the following summary by Gribas, may be considered to offer as fair an appreciation of its properties, as can at present be made. It accords with my own experience.

1. Arsenious Acid has real febrifuge properties in intermittents the product of marsh miasma.

2. It succeeds in tertians better than in quartans and quotidians.

3. It has no appreciable action on enlargement of the spleen or on the system generally.

4. The tolerance of Arsenious Acid administered up to 1½ gr. and even a little more daily, has been complete in one-half the patients.

5. The disturbances of the system it has caused, have seldom been of importance.

6. This tolerance does not necessarily require the aid of of a copious diet and good supply of wine.

7. The employment of emeto-cathartic medicines has the triple advantage, of facilitating the tolerance of the medi-

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* Op. Cit. † Medical Board's Report, 1851.

cine, of stopping all its disagreeable effects, and of helping to cure the fever. Jacquot's Report goes to show that emetics increase much the effect of Arsenic, while their action is indifferent with Quinine.

8. It is prudent to suspend the use of the medicine on the occurrence of pain at the epigastrium, colic, nausea or diarrhœa.

9. The Arsenious Acid should be given by the mouth, during the intermissions or the decline of the paroxysm.

10. When the paroxysms have been stopped, the use of the medicine should be gradually diminished, as it was commenced.

11. The preparations of Cinchona administered after Arsenic, appear to be more efficacious, than when simply administered by themselves. This is denied by Jacquot, probably with reason.

12. The arsenical treatment is less powerful and less sure than Quinine.

13. Relapses do not appear to be either more or less frequent under the one or the other treatment.

14. The arsenical treatment should not be adopted in the treatment of pernicious fevers.

These remarks appear to me fair and impartial, and correspond with the general feeling of Indian practitioners. They often use Arsenic with success in rebellious intermittents, but never would trust to it alone in a bad remittent, although there is no objection to continuing its use throughout a paroxysm, or to the joint use of Arsenic and Quinine, as recommended by Masselot and others.

Dose and administration.—The most simple and sure preparation is a mixture of well pounded Arsenious Acid with Sugar of Milk equally well pulverized, in the proportion of 1 to 30, and to be taken in a fluid vehicle. We may begin by about 3-10th gr. of Arsenious Acid twice in the six hours, and increase up to 1½ gr. taken in divided doses three or four times a day. Native practitioners give 1-14th part of a grain rubbed up with Sugar twice daily. The French think Arsenious Acid most efficacious, but the English have always preferred Fowler's solution, or the Liquor Potassæ Arsenitis. The dose may be counted about 10 to 15 drops three times a day; owing to its tastelessness, it is sometimes given to children: 2 drops thrice a day may be given to a child two years old.

Arsenic has also been considered a prophylactic against fevers. I have no confidence in it as such, nor have I heard

of its use in India. Jacquot is very certain that it is no prophylactic.

I cannot leave the subject of Arsenic, without expressing a hope that further trials may be made of the simultaneous use of Arsenic and Quinine. Dr. Johnstone, late of H. M. 70th, found such practice particularly efficacious in the obstinate cases of fever sent to Landour, and others, as Dr. Gordon of H. M. 10th, have done so, although, as we have seen, the salt composed of the two, has only the efficacy of the Arsenic it contains. Dr. Johnstone informs me that he used a mixture of the amorphous solution of Quinine with Liquor Arsenicalis.

The *Arseniate of Iron* has been lately very highly recommended as the best of all arsenical preparations in skin diseases. If, as the French author affirms, it may be taken in quantities gradually increased up to 3 grs. a day without producing disagreeable effects, it is well worthy of being tried in fever.

The other articles from the inorganic world, will not require a long notice.

Sulphate of Zinc—Being considered tonic and antispasmodic, has been employed as a febrifuge. It was given by Sir J. McGrigor in the Peninsula, with some success. Dr. Jos. Brown recommends its use, and thinks it comes next to Arsenic in efficacy.

Some Navy Surgeons found it useful in the West Indies. But the Madras Report cannot say much in favour of its use—and I believe that in India it has nearly fallen into oblivion. Given as an emetic, it must have a certain degree of efficacy in fever.

The *Oxide* of Zinc has been used with effect in H. M. 10th. Dose, 2 to 5 grs. every six or eight hours, with some ginger or conserve.

Sulphate of Copper and *Ammoniated Sulphate of ditto.*—These substances have been applied on the same principles as the last one. The first is considered by Dr. G. B. Wood, to be one of the most efficient metallic antiperiodics, especially given in connexion with Quinine. The latter was formerly much esteemed and admired, by McCausland, Bianchi, and others. The so called antimiasmatic tincture of Köchlin was carbonate of copper dissolved in hydrochloric acid, then mixed with hydrochlorate of ammonia. It is obsolete, though still retained in the Saxon Pharmacopœia. I do not know that sulphate of copper is ever used in India in fever.

Dose, $\frac{1}{4}$th of a grain, with as much Opium, 4 times a day.

Mercury—Though a Medicine of high importance in the subsidiary treatment of fever, cannot be counted antiperiodic. It is never used as such, although Annesley seems to have thought scruple doses febrifuge, and Dr. Baillie had great faith in its action in the cure of ague. It need not therefore be treated of here, any more than other purgatives, or alteratives, which may prove useful in fever.

Antimony.—Often a most valuable remedy in the treatment of fever, cannot be considered a febrifuge. Its emetic and depressing action constitutes its value.

Some however have confidence in it as an antiperiodic, and an old specific "Peysson's potion," (divided doses of it) has still a reputation in France. Assistant Surgeon T. Moore in this country has called attention to the use of Antimony in intermittents, but he expressly states that he does not count it antiperiodic.

I have already observed that many practitioners in India are in the habit of administering Antimony with Quinine, and I have an opportunity of here noticing a new salt of that medicine, *Antimoniate of Quinine*.

This is a new medicine, which comes to us from Italy, where it was prepared by Palombo, and which seems well worthy of attention. This salt, as prepared from the mixture of a solution of Antimoniate of Potass in cold water, and of Sulphate of Quinine in hot water, occurs crystallized in the form of minute spiculæ, resembling the plume of a feather. It has a bitter, austere taste, is slightly soluble in cold water, more so in hot, and still more so in ether and alcohol.

M. Palombo says, that this substance is extremely valuable in simple and complicated periodic affections, in the subcontinued fevers of Torti, and even in real pernicious fevers. Experience has shown that it prevents relapses in the maladies just mentioned. It should be preferred to all antiperiodics in the obscure forms of intermittent maladies, which are often masked under the pseudo-continued shape. Among all the facts described by the author, which are both numerous and incontestable, there was no single case of periodic fever, which though refractory to other preparations of Quinine, did not yield to this one! It often acts also as a cathartic, emetic and diaphoretic.

I am quite inclined to think that this salt will be found useful in tropical practice.

The dose is 6 to 8 grs. during the apyrexia; a second dose is seldom required.

Ferri Sulphas.—Sydenham and Stoll were taught by ex-

perience that ferruginous preparations were useful additions to bark. The Salts of Iron have been much given popularly in a few districts in England, such as Essex, for ague; a combination of Sulphate of Iron with Nitre was formerly celebrated, as the febrifuge salt of Moebius. But Marc in 1810, appears to be the first who attributed a direct febrifuge effect to Sulphate of Iron. He was followed by Martin and Anteer. M. Corvisart was appointed to inquire into the practice, and reported favourably.

However the practice was never common, and fell into disuse. Mr. Waring* has lately attempted to revive it. "During the last 18 months he has employed it in between 100 and 200 cases of ordinary intermittents, quotidian, tertian and quartan in the Tenasserim Provinces, and in upwards of $\frac{3}{3}$rds a speedy and complete cure was obtained. It was unsuccessful in some cases where Quinine failed." He did not try it in the short or plethoric.

It is to be borne in mind that under almost any treatment a certain number of cases recover, and that Mr. Waring was careful that a low diet shonld be observed, the bowels be carefully regulated and acid fruits avoided. However his practice certainly deserves a trial.

Dose, grs. viii. to x. daily in divided doses during the intermission, in form of pill, with a grain or two of Ext. of Hyoscyamus, or fluid with Infus. Quassia.

Ferri Percyanidum.—Prussian blue. This substance was brought into notice some years ago, by Dr. Zollickoffer, of Maryland, and met with many advocates. Rodriguez considered it particularly adapted for children, and Zollickoffer thought it superior to Bark.

Dr. Samuel Jackson, of Pennsylvania, employed it with great success, though he did not think it equal to Bark. Out of 200 cases in which it was given by him, it failed to produce an immediate suspension of the paroxysm only in a fifth or sixth of the cases, and in most of them proved successful in the second, third, or fourth interval. Dr. G. B. Wood used the medicine when it came into notice—but though its employment was attended with some success, the Bark proved so much more certainly efficacious, that he speedily abandoned it. Dr. Von Dreyer, in Russia, combines it with Quinine in obstinate fevers.

Dr. Zollickoffer gave about six grains twice or thrice daily. Dr. Jackson one or two drachms in the intervals.

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* Manual of Therapeutics.

Hydroferrocyanate of Potass and Urea.—This monstrous compound has of late years been made and experimented on, it is said, successfully in France. We do not want it.

Ferri Perserquinitratis Liquor.—This salt has been lately used with great advantage by Mr. Kerr, of West Canada, (1851.) It is unknown in India. Dose—ɱ x. to xl. in water.

Before leaving the martial preparations, it may be well to remark, that though the evidence in favour of their strictly febrifuge powers is not very strong, yet there is no question that they are of infinite value in the cachectic and anæmic state, accompanying old fevers and spleen disease. If the enlargement of the spleen be too old to yield at once to quinine, some preparation of iron should be, and is generally used; of these the Iodide of Iron has been found by me perhaps the most efficacious.

Hydrated Iron, and some of the new compounds of *Iron* and *Manganese* have been recently vaunted, and may deserve a trial in such cases.

Tincture of Iodine—Has been found efficacious by M. Seguin. It is given in America in doses of 30 drops repeated three times during the apyrexia, and increased if necessary to 40, 50, or 60 drops, especially in very obstinate cases. I have no knowledge of its effects.

Sulphur.—From having been used in cases of spinal irritation, to which cause some attribute the ague fit, this substance has come to be used as a febrifuge—and has even been highly spoken of, particularly in America. Dr. Chapman gives a favorable opinion of it: and Dr. Dickson of Charleston, considers it a most valuable remedy in various intermittent diseases, and especially applicable to intermittent fever, where the apyrexia is incomplete.

Though these statements must be received with great caution, perhaps it may be worth while to observe, that in the plan of curing intermittent fevers, proposed by Mr. Blackall, and circulated to the service by the Madras Medical Board, $\frac{1}{6}$th of sulphur was added to the phosphate of lime, of which 5 scruples were taken, and that consequently the patient would take about 1 scruple of sulphur daily.

Alum.—Once enjoyed a high reputation as a febrifuge, and was employed by Boerhave, Lind and Munro. More lately Müller and Fontana have said that it is to be classed as a remedy with quinine.

The dose used to be, 1 scruple with nutmeg, mace, or nitre every hour before the approach of the fit, but it seems now to be seldom or never employed.

Hydrochlorate of Ammonia—Has been used as a febrifuge, but it probably owes any power it possesses to its diaphoretic and antacid powers. However it was much used in the treatment of ague by Sennert, Primrose, &c., but especially by Muys (1704.) It has also been commended by Boerhave and others. Dr. John Hunter gave it in the West Indies along with bark with occasional benefit. Oesterlen thus speaks of this remedy—"In some places, as in the North of Europe, Sal-ammoniac is still in high repute in agues—not only in their gastric complications, but, also to prevent the paroxysm; it is generally given in large doses. Without doubt slight cases may recover under the use of this as of a hundred other remedies—yet it does not deserve much confidence; besides it is usually given along with quinine."

Dose from 20 to 30 grs., an hour before the paroxysm.

Carbonate of Potass—As Sal-Absinthii, had some name as an antiperiodic, and has been in some cases thought antispasmodic, and has even been used in tetanus; in fever it can only have acted as an adjuvant and antacid.

Chloride of Soda—Best known as a disinfectant, as Liquor Sodæ Chlorinatæ, has of late years been brought forward in France as an antiperiodic. Drs. Lalesque and Gouzu in 1835, stated that it possessed as certain and as active febrifuge properties as cinchona;—a Committee reported on these statements, that it does possess some febrifuge properties, but is not to be compared with quinine. In 1839, M. Thomas attempted to prove that chlorinated soda was particularly efficacious in preventing relapses, and that in this respect it was superior to quinine. But this opinion has not been acquiesced in, and the medicine is very little used.

Dose ℈ss. of chloride, or ℥iv. of the solution daily.

Chloride of Sodium or common salt. Mondezert has lately, he considers, discovered one of the best febrifuges in this common substance, and Piorry, with his ever ready plessimeter, has felt the spleen diminish in size under its administration.

Piorry has thus expressed himself. "In Civil and Military Hospitals and Dispensary practice, in armies and especially for Algiers, in districts where affections of the spleen are endemic, and relapses so frequent, the employment of culinary salt must be of vast utility."

On this M. M. Levy remarks—that Military Surgeons in Algiers have tried it and always with very poor success, and that M. Cazales in the Hospital of Val de Grâce found it of

little use, and he concludes with the following more general observations on the subject, which I give, as they have a great deal of truth in them, and are of general application.

"There are some medicines which cannot be experimented on every where with the same advantage. Is Paris a good field for determining the action of febrifuges? Is it in the Hospitals of Paris, that we are to recognize the success of Cinchona as a febrifuge? A great many substances have been recently tried as substitutes for quinine. One of these has been experimented on in Paris, and it is said with success. The Minister of War interested himself in the question, and salt was tried at Perpignan, in Corsica, and in Rome. The results in these places have not agreed with those of Paris. The reason is, that the Paris fevers are so much slighter, and that fevers of Corsica or Africa improve rapidly of themselves in Paris, or under the expectant system. M. Cazales has published a table showing that of 150 cases thus treated at Val de Grâce, only by bitters or evacuants, 130 of the patients recovered, and only 13 of these had relapses; no wonder then, if culinary salt has had a certain degree of success in Paris!"

Others however, especially in America, are inclined to confirm the original favorable accounts of its use, and Dr. Hutchinson of Brooklyn (1854,) comes to these conclusions:—

1. That, although inferior to Cinchona and its preparations, it forms a very good substitute for them in intermittent fever, having failed to produce a speedy cure in only 31 per cent. of cases.

2. It may be used instead of quinine and indeed preferably, in cases where the latter is forbidden owing to the production of disagreeable head symptoms, or when quinine through repetition has lost its effect: also on the score of economy, and of being always to be had, though quinine may not be at hand.

Dr. Hutchinson has found it more energetic than any substance except bark and its preparations, and thinks it should be preferred to arsenic, which is a dangerous remedy.

On the whole, what I have read, does not give me a very favorable idea of the value of salt. I have not used it.

The dose is 8 to 12 drachms during the apyrexia; children require larger proportional doses. Dr. Hutchinson gave it in mucilage of elm to disguise the taste.

CERTAIN OTHER ANTIPERIODICS.

From the Animal Kingdom.—The names merely of musk, castor, phosphorus, gelatine and cob-web—can be here enumerated.

Diffusible Stimulants.—Can scarcely be termed antiperiodics, yet some of them have been used as such. *Æthers* have been prescribed in large doses either alone, or with camphor and opium shortly before the paroxysms, with the view of shortening the cold stage. Jacquot and Beylot think their combination with Quinine particularly useful in comatose intermittent, both by the mouth, and in injections.

Ammonia has been used in the same way.

Delioux has used *Chloroform* internally for the same purpose. In all such cases, diffusible stimulants if given alone, must be exhibited in very large doses, if they are to have sufficient action on the nervous system to keep off the paroxysm —consequently they are not practically of very much value.

I have not heard of the inhalation of chloroform being used to keep off a paroxysm, but I have no doubt that it would do so, just as Jacquot tells us that the Romans cure bad quartans, by making themselves dead drunk on the day when the fever is expected. Such a remedy is however in no degree wanted, and there might be danger, if the experiment were made very close on the expected cold stage.

It may nevertheless be well to give Delioux's last account of his use of chloroform.

He says that fevers, on which no other treatment had previously made an impression, and fevers treated unsuccessfully with quinine or arsenic, have yielded to chloroform. By the side of the cases telling favorably for chloroform as an antiperiodic, he has had more than one failure. Thus it cannot be repeated too frequently, as to all substitutes for arsenic and quinine, that their merit is only of a secondary kind.

It is enough, that chloroform may be inscribed in the list of remedies, that may cure fevers that are not very obstinate or very serious, or those which have resisted the action of quinine, either owing to the system being habituated to it, or to the idiosyncracy of the patient resisting its influence.

He gives chloroform in syrup, 1 part of it to 20 of the vehicle. The quantity of the syrup, taken in a mucilaginous fluid, is about ½ an ounce up to 1½ oz., which is divided into repeated doses during the apyrexia.

It is well to give the last dose three or four hours before the next expected paroxysm. If it be given at too long an

interval, there is less chance of the antiperiodic effect being obtained.

Emetics.—There is no doubt that in the case of mild intermittents, a sharp emetic an hour before the expected paroxysm, or the nauseating effects of Ipecacuanha or still better Tartar emetic for some hours before the paroxysm, will in many instances prevent the return of the access of fever.

These remedies appear to give a shock to the nervous system, which is thus rendered unable to take on the consensual action necessary for the production of an ague fit or paroxysm.

This I have myself frequently seen, having tried it often with Sepoys, and occasionally with Europeans.

In fact there are very few fevers in India, whether intermittent, remittent or pseudo—continued, in which in the early stage, the use of an emetic is not attended with the best effect.

Revulsives.—M. Hespin has lately used foot baths of mustard and hot water, applied half an hour before the expected access, with very favorable results; electric frictions and dry cupping along the spine have been tried—with some slight degree of success in France; nay one German practitioner Dr. Zimmerman assures us that by applying 20 to 30 cupping glasses on each side of the spine and taking blood, the paroxysm may always be kept off, but we would rather be excused from following such bloody practice. Perhaps under this head may come the smelling of burnt feathers, or the Bengalee practice of inhaling the odor of the roots of the Oprajeeta, the Clitoria Ternatea.

Blisters.—Put on 6 or 7 hours before the paroxysm, and applied to the nape of the neck, so as to be in full operation when the access is expected, have been recommended, and I have occasionally found them useful.

General Blood-letting—Practised during the intermissions has been known to keep off the paroxysms occasionally. Twining also remarks—"In some seasons I find blood-letting in the cold stage of regular intermittents arrest the paroxysm, and prevent its return in almost every case." But Mackintosh's plan of bleeding in the cold stage is now universally condemned and abandoned. Even if the theory of its employment were correct, the practice is quite unnecessary.

The Shock of Cold Water—Has often effected a cure—there is not a hydropathic institution, where such cures are not proclaimed. M. Baud and Fleury have recommended (1852) the cold douche as a powerful febrifuge.

The Madras Report states, that in several instances daily immersion in the sea had proved the happy means of checking agues, which had baffled every exertion that had been made to conquer them.

Tourniquet.—Finally a plan of Dr. Kellie of Leith, has met with some supporters. He was of opinion, that if tourniquets be applied, one on the thigh of one side, and the other on the arm of the opposite side, previously to the accession of the paroxysm, the cold stage will be generally prevented, and that, whether the cold stage be entirely prevented or only shortened, the following hot stages will be rendered both milder and of shorter duration. There is no satisfactory theory of these effects. M. Bailly strongly recommends the adoption of this plan in bad intermittents—and Bourgery has followed him.

This practice was not long ago brought to the notice of the Profession in India, by my friend Dr. Wise, late of Dacca.* Dr. Wise found, that when the tourniquet was applied to one of the limbs previous to the accession of the paroxysm of ague, the cold stage was entirely prevented, and a slight attack of synochus followed.

Dr. Wise writes. "I have now before me the particulars of 77 cases of intermittent and remittent fever, all of which were very much benefited or entirely cured by the employment of the ligature; of these—

27	were cured	by one application.
26	„	by two or three applications.
14	„	by from four to six
5	„	by from seven to ten."

These cases were many of them examined by Mr. George Lamb, the late Physician General, and he informed me, that he entertained no doubt that the tourniquet had the effect attributed to it.

But it may be questioned, whether any thing that strongly excited the interest of the patient, especially if attended, as in this case, with disagreeable sensations, would not have produced the same effect; a few strokes of a lash would probably be as efficacious, as the remedy in question.

Change of Scene and Change of Climate—Are among the most powerful antiperiodics we have. Every one can attest their virtues, but to enter into a discussion of this remedy,

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* McClelland's Journal, vol. vi.

or of the interesting subject of the climates to which the Indian invalid may resort, would not be within the scope of these pages.

It is surprising, how small a change of place may be sufficient to break the periodicity of slight attacks, while it may take a couple of years residence in Europe or more, to shake off entirely an obstinate one.

APPENDIX.

Cinchonine.—While these sheets were in the book-binder's hands, I received the Supplement to Bouchardat's Annual for this year, and find that it contains an elaborate memoir by M.M. Bouchardat, Delondre and Girault on the important subject of Cinchonine, to which I have alluded in the introduction, and at pp. 26, 27.

Every thing which they say goes to prove that, in the great majority of cases, Cinchonine may be substituted for Quinine. M. Forget's unfavorable report turns out to be a mistake; he experimented with Cinchonicine, not Cinchonine. M.M. Laveran and Wahu have reported on the effects of Cinchonine in the fevers of Algiers, the latter very favorably. But neither of them seems to have fully tested its powers in the worst fevers, being unwilling to omit the use of a remedy like Quinine, on the certainty of which they could, from former experience, depend. M. Wahu thus expresses himself:

"After these two series of experiments, I think I may say, without being considered merely an enthusiastic advocate of what is new, that I have found Cinchonine and Quinine identical as respects their curative effects in cases of paludal fever. I say their curative effects, because in their physiological, or to speak more correctly, in their pathogenic actions, there was a difference between Cinchonine and Quinine, the former alkaloid occasioning only exceptionally the deafness and singing in the ears, so often produced by the latter."

As their views of the physiological action of Cinchonine differ a little from those of Briquet, I shall give here the general conclusions and comparisons of the effects of Cinchonine and Quinine in their physiological and therapeutic relations, with which M.M. Bouchardat, Delondre and Girault conclude their memoir:

"In its physiological and therapeutic actions Cinchonine is not, as has been hitherto supposed, exactly to be compared with Quinine. The opinion that Cinchonine was merely a weaker Quinine, is not borne out by a rigorous interpretation of all facts.

"Given in equal doses sulphate of Cinchonine kills frogs more certainly than Quinine; a smaller quantity of sulphate of Cinchonine than of sulphate of Quinine injected into the veins of a dog will cause death.

"The action of sulphate of Cinchonine on man in a state of health certainly has considerable resemblance to that of sulphate of Quinine; but there are certain differences which show, that there is something more than a mere difference in the intensity of action.

"Sulphate of Cinchonine given in the same dose as sulphate of Quinine does not so rapidly produce singing of the ears, and disturbance of

vision, but given in smaller doses, it produces, and with greater constancy than Quinine, a special sort of headache seated chiefly in the anterior portion of the head, and accompanied with a very remarkable feeling of compression. These phenomena are produced by doses of from 9 to 15 grs. With these doses, we observe, and much more frequently and energetically than with sulphate of Quinine, præcordial pains and flutterings of the heart, indeed a very well-marked reduction of the vital powers, which may go on to syncope.

"If sulphate of Quinine is to be preferred to that of Cinchonine in the treatment of pernicious intermittents, on the other hand in non-pernicious fevers Cinchonine is quite equal to Quinine.

"The proper dose for one day is 7½ grs. taken at once. In Algiers the dose may be as much as 15 grs.

"Finally we must observe, and this is a matter of great importance, that while sulphate of Quinine in an equal dose suppresses an access of fever more surely and rapidly than sulphate of Cinchonine—yet in ordinary cases where time is no great object, and where pernicious accesses are not dreaded, Cinchonine is at least as sure as Quinine."

If introduced into India, Cinchonine would thus not supersede, but most effectively supplement, Quinine.

Apiol.—M. Dubail has studied this substance, and confirms all the results of M. M. Homolle and Joret, as given above.

Effects of Quinine given during the Paroxysm.—With reference to Briquet's remarks, p. 36 suprâ, that a large dose of Quinine given close on or after an accession of fever may prove injurious in various ways, I would say that those bad effects appear to me to have been theoretically inferred. Practically, those who suffer much from fever, find that a large dose taken just before, or even after the setting in of the fever, breaks the violence of the access. In several instances where it has been taken after the premonitory symptoms of the paroxysm had been felt, I have seen a curious struggle between the Quinine and the fever, as to which should have the mastery; in such cases the cold fit was often suppressed, and the duration and intensity of the whole paroxysm generally diminished. This in no degree militates against Briquet's and the received opinion, that Quinine is most efficaciously given during the apyrexia, or in the third stage of the paroxysm.

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