Subtitle: Comparative Studies in the Pathology and Host Physiology of Malarias: Plasmodium coatneyi malaria.

Investigators: Robert S. Desowitz, Louis H. Miller, Richard D. Buchanan, Vithume Yuthasastrkosol. Barnyen Permpanich

Because of the multiplicity of host-parasite relationships in the genus Plasmodium a full understanding of host pathology necessitates a comparative approach. Not only do the different species. of Plasmodium produce a variety of diseases but also the type of infection any single species may induce can vary within its host range. A familiar example of this is the benign course of P. knowlesi in Macaca irus as compared to the fatal infection produced in M. mulatta.

Although the work of Maegraith and his colleagues on P. knowlesi over the past two decades has greatly contributed to the understanding of malarial pathophysiology, many other malarias have not been similarly examined. In view of this hiatus it is the aim of these present studies to describe and compare the disease produced by various malarias in different hosts. This initial paper is concerned with a primate malaria of S.E. Asia, P. coatneyi (Eyles et al. 1962), in the rhesus monkey. This parasite shares many characters in common with P. falciparum. With the exception of the gametocytes, the morphology is similar and it exhibits a tertian periodicity with deep vascular schizogony (Eyles et al. 1962). There is also evidence that P. coatneyi is antigenically related to P. falciparum (Stein and Desowitz, 1964; Desowitz, Saave, and Stein, 1966). For these reasons P. coatneyi is of special interest as a possible model for human malignant tertian malaria.

Methods

Adult rhesus monkeys from Northern India (M. mulatta mulatta) and Thailand (M. mulatta siamica) were used in these experiments. Repeated blood examinations gave no evidence of malaria and tuberculin skin tests showed all to be free of tuberculosis. Some animals were splenectomized prior to experimental infection. The monkeys were infected by intravenous or intraperitoneal inoculation of parasitized blood. The description of each animal will be given under Results. Four animals were maintained as uninfected controls.

The principles of laboratory animal care as promulgated by the National Society for Medical Research were observed.

The course of infection was studied in terms of parasitaemia, temperature, haematologic values, various blood chemistries, urinalysis, and tissue pathology. Haematology and blood chemistries were obtained on all animals prior to infection. The methods employed were as follows:

1. Parasitaemia. Blood films were obtained each morning. The parasitaemia was assessed by counting the total number of asexual forms in fifty high-power oil immersion fields of the Giemsa stained thin blood film.

2. Temperature. Rectal temperatures were taken each morning.

3. Haematology. One ml. of blood was drawn weekly into a heparinized syringe. In some animals blood was obtained more frequently as to be described in the results. Haematocrit, haemoglobin, red blood cell count, reticulocyte count, and white blood cell count and differential were performed. Bone marrow aspirations were obtained from selected animals. A bone marrow needle was inserted into the greater trochanter and the marrow smear stained with Giemsa-Wright.

4. Blood chemistries. At the time the blood was drawn for haematology another seven ml. was obtained for blood chemistries. This was allowed to clot, the serum obtained and refrigerated as 5°C. Transaminases and alkaline phosphatase determinations were carried out that same day. The remainder of the sample was stored at—70°C and the other analyses made within three days.

appeared ill and was lethargic. The BUN attained a maximum level of 51 mg. Per cent. By the 11th day the haematocrit showed no further decrease. The haemoglobinuria had disappeared and the animal was again walking about its cage. BUN and transaminases had fallen, but over the next three days the transaminases rose again. The creatinine remained normal and the BUN continued to be slightly elevated. On the 14th day there was a marked reticulocytosis of 21% and 169 normoblasts per 100 white blood cells.

Throughout the entire two week period of the acute phase the only abnormal temperature noted was on the 12th day when it fell to 97^{5}°F. The akaline phosphatase declined from a preinfection level of 17.6 sigma units to 6.4 on the 14th day. There was also some decrease in cholesterol over this period. Other than the transient haemoglobinuria no other abnormalities were observed in the urine during the acute or chronic infection.

MS2. (splenectomized Thai rhesus). The monkey received an intraperitoneal inoculation of $5x10^6$ parasites. The primary attack was characterized by a high, unrelenting parasitaemia for 7 days followed by a second rise in parasitaemia with its peak on the 33rd day (fig. 5). Thereafter, the infection became chronic with a low-grade parasitaemia of tertian periodicity. The onset of anaemia at the 7th day occurred before the peak parasitaemia. During the period of the primary parasitaemic attack the transaminases. BUN, and creatinine rose. These blood chemistries returned to normal by the 30th day except the elevated SGOT which persisted for approximately 4 more weeks. Despite the abnormal SGOT a liver biopsy taken on the 23rd day was normal except for a heavy deposit of pigment in the Kupffer cells.

A peak of 20 per cent reticulocytes occurred on the 20th day and returned to a pre-infection level as the anemia disappeared with the onset of chronicity. Concurrent with the maximal reticulocytosis the highest number of normoblasts, 31,000 per mm^3 , was present. The bone marrow on the 30th day showed erythroid hyperplasia with a M:E ratio of 1:3. There was a persistent leucocytosis that began during the acute infection and continued for the five month observation period. During the early chronic period the monocyte count rose to 45 per 100 WBC. No abnormal blood chemistries were evident during the chronic period.

MS18. (splenectomized Thai rhesus). The animal received an intraperitoneal inoculation of $5x10^6$ parasites. For the first 60 days a parasitaemia of 200 to 500 parasites per 50 thin film fields appeared with regular tertian periodicity (fig. 6). After day 75 the parasitaemia was of a chronic, low grade nature. A progressive anaemia developed during the first two weeks of infection and persisted until approximately day 75. There was a reticulocyte response of fluctuating intensity with a maximum of 9 per cent during the period of anaemia. With the onset of the low-grade chronic parasitaemia the haematologic values returned to normal. Normoblasts were first seen on day 21 and were present throughout chronicity with a maximum of 14/100 WBC. Bone marrow specimens taken on the 88th and 115th days were hyperplastic with M:E ratios of 1:2 and 1:3.5, respectively. There was no abnormality of white blood cell count at any time. Blood chemistries remained normal throughout the observation period with the exception of a rise in alkaline phosphatase. Urines on 63rd and 73rd days were normal.

A liver biopsy obtained on the 17th day showed increased activity of reticuloendothelial elements, much finely divided malarial pigment in the Kupffer cells and marked granularity and basophilia of the parenchymal cytoplasm.

KL1. (intact Indian rhesus). This animal developed a moderate primary parasitaemia which decreased progressively to a persistent low grade infection (fig. 7). It became severely anaemic by the 12th day followed by a gradual recovery towards normal. The anaemia was accompanied by a reticulocytosis, the presence of normoblass in the peripheral blood, and increased unconjugated serum bilirubin. There was no significant alteration in the white blood cell count. The BUN rose to 32 mg. per cent on the 12th day and was normal thereafter. There was no coincidental rise in creatinine. The trasaminases and alkaline phosphatase did not, at any time, alter markedly. Cholesterol was decreased from a preinfection level of 162 mg. Per cent to 93 mg. per cent on the 17th day and returned to normal over the next two weeks. A liver biopsy carried out on the 26th day was normal except for pigment in the Kupffer cells.

KL2. (intact Indian rhesus). This animal was inoculated intravenously with $7x10^7$ parasites. The course of infection was characterized by a primary parasitaemia which became periodic after the 20th day (fig. 8). A peak parasitaemia of 542 parasites per 50 thin film fields occurred on the 26th day. After the 38th day the parasitaemia was scanty. The haemogram indicated a marked anemia by the 12th day. At that time a bone marrow specimen sbowed erythroid hyperplasia with a M:E ratio of 1:2. Further evidence of bone marrow activity was a peak reticulocytosis of 18 per cent on the 18th day and 46 normoblasts per 100 WBC. There was no alteration in the white blood cells. Neither transaminases, direct bilirubin, BUN nor creatinine on the 4th, 7th, and 11th days showed any alteration from baseline normal values. During this acute phase the alkaline phosphatase fell from a baseline average of 17 sigma units to 4. It remained at this low level until the onset of chronicity at the 40th day. A liver biopsy on the twelfth day showed nuclear irregularity and intense cytoplasmic basophilia in the parenchymal cells, histologic evidence of increased liver cell activity. Kupffer cells contained finely divided pigment. The sole abnormality of the kidney biopsy was minimal swelling of the glomeruli.

During the period of the 20th to the 38th day, a time when the animal was subjected to repeated parasitaemic attacks of moderate severity, the anemia persisted. With the decline in parasitaemia there was a return of haematologic values towards normal. From the 40th to 61st days there was an elevation of unconjugated bilirubin, an occurrence that had not been found in other monkeys during the chronic phase. The elevated bilirubin is probably a result of haemolysis and it is of interest to note that there was also a concurrent reticulocytosis. The cause of this haemolysis during a time of low parasitaemia was not known. Other than the unconjugated bilirubin and alkaline phosphatase there were no changes in blood chemistries.

On 10 separate days the temperature rose above 104°F. During 69 days of daily preinfection temperatures the maximum recorded was 103.6°F. There was no relationship between fever and parasitaemic periodicity.

SP1. (intact Thai rhesus). This animal received an intravenous inoculation of $9x10^7$ parasites. The infection was of a mild nature with a parasitaemia that never exceeded 100 parasites per 50 thin film fields. From the onset, there was a tertian pattern of parasitaemia. After the second week, the infection became chronic with parasite numbers of not more than 10 per 50 thin film fields. Relatively little anaemia was produced and this only during the second week of infection. At this time the haematocrit had fallen from 33 to 21 per cent, with a concomitant reticulocytosis of 5 per cent. No alteration in transaminases, alkaline phosphatase, BUN or creatinine were observed. Cholesterol decreased from 145 mg. per cent to 90 mg. per cent early in the infection and remained low for five weeks, after which it gradually returned to the preinfection level. Urines collected daily for the first month of infection contained no protein.

DISCUSSION

The models commonly employed for physiologic studies, P. berghei in mice and P. knowlesi in the rhesus monkey, generally produce fatal infections. However human malaria differs from these in that the severity of disease is highly variable. Similar to human malaria P. coatneyi produced a spectrum of disease, ranging from a fulminating fatal infection as in KL12 and 13 to a mild chronic course as in SP1. The intensity of disease for experimental purposes can be controlled by using splenectomized or intact rhesus.

In general, the pathologic effect as manifested by alterations in haematology, blood chemistry and tissue pathology was related to the degree of parasitaemia. Exceptions to this did occur. A relatively low parasitaemia, produced a fatal infection in KL12 and a severe anemia in KL1. However, the limitations in parasite enumeration must be taken into account. Marked hourly flucuations in parasite density were seen in KL3, and thus in many of our animals from which blood films were only taken daily the true peak parasitaemia may well have been missed. Furthermore since schizogeny occurs in the deep vasculature, enumeration from peripheral blood would not give a true account of the total parasitaemia.

The most consistent pathologic effect was anaemia. In most cases, onset and degree of anaemia paralleled the rise in parasite numbers of the primary attack. However in one animal, MS2, an anaemia was produced on the 7th day, a time when the parasitaemia was still low. In the three acutely infected animals, KL12, KL13, and KL3, the rapid onset of anaemia was accompanied by haemoglobinuria (lytic phase), a phenomenon shown to occur in P. knowlesi (Devakul and Maegraith, 1959).

In KL3 a definite haemoconcentration occurred early in the infection, prior to the lytic phase. This event was associated with marked signs of illness and biochemical change. Haemoconcentration with an associated shock-like syndrome has been described by Devakul and Maegraith (1959), Skirrow (1962) and Chongsuphajaisiddhi (1966) in P. knowlesi infections and by Kean and Taylor (1946) in P. falciparum. This may be caused by a decrease in plasma volume which in turn may be related to the vascular permeability increasing factor in the serum of malaria infected monkeys (Desowitz and Pavanand, 1967). A haemoconcentration phenomenon may be extremely important in contributing to the early pathogenesis of malaria but it will require further detailed study on haematology, plasma volume and red cell mass to elucidate its frequency and mechanism.

In non-fatal infections there was a vigorous host response to the anaemia as evidenced by reticulocytosis, nucleated red blood cells in the peripheral smear and erythroid hyperplasia of the marrow. In most animals the peak reticulocytosis occurred approximately one week after maximum anemia. The duration of anemia seemed to depend upon parasite numbers.

Liver pathology was evident in some animals, notably those which sustained an acute infection. In these, centrilobular necrosis of the liver was accompanied by transaminase elevations. Centrilobular necrosis has previously been described as a consequence of P. falciparum in man and P. knowlesi in the rhesus monkey (Rigdon and Stratman-Thomas, 1942; Andrews, 1948). It is possible that two events are involved in the process of liver pathology due to P. coatneyi. In two acutely infected monkeys studied in detail KL3 and KL13 there was an initial rise in transaminase with biopsy evidence of patchy centrilobular necrosis in one. This was followed by a decrease in transaminase levels and secondary elevation at or shortly after the lytic phase. The SGOT usually rose to higher levels than the SGPT which is in keeping with Maegraith's findings for P. knowlesi (1966). However, Sadun et al. (1966) found that the SGPT increment was greater than SGOT in chimpanzees infected with P. falciparum. This difference might be attributed to the host species studied.

Of the five moderately infected animals, only MS2 had an elevated transaminase but there was no histologic evidence of hepatic necrosis. In the other monkeys there was no transaminase elevation over the period of rapidly developing anaemia. Maegraith (1966) has raised the point that hemolysis might contribute to a transaminase elevation but we have no evidence for this in either these experiments or in gibbon malaria which is to be reported in a subsequent paper.

The two biochemical indicators of liver function employed in this study, direct bilirubin and alkaline phosphatase, showed no abnormal elevation in either acutely or moderately infected monkeys. In fact, there was a tendency for alkaline phosphatase level to fall. This is similar to the finding of Sadun et at (1965) for mice infecled with P. berghei. At present, it is difficult to account for this decrease in alkaline phosphatase during malaria. It has been shown that this enzyme is high in growing animals and falls when growth is retarded (Gutman, 1959). It is possible that malaria inhibits the growth process and that the serum alkaline phosphatase level might reflect this.

Similar to hepatic changes, renal abnormalities were most frequently observed in the acutely infected animals. In both KL3 and KL13 the BUN and serum creatinine were abnormably high. In KL3 this occurred early, at the time of haemoconcentration and inital rise in transaminases, while in KL13 this increase was a terminal event. Despite the abnormal biochemistry, the kidney pathology of the autopsy specimen of KL13 showed remarkably little change. That severe histopathologic alteration of the kidney may occur was shown in KL12 where the picture was similar to that described for P. knowlesi of the rhesus (Rigdon and Stratman-Thomas 1942).

In the more moderate infections renal abnormalities were less consistently observed. MS2 exhibited an elevation of both creatinine and BUN, coinciding with a rise in transaminases. In KL1 only the BUN increased without any alteration in either creatinine or transaminases. The elevation of BUN when it occurs without coincidental rise in creatinine may be attributed to an increased metabolic production of urea. An abnormal serum creatinine without tissue pathology suggests a decreased renal blood flow. Evidence for renal blood flow abnormality has been presented by Chongsuphajaisiddhi (1966) for P. knowlesi and Sitprija et al (1967) for three patients with severe P. falciparum infections.

Transient decreases in cholesterol were seen in five of seven monkeys. The significance of this will be discussed in a subsequent paper when a comparison of cholesterol alterations in malarias will be made.

There was no consistent relationship between temperature elevations and parasitaemia or other manifestations of disease. The inconsistent finding of pyrexia in this disease and its virtual absence in P. knowlesi malaria (Menon and Nair, 1955) is in sharp contrast to the human host who, in this respect, would seem to be exquisitely sensitive to the parasite. The temperature fell late in the acute infections and this may be related to shock.

While it is obvious that there is no perfect model for human falciparum malaria we feel that P. coatneyi infection in the rhesus monkey approaches this ideal more closely than any other primate malaria studied hitherto. Not only is it morphologically and antigenically related but as has been shown in this paper the general pathogenic effects are, in many respects, similar to the human infection. However it is not our intention at this time to present a detailed comparative host pathophysiology between various malarias. This will be reserved until a later time when we have presented out studies in other primate malarias.

SUMMARY

1. Splenectomized and intact rhesus monkeys were infected with P. coatneyi. The course of infection was studied sequentially in terms of parasitaemia, haematology, blood chemistry, and tissue pathology.

2. Splenectomized Indian rhesus became acutely ill with the infection terminating in death in two of three animals. The acute infection was characterized by anaemia, haemoglobinuria, elevated transaminases, BUN and creatinine. The liver exhibited centrilobular necrosis and the kidney of one animal showed hyaline droplet degeneration.

3. Splenectomized Thai rhesus and intact Indian rhesus had milder infections. Anaemia was the outstanding abnormality. A vigorous response of the bone marrow was evidenced by reticulocytosis, normoblasts in the peripheral blood and erythroid hyperplasia. The haemogram returned towards normal with the onset of chronicity. Of the five moderately infected rhesus only one, a splenectomized Thai rhesus, had elevated transaminase, BUN and creatinine.

4. During the chronic phase no haematologic or blood chemistry abnormalities have been observed to date.

Acknowledgements: We are indebted to Cpt. Iber, SFC C. Horton, and SFC G. Clary of the Laboratory Service, Clinical Research Center for their technical assistance. We should also like to express our appreciation to Cpt. J. Stanton and Dr. Prayoth of the Dept of Veterinary Medicine, for their help in maintaining the experimental animals.

TABLE I — Haematology and blood chemistry values of serial samples from control rhesus SP9

Day	Haematology					Blood Chemistry							
	WBC /mm³	RBC x10⁶ / mm³	Reticulocytes %	Haematocrit %	Haemoglobin gm%	Bilirubin mg%		SGOT S.F. Units	SGPT S.F. Units	Alkaline Phosphatase Sigma Units	BUN mg%	Creatinine mg%	Cholesterol mg%
						Direct	Total						
0	8,700	4.81	0.5	37	11.0	0	0.1	42	33	1.1	21.0	1.1	136
7	7,600	4.46	0.4	34	10.0	0	0.1	31	20	3.2	15.0	0.9	139
14	5,800	4.35	0.0	30	10.0	0	0.1	41	15	2.0	19.7	0.8	139
20	8,000	4.44	0.4	30	9.7	0	0	30	34	4.2	13.9	0.9	146
27	7,200	3.42	0.7	30	9.4	0	0.1	29	23	3.2	11.8	1.1	146
34	8,500	4.02	0.4	33	10.2	0	0.2	35	23	2.1	14.9	0.9	141
41	7,600	4.48	0.6	34	9.8	0	0	29	18	2.8	15.9	0.9	146
55	11,800	3.67	0.8	32	9.3	0	0	27	17	5.6	12.1	1.0	113
61	9,800	4.33	0.5	33	9.9	0	0.1	26	13	4.0	16.2	0.9	127
68	8,100	4.78	0.6	34	10.1	0.1	0.3	28	16	3.2	10.7	0.8	155
75	9,100	4.77	0.8	35	10.1	0.05	0.1	18	17	4.2	9.3	1.0	145
Range	5,800–11,800	3.42–4.81	0.0–0.8	30–37	9.3–11.0	0.0–0.1	0.0–0.3	18–42	13–34	1.1–5.6	9.3–21.0	0.8–1.1	113–155

TABLE II — Haematology and blood chemistry values of serial samples from control rhesus MS37

Day	Haematology					Blood Chemistry							
	WBC /mm³	RBC x10⁶ / mm³	Reticu— locytes %	Haemato— crit %	Haemo— globin gm%	Bilirubin mg%		SGOT S.F. Units	SGPT S.F. Units	Alkaline Phospha— tase Sigma Units	BUN mg%	Creati— nine mg%	Choles— terol mg%
						Direct	Total						
0	10,700	3.90	0.2	32	7.6		0	20	15	9.2	14.2	0.8	122
7	8,500	4.30	0.2	30	7.8		0.1	24	17	6.0	10.1		121
21	6,600	3.80	0.3	25	6.6		0.2	48			11.8	0.6	129
29	6,900	4.52	0.2	27	7.4	0.1	0.2	35	25		15.3	0.8	117
35	5,500	3.01	0.4	28	7.2	0	0.1	37	24	6.0	10.3	1.1	133
42	10,200	4.66	0.2	39	8.7	0	0	41	20		8.5	1.0	121
49	7,200	3.91	0.4	30	7.6	0.2	0.3	35	20		17.6	1.1	125
56			0.3	28	7.2	0	0.1	47	21	5.8	9.3	1.3	116
62	5,800	3.41	0.5	24	6.0	0	0.1	40	14	6.2	11.0	0.8	138
69	5,800	3.35	0	26	6.0	0.1	0.1	51	12	6.1	14.9	1.3	162
75	6,200	4.58	0.4	29	7.2	0	0	47	17	9.4	11.7	1.2	136
83	6,600	4.22	0.3	30	7.6	0	0	31	19	7.8	12.8	0.9	114
89	9,000	4.22	0.2	30	7.4	0.05	0.3	42	23	8.8	14.3	1.1	131
96	9,100	3.99	0.2	27	6.5	0	0	53	25	10.0	18.3	1.2	112
103	5,700	3.90	0.4	26	6.5	0	0.1	48	29	9.8	15.6	0.9	138
116	6,000	5.17	0.2	28	7.8	0	0	29	15	11.8	19.4	0.8	128
123	11,100	4.36	0.3	30	7.8	0.05	0.1	42	20	9.6	14.6	1.2	130
130	6,700	4.38	0.4	30	7.1	0	0	23	17	13.8	12.0	1.2	126
Range	5,500—11,100	3.01—5.17	0.0—0.5	24—39	6.0—8.7	0.0—0.2	0.0—0.3	20—53	12—29	5.8—13.8	8.5—19.4	0.6—1.3	112—162

TABLE III — Haematology and blood chemistry values of serial samples from control rhesus KL2

Day	Haematology					Blood Chemistry							
	WBC /mm³	RBC x10⁶ / mm³	Reticu—locytes %	Haemato—crit %	Haemo—globin gm%	Bilirubin mg%		SGOT S.F. Units	SGPT S.F. Units	Alkaline Phospha—tase Sigma Units	BUN mg%	Creati—nine mg%	Choles—terol mg%
						Direct	Total						
0	9,400	4.41	0.3	34	10.3	.1	.3	36	24		18.4	.8	154
11	6,100	4.05	0.3	34	9.7	0	.1	47	24	16.6	21.6	.7	154
18	7,000	3.52	0.2	33	9.1	0	.1	48	22	16.2	19.7	1.1	170
25	5,200	4.14	0.3	33	9.3	0	0	43	22	19.0	18.8	0.9	158
31						0	.1	38	25	17.6	19.3	0.8	162
37	5,800	4.28	0.6	32	9.2	0	.1	56	24	18.6	13.2	1.1	162
44	8,700	4.51	1.2	35	9.7	.05	.3	52	28	19.8	13.2	0.7	170
51	8,700	4.10	.4	34	9.5	.05	.1	41	23	15.2	14.4	0.9	170
58	8,400	4.65	1.3	28	9.4	.10	.2	47	24	11.7	17.9	0.8	162
65		4.40	.5	35	10.4	0	.1	31	17	18.2	17.9	0.9	144
Range	5,200—9,400	3.52—4.65	0.2—1.3	28—35	9.1—10.4	0—.1	0—.3	31—56	17—28	11.7—19.8	13.2—21.6	0.7—1.1	144—170

TABLE IV — Haematology and blood chemistry values of serial samples from control rhesus SP1

Day	Haematology					Blood Chemistry							
	WBC /mm³	RBC x10⁶ / mm³	Reticu— locytes %	Haemato— crit %	Haemo— globin gm%	Bilirubin mg%		SGOT S.F. Units	SGPT S.F. Units	Alkaline Phospha— tase Sigma Units	BUN mg%	Creati— nine mg%	Choles— terol mg%
						Direct	Total						
0	5,400	4.10	0.7	32	9.4	0	0	55	16	8.8	17.8	1.2	146
8	8,200	4.24	1.0	31	9.7	.1	.2	71	14	8.6	15.8	.9	138
15	8,100	4.70	1.3	32	9.4	0	.1	67	17	7.8	21.8	.7	133
21	6,000	4.37	1.4	34	9.9	0	.1	66	15		17.9	1.2	154
27	8,000	4.92	1.5	35	10.6	.05	.1	70	20	12.0	19.2	1.0	154
34	4,300	3.87	1.0	31	9.3	0	0	67	18	9.0	17.8	0.8	146
41	5,700	3.94	1.4	31	9.0	.2	.4	74	22	11.6	17.9	1.2	146
48	8,400	4.53	0.7	35	9.8	0	.1	66	24	8.2	19.4	.9	138
55	8,000	4.65	0.3	32	9.7	0	0	53	12	11.8	14.8	1.3	142
Range	4,300— 8,400	3.87— 4.92	0.3— 1.5	31— 35	9.0— 10.6	0— .2	0— .4	53— 74	12— 24	7.8— 12.0	14.8— 21.8	.7— 1.3	133— 154

TABLE V — Haematology and blood chemistry values for monkeys prior to infection

Day	Haematology					Blood Chemistry							
	WBC /mm³	RBC x10⁶ / mm³	Reticulocytes %	Haematocrit %	Haemoglobin gm%	Bilirubin mg%		SGOT S.F. Units	SGPT S.F. Units	Alkaline Phosphatase Sigma Units	BUN mg%	Creatinine mg%	Cholesterol mg%
						Direct	Total						
KL14	10,900	4.0	1.4	32	9.3	.05	0.1	37	22	19.8	24.5	0.9	168
KL3	11,200	5.9	1.2	37	11.0	0	0.1	34	14	17.6	13.4	0.9	182
KL2	8,400	4.4	.5	35	10.4	0	0.1	31	17	18.2	17.9	0.9	144
KL12	15,800	5.1	.4	36	10.1	.05	0.2	43	26	17.0	19.2	1.1	178
	12,500	5.7	.3	37	10.5	.05	0.1	52	23	17.6	16.7	1.0	178
	11,400	4.4	1.7	36	10.1	0	0.1	35	19	17.6	15.0	1.2	184
KL13	9,200	4.8	.3	38	11	.05	0.2	48	28	21.6	14.5	1.3	162
	6,600	5.2	.5	38	11.2	0.1	0.1	73	26	24.0	17.4	1.3	172
	5,700	5.4	.6	34	10.1	—	0.1	60	25	22.0	14.7	1.0	160
KL1	13,900	5.1	1.0	38	10.4	—	0.1	46	31	15.8	15.1	0.9	162
SP2	20,600	5.0	—	35	11.3	—	—	—	—	—	17.0	0.6	—
SP4	11,200	6.3	—	—	—	—	—	—	—	—	15.9	—	—
SP5	7,000	5.1	—	33	10.2	—	—	—	—	—	15.2	0.9	—
	8,400	4.7	—	36	10.2	—	—	—	—	—	13.2	0.9	—
	7,000	5.6	—	36	10.2	—	—	—	—	—	13.3	—	—
SP1	8,000	4.7	0.3	32	9.7	0	0	53	12	11.8	14.8	1.3	142
SP9	8,700	4.8	0.5	37	11.0	0	0.1	42	33	1.8	21.0	1.1	136
MS18	6,400	4.5	1.0	33	8.9	0.1	0.2	40	29	6.6	16.0	1.2	105
MS37	10,700	3.9	.2	32	7.6	0	0	20	15	9.2	14.2	0.8	122
MS2	8,300	5.1	.5	40	12.0	0.2	0.4	48	33	6.4	13.4	1.8	162
Range	5,700—15,800	3.9—6.3	0.2—1.7	32—40	7.6—12.0	0—.2	0—0.4	31—73	12—33	1.8—24.0	13.2—24.5	0.6—1.8	105—184

Fig. 1 Parasitaemia, haematologic and blood chemistries of KL13

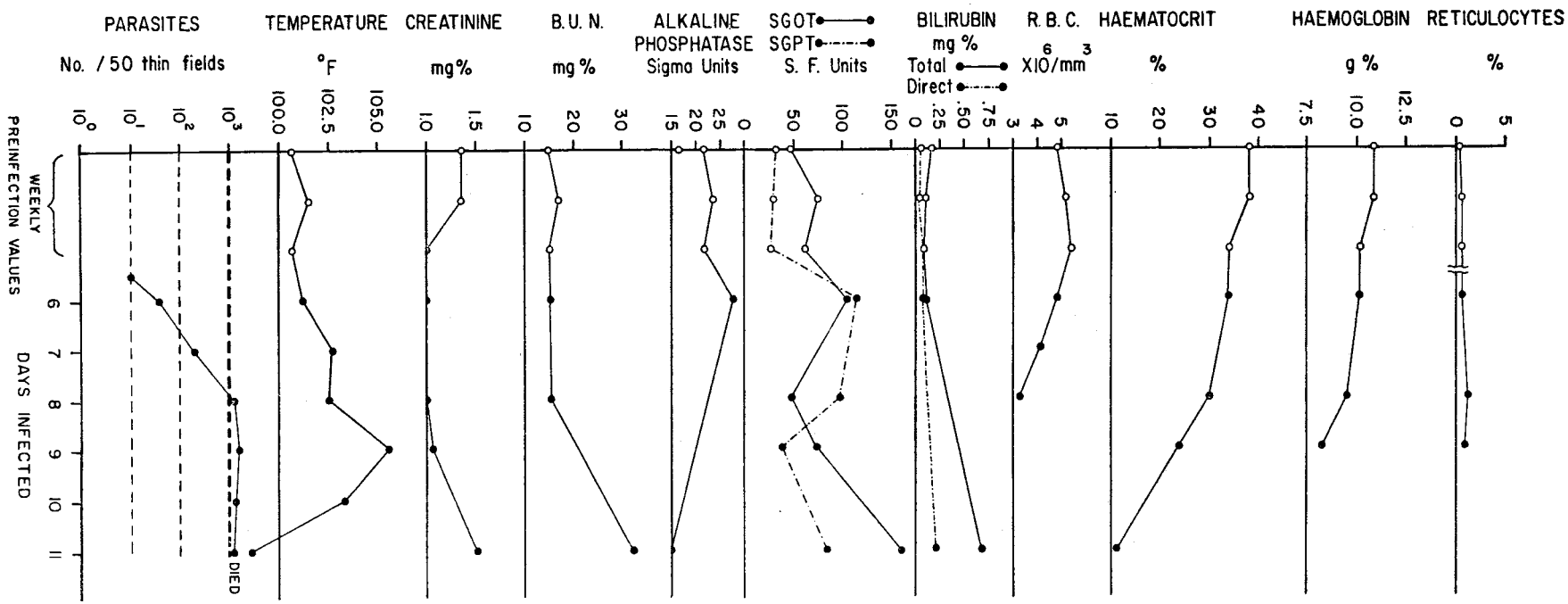


Fig. 2. Liver KL13 showing of centrilobular necrosis

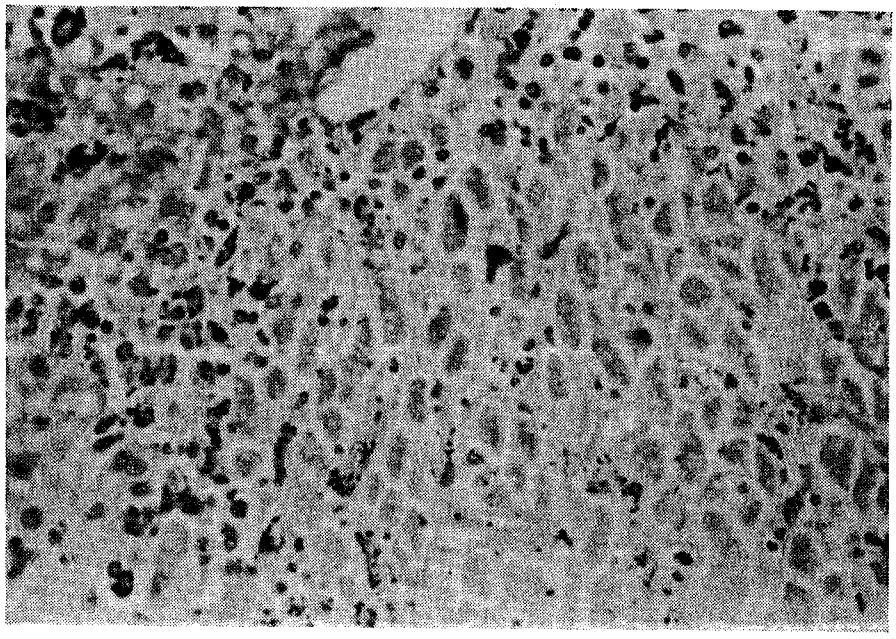
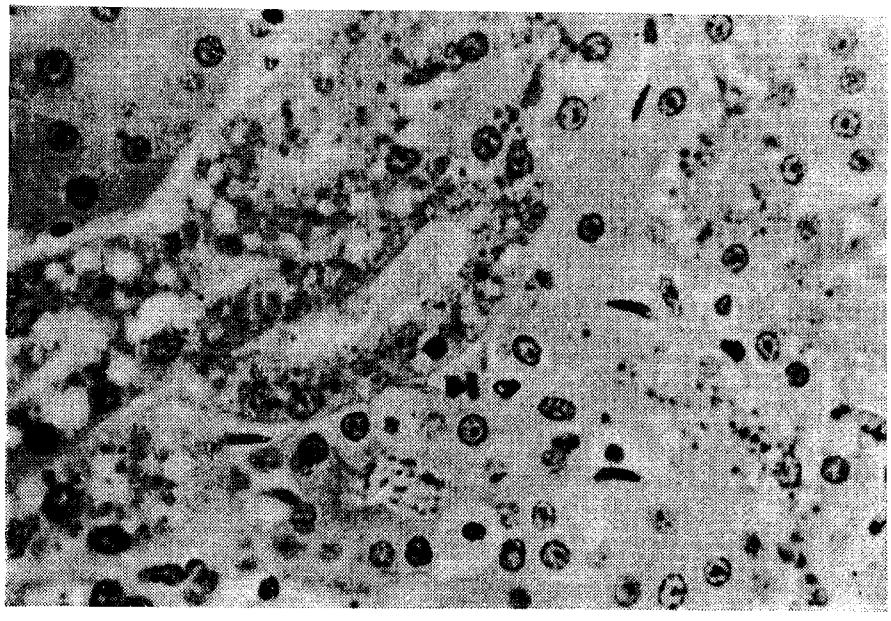


Fig. 3. Kidney of KL13 showing hyaline droplet degeneration, hemoglobin casts and fluid in Bowman's space



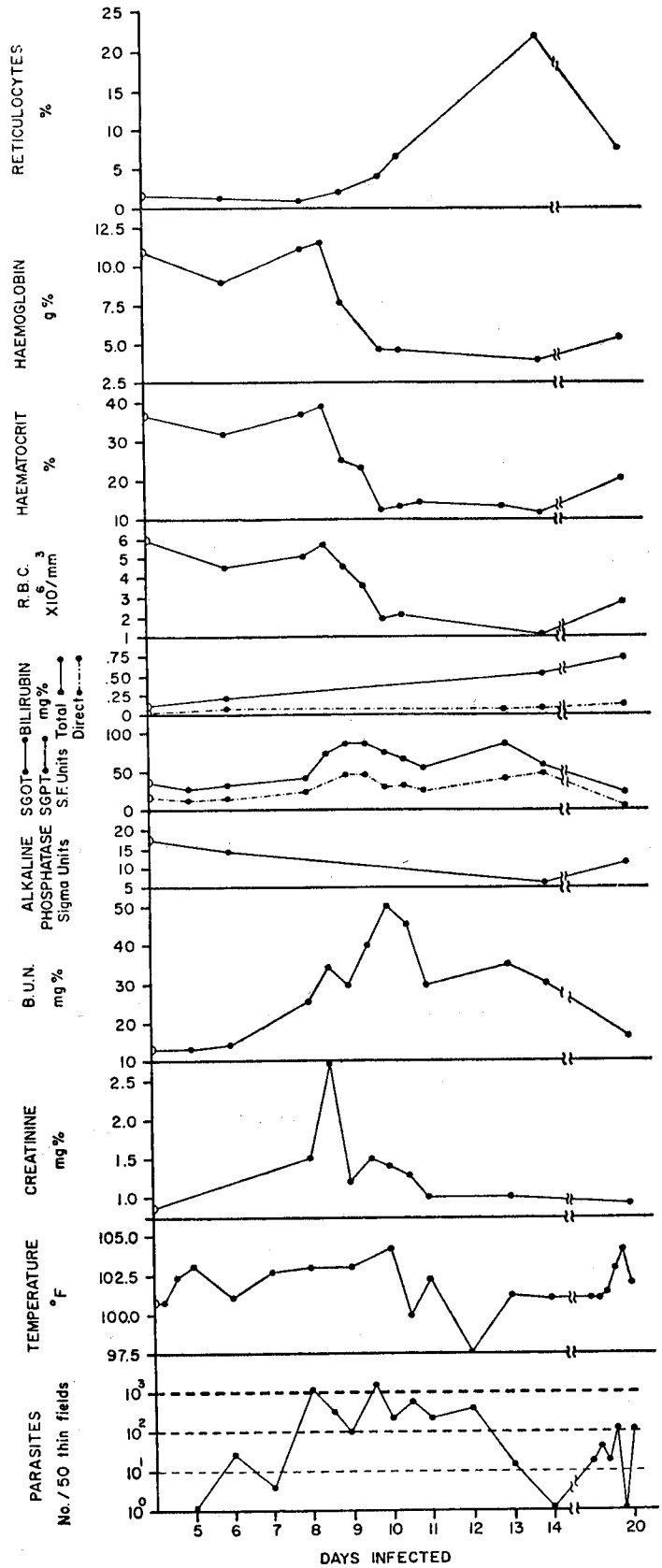


Fig. 4. Parasitaemia, haematologic and blood chemistries of KL3

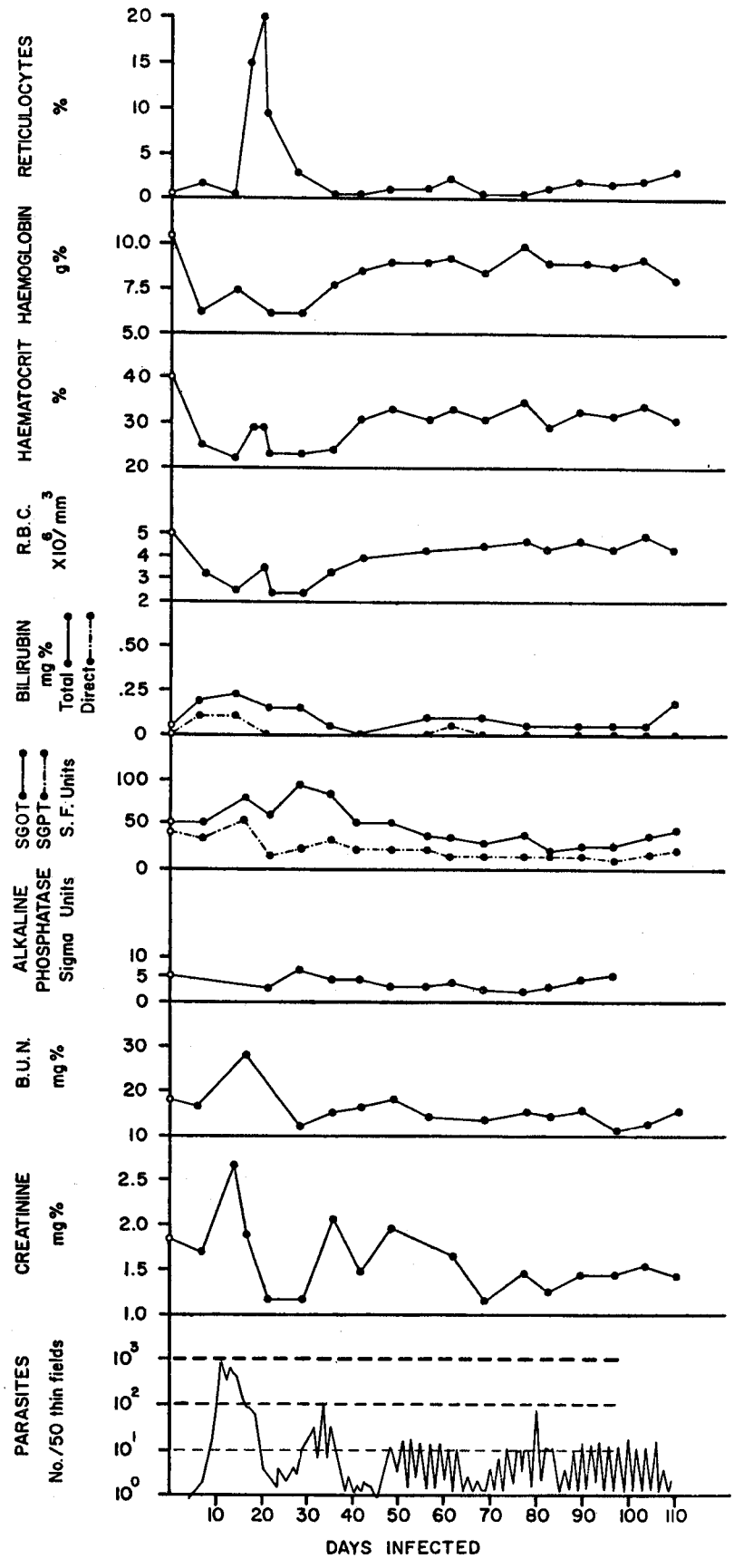


Fig. 5. Parasitaemia, haematologic and blood chemistries of MS2

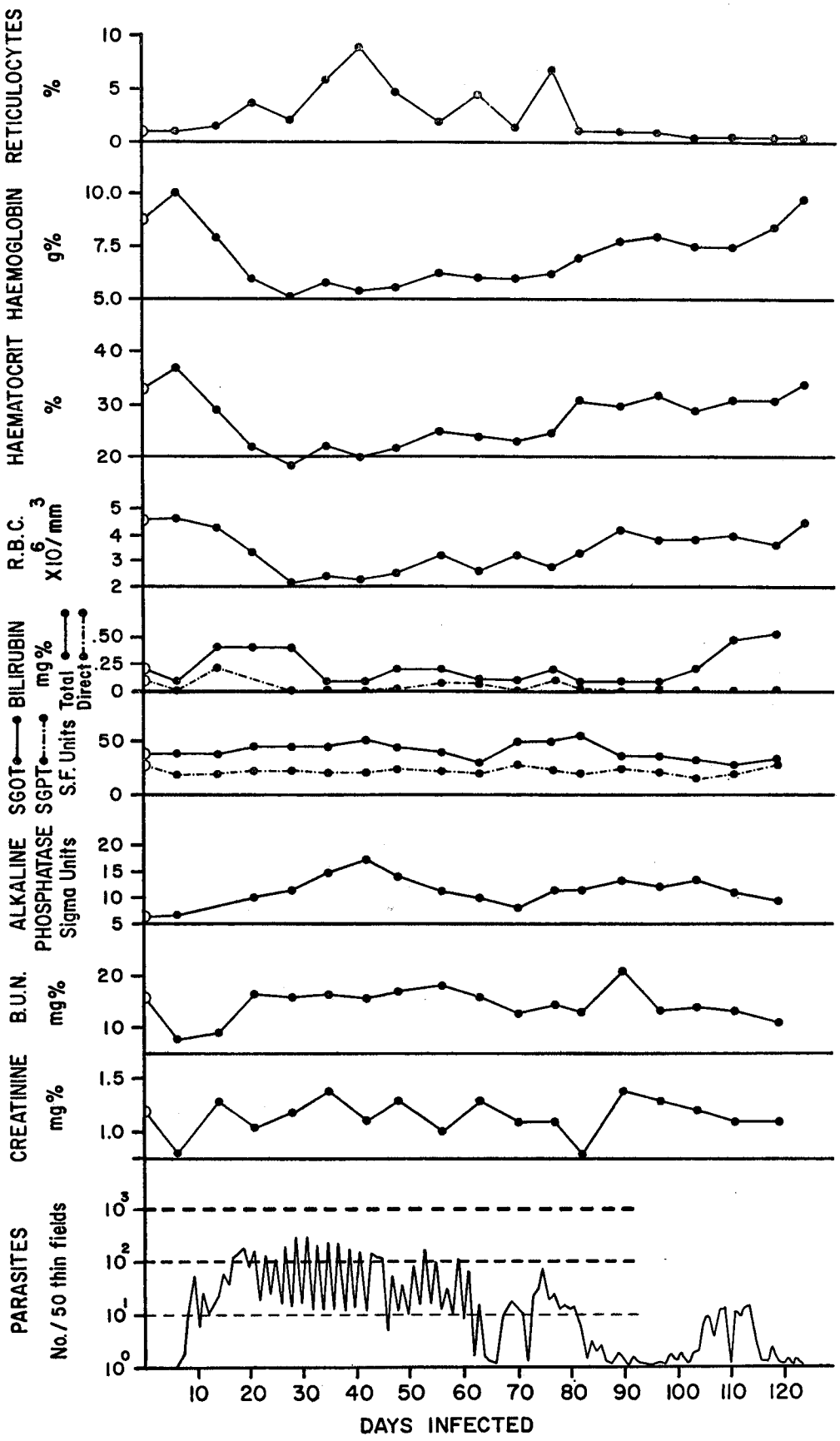


Fig. 6. Parasitaemia, haematologic and blood chemistries of MS18

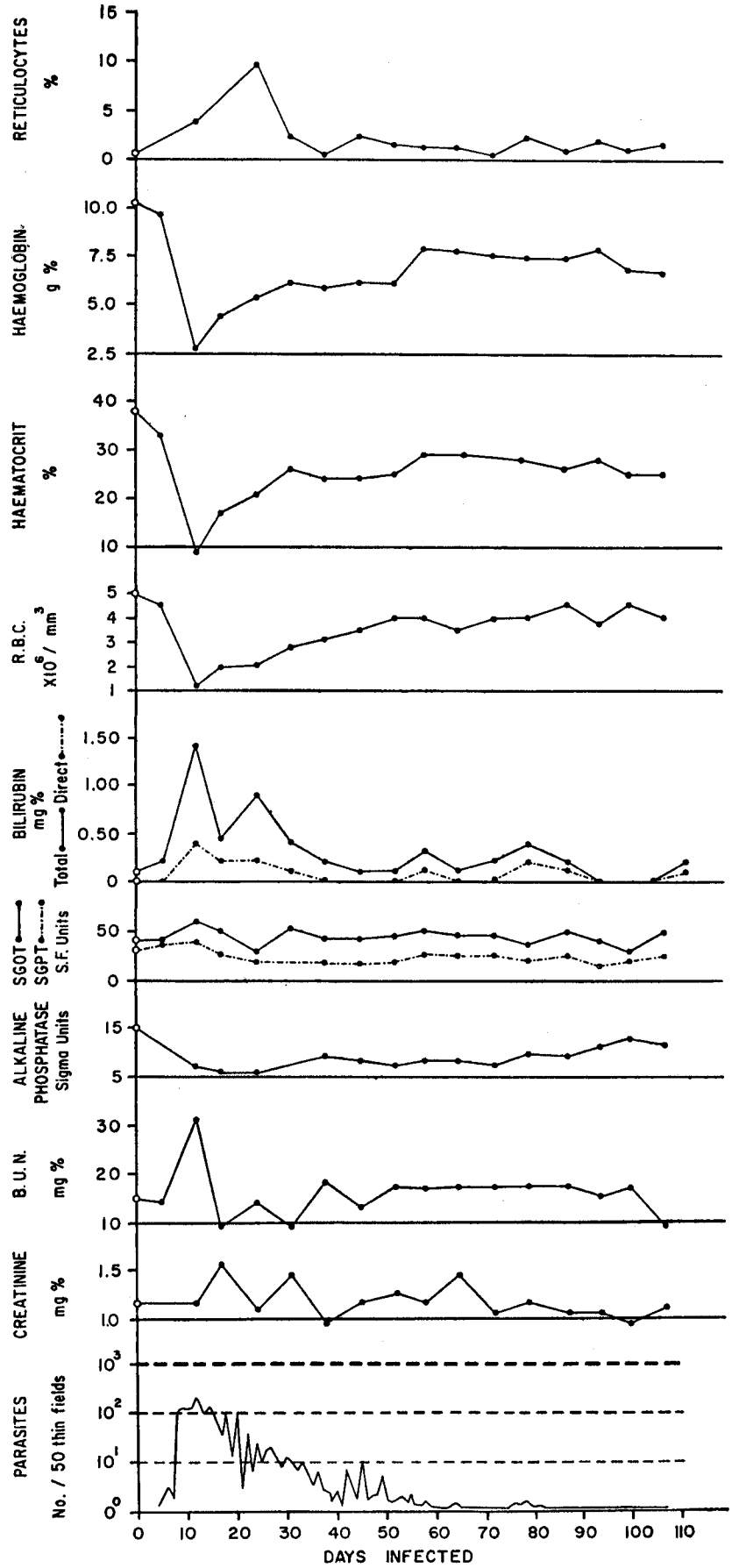


Fig. 7. Parasitaemia, haematologic and blood chemistries of KL1

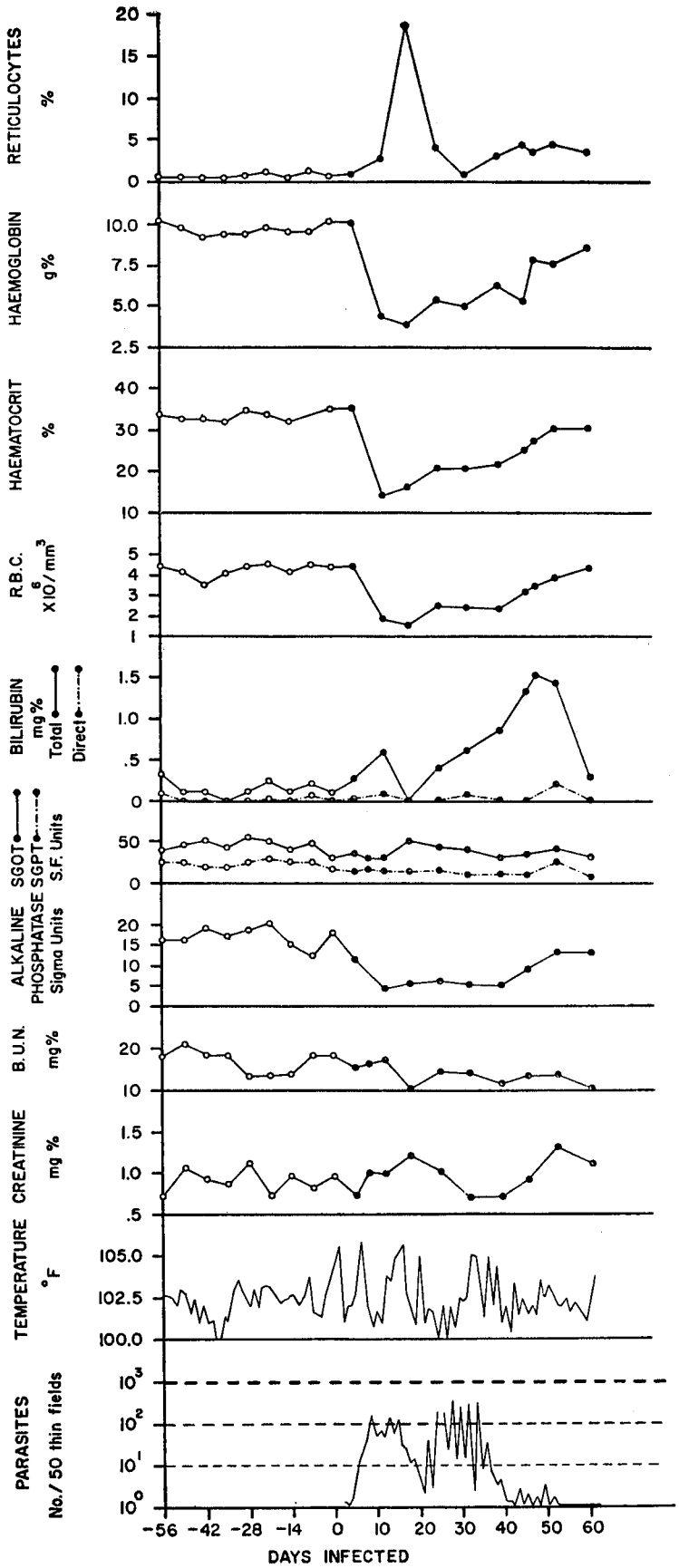


Fig. 8 Parasitaemia, haematologic and blood chemistries of KL2