LXXXVII. THE TRANSMISSION OF VITAMIN A FROM PARENTS TO YOUNG IN MAMMALS.

III. EFFECT OF THE FAT CONTENT OF DIET DURING PREGNANCY ON THE TRANSMISSION OF VITAMIN A TO THE FOETAL RAT.

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In an earlier paper [Dann, 1932] a preliminary investigation of the factors controlling the transmission of vitamin A from mammalian mothers to their young was described, most of the work being done upon the rat. One of the conclusions reached, which is further examined in the present communication, was that "the amount of vitamin A in the liver of the foetal rat at birth is small and subject to little variation. It cannot be increased by giving large amounts of carotene to the mother before or during pregnancy." The provitamin A, carotene, was used in those experiments because at that time no rich concentrate of vitamin A was available in the quantities required. Since the publication of the earlier paper, however, concentrates of vitamin A have become available in large quantities, and it has been thought advisable to repeat the work upon the rat using vitamin A itself in the diet. The repetition (described below) led to a conclusion similar to that reached from the earlier work, namely that the amount of vitamin A in the liver of the foetal rat remains small even when the parent doe receives large amounts of vitamin A before or during gestation.

Having established this point, it remained to be seen whether other constituents of the diet exercised any marked effect on the amount of vitamin A transmitted to the foetus during gestation when there was a liberal amount of it in the doe's diet. A factor which might *a priori* be expected to exercise some effect is the fat content of the diet, and in the present paper an investigation of the effect of the fat content of the maternal diet on the transmission of vitamin A to the foetus is described.

Experimental.

The effect of a diet rich in vitamin A on its transmission to the foetus.

For this work piebald rats from the breeding colony of this laboratory were used. The sexes were segregated at weaning and all the animals kept on the stock diet for breeding animals, consisting of bread, milk, mixed corn, green stuff and meat. At 12 weeks old, the diet was changed to one made up to resemble the carotene-rich diet used in previous experiments [Dann, 1932], which consisted of maize meal 1060, whole milk powder 400, whole grain flour 200, yeast 200, wheat germ 60, calcium phosphate 60 and salt mixture 20; for each 90 g. of this basal

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diet 10 g. of red palm oil were allowed and mixed in. In place of the red palm oil for the present experiment was substituted the same weight of a 0·5 % solution of B.D.H. vitamin A concentrate in arachis oil. When the animals were 16 weeks old, bucks and does were placed together in a single large cage, and when the does were seen to be pregnant they were removed to separate cages but kept upon the same diet. At birth of the litters both parent and young were immediately killed and the liver of the doe was removed for estimation of its vitamin A content colorimetrically with antimony trichloride. The young were examined similarly in batches of four or five instead of singly, and the vitamin A content of the carcase after removal of the liver was also determined in every case to be negative. The results of the liver examinations are set out in Table I.

Table I. *Transmission of vitamin A to foetal rats, when the parent receives much vitamin A.*

Doe	1	2	3	4	5	6
Vitamin A content of doe's liver at parturition (in B.U.)	300,000	300,000	300,000	200,000	200,000	180,000
Vitamin A content of liver of foetus at birth (in B.U.)	25	33	30	20	35	20

The effect of the fat content of the diet.

For this work also our own stock breeding animals were used. At weaning the sexes were segregated and kept in large cages on the stock diet described above.

At the age of 16 weeks, when the experimental period began, the does were divided into two groups matched in weight, and each group was put into a single large cage, together with a suitable number of bucks of the same age. One group then received a diet poor in fat and the other group a diet rich in fat, each diet containing the same liberal amount of vitamin A. In order to ensure that these conditions were strictly observed, the diets were prepared as follows. A basal diet free from fat and vitamin A was composed of 600 g. maize meal, 200 g. skim milk powder, 200 g. dried yeast and 50 g. salt mixture; weekly batches of this diet were prepared. The two experimental diets were prepared fresh daily by the addition of the requisite quantities of arachis oil and vitamin A to the basal diet. A commercial concentrate of vitamin A (obtained from The British Drug Houses, Ltd.) was taken, and 1 g. was dissolved in 19 g. of arachis oil. Each day 1·5 g. of this were weighed out and mixed into 148·5 g. of the basal diet, giving an experimental diet containing 0·05 % of the vitamin A concentrate and 1 % of fat. A further 1·5 g. of the oil was weighed out and mixed with 28·5 g. of arachis oil; the 30 g. of dilute vitamin A solution were then mixed into 120 g. of the basal diet giving an experimental diet containing 0·05 % of the vitamin A concentrate and 20 % of fat. By adopting the procedure of daily preparation of diets in this way any change in the potency of successive batches of the vitamin A concentrate is prevented from contravening the conditions stipulated above, since the two diets on any one day will always contain the same percentage of vitamin A and one will always contain twenty times as much fat as the other.

When a doe was seen to be pregnant she was at once removed to a separate cage but kept on the same diet as she had previously received. At parturition the young were removed immediately and decapitated, and the carcases were digested in aqueous KOH, from which the vitamin A was removed by extraction with ether and estimated by the antimony trichloride reaction.

Two experiments performed in this way are reported here. In the first, twelve piebald does were used; in the second, eight albino does. The results are collected in Tables II and III.

Table II. *Transmission of vitamin A to foetal piebald rats. The diet of each doe during gestation contained 0·05 % of vitamin A concentrate, but some received 1 % and others 20 % of fat.*

Doe	1	2	3	4	5	6	7	8	9	10	11	12
Fat content of doe's diet during gestation	20 %	20 %	20 %	20 %	20 %	20 %	1 %	1 %	1 %	1 %	1 %	1 %
Number of young in litter	9	8	8	10	6	9	12	8	8	10	8	8
Vitamin A store of each foetus (in B.U.)	31	25	33	35	37·5	50	25	33	25	19	25	25
Total amount of vitamin A transmitted to the whole litter (in B.U.)	279	200	264	350	225	450	300	264	200	190	200	200

Table III. *Transmission of vitamin A to foetal albino rats. The diet of each doe during gestation contained 0·05 % of vitamin A concentrate, but some received 1 % and others 20 % of fat.*

Doe	1	2	3	4	5	6	7	8
Fat content of doe's diet during gestation	20 %	20 %	20 %	20 %	1 %	1 %	1 %	1 %
Number of young in litter	9	9	12	7	6	10	10	9
Vitamin A store of each foetus (in B.U.)	11·5	37	46	16	21	30	16	9
Total amount of vitamin A transmitted to the whole litter (in B.U.)	104	243	552	112	186	300	160	81

Discussion.

The first part of the experimental work described shows that the amount of vitamin A transmitted to the foetal rat during gestation is still strictly limited when the parent animal has an enormous reserve of vitamin A in her own liver and receives a diet rich in vitamin A during gestation. The amount of vitamin A found in the foetal rats at birth was however greater in these experiments than in the author's previous experiments where the provitamin carotene was included in the diet of the parent, but it must be borne in mind that in the present experiments the does received at a moderate estimate five thousand times the necessary minimum of vitamin A in their diet.

Turning to the effect of fat in the maternal diet, it can be seen from the figures collected in Table II that the average amount of vitamin A found in the foetal piebald rats at birth was 35 B.U. when the doe received during gestation a diet containing 20 % of fat and 0·05 % of vitamin A concentrate, and 25 B.U. when the doe received a diet containing 1 % of fat and 0·05 % of vitamin A concentrate. The average figures for the total amounts of vitamin A transmitted to the whole litter during gestation were 294 B.U. and 226 B.U. for does receiving high fat and low fat diets respectively. From Table III the average figures for the albino rats are 27 B.U. and 19 B.U. transmitted to each foetus, and 253 B.U. and 182 B.U. transmitted to the whole litters, on high fat and low fat diets respectively.

From these figures it appears that an increase in the proportion of fat in the diet of a pregnant doe will in general cause an increased transmission of vitamin A to the foetus. It is plain however that with the wide differences in fat content now tested, the variation in the amount transmitted is so small (though definite) that the effect of ordinary variations in the fat content can be neglected when the diet is rich in the vitamin.

SUMMARY.

1. When the female rat receives large amounts of vitamin A (of the order of 5000 times the necessary minimum) in her diet before and during gestation, her young have only a small store of vitamin A in their livers at birth. The amount is generally between 20 and 35 B.U. of the vitamin. In the body apart from the liver no vitamin A can be detected.

2. The amount of vitamin A transmitted to the foetal rat during gestation when the parent doe receives large amounts in her diet is affected by the fat content of the diet and is increased as the fat content increases. This increase in transmission is small and for ordinary ranges of variation of fat content is probably negligible.

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REFERENCE.

Dann (1932). *Biochem. J.* **26**, 1072.