

## THE BODY TEMPERATURE IN RATS ON NORMAL AND DEFICIENT DIETS.

Preliminary Report.

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PREVIOUSLY, I have emphasized the importance of clinical examinations of the animals in nutrition experiments [Gudjonsson, 1930*a*]. But the investigations reported in this paper were really undertaken on account of my observations on the periocular reaction [Gudjonsson, 1930*b*]. I had interpreted the periocular reaction as a sort of focal reaction or demarcation process, appearing when A-avitaminotic rats are supplied with a considerable addition of vitamin A. It was then natural to imagine that this focal reaction would be accompanied by a rise of body temperature, a feature that is well known from clinical observation in inflammatory reactions. On autopsy, however, the A-avitaminotic animals show but a very slight reaction around the numerous abscesses usually encountered—*e.g.* at the base of the tongue, in the cervical glands, urogenital organs, etc. These severe infections often take a chronic course without any particular reaction in the surrounding structures.

So my working hypothesis was as follows: on account of the vitamin A deficiency, the organism is incapable of reacting normally to these focal infections. And an animal supplied with an adequate addition of vitamin A will again be able to react with the acute processes of inflammation and resulting fever. But the results of my experiments have not corroborated this working hypothesis. The results are about the opposite of what I had expected. Still, I did find something—and it may be that further investigation along this line will throw more light on the rather obscure patho-physiology of A-avitaminosis.

Pembrey [1895] has examined the rectal temperature of adult rats with a mercury thermometer, and he finds the normal temperature to be 37.5° C. MacLeod [1907] has also used a mercury thermometer to

measure the rectal temperature in adult rats, and in his experiments it varies between 37.5 and 38.5° C., with an average of 37.9° C. He further finds that if the temperature of the air rises above 37.5° C., the body temperature of the rats rises rather rapidly, and the animals die with hyperpyrexia. Congdon [1912], who also employs a mercury thermometer, finds 37.9° C. as the normal rectal temperature in young rats; in adult rats, living at an environmental temperature of 16° C., he finds a body temperature of 36.2° C., whereas he finds a body temperature of 37.2° C. in adult rats living at an environmental temperature of 33° C. In new-born rats the body temperature is subject to great variation, dependent upon the environmental temperature. When the rat is 10 days old its body temperature is more stable, though it is never altogether well regulated [Donaldson, 1924]. The body temperature is said to be higher in female rats than in males, and it falls a little in the evening [Bierens de Haan, 1922*a, b*]. Graham and Hutchinson, [1914], who employ a thermoelectrical measuring method, find that the body temperature in rats varies greatly with variations in the environmental temperature. Thus, several investigators have found that the normal body temperature of the rat is about 37.5–37.8° C., and that it is rather unstable, with a tendency to poikilothermia.

According to the aforementioned hypothetical view as to the reaction of A-avitaminotic rats when supplied with vitamin A, I have made two series of experiments that are partly parallel.

*Exp. 1.* Ten rats of the same litter, 30 days old and weighing *ca.* 50 g., are first placed on the usual vitamin A-free diet. Each rat is kept in its separate wire cage, and they all stay in a room with a constant temperature of *ca.* 22° C. Every day, at the same time (about 2 P.M.), the rats are brought into an examination room where the temperature is also about 20–22° C. After staying in this room about half an hour, the rectal temperature is taken with a thermoelectrical probe, measuring *ca.* 1.5 mm. in diameter. Before and after this procedure, the accuracy of the thermoelectrical apparatus is checked by comparison with a standardized mercury thermometer; and, of course, the temperatures obtained in the rats are corrected accordingly if any correction is to be made. After the rats have been on this diet for about 3 weeks, they begin to show clinical signs of A-avitaminosis: they stop gaining in weight, and the first symptoms of xerophthalmia make their appearance. The rats are kept a couple of weeks more on the vitamin A-free diet, so as to ensure that they all have focal infections. They are then divided into two groups. The first group of 5 rats is now supplied with a daily addition

of shark-liver oil—50 mg. daily per rat, which is ten times the optimal dose of vitamin A. The other group is kept on the vitamin A-free diet.

Two rats of the first group, which had an addition of vitamin A, died 1–2 days after they were supplied with this addition. Of the remaining 3 rats, 1 lived 4 weeks on this diet with addition of shark-liver oil, and 2 lived throughout the experimental period, *i.e.* 8 weeks. These 3 rats recovered from the symptoms of A-avitaminosis, and they gained

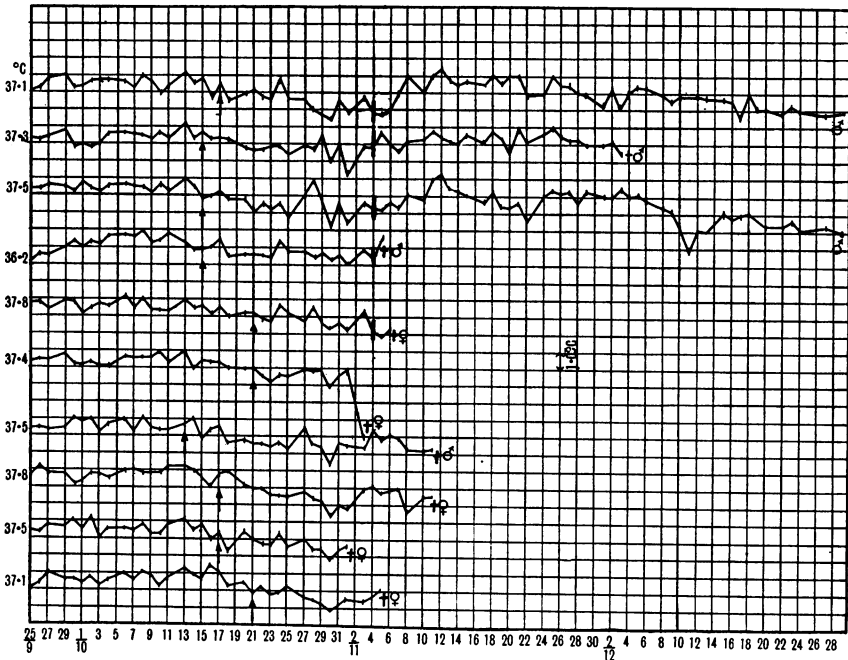


Fig. 1. Curves of rectal temperature in rats on vitamin A-free diet with and without addition of vitamin A. The arrow indicates the time of the appearance of xerophthalmia. The vertical line shows the time when the rats are first supplied with shark-liver oil.

considerably in weight, though hardly to a normal degree—they had been too ill before they were supplied with vitamin A. In fact, the autopsy revealed signs of severe pathological changes, urinary calculi and nephritis.

During the first 3 weeks, all the rats show a fairly constant rectal temperature, averaging 37.5° C., ranging from 36.2 to 38.2° C., as shown in Fig. 1. About the time when the clinical symptoms appear, or a little before, the rectal temperature begins to be less stable and shows a

tendency to fall. The next 2 weeks the rectal temperature averages  $36.6^{\circ}\text{C}$ .—*i.e.*  $1^{\circ}$  below the normal—ranging from  $35.2$  to  $37.9^{\circ}\text{C}$ . After the rats had been getting a daily addition of vitamin A, they show some remissions of the rectal temperature with a tendency to a higher level. Still, the rectal temperature does not reach the level registered in the same rats before the A-avitaminosis, but stays about  $\frac{1}{2}^{\circ}$  lower—averaging

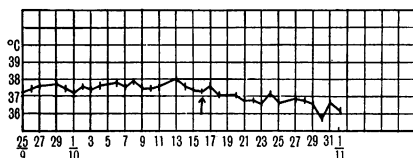


Fig. 2. Average curve of rectal temperature in 5 rats on vitamin A-free diet. The arrow indicates the time of the appearance of xerophthalmia.

$36.9^{\circ}\text{C}$ . In this period the highest measured temperature is  $38.3^{\circ}$ , the lowest  $34.0^{\circ}\text{C}$ .

Fig. 2 gives the average curve of rectal temperature in the 5 rats of group 2 which were kept on a vitamin A-free diet throughout the experimental period. It illustrates very clearly the fall of the body temperature of these rats in the period of A-avitaminosis.

Fig. 3 shows the average curve of rectal temperature in A-avitaminotic rats that are having their after-period prolonged by addition

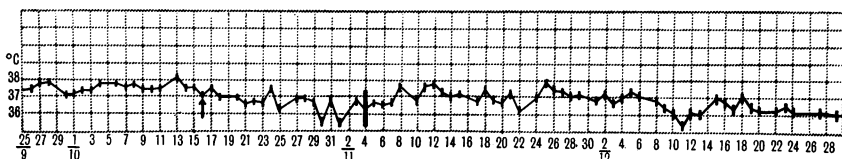


Fig. 3. Average curve of rectal temperature in 3 rats on vitamin A-free diet plus an addition of shark-liver oil in the after-period. The arrow indicates the time of the appearance of xerophthalmia. The vertical line shows the time when the rats are first supplied with shark-liver oil.

of shark-liver oil to the vitamin A-free diet. The curve illustrates the fall of the temperature during the period of avitaminosis and the subsequent irregular rise of the temperature which does not reach the normal level.

In this series of experiments, then, one finds the peculiar outcome that when the animals begin to suffer from A-avitaminosis and are ill with xerophthalmia and other infections, their body temperature falls on an average *ca.*  $1^{\circ}\text{C}$ . below the normal. If these animals are now supplied with vitamin A so that they apparently recover and their

growth is restored, their body temperature rises to some extent but not up to the normal level. I had expected that the animals would have fever in the beginning of this period of improvement. But this was absolutely not the case. In human individuals with such infections as are found in the rat during the A-avitaminotic period, one would find a marked elevation of the temperature.

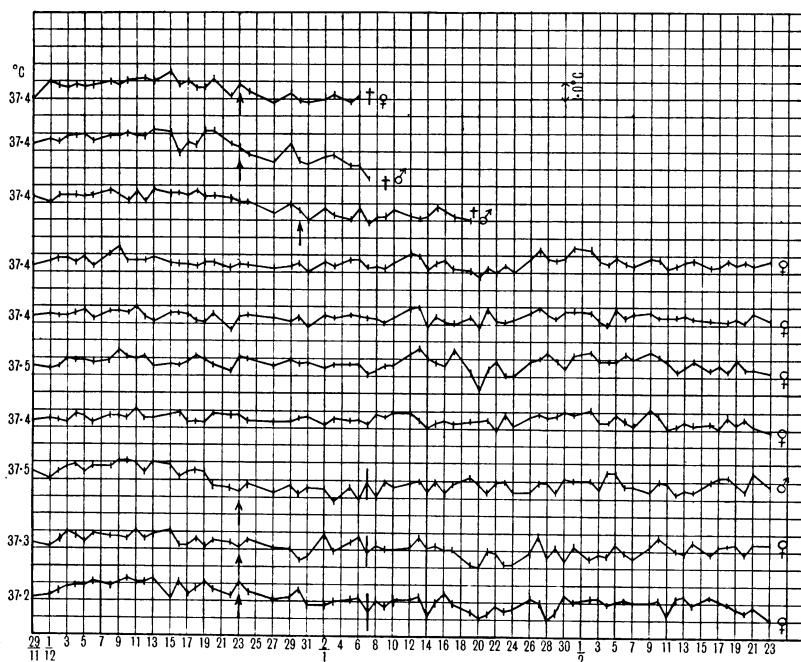


Fig. 4. Curves of rectal temperature in rats on normal and vitamin A-free diets. The upper three come from rats on vitamin A-free diet, the middle four from rats on normal diet, and the lower three from rats on vitamin A-free diet plus an addition of shark-liver oil in the after-period. The arrows indicate the time of the appearance of xerophthalmia. The vertical line shows the time when the rats are first supplied with shark-liver oil.

To corroborate this unexpected result, the following experiments were performed.

*Exp. 2.* Ten rats of the same litter, 30 days old, were divided into two groups. Four rats were placed on the normal rat diet employed in this laboratory—6 were placed on the usual vitamin A-free diet. All the animals lived under the same experimental conditions as described above, and their rectal temperature was measured in the same way as above. The experiment lasted 88 days.

Fig. 4 gives the temperature curves in this experiment. The results are quite in keeping with those obtained in Exp. 1.

The average temperature of the normal rats lies midway between 37 and 38° C. This is also evident from Fig. 5, which shows a curve for all the rats in the period before any of the rats showed signs of A-avitaminosis, and before the temperature began to fall. This is further illustrated in Fig. 6, which shows the average temperature of the 4 rats on normal diet throughout the experimental period. Here the values are also between 37 and 38° C. So the normal temperature of the rat as obtained in these experiments agrees with that reported by other investigators as mentioned in the beginning of this paper.

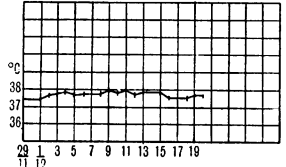


Fig. 5. Average curve of rectal temperature in 10 rats, covering a period of 20 days, during which 4 have normal diet while 6 have vitamin A-free diet.

Of the 6 rats that were placed on vitamin A-free diet, 3 were kept on this diet till they died. As in the preceding experiment, the temperature

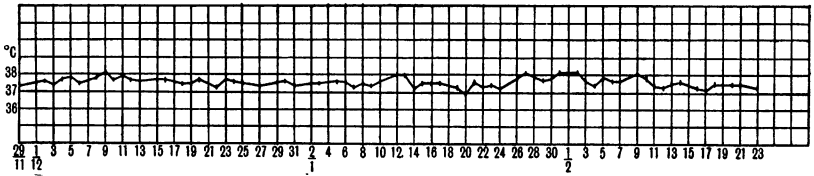


Fig. 6. Average curve of rectal temperature in 4 rats on normal diet.

of these rats began to fall some days before they showed signs of xerophthalmia. The temperature continued to fall, and just before death it was

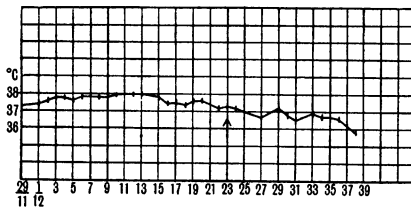


Fig. 7. Average curve of rectal temperature in 3 rats on vitamin A-free diet. The arrow indicates the time of the appearance of xerophthalmia.

1.5° C. below the average temperature registered by the same rats in the period prior to the A-avitaminosis—see Figs. 7 and 4. The other 3 rats of this group on vitamin A-free diet had in the after-period an addition

of shark-liver oil (about ten times the optimal dose). In this experiment the shark-liver oil was given earlier in the after-period than in Exp. 1. Apparently, all 3 rats recovered. All signs of xerophthalmia disappeared, and the rats were gaining in weight. The rectal temperature of these rats showed the same peculiarity as that of the corresponding rats in Exp. 1: it rose, but it never quite reached the normal level nor its level in the same rats during the period prior to the A-avitaminosis, the average temperature of the after-period being about 0.6° C. lower than that of the fore-period—see Figs. 4 and 8.

This experiment shows, then, that in A-avitaminosis the temperature of the rat falls to a level 1–2° C. below the normal. Still, as mentioned before, in this period the rats are suffering from extensive infections. When such rats are supplied with an adequate amount of vitamin A,

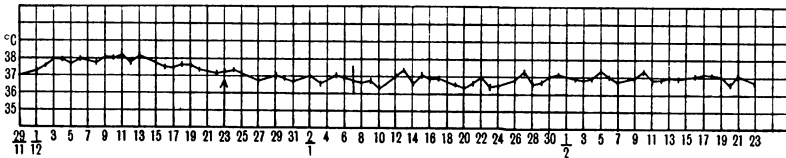


Fig. 8. Average curve of rectal temperature in 3 rats on vitamin A-free diet plus an addition of shark-liver oil in the after-period. The arrow indicates the time of the appearance of xerophthalmia. The vertical line shows the time when the rats are first supplied with shark-liver oil.

they get no fever, but their temperature curve shows a slow and gradual but incomplete rise. The striking peculiarity is the fact that the temperature does not quite reach the normal level. It may be that it might have reached the normal level if the experimental period had been extended further, but it is not very likely.

These experiments further confirm what has been found before, that the body temperature of the rat is rather unstable. I shall not advance any interpretation of these results. But they suggest that A-avitaminosis lowers or alters the metabolism; or perhaps it affects the thermo-regulating apparatus of the animals in some way or other.

#### SUMMARY.

1. In two series of experiments the body temperature in rats on normal and vitamin A-free diets was measured.
2. The body temperature is rather unstable, but normally it lies midway between 37 and 38° C.

3. In A-avitaminosis the temperature falls, and in the last part of the A-avitaminotic period it lies about  $1.5^{\circ}$  C. below the normal.

4. On addition of large amounts of vitamin A to the vitamin A-free diet, the rats under this treatment show a rise of temperature, though this does not reach the normal level—not in 8–10 weeks, at any rate—notwithstanding the fact that in all other respects these animals recover from the A-avitaminosis apparently completely. .

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