

## Public Health Section

## THE TREATMENT AND PREVENTION OF VITAMIN-B<sub>1</sub> DEFICIENCY IN INFANTS: A PUBLIC HEALTH EXPERIMENT

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AYKROYD AND KRISHNAN (1941) reported cases of infantile beri-beri in the Northern Circars area in the Madras Presidency, where beri-beri in adults was known to be common\*. They found that in three towns, Bezwada, Cocanada and Vizagapatam, a peak in infant mortality occurred at the fourth month of life, while this peak was absent in other towns outside the beri-beri area. They concluded that infantile beri-beri was the chief cause of the unusual infant mortality. No direct clinical evidence was, however, available as to the prevalence of the disease, nor had any systematic attempts at prevention or treatment been made. To follow up the preliminary investigations, an 'infantile beri-beri enquiry' was undertaken in 1942 in Cocanada under the auspices of the Indian Research Fund Association. With the co-operation of the municipal authorities, the municipal health officer and the director of public health, Madras, one of the municipal infant welfare centres in Cocanada was taken over for purposes of the enquiry, and this was placed in charge of a lady health officer.

The present paper gives an account of the work of the centre. It confirms the provisional conclusion that infantile beri-beri is common in this part of India and indicates ways and means of attacking an important public health problem by the use of preparations of synthetic vitamin B<sub>1</sub>.

### Clinical

'Infantile beri-beri' is not a satisfactory name for the condition in infants with which

this paper deals. This condition does not, in its symptomatology, closely resemble adult beri-beri in its classical forms. Since it responds dramatically to treatment with pure vitamin B<sub>1</sub>, and appears to be closer to an unmixed single vitamin deficiency than any other condition reported in human beings, it could reasonably be called 'vitamin-B<sub>1</sub> (or thiamin) deficiency in infants'. This is, however, a clumsy title. The population of the Northern Circars has coined a word—'anasa'—which is used to describe the disease, but, while most 'anasa' is vitamin-B<sub>1</sub> deficiency, the same name is also applied to other forms of disease in infants. Hence 'anasa' is scarcely appropriate as a scientific medical term.

The following clinical account of the condition was given by Aykroyd (1943):

'Infantile beri-beri occurs in breast-fed infants usually from the second to the fifth month of life. In the acute form, known to the Chinese as "Fung-Team" or "wind-mucus", the infant may suddenly become cyanosed, with dyspnoea and tachycardia, and die in a few hours. The disease may show itself in an infant in apparent health with few premonitory signs. Because of their acute fulminating nature, such cases may rarely be seen by the physician or welfare worker, but mothers with infants showing the condition in less desperate form may give a history of the sudden death in this fashion of other infants in early infancy. In Singapore (Faris, *loc. cit.*) the mother may make the simple and dramatic statement that one or more of her infants has "turned blue, sighed and died".

'In the more usual type of case, the child is seized with screaming fits and attacks of colicky pain. During severe paroxysms the infant may straighten out its body and become rigid. Convulsions may occur. There is some vomiting and diarrhoea and the infant appears restless, pallid and ill. It may rapidly become worse—it is in fact in an acutely dangerous condition—but the disease may not prove immediately fatal and may follow a more chronic course. One very characteristic sign, usually encountered only in fairly severe cases, is partial or complete aphonia. The infant's cry may be thin and almost inaudible and in some instances it may go through the motions of crying, without any sound proceeding from its mouth. The aphonia, sometimes accompanied by signs of bronchitis, may suggest that respiratory disease is the primary cause of the infant's condition and confuse the diagnosis. Oedema is not a common feature. Textbook accounts of infantile beri-beri usually include a picture of a swollen oedematous infant and such pictures have, in my opinion, often hampered the recognition of the disease. According to some writers there may be localized oedema in certain cases, *e.g.* of the face, but this has not yet been observed in the series of cases treated in Cocanada. Enlargement of the right side of the heart and loss or diminution of the knee jerks are said to occur in some cases, but neither of these signs is easy to detect in a screaming and restless infant. Excoriation of the skin and mucous membrane at the angles of the mouth and in the region of the anus appears to be a fairly common sign. It has been observed in Cocanada but has not been recorded by other writers.

'In the more chronic form of infantile beri-beri, the clinical picture does not greatly differ from that of chronic malnutrition and marasmus of a less specific kind. There is pallor, vomiting, constipation, loss of

\*The epidemiology of beri-beri in India has been fully considered in various papers from the Nutrition Research Laboratories. The prevalence of beri-beri in the Northern Circars is due to the fact that in this area machine-milled raw rice is consumed by all sections of the population.

weight and retarded growth. The nutritional disorders may be complicated by bronchitis or other infections. It is easy to understand how a condition originally caused by one particular dietary abnormality may become one of generalized malnutrition through failure to retain and assimilate milk in sufficient quantities.

Since infantile beri-beri as described resembles other forms of disease and malnutrition among infants, the therapeutic test is of primary diagnostic importance. The injection of 2 milligrams or thereabouts of vitamin B<sub>1</sub> has a remarkable and dramatic effect on infants suffering from the disease. Within 24 hours the change for the better is unmistakable. The screaming fits and paroxysms cease, the infant appears placid, and its general appearance has visibly improved. A few more injections, given at intervals of one or two days, will complete the cure for the time being. Sometimes even infants who appear moribund can be saved by this treatment.

#### *Work of the infant-welfare centre*

*Curative.*—Up to the end of April 1945, 1,145 infants suspected of suffering from vitamin-B<sub>1</sub> deficiency have been treated by injections of vitamin B<sub>1</sub>. The infants were breast fed and ranged in age from 1 to 12 months. The highest incidence was among infants aged 2 to 4 months, and most of the acute cases occurred in infants under 6 months. About 8 per cent were acute fulminating cases, and 7 per cent 'chronic'; the remainder may be described as sub-acute. The 'chronic' form was most commonly seen in infants over 6 months. The majority of mothers showed mild signs of peripheral neuritis, e.g. pain and tingling in the extremities and weakness of the extremities. Some were, however, free from such signs. A history of having lost previous infants from 'anasa' was common throughout the series. The majority of the mothers belonged to the poorer classes, and were living on a diet mainly composed of machine-milled raw rice.

Of the infants treated, 980 were discharged as cured. The condition recurred, however, in 68 of these, after intervals varying from 15 days to 3 months. Further similar treatment of recurrent cases was successful. It was noted that recurrence was uncommon among infants of mothers who were given tablets of vitamin B<sub>1</sub> as a daily dose.

At the date in question (31st March, 1945), 135 infants were under observation and treatment. Sixteen infants died in spite of treatment and 14 infants could not be traced after incomplete treatment. Those that died were mostly infants brought to the clinic in a very acute or even moribund condition.

*Preventive.*—An attempt was made to prevent the occurrence of vitamin-B<sub>1</sub> deficiency in infants by supplying vitamin B<sub>1</sub> tablets to mothers for 3 months before delivery and 6

months after it. The mothers were given a daily tablet containing one milligram of the vitamin during this period. Some mothers have received this prophylactic treatment, and its effects have been observed as far as possible. In one group of 54 mothers who gave a previous history of having lost babies from 'anasa' and showed evidence of peripheral neuritis, vitamin-B<sub>1</sub> deficiency occurred in 28 infants in spite of prophylactic treatment; this, however, readily responded to injection of the vitamin and no deaths occurred. A small group of 12 mothers with a similar history were given no prophylactic treatment and kept under observation; eight living children were delivered and all of these developed infantile beri-beri which was successfully treated. A high incidence of vitamin-B<sub>1</sub> deficiency was also observed in the infants of mothers showing no evidence of peripheral neuritis but giving the familiar history of previous deaths from 'anasa', whether vitamin B<sub>1</sub> tablets were given or not. A considerably larger group of mothers—some 500—who were free from signs of peripheral neuritis and gave no history of previous infant losses from 'anasa' were also observed. The incidence of vitamin-B<sub>1</sub> deficiency in the infants of these mothers was much smaller than in the groups mentioned above, and the administration of vitamin B<sub>1</sub> tablets to mothers appeared to have some preventive effect. Some mild cases did, however, occur in infants whose mothers received treatment. The general impression gained from these observations is that the regular administration of one milligram tablets of vitamin B<sub>1</sub> to expectant and nursing mothers is of some value in prophylaxis, and modifies the severity of symptoms in infants who develop this disease, but that such a dosage is too small for satisfactory prevention. The women given treatment were, in general, living on a diet grossly deficient in the vitamin and a supplement of one mg. daily fails to meet entirely the demands imposed by pregnancy and lactation, and to give infants complete protection from the danger of vitamin-B<sub>1</sub> deficiency.

A striking feature of the work of the centre has been its growing popularity. In the early stages attendances were relatively small, and many women in the town preferred to take infants suffering from the dreaded 'anasa' to quacks. But it was gradually learnt that an effective cure for 'anasa' was available at the centre, and attendances have gradually risen until at the present time 50 or more mothers, bringing their infants, attend daily. (Not all the infants, of course, are suffering from vitamin-B<sub>1</sub> deficiency.) The disease, as has been previously pointed out, is prevalent throughout the Northern Circars and women from towns as far distant as Vizagapatam have brought infants for treatment. The following table shows the numbers of infants from towns other than Cocanada treated for vitamin-B<sub>1</sub>

deficiency, and the distance of these towns from Cocanada :

Name of place	Number of cases	Distance from Cocanada (miles)
Vizagapatam ..	27	103
Ellore ..	14	99
Pittapur ..	12	12
Rajahmundry ..	11	36
Ramachandrapur ..	8	20
Samalkota ..	7	8
Narasapatnam ..	6	80
Anakapalle ..	4	83
Razole ..	3	40
Bezwada ..	2	135
Yellamanchili ..	2	70

#### Public health policy

The work carried out to date has established the fact that infantile beri-beri is common in Cocanada and neighbouring areas. The proportion of all infants born that develop beri-beri, and the quantitative effect of the disease on the infantile mortality rate, have not yet been ascertained; it is hoped to obtain data on these questions. The fact has, however, been clearly established that infantile beri-beri is an important public health problem which calls for suitable public health measures. There would be no obvious difficulty in establishing treatment centres for infantile beri-beri throughout the beri-beri area. Vitamin B<sub>1</sub> in tablet form is cheap and available in quantity. At the Cocanada centre infants have been treated by injection of the vitamin, which produces better and quicker results than administration by mouth. Ampoules purchased in the market are considerably dearer than tablets containing an equivalent amount of the vitamin, but a solution could be put up cheaply in bottles for subcutaneous administration.

Prevention by the use of the synthetic vitamin is a more difficult problem. The dosage required, and the necessary period of administration to mothers, have yet to be satisfactorily established. Its routine distribution to expectant and nursing mothers throughout a large area would require considerable organization, and the task of accustoming the people to this method of prevention would be a difficult one. The all-round improvement of the diet, so that it contains less rice and more pulses and other foods, would be the best method of eradicating the disease, but this can be achieved only by long-term measures to adjust and increase agricultural production and improve the economic condition of the people. The possibility of increasing the amount of vitamin B<sub>1</sub> supplied through the medium of the staple food, rice, must be carefully considered. The raw rice at present consumed is not highly milled, since the rice milling order of the Government of Madras prohibits the double polishing of rice. It is clear, however, that the rice at present con-

sumed does not supply enough vitamin B<sub>1</sub>. In some families the rice purchased through the government ration shops is pounded in the home with the object of removing the pericarp that remains after milling and making it whiter. This may be one of the reasons why the milling order has not effectively prevented infantile beri-beri. Further, as Swaminathan (1942) has shown, the washing of raw rice removes as much as 60 per cent of the vitamin B<sub>1</sub> previously present. It is possible that the kind of raw rice at present in supply, while richer in vitamin B<sub>1</sub> than highly polished raw rice, is deprived of so large a proportion of its vitamin-B<sub>1</sub> content by washing and cooking that it falls below the danger-point when consumed as the principal article of diet. All these questions require investigation. No information is available as to whether the rice milling order has reduced the incidence and severity of infantile and adult beri-beri in the Northern Circars; it has probably done so. The present investigation, however, shows that it has not effectively prevented infantile beri-beri.

Parboiled rice even after milling and washing, generally speaking, contains enough vitamin B<sub>1</sub> to prevent beri-beri, as is shown by the epidemiology of the disease in India. The popularization of parboiled rice in the beri-beri area has been advocated as a method of preventing beri-beri. 'Converted' rice, which is essentially similar to parboiled rice in its nutritive properties, would have the same effect. The people are, however, fully accustomed to raw rice and dislike parboiled rice, so that it would be difficult to bring about such a change of habit.

It has been clearly shown that infantile beri-beri is an important public health problem in the part of Madras in which adult beri-beri has long been prevalent. While the latter is unquestionably rare in areas in which parboiled rice is the staple food, it is not impossible that infantile beri-beri occurs in mild form in the infants of mothers consuming such rice. It is important that this question should be brought to the notice of those concerned with the care of infants in rice-eating areas outside the beri-beri area. The treatment of infants who are ailing from no obvious cause by injections of vitamin B<sub>1</sub> would throw light on this question.

Whatever the prospects of preventing infantile beri-beri by general improvement in the diet or by a change in the nature of the rice used as the staple cereal, efforts should be made in the meantime to make curative treatment by the pure vitamin more widely available. This offers a means of saving many infant lives, improving the health of infants, and preventing unnecessary suffering.

#### Summary

(1) A public health experiment which has as its objective the treatment and prevention of

infantile beri-beri is proceeding in Cocanada. The work has been carried out at an infant-welfare centre in that town.

(2) It has been found that infantile beri-beri is a common disease in breast-fed infants. It can be successfully treated by the injection of pure vitamin B<sub>1</sub>.

(3) An attempt was made at prevention by the administration of the vitamin to expectant and nursing mothers, the prophylactic dose being 1 milligram of vitamin B<sub>1</sub> daily. While this treatment was not without effect, the dosage employed appeared to be too small for the fully effective prevention of vitamin-B<sub>1</sub> deficiency in infants.

(4) The public health aspects of the problem are discussed, and it is recommended that cura-

tive centres should be established elsewhere in the beri-beri area.

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 SWAMINATHAN, M. (1942). *Ibid.*, **30**, 409.

## Current Topics

### Inactivation of Malarial Parasites by X-Rays

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 21st April, 1945, p. 1058)

THE selective sensitivity of various diseased tissue to x-rays has important medical implications. Recently Bennison and Coatney tested the sensitivity of some species of malarial parasites to x-rays. *In vitro* both the sporozoite and the trophozoite forms of an avian malarial organism were found to be sensitive to x-rays. Of the two, the sporozoite form could be more easily inactivated. While doses of x-rays of less than 10,000 roentgens do not cause inactivation of the trophozoite form, there was a somewhat increased survival time of infected chicks. Also there was a noticeable increase in time after injection of infected blood before the birds showed positive blood smears. With this sensitivity in mind infected birds were irradiated, and under the conditions used there was no significant change in the survival time. *Plasmodium malariae* was irradiated *in vitro* and this treated blood then injected into a patient suffering from syphilis of the central nervous system. In the following thirty-two days no symptoms of malaria developed and no parasites were found in the blood smears. It appears that the organisms had been completely inactivated under the conditions of irradiation. The subject was later treated with the unirradiated blood and developed typical malaria. The prolonged prepatent period and also the increase in survival time of the chicks receiving the irradiated organism suggests that some of the parasites were totally inactivated, thus leaving only a small number to initiate the infection. It is believed that the cells most sensitive to x-rays are those in the process of division. It may be possible to inactivate selectively the malarial organism while it is in the process of reproduction. This would be difficult with the avian strain used, since all stages of the cycle are present in the blood stream at one time. However, in the highly synchronous infections with *Plasmodium malariae* of man practically all the parasites at a given time are at the same stage of development and one of these phases may well be sensitive to x-rays.

### Methylene Blue Test for Urinary Bilirubin

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 21st April, 1945, p. 1058)

A SENSITIVE test that would reveal the prejaundice stage of liver damage would be useful. In 1933 Fellingner and Menkes described a method for the quantitative

determination of bilirubin in the urine with methylene blue. The qualitative test as described by Myers consists in adding two drops of Loeffler's methylene blue to 10 c.c. of urine. The solution remains dark blue if negative but turns a brilliant green if positive. The test is immediate and is not changed by temperature or the acidity or alkalinity of the urine. It can be read in natural or artificial light. In determining the quantitative value of the methylene blue test a method of simple dilution of the urine was done routinely. To keep the volume at 10 c.c., 1 c.c. of urine was replaced by 1 c.c. of water for the first dilution, 2 c.c. of urine by 2 c.c. of water for the second dilution, and so on until a negative test was obtained. In all cases in which positive methylene blue tests of the urine occurred, a serum bilirubin test was done immediately. Of the 59 cases of elevated serum bilirubin found among a group of employees exposed to tetrachlorethane, not one was found in which the methylene blue test of the urine was negative at the onset. The test was used on patients hospitalized for acute toxic hepatitis. Urine specimens were obtained each day on which a serum bilirubin test was done. The peak of the rise of bilirubin in the urine was present several days before the bilirubin in the serum reached its highest level. As improvement occurred, the urine became negative more promptly than the serum reached its normal level. More information is necessary to evaluate accurately the methylene blue test. Judging from the cases reported it is valuable in detecting early liver damage and thus avoiding further exposure to the toxic tetrachlorethane fumes.

### The Indian Journal of Medical Research, Vol. XXXII, No. 2, October 1944

THE following is the list of contents:—

- (1) Kirwan, E. O'G., Sen, K., and Bose, N. Vitamin-B<sub>2</sub> deficiency as a cause of eye diseases in Bengal.
- (2) Sarma, P. S. The estimation of pyridoxine (vitamin B<sub>6</sub>) in foods using rice-moth larvæ (*Coryca cephalonica* St.).
- (3) Kamala Bhagvat and Devi, P. Anti-thiamine factor in carp.
- (4) Kamala Bhagvat and Devi, P. Inactivation of thiamine by certain foodstuffs and oil seeds. Part I.
- (5) Kamala Bhagvat and Devi, P. Inactivation of thiamine by certain foodstuffs and oil seeds. Part II.