INFANTILE BERIBERI IN THE PHILIPPINES

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There are problems of beriberi in general and of infantile beriberi in particular which are still unclear, and probably will remain so for a long time, since "medicine is not, and never will be, an exact science." In this report, we have restated some of the most important of these problems, in the hope that by considering them against the background of data gathered from 968 cases of infantile beriberi seen in the Pediatrics Ward of the Philippine General Hospital from 1914-1946, possible solutions or fresh approaches might become apparent.

Etiology.—Although beriberi was known to the Chinese as early as 2600 B. C. and to the Romans as early as 24 B. C.(2), its etiology is not settled. The prevailing opinion is that it is a nutritional deficiency disease. Until recently we accepted this opinion and believed that Vitamin B_1 was the deficient factor. However, recent studies have forced us to modify this opinion.

a. Race.—In 1931, Albert reported a series of 500 cases of infantile beriberi in which he pointed out that the condition was not seen among Caucasians or among the offspring of Caucasian-Malayan parents. The explanation given was the difference in diet and social scale; but low-income families, where the diet is obviously inadequate, are found in all groups—Caucasian, mixed, and Malayan.

b. Age.—Infantile beriberi, as the term implies, occurs almost exclusively during the first year of life. As can be seen in Table 3 the most dangerous period is 1-4 months. During this time, the disease is most frequent as well as more severe. Guerrero and Quintos(9) stated that the greater number belong to the group between one and three months old. Beyond the age of one year we do not see the disease. Why does beriberi affect only infants and adults and spare young children? Obviously, a thiamin-deficient diet cannot be the only answer.

* Doctor Albert died on August 13, 1946.

c. Monthly Variations.—Humidity, rainfall, temperature, atmospheric pressure probably exert some influence, for although infantile beriberi is found throughout the year, the incidence is significantly lower during the months of May and June and highest during November, December and January (Table 2).

d. Yearly Variations.—In May, 1928, Albert and Ocampo(3) published a paper wherein they voiced the opinion that "infantile beriberi was disappearing at least in Manila and its environs." They attributed this success to the combined efforts of the Government, through its health agencies, private physicians, nurses, etc., who have popularized the use of tikitiki extract, and to the education of the masses in proper infant feeding.

This situation did not last long. For the very next year, 1929, the incidence of the disease began to rise again and remained high for the next eleven years. Then from 1941 to the middle of 1946, another period of decline set in. In other words, the cycle from decline to decline seems to be 12-13 years. The first period of decline, lasting for three years, began in 1926; the next period of decline started in 1941 and continued up to the middle of 1946. From the other services in our Hospital (Medical and Obstetrical) and from other clinics in Manila, the same decline was noted. This period coincided with the Japanese occupation when food shortages became acute and death from starvation was an everyday affair. Generalized malnutrition, "hunger edema," xeropthalmia, keratomalacia, hyperkeratosis, and cancrum oris were frequently seen in our Out-Patient Clinics as well as in the wards. And yet infantile beriberi practically disappeared during this period.

e. Associated Diseases.—Infection plays an important though undetermined role in the etiology as well as the course and prognosis of infantile beriberi. Guerrero and Quintos(9) classified infantile beriberi into pure and mixed, the latter being associated with gastroenteritis, bronchitis or convulsions. In our cases, more than half were seen with some form of infection, either frank or subclinical, since fever, cough, or diarrhea was frequently present. The most commonly associated diseases were bronchopneumonia, bronchitis, and enteritis. These were often responsible for the flaring up of symptoms, and were often the cause of death in the cardialgic forms of beriberi.

f. Feeding.—All observers recognize breast-feeding as the condition "sine qua non" for the development of infantile beriberi. However, from time to time, cases occurring in bottle-fed infants are reported. Chapman(12) described 8 such cases in 1927. Since 1931, I have seen twelve cases among bottle-fed and forty-five among mixed-fed babies. In the last group, the information was usually obtained that the infants were nursed by their mothers for a period varying from one week to two months from birth. When the symptoms first became apparent, they were being artificially fed, and had been so for some time.

In view of all the above considerations, the conclusion seems inescapable that infantile beriberi is not simply a vitamin deficiency disease, and that other factors, besides lack of thiamin, are involved. Of course the most important factor seems to be faulty nutritional habits. The nursing mother of the stricken infant, when carefully questioned, usually revealed that she had been subsisting on a monotonous diet consisting of excessive quantities of polished rice, some fish, and little or no meats and vegetables. According to McCarrison(13) such a diet has at least four faults, namely, poverty in protein, excess of starch, deficiency of calcium, sodium and chloride, and lack of Vitamin A and B. Just exactly what role the secondary factors, enumerated above, play in bringing about the full-blown clinical picture of infantile beriberi cannot be determined at this time.

CLASSIFICATION

Various ways of classifying infantile beriberi have been proposed, based mostly on symptomatology. After studying our 968 cases, we believe that they can be divided into five groups.

1. *Pure Cardialgic, Fulminant or Pernicious Type.*

The onset is characteristically explosive. Vomiting after sucking may be the only prodromal symptom. The most important features in the clinical picture are as follows:

a. The baby is plump and apparently well nourished.

b. The baby's cry is a peculiar loud, piercing, and persistent scream repeated in paroxysms, apparently denoting severe suffering. This gradually gives way to a moaning or whining sound, as the child becomes exhausted.

c. The face is markedly pale, with a cyanotic tinge around the mouth.

d. The patient's body is stretched out, it may become stiff, and towards the end, convulsions may be noted.

e. The abdomen shows some rigidity, simulating flatulent colic.

f. Respiration is labored. In the agonal stage, the baby gasps for breath, the eyes staring upward.

g. Auscultation of the heart reveals accentuation of the second pulmonic.

h. Roentgenography shows an enlarged heart.

i. Therapeutic test with thiamin elicits a dramatic change in the clinical picture within one-half to six hours. On the other hand, cardio-tonics as caffeine, digitalis, and strophantin are ineffective.

The clinical picture derived from the above manifestations is almost characteristic. A baby around three months old, apparently in good health, nursed entirely by its mother, is abruptly seized with an attack of screaming. As he utters his loud piercing cry, his body stretches, the abdomen becomes hard, the pulse thready, the respiration labored, his face either deathly white or cyanotic, and an expression of profound terror or suffering grips his entire being. This state may last anywhere from one half to one hour. It disappears spontaneously, only to recur with increasing severity and frequency until death supervenes, or the specific treatment is promptly administered.

The Aphonic Type

Unlike the first group, this is characterized by an insidious onset and a long duration. It is much less serious than the cardialgic form. The outstanding feature is the dysphonia in some cases and complete aphonia in others. These cases usually begin with a slight fever and cough, or choking, and for this reason, are often mistaken for upper respiratory tract infection. As in the first, pallor of the face, with cyanosis around the mouth, is also seen. Restlessness, paroxysmal polypnea, oliguria and edema are often noted.

The aphonia may be severe. We saw a case in which restoration of the voice did not come until after some months, although all other symptoms had long since disappeared. When well developed, it also gives an unforgettable picture. As in the cardialgic type, the baby seems to be crying, but because of the loss of voice, no sound comes from him, and only his grimaces and twitching of his face offer evidence of the sufferings he is undergoing.

The laryngological examination is revealing. Alcantara and Ocampo(15) reported their findings in 37 cases in 1939:

"The five infants with acute cardialgic beriberi in whom impairment of voice was slight showed only congestion of the vocal cords, motility being normal. All the rest had impairment of motion. The right vocal cord was paretic or could not move to the median line in 4 cases, stayed immobile in the middle in 9 cases and assumed a cadaveric position in 3 cases. The left vocal cord was paretic in 5, completely immobile in the median line in 9 and cadaveric in 1 case. The vocal cords were bilaterally affected in 3 cases. In some cases, the paretic vocal cord appeared at a lower level than normal." This group showed the poorest response to thiamin.

The Pseudomeningitic Type

This type, first described by Albert in 1917, presents a distinct picture from the first two types. It is also less common, and is more often observed in older infants, between 6 and 12 months of age.

The typical picture is that of a well-nourished baby, breast-fed, who gradually becomes peaceful and quiet, as if he has forgotten how to cry or smile. He wears a languid and indifferent look, his eyelids are but half open. Sometimes, in addition to the ptosis of the upper lids, there is strabismus or nystagmus, suggesting encephalitis or tuberculous meningtis. There is, however, generally no nuchal rigidity. There may be spasmodic contraction of the facial muscles or choreic movements of the arms and hands. Sometimes there may be convulsions so severe as to require lumbar puncture. Vomiting and moderate constipation are noted. The temperature may rise to 38°C.

In 1934-1935, when we had an unusual number of these cases, the junior author made an observation which we thought might be useful in the differential diagnosis. We noticed that these cases of pseudomeningitic beriberi, in spite of their lethargic appearance, responded normally to certain stimuli. When a toy or any object was presented to one of these patients, in spite of his apparent stupor, he would reach out an unsteady arm to get the object offered to him. A similar stimulus given to patients with encephalitis or meningitis brought no response.

Often these cases are erroneously diagnosed as meningitis and progress to a fatal termination. Such errors are all the more tragic

because of the fact that these cases respond promptly to large doses of thiamin.

The Mixed Type

In this group are included those patients who show a combination of symptoms of the first three groups. Thus we have the (a) cardialgic-aphonic type (b) the cardialgic-pseudomeningitic, and (c) the aphonic-pseudomeningitic.

The cases that fall into any of the four groups described above are not hard to diagnose. There are, however, certain cases that present only a part of the symptom complex and thereby become major diagnostic problems. In some, the gastro-intestinal symptoms are most prominent, in others cyanosis. The diagnosis is often made by inference and the response to specific therapy. This group may probably be labelled the attenuated form or the "formes frustes."

THE PROBLEM OF THERAPY

Chamberlain and Vedder reported in 1912([18]) that an extract of rice polishings (tiki-tiki) was effective in beriberi. Since then confirmation has come from all parts of the world. The reduction of infant mortality in the Philippines from 65% to about 20% is considered to have been largely due to the extensive use of tiki-tiki extract. Its prophylactic and curative effects can no longer be doubted. In spite of this, however, we find that only about 31% of our cases were cured; the rest died or were discharged partly improved. We offer the following tentative explanation:

1. Those recovered were pure uncomplicated cases of the cardialgic and pseudomeningitic types who were brought in for early treatment.

2. Those that died were brought in too late or had some complicating acute infection.

3. Those that showed partial improvement only, without complete recovery, were mostly cases of the aphonic type. Although the symptoms of restlessness, pallor, edema, oliguria, etc. disappeared rapidly with the specific treatment, aphonia or dysphonia persisted for months. In this case, thiamin apparently had no effect on the paretic vocal cords.

These questions therefore come up: Is aphonic infantile beriberi true beriberi or something else? If it were true beriberi, why is

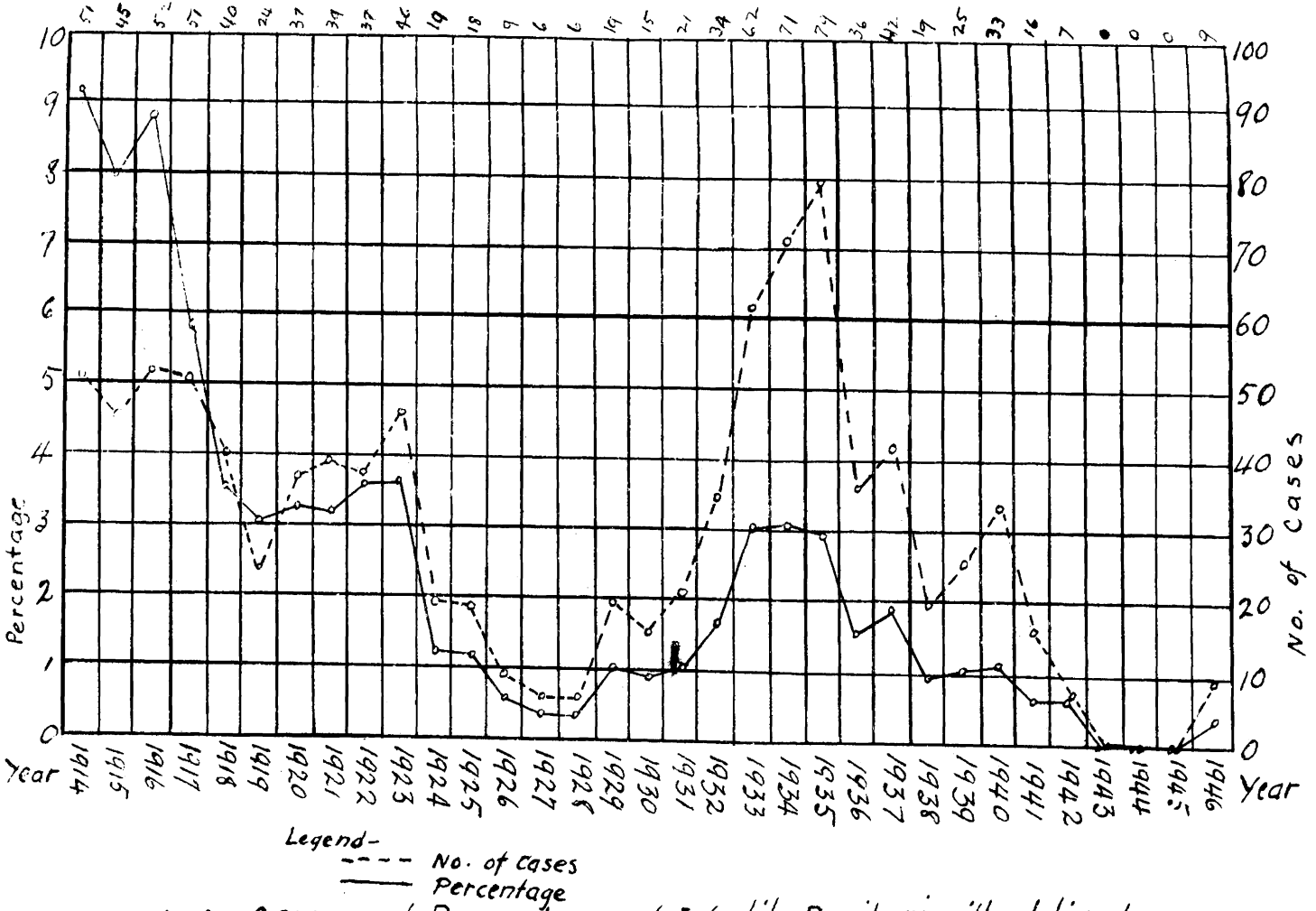

Fig. 1. Cases and Percentage of Infantile Beriberi with relation to Total Admissions

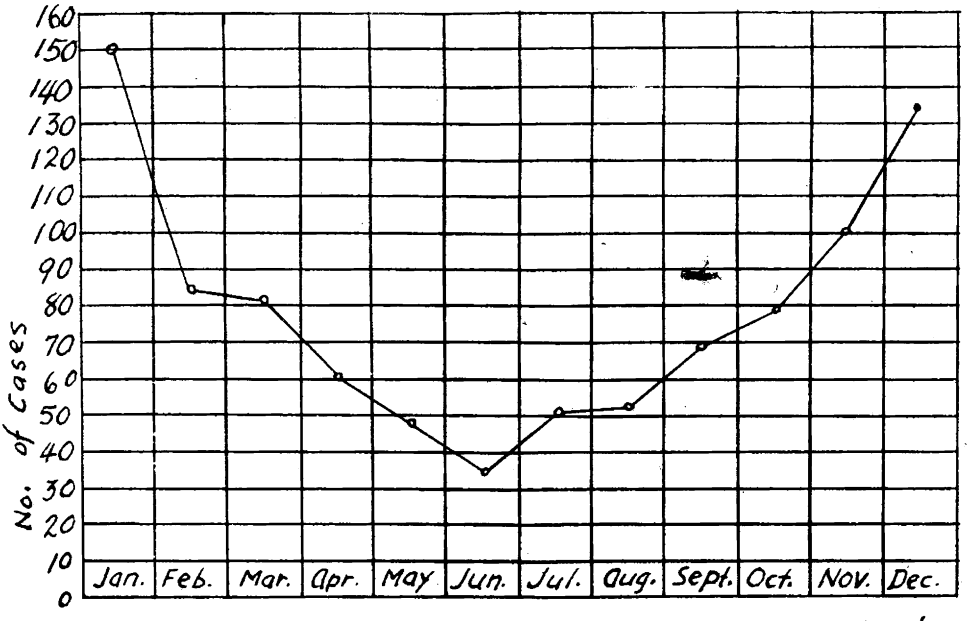

Fig. 2. Monthly Distribution of Inf. Beriberi

thiamin ineffective? Does it represent one of the irreversible stages of polyneuritis?

Remembering that most of the symptoms associated with the aphonia were quickly and favorably influenced by thiamin, one is inclined to consider that this type is a true beriberi.

Doubt about thiamin being an "antineuritic vitamin" has been expressed in various quarters. Thus it is well known that in adult beriberi it is ineffective, except for the relief of cardio-vascular manifestations. Aring and Spies(20) and Ming(21) believe that the initial prompt improvement with thiamin in cases of nutritional deficiency is humoral in nature. Peters(22) thinks that it acts as a catalyst in the carbohydrate metabolism of the nerve cell and of the heart muscle, so that its action in beriberi subjects is concerned with the reestablishment of the normal metabolism of the carbohydrate in the tissue. Walse(23) accordingly says: "To speak of Vitamin B_1 as 'antineuritic' is wholly erroneous except in relation to cases (human and avian) receiving a high carbohydrate diet." Meiklejohn(24) makes the following conclusions:

1. Thiamin is capable of curing a specific metabolic disturbance in the nervous system in animals. This disturbance has been incorrectly referred to as "polyneuritis" by many authors.

2. There is yet no clear experimental evidence showing that true anatomic polyneuritis in animals is curable by thiamin.

Thiamin deficiency in animals disturbs not only the normal metabolism of the nervous tissue, but also, and in a similar manner, the metabolism of the kidney, heart and probably other organs. It so happens that the metabolic disturbance of the nervous tissue manifests itself externally in a dramatic manner, while a similar disorder proceeding in the kidney and elsewhere produces no such obvious effects. This has given rise to the erroneous belief that thiamin has a specific effect on the nervous tissue. It is probably safe to say that thiamin is necessary for the normal metabolism of almost all tissues. It would seem that so far as the evidence from laboratory experiments is concerned, there is really no great justification for referring to thiamin as the "antineuritic vitamin."

SUMMARY

1. A study based on 968 cases of infantile beriberi seen in the Pediatrics wards of the Philippine General Hospital is presented.

2. The disease seems to have definite phases of intensity and decline, following a cycle of 12-13 years.

3. Seasonal variations, age, sex, etc. are definite secondary factors in the etiology.

4. The disease, as usually observed in our wards, usually occurs in association with upper respiratory tract or gastro-intestinal infection.

5. Classification of the disease, based on symptomatology, is presented.

6. Evidence that the condition is not due solely to vitamin B_1 deficiency is given.

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TABLE I.—*Percentage of Infantile Beriberi*

Year	No. of Cases of Infantile Beriberi	Total Admission	Percentage of Infantile Beriberi
1914	51	547	9.32
1915	45	577	7.79
1916	52	591	8.79
1917	51	866	5.89
1918	40	1127	3.55
1919	24	792	3.03
1920	37	1091	3.39
1922	39	1171	3.33
1921	37	1030	3.59
1923	46	1276	3.61
1924	19	1369	1.39
1925	18	1383	1.30
1926	9	1408	0.64
1927	6	1316	0.46
1928	6	1344	0.45
1929	19	1573	1.15
1930	15	1712	0.88
1931	21	1853	1.13
1932	34	1955	1.74
1933	62	2092	3.01
1934	71	2318	3.07
1935	79	2767	2.85
1936	36	2377	1.51
1937	42	2306	1.82
1938	19	1953	0.97
1939	25	2008	1.24
1940	33	2390	1.38
1941	16	2157	0.70
1942	7	928	0.75
1943	0	916	0
1944	0	907	0
		From July 16-Dec. 31	
1945	0	916	0
1946	9	2648	0.34

TABLE II.—*Monthly Distribution of Cases*

Year	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1914	5	4	3	1	1	2	2	2	6	6	11	8	51
1915	4	3	1	3	6	2	1	1	4	5	6	9	45
1916	8	6	3	2	2	3	3	3	1	4	8	9	52
1917	4	2	3	11	2	3	3	2	3	7	4	7	51
1918	5	7	6	6	1	2		1	2	1	1	8	40
1919	7	1	1	1	2	1		2	1	2	1	5	24
1920	3	1			2	1	1	1	4	4	7	13	37
1921	14	1	6	4	2		1		1	2	3	5	39
1922	3	2	4	3	3		3	3	5	2	3	6	37
1923	7	1	10	2	3	1	4	5	2	3	3	5	46
1924	3	2	2	2	2	0	2	4	1			1	19
1925	1	4	3	2	1	1	1	1		2	1	1	18
1926			2		1	1			2	1	1	1	9
1927					1			1	1	1	1	1	6
1928	2					1			1		1	1	6
1929	3	1	1		1	1	2	2		3	1	4	19
1930	1	1			1		3	3	3	2		1	15
1931	1	2	1	3		2	3	1		1	1	6	21
1932	5	2	3		1	1	1	4	2	4	6	5	34
1933	8	9	10	5	4	3	3	5	5	1	6	3	62
1934	5	8	5	1		3	6	3	3	8	7	22	71
1935	27	11	7	6	4	2			3	6	8	5	79
1936	9	2	4	2	4	1	1	2	4	3	3	1	36
1937	8	7	3	3	1	3	2	1	4	1	7	2	42
1938	4	4	1	2	1	1	2			2		2	19
1939	2	1	2				3	2	4	3	7	1	25
1940	8	3		2	2	1	1	1	4	3	4	4	33
1941	3	1	2	1	1		2	2	1	2	1		16
1942							2	1	3	1			7
1943													0
1944													0
1945													0
1946		1			1				4	1	1	1	9
Total	150	86	84	62	49	37	52	53	74	81	103	137	968

TABLE III.—*Incidence of Infantile Beriberi by Age Group*

Year	0-1 Wk.	2-4 Wk:.	1-3 Mos.	4-6 Mos.	7-12 Mos.	Total
1914	1	9	34	4	3	51
1915	1	9	22	8	5	45
1916		7	33	9	3	52
1917		4	33	8	6	51
1918		4	19	8	9	40
1919		7	7	3	7	24
1920		5	20	7	5	37
1921		5	17	9	8	39
1922		7	18	6	6	37
1923	2	8	26	9	1	46
1924		2	12	2	3	19
1925		3	13	1	1	18
1926			2	4	3	9
1927			4	2		6
1928			3	1	2	6
1929			10	6	3	19
1930			4	3	8	15
1931			10	2	9	21
1932			18	10	6	34
1933			34	15	13	62
1934			29	20	22	71
1935			31	23	25	79
1936			18	15	3	36
1937		1	20	14	7	42
1938			10	6	3	19
1939			12	5	8	25
1940			18	12	3	33
1941			9	4	3	16
1942			2	1	4	7
1943						0
1944						0
1945						0
1946			6	3		9
Total	4	71	494	220	179	
Percentage	0.41	7.33	51.03	22.72	18.80	

TABLE IV

	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946	TOTAL
A. No. of Cases	21	34	62	71	79	36	42	19	25	33	16	7	0	0	0	9	454
B. Types:																	
1. Cardialgic	13	20	26	43	36	16	16	6	5	12	4	2	0	0	0	4	203
2. Aphonic	3	7	26	6	11	9	7	2	4	9	6	2				2	94
3. Pseudomeningitic	5	6	5	7	11	3	4	1	7	5	1						55
4. Mixed:																	
a. Card.-Aphon.			1	6	10	7	14	9	8	7	5	2				3	72
b. Card.-Pseudo				1	2												3
c. Aphon.-Pseudo.				2								1					3
5. Frustrated: (attenuated)																	
a. Gastro-intes.				3	1												4
b. Cyanotic		1	4	3	8	1	1	1	1								20
C. Sex:				41	48	20											
1. Male	11	19	35	30	31	16	30	10	12	18	9	6				5	264
2. Female	10	15	27				12	9	13	15	7	1				4	190
D. Feeding:																	
1. Breast alone	19	27	61	55	71	30	39	18	21	31	12	4				9	397
2. Bottle fed		2		1	1	2	1	1		1	1	2					12
3. Mixed fed	2	5	1	15	7	4	2		4	1	3	1					45
E. Outcome:																	
1. Recovered	8	10	16	21	23	12	14	6	9	10	5					7	141
2. Improved	3	7	28	16	23	10	19	10	11	20	9	4				1	161
3. Unimproved					3	1				2							6
4. Died	10	17	18	34	30	13	9	3	5	1	2	3				1	146