LI. THE ZINC CONTENT OF EPIDERMAL STRUCTURES IN BERIBERI

By WILLIAM GEORGE ELFORD EGGLETON

*From the Division of Physiological Sciences, Henry Lester
Institute of Medical Research, Shanghai*

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THE author [1938] has shown by calculation from the known Zn contents of a large variety of foodstuffs that the average amount of Zn ingested per day in a balanced diet is about 12 mg. and that this figure agrees with the average amount of Zn found by several workers to be eliminated daily in the faeces and urine of normal individuals. The author has also drawn attention to the fact that each of the three foods, sea fish, cooked polished rice and cabbage, which form the bulk of the diet of the poorest class of Chinese in South China, contains less than 6 mg. Zn per kg. of food as eaten. Since the amount of food consumed in a day by a person existing on such a restricted diet would not appreciably exceed 1 kg., it may be assumed that this represents the approximate daily Zn intake. Small additions of other foodstuffs richer in Zn will not materially augment this figure.

At this point it was realized that apart from containing little Zn, the three foodstuffs mentioned were also poor in aneurin. An examination of the available published data revealed strong evidence of a positive correlation between the Zn and aneurin contents of foodstuffs as shown in Table I and Fig. 1. For

Fig. 1. Zinc and aneurin contents of foodstuffs.

this reason a diet supplying inadequate aneurin should also supply subnormal amounts of Zn and it would be reasonable to suppose therefore that sufferers from beriberi would show a reduction in the Zn content of their tissues.

Table I

Foodstuffs	Moisture† content %	Zn content*			
		Fresh matter			Dry matter p.p.m.
		Range p.p.m.	Mean p.p.m.	No. of observations	
Egg white	87.5	Nil-trace	Nil-trace	(4)	Nil-trace
Polished rice	15	9.7 - 14.5	13	(7)	15
Wheat bread (white)	33	4.1 - 8.0	5	(3)	8
Wheat flour (white)	20	6.5 - 8.0	7	(3)	9
Whole rice	15	14.65- 22.4	18	(3)	22
Cow's milk	86.5	2.07- 5.6	3.1	>(30)	23
Sea fish	80	0.3 - 8.0	4	(6)	20
Smooth pea	10	28.0 - 40.4	33	(4)	36
Soy bean	8	27.3, 38.0	33	(2)	36
Whole barley	15	—	27	(1)	31
Whole rye	15	—	17	(1)	20
Whole maize	54	—	25	(1)	55
Whole wheat	15	22.1 - 84.8	45	(5)	53
Whole oats	15	31.71- 77.5	45	(6)	53
Wheat bran	10	74.0 -139.2	100	(7)	111
Cabbage	94	2.6 - 3.7	3	(3)	55
Egg yolk	53	23.0 - 56.7	40	(8)	86
Beef liver	69	34.5 - 84.0	54	(7)	175
Baker's yeast (dried)	—	36.4 -305	194	(4)	194
Rice bran (dried)	—	67.4, 70	69	(2)	69
Wheat germ	10	140, 145	142	(2)	158

Foodstuffs	Moisture† content %	Aneurin content‡			
		Fresh matter			Dry matter i.u./g.
		Range i.u./g.	Mean i.u./g.	No. of observations	
Egg white	87.5	Nil-trace	Nil-trace	(2)	—
Polished rice	15	0.0 - 0.30	0.15	(4)	0.18
Wheat bread (white)	33	0.07 - 0.30	0.18	(18)	0.27
Wheat flour (white)	20	0.0 - 1.2	0.38	(11)	0.47
Whole rice	15	0.2 - 1.2	0.68	(21)	0.80
Cow's milk	86.5	0.06 - 0.25	0.15	(16)	1.1
Sea fish	80	0.0 - 1.0	0.22	(17)	1.1
Smooth pea	10	0.4 - 1.3	1.0	(4)	1.1
Soy bean	8	0.45 - 1.5	1.0	(8)	1.1
Whole barley	15	1.0 - 1.2	1.1	(4)	1.2
Whole rye	15	1.0 - 1.36	1.1	(3)	1.3
Whole maize	54	0.05 - 1.0	0.59	(5)	1.3
Whole wheat	15	0.75 - 3.40	1.7	(26)	2.0
Whole oats	15	1.1 - 3.25	1.9	(3)	2.3
Wheat bran	10	1.3 - 3.6	2.3	(6)	2.6
Cabbage	94	0.076- 0.25	0.19	(7)	3.1
Egg yolk	53	1.4 - 1.6	1.5	(2)	3.2
Beef liver	69	1.2 - 1.6	1.4	(4)	4.6
Baker's yeast (dried)	—	2.4 -10.0	5.1	(14)	5.1
Rice bran (dried)	—	4.2 - 7.6	5.8	(3)	6.4
Wheat germ	10	6.5 -22.0	90	(20)	10.0

* Derived from various sources quoted by Eggleton [1938].

† Derived from Read *et al.* [1937].

‡ Derived mainly from sources quoted by Fixsen & Roscoe [1938] but including also some values given by Pyke [1937].

Since epidermal structures are obtainable with equal ease from the living as from the dead and since they show little post-mortem change compared with internal viscera, it was decided to test the suggested correlation by investigating the Zn content of epidermal structures of patients with beriberi and normal individuals.

It is apparent that an abnormally low content of Zn in the epidermal structures might result also from low intake of food of normal Zn content. This starvation factor in the case of patients with beriberi cannot be ignored, but the correlation between the Zn and aneurin contents of foodstuffs shows that reduced epidermal Zn in beriberi is not wholly due to reduced food intake.

Methods

The samples were obtained partly from autopsies and partly from living persons, choice of material being governed by the need for keeping the comparison as unbiased and clear-cut as possible. It should be mentioned that in one case beriberi was complicated by amoebic dysentery with perforation which caused death. In another, a survival case, the beriberi had developed after cholera. The normal subjects were chosen from healthy living persons or from healthy accident cases or suicides showing no gross pathological changes. With three exceptions all samples were taken under the author's supervision.

The method of analysis used was essentially that described by Sylvester & Hughes [1936], which involves dry-ashing the clean, ether-extracted material, dissolving in HCl and extracting with dithizone at a specified pH. The Zn, after isolation from the dithizone, was estimated by the volumetric method of Lang [1929; 1933]. Several modifications making for increased accuracy and speed have been introduced and will be described elsewhere.

Results

The analytical results given in Table II show that the Zn content of the hair, nails and skin of patients with beriberi is about half that of those not suffering from the disease and that the ash contents of the nails and skin appear

Table II. *Zn and ash contents of epidermal structures in beriberi*

	Zinc content (p.p.m. of fat-free dry material)			
	Beriberi		Non-beriberi	
	Range	Mean	Range	Mean
Head hair (pigmented)	110-229	173 (6)	84-444	225 (11)
Head hair (unpigmented)	145	—	198, 222	210 (2)
Beard hair	—	—	130, 167	149 (2)
Pubic hair	45-115	83 (4)	71-342	197 (8)
Finger nails	22-184	88 (13)	121-260	195 (13)
Toe nails	31-153	90 (6)	96-340	198 (11)
Skin (whole)	6- 21	13 (7)	12- 55	26 (8)
Epidermis	—	—	97	—
Ash content (% of fat-free dry material)				
Head hair (pigmented)	0.16-0.39	0.28 (7)	0.23-0.73	0.45 (10)
Head hair (unpigmented)	0.095	—	0.53, 0.72	0.63 (2)
	0.091	—		
Beard hair	—	—	0.31, 1.03	0.67 (2)
Pubic hair	0.18-0.70	0.51 (6)	0.10-0.75	0.40 (7)
Finger nails	0.22-3.35	1.18 (14)	0.07-0.56	0.30 (10)
Toe nails	0.42-1.53	0.68 (7)	0.15-0.72	0.39 (8)
Skin (whole)	2.33-3.90	2.92 (7)	1.37-2.56	2.08 (5)
Epidermis	—	—	0.12	—

Figures in brackets indicate number of subjects examined.

to be increased in beriberi. Why the ash content should be increased is not clear unless it be the result of diminished keratin formation arising from diminished protein intake. The determination of the ash in the small quantities of material

used is not so accurate as the determination of the Zn, so that less emphasis can be placed on the figures obtained, but the figures for Zn are clear-cut and leave no room for doubt.

Discussion

The idea of an association between the mineral content of a foodstuff and its aneurin content is not new. Schaumann [1908] pointed out that diets producing peripheral neuritis were invariably poor in phosphorus. In the erroneous belief that nucleic acid was the active principle he suggested that the P content of antineuritic substances was a direct measure of potency. Haag & Palmer [1928] have also drawn attention to the fact that some symptoms of aneurin deficiency are similar to those of Ca and P deficiency. Kilbourne [1910] has also pointed out that the potassium of rice meal is of diagnostic value as an indicator of its antineuritic potency, in which connexion it is interesting to note that Shiuzo [1926] has claimed to have produced a beriberi-like disease in rabbits by a diet deficient in K. According to Bliss [1930] foods rich in vitamin B₂, such as beef, liver, egg-yolk and yeast (also rich sources of aneurin), are all iron-containing foods. Bliss has even gone so far as to suggest that pellagra is an iron deficiency disease since he obtained encouraging results from injection of iron in severe cases.

It would therefore appear likely that some of the symptoms commonly associated with beriberi and usually ascribed to aneurin deficiency may arise from, or be intensified by, deficiencies in certain elements commonly found in foodstuffs in association with aneurin. It is considered that Zn may have some importance in this regard. Curiously enough Hove *et al.* [1937] had found that rats fed on diets containing minimal amounts of Zn developed pellagra-like lesions round the eyes, at the mouth corners and on the feet and lost neck and shoulder hair. These abnormalities did not appear when the animals received a small supplement of Zn.

SUMMARY

In beriberi the Zn contents of the toe nails, finger nails and skin are reduced to half their normal value and there is a strong indication that the ash content is increased. Data are produced to show that the amount of Zn in natural foodstuffs is positively correlated with that of aneurin. It is suggested that Zn deficiency may be a factor in the beriberi syndrome.

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REFERENCES

- Bliss (1930). *Science*, **72**, 577.
- Eggleton (1938). *Caduceus, Hongkong*, **17**, 103.
- Fixsen & Roscoe (1938). *Nutrit. Abstr. Rev.* **7**, 823.
- Haag & Palmer (1928). *J. biol. Chem.* **76**, 367.
- Hove, Elvehjem & Hart (1937). *Amer. J. Physiol.* **119**, 768.
- Kilbourne (1910). *Philipp. J. Sci.* **5**, 127.
- Lang (1929). *Z. anal. Chem.* **79**, 161.
- (1933). *Z. anal. Chem.* **93**, 21.
- Pyke (1937). *Biochem. J.* **31**, 1958.
- Read, Lee & Cheng (1937). Shanghai Foods. Chinese Med. Ass. Spec. Rep. Ser. no. 8.
- Schaumann (1908). *Arch. Schiffs- u. Tropenhyg.* **12**, 37.
- Shiuzo (1926). *Sci. Rep. Govt. Inst. Infect. Dis., Tokyo*, **5**, 591.
- Sylvester & Hughes (1936). *Analyst*, **61**, 734.