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GOVERNMENT OF MADRAS.

PUBLIC DEPARTMENT.

22nd January 1879, No. 83.

Cinchona Febrifuge.

Read the following paper :—

No. 42. *From Surgeon-General G. SMITH, M.D., Indian Medical Department, to the Acting Chief Secretary to Government, dated Fort St. George, 25th September* 1878, *No.* 527.

I have the honor to submit, for the consideration of His Grace the Governor in Council, the opinion called for in G.O., No. 1011, of 27th June 1878, touching the recommendation of the Government of India that "only one-fourth of the quantity of quinine hitherto supplied should in future be issued to Native Civil Hospitals and Dispensaries, the remaining three-fourths being made up by the cinchona febrifuge prepared at Runghee," a recommendation which has been extended so as to include Native Military Hospitals.*

* *Vide* letter from Supreme Government to Secretary of State, No. 45, dated 17th June 1878, paragraph 3. Pamphlet, page 73.

2. A careful review of the evidence available in this Presidency and in the Presidency of Bengal, bearing upon the proposed substitution, constrains me to hesitate before assuming the responsibility of advising Government to accept this recommendation of the Government of India, and, as the question is one of grave importance, I shall now place before Government the grounds which seem to me to justify this hesitation.

3. Setting aside altogether the recorded experience detailed in the communication from this office, No. 520, dated 16th September 1876, I would solicit the attention of Government to the experience of Bengal as recorded in the official pamplet entitled "Collection of papers showing the recent results of the trial of cinchona febrifuge, quinetum, alkaloids, and sulphate of quinetum," which has been sent for my information.

4. In the appendix of this letter will be found a tabular analysis of the experience of fifty-six medical men in Bengal, who were called upon to report on the therapeutic properties of these preparations. The results as regards each of these preparations are recorded, but I propose to confine my attention to those which refer to the Sikkim cinchona febrifuge (a preparation of the mixed alkaloids as they exist naturally in the red bark), inasmuch as that is the preparation which Government has been requested to accept as a substitute for 75 per cent. of the supply of quinine required in this Presidency.

Vide Annexure A.

5. Reports 1 to 18 inclusive concern quinetum alkaloid and quinetum sulphate; reports 19 to 66 inclusive have reference to the medical experiences of the Sikkim cinchona febrifuge as a therapeutic agent in the treatment of fever. These latter are thirty-eight in number, and a careful inspection of the reports shows that, whilst there is a general concurrence of opinion regarding the febrifuge properties of the drug in the treatment of ordinary and uncomplicated cases of fever, there is a very marked difference of experience as regards the toxic properties of the same.

The preparation possesses marked therapeutic with little or no toxic properties according to one group of observers. According to the other group it has marked therapeutic with objectionable toxic properties.

6. In twenty-three of the thirty-eight reports tabulated, that is, in 60·5 per cent. of the whole, the febrifuge action of the preparation was associated with more or less marked effects of an objectionable kind, such as nausea, vomiting, diarrhœa, giddiness, headache, and, in some instances, a tendency to depression. These symptoms were not all present in each instance, nor were they all present in the same intensity. They were, however, present to an extent in each case meriting special notice.

7. That this result, bearing as it does directly upon the therapeutic value of the cinchona febrifuge, has attracted the attention of medical men in Bengal, of the Government of Bengal, and of the Supreme Government the official pamphlet* clearly and repeatedly shows, as the marginal references† prove.

8. Recommendations moreover touching the proper expedients for securing high therapeutic with a minimum‡ of toxic properties are made by Dr. King and Mr. Wood at page 47. These recommendations involve the substitution for the cinchona febrifuge of a new compound containing the sulphates of quinine, cinchonidine, and cinchonine, but, omitting quinidine and amorphous alkaloid, the selected alkaloids being converted into crystallizable sulphates. Dr. King and Mr. Wood, however, express doubts regarding this combination, thinking it possible that cinchonine may have contributed to the objectionable symptoms attended upon the use of the cinchona febrifuge. This suggestion, if acted upon, would reduce the ingredients of the new cinchona febrifuge to two, viz., the sulphates of quinine and cinchonidine, a combination not unfrequently met with in the impure quinine of the shops. Finally these gentlemen recommend a mixture of the commercial sulphates of quinine, cinchonidine, and cinchonine in the proportion of 4, 3, and 2 parts, respectively, the proportions in which they are said to exist in red bark. At page 70 of the pamphlet the Committee on the Cinchona Febrifuge accepts the formula of Messrs. King and Wood, and further give it as their opinion "that, while the experiments which they have above recommended are being carried on, the manufacture of cinchona febrifuge should by no means be discontinued, but on the contrary that it should be carried on on the present scale, which (they understand) is not at all in excess of the current demands." This recommendation appears to me to be somewhat of a *non sequitur*. They also recommend that the preparation suggested by Messrs. King and Wood and approved of by the Surgeon-General be issued for trial and report to a limited number of medical officers who, in the opinion of the Surgeon-General, may have good opportunities and who may be well qualified to give it a full, fair, and unprejudiced trial.

9. Medical men are well aware that with the sulphate of quinine the *therapeutic* without the *toxic* effect of the drug can be secured in the great majority of cases; they are also unanimous in stating that in the severe and complicated cases of fever no preparation can be so trusted as that alkaloid, and it is not to be wondered at if they prefer a medicine which is of high value in every type of malarial fever to one which is principally useful in a limited and less urgent field, and which has its febrifuge qualities associated with physiological actions of a more or less serious import.

10. The evidence adduced is sufficient, I think, to enable Government to come to a decision on the point at issue. I am of opinion that it does not bear out the advisability of accepting 75 per cent. of our *supply* of quinine in the form of the cinchona febrifuge, nor do I think that, were such suggestion accepted, it would be regarded by the Medical Department of this Presidency as the fair expression of their experience. I am, however, prepared to accept the *separate* issue of the cinchona alkaloids selected by the Calcutta Committee in the following proportion and as a tentative arrangement till an equally efficient substitute can be found at a cheaper rate. The sulphates referred to are crystallizable salts:—

Sulphate of Quinine	25*	per cent.
„ Cinchonidine	50	„
„ Cinchonine	25	„
	100·0	

In Bengal the experiment is to be made with a mixture of these alkaloids. I propose that in Madras there should be a repetition of the experiments of 1867 and 1868 with these alkaloids separately, so that by comparing results alterations in the quantities of each indented for may be made as experience shall dictate. The sulphates of cinchonidine and cinchonine are inexpensive preparations, the cost prices in London of the supplies now in stock in the Medical Depôt having been as per margin. In offering this suggestion I contemplate the provision of pure, not of impure preparations. Further information regarding the febrifuge value of the sulphates of cinchonidine, cinchonine, and quinidine will be found in the Proceedings of Government marginally noted.

	Per Pound. Rs.	A.	P.
Cinchonidiæ sulphas	17	8	0
Cinchoniæ sulphas	5	0	0

G.O., No. 1671, dated 15th June 1868.
„ 652, „ 19th March 1867.

11. There is moreover a difficulty to be contemplated in this Presidency with reference to any attempt to place the Sikkim febrifuge in the hands of the people at large, viz., that, owing to its marked difference in appearance from that of quinine, it is likely to be regarded with suspicion. In all parts of the country the Madras native is quite familiar with the physical characteristics of sulphate of quinine, and we know from experience that he would not readily accept any substitute which in appearance should be different from that drug. One great advantage attending the use of the European-made sulphates of cinchonine and cinchonidine will be that, in consequence of their similarity to quinine, they will at once pass current as substitutes for it.

12. It is also doubtful whether Local Fund Boards and Municipalities, who pay for their supplies of medicines, will be found willing to buy a preparation of which we have had comparatively but little experience, and that experience not altogether of a favorable character.

13. With reference to the further trial of the Sikkim febrifuge ordered in Government Order, Public Department, No. 134, of 7th February 1877, I have to report that a supply of the drug, although at once asked for, was not received until October 1877. It was then distributed to a number of stations, and, as soon as the whole of the reports of the trial have come to hand, a further communication will be submitted to Government. Meanwhile a reminder calling for the reports still due has been sent in circulation.

* Annexure B.

† Letter from Govt. of Bengal, to Surgeon-General, I.M.D., No. 2337, 22nd June 1878,—*vide* para. 3 (page 41).
Letter from G. King, Esq., M.D., and C. H. Wood, Esq., to Surgeon-General, I.M.D., No. 130-Q, 26th July 1877,—*vide* para. 2 (page 47).
Letter from Surgeon-General, I.M.D., to Govt. of Bengal, No. 620, 27th July 1877, para. 3 (page 46).
Letter from Surgeon-General, I.M.D., to Govt. of Bengal, No. 1605, 30th Jan. 1878,—*vide* para. 4, Sec. (b), and para. 5 (page 68).
Letter from J. H. E. Innes, Esq., Surgeon-General, B.M.S., to the Govt. of India, No. 536-B, 22nd May 1877,—*vide* para. 1 (page 56).
Letter from J. H. E. Innes, Esq., Surgeon-General, B.M.S., to the Govt. of India, No. 599-B, 28th Dec. 1877,—*vide* para. 2 (page 59).
Report of Committee on Cinchona Febrifuge, 27th Aug. 1877,—*vide* paras. 2, 3, and 4 (page 60).
Letter from Govt. of India, to Her Majesty's Secy. of State, No. 45, 17th June 1878,—*vide* paras. 2, 3, and 5 (page 73).

‡ All salts of quinia possess *toxic* properties more or less. They are all protoplasmic poisons.

* Of this aggregate 6 per cent. should be in the form of the neutral sulphate for hypodermic injections.

No. 43. ORDER THEREON, 22nd January 1879, No. 83.

His Grace the Governor in Council considers the suggestion of the Surgeon-General in regard to the extended use of cinchonidine and cinchonine, and their separate issue, to be unobjectionable, while it is also desirable that their value should be fully tested especially as the measure is expected to be equally economical with that suggested by the Government of India.

2. It is most necessary, at the same time, that full and systematic trial of the Sikkim febrifuge should be carried on under careful supervision in Civil Dispensaries and Hospitals as well as in Military Hospitals. Reports should be rendered half-yearly of the results. A recent paragraph in the *Pioneer* states it has been found very effective in Afghanistan in combination with certain other drugs.

3. The Surgeon-General, Indian Medical Department, will report, at an early date, the quantities of the Sikkim febrifuge, as well of cinchonidine and cinchonine, he requires to be supplied for the use of his department.

4. It will be intimated to the Government of India that His Grace the Governor in Council has directed an extended use of the Sikkim febrifuge in both Military and Civil Hospitals as also extensive trial of cinchonidine and cinchonine, but, as at present advised, is not prepared to direct the substitution of the febrifuge for quinine in this Presidency.

(True Extract.)

Acting Chief Secretary.

To the Surgeon-General, Indian Medical Department.
" Revenue Department.
" Military Department.

No 427

1st Feb 79

Encl. J. W. Fischer.

14 Febr. [illegible]

Received 1879 Sept

No 427, 1 February 1879

Write Order

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