2. The ether-soluble faecal lipids were fractionated into unsaponifiable matter, total sterol, total acids and light petroleum-insoluble acids (Table 2). The distribution of the faecal lipids was determined (Table 3).

3. The deposition of unsaponifiable matter and sterol in the livers, carcasses and gut was determined (Tables 5 and 6).

4. Balance sheets of the cholesterol metabolism have been made both on differences in unsaponifiable matter (Table 7) and the differences in sterol (Table 8) between cholesterol-fed and control animals. Calculated as unsaponifiable matter an average of 24 % of the cholesterol ingested was metabolized in guinea pigs and in rabbits (one experiment) 24 %. As sterol the guinea pigs and

rabbits metabolized 54 %. For rats these values are, unsaponifiable matter, 18 % and sterol 44 %.

5. In guinea pigs there was an increased excretion of total faecal fatty acids in the cholesterol-fed animals. In the rabbit this increase is slight.

The light petroleum-insoluble acids were slightly increased in the faeces of cholesterol-fed guinea pigs, but in the rabbit more light petroleum-insoluble acids are present in the faeces of control animals than there are in those fed cholesterol.

6. The significance of these findings in relation to the pathological lesions produced in these different species by feeding excess cholesterol in this diet is discussed.

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Vitamin A in the Kidney of the Rat

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Johnson & Baumann (1947*a, b*) reported that when rats were kept on a diet deficient in vitamin A with supplements of 35 i.u. of carotene daily, or of small doses of preformed vitamin A, more vitamin A was accumulated in their kidneys than in their livers. With higher doses, however, the usual predominance of the liver as the main site of storage was asserted.

In a preliminary communication we have reported experiments which confirmed this interesting observation (Eden & Moore, 1950). The purpose of the present paper is to present our results in detail. Since Moore & Sharman (1950) have recently found that the distribution of vitamin A between the liver and kidneys is influenced by sex our results on male and female animals will be considered separately.

EXPERIMENTAL

In most of our experiments groups of young piebald rats, weaned from mothers receiving an adequate mixed diet, were given for 4-7 weeks a diet of casein 20 %, sugar 45 %,

dried brewer's yeast 10 %, minerals 5 % and either lard (groups 1, 2, 3, 6 and 7 in Table 1) or cod liver oil 20 % (groups 5 and 8). The diet with lard, and without supplements of vitamin A, caused the disappearance of vitamin A from both the liver and kidneys within 5 weeks. Groups 1-3 received daily supplements of 20 i.u. of synthetic vitamin A acetate, which was kindly supplied by Roche Products Ltd. The animals of groups 6 and 7 received only a single dose of 2000 i.u. of vitamin A acetate 48 hr. before they were killed. The cod liver oil supplied to groups 5 and 8 was of a high class medicinal grade containing about 800 i.u./g. of vitamin A, and was mixed freshly each day with the solid components of the diet. The rats in group 4 were adult males, about 1 year old, which had been used for breeding purposes; their diet had been made up of bread, milk, meat and vegetables, with occasional doses of cod liver oil.

It may be mentioned that the rats in groups 1, 2, 5, 6 and 8 received a diet lacking in vitamin E. The animals in groups 3 and 7 were each dosed with 2 mg. of ($\pm$)- α -tocopheryl acetate weekly, while those in group 4 had derived adequate supplies from their mixed diet. Although it is known that vitamin E may influence the storage of vitamin A in some

Table 1. *The accumulation of vitamin A in the livers and kidneys of rats at various levels of intake*

Sex	Group no.	Rat no.	Weight		Vitamin E	Daily intake vitamin A (i.u.)	Time given vitamin A (days)	Form of vitamin A given	Vitamin A (i.u.) total in		Vitamin A (i.u./g.) in			
			Initial (g.)	Final (g.)					Liver	Kidney	Liver	Kidney		
Male	1	1	36	126	-	20	28	Acetate	71	103	10.4	70		
		2	40	130	-	20	28	Acetate	71	96	9.8	68		
		3	50	145	-	20	28	Acetate	33	83	4.3	59		
Male	2	4	51	200	-	20	34	Acetate	28	75	2.6	40		
		5	52	185	-	20	34	Acetate	83	59	9.3	37		
		6	55	212	-	20	34	Acetate	26	69	2.3	35		
Male	3	7	38	138	+	20	28	Acetate	330	91	42	67		
		8	38	145	+	20	28	Acetate	93	200	11	140		
		9	33	121	+	20	28	Acetate	80	103	10	80		
Male	4	Final weights $\simeq$ 350 g.					Means for groups 1-3 combined							
		10				+		Approx. 365	Mixed diet	2,700	28	250	16	
		11				+		Approx. 365	Mixed diet	3,700	36	300	20	
		12				+		Approx. 365	Mixed diet	4,000	32	320	16	
		13				+		Approx. 365	Mixed diet	3,200	38	310	20	
		14				+		Approx. 365	Mixed diet	1,600	33	110	17	
		15				+		Approx. 365	Mixed diet	3,120	29	320	13	
		16				+		Approx. 365	Mixed diet	2,300	52	210	27	
		17				+		Approx. 365	Mixed diet	4,600	15	400	9	
Male	5						Means for group 4							
		18	45	218	-		Approx. 2,000	50	Cod liver oil	16,000	570	1,400	190	
		19	38	163	-		Approx. 2,000	52	Cod liver oil	26,000	520	4,100	330	
		20	33	154	-		Approx. 2,000	52	Cod liver oil	57,000	180	6,700	100	
		21	43	166	-		Approx. 2,000	52	Cod liver oil	7,900	17	1,200	8	
Female	6						Means for group 5*							
		22		122	-		Approx. 2,000	1	Acetate	360	15	57	11	
		23		149	-		Approx. 2,000	1	Acetate	320	35	47	22	
		24		154	-		Approx. 2,000	1	Acetate	360	41	46	23	
		25		127	+		Approx. 2,000	1	Acetate	270	10	45	8.5	
		26		140	+		Approx. 2,000	1	Acetate	240	17	34	11	
		27		120	+		Approx. 2,000	1	Acetate	460	24	69	16	
Female	8						Means for groups 6 and 7							
		28	47	112	-		Approx. 2,000	29	Cod liver oil	3,900	16	600	10	
		29	38	104	-		Approx. 2,000	29	Cod liver oil	6,000	14	840	10	
		30	40	97	-		Approx. 2,000	29	Cod liver oil	7,500	6	1,200	6	
								Means for group 8				12	880	8.7

* In our preliminary communication (Eden & Moore, 1950) the means for the kidneys in this group were miscalculated.

circumstances (Moore, 1940) there was no plain evidence of this effect being exercised in the present experiments, which were too short to cause an acute deficiency of vitamin E. In taking averages, therefore, the values for the groups with and without vitamin E at the same levels of dosing with vitamin A have been combined.

In most instances the animals were killed for the estimation of vitamin A in their livers and kidneys, but those in group 5 died spontaneously or accidentally. The vitamin was extracted from the tissues after they had been digested with alkali according to the method of Davies (1933), and was measured by the antimony trichloride method applied with a photoelectric absorptiometer. In Exp. 4 the rats nos. 10–13 were killed with coal gas and nos. 14–17 with CHCl_3 , but the mode of killing has no obvious effect on the distribution of the vitamin. Two of the animals in group 5 died from profuse bleeding from minor accidental wounds in their paws, while another had subcutaneous and intramuscular haemorrhage in the inguinal region. These injuries were presumably caused or exacerbated by the heavy intake of cod liver oil. The results obtained are given in Table 1.

Vitamin A in other tissues. Estimations of vitamin A were not made systematically in tissues other than the liver and kidney. In specimens of lungs, suprarenals and retinas collected from different groups, however, the total amounts of vitamin A were invariably much smaller than in the kidneys, and were seldom sufficient, except in the lungs, to produce blue colours discernible to the eye in the antimony trichloride reaction.

DISCUSSION

Males. From Table 1 it will be seen that in the nine male rats of groups 1–3 which were given 20 i.u. of vitamin A daily, the concentration of the vitamin was invariably greater in the kidney than in the liver, with means of 66 and 11 i.u./g., respectively. In seven instances the total amounts of vitamin A were greater in the kidneys than in the liver, with means of 98 and 91 i.u. In the eight rats of group 4, which had received an adequate mixed diet for about a year, the normal relationship between the concentrations in the kidneys and liver was found, with values of 17 and 280 i.u., respectively. In the four rats of group 5, which received large amounts of cod liver oil for 7 weeks, the mean concentrations were

160 i.u./g. in the kidneys, and 3400 i.u. in the liver. These results confirm the statement of Johnson & Baumann (1947*a, b*) that the kidney is the main site of storage of vitamin A at low levels of dosing. The changes in the concentration of vitamin A in the kidneys in response to increased intakes of vitamin A, however, were surprisingly inconsistent. From the limited number of results which are at present available it would appear that the amounts of vitamin A in the kidneys are high at rather low and very heavy levels of intake, and lower at intermediate intakes. The complicating factor that the rats in group 5 died, whereas those in the other groups were killed, must not however be overlooked. The effect of very heavy doses of vitamin A in raising its level in the kidneys has already been reported by Davies & Moore (1934).

Females. In the female rats of groups 6–8 the intakes of vitamin A were too high to allow the concentrations reached in the kidneys to exceed those found in the liver. The results may be interesting, however, as further evidence of a lack of simple proportionality between the concentrations in the liver and kidneys. Thus in the combined groups 6 and 7 the kidney and livers averaged 15 and 50 i.u./g., respectively. Although in group 8 the mean concentration of 880 i.u./g. in the liver was nearly twenty times higher, the level in kidneys was only 8.7 i.u./g.

SUMMARY

1. The priority of the kidneys over the liver in accumulating vitamin A at low levels of intake was confirmed in young male piebald rats.

2. The usual predominance of the liver was asserted at higher levels of intake. In both male and female animals no simple relationship could be found between the concentrations in the liver and kidneys.

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