

SULPHONE LEVELS IN BREAST MILK OF  
MOTHERS ON SULPHONE THERAPY

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Of the many sociological problems that arise in the treatment of people with leprosy, one of the most difficult is that of the care of uninfected children of infected parents. In some places the problem is ignored entirely, and the children are left with their parents, there being no attempt whatever to separate healthy children from active cases of leprosy. There are many attempts at partial isolation. The ideal, however, is complete segregation, examples of which are the Preventoria of Brazil (1, 2, and 3).

There have been many detailed epidemiological studies (4) which have presented evidence which few leprologists will question. The most notable and thorough, perhaps, are those which have been carried out in the Philippines. Briefly, some conclusions are: (1) children are much more susceptible to infection than adults; (2) leprosy is almost always contracted in early childhood; (3) leprosy is not inherited, nor is it an *in utero* infection; (4) and if a new born infant is removed at once from its infected mother and has no contact with an active case, the child will not develop leprosy.

After a study of these findings, it is evident that the ideal way to prevent the children of parents with leprosy from contracting the disease is to remove the children from their parents at birth and to care for them in nurseries or preventoria. This is what is being done in the Kano Leprosy Settlement of the Sudan Interior Mission in Nigeria. At this Leprosy Settlement we have two baby homes, which we call "creches." In one creche we have the children who have been delivered in the Settlement. When the expectant mother is near term, she is admitted to the maternity building, where she stays until after she delivers her child. At the time of delivery, she is attended by the missionary doctor or, in his absence, by a missionary nurse. This delivery is carried out under sterile conditions and the new born infant is taken immediately to this creche, which is under the supervision of a woman missionary and a staff of African nurses who have never had leprosy. The baby is put on a formula which is altered according to weight and age, and as it develops, supplemental feeding, vitamins and an antimalarial drug are added at the recommended times. This system has proved satisfactory, but, as it requires more staff and costly feedings, it is expensive compared with the practice of allowing the mothers to nurse their children. It is gratifying, however, in that none of our children thus raised has ever developed leprosy.

Before proceeding to the main study to be presented in this paper, we shall complete the description of our creche system. The second baby home at our Settlement is referred to as the 'contaminated creche.' To this home are admitted the children who accompany their parents to our Settlement, but who on clinical and laboratory examination have no evidence of the disease. These children have had contact with active cases of leprosy for varying lengths of time and have had opportunity to become infected. At the time of admission, they show no clinical evidence of the disease but they may do so later. These children are kept under constant observation and if any clinical manifestation of leprosy develops, they are transferred to the Settlement and active treatment started. It is interesting to note that a child taken away from its source of infection seldom develops clinical leprosy. Since these children are potentially infected, they are kept separated from the children in the other creche.

In some institutions the care of the healthy child will vary with the type of disease of the parents. Often only the children of leproumatous, or so called open, infectious cases of leprosy are cared for in a preventorium; whereas, the tuberculoid or so called closed, non-infectious cases are permitted to keep their children. It is our opinion, and it has been adequately substantiated, we feel, by epidemiological studies, that all active cases of leprosy are infectious, although there are marked degrees of infectivity. Thus we treat all of our children alike regardless of the classification of leprosy into which their parents may fall.

It is evident that such a system as we have described, even though it is what we feel to be scientifically correct and ideal, causes new sociological problems. The mother has no part whatsoever in the care of her child and often loses interest in its development. This is not good for either the child or the parents, for the ultimate goal is to re-unite the family when the parents' disease becomes arrested. It was with a twofold purpose that we started the study to be described—to make the mother feel that she was having an active and vital part in the raising of her child and to cut down the cost of feeding, a problem facing every missionary working on a limited budget.

At first, the mothers' breasts were pumped by an attendant but later they were taught to carry out this procedure themselves at regular intervals during the day. They brought their milk to the creche where it was sterilized by boiling and then bottle fed to their babies, their feedings being supplemented by the stock formula. This proved to be a satisfactory plan. The mothers were happy and took greater interest in their children, and the children

actually seemed to do better even though the volume of mother's milk they received was not nearly enough to meet their daily requirements.

It was about this time that the author attended the Nigeria Central Leprosy Advisory Board Meeting, where during the proceedings the problem of the prevention of leprosy was discussed. One government leprologist suggested the possibility that mothers with leprosy who were being treated with sulphone drugs might possibly be secreting enough of the sulphone in the breast milk to act as a prophylactic dose to the nursing children. Questioning such a possibility and reviewing the available literature, however, revealed that little was known concerning the secretion of sulphone in breast milk. If it were secreted in breast milk, was there enough to cause an appreciable blood level in the nursing child, would it be enough to act as a prophylactic?

Answers to these questions could prove very interesting since if prophylaxis could thus be obtained, we could do away with the very expensive creche system, and still know that we were preventing the healthy children from developing leprosy. Many problems could thus be solved and considerable money saved.

The following study was an attempt to answer some of these questions:

At the time of this study, there were at the Kano Leprosy Settlement six mothers who were bringing their milk to the creche for their babies. All these infants were less than three months of age. Five of these mothers were on sulphetrone treatment. They were receiving this drug twice weekly by I.M. injection of 50% aqueous solution. The sixth was on oral diaminodiphenyl sulphone twice weekly. The dosage of these drugs had been regulated by weekly hemoglobin determination and monthly blood sulphone levels as well as by clinical observation.

All the mothers were given a week's rest from treatment in order to bring their blood level to zero as a base line for this study. They were then given 10 c.c. of a 50% aqueous sulphetrone solution I.M. (5 gms. of sulphetrone) and blood sulphetrone determinations were taken before treatment and at 2, 4, 6, and 24 hours after treatment. The sixth mother was given 0.5 gms. of diaminodiphenyl sulphone orally and diaminodiphenyl sulphone blood level was taken at the same intervals. At the same time, samples of breast milk were taken before and at 4, 6, and 24 hours after treatment. These time intervals were chosen because we had shown by studies in our own laboratory, and had read reports by other investigators, that we could expect the peak blood level at about 2-6 hours after treatment, the level gradually returning towards the base line over the next 72 hours.

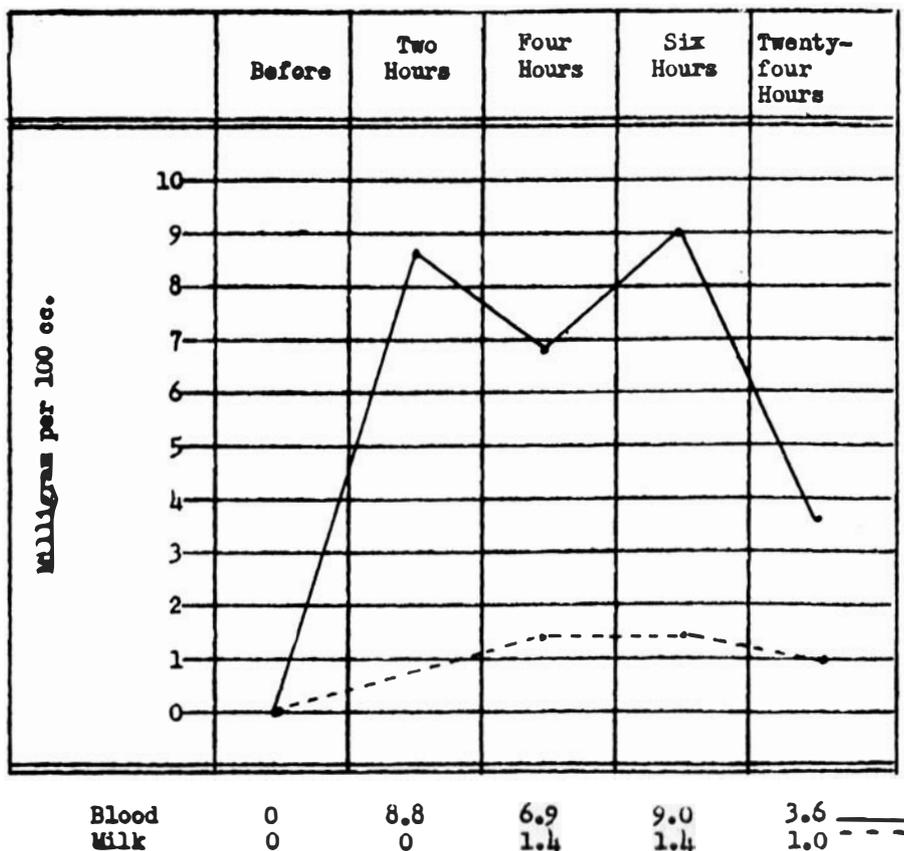
These studies were repeated on two occasions several weeks apart and the accompanying graph represents an average of the findings of these studies:

The blood sulphetrone levels were determined by the Branton Marshall (5) method, using the Loviband comparator. The blood diaminodiphenyl sulphone level was determined also by the Branton Marshall (6) method, using a known standard for a control and using the Kelt-Duboscq colorimeter for comparison.

The sulphetrone and diaminodiphenyl sulphone levels of the breast milk were determined the same way. There were some technical difficulties encountered which took some time and minor modification of technique before we could obtain a clear solution for colorimetry. After we had worked out those modifications, however, we were able consistently to obtain a clear solution and attain consistent readings.

A study of the graph will reveal that there is an appreciable

Curve showing levels of Sulphetrone in Blood and Milk



amount of sulphetrone excreted in the breast milk. More detailed studies, not being reported in this paper, led us to believe that the peak of milk sulphone was about six hours after treatment, and that it appeared more slowly and returned to the base line more gradually, but sooner, than the blood sulphone level.

In the light of these studies we now know that mothers on adequate sulphone therapy did secrete definite, measurable amounts of the respective sulphone drugs.

The next step was to find if the infants fed on breast milk from mothers receiving sulphone therapy ingested enough of the milk sulphone to have a measurable blood sulphone level.

For this part of the study, we chose the following method: The mothers' breasts were pumped six hours after treatment and the milk after sterilization by boiling was bottle fed to their infants. We should expect to find the highest milk sulphone content in this specimen of milk. We had planned to do repeated vein puncture on these infants and run blood sulphone levels on the samples. In view of the fact that these infants were all small, however, and repeated vein punctures were not only difficult but possibly deleterious, we altered our plan to that of collecting urine from the infants. This was much easier and of no harm to the infant. We took urine specimens four hours after ingestion of the breast milk, and the respective sulphone urine levels were determined. An average of these determined was 2.6 mgms. per cent. Although we do not know what the sulphone blood levels were in these infants, we do know that a very definite and measurable amount was excreted in their urine. It is conceivable that these blood levels, even though they undoubtedly were low and much under the optimal therapeutic level, might possibly be of prophylactic value. The actual evaluation of such a possibility is a study that will take years of observation and study fraught by many difficulties, and also possibilities of error. For example, the child in our country is weaned at 2 years of age, at which time he no longer would be getting sulphone from his mother. Of course, by that time his mother might be arrested and the problem no longer exists. But even at best, it would take 10-20 years of observation to know if these children later developed the disease, and in our country where follow-up studies are often difficult, there is the possibility of losing track of many cases. At best, it would take a great deal of very wise and unbiased judgment properly to evaluate the findings.

I do not feel that the many difficulties encountered in such a long time study should deter us from embarking on it, for it is the only way we will be able to answer the question of prophylaxis in the prevention of leprosy.

## SUMMARY AND CONCLUSIONS

A study has been reported in which an attempt was made to answer some questions relative to the possibility of nursing infants receiving enough sulphone in breast milk, from mothers with leprosy on sulphone treatment, to act as a prophylactic in the prevention of leprosy.

1. Nursing mothers on adequate treatment with sulphone do secrete measurable amounts of the sulphone in their breast milk.

2. Infants fed on this milk obtain enough sulphone to cause it to be excreted in their urine in measurable amounts.

3. The final answer to the problem of prophylaxis will come only after long study and the solution of many difficult problems.

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