THE VITAMIN C CONTENT OF THE LIVER OF NEWBORN INFANTS

BY

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Until recently workers have been entirely dependent on feeding experiments in order to determine the amount of vitamin C present in tissues. This method, however, is difficult to apply to the study of small amounts of tissue, neither is it possible to study in this way the small variations of the vitamin C content of the different organs. After the identification of ascorbic acid as vitamin C, verified by nearly all investigators, the development of a direct chemical method for the estimation of this substance in small amounts of tissue has made possible a new approach to the study of the storage of vitamin C in the human organism. It is known, however, that the chemical reaction is not absolutely specific for the vitamin present. Nevertheless this method gives in a very short time a more precise measure of the vitamin content of the tissue than feeding experiments, even if large quantities of tissue are used and a long time is spent on the performance of the animal experiment.

During the last two years the livers from fifty-six new-born infants have been examined as to the ascorbic acid content. The method used was learnt in the Nutritional Laboratory of the University of Cambridge and is described in detail by Birch, Harris and Ray¹. The ascorbic acid used for the titration of the 2:6 dichlorophenolindophenol was very kindly sent me from the British Drug Houses Ltd., London.

Of the fifty-six new-born infants examined thirty-one were full-term infants and twenty-five were premature infants.

From table 1 it will be seen that the ascorbic acid content varies from 2.7 mgm. to 10.4 mgm. per 100 gm. of fresh liver substance. These two extreme figures represent only two cases, no. 134 and 142 of the premature infants. Most of the other cases show about 6 and 7 mgm. per 100 gm. of liver substance. The average figure is 6.05 mgm. for premature infants and 7.01 mgm. for full-term infants.

The normal ascorbic acid content of new-born infants' tissues is not yet known. Only a few studies are available in the literature of ascorbic acid-content of human tissue. One of these is by Yavorsky, Almaden and King², who found the average figure for liver from infants one to thirty days old is 14.9 mgm. per 100 gm. of tissue. They noted great variation from one

TABLE 1.
FULL-TERM INFANTS.

No.	Weight : gm.	State of infant	Ascorbic acid : mgm. per 100 gm. of liver	Mother's condition during pregnancy	Findings at autopsy.
105	2800	Stillborn	7.0	Poor diet, bleeding	Cerebral haemorrhage
108	3600	"	8.0	Poor diet	Perforation
111	4200	"	9.3	Poor diet	Perforation
112	4700	"	7.4	Good diet	Perforation
113	4500	"	5.6	Average diet	Perforation
115	3530	"	8.8	Good diet	Perforation
118	3500	"	4.9	Good diet	Nil
121	3330	Lived $\frac{1}{2}$ hr.	6.7	Poor diet, mother anaemic	Nil
123	4300	Stillborn	6.2	Poor diet, mother anaemic	Perforation
127	3430	Lived 3 days	7.1	Good diet, felt well	Cerebral haemorrhage
129	3170	Stillborn	7.4	Good diet, hyper- tension, albuminuria	Cerebral haemorrhage
131	3630	Lived 5 hr.	6.1	Poor diet, felt well	Nil
137	2900	Lived 3 hr.	3.3	Poor diet, haemorr- hage, Caesarian section	Cerebral haemorrhage
138	4000	Stillborn	8.1	Good diet, slightly anaemic	Cerebral haemorrhage
139	2850	Lived 28 hr.	7.6	Average diet, albu- minuria	Broncho- pneumonia
140	3410	Stillborn	7.5	Good diet, felt well	Perforation
141	3000	"	6.9	Average diet, felt well	Maceration
143	3500	"	6.0	Good diet	Perforation
144	3470	Lived 2 days	9.0	Good diet	Haemorrhage in spinal canal
147	3800	Stillborn	7.3	Average diet	Cerebral haemorrhage
148	3540	"	5.8	Poor diet, bleeding	Perforation
150	3500	"	6.9	Average diet, mother anaemic	Perforation
151	4070	Lived 6 days	6.4	Poor diet, mother anaemic	Cerebral haemorrhage
152	3690	Lived $\frac{1}{2}$ hr.	6.3	Average diet, felt well	Cerebral haemorrhage
154	3680	Stillborn	7.6	Average diet, felt well	Nil
155	3100	"	6.0	Average diet	Maceration
156	3050	"	7.4	Average diet	Nil
157	2800	"	8.1	Average diet	Nil
158	3360	"	7.5	Good diet	
163	3450	"	8.0	No information on diet	Perforation
164	4830	Lived 4 days	7.1	No information on diet	Cerebral haemorrhage Adrenal haemorrhage

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TABLE 2.
PREMATURE INFANTS.

No.	Weight : gm.	Age of foetal life in weeks	State of infant.	Ascorbic acid : mgm. per 100 gm. of liver	Mother's condition during pregnancy	Findings at autopsy.
103	1600	34	Stillborn	7.4	Average diet, albu- minuria, anaemia	Nil
104	2000	36	„	6.0	Poor diet, chronic nephritis	Nil
106	1670	34	Lived 24 hr.	6.6	Average diet, un- married	Cerebral haemorrhage
107	1500	32	Stillborn	8.2	Good diet, hyper- tension	Spinal haemorrhage
117	1600	30	„	5.5	Good diet, felt well	Nil
120	1600	30	Born alive	5.8	Poor diet	Broncho- pneumonia
122	1230	30	Stillborn	5.7	Average diet, bleed- ing, anaemia	Spinal haemorrhage
124	1390	30	„	4.9	Poor diet, bleeding, Caesarian section	Cerebral haemorrhage
125	2440	34	„	4.4	Poor diet, hyper- tension	Spinal haemorrhage
126	1900	36	„	5.7	Average diet, eclamptic attacks	Cerebral haemorrhage
128	2250	36	Lived 2 hr.	8.6	Good diet	Nil
130	2330	38	Lived 3 days	6.2	Average diet, cys- titis	Atresia ani
132	2100	36	Stillborn	7.6	Good diet, habitual abortion	Nil
133	2400	38	„	6.6	Average diet	Nil
134	2220	36	„	2.7	Good diet, felt well	Congenital heart defect
135	1400	30	„	4.7	Average diet, eclamptic attacks	Nil
136	1760	32	Lived 8 hr.	6.2	Good diet	Cerebral & spinal haemorrhage
142	2530	38	Stillborn	10.4	Average diet, hyper- emesis	Spinal haemorrhage
145	2770	38	Lived 8 hr.	8.0	Good diet, chronic nephritis	Nil
146	1300	32	Stillborn	3.5	Average diet, hyper- tension	Nil
149	1690	32	Lived 14 hr.	7.5	Average diet	Cerebral haemorrhage
153	1300	32	Born alive	7.4	Average diet, albu- minuria, hyper- tension	Cerebral haemorrhage
160	2000	36	Stillborn	5.6	Good diet, hyper- tension	Cerebral haemorrhage
161	1400	30	„	6.5	Uterine tumour, poor condition	Nil
162	600	26	„	4.5	Good diet, habitual abortion	Nil

individual to another. These authors also found that the distribution of vitamin C of human tissue corresponds fairly well to data obtained from titration of guinea-pig tissues. Here the value found with early scorbutic symptoms was determined to be 3 mgm. as far as the liver is concerned.

In the findings of the present investigation the average figures of 6 and 7 mgm. were considerably lower than the average of the above-mentioned investigations, though it must be considered that these infants, one to thirty days old, may have had some antiscorbutic foodstuff given to them during the days of post-uterine life. There is only one infant in these authors' series which may be compared with the present cases, namely a still-born one, showing 11 mgm. One twenty-four days' old infant showed only 7.4 mgm., a figure nearly the same as the average figure of the full-term infants in the present series.

It is not yet known what must be accepted as the level of ascorbic acid content in the liver associated with scorbutic symptoms in children. If, however, according to the findings of the above-mentioned authors conclusions are drawn from the human and guinea-pig studies, 3 mgm. correspond with early scorbutic symptoms. In the present series there is one case with a value below this figure. Six more cases show values close to this, that is they are all below 5 mgm. per 100 gm. of liver substance. These seven cases may, then, be looked upon as suffering from latent scurvy. Of these infants only two were full-term, the other five were all premature infants.

When these infants with a vitamin content below 5 mgm. are considered in detail, it is seen from table 1 that the full-term infant no. 118 with an ascorbic acid content of 4.9 mgm. was born of a mother who received a good diet during pregnancy. No pathological findings were noted at autopsy. The other full-term infant, no. 137, with a low ascorbic acid content (3.3 mgm.) was born of a mother who received a poor diet during pregnancy and she had several haemorrhages the last fourteen days before delivery. The infant showed a small haemorrhage in the cerebral meninges at autopsy. As to the five premature infants, no. 124 (table 2) with an ascorbic acid content of 4.9 mgm. was born of a mother who had poor diet during pregnancy. A Caesarian section was performed on account of a premature separation of the placenta. At autopsy a large cerebral haemorrhage was found in the infant. The infant no. 125, with a content of 4.4 mgm. was also born of a mother who received a poor diet during pregnancy. This mother was suffering from a toxæmia with albuminuria during her pregnancy. At autopsy on the infant a haemorrhage was found in the spinal canal. The infant no. 134, with the lowest content found in this series, namely 2.7 mgm., had a severe congenital heart lesion. This infant's mother received a good diet during pregnancy. The mother of infant no. 135 showing 4.7 mgm., had a severe toxæmia with albuminuria and eclamptic attacks in the last part of pregnancy. The diet of the mother was an average one. As far as the last case is concerned, no. 162, this infant's mother

was suffering from habitual abortion (seven still-born infants previously). Her diet was good throughout pregnancy. The autopsy findings were negative.

It is thus found that with one exception—the full-term infant no. 124—the rest of the infants with the vitamin content below 5 mgm. per 100 gm. of liver substance, were born of mothers having had either a poor diet during pregnancy or having suffered from toxæmia or habitual abortion during this time or the infant itself was pathological in some respect. The conditions here mentioned may explain the low vitamin C content of the liver in these infants.

In eight cases other organs besides the liver have been examined. The content of the adrenals has varied from 10 to 13 mgm.; of the kidneys from 2 to 3 mgm.; of the thymus from 1 to 2 mgm.; and in one instance the lung was examined with the result of 5.18 mgm. per 100 gm. These values are all below those of Yavorsky, Almaden and King.

Such low values for the liver, as well as for the other organs, indicate that the vitamin C content actually is very low at birth in Norwegian infants. This fact has, therefore, to be considered, in the regulation of the pre-natal and post-natal diet of the mother and the child.

The early development of scorbutic symptoms, as demonstrated by Prof. Frølich at a meeting of the Norwegian Paediatric Society in November, 1934, consisting of hæmaturia in a three-months' old infant, disappearing on antiscorbutic treatment, can only be explained on the basis of a low congenital store of vitamin C in the organism. The time of development of symptoms of scurvy will depend partly on the congenital store of vitamin C present and partly on the deficiency of the post-natal diet. As a third factor has to be considered infections present in the infant's post-natal life. Here a vicious circle occurs as the infections are partly a result of the deficiency of the vitamins in the infant's organism. At the same time the infection, with the increased general metabolism and the low food intake and poor absorption, will contribute in lowering the vitamin store of the organism, and render the infants even more susceptible to different infections.

In such infants there is usually not only a deficiency of one vitamin but a general vitamin depletion. This has been confirmed by examining the storage of the vitamins A and D in a larger series of new-born infants, including those in this series. The storage of A and D has been low and in some infants hardly detectable. The result of these investigations will be published in a separate article.

Summary.

The ascorbic acid content has been examined in the liver of fifty-six new-born infants of which thirty-one were full-term and twenty-five premature infants,

The average value for the full-term infants was 7.01 mgm. and for the premature infants 6.05 mgm. per 100 gm. of fresh liver with variations from 2.7 to 10.4 mgm.

The significance of the low content of ascorbic acid at birth for the early development of scurvy in infancy is discussed.

I am indebted to Prof. Harbitz and Prof. A. Sunde for the opportunity of using the material.

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