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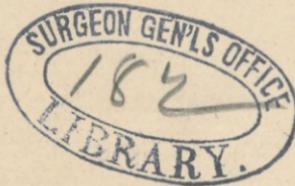
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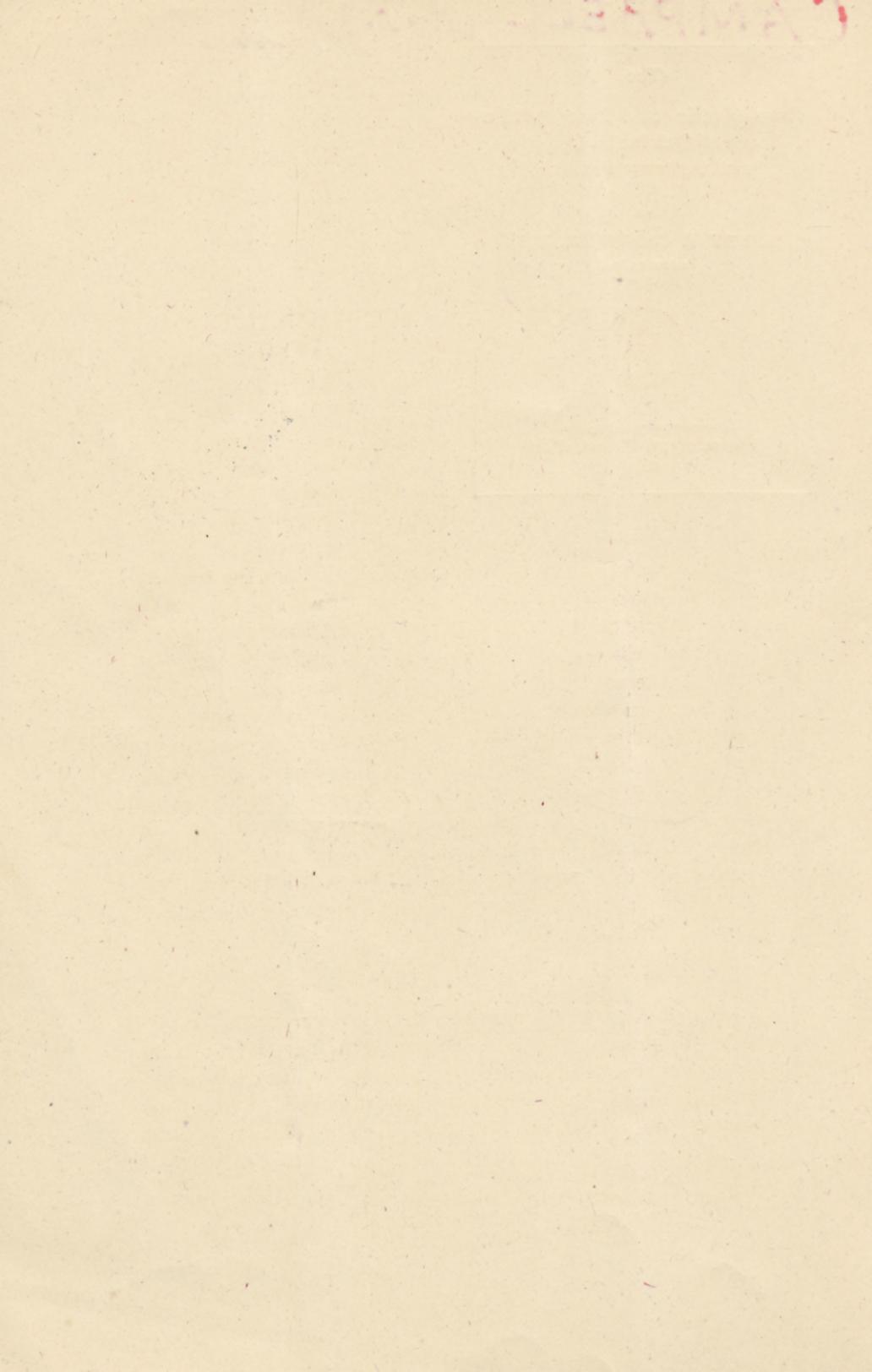
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AUGUSTA, GA.



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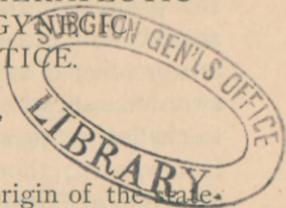




Dr E. S. Gaillard  
With Compliments of  
The Author.

THE PROPHYLACTIC AND THERAPEUTIC  
VALUE OF QUININE IN GYNECIC  
AND OBSTETRIC PRACTICE.

BY HENRY F. CAMPBELL, M. D.,  
Augusta, Georgia.



EVERY one present will recognize the origin of the statement when I give my full indorsement to the principle that "medical gynecology should bear as important a part in the work of the Society as uterine surgery."<sup>1</sup> In the remarks which I am about to make I am glad it has fallen to me to find myself at this time in that less brilliant, though perhaps not less useful, minority who are giving attention to uterine therapeutics; or, as I would qualify the expression, to the therapeutics pertaining to abnormal conditions of the uterine system. Adhering strictly to the programme for to-day, I will confine myself to the consideration of a single medicinal agent, — *quinine*. I shall endeavor, from the observation and experience of many years, in a region in which its applications have been as varied and abundant as perhaps in any other portion of the world, to contribute my quota in estimating and defining its value in gynecic and obstetric practice.

QUININE IN PREGNANCY.

*Abortivant effects of quinine.* — At a period not very remote from the present, though I have not seen much concerning it of late, the medical journals of this country contained frequent articles discussing and most of them strongly asserting the *oxytocic* properties of quinine. The tendency

<sup>1</sup> Fordyce Barker. Second Annual Address. By the President. "Medical Gynecology." *Tr. Am. Gynec. Soc.*, vol. ii., p. 25, 1877.

and the precept of all these papers were to lead to the establishment of the opinion that the preparations of cinchona are not only inapplicable, but positively dangerous and subversive, in any and all the stages of pregnancy. Abortions, miscarriages, and premature labors were constantly attributed to its administration. Why this fusillade against this prominent and important article of the pharmacopeia should have ceased, I am at a loss to divine, unless upon one or other of two very different assumptions; either "the sword was sheathed for lack of argument," as no one seemed to challenge the statements, or it was considered that the fact was too thoroughly established to require either reassertion or farther confirmation.

To this opinion in regard to the action of quinine under a proper, or in any degree prudent, application of the agent, my own daily observation for nearly forty years gives an unconditional denial. "Woe to her that is with child!" would it indeed be, to all the women of our malarial districts of the South, and in many portions of the West, did quinine, the daily and long-continued taking of which constitutes an important condition of their very existence, produce such calamitous results! The very suggestion of the circumstances, without argument, must certainly at once refute all charges against quinine as an oxytocic. We have only to be reminded of the thousands of pregnant women who must daily use the drug to prevent or to break the force of paroxysms of fever, and to know the fact that the question of such an effect never enters the mind of either patient or physician on its administration, to be fully convinced of the fallacy regarding its abortivant effects. Notwithstanding all that has been written on the subject, and though many of them are fully aware of the charges of oxytocic properties made upon quinine, I do not know a single practitioner in the widely extended region of the South with which I am familiar, who is at all influenced by them or who would hesitate to administer quinine freely to a pregnant woman at any stage, as the very *sheet-anchor* of her safety in paroxysmal fever. Among the hundreds who pre-

scribe it and the many thousands who take it under these circumstances, we might suppose that the barely casual observation of the doctors, or even the common sense of the people would long ago have discovered some connection between cause and effect had any such relation existed. I am particular to say here that miscarriages do, nevertheless, occur often in these regions that are in no way attributable to quinine, but rather the reverse. This, however, brings us to a different but very important examination of this portion of our subject. It should have a much more elaborate consideration than I am at present able to engage in.

*The paroxysmal neuroses endanger the prosperity of pregnancy.*

Many years ago I had occasion to tabulate the neuroses with the object of making a comprehensive classification of febrile diseases on the basis of the nervous system.<sup>1</sup> The definition then given to the neuroses will indicate the relation which paroxysmal fever—considered as one of them—may hold to the pregnant uterus as endangering the welfare of the fetus: “NEUROSES. Diseases in which any portion of the nervous system may be recognized as the *primary dynamic source of either their functional manifestations or of their structural changes.*”<sup>2</sup>

In this paper it will be found that paroxysmal fever of every grade and type is regarded as a paroxysmal cerebro-spinal neurosis, differing from neuralgia in the essential feature of pyrexia. Regarding, then, every paroxysm of intermittent fever as a temporary *erethismic* condition of the cerebro-spinal nerves and centres, attended with aberrations of sensation and of motion,—ague-shake,—even to the extent of convulsions, as in infants, it is not difficult to estimate the liability of such paroxysms to excite abnormal contractions of the pregnant uterus; and in connection with

<sup>1</sup> “The Nervous System in Febrile Diseases, and the Classification of Fevers by the Nervous System.” *Trans. Amer. Med. Assoc.*, vol. xi., p. 549. Washington, May, 1858.

<sup>2</sup> *Op. cit.*, Tabular Statement, p. 715.

these contractions, the inestimable value of any agent which might lessen, or control, or entirely prevent the advent of a condition so hazardous to the continuance of pregnancy must be self-evident.

Many considerations which, as physiologists, some might engage in, present themselves as to *rationale* and as to direct and reflex instrumentalities; but I have placed the subject in such a relation, that, holding the views I have stated, the point to which I am tending is already obvious to all. It is this, that instead of withholding quinine from a fear that it may produce abortion or premature labor, I give it most punctiliously to *prevent abortion*, or rather to prevent the paroxysms and the attendant calamities—abortion among them—that are threatened thereby. In the classic bluntness of Dr. Gooch, “Take care of the woman and the womb will take care of itself.”

In paroxysmal fever, when the neurotic irritation is reflected upon the pregnant uterus, it will be observed that the uterine “pains” recur *with* the paroxysms of fever, and abate or disappear entirely during the remissions or intermissions. They may continue to complicate the paroxysms as long as they recur, and even for a considerable length of time, without ending in catastrophe. At other times, without any obvious general pyrexia, the woman may, each night, have pain in the back, aching of the lower extremities with recurring uterine pains strongly simulating the pains of incipient labor. During the entire day, there is generally an absence of the lumbago and aching of the limbs with perfect quiet in the uterus.—The above sketch accurately describes a large number of cases tending to threatened expulsion, for which I, and doubtless many others in the South, are often consulted. In both these classes of cases, the apyrexia as well as those in which there is general fever, I invariably resort to efficient doses of quinine during the intermission, and almost as invariably have I found every threatening symptom to disappear; relieving the mind as well as the body of the patient. The extreme result of such cases in actual expulsion of the fetus has but

seldom been observed by me for the reason, that even after many returns of such paroxysms of uterine pain, the administration of quinine arrests their progress and restores quiet to the pelvic regions. Without the administration of quinine, as above suggested, I should have but little confidence in arresting such pains or of preventing the abortion often imminently threatened. My inquiries into the history of several of the abortions that have actually taken place — progress having advanced too far to be stayed — have developed the fact, that in more than one of them the accident had been preceded by nightly or daily paroxysms such as are above described.

A condensed statement from notes taken at the time exhibits the effects of the willful withholding of quinine when most grievously required, the opportunity of observing which was forced upon me. I was hastily called to a young lady from a malarious district. On my arrival, I was told by her married sister that she had been having "chills and fevers" every other night for more than a week, at which times she had been very restless, groaning often and in great pain. She stated that her present anxiety was occasioned by some inquiries which had developed the fact that no menstrual discharge had occurred for at least four months; but that now there being a slight show she candidly stated her apprehensions, and desired me to make an examination, that the family might know how to act. This examination was made at once, and at that time of the day, afternoon, when the pains had begun, as for a week or more, to come on. I found the abdomen somewhat enlarged, uterus slightly above the pubes, vagina relaxed and very moist, os tincæ soft and dilatable, neck not obliterated, of course, nor was there dilatation at the time of the recurring pains. The mucous discharge when examined was found to be decidedly tinged with blood. The case was clearly one of pregnancy at four months, — abortion from paroxysmal fever being strongly threatened.

Had this young lady been a wife desirous of offspring as heir to a boundless estate, according to my observation and

experience, her best chance of being gratified would have rested in the free use of quinine carefully adjusted to the type of her paroxysms. Far advanced as the prodromata of miscarriage were found to be at my first examination, I believe the uterine disturbance would have been arrested and the continued progress of gestation secured by its faithful and judicious administration. No less faithfully in this case, than in one where offspring was most ardently desired, did I urge, as was my conscientious duty, the observance of the course I thought best calculated to prevent the catastrophe, namely, An enema of laudanum to quiet her present *uterine* pains, a strict observance of the horizontal position in bed, and, above all, *fifteen or twenty grains of quinine, each day in divided doses, to prevent the recurrence of the daily paroxysms* which I regarded as the one great cause of the present threatening. She listened most attentively to my discussion of the case with an apparent disposition at first to acquiesce in my advice, but in the end told me, with the flattest candor, that nothing on earth could induce her to obey my directions in the slightest particular. She said she was glad to know she was in danger of miscarriage, and that death to her was preferable to exposure. In this immovable determination I was not surprised to find that she was most strongly upheld by her sister and another member of the family, who was cognizant of the deplorable facts of the case, and who took in very fully all the bearings of my prophylaxis.

On the second night, I was called again to the case. I found her with only a moderate degree of fever, but suffering with what appeared to be labor-pains, which recurred at intervals varying from twenty minutes to an hour. There was but little alteration in the condition of the os during the pain, though I thought the cervix had been slightly shortened, and there was more dilatability and softness of the mouth of the womb. I urged quinine again,—now merely *pro forma*. The pains entirely disappeared and did not return again till the second day after, when I was called in the middle of the night. I found quite a full dila-

tation of the os with an arm protruding into the vagina; delivery was easily accomplished by manipulation. The fetus was one of nearly six months and still-born. After the expulsion of the fetus quinine was freely prescribed to break up the paroxysms and faithfully taken. The young lady made a good recovery, with no bad results of any kind, so far as I know, accruing from the narrows through which she had passed. I believed then, as I do now, that quinine would have prevented this miscarriage. Even as an army surgeon I have never used "military authority," and much less *force*, to compel any adult of sound mind to take medicine, or to submit, against his will, to an operation. Some of the rights of patients are inalienable. The exercise of free will, in such cases, I believe to be one of them.

The pyrexia conditions under which quinine is given in malarial paroxysms, complicating pregnancy, I have not thought necessary to illustrate by the rehearsal of individual cases. It has been distinctly and undeniably stated that pregnancy, so far from being a bar to its administration, — especially where abortion, or miscarriage, or premature labor is threatened, — becomes the one most imperative indication for its effectual exhibition. I think I shall be indorsed in this statement by nearly all practitioners of experience in the malarial regions of this country.

*Apyrexia paroxysms of a local or general form often threaten the continuance of pregnancy.*

But it is not alone in the well-marked paroxysms of malarial fevers, where "the cold, the hot, and the sweating stages" succeed each other in classic order, that the integrity of the gestative term is imperiled. Apyrexia neuroses of a peculiar but by no means unfamiliar character, simulating in mode of access, in type of period, in duration and decline of paroxysm most closely the malarial paroxysm, scarcely less frequently invade the nervous systems of pregnant women, and cause the most serious alarm by the unmistakable threatenings of expulsion by which they are accompanied. A prolonged observation of many of these

paroxysms has led me to the opinion, that though attended with much suffering and giving rise to much alarm on the part of the patient, even without treatment they do not invariably result in catastrophe. Our object, nevertheless, is more to illustrate the therapeutic value of quinine in such cases, than to claim for it here the prophylactic power against abortion, to which, however, it is most unquestionably entitled in these cases. In many histories of miscarriages, as related to me by patients, many nightly paroxysms, attended by pains almost identical with labor-pains, recurring regularly in back and hypogastrium at half-hour or ten-minute intervals, and subsiding gradually in the morning, had preceded the one in which rupture of the membranes and expulsion of the fetus took place. These are "the false pains of pregnant women." That they do not, even when neglected, always end in the production of "true pains" producing expulsion I will not deny, but that this is their tendency, and that they are most dangerous to pregnancy, I do most confidently assert. My largest number of recorded observations, in which I have prescribed quinine with distinct reference to the uterine disturbance with the more important object distinctly in my mind of *preventing* miscarriage, belong to this class of apyrexial paroxysms. As some of them are quite striking, I will summarize one or more from different stages of gestation. The following case will be found to illustrate the observance of the hebdomadal course for the relapses of the uterine neuroses which simulated and seemed to threaten abortion.

CASE I. — *Paroxysmal uterine neurosis in earlier periods of pregnancy.* Mrs. P. H. J., aged about twenty-three years, became pregnant after rather prolonged treatment for cervical stenosis with cervicitis, from which she had suffered from an early period of her menstrual life. In the third month of pregnancy, having called me, she stated that she "had fears that she might miscarry." She said that for a part of every day, for more than a week past, she began to have pains in the lower part of the abdomen and small of the back about one o'clock in the day. These

pains would recur in paroxysms at intervals of half an hour or more, but there was a continued feeling of heaviness as if something were pressing out. She stated, that at first these paroxysms and unpleasant sensations lasted but a few hours, leaving her in the evening quite comfortable; but more recently they had continued after going to bed, sometimes keeping her awake at night by the recurrence of the contractions.

Supposing these uncomfortable sensations to be due to gravid displacement or descent incident to the approach of quickening, I made a digital examination. The uterus was low in the pelvis and somewhat retroverted, the os was not at all influenced by the pains, being closed and natural. Replacing the uterus in genupectoral position, and instructing her to observe nightly self-replacement with the pneumatic repositer, I asked her to report. Being called a few days after to see this lady, she informed me that though the replacement had relieved, to a considerable extent, the downward pressure and heaviness, the paroxysms continued to return each day, repeating themselves at intervals during many hours of the day. She regarded her symptoms as seriously indicating the approach of miscarriage. She seemed free from fever and reported herself well in every other respect.

The regularity with which these paroxysms of "false pain" returned, and the completeness of the intermissions alternating with them, suggested to my mind the necessity for antiperiodic treatment. I prescribed to be taken next day fifteen grains of sulphate of quinine in three five-grain capsules, three hours apart. This to be repeated for the next two days.

Four days after she reported that on the day of taking the quinine every symptom of her uterine pain had disappeared. On the second day she had taken but nine grains of quinine — three three-grain doses — as she had been very disagreeably impressed by fifteen grains, it being more than she could bear. She said that since taking the quinine "she had felt like a new being." After two weeks of entire freedom from the above distressing feelings, this lady sent for me and stated that she was suffering from a return of her symptoms, and asked if she should take quinine again as before. Quinine was again prescribed to the extent of nine grains a day for two days; full cinchonism was produced with the effect of a complete prevention of the paroxysms. In this case, pregnancy being normal in every other respect, there were several other hebdomadal relapses of the neurosis, the in-

tervals being at two and sometimes at three weeks. The relapses ceased after the sixth month. She was delivered at full term of a healthy living child.

The above case is the more valuable on account of the comprehensive illustration afforded by it, both of the hebdomadal recurrence of the peculiar neurosis, continued through various stages, to an advanced period of pregnancy, and also of the invariably beneficial effect of quinine in all these stages of gestation.

CASE II. — *Paroxysmal uterine neurosis simulating labor near the end of gestation.* Mrs. G. P., an Irishwoman, aged about forty years, health robust, was pregnant with her tenth child; had never had any difficulty in labor, and had generally been attended by a midwife. I was called to visit her after midnight, her husband urging immediate attendance, as he was sure labor had begun. He said, according to her "calculation" her time was *up*. I found her in bed, and in what, to all appearance, was the fullest activity of the second stage of labor. I have seldom witnessed more violent pains, or pains in which the abdominal muscles and all the muscles auxiliary to them in expulsive efforts were more strongly or more universally brought into action at each return; they were not always rapid, but irregular, returning at intervals of from ten minutes to half an hour. On examination, I found the os tinæ, to my unbounded surprise, not in the least affected by the violent muscular contractions. The neck was obliterated, the os soft and quite patulous, but neither thinning nor dilating at any time during these paroxysms of pain. The bearing down and straining seemed to be entirely involuntary, and she would each time seize the hands of those around her, seemingly expecting very early delivery. They were *not* the pains of the first stage in any appearance; but, as I have said, each paroxysm was the exact pantomime of an expulsive pain.

As the patient reported herself as generally having "quick labors," and as in some multipara the characteristics of the first and second stages I had found to be crowded together, completion of labor occurring anomalously with unlooked-for rapidity, I consented to remain till morning. Several repeated examinations during the paroxysms revealed no advance in the dilatation of the os. One sixth of a grain of morphine, repeated in an hour,

produced no decided abatement in the violence of the paroxysms. The returns, however, became less frequent after daylight; and when I left at 9 o'clock, A. M., at which time the os tinæ had not changed its condition, I felt confident that true labor would begin sometime in the next twenty-four hours, and told the family to send for me in case of an active return of the paroxysms.

Not being called to this patient, nor hearing from her during the entire day, nor the following night, nor during the second day, I had concluded that labor had come on, perhaps, suddenly, and that she had been attended by her midwife.

On the second night, again after midnight, I was called to this patient, and found her in the midst of the same dramatic representation of violent parturition in the second stage. In no particular, either of process or results, did my second night's useless expenditure of fatigue and expectancy differ from that two nights before! Morning came, and with it the gradual subsidence of the paroxysms, and I left her in sound and undisturbed sleep.

Recognizing, now, that the case was one of paroxysmal uterine neurosis of the tertian type, or if not that, and perhaps more correctly, a paroxysmal excito-motory neurosis of the abdominal muscles of the tertian type, I determined — although, according to the woman's statements, and to all appearance, the term of gestation was completed — to administer quinine in decided antiperiodic doses.

Prescribed fifteen grains of quinine, in three doses, to be given between twelve and six o'clock of that day, and that, on the following day when paroxysms were expected, the doses should be repeated in such a manner as to secure *decided cinchonism* by midnight.

Calling to inquire the day after, I found she had taken, on the day preceding the night of the expected paroxysms, eighteen grains of quinine, in three-grain doses, and that decided cinchonism had been produced, "ringing-in-the-ears" having not yet subsided. She had slept soundly and somewhat heavily the entire night, and had not experienced the slightest indication of the "coming on of her labor," as they called it.

Now deeply interested in the case, I inquired of her husband in regard to Mrs. P.'s condition. His answer was, "Why, Doctor, she's as well as ever she was in all her life. I don't believe she's going to have any baby at all! Your quinine has just stopt her up entirely!"

Fully two weeks after this last visit, I was called in the daytime to attend this patient. I found her in the first stage of labor, the os dilating gradually but satisfactorily, with favorable position of the head. She was delivered naturally of twins, both living, and her getting up was without incident. I advised that moderate doses of quinine should be taken for some days after labor, with the view of preventing the return of neurotic paroxysms. I am not informed whether it was taken or not.

The report made as to labor being *due* at my first call to attend her, two weeks previously, was probably a mistake in the calculation of the patient. Whether labor would have been super-induced prematurely had the quinine been withheld, I cannot confidently decide. Such violent exhibitions of reflex muscular action, had they been often repeated, could not fail, it would seem, to excite the uterus to action.

The two or three cases above cited at length in the earlier and later stages of pregnancy, are but fair representatives of a large number in all periods of gestation in which paroxysmal neurosis of the gravid uterus, tending apparently to the immediate expulsion of its contents, was checked "as by a charm" by efficient medication with quinine. Indeed, as I have said, without its aid I should have felt myself helpless in innumerable instances of a like kind of impending miscarriage. Many others, even more striking in some respects than the above, might be given, — one in which the hebdomadal returns, beginning about the seventh month, were repeated every two or three weeks, till the end of pregnancy, would illustrate even more plainly than any the reliable value of cinchonism in preventing the paroxysms, and thereby evading the catastrophe of premature labor. The time allowed for the presentation of these observations must, however, defer any further detail of cases, as well as prolonged discussion of the morbid conditions of pregnancy requiring the application of the remedy. As a promoter of labor at term, I have seldom applied quinine, though I have no doubt of its value, which must rest principally upon its roborant influence on the general nervous system, and not upon any special power it possesses of producing ute-

rine contractions. During the entire term of pregnancy, and up to the last moment of the term, I have exhibited this alkaloid whenever, from any cause, it seemed to be required, and in no single instance have I ever discovered the slightest indication that expulsive uterine contractions were superinduced under its influence. The following remarks, published by me in 1857, will be found in volume xi., "Transactions of the American Medical Association."

"Many facts to be observed in the obstetric department of medicine can be made to illustrate very clearly the influence exerted by the cerebro-spinal nervous centres over the pelvic viscera in both excito-motory and excito-secretory (vaso-motor) action. Dr. Tyler Smith has demonstrated the first so fully that little can be added to his observations upon the subject except so far as relates to the connection which this reflex action bears to malarial fever. On this point, we have constantly observed that miscarriages are frequently produced by spinal irritation, which, for days preceding this catastrophe, if closely watched, would be found to manifest itself *in paroxysms* of either a quotidian or tertian type, and which, if timely treated by revulsives to the tender region of the spine and proper doses of quinine, will be arrested, and premature labor thus often prevented. These paroxysmal manifestations, *without any general fever*, often show a strong disposition to assume the hebdomadal-relapse character, and the evil which is averted *now* may be consummated in fourteen or twenty-one days from the attendant's inadvertently failing to anticipate the relapse period, with the application of this proper and simple remedy."<sup>1</sup>

*Paroxysmal neuroses amenable to quinine, often disturb and interrupt the normal processes of childbed.*

Having, somewhat at length, discussed the conditions of pregnancy in which quinine has proved valuable, I will endeavor, presently, to illustrate, principally from my own experience, its value in some of the accidents and liabilities

<sup>1</sup> *Report on Nervous System in Febrile Diseases.*

of those critical and often dangerous periods attendant upon and succeeding labor.

#### QUININE DURING LABOR.

As its administration during the actual progress of parturition has recently attracted some attention, I will make a few brief remarks upon quinine in labor, before giving my views as to its post-partum applications, which I regard as much more frequent and therefore more important. To begin with ; I have never made it a practice to resort to quinine as a promoter of contractions in retarded labor, whether in the first or second stage. It has not, in my opinion, any power *per se* to provoke or to enhance uterine contractions. There are, however, three distinct conditions, all analogous and kindred to each other, in which I have found quinine during labor to be of the highest value : *First*, If my patient is reported to me to have been the subject of quotidian or of tertian paroxysms, and if the type should coincide with the hours to be occupied by the labor, my first care always is to avoid the complication of a paroxysm of fever with the distresses of parturition ; and to this end I produce cinchonism, by the most speedy and efficient means at my command. If I fail in this, I know full well that I am to expect a most distressing, irregular, and possibly a dangerous labor. All the normal reflexes of the act of parturition will be disturbed and most probably exaggerated, by the superimposed reflex excitability of the cord which, according to my pathology,<sup>1</sup> constitutes the initial factor — the very essence of the febrile paroxysm ; *second*, In cases where even no history of paroxysmal fever has been given, but in which there is marked irritability, — pain incessantly recurring but without contractions — I think it always advisable to bring about cinchonism in order to depress this abnormal reflex excitability of the spinal cord, and thus allow the merely functional reflexes to have sway.

<sup>1</sup> *Transactions Am. Med. Association*, vol. xi., May, 1858, Report on Nervous System in Febrile Diseases. Section Cerebro-Spinal Fevers, etc., etc.

Under such circumstances I have found uterine action to become more steady, so to speak, contraction being more efficient, and dilatation, if in the first stage, more progressive under quinine. For this purpose, however, I do not often select it as the best agent. I find either chloral or morphine, or a few inhalations of chloroform far more prompt and equally efficient in quelling the evanescent reflex excitability upon which these perturbations unquestionably depend.

*Thirdly*, Of all the accidents of childbed, none are more startling, disconcerting, or alarming than *eclampsia*, yet by a careful and attentive consideration, on the part of the medical attendant, the cases in which convulsions are liable to occur may generally be recognized even in the earlier stages of labor. Whichever one of the many theories we may adopt in regard to the ultimate cause, whether plethora, anemia, uremia, or malaria be the irritant, we are irresistibly forced to recognize unduly excited cerebro-spinal centres, with afferent and efferent nerves, as the instrumentalities through which the frightful drama is enacted. The one grand and paramount indication is to prevent or to combat reflex excitability. After the convulsions have begun, opium by puncture or otherwise with the bromides, chloral, chloroform, and blood letting are of course our most ready and efficient means for restoring order to the muscular system. But among prophylactics, well established cinchonism, in the beginning and maintained to the end of labor, is surpassingly the most valuable in all cases where convulsions are foreshadowed.

Referring to my notes in another department of practice, I find the most abundant confirmation of my faith in quinine to modify the convulsions of the puerperal state. As early as October, 1849, there will be found in vol. v. of "The Southern Medical and Surgical Journal," p. 591, a paper entitled "Infantile Paroxysmal Convulsions and their Treatment with Sulphate of Quinine." Six cases are there carefully reported in which children from twelve months to five years were treated by large doses of quinine admin-

istered per anum, during the convulsion, with remarkable and invariable success; from five to ten grains being thus given at a time.

Among the apyrexia neuroses none equals in its severity, its inveteracy and fatality, traumatic tetanus, and of all neuroses, pyrexia and apyrexia, no one presents a more typical and well defined exhibition of reflex motory domination. Since the use of chloral, chloroform, and the bromides, this disease has come to be considered not so uniformly fatal as once it was regarded; but long previous to their application, from the observation of cases treated by what would even now be regarded as enormous doses of quinine at the hands of Dr. Robert Campbell, — over 1,300 grains having been taken during twenty-seven days, — I had been convinced, and have no reason to change my opinion, that it is by far the most reliable means for combating the symptoms, and for finally curing this perhaps by far the most unmanageable of all the morbid reflexes. Many cases of hysteria both gravid and non-gravid, emotional and convulsive, I have found to yield like magic to quinine.

From the above, it will be clearly apprehended that in the administration of quinine for the subversion of the dangerous conditions, whether of pregnancy or childbed, no special applicability is claimed for the agent on account of what may or may not be regarded as the specific cause operating to produce any of the varied manifestations. No more do I adjust the treatment in respect to the "morbific cause" in the case of exhausting uterine irritability or to that of the threatened eclampsia, or even to that of the approaching malarial paroxysms, than I did to the cases of traumatic tetanus, so entirely outside, probably, of all considerations, based upon any toxemia whatever. It is adjusted, in all these instances *indifferently* to the dominant reflex motor excitability, whether, as in pregnancy, the calamity to be evaded be spasm restricted to the uterine muscle alone, threatening premature expulsion, or as during labor, the wide-spread exhibitions of the eclamptic seizure. The one essential condition, common as the result of many

varied causes, has been arrived at. This is exaggerated reflex excitability of the brain and spinal cord. The quinine is given to depress that — no matter which particular one of the causes in any given case may have been operative in its production.

#### QUININE AFTER LABOR.

In the consideration of the liabilities and accidents pertaining to pregnancy and, more strictly still, in those which are to be dreaded during the progress of parturition, it is singularly manifest that the cerebro-spinal system and the muscular apparatuses directly or indirectly under its influence are invariably and almost exclusively the organs concerned in the production of the phenomena. Thus during pregnancy, morbid reflex excitability of the cord, whether produced by malaria or by any other blood poison, tends to premature labor by excito-motory excitation of the uterine muscle; and again during labor, the same reflex excitability of the spinal and cerebral centres, whether produced by malaria, uremia, or by centripetal excitation beginning in the womb itself, may be distributed to the general muscular system and afford us the alarming exhibition of eclamptic convulsions.

The strictly apyrexia and non-inflammatory character of nearly all the neuroses which disturb the quiet of pregnancy, and no less that dreaded one, eclampsia, which endangers the life of the woman during labor, distinguishes them in a most remarkable manner from the disorders — also in my opinion essentially neuroses — which always are the dread and often the burdensome responsibility of the medical attendant, after parturition. No longer have we to deal with the dynamic influence of nerves and nerve-centres restricted to a single tissue as found in the muscular apparatuses of the womb and of general volition, but with blood-vessels, lymphatics, glandular bodies, and mucous linings; with connective tissue and with the parenchyma of every organ and structure which phlogosis can invade and fibrific action deteriorate. The conditions we

have now to encounter are those of fever and of inflammation.

Of the many and varied liabilities of the post-partum puerperal state which I have found to be guarded against and evaded by the careful and judicious use of quinine, time and the space allowed to observations of this special character will permit me to discuss, and that only briefly, but two classes. These two I have selected on account of their being the most common, therefore the most important to us as practitioners: *First*, The disturbances of Involution; and *secondly*, The disturbances of Lactation.

*Involution.* I do not know who it was who first compared the recently evacuated uterus to an organ in a traumatic condition with all the liabilities and ready susceptibilities to the invasion of irritation, congestion, and active inflammation, which any other organ of the human body recently wounded would thereby acquire. If it was the somewhat erratic author of the "Chrono-thermal Theory of Disease,"<sup>1</sup> which is my impression, I willingly accord him credit for two good ideas instead of one, which only failed of success because somewhat imperfect and "born before its time." The analogy at least is worthy of consideration, the quasi-laceration caused by separation of the placenta, the exfoliation of the entire mucous surface, the melting down and draining away of lymph-matters, and the unique and unexampled activities incident to "denidation," — all suggest the idea of a critical and ticklish condition opportune and ready for the awakening of inflammation, from whatever source, external or internal, the influence may arise. Every practitioner is too well aware how often this necessary and adequate occasion is afforded, and how frequently the natural process of involution is midway arrested, the organ never again, or not for a long time, returning to its normal condition. The sudden occurrence of fever in the midst of this normal, but most critical process, as is well known, is one of the most frequent causes resulting in subinvolution.

<sup>1</sup> Samuel Jackson, of London.

It has been seen in the foregoing portion of these observations that reflex excitability of the cord is often one of the prominent characteristics of the innervation of pregnant women. In such women this reflex excitability before parturition seems to manifest itself only in the excito-motory phenomena, as locally in uterine contractions, and sometimes generally, in puerperal convulsions.

But it is well known, as expressed in the words of Marshall Hall,<sup>1</sup> that "The diastaltic nervous system is divided into *two* sub-systems: (1.) Excito-motory. (2.) Excito-secretory. The former is extended to the muscular system; the latter is diffused over the general system as the blood is diffused over the system."

The former of these two sub-systems, we have shown, is more particularly concerned in the morbid reflex phenomena that sometimes disturb pregnancy, and that exhibit themselves during labor in eclampsia. It is with the latter, however, namely, the reflex relations subsisting between the spinal cord and the ganglionic or secretory system, controlling circulation in the uterus and elsewhere, that we have to deal in our consideration of the post-partum troubles now under review. The abiding morbid reflex excitability of the cord now acts disturbingly and disastrously upon the circulation of the womb and uterine system, first deranging involution, and next, or simultaneously, upon the general system, producing fever and constitutional disturbance. Reflex excitability of the cord, then, is at least one of the factors in the morbid processes, subsidiary to involution, — in my opinion the most important factor.

From a certain familiarity with surgical injuries, and the treatment of patients after surgical operations, no one conviction has more fully taken possession of me than this, that quinine, above all other medicinal agents, is a preventer and controller of traumatic inflammation. For more than thirty years no surgical injury, nor any case requiring surgical operation, has been conducted in its after treat-

<sup>1</sup> *London Lancet*, March, 1857.

ment by me without the free administration of quinine as one of my chiefest reliances in securing a mild progress and an ultimately favorable result. So far back as May, 1858, this subject, cognate to the one now under consideration, was discussed in the following language: "We are not aware that the observation has been recorded elsewhere that the phenomena succeeding surgical and other wounds are of a decidedly paroxysmal character. This feature we have so frequently — we may say so invariably — observed, that its existence in such cases appears to be the rule. We are all familiar with the common expression 'fever in the wound,' or 'fever in the stump.' Few, we apprehend, have remarked that this fever observes an intermittent course."<sup>1</sup> Much observation has rendered it unquestionable to my mind that each one of the essential characteristics of traumatic inflammation, — the pain, the redness, the heat, and the swelling, — were only clearly explicable by a *rationale* involving the injured sensory nerve of the wounded part and its excitor relations to the spinal cord, giving rise to reflex-secretory (vaso-motor) disturbance. These manifestations of excito-secretory disturbance are marked by alternations of rest and activity; which last we recognize as paroxysms, and which I have always found amenable to quinine in the most marked and satisfactory degree.

That there is an intermittency — sometimes a remittency only — of the most marked and obvious character, signalizing the course and method of the febrile and inflammatory phenomena attending the post-partum affections under consideration, my own observation and that of many others will substantiate. A less frequent pulse, a lower temperature, diminished peritoneal tenderness, and indications of better comfort, more frequently mark the earlier hours of the day; while the reverse of these conditions are found to signalize the paroxysm, most frequently in the hours of the afternoon.

Quinine, in efficient portions, now becomes our obvious, as it is our most reliable, resource. If we neglect to apply

<sup>1</sup> *Trans. Amer. Med. Assoc.*, vol. xi., p. 615, May, 1858.

the power at our command, these exacerbations, perhaps mild at first, become day by day of graver and more alarming import, till, by repetition or by long continuance, greater disturbance and more damaging complications dispel the chances of an "easy getting up." Septic fever, and perhaps death, may terminate the case. Escaping this, such cases are not uncommonly drifted out into a sea of troubles beyond the check and guidance of the medical attendant. Ovaritis, endo-metritis, uterine engorgement, and hyperplasia, with all the functional chaos and life-long crippling of subinvolution now destroy all hope of child-bearing, besides rendering life a heavy burden.

For specific measures of treatment after labor, comprehending quinine and other means, I refer to the pages following the consideration of the disturbances of lactation.

*Lactation.* — The intimate relations subsisting between the mammary gland and the uterus, — whether non-gravid, gravid, or puerperal, — are too well recognized and familiar for any extended comment. The breasts develop under the advance of puberty, they enlarge and become tender during menstruation, they color their areolæ after conception; while, during pregnancy and after labor, the relation is even still more striking and mutual. The nursing infant excites painful, but often beneficial, uterine contractions, and the uterine processes seem intimately connected with the establishment of lactation.

All the above phenomena, heretofore ignorantly attributed to "sympathy," are now recognized as the result of normal reflexes in the spinal cord. That an exaggerated reflex excitability in the cord would be competent to disturb, aggravate, and render morbid the process of lactation, I do not think any one giving assent to the accepted results of modern physiology would pretend to deny. Solely for the benefit of any other class, I cannot enter into any extended argument to prove that which both observation and experiment seem pretty fully to have demonstrated. It is a matter of common observation by practitioners that ex-

cessive activity in the establishment of the milk-flow is nearly always attended by pain, and that in the majority of the cases more or less general excitement, with increased temperature and accelerated circulation, is an accompaniment of lactation. Hence, at the end of the second day or the beginning of the third, so familiar have been these phenomena to ordinary observation, that this period has been universally set apart for what is termed "the milk-fever of child-bed." It may continue for only a number of hours, or it may persist during many days. The excessive activity may extend to actual inflammation, with great tumefaction, ending in suppuration and destruction of the cellular tissue, or even a portion of the gland-substance itself.

The course of events above described is not infrequently initiated by a chilly sensation in the region of the gland, — the true "breast ague" of common parlance, — or there may be a general chill, with distressing nervous agitation and lancinating pain, succeeded by fever of a more or less active character. According to an observation extending over many years, the phenomena, both local and general, which mark the existence and progress of mammary inflammation, whether eventuating in abscess or not, I have found to be almost invariably of an intermittent or remittent character. The nervous and vascular perturbation in and about the affected gland, as marked by the pain, redness, heat, and swelling, as a rule, manifest their highest activity during the hours of the afternoon and early night, while they undergo an abatement towards morning, under which comparative comfort and freedom from febrile symptoms are maintained till the rise of the distinct and obvious paroxysm again in the afternoon of the succeeding day.

With each recurrence of the paroxysms, which are not always quotidian, but sometimes tertian, in type, the inflammatory characteristics of the local affection become more and more marked, seeming only to make progress during the period of exacerbation, but deepening with each return, until the stage of suppuration has been reached, and the deplorable condition and results of mammary abscess have been accomplished.

It may here be asked, Is the process of inflammation to be regarded as intermittent, and is its advance marked by paroxysms? To this I can only answer that such has been unquestionably the result of my own observation, not only in regard to inflammatory processes occurring idiopathically in the mamma, but also in respect to all traumatic inflammation in a marked degree, and more or less to true inflammation of every kind, in whatever organ it may occur. And further, that the timely and judicious application of quinine greatly modifies and ameliorates its severity, and often, in its earlier stages, arrests its progress and effectually aborts its damaging results.

#### THE PHYSIOLOGICAL ACTION OF QUININE.

Of the many explanations given in regard to the therapeutic action of quinine, that which attributes to it an influence in lessening or depressing the reflex excitability of the spinal cord seems to be the one best demonstrated by experiment and most clearly answering to the observed results of its influence over disease. Whether this result is secured by its direct action upon the nervous structures (neurine) of that centre, according to Sedgwick,<sup>1</sup> or by lessening the blood-supply to it by contraction of the capillaries supplying this neurine, as shown by Robert Campbell,<sup>2</sup> is not very important to the result as claimed in the present discussion.

The former of these writers, in a paper of much physiological and therapeutic value, considers the theories of Setschenow, Herzen, Goltz, Freusberg, Meihuizen, and

<sup>1</sup> "The Influence of Quinine upon the Reflex Excitability of the Spinal Cord." By Wm. T. Sedgwick, Ph. B., Fellow of Johns Hopkins University, Baltimore, Md. *Journal of Physiology*, vol. iii., No. I, p. 22.

<sup>2</sup> "It relieves, entirely or partially, all those diseases which depend upon engorgement, resulting from vascular exhaustion or debility, such as would proceed from relaxation of the middle coat, whether occurring in a vascular organ, as lung, spleen, or liver, or in a nervous centre, as brain, spinal cord, or ganglion." — *Southern Med. and Surg. Journal*, April, 1857.

others, in regard to reflex irritability as bearing upon the action of quinine, and then, as the result of a series of carefully conducted experiments on the frog in the physiological laboratory of the Johns Hopkins University, he arrives at conclusions that are quite definite, and which in most respects appear quite unassailable. "Meihuizen found, — and I agree with him in this," — says Sedgwick, "that although in the frog, whose medulla has been divided, small doses of quinine do not seem to affect either the heart-beat or the reflex excitability, large doses do, on the contrary, affect both. They slow the heart-beat and depress the reflex excitability." . . . . "Under large doses of quinine I have repeatedly seen the reflex excitability grow feebler and feebler, till it finally disappeared altogether. In such cases I have almost invariably found the heart still beating, though the circulation in the web-vessels was usually stopped."<sup>1</sup>

The diligent researches of Sedgwick seem to have in view the confirmation of the "simultaneous stimulation" theory of Goltz and Meihuizen, as opposed to that of Setschenow, which affirms the existence of special inhibitory centres in the brain through the medium of which the quinine is supposed to act in repressing reflex excitability of the cord. These observations were necessarily confined to a restricted field, being devoted almost exclusively to the heart and pneumogastric nerve. They may be regarded, however, as conclusive in their results as applying to centric reflex excitability observed everywhere in the phenomena of any organ, or sets of organs, under its domination. In the conditions which our discussion has under particular consideration, it is applicable to all the muscular system as in threatened abortion and eclampsia ; to the uterus, the ovaries, and the post-partum mamma, as well as to the heart and other organs simultaneously acted upon during the puerperal period. "Freusberg (1875), and others," says he, "have tested and finally abandoned the doctrine of special reflex inhibition centres. Nevertheless, this doctrine still offers

<sup>1</sup> *J. Physiol.*, III. p. 26.

the readiest explanation of numerous phenomena in physiology, one of which is *the remarkable loss of reflex excitability following the administration of a small dose of quinine to a normal frog.*"<sup>1</sup> He has shown that in large doses the effect is produced even after extensive mutilation of the nerve-centres. "In the pithed frog," larger doses are required and "the drug possibly acts as a direct poison on the cord."

Though fully agreeing with Sedgwick that "quinine does not depress the reflexes by the mediation of any special inhibitory centres," in the present discussion, it is a matter of less consequence that Goltz's theory is supported and that of Setschenow much weakened. *Our* occasion demands, as the one main and all-important result, the clear demonstration he and others have given us, *that quinine does unquestionably depress the reflex excitability of the cord*; for by this guiding fact we are conducted to the explanation of its magic influence in controlling the reflexes which form so important a part in much that we have to contend with in pregnancy, in labor, and in *post-partum* practice. In each of these conditions, reflex excitability of the cord is the underlying provocative to all the alarming and destructive phenomena,—no less to the obscure and fatal peritonitis and septic fever, to the deplorable subinvolution, to the distressing mammary abscess and irritative fever, than to the plainer and more easily recognized reflexes concerned in premature labor, in eclampsia, and hysteria. In these last the centric excitability explodes in a sudden and convulsed activity of the muscular organs, through excitomotory channels, while in the former it is propagated more slowly but even more surely and disastrously through the ganglia and filaments of the secretory or vaso-motor system, disturbing and obstructing the capillary circulation, and upsetting all the important processes of elimination, of metamorphosis, of nutrition, and of *blood-heat* involved in its normal activity.

Three distinct lines, then, may be recognized as the open paths by which morbid reflex-excitability of the cord may

<sup>1</sup> The Italics are mine.

travel, to superinduce in the organs the varied phenomena of which it is so often the primary dynamic source: First, by way of a sensory nerve, producing direct or reflex neuralgia or other aberrations of sensation, as chills or flushes; secondly, by motory channels, we may have convulsive or spasmodic symptoms; and thirdly, by virtue of the intimate connection of the spinal with the ganglionic system, irritation may be transmitted through the ganglia and filaments supplying and controlling the blood-vessels of the several organs, resulting in congestion, inflammation, and change of tissue. This latter neurotic condition, it will be seen, is not only a modifier of functional manifestation, but becomes truly the dynamic source of *structural change* in the parenchyma of the organs.

Quinine, as has been seen, by depressing this centric reflex excitability, controls, better than any other agent, all three of the above classes of reflexes. And besides this, we hope to show, hereafter, that by the contractile power directly exerted by it on the capillaries of the congested and inflamed organs, it, in another way, disperses the hyperemia lying at the foundation of each special morbid state.

THE PRIMARY ACTION OF QUININE DUE TO ITS CONTRACTILE EFFECT ON THE CAPILLARIES. ROBERT CAMPBELL. 1858.

Long previous to the demonstration that the physiological action of quinine was dependent upon its influence in depressing reflex excitability of the cord, was the announcement and formal record of an explanation of its therapeutic power, even more profound and comprehensive in its significance, so far as relates to the class of diseases we are called upon to consider in the present discussion. Fortunately for us it does not contradict, but on the contrary confirms, and in a great measure explains, the postulate in regard to its control of the reflexes through the cerebro-spinal centres. The doctrine, however, does more than this — it asserts that the controlling influence of the agent is not confined solely to its depressing action on the cord, but claims that its curative power extends also to a

*direct action* upon the congested and inflamed *organs* themselves.

That "Quinine is to be regarded as a disseminator and equalizer of the *circulation* and acts by dispersing, wherever found, all vascular accumulations, possibly *by giving tone to the vascular tissue*, and that it has control over the nervous system by *dispersing* such engorgements in its centres," is a proposition of Dr. Robert Campbell of Georgia.<sup>1</sup> "Quinine exercises its primary action upon the middle or fibrous coat of the blood-vessels, and upon its influence in that tissue all its observed effects depend." The following propositions may be said to summarize his view of the subject as presented to the Medical Association of Georgia in April, 1859:—

"*First.* That quinine does not act *primarily* upon the nervous system.

"*Second.* That its effects upon the nervous system are neither those of a stimulant nor sedative.

"*Third.* That its manifest uniform phenomena are at variance with those of any known neurotic.

"*Fourth.* That there is no concordance between the degree of its *apparent* influence over the nervous system and the size of the dose, as obtains with all neurotics.

"*Fifth.* That its phenomena are varied in character and degree, more in accordance with an associate condition of the *vascular*, than of the nervous system.

"*Sixth.* That its action is *primarily* exerted upon the *vascular system*, by a specific agency directed to the fibrous coat of the vessels, and having the power of condensing or contracting that tissue — probably by chemical union with its elements, similar to that of the vegetable astringents. By virtue of this property it overcomes all engorgements —

<sup>1</sup> *The Southern Medical and Surgical Journal*, Augusta, Ga., February, 1858. This very important and philosophic explanation of the action of quinine has been of late more than once, either willfully or ignorantly, presented as more or less original with the writers referring to the subject. It is hoped that the claim of the author will hereafter be fully recognized.

*by constringing the vessels.* Thus it relieves, entirely or partially, all those diseases which depend upon engorgement, resulting from vascular exhaustion or debility, such as would proceed from relaxation of the middle coat—whether occurring in a vascular organ, as lung, spleen, or liver [or uterus]; or in a nervous centre, as brain, spinal marrow, or ganglion.

*Seventh.* That this interpretation is the only one which can furnish a satisfactory explanation of the phenomena consequent upon the administration of quinine."

Much more recently Meihuizen has formed a theory somewhat corroborative of the above, in regard to the influence of the circulation upon the reflex excitability of the centres. He has found that no great loss of spinal excitability ever precedes the cessation of the heart-beat. He has, therefore, builded the theory that in frogs with divided medullas *quinine depresses the reflexes by producing grave disturbances in the circulation.* This in some degree is an experimental confirmation of the theory of Robert Campbell.

Sedgwick, in disagreeing with Meihuizen, says: "I next proceeded to estimate directly the influence upon the reflexes of profound disturbance of the circulation." He then exposed the heart of the frog, "and passed a ligature tightly around it, so that all circulation was stopped at once." He found that in this total stoppage of the circulation the effect was less rapid upon the reflexes than even after large doses of quinine." He comes, then, to the decision, which I cannot regard as entirely free from fallacy, that "we must conclude that quinine does not act primarily upon reflex excitability by diminishing the blood-flow."

I am inclined to arrive at a directly opposite conclusion, and one that will confirm, by his own experiment, Meihuizen's views, and especially that of Robert Campbell. Cutting off the circulation by ligature of the heart should not, perhaps, be expected to exsanguinate the capillaries of the spinal centres immediately. There would be, on the one hand, at least for a time, capillary stasis which would main-

tain the reflex excitability until failing by chemical interchange to maintain functional activity ; on the other hand, quinine, acting directly on the capillaries of the nerve-centres, would begin by constringing their middle coat, exsanguinating at once the structure of the centric neurine, and thus starve out, as it were, its reflex activity in a shorter time than even ligation of the heart could effect. This view of the subject is placed beyond all question by his statement that "under large doses of quinine I have almost invariably found the heart still beating, though the circulation in the web-vessels was usually stopped."

This, I think, is the legitimate interpretation that can be given to Sedgwick's ingenious experiment. It is extremely valuable, for it shows conclusively where and by what instrumentalities quinine acts in depressing reflex excitability ; not from slowing or even stopping of the heart, which we know it does, but by effecting a prompt and decided contraction of the capillaries supplying the intimate structure of the spinal centre, depriving it of the blood necessary to maintain either its functional or morbid responsiveness.

The following remarks from a recent paper on the subject, on a different application of the agent,<sup>1</sup> will sum up its value and well describes its widespread influence in morbid conditions : "Besides this action on the local circulation of the organ itself, the same effect is simultaneously exerted on the entire circulation, and, with the rest, on that of the nerve centres, both cerebro-spinal and sympathetic, so that the general febrile and other reactive processes liable to occur after surgical operations, are either warded off entirely or modified in their intensity ; and again, the sympathetic ganglia presiding over the local vascularity and nutrition, through the same tonic influence on their own circulation, receive, no doubt, at the same time, a renewed

<sup>1</sup> *Ophthalmic Operations, with Remarks on After-Treatment, — the Ophthalmic Use of Quinine, and its Therapeutic Action* ; read before the Medical Association of Georgia, April, 1880. By A. Sibley Campbell, M. D., of Augusta, Georgia.

impulse in aiding the blood-vessels of the local circulation of the organ to overcome the hyperemia, stasis, and their various sequelæ; so that we have, both locally and generally, at the centre and at the periphery, in the organ and throughout the system, as long as the agent is continued or its effects remain, an influence exerted, hostile to, congestion, inflammation, suppuration, and the long train of special symptoms and conditions which they either include or may develop."

The foregoing brief but, I hope, comprehensive statement of the action of quinine is placed in relation with our subject, from the belief that there is no class of diseases in which, on the one hand, reflex spinal excitability more constantly exists, nor on the other, is there any class in which vascular congestion, engorgement, and active inflammation are more common and destructive, than in the puerperal and post-puerperal periods of child-bearing life.

#### MALARIAL TOXEMIA IN CHILDBED.

One of the most difficult studies connected with the subject under consideration is the exact estimate that should be made of the influence exerted by what is understood as malaria in the etiology of the morbid conditions met with in the puerperal state. Recognizing, as I do, reflex excitability of the cord as a profound neurotic condition in which a large proportion of these affections is radicated; and, further, recognizing in this polarized condition the dynamic instrumentality by which the morbid manifestations are guided and controlled, I do not, for a moment, ignore the still more profound and yet unquestionable toxemia which underlies and originates and continues to magnify everything that is aberrant in the varied tableau of morbid phenomena. Poisoned blood, to the nerve, and to the nerve-centre, is, in a vast majority of cases, what too much or too little, or the wrong kind, of oxidizing fluid is to the metallic elements of the cell in electro-dynamics. These nerves and nerve-centres — immersed as they are in this solution of foreign irritating matters — become, indeed, the manifestor

and the measurer of the deleterious agent that is to excite and aberrate their functional activities — the nervous system is truly now a delicate toximeter of the blood, and by its disturbances are manifested the kind and the amount of poisonous matter any given blood-system may contain.

But is malaria, indeed, the only one of the blood-poisons which, having awakened or enhanced the reflex excitability of the spinal centres, is capable of manifesting this excitability by paroxysmal phenomena? This question, so deeply concerned in the decisions of treatment, I am strongly inclined, nay, faithfully impelled, to answer in a decided negative. Periodicity, in my belief, is more an inherent attribute of the cerebro-spinal centres, both in health and in disease, than it is an attribute of any one cause operating upon these centres to evoke periodic phenomena. Malaria, as we recognize it, is by the consent of all, an exaggerator of the reflex excitability of the spinal cord, — a producer of morbid excitability; but, according to my own observation, it is only one of many causes which are capable of producing a like result or condition. Many other poisons, on being absorbed into the blood, as the septic and semi-putrescent matters of childbed, as also many external influences, as reflected peripheral irritation, — as in “urethral intermittents” in all regions of the world, — will all give rise to the reflex excitability. This will be manifested by paroxysms, and these paroxysms can be subjugated or at least modified by cinchona.

This question lies at the very foundation of our practice, and is therefore one of the most important in determining the administration or the withholding of quinine. Upon the sometimes accidental and often precarious decision of the attending physician, whether malaria in any given case is to be recognized or not, depends the giving of quinine, so paramount in importance to the depressing of reflex excitability, to the exsanguination of the turgid and engorged organs, and, indeed, to the well-doing and final restoration of the patient. That in the puerperal condition other and various blood-poisons besides malaria may ope-

rate to superinduce excessive polarity, it is but reasonable to consider; we have a wombful of disintegrating blood-clots; often with exfoliations and drainage,—frequently offensive,—sometimes irritating, muco-purulent, or quasi-purulent. These are in contact with the denuded uterine wall and ragged placental surface,—open avenues to the circulating blood as it bathes and percolates the spinal and cerebral ganglia, modifying their activity, and increasing their reflex excitability.

Besides the above, we must remember the functionally high development and polarity of the recently pregnant woman's nervous organization, her augmented nervous apparatus for the production of an amount of trophic nerve-force adequate to the augmented demand<sup>1</sup>—nidation, fetal nutrition, parturition, involution, and lactation. Under blood-intoxication, whether septic or malarial, it may be well estimated how powerfully these temporarily augmented and exalted ganglia of brain and spinal cord might act like drunken giants in disordering and disorganizing the entire realm over which they hold their sway.

It has become very much a fashion of the day to *condition* all the benefits that have been derived or that are to be derived from quinine, by the presence of malaria as the etiological starting-point and abiding sustainer of the diseased condition so relieved. If the symptoms yield promptly to cinchona, like the spear of Ithuriel, the test has been applied, and the disease is decided at once to be malarial; thus is a questionable diagnosis verified by a foregone conclusion in therapeutics. As the applications of quinine become extended, and its efficiency in relieving conditions previously not treated by it has become recognized, whether in central jungle, border plain, or metropolitan city, it is at once discovered that "a new type of disease has appeared, and that malaria has begun to complicate everything." So fixed is the two-sided proposition in the minds of the leaders of our profession, namely, that paroxysmal morbid phenomena are evoked only by malaria, and that quinine is

<sup>1</sup> Robert Lee.

only beneficial where malaria is the etiological factor, and so difficult — nay impossible — is it to disprove the existence of malaria anywhere, that all questioning of the doctrine has been long silenced, and the impregnable theory, it seems, must ever remain in the minds of most of the profession as one of our guiding principles. Fortunately the disastrous results that might accrue from this conditional administration of quinine are being every day more and more evaded, as the assumption is becoming general, that malarial influences are widening their sway, and with this assumption the omissions of quinine in conditions demanding its use are becoming less and less frequent.

Among those whose influence has been exerted to extend the use and urge the value of quinine in the puerperal condition, a distinguished Fellow of this Society has been most prominent. Dr. Fordyce Barker, adhering to the doctrine of malarial toxemia, designates some of his cases as "Malarial Puerperal Fever." The morbid phenomena were recognized as of a paroxysmal type, and the administration of quinine in decided doses resulted in their rapid recovery. Certain cases of puerperal eclampsia decided by him to present the same complication were treated by large doses of this alkaloid with a like fortunate result. Though by no means fully assenting to the decision, that such cases, on account of being paroxysmal, were necessarily and invariably malarial, I would respectfully ask to relate to my distinguished friend — our master in "Puerperal Diseases" — the result of my own experience of more than twenty years. Daily observation on the James,<sup>1</sup> and on the Mississippi,<sup>2</sup> as well as on the Savannah,<sup>3</sup> has but confirmed me in the belief that there is no febrile condition of the puerperal state which is not, in the majority of cases, greatly benefited by quinine, whether regarded as malarial or not; and further, that its invariable use after labor would greatly

<sup>1</sup> Richmond, Virginia, during our late war, 1861-1865.

<sup>2</sup> New Orleans, Louisiana. Winter of 1866-67, and of 1867-68.

<sup>3</sup> Augusta, Georgia. From 1842 to the present time with the above exceptions.

lessen the frequency of many of the dangerous sequelæ now so much to be dreaded in post-partum practice.

Whether these clinical observations, made always, as has been shown, within the sphere of malarial influences, will serve to weaken or to confirm the almost universally adopted views I am disposed to question is, as it should be, a matter of indifference. They are not given to advocate any particular idea,—malarial or anti-malarial,—but to further the cause of truth in regard to the benefits of quinine everywhere, as argued upon the broader field opened to us by experimental inquiries demonstrating its ultimate physiological action.

More widely influential than even clinical reports, in extending the applications of quinine, not only in obstetric but also in general practice, will be the elaboration and general diffusion of such views in regard to its physiological action as those of Sedgwick, Robert Campbell, Goltz, and Meihuizen. They demonstrate its applicability to conditions independently of theoretical causes. Of a like value, with the experiments in the Physiological Laboratory of Johns Hopkins University, are those made, not long previously, by Dr. Mary Putnam Jacobi,<sup>1</sup> in which, in the human subject, she was enabled to estimate, by the sphygmograph, the marked diminution of cerebral tensions under the influence of twenty grains of quinine, in the case of a boy with exposed cerebral hemisphere.

#### CINCHONISM AND LISTERISM.

What is called the “germicidal property,” so generally accorded to quinine, may afford one of its modes of action for combatting in the blood foreign organic agencies, that

<sup>1</sup> “All these circumstances tended to prove that under the influence of a ‘sedative’ dose of quinine . . . the amount of blood in the brain was diminished.” Also, in a case of “reflex hyperemia of the brain,” fifteen grains of quinine in divided doses repeated for two days — child ten months of age — relieved permanently the most serious symptoms. “I attribute the effect to a depletion of the cerebral blood-vessels.” *Archives of Medicine*, February, 1879, article, “Effect of Quinine on Cerebral Circulation,” p. 33.

increase centric excitability. This also may furnish to some another reason for recommending it in post-partum and other gynecic conditions, more or less tending to septicemia and pyemia. If Listerism can be allowed to have any rival, in its power to prevent and repress suppuration, and to secure uninterrupted plastic union or resolution in wounds, that rival is cinchonism. Not, as I believe, altogether by destruction of germs, though I do not deny their existence, but by its power to repress centric excitability and its consequent reflex in the capillary circulation of the wounded part.

Though according full credit to Mr. Lister, and fully recognizing the advantages claimed for his system, the explanation given of its valuable results is not always acceptable, on account of the necessity it involves of predicating hypothetical germs and their destruction as an essential part of it. Other views, more consistent with the present discussion and equally plausible, may very well be adopted. Since 1850, reflex irritations originating in peripheral sensory nerves, and modifying ganglionic power over the capillaries have been recognized as influential in altering structural conditions as well as nutrient and secretory processes.<sup>1</sup> The reflex character of inflammatory and suppurative processes, and their relation to both peripheral and centric activities, have been thus described in a former discussion. "The true account of these phenomena has been already suggested by us when discussing the subject of suppuration in reference to its periodicity, namely, that when any part of the surface is wounded, either by incision, puncture, or the persistent presence of a foreign body, a number of sensory filaments of the cerebro-spinal system is necessarily injured; these filaments, thus impressed, communicate excitement to the spinal centre, thence it is reflected to the secretory ganglia and filaments directly controlling the vessels of the wounded part; these are aberrated in their action, and the modified circulation and the forma-

<sup>1</sup> *Southern Med. & Surg. Journal*, June, 1850, "The Influence of Dentition in Producing Disease," vol. vi., p. 18.

tion of pus are the results of this reflex aberration in the two nervous systems. The phenomena of suppuration, then, under the above circumstances, may be fairly considered as true excito-secretory phenomena. That the cerebro-spinal (or peripheral) irritation is an important element in the various processes of inflammation, the experiments of Magendie and others will fully establish. . . . *Whatever amount of pain there may be succeeding such wounds, it is always paroxysmal. These paroxysms are followed by suppurations, and an interruption of the healing process, and therefore we give quinine when such is the nature of the pain, and our experience is that the pain is much lessened or prevented, and that the suppuration is either prevented or retarded.*"<sup>1</sup>

From the above it will be seen that the elements in the inflammatory and suppurative processes are: 1st, The wounded sensory or afferent nerve; 2d, The excited spinal centre, and 3d, The vaso-motor filaments controlling the capillaries of the injured part. Suppuration, then, is a reflex initiated by the wounded sensory nerve, and propagated by the excited cord to the capillaries. Any influence capable of annulling the inceptive or transmitting power of the sensory nerves will arrest or prevent the process *ab initio*; on the other hand, any influence or agent capable of annulling the reflex excitability of the spinal centre will as effectually prevent suppuration by abstracting the dynamic power necessary to the process. This centric depression, we have seen, is exerted by cinchonism, while the anesthetic power of carbolic acid continuously applied to the injured part, and constituting the essence of Listerism, acts by annulling centripetal irritation, thus interrupting peripherally the reflex equally indispensable to the capillary disturbance. This peripheral paresis, produced by carbolic acid, I regard as the true explanation of Listerism.<sup>2</sup> Cinchonism acting

<sup>1</sup> *Trans. of the Amer. Med. Assoc.*, for 1858, vol. xi., pp. 616-617.

<sup>2</sup> After writing the above, my attention was called to the remarks of Dr. J. H. Bill, *Amer. Jour. Med. Sciences*, July, 1872. I find he adopts a similar view as to the power of "Carbol" to depress sensibility in

centrically may be regarded as equally powerful, if not superior, in repressing inflammation and its *consequent* suppuration. It can easily be recognized how both these agencies acting conjointly, one dulling traumatic sensibility at the periphery, and the other depressing reflex excitability at the centre, combine to constitute a controller of both inflammatory and febrile activity of the most efficient and available kind.

The value of judicious carbolic irrigation,<sup>1</sup> then, after labor, it may be seen, is greatly enhanced by the use of quinine in conjunction. We may thus shut out both febrile and inflammatory disasters so often the terror of post-partum conditions.

#### THE RECOGNITION OF PRINCIPLE AFTER PRACTICE.

That "the foundation of therapeutics is laid in empiricism, and that practice precedes principle,"<sup>2</sup> applies as fully in the case of quinine as to that of most remedial agents. Even in the present advanced state of medicine Sydney Ringer, referring to quinine in intermittent fever, makes the candid acknowledgment that "how it acts is at present quite unknown." And yet quinine has been empirically curing intermittents since 1820.

the wound. He does not, however, refer to the spinal cord as being a factor in the result, but, as I understand him, "the sympathetic ganglion." This is not what I call "excito-secretory action."

<sup>1</sup> For some well-timed remarks on this subject, I here refer to a paper read before the Obstetrical Society of Dublin, by Dr. W. J. Smyley, on "Utero-vaginal Injections in Childbed." He recommends great care, and reports a death under his observation at the Rotunda Hospital, from entrance of air into the veins of the uterus during the injection of Condy's fluid. "Suddenly the woman became collapsed, respiration ceased, the pulse at the wrist became indistinguishable, and the cardiac impulse, which could faintly be felt for some time, soon ceased." The woman was dead in twenty minutes from the accident. The post-mortem examination showed a quantity of frothy blood in the right heart. He thinks very frequent irrigation ought to be discouraged except in cases tending to septicemia. I witnessed some alarming symptoms from carelessness on part of nurses, but no death. From *British Med. Journal*. See *N. Y. Med. Gazette*, April 30, 1881.

<sup>2</sup> Elisha Bartlet, *Medical Philosophy*.

In the department of obstetrics and gynecology, and longer in general surgery, the use of quinine has been familiar to me as a safe and most valuable adjunct for more than twenty years. Long previous to the unquestionable experimental data now afforded us, and by which we are enabled to investigate its mode of action as presented in this paper, I constantly availed myself of its valuable aid in traumatic fever and many allied conditions. Accustomed since 1857 to administer quinine in the treatment of all surgical injuries, and after surgical operations, it became my habit to regard it as indispensably necessary after any aggression whatsoever upon the system, whether trivial or severe, — after the application of male bougies in urethral stricture, after the sponge-tent in cervical stenosis, as well as in lithotomy in the male, or in grave incisions of any kind in the female.

Not leaving out of view certain blood-conditions that quite often exist, traumatic fever may be regarded as a reflex from the wound through the sensory nerves and spinal cord to the general vascular system. Morbid uterine conditions I have ever regarded as fully capable of producing identical results, and as requiring remedial agencies of like character and power for their abatement and control.

#### THE PROPHYLACTIC AND CURATIVE USE OF QUININE IN CHILDBED.

From considerations like the above, and for reasons given earlier in this discussion, it will doubtless surprise no one when I say that during the time mentioned, as well as at the present, it is a distinct and important feature of my attendance to administer quinine invariably after parturition. Whether the case be one of labor at full term or of premature delivery, or the earliest abortion, my method is the same in regard to the administration of quinine, whether as a prophylactic or curative agent. Beginning on the morning of the first or second day after labor, it is my object to secure to my patient at a reasonably early time a moderate degree of cinchonism which is to be maintained for at least a

week or ten days from the date of childbirth. The amount of the alkaloid necessary for this I find to vary from ten or even six grains to fifteen or twenty for the daily administration. After the influence is established, I find in most women but a moderate quantity is required to maintain what I would term the protective degree of cinchonism as long as I may suppose it to be desirable. I have found divided doses of from three to five grains, two hours apart, preferable to a single dose, as less liable to disturb the stomach or to produce agitation. The entire quantity to be taken each day I endeavor to have given by noon or not long after.

The above daily routine may generally be omitted after a week or ten days, or at the end of this time, as I have found the local as well as the febrile disturbances of lactation, and the more serious febrile disturbances incident to involution, among which peritonitis, septicemia, and subinvolution are most to be dreaded, have in most cases been eyaded, and the patient tided over the period in which nearly all the dangers of the puerperal condition are past. If, as in rare cases, there be manifestations of febrile excitement after the cessation of quinine, I advise the immediate resumption of the course, to be continued as long as found desirable.

*Modifications.* There are cases in which I find it desirable to vary the "routine." Some delicate women are rendered excessively "nervous," by even moderate quantities of quinine. I have then alternated the doses of quinine by portions of bromide of potassium until the required amount of quinine has been taken; thus two or three grains of quinine, and fifteen or twenty grains bromide of potassium at alternate hours.

*Idiosyncrasies.* Inocuous as quinine, as a general rule, is found to be, there are persons of peculiar temperament to whom even the most moderate dose of any of the preparations of cinchona would be not only very distressing but positively dangerous. I have witnessed the most alarming heart-perturbations and "sinking" as an occasional result.

This may be the effect of exaggerated depression of reflex power. But the most common and alarming disturbance arising from idiosyncrasy is the sudden occurrence of an efflorescence with intense redness and tumefaction of the skin. I have regarded this distressing exanthem as urticaria. It is not always confined to the cutaneous surface, but I have seen the buccal mucous membrane, the fauces, and pharynx puffed and swollen, a most distressing dyspnea threatening the patient with asphyxia. Many of these persons, I believe, would be killed by ten or even five grains of quinine, if not speedily relieved. Bromide of potassium moderates the severity of the symptoms, and morphine, I have found, in cases where these alarming effects have been unwittingly produced, very soon relieves them.

*Salicine.* In cases like the above I have found a most valuable substitute for quinine in salicine, which I invariably prescribe in doses adequate to the full effect of the quinine required after labor.

#### RESULTS OF TREATMENT.

In estimating the results of a method of treatment in which prophylaxis is the object mainly contemplated, it is of course difficult to present that appearance of statistical or tabular exactness which is seen in the results of curative measures. Cases of disease prevented are not so obvious and tangible as cases of cure. We can still, however, arrive at conclusions which place the results entirely on the side of the method in question. The comparative infrequency of grave cases of puerperal disease under this method, as compared with results under its omission, has been very obvious. Since quinine has been administered immediately after labor, and continued as above described, mammary inflammation and abscess, peritoneal tenderness, uterine sensitiveness, peritonitis, cellulitis, irritative and septic fever, besides subinvolution and its many concomitants, have been greatly diminished in the scope of my attendance, — indeed, I may say, are almost unknown. In a community of highly intelligent medical men and among us, many independent

thinkers and careful observers, a treatment savoring so decidedly of "routine" as the invariable giving of quinine after labor, could not expect to escape inquisition. Twenty years ago criticism was often adverse though never unfriendly. Among these gentlemen, and among a very large body of younger practitioners reared under their influence, I may say, that I know scarcely of one who does not at the present day pursue a more or less similar or modified plan in their post-partum practice. If not beginning with quinine *unconditionally*, as I have done, all keep a most watchful eye upon every case, and on the slightest indication of lagging convalescence the free and continued administration of quinine becomes the most prominent and essential feature of their management. On the other hand, though in comparatively scant proportion, many opportunities have been afforded me of estimating the curative results of quinine, as a measure of post-partum treatment, as in cases originally under the care of midwives and others who may have neglected prophylactic measures. Of these, tender and enlarged or inflamed mammae, or even fully formed abscesses, besides peritoneal and uterine tenderness, cellulitis, tardy involution, and subinvolution, are constantly found to yield to quinine in the most striking manner. Among these results none are more obvious than its apparent power to prevent and to retard suppuration anywhere, but most frequently in the mamma,<sup>1</sup> or in any lymphatic or other gland which may be the subject of inflammation after labor. For all these varied conditions I have found quinine as the main basis of treatment to far transcend every other method, or all others combined, in its immediate and striking efficiency, as well as in its valuable results.

Both as a promoter of involution, as well as dispeller of subinvolution, the quinine treatment is modified by my

<sup>1</sup> As incidentally connected with our subject I refer here to the measure of making firm compression by bandage or light corset in threatened mammary abscess, first suggested many years ago by my distinguished friend, Dr. L. A. Dugas, Professor of Surgery in the Medical Department of the State University.

friend Dr. J. S. Coleman of Augusta. He combines with it, in alternating doses, fifteen to thirty minims of fluid extract of ergot, beginning the day after labor and continuing at intervals of six hours as long as the quinine is used. Theoretically, this combination is admirably calculated to lessen uterine congestion and to promote shrinkage. In my own cases, however, I have seldom had occasion to use the ergot, finding quinine alone fully adequate to secure me generally against all accidents to involution. As an addition to the treatment of uterine fibroids by ergot, I have found quinine valuable as an adjunct; I have thought in such cases the rapidity of growth was somewhat repressed and the amount of hemorrhage lessened, but of actual cures I have none to report.

Mr. President: In the course of these rather extended remarks on the value of quinine in our department of medicine, I have been careful to state that my observations have been made constantly within the sphere of malarial influences. A spirit of candor and of scientific fairness has alone prompted me in giving this warning, as with some it may measure the estimate to be given to one or more of my conclusions. I am aware that under malarial intoxication diseases are supposed to, and probably do, acquire a widely assimilated type. That when we come to discuss the effectiveness of quinine in their treatment, there is ever a suspicion that, instead of extending the applications of the agent, we are dealing constantly with but a single form of toxemia, common to all classes of morbid phenomena existing in these regions. As "all things look yellow to a jaundiced eye" so are we regarded as walking ever in an enchanted circle in which every phase of disease is colored by malaria, and hence no experience is of any value except as illustrative of our resources in combating its influence.

While to a considerable extent there may be truth, and some wholesome discrimination, in the above view of the subject, I am convinced that the *dictum* upon which this momentous question has so often been settled, has more in it of plausible triteness than of sound philosophy. Since the

careful observations and experimental researches into the physiological action of quinine, a new illumination may be said to have dawned upon this particular field of study. By these valuable investigations it is now demonstrated, that the administration of quinine in child-bed and under other circumstances is no longer to be dependent upon the theoretical assumption of the presence of malaria; but upon conditions easily recognizable and fully adequate to account for the morbid phenomena. In the puerperal condition, the laxity of tissue, and the excessive amplification of the uterine and pelvic vascular system, no less than the morbid reflex excitability of the cord, are both rapidly overcome and kept under control by the power of quinine to diminish the calibre of the blood-vessels. This curative exsanguination in the capillaries of the cord, as well as in the vessels of the mamma and pelvic organs, may now be held to result from its action, whether it be malaria or any other cause, internal or extraneous, that may have been remotely concerned in the production of the morbid manifestations.

The following are some of the principles which may be derived from our discussion of quinine in its relations to obstetric practice:—

*First*, That an exalted reflex excitability of the cerebro-spinal centres, as well as general plethora, may be recognized as a characteristic condition of the pregnant woman from the date of conception to the completion of involution. This may be termed "the gravid development and exaltation of the nerve-centres."

*Second*, That this provisionally increased development and polarity, intended for the purposes of fetal and uterine growth, renders the woman, during its continuance, eminently liable to become the subject of various morbid reflexes more or less peculiar to her condition.

*Third*, That these morbid reflexes are of two perfectly distinct and dissimilar kinds, differing widely as they may happen to occur, before or after parturition.

*Fourth*. During the entire period of pregnancy, and until after labor, the reflexes are of an *excito-motory* character,

restricted to the muscular apparatuses of the uterus and of general volition. They are apyrexia and non-inflammatory. Their paroxysms threaten premature expulsion of the fetus in pregnancy, and eclamptic convulsions in labor.

*Fifth*, After parturition, the reflexes are of an *excitatory* character. They are propagated, through the ganglionic or vaso-motor nerves, to the blood-vessels and capillaries of the pelvic organs and tissues and of the general system. They are marked by fever, congestion, and inflammation, with their products and consequences. Septic fever and peritonitis, with arrest of involution and mammary abscess, are their not uncommon results.

*Sixth*, That quinine, by its contractile action on the capillaries of the cerebro-spinal centres, exsanguinates their nervous structure and, more than any known agent, depresses the reflex excitability from which the varied morbid phenomena of both pregnancy and child-bed originate.

*Seventh*, That quinine, except in cases of idiosyncrasy or from an injudicious administration of the agent, exercises no influence whatever to superinduce premature expulsion of the fetus.

*Eighth*, That moderate cinchonism adjusted to the type and approach of the paroxysmal neuroses, which endanger the welfare of the fetus during pregnancy, is one of our most efficient resources in many cases of threatened abortion and of premature labor. During parturition it may give "steadiness" to irregular uterine contractions; and, continued during labor, cinchonism is, in a most valuable degree, prophylactic against threatened eclampsia.

*Ninth*, That the reflexes of child-bed, pertaining as they do, primarily and principally, to the recently evacuated uterus — well likened to an organ in a traumatic condition — opportune and ready for the awakening of fever and inflammation, are of the gravest character, frequently tending to disorganization and death, or else to permanent and irreparable injury. These "reflexes" constitute a dreaded class of diseases, most commonly called "puerperal," which, by universal consent, must be *prevented* rather than trusted

to efforts, so often unavailing, for their cure. To this end, the most valuable and reliable prophylactic method will be found to consist in *the daily administration of quinine to the degree of moderate cinchonism* from the day of parturition and to be continued daily until normal involution is safely secured. By the observance of this "routine" as a rule it is believed that the occurrence of puerperal diseases will be largely prevented, and that the rate of child-bed mortality will be greatly diminished.

*Tenth*, That cinchonism in its quality of preventing and controlling inflammation, whether traumatic or idiopathic, and of suppressing suppuration, — all of which is due to its power over reflex excitability of the cord and its action on the capillaries, — has a claim to antiseptic value superior to Listerism, and is less to be dispensed with than carbolic acid or any of the means and appliances of the recognized "antiseptic method." In general surgery and especially in uterine surgery, as well as after parturition, the combination of carbolized irrigations and applications to diminish *peripheral* excitability with persistent *cinchonism* to depress *centric* excitability should constitute hereafter an antiseptic method more reliable, generally practicable, and less to be dispensed with than the most faithful observance of the complex Listerian process.

