A RELATIONSHIP OF VITAMIN E TO NUCLEIC ACID METABOLISM*

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The data to be presented show that vitamin E-deficient rabbits excrete large quantities of allantoin as compared to comparable control rabbits. These results, together with data obtained by determinations of tissue nucleic acids, indicate that nucleic acid metabolism is deranged in vitamin E-deficient rabbits.

EXPERIMENTAL

White, male, New Zealand rabbits weighing approximately 1200 gm. were placed in individual metabolism cages and given a diet of casein 15 gm., sucrose 39.3 gm., corn starch 36.0 gm., lard 3.0 gm., cod liver oil 3.0 gm., salt mix (1) 3.0 gm., inositol 0.1 gm., choline chloride 0.1 gm., nicotinamide 20 mg., pyridoxine hydrochloride 0.5 mg., thiamine chloride 0.5 mg., riboflavin 0.5 mg., calcium pantothenate 1.0 mg., folic acid 0.5 mg., biotin 0.005 mg., 2-methylnaphthoquinone 0.025 mg., and vitamin B\textsubscript{12} 4.5 \gamma. One group received this diet without supplement; another group received the basal diet plus oral supplements of 4 mg. of \alpha-tocopherol acetate per kilo of body weight on alternate days. A third group was given a diet of rabbit chow. The animals were weighed frequently, food intake records were kept, and urine was collected daily for determination of creatine and creatinine (2) and allantoin (3). Blood counts were made at frequent intervals. After appropriate time intervals, tissues were taken for determination of ribonucleic acid and desoxyribonucleic acid (4).

Results

The rabbits ate the purified diet readily and those receiving supplements of vitamin E gained weight throughout the experiment, although not as rapidly as animals eating the chow diet. After 2 to 3 weeks the animals receiving the deficient diet developed the typical symptoms of muscular dystrophy (5). Creatine excretion responded as has been described (5),

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and, since the results merely confirm many previous reports, the data are not presented.

Fig. 1 presents data on allantoin excretion by rabbits receiving the deficient diet, and by rabbits receiving this purified diet with supplements of α-tocopherol acetate. The curves are averages for four deficient rabbits and three control rabbits. Beginning about the 14th day of feeding, the rabbits receiving the deficient diet excreted increased amounts of allantoin. This was very consistent for all rabbits receiving the deficient diet, and by the time that overt symptoms of muscular dystrophy occurred the allantoin excretion by these animals was elevated 3- to 8-fold when compared either to their own initial values or to comparable rabbits receiving the same diet with supplements of α-tocopherol. Creatine excretion by the deficient rabbits followed a course very similar to allantoin excretion.

Fig. 2 shows typical results of a recovery experiment. This rabbit was fed the deficient diet and, after manifesting deficiency symptoms, was treated orally with 10 mg. of α-tocopherol acetate per kilo of body weight.
daily. It may be seen that the elevated allantoin excretion of vitamin E deficiency very promptly responds to the appropriate therapy.

Rabbits receiving the chow diet consistently excreted more allantoin than rabbits receiving the purified diet plus vitamin E. Since the nucleic acid content of the chow was not determined, it is not possible to evaluate this observation at the present time.

![Graph](http://www.jbc.org/content/235/1/745/F3)

**Fig. 2.** The effect of therapy with α-tocopherol acetate on the increased allantoin excretion by a vitamin E-deficient rabbit.

Table I presents data on nucleic acid concentration in liver and skeletal muscle of control and deficient rabbits. Both ribonucleic and desoxyribonucleic acids were elevated in muscle from vitamin E-deficient animals. Liver ribonucleic acid was not significantly different in the deficient animals; however, liver desoxyribonucleic acid was elevated in the deficient animals. The tissue nucleic acid concentration in the rabbits fed the chow diet was quite similar to that in animals receiving the purified diet with supplements of α-tocopherol acetate.

Rabbits with muscular dystrophy invariably exhibited a leucocytosis. However, this observation was complicated by the fact that some of the
animals receiving the purified diet with supplements of vitamin E also exhibited a leukocytosis. More data are required to determine whether vitamin E deficiency in the rabbit has any direct effect on peripheral white blood cells.

**Table I**

Ribonucleic Acid Phosphorus (RNAP) and Desoxyribonucleic Acid Phosphorus (DNAP) in Liver and Skeletal Muscle of Rabbits Fed Various Diets

The results are expressed as mg. of P per 100 gm. of wet weight of tissue.

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Diet</th>
<th>Skeletal muscle</th>
<th>Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RNAP  DNAP</td>
<td>RNAP  DNAP</td>
<td>RNAP  DNAP</td>
</tr>
<tr>
<td>2</td>
<td>Purified + vitamin E</td>
<td>23   4   5.7</td>
<td>91   17   5.4</td>
</tr>
<tr>
<td>3</td>
<td>&quot; + &quot; + &quot; &quot;</td>
<td>21   9   2.3</td>
<td>92   20   4.6</td>
</tr>
<tr>
<td>6*</td>
<td>&quot; + &quot; + &quot; &quot;</td>
<td>28   12  2.3</td>
<td>53   14   3.8</td>
</tr>
<tr>
<td>Average</td>
<td>24   8   3.0</td>
<td>79   17   4.6</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Purified - vitamin E</td>
<td>54   21  2.5</td>
<td>91   24   3.8</td>
</tr>
<tr>
<td>5</td>
<td>&quot; - &quot; - &quot; &quot;</td>
<td>37   19  1.9</td>
<td>88   27   3.3</td>
</tr>
<tr>
<td>7</td>
<td>&quot; - &quot; - &quot; &quot;</td>
<td>53   15  3.5</td>
<td>114  33   3.5</td>
</tr>
<tr>
<td>8</td>
<td>&quot; - &quot; - &quot; &quot;</td>
<td>42   18  2.3</td>
<td>85   36   2.4</td>
</tr>
<tr>
<td>Average</td>
<td>47   18  2.6</td>
<td>95   30   3.2</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Chow</td>
<td>37   9   4.1</td>
<td>94   20   4.7</td>
</tr>
<tr>
<td>10</td>
<td>&quot;</td>
<td>27   4   6.7</td>
<td>81   19   4.3</td>
</tr>
<tr>
<td>Average</td>
<td>32   7   5.4</td>
<td>88   20   4.4</td>
<td></td>
</tr>
</tbody>
</table>

* Fed the purified diet minus vitamin E until deficiency symptoms developed, then recovered with oral supplements of \( \alpha \)-tocopherol acetate.

**Discussion**

The rabbits receiving the purified diet without supplement lost approximately 20 per cent of their body weight during the deficiency stage. The extra allantoin excreted by these animals would be equivalent to approximately 350 mg. of nucleic acid phosphorus per rabbit. This in turn represents the amount of nucleic acid present in approximately 1 kilo of skeletal muscle. It then becomes obvious that the extra allantoin excreted by the deficient animals was not due simply to loss of muscle tissue. The data suggest that during the state of vitamin E deficiency in the rabbit the rate of turnover of nucleic acids is greatly accelerated. An alternate explanation would be that the increased allantoin excretion re-
reflects an accelerated purine synthesis without their incorporation into nucleic acids. The former interpretation seems more probable.

SUMMARY

1. Vitamin E-deficient animals were found to excrete much greater quantities of allantoin than comparable control rabbits.
2. The elevated allantoin excretion of vitamin E-deficient rabbits was reduced to normal by oral therapy with α-tocopherol acetate.
3. Skeletal muscle from vitamin E-deficient rabbits contained more ribonucleic acid and desoxyribonucleic acid than did the tissues from control animals.
4. The concentration of desoxyribonucleic acid in liver was elevated in vitamin E-deficient rabbits, but ribonucleic acid was not significantly altered by the deficiency.
5. It is suggested that the turn-over rate of nucleic acids is accelerated in vitamin E deficiency, especially in skeletal muscle.

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