

CHAPTER IV

RESULTS

(1) Radioisotope study for erythrophagocytosis.

The body weight, haemoglobin and haematocrit values, the half-disappearance time ($T_{1/2}$) and the fractional turnover rate (K) of ^{51}Cr -labelled human red cells in the normal and in the ethpalm monkeys are shown in Table 1 and 2, respectively.

Table 1 The half disappearance time ($T_{1/2}$) and the fractional turnover rates (K) of ^{51}Cr -labelled red cells in the normal rhesus monkeys.

No.	B.W. (Kg)	Hb (g%)	Hct (%)	$T_{1/2}$ (min)	K (hr^{-1})
M-27	3.0	10.3	32	154	0.270
M-30	2.5	9.2	31	144	0.289
M-31	3.3	12.5	42	130	0.320
M-33	2.2	10.9	33	138	0.301
M-34	3.8	12.2	38	140	0.297
M-35	2.9	9.7	33	140	0.297
Mean	3.0	10.8	35	141	0.296

Table 2 The half disappearance time ($T_{1/2}$) and the fractional turnover rates (K) of ^{51}Cr -labelled red cells in the ethpalm rhesus monkeys.

No.	B.W. (Kg)	Hb (g%)	Hct (%)	$T_{1/2}$ (min)	K (hr^{-1})
<u>15% ethyl palmitate, 1.5 g/Kg</u>					
M-37	3.4	10.9	36	189	0.220
M-44	4.05	12.5	39	167	0.248
M-43	3.1	9.4	31.5	200	0.208
Mean	3.5	10.9	35.5	185	0.225
<u>20% ethyl palmitate, 2 g/Kg</u>					
M-4	2.5	9.7	33	184	0.226
M-29	2.5	11.9	39	300	0.139
M-30	2.2	6.9	24	303	0.137
M-34	3.2	8.1	32	324	0.128
Mean	2.6	9.2	32	278	0.158

The blood disappearance curves of the radioactivity in these monkeys are illustrated in Fig. 3. It is apparent from the figure that the disappearance rate followed a first order reaction over the range that was observed. The disappearance rates in the ethpalm monkeys were found to be slower than those of the normal monkeys. The mean half disappearance time ($T_{1/2}$) in the normal monkeys (141 minutes, range 130-154 minutes) was lower than the mean value of 185 minutes (range 167-200 minutes) in the 15% ethpalm monkeys ($P > 0.05$) and 278 minutes (range 184-324 minutes) in the 20% ethpalm monkeys ($P > 0.05$). The individual values of $T_{1/2}$ and K in these monkeys are shown in Fig. 4 and 5, respectively.

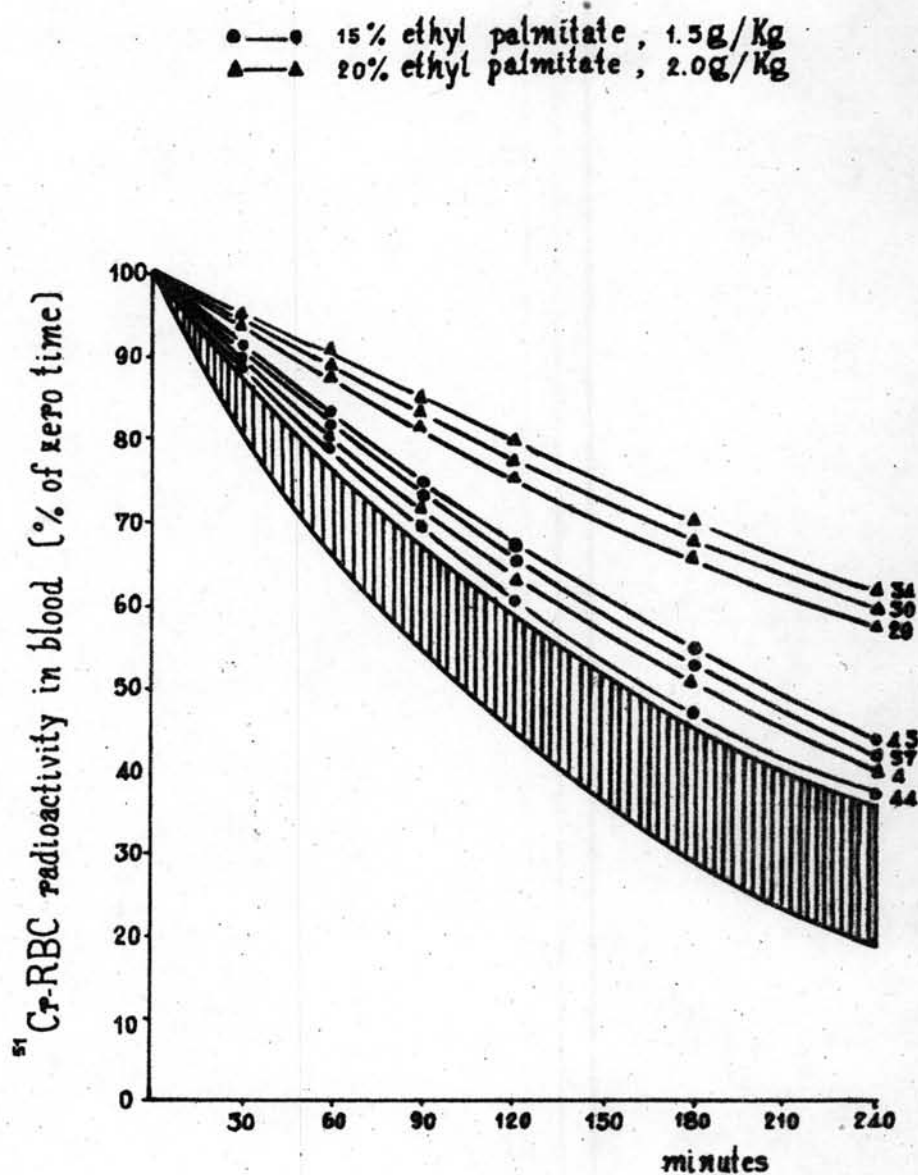


Fig. 3 - ^{51}Cr -RBC disappearance curves for 6 normal monkeys (vertical lines) and 7 ethypalm monkeys (numbered lines).

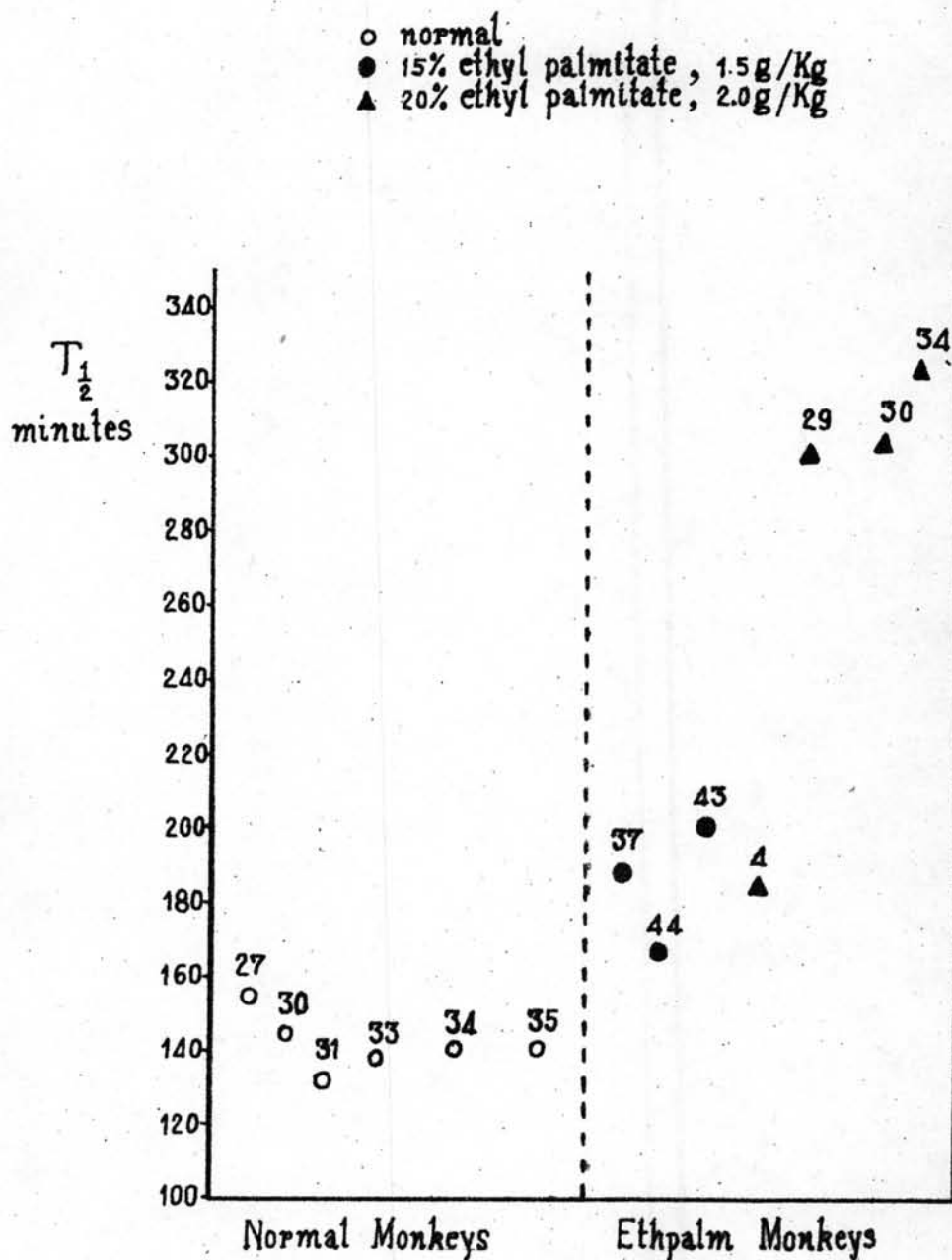


Fig. 4 - The individual values of half disappearance time ($T_{1/2}$) of ^{51}Cr -labelled red cell in normal and ethpalm rhesus monkeys.

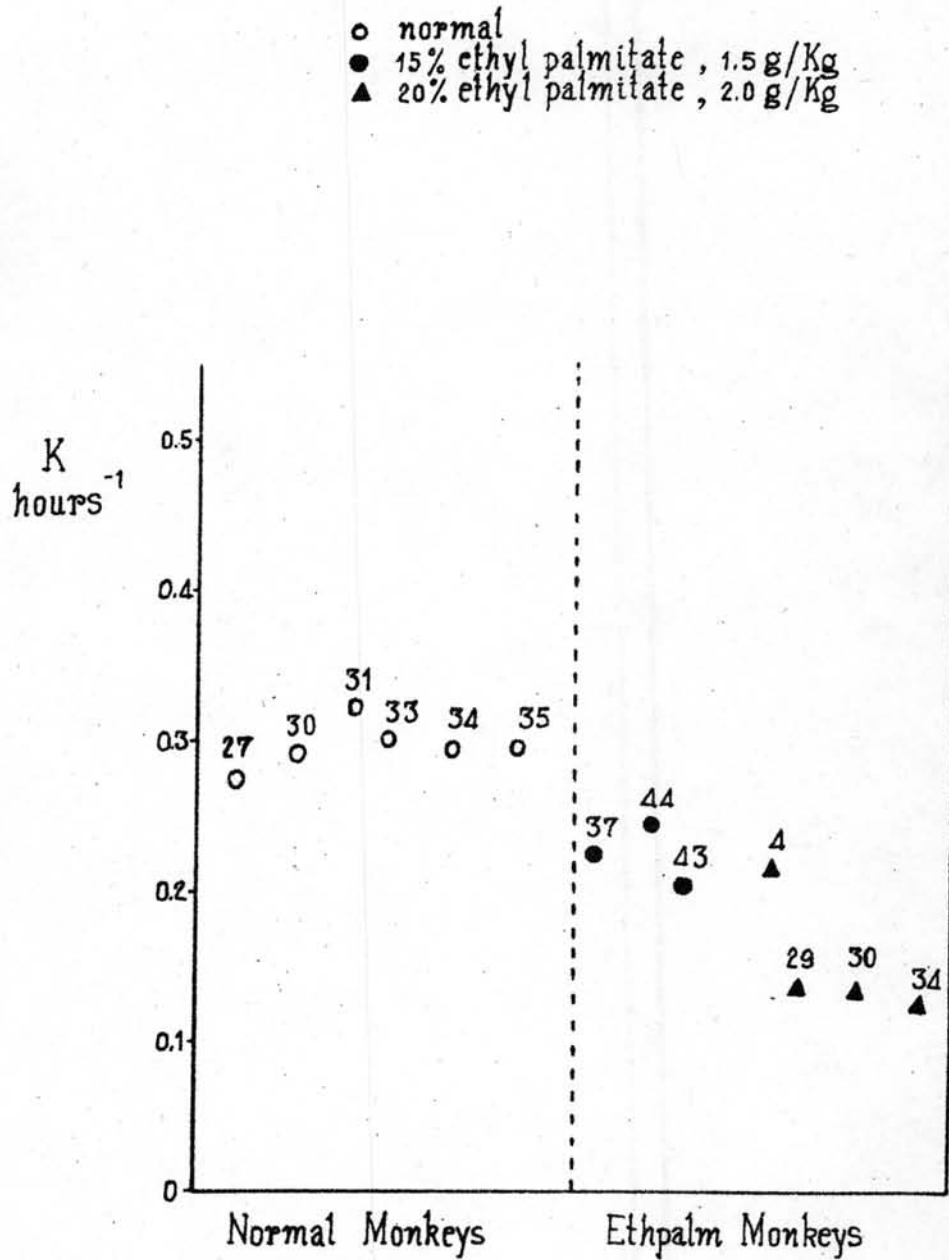


Fig.5 - The individual values of the fractional turnover rates (K) of ⁵¹Cr-labelled red cell in normal and ethpalm rhesus monkeys.



(2) Radioisotope study for a sinusoidal liver blood flow and phagocytic activity of the reticuloendothelial system.

The results of the maximal rate of blood clearance (K_e) after giving 0.03 mg/Kg of $^{131}\text{I-AA}$ and the sinusoidal liver blood flow calculated by equation (5) from 9 normal monkeys are shown in Table 3. The mean values of sinusoidal liver blood flow were found to be 107.2 ml/min (range 52.7-193.3 ml/min) or 1.00 ml/min/gm of liver weight (range 0.57-1.20 ml/min/gm of liver weight), respectively.

Table 3 Sinusoidal liver blood flow in normal rhesus monkeys, measured with $^{131}\text{I-AA}$ 0.03 mg/Kg body weight.

No.	B.W. (Kg)	Hb (g%)	Hct (%)	T½ (min)	K (min ⁻¹)	K _e (min ⁻¹)	Sinusoidal liver blood flow	
							ml/min	ml/min/gm of liver weight
M-1	2.9	11.7	38	1.60	0.190	0.433	81.8	0.85
M-2	5.8	10.9	38	1.80	0.168	0.384	145.5	1.20
M-3	4.0	11.5	40	1.71	0.178	0.406	100.6	1.03
M-6	4.4	10.6	33	1.40	0.217	0.495	131.7	1.20
M-12	5.8	10.9	38	1.36	0.224	0.510	193.3	1.60
M-13	3.8	11.5	40	3.00	0.101	0.231	59.4	0.57
M-14	3.4	9.7	32	1.40	0.214	0.488	99.1	0.98
M-15	3.1	10.6	34	1.43	0.212	0.484	92.0	0.94
M-17	2.2	11.9	40	1.95	0.156	0.355	52.7	0.60
Mean	3.9	11.0	37	1.74	0.184	0.420	107.2	1.00

The sinusoidal liver blood flow in the present experiments was in the same order of magnitude as the other species of animals reported previously (see Table 4).

Table 4 Values of the maximal rate of the blood clearance (K_{max} and K_e) and sinusoidal liver blood flow using $^{131}\text{I-AA}$ below the "critical dose" in different animal species.*

Species	Critical dose mg/100gm	K_{max}	K_e	Sinusoidal liver blood flow	
				ml/min	ml/min/gm of liver weight
Mouse	0.51	0.360	0.833	1.47	1.30
Rat	0.43	0.300	0.700	6.95	1.13
Guinea-pig	0.36	0.300	0.687	15.6	1.30
Rabbit	0.19	0.285	0.659	106.0	1.15
Man	0.25	0.139	0.318	1445.0	0.73
Monkey**	0.12	0.188	0.401	109.1	0.91

* This data was adapted from Stiffel et al., (1970).

** From present studies, calculated from the data of 0.03 mg/Kg of $^{131}\text{I-AA}$.

The phagocytic activity of the R.E.S. was studied by using 5 mg/Kg of ^{131}I -AA in 10 normal monkeys. The calculated values of $T_{1/2}$ and the phagocytic index (K) calculated from equation (2) are shown in Table 5. The mean values of $T_{1/2}$ and K were found to be 5.6 minutes (range 3.7-8.5 min) and 0.056 (range 0.036-0.082) min^{-1} respectively.

Table 5 The half disappearance time ($T_{1/2}$) and the phagocytic index (K) in normal rhesus monkeys, measured with ^{131}I -AA 5.0 mg/Kg body weight.

No.	B.W. (Kg)	Hb (g%)	Hct (%)	Phagocytic Activity	
				$T_{1/2}$ (min)	K (min^{-1})
M-1	2.9	11.7	38	8.50	0.036
M-2	5.8	10.9	38	4.30	0.070
M-3	4.0	11.5	40	6.30	0.048
M-6	4.4	10.6	33	3.70	0.082
M-15	3.1	10.6	34	7.20	0.042
M-17	2.2	11.9	40	5.10	0.060
M-4	1.9	11.0	34	4.20	0.072
M-5	1.9	11.5	37	4.50	0.067
M-16	1.7	9.4	28	5.80	0.052
M-18	2.9	11.7	38	7.90	0.038
Mean	3.1	11.7	36	5.60	0.056

The phagocytic activity and the corrected phagocytic index from the present study was in accordance with dose of the other species of animals (see Table 6).

Table 6 Values of phagocytic activity established for the dose of 5 mg ^{131}I -AA per 100 gm of body weight in various normal animal species.*

Species	K	K x D	Wls (gm/100 gm)	α
Mouse	0.042	0.210	5.5	6.3
Rat	0.026	0.130	4.2	7.0
Guinea-pig	0.022	0.110	4.0	6.8
Rabbit	0.011	0.055	3.4	6.5
Man	0.007**	0.035	3.0	6.3
Monkey***	0.006**	0.029	3.2	5.4

* This data was adapted from Stiffel et al., (1970)

** Calculated from K = 0.07 and 0.05 respectively for the dose of 5.0 mg/Kg

*** From present studies.

The body weight, haemoglobin and haematocrit values, and the sinusoidal liver blood flow in the ethpalm monkeys, measured with 0.03 mg of $^{131}\text{I-AA/Kg}$ body weight, are shown in Table 7. There was a difference in the mean value of the $T_{1/2}$ of 10% ethpalm monkeys (2.16 minutes) ($P < 0.05$); 15% ethpalm monkeys (1.83 minutes) ($P > 0.05$); 20% ethpalm monkeys (1.34 minutes) ($P > 0.05$) and of normal monkeys (1.74 minutes). The mean values of K_e were slightly lower in the 10% and 15% ethpalm monkeys but higher in the 20% ethpalm monkeys than that of the normal monkeys. The mean value of the sinusoidal liver blood flow was also lower in the ethpalm monkeys [50.4 ml/min or 0.55 ml/min/gm liver for 10% ethpalm monkeys ($P < 0.05$); 87.8 ml/min or 0.85 ml/min/gm liver for 15% ethpalm monkeys ($P > 0.05$) and 81.5 ml/min or 0.82 ml/min/gm liver for 20% ethpalm monkeys ($P > 0.05$)] than that of the normal monkeys (107.2 ml/min or 1.00 ml/min/gm liver). The individual values of the sinusoidal liver blood flow in these monkeys are illustrated in Fig.6 and 7.

Table 7 Sinusoidal liver blood flow in ethpalm rhesus monkeys, measured with $^{131}\text{I-AA}$ 0.03 mg/Kg body weight.

No.	B.W. (K)	Hb (g%)	Hct (%)	T½ (min)	K (min ⁻¹)	K _e (min ⁻¹)	Sinusoidal liver blood flow	
							ml/min	ml/min/gm of liver weight
<u>10% ethyl palmitate, 0.75 g/Kg</u>								
M-15	2.8	7.1	27	2.15	0.142	0.323	50.2	0.53
M-18	2.4	7.1	27	1.70	0.179	0.408	54.3	0.60
M-22	2.4	9.8	30	1.52	0.196	0.456	63.9	0.71
M-4	2.1	9.9	33	1.45	0.210	0.479	61.8	0.72
M-15	2.6	8.9	31	2.76	0.110	0.251	38.0	0.41
M-22	2.8	7.3	33	3.38	0.093	0.205	34.4	0.35
Mean	2.5	8.4	30	2.16	0.155	0.354	50.4	0.55
<u>15% ethyl palmitate, 1.5 g/Kg</u>								
M-44	4.1	12.5	39	1.52	0.20	0.456	122.6	1.14
M-37	3.4	10.9	36	2.39	0.127	0.289	62.1	0.61
M-43	3.1	9.4	31.5	1.59	0.190	0.433	78.6	0.80
Mean	3.5	10.9	35.5	1.83	0.172	0.393	87.8	0.85
<u>20% ethyl palmitate, 2 g/Kg</u>								
M-30	2.2	6.9	24	1.45	0.210	0.478	54.1	0.44
M-34	3.2	8.1	32	1.22	0.252	0.570	108.9	1.19
Mean	2.7	7.5	28	1.34	0.231	0.524	81.5	0.82

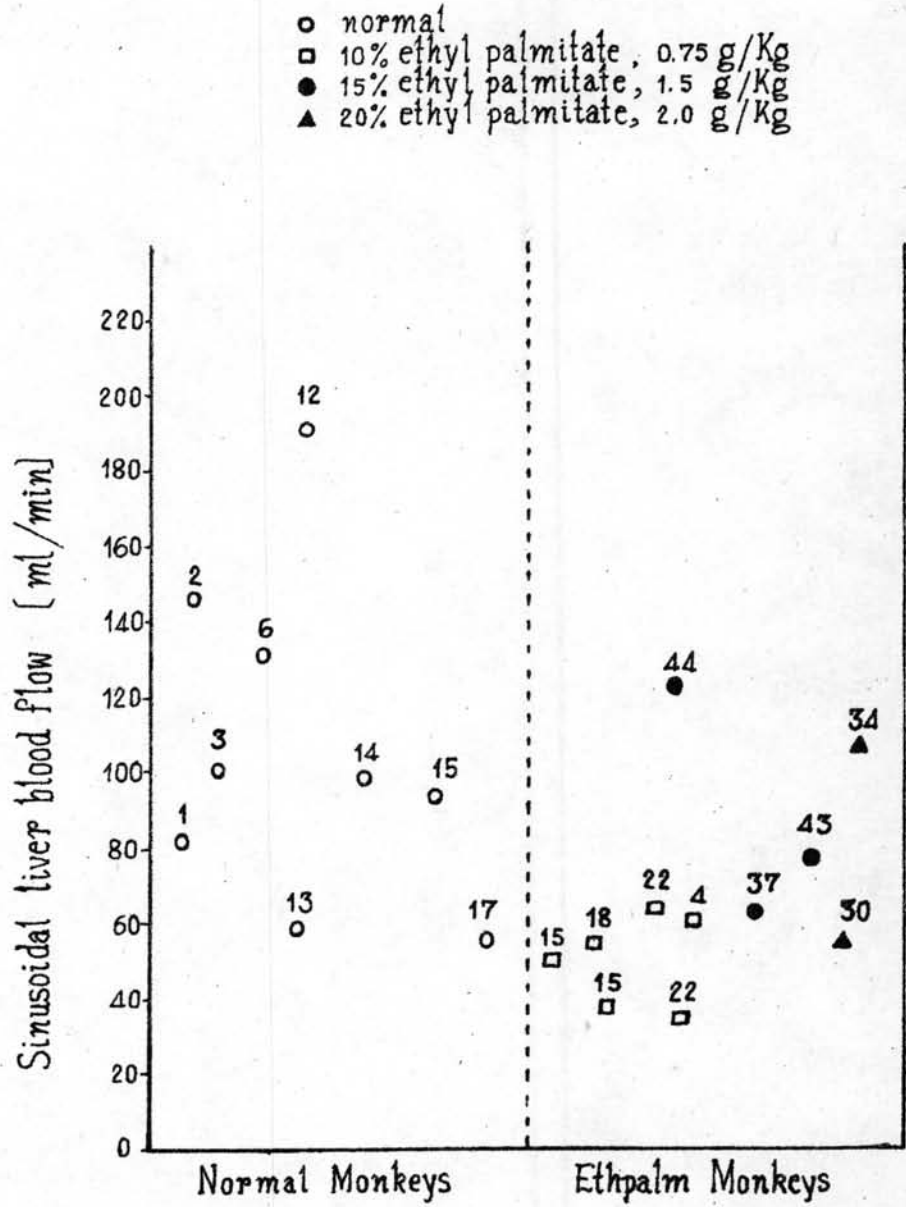


Fig. 6 - The individual values of the sinusoidal liver blood flow (ml/min) in normal and ethpalm rhesus monkeys, measured with ¹³¹I-AA 0.03 mg/Kg body weight.

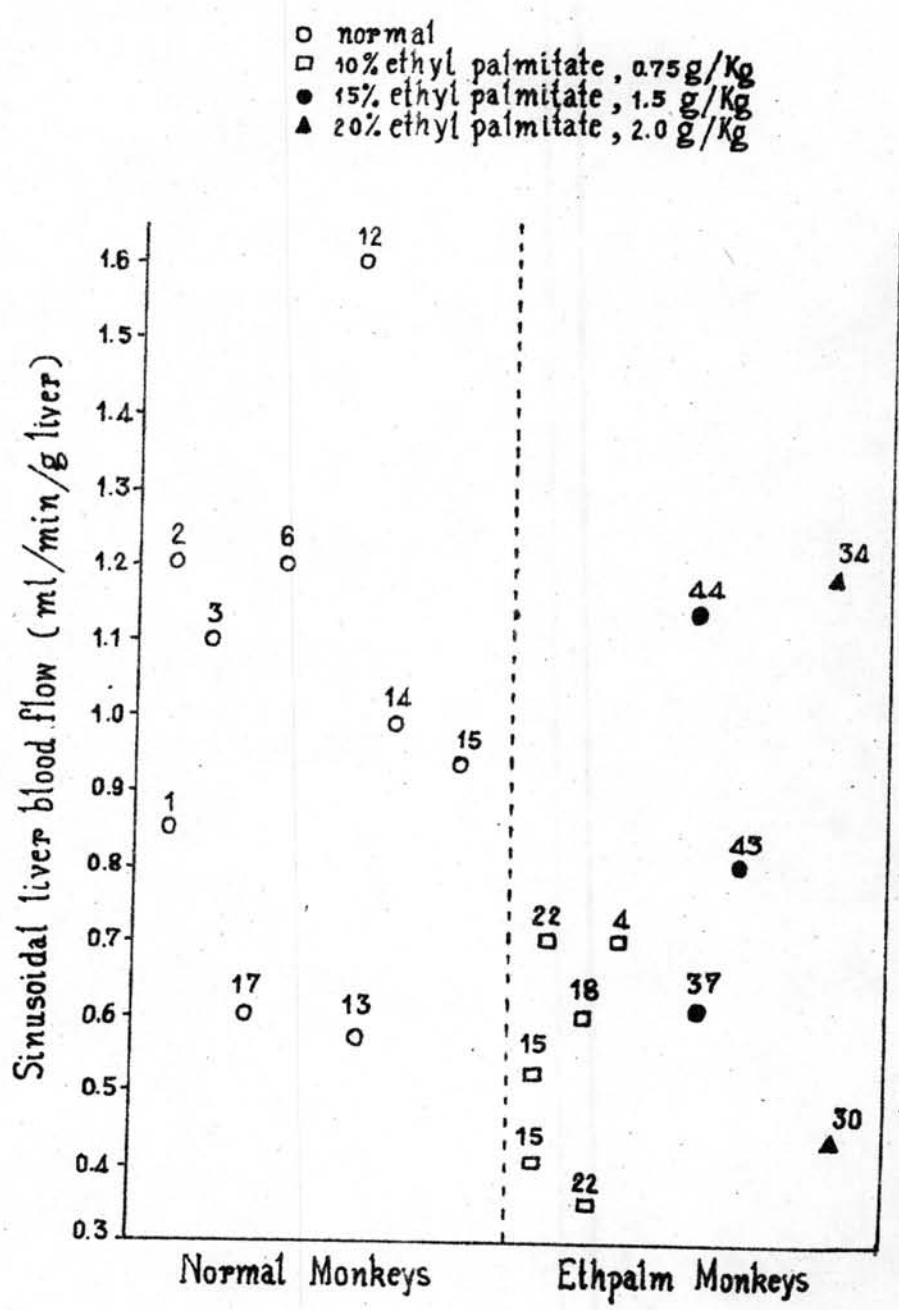


Fig. 7 - The individual values of the sinusoidal liver blood flow [ml/min/g liver] in normal and ethpalm rhesus monkeys, measured with ¹³¹I-AA 0.03 mg/Kg body weight.

The phagocytic activity of the R.E.S. in 12 ethpalm monkeys are shown in Table 8. There was a difference in the $T_{1/2}$ ($P > 0.05$) of the normal monkeys (5.60 minutes) and the ethpalm group (3.18 minutes of 10% ethpalm monkeys, 4.45 minutes for 15% ethpalm monkeys and 3.18 minutes for 20% ethpalm monkeys). The mean phagocytic index, K , ($P > 0.05$) of the ethpalm (0.103 min^{-1} for 10% ethpalm monkeys; 0.073 min^{-1} for 15% ethpalm monkeys; 0.101 min^{-1} for 20% ethpalm monkeys) was also higher than that of the normal group (0.056 min^{-1}). The individual values of the phagocytic index and $T_{1/2}$ in these group of monkeys are illustrated in Fig.8 and 9, respectively.

Table 8 The half disappearance time ($T_{1/2}$) and the phagocytic index (K) in ethpalm rhesus monkeys, measured with $^{131}\text{I-AA}$ 5.0 mg/Kg body weight.

No.	B.W. (Kg)	Hb (g%)	Hct (%)	Phagocytic activity	
				$T_{1/2}$ (min)	K (min^{-1})
<u>10% ethyl palmitate, 0.75 g/Kg</u>					
M-15	2.8	7.1	27	2.22	0.137
M-18	2.4	7.1	27	2.34	0.130
M-22	2.4	9.8	30	3.37	0.088
M-4	2.1	9.9	33	2.28	0.133
M-15	2.6	8.9	31	3.80	0.080
M-22	2.8	7.3	33	5.07	0.060
Mean	2.5	8.4	30	3.18	0.103
<u>15% ethyl palmitate, 1.5 g/Kg</u>					
M-44	4.1	12.5	39	4.36	0.070
M-37	3.4	10.9	36	5.42	0.056
M-43	3.1	9.4	31.5	3.58	0.085
Mean	3.5	10.9	35.5	4.45	0.073
<u>20% ethyl palmitate, 2 g/Kg</u>					
M-29	2.5	11.9	39	4.30	0.070
M-30	2.2	6.9	24	2.60	0.117
M-34	3.2	8.1	32	2.64	0.115
Mean	2.63	9.0	35	3.18	0.101

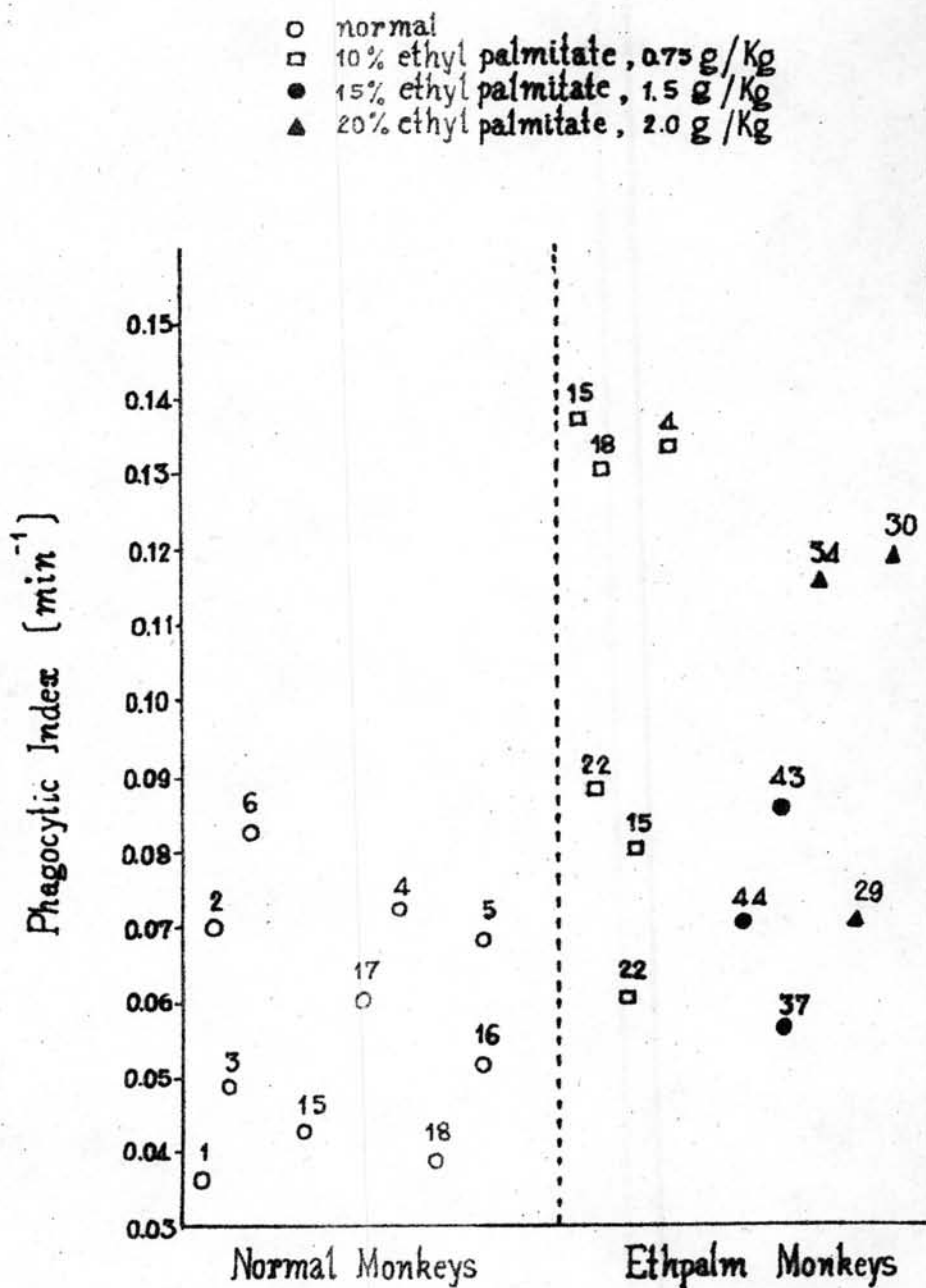


Fig. 8 - The individual values of the phagocytic index (K) in normal and ethpalm rhesus monkeys, measured with ¹³¹I-AA 5 mg/Kg body weight.

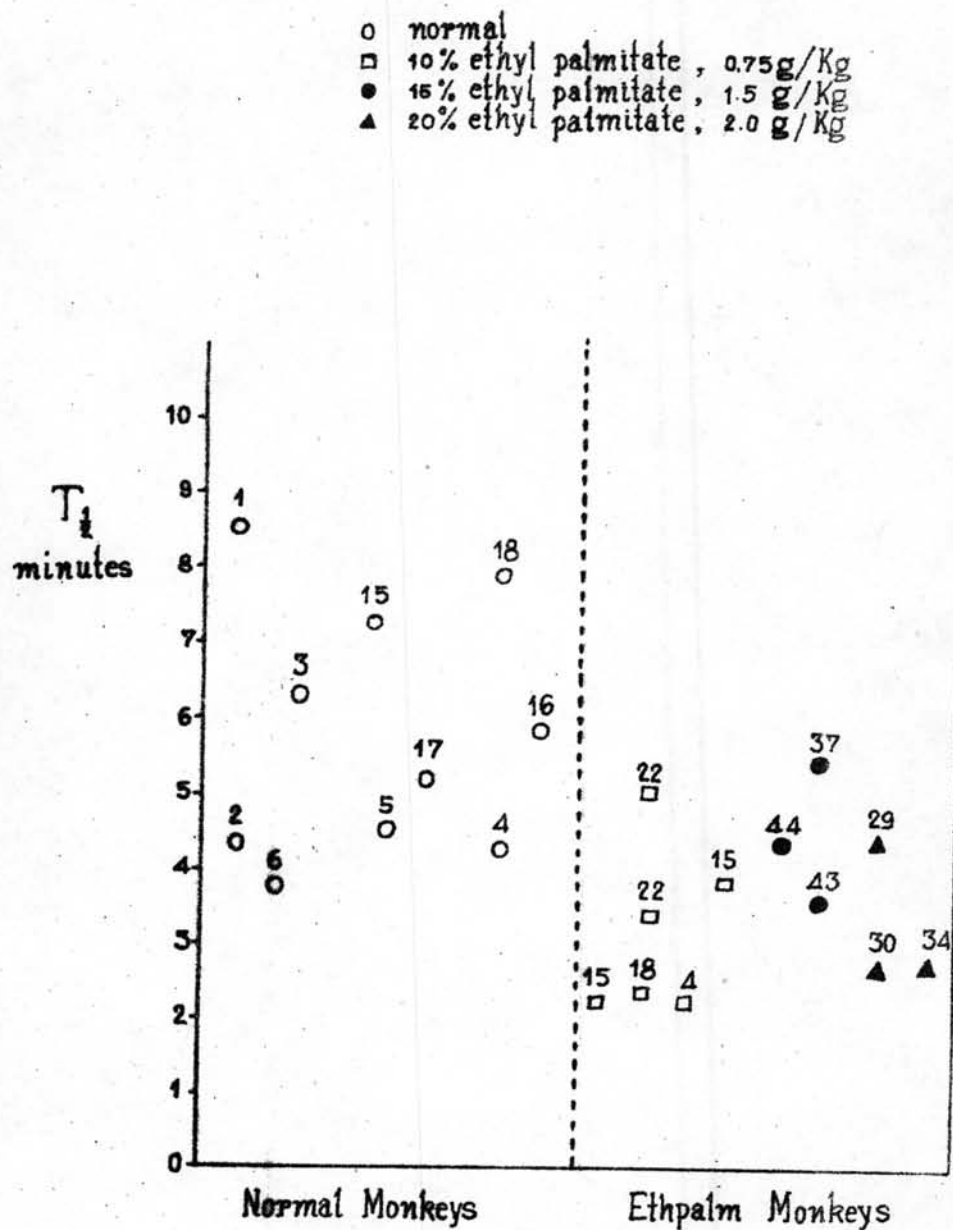


Fig 9 - The individual values of the half disappearance time ($T_{1/2}$) in normal and ethpalm rhesus monkeys, measured with $^{131}\text{I-AA}$ 5 mg/Kg body weight.

(3) Histological examination

Microscopic examination of the liver in monkeys receiving 10% and 20% ethyl palmitate emulsion showed congestion, cloudy swelling and some hydropic degeneration of the liver cells; dark brown pigment; several degenerative change at portal area and periphery central vein; mild fatty metamorphosis of liver cell, hyperplasia, proliferation and accumulation of Kupffer cell (See Fig. 10 and 11).

Section of spleen in monkeys, showed no definite change of necrosis, proliferation of malpighian corpuscle in R.E. cells and portal veins.

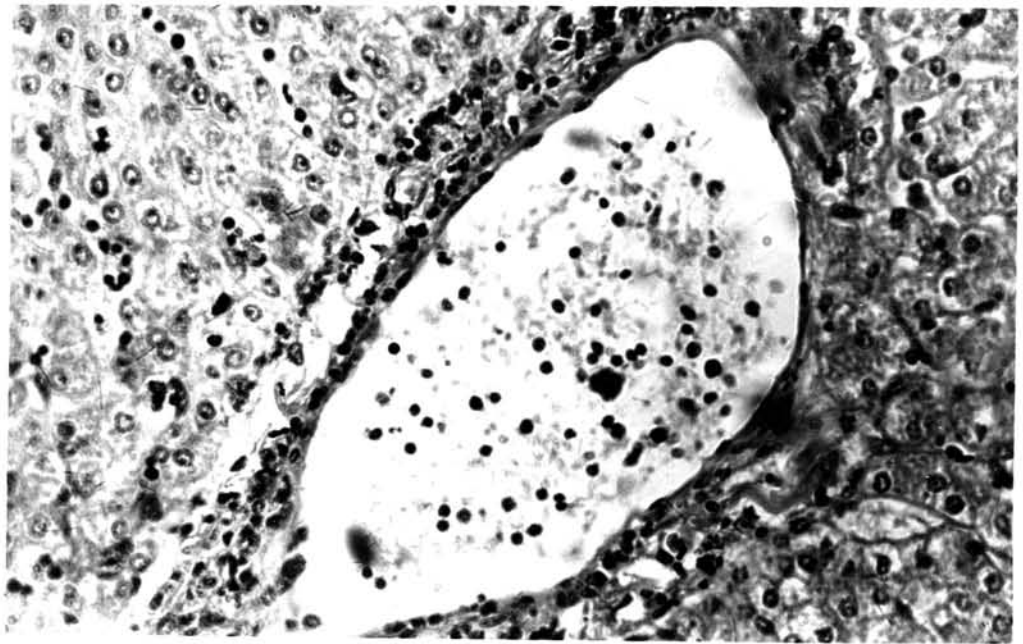


Fig 10 - Histological section of the liver of a monkey (M-22)
receiving 10% ethyl palmitate.

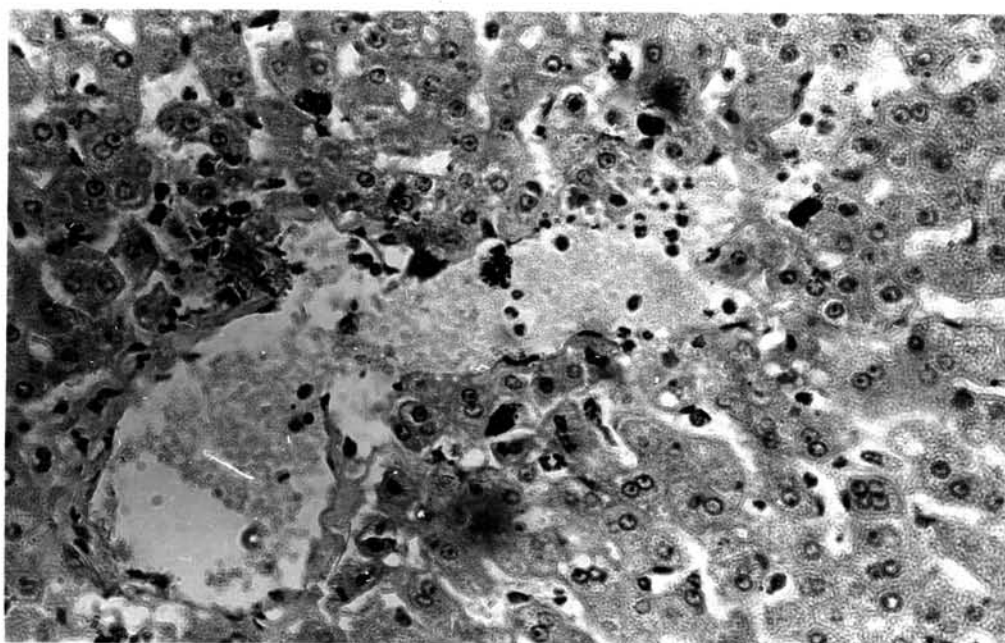


Fig 11 - Histological section of the liver of a monkey (M-34)
receiving 20% ethyl palmitate.