Influence of Vitamin B₁ on Arakawa's Reaction and Inorganic Sulphate Content of Human Milk.

99th Report of the Peroxidase Reaction.

By

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Introduction.

In a preceding paper¹⁾ (83rd Report of the Peroxidase Reaction) I have made an investigation into the relation between the Arakawa reaction* and the content of human milk in inorganic sulphate, and found that there is a rough parallelism between them, and it will be quite natural to assume that the amount of inorganic sulphate in human milk will decrease on an administration of vitamin B₁ to the lactating mother.

In the present paper I want to report of the influence of vitamin-B₁ on Arakawa's reaction and inorganic sulphate content in human milk.

Method of Clinical Experiment.

Materials: Mothers of sick infants who visited our Dispensary or were admitted into our Department. To these lactating women, vita-

1) Ky. Yoshino, Tohoku J. Exp. Med.,

* Arakawa-positive may be used in two different senses. One of these is: Arakawa-positive in a biochemical sense. A sample of human milk is said to have become Arakawa-positive, when it becomes blue on the addition of Arakawa's reagent. There it means that the sample is not negative to Arakawa's reaction. Arakawa-positive in a clinical sense: A sample of human milk is clinically Arakawa-positive only when it shows such a reaction as ++ or +++ in one minute of the addition of Arakawa's reagent. Another sample of human milk may be Arakawa-positive in the first described sense, but yet clinically negative.

min B₁ was administered, though to some of them yakriton,^{2,3)} the detoxicating hormone of the liver, was also used (Cf. the paper of Takamatsu²⁾ and Kimura³⁾) besides the vitamin. Arakawa's reaction and sulphate content of their milk were examined.

Method of sulphate determination: This was my own micro-method⁴⁾ for the determination of inorganic sulphate in human milk.

Results of Experiment.

Case 1. Y. Kansaku, female, aged one month. Diagnosis: Malnutrition (B-avitaminosis).

After the infant's admission to our Department, Arakawa's reaction of the mother was almost completely negative on both breasts for a long time, and, as will be seen in the following Table (Cf. Table 1), a daily administration of vitamin-B₁** preparation was given perorally or subcutaneously. Then 1/2 R. A. U. of yakriton^{2,3)} was used besides the vitamin B₁. Arakawa's reaction became more or less stronger on both sides, and antecedent to it, inorganic sulphate content became smaller and smaller.

TABLE 1.

Case 1. Y. Kansaku.

Date	Right							Left							Remarks
	Arakawa's reaction						SO ₂ (mgms.)	Arakawa's reaction						SO ₂ (mgms.)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
5. XII	—	—	—	—	—	—	14.4	—	—	—	—	—	—	15.8	From December 2nd on mother was given vitamin-B ₁ * (Oryzamin powder 5 gr. and Ebios 3 gr.) per os daily
9. "	—	—	—	—	—	—	10.0	—	—	—	—	—	—	11.9	
14. "	—	—	—	—	—	—	12.8	—	—	—	—	—	—	11.9	
16. "	—	—	—	—	—	—	5.6	—	—	—	—	—	—	6.7	
18. "	—	—	—	—	—	—	6.7	—	—	—	—	—	—	7.9	
23. "	—	—	—	—	—	±	6.7	—	—	—	—	—	—	5.6	
28. "	—	—	—	—	—	—	5.6	—	—	—	—	—	—	6.7	
6. I	—	—	—	—	—	—	5.6	—	—	—	—	—	—	5.6	

2) A. Takamatsu, Tohoku J. Exp. Med., 1934, **23**, 372.3) J. Kimura, Tohoku J. Exp. Med., 1936, **28**, 55.4) Ky. Yoshino, Tohoku J. Exp. Med., 1937, **30**, 501.

** Cf. Table 1.

Date	Right							Left							Remarks
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
8. "	-	-	-	-	-	-	7.9	-	-	-	-	-	-	9.0	During this period mother was injected with vitamin-B ₁ * (Injectio oryzanin fortior 1 c.c.) and 1/2 R.A.U. of yakriton 5 times
11. "	-	-	-	-	-	-	9.0	-	-	-	-	-	±	7.9	
13. "	-	-	-	-	-	-	6.7	-	-	-	-	±	±	5.6	
15. "	-	-	-	-	-	-	5.6	-	-	-	-	-	±	6.7	
18. "	-	-	-	-	-	-	5.6	-	-	-	-	-	-	5.6	
25. "	-	-	-	-	-	-	6.7	-	-	-	-	±	±	6.7	From January 25th on mother was given vitamin-B ₁ * (Oryzanin powder 5 gr. daily
30. "	-	±	±	+	+	+	5.6	-	-	±	±	+	+	6.7	
4. II	-	-	±	±	±	+	2.9	-	-	±	±	±	±	4.3	
6. "	-	-	±	±	±	±	4.3	-	-	±	±	±	±	5.6	Suspension of the medication
19. "	-	±	±	+	+	+	-	-	-	±	±	±	±	-	
22. "	±	+	+	++	++	++	-	±	+	+	++	++	++	-	

* Vitamin-B₁ preparations used in this experiment were as follow:

Injectio oryzanin (Sankyo)=claimed to contain in 1 c.c. 33.3 international units.

Injectio oryzanin fortior (Sankyo)=claimed to contain in 1 c.c. 333 I.N.U.

Liquor oryzanin (Sankyo)=claimed to contain in 1 c.c. 6 I.N.U.

Oryzanin powder (Sankyo)=claimed to contain in 1 gm. 40 I.N.U.

Liquor beriberol (Radium Co.)=claimed to contain in 1 c.c. 1.02 I.N.U.

Paranutrin powder (Shionogi)=claimed to contain in 1 gm. 10 I.N.U.

Injectio abery (Daiichi-Seiyaku) is unknown.

Case 2. R. Sakamoto, female, aged 3 months. Diagnosis: Infantile beriberi.

In this case, the mother had been injected with vitamin B₁ preparation since one month before the experiment. Arakawa's reaction of the mother improved, though the decrease of inorganic sulphate content was not remarkable. (Cf. Table 2).

Case 3. T. Kikuchi, male, aged 47 days. Diagnosis: Dyspepsia.

Arakawa's reaction of the mother was negative, and vitamin B₁ preparation was given to her daily. Though Arakawa's reaction was almost unchanged,* inorganic sulphate content showed a decrease (Cf. Table 3).

* "Unchanged" means the reaction up to the 5th minute of the reaction; (-)5' may mean (+)6', (++)10' or (-)15'.

TABLE 2.
Case 2. R. Sakamoto.

Date	Right							Left							Remarks
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
9. XII	—	—	±	+	+	++	7.9	—	—	—	±	±	±	9.0	Until from December 2nd to November 18th mother was injected with vitamin-B ₁ *(In- jectio abery 3 c.c.) 17 times Suspension of the medication
14. "	±	+	++	++	++	++	6.7	—	±	+	+	+	++	9.0	
16. "	—	±	+	+	++	++	7.9	—	±	+	++	++	++	6.7	
18. "	±	+	+	+	++	++	9.0	±	+	+	+	++	++	9.0	
23. "	±	++	++	++	++	++	7.9	—	+	++	++	++	++	7.9	

* Cf. Foot note to Table 1.

TABLE 3.
Case 3. T. Kikuchi.

Date	Right							SO ₃ (mgrms. %)	Left							SO ₃ (mgrms. %)	Remark
	Arakawa's reaction								Arakawa's reaction								
	0'	1'	2'	3'	4'	5'	0'		1'	2'	3'	4'	5'				
7. I	—	—	+	+	+	++	7.9	—	—	+	+	+	++	7.9	From January 11th on mother was given vita- min-B ₁ * (Liqu- or oryzanin 20 c.c.) per os daily		
9. "	—	—	±	+	+	+	7.9	—	—	—	±	±	±	9.0			
11. "	—	±	+	+	++	++	4.7	—	—	±	±	+	+	5.6			
13. "	—	±	+	+	++	++	4.3	—	—	±	±	+	+	4.7			
15. "	—	±	+	+	+	++	4.7	—	—	±	±	±	+	5.6			

* Cf. Foot note to Table 1.

Case 4. M. Takahashi, male, aged 8 months. Diagnosis: Bronchitis.

Arakawa's reaction of the mother was weakly positive. After administration of vitamin B₁ preparation, Arakawa's reaction slightly improved, but inorganic sulphate content showed only a slight decrease (Cf. Table 4).

Case 5. E. Sasaki, male, aged one year. Diagnosis: Influenza.

Though administration of a vitamin B₁ preparation was given perorally, Arakawa's reaction of the mother was almost unchanged.

TABLE 4.
Case 4, M. Takahashi.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
21. I	±	±	+	+	++	++	11.9	+	+	++	++	++	++	10.9	From January 25th on mother was given vitamin-B ₁ * (Liquor oryzanin 20 c.c.) per os daily
27. "	—	±	±	+	+	+	15.2	—	—	—	±	±	±	13.6	
29. "	—	±	±	+	+	+	10.0	±	+	+	++	++	++	10.0	
1. II	±	±	+	+	+	+	10.0	±	±	+	+	++	++	10.9	
4. "	—	±	±	+	++	++	11.9	—	++	++	++	++	++	10.0	

* Cf. Foot note to Table 1.

But inorganic sulphate content decreased rather remarkably (Cf. Table 5).

TABLE 5.
Case 5. S. Sasaki.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
19. I	-	-	-	-	-	-	—	-	±	±	+	+	++	—	From January 23rd on mother was given vitamin-B ₁ * (Liquor oryzanin 20 c.c.) per os daily
21. "	-	-	-	±	±	+	11.9	±	±	+	+	++	++	10.9	
23. "	-	-	±	+	+	+	9.0	-	-	±	±	±	±	10.0	
25. "	-	-	-	-	±	±	6.7	-	-	±	+	+	+	6.7	
27. "	-	-	-	-	-	-	6.7	-	-	-	±	+	+	7.6	
29. "	-	-	-	-	-	-	10.0	-	-	±	±	+	+	9.0	
1. II	-	-	-	-	±	±	6.7	-	±	+	+	++	++	5.6	
4. "	-	-	±	+	+	+	6.7	-	-	±	+	+	+	6.7	

* Cf. Foot note to Table 1.

Case 6. S. Wajima, female, aged 2 months. Diagnosis: Dyspepsia.

In spite of subcutaneous medication of vitamin B₁ and 1/2 R.A.U. of yakriton²³⁾ to the mother, Arakawa's reaction remained always negative. But inorganic sulphate content showed a rather remarkable decrease (Cf. Table 6).

TABLE 6.
Case 6. S. Wajima.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₃ (mgrms.)	Arakawa's reaction						SO ₃ (mgrms.)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
2. II	—	—	—	—	—	—	18.4	—	—	—	—	—	—	18.0	From February 3rd on mother was injected vitamin-B,* (Injectio oryzanin 1 c.c.) and 1/2 R.A.U. of yakriton daily
5. "	—	—	—	—	—	—	12.5	—	—	—	—	—	—	11.9	
8. "	—	—	—	—	—	—	14.7	—	—	—	—	—	—	11.9	
15. "	—	—	—	—	—	—	10.9	—	—	—	—	—	—	11.9	

* Cf. Foot note to Table 1.

Case 7. T. Nikaido, female, aged 2 months. Diagnosis: Malnutrition and dyspepsia.

Her mother suffered from beriberi two years ago and was given vitamin B₁ preparation perorally or subcutaneously at that time. Now, from February 16th to May 3rd the mother was injected with vitamin B₁ preparation and 1/2 R.A.U. of yakriton²³⁾ 22 times. Arakawa's reaction of the mother remained completely negative for a rather long

TABLE 7.
Case 7. T. Nikaido.

Date	Right						Left						Remark		
	Arakawa's reaction					SO ₃ (mgrms. %)	Arakawa's reaction					SO ₃ (mgrms. %)			
	0'	1'	2'	3'	4'		5'	0'	1'	2'	3'			4'	5'
5. II	—	—	—	—	—	—	13.6	—	—	—	—	—	—	11.9	Until from February 16th to May 3rd on mother was injected with vitamin-B ₁ * (Injectio oryzanin 1 c.c.) and 1/2 R.A.U. of yakriton 22 times
18. "	—	—	—	—	—	—	9.0	—	—	—	—	—	—	7.9	
6. III	—	—	—	—	—	—	10.0	—	—	—	—	—	—	11.9	
16. "	—	—	—	—	—	—	10.0	—	—	—	—	—	—	10.9	
22. "	—	—	—	±	±	+	7.9	—	—	—	±	±	+	5.6	
22. IV	—	—	+	+	+	+	4.3	—	—	±	+	+	+	5.6	
16. "	—	—	—	—	—	±	5.6	—	—	±	+	+	+	7.3	
3. V	—	±	±	±	±	+	5.6	—	±	±	+	+	+	5.6	

* Cf. Foot note to Table 1.

time. Then, however, the reaction became gradually better and better, and inorganic sulphate content also became smaller and smaller and decreased remarkably (Cf. Table 7).

Case 8. K. Muraki, female, aged 2 months. Diagnosis: Hypogalactia.

Previous to admission, the mother had been taking vitamin B₁ preparation. During this experiment Arakawa's reaction showed an improvement. But inorganic sulphate content showed only a slight decrease or may be considered to have shown no change (Cf. Table 8). But it is to be noted that her inorganic sulphate might already be within normal limits.

TABLE 8.
Case 8. K. Muraki.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
10. II	—	—	—	±	±	±	5.6	—	—	—	—	—	—	6.7	From a few month ago mother had been taking vitamin-B ₁ * (paranutrin powder) daily
23. "	—	±	+	++	++	##	9.0	—	—	±	+	+	++	9.0	
9. III	—	±	+	+	++	++	7.9	—	—	±	+	+	++	5.6	
1. IV	±	++	++	++	++	##	6.7	—	±	±	+	+	++	5.6	

* Cf. Foot note to Table 1.

Case 9. N. Nagasawa, male, aged one year. Diagnosis: Bronchopneumonia and malnutrition.

After admission into our Department, Arakawa's reaction of the mother became weaker on both breasts, and from March 1st a daily administration of vitamin B₁ preparation was given perorally. Arakawa's reaction of the mother improved only slightly, but inorganic sulphate content showed a definite decrease (Cf. Table 9).

Case 10. H. Uchigasaki, male, aged 10 months. Diagnosis: Bronchitis.

Arakawa's reaction of his nurse was negative, but after the administration of vitamin B₁ preparation the reaction improved fairly. It, however, became worse again. From the beginning of this experiment, inorganic sulphate content in his nurse's milk showed minimal

TABLE 9.
Case 9. N. Nagasawa.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₃ (mgrms. %)	Arakawa's reaction						SO ₃ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
24. II	—	+	+	++	+++	+++	14.4	—	±	±	±	±	+	14.4	From March 1st on mother was given vitamin- B ₁ * (Liquor ber- berol 20c.c.) per os daily
26. "	—	—	—	—	—	—	11.9	—	—	—	—	—	—	10.9	
3. III	—	—	—	—	±	+	12.8	—	—	—	—	±	±	11.9	
5. "	—	—	—	—	—	±	9.0	—	—	—	—	±	+	10.0	
6. "	—	—	—	±	±	±	10.9	—	—	—	±	±	±	10.0	

* Cf. Foot note to Table 1.

physiological values. The change of sulphate seen in Case 10 was most probably only physiological (Cf. Table 10).

TABLE 10.
Case 10. H. Uchigasaki.

Date	Right							Left							Remark
	Arakawa's reaction						SO ₂ (mgrms. %)	Arakawa's reaction						SO ₂ (mgrms. %)	
	0'	1'	2'	3'	4'	5'		0'	1'	2'	3'	4'	5'		
22. II	—	—	±	+	++	++	2.9	—	—	±	++	++	++	4.3	From February 11th on his nurse was given vitamin-B ₁ * (Liquor oryza- nin 30 c.c.) per os daily
25. "	—	—	+	+	++	+++	2.9	—	—	±	+	+	++	2.9	
26. "	—	±	+	++	+++	+++	4.3	—	±	+	++	+++	+++	5.6	
28. "	—	±	+	++	+++	+++	4.3	—	±	+	++	+++	+++	2.9	
3. III	—	—	—	±	+	++	5.6	—	—	—	±	+	++	4.3	
5. "	—	—	—	—	—	±	2.9	—	—	—	—	—	±	4.3	
7. "	—	—	±	+	+	+	2.9	—	—	—	±	+	+	2.9	

* Cf. Foot note to Table 1.

Comment.

Though it was my intention to observe these 10 mothers for a rather long time, I was able to do it for only a very short period except for two cases. In these two cases (Case 1 and 7), Arakawa's

reaction showed a tendency to become positive, though the tendency was not a strong one, while the reduction of sulphate content was rather remarkable in both cases. The influence of vitamin B₁ on Arakawa's reaction and inorganic sulphate will be seen from the result in these two cases. In all the other cases (except Case 10) of short-timed observation, Arakawa's reaction improved or did not yet show a remarkable improvement, but as to sulphate content, either there was a rather remarkable reduction, or a certain tendency of its reduction was seen. Only Case 10 warrants special attention. Here Arakawa's reaction became worse again after an improvement. The cause was unknown, but such a psychic factor as anxiety can make Arakawa's reaction worse,^{5,6)} which fact should not be overlooked. In this case it is further interesting to see the sulphate figures, which were already very small at the beginning of the experiment. The fluctuation of sulphate in this case must be quite physiological. Besides, it is not to be excluded that the initial small sulphate figure might have been due to vitamin B₁, which the nurse had already been taking for about 10 days before the sulphate determination.

Of course this experiment was not a clinical experiment of itself, but an observation during the treatment of the 10 cases. As they did not continue to visit us as soon as their infants got well, the duration of the experiment was too short to give a more decisive conclusion in most cases. But a close relation between Arakawa's reaction and sulphate content of human milk will be seen from the result of the present investigation.

Summary.

In a preceding paper¹⁾ I stated that preformed or inorganic sulphate is poor in human milk positive to Arakawa's reaction and that it is abundant in Arakawa-negative milk. Human milk poor in inorganic sulphate is therefore probably a "good milk" generally. Now as Arakawa-negative milk is a milk secreted from a B-avitaminotic body, then it will be natural to conclude that, if vitamin B₁ is administered to a mother with milk abundant in sulphate, then she will come to secrete sulphate-poor milk.

In the present paper I administered vitamin B₁ to 10 lactating women and saw the change of sulphate content in their milk. And the

5) A. Sato and Y. Moriwaki, *Tohoku J. Exp. Med.*, 1936, **29**, 384.

6) A. Sato, *Nisshinchiryō*, 1937, **230**, 69.

result is that sulphate content decreased in most cases on administration of the vitamin B₁. And the decrease of it will occur more early than the improvement of A r a k a w a's reaction.

Conclusions.

1. A certain relation seems to exist between inorganic sulphate content of human milk and vitamin B₁.
 2. The present paper may be a further proof that human milk poor in inorganic sulphate is generally a "good milk".
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