

PLATE I

An untreated pig with advanced
hereditary lymphosarcoma.



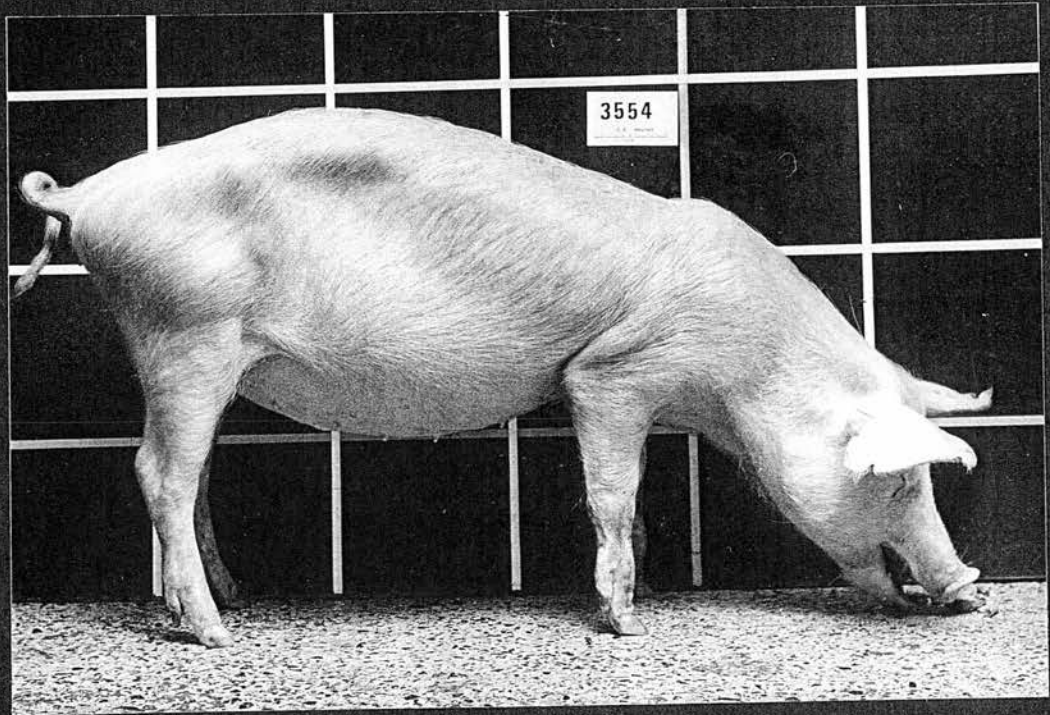


PLATE 2

A lymphosarcoma case (3637) before
treatment with prednisolone.

PLATE 3

The same lymphosarcoma case after
treatment with prednisolone.

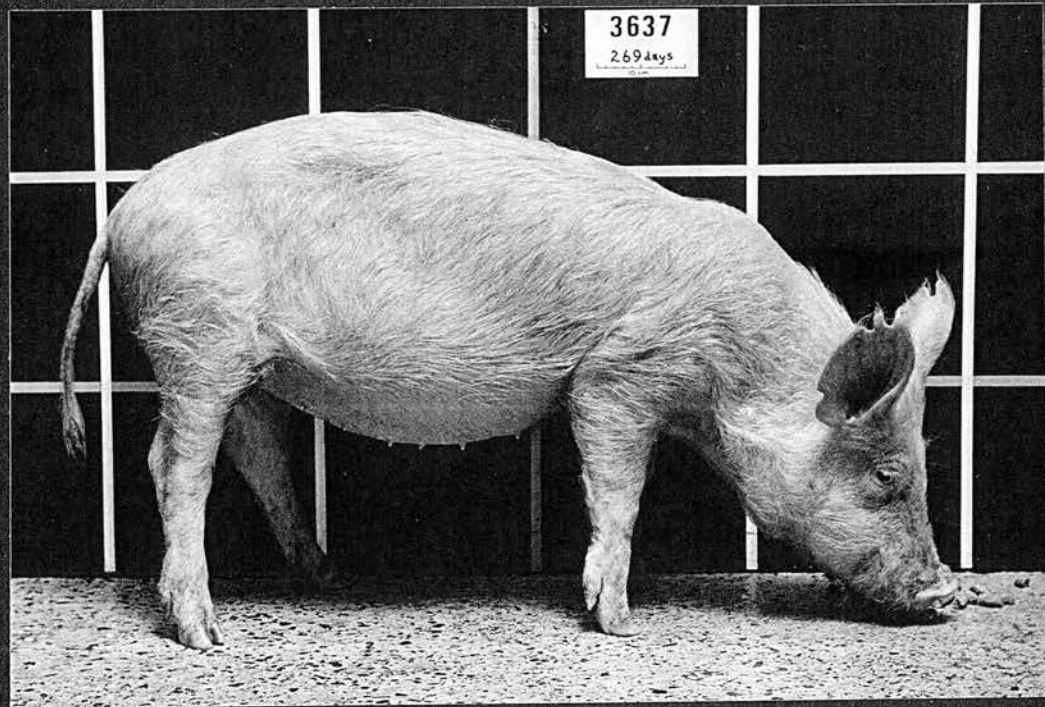
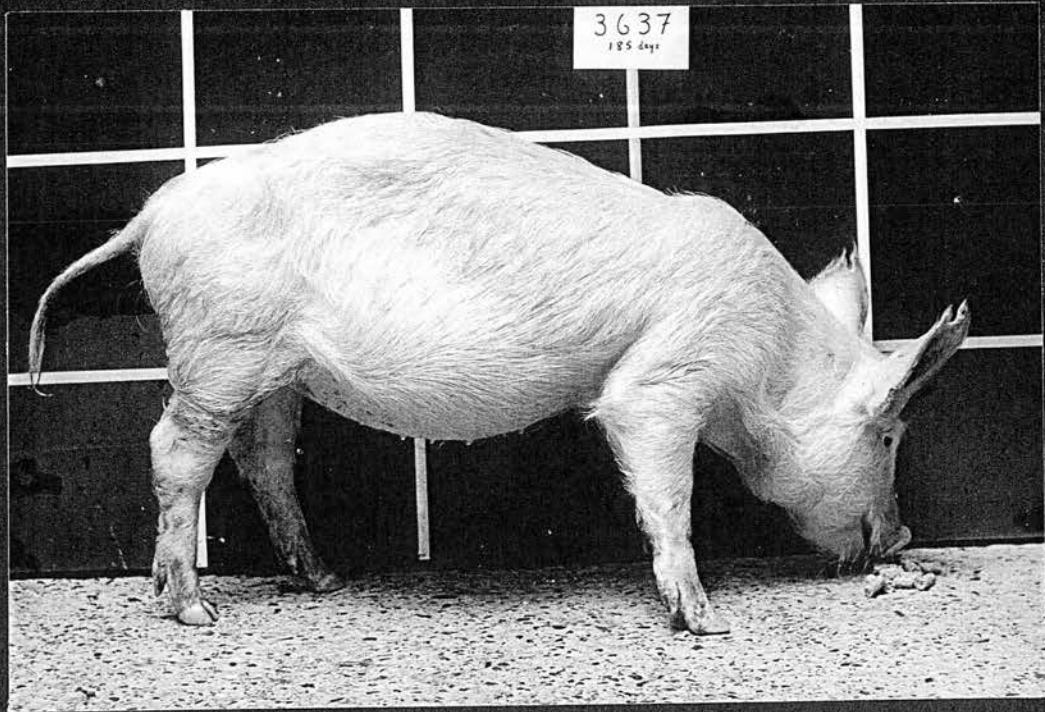


PLATE 4 Inguinal lymph nodes of
pig 3637 before treatment.

PLATE 5 Inguinal lymph nodes of
pig 3637 after prednisolone.

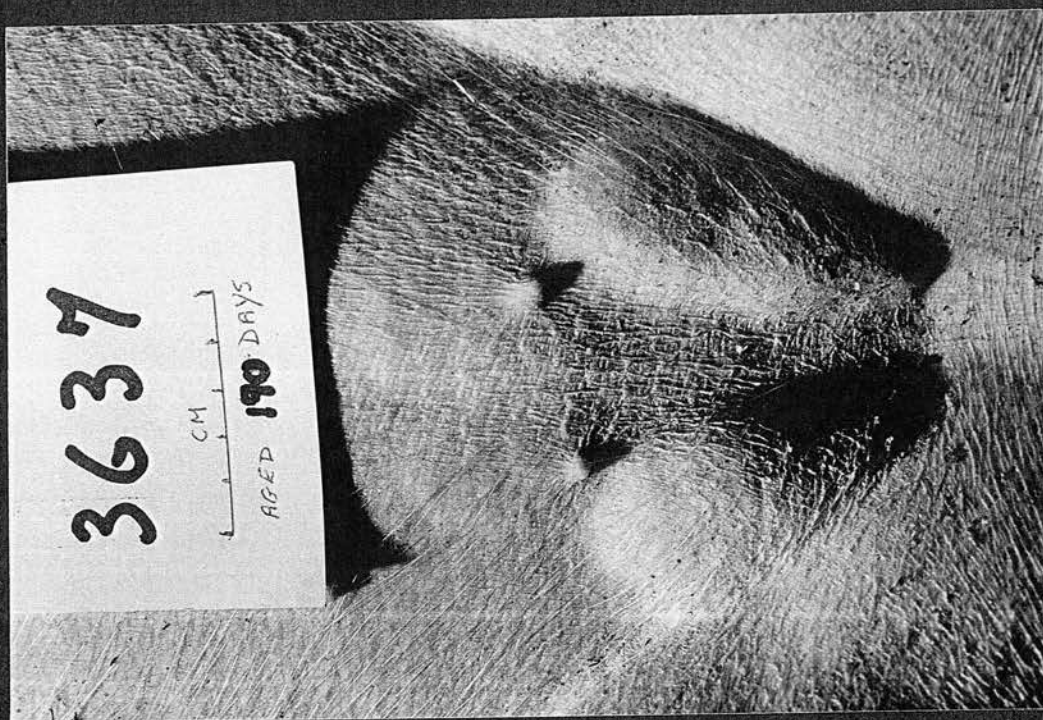


PLATE 6 Haemorrhages on abdomen of non-
lymphosarcomatous pig 41 which died after
4mg/kg adriamycin.



41

9 days after

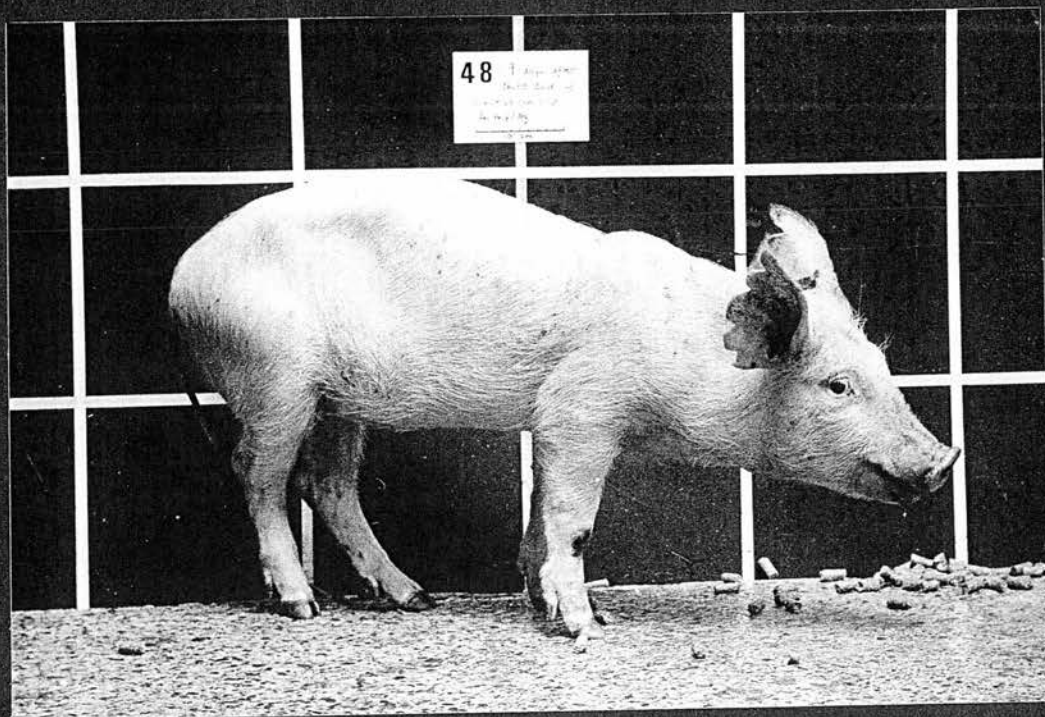
4 mg/kg

Doxorubicin i/v.

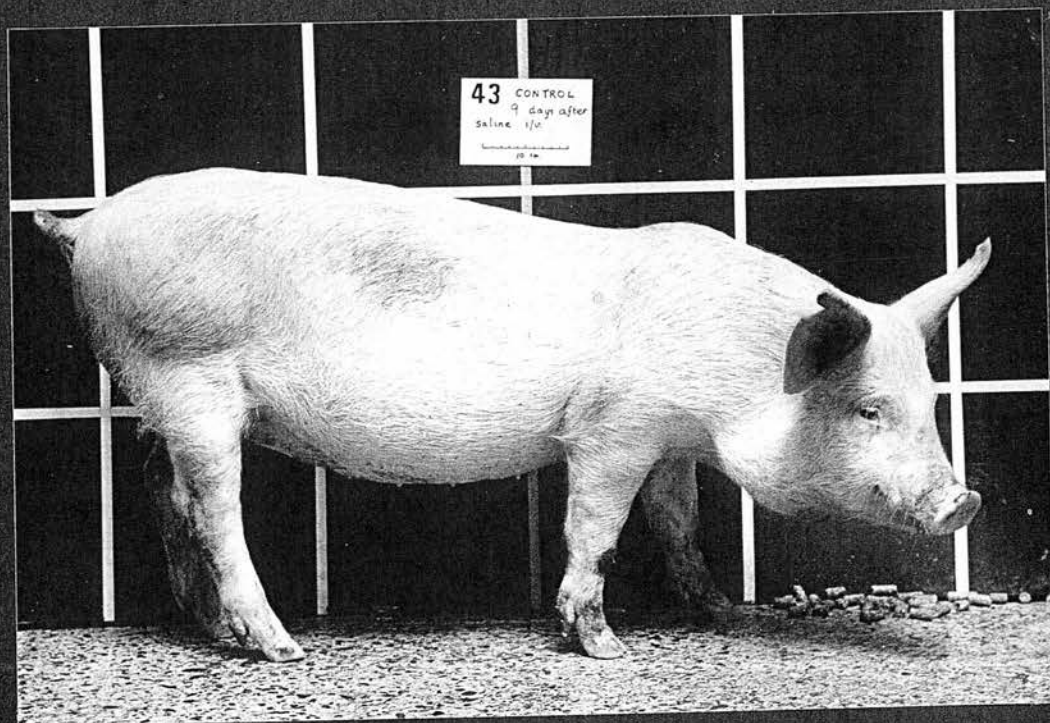
10 cm

PLATE 7 Non-lymphosarcomatous pig (48)
after three doses of 4mg/kg
adriamycin.

PLATE 8 Normal saline-treated control (43)



48



43 CONTROL
9 days after
saline 1/10

PLATE 9 Lymphosarcoma case 3785 before
treatment with adriamycin.

PLATE 10 The same lymphosarcoma case after
treatment with 2mg/kg adriamycin
shortly before it was destroyed.
The skin was bright yellow.

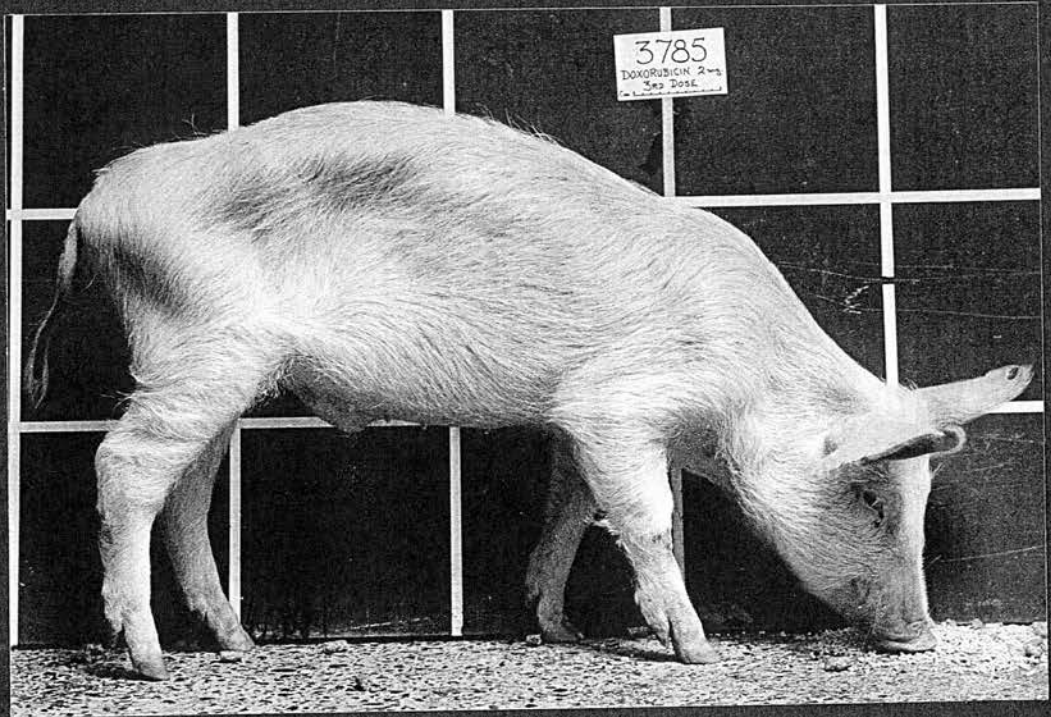
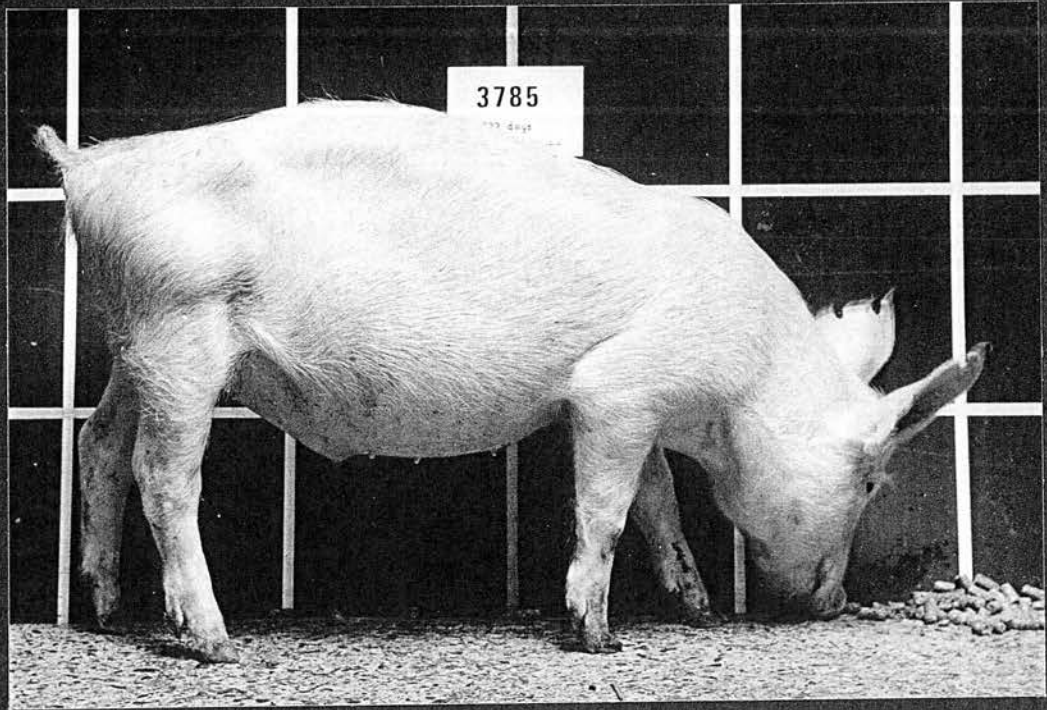


PLATE 11

Lymphosarcoma case 192 before
treatment.

PLATE 12

The same pig after eight doses
of 1mg/kg adriamycin.

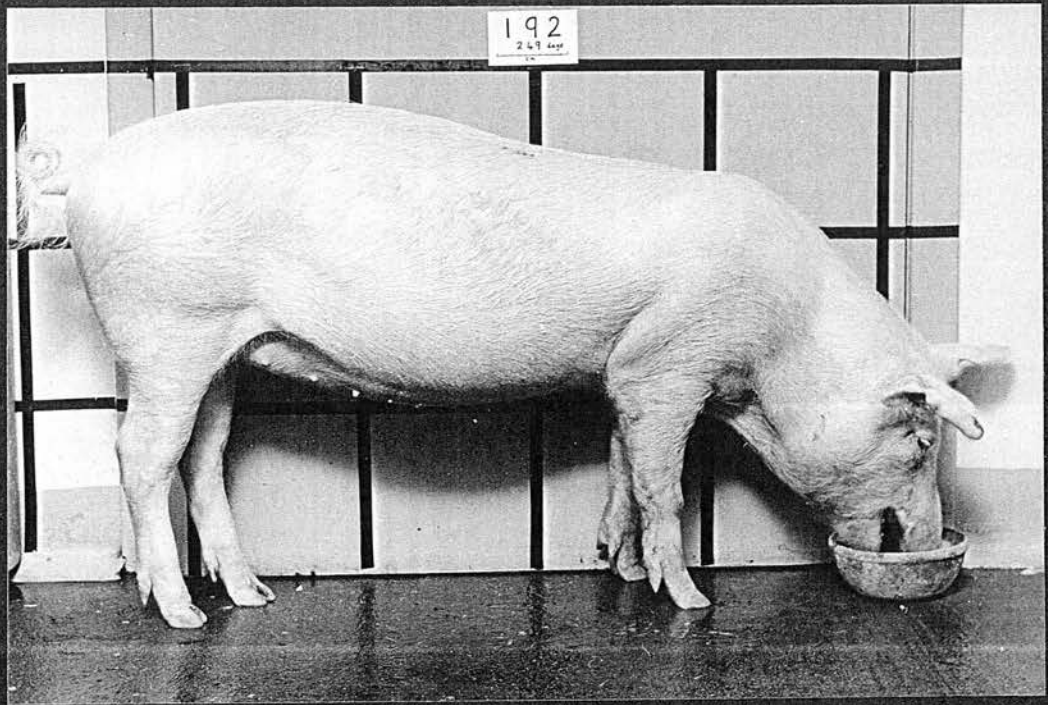
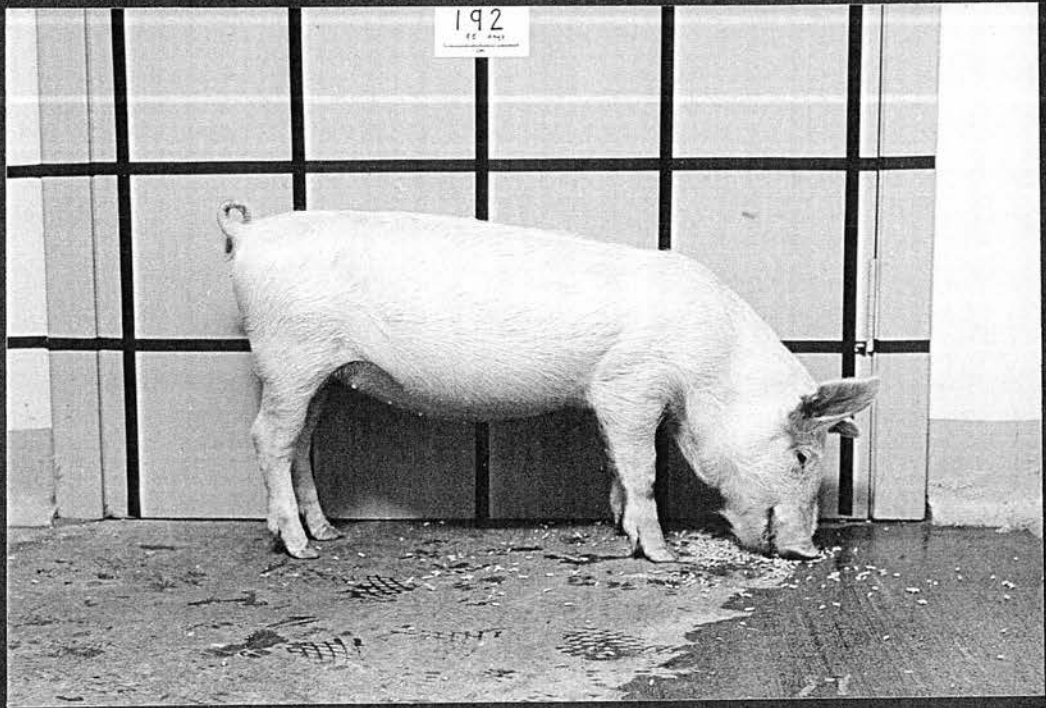


PLATE 13

Lymphosarcoma case 194 before
treatment.

PLATE 14

The same pig after eight doses of
1mg/kg adriamycin.

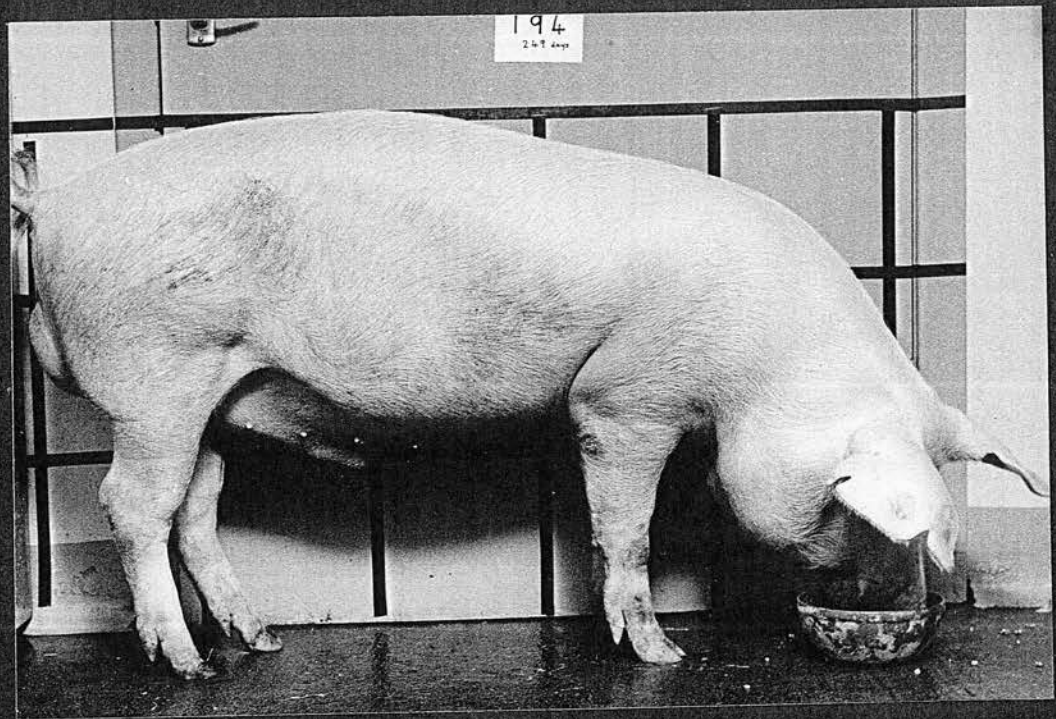
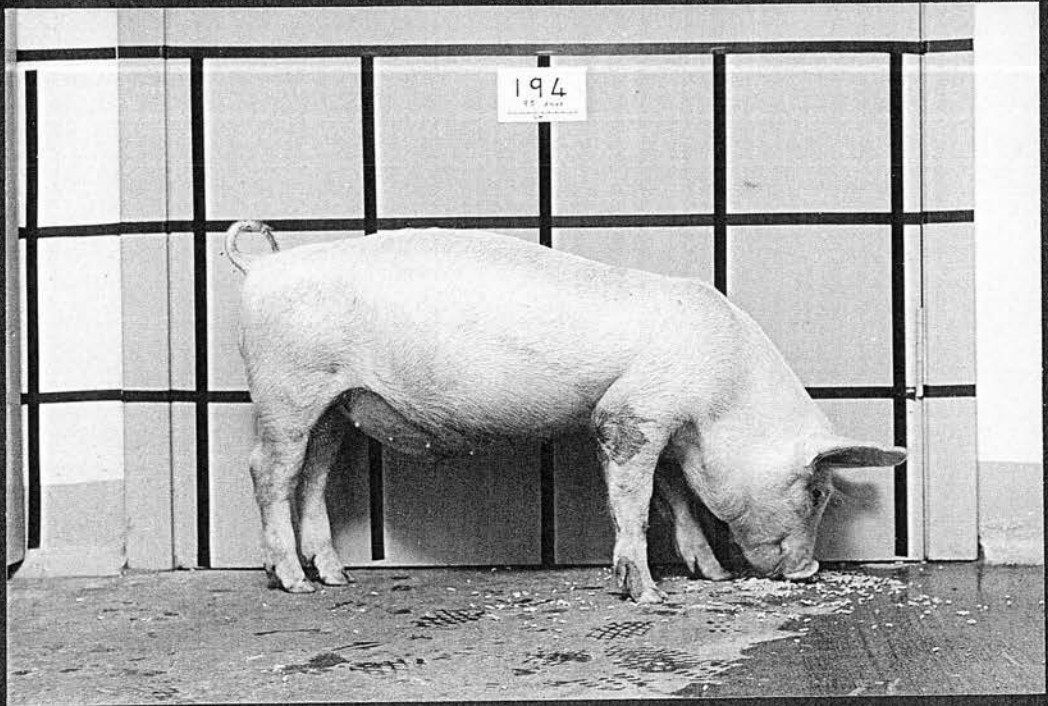


PLATE 15

Lymphosarcoma case 192 - normal.

PLATE 16

Lymphosarcoma case 192 - right ear 6
days after accidental intra-arterial
injection of adriamycin.

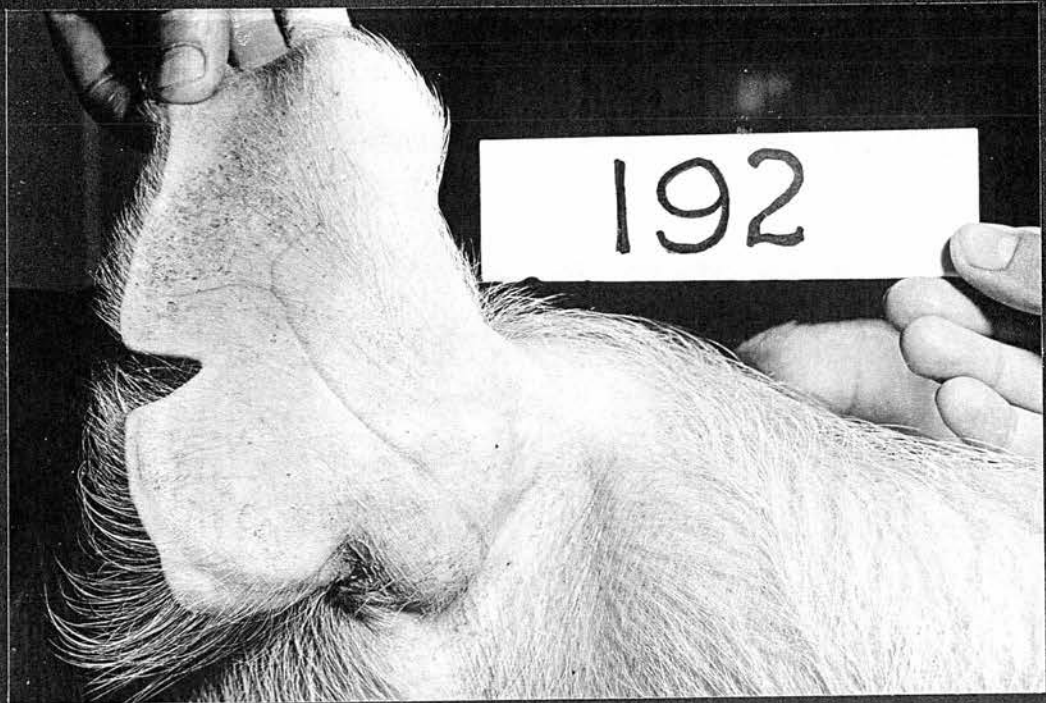


PLATE 17

Lymphosarcoma case 192 - right ear
7 weeks after accidental intra-
arterial injection of adriamycin.



192

249 days

cm

PLATE 18

Lymphosarcoma case 362 before treatment.

PLATE 19

Pig 362 at the end of treatment with cyclophosphamide.

PLATE 20

Pig 362 in relapse.

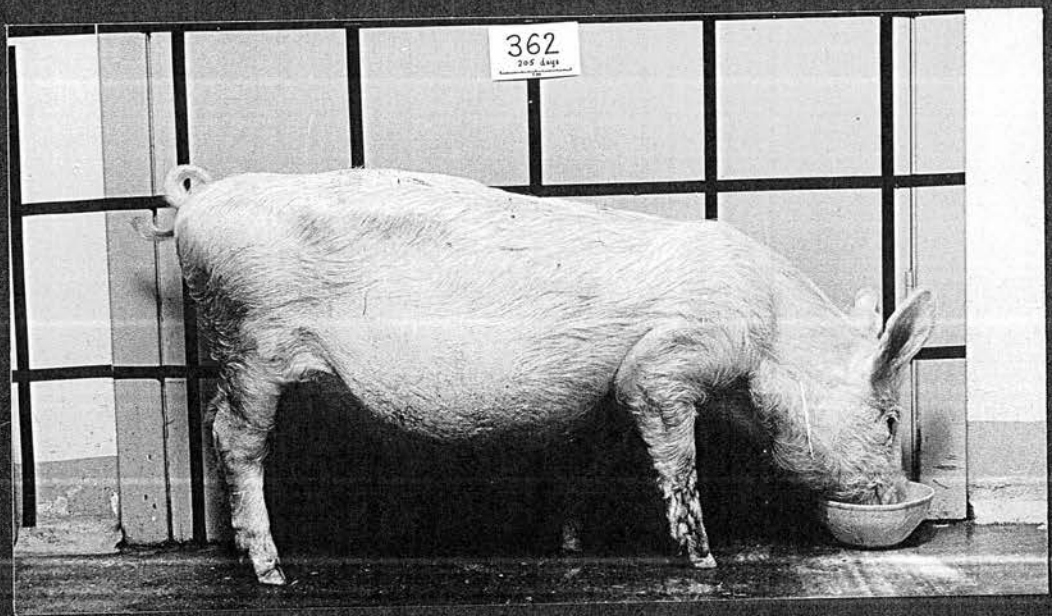
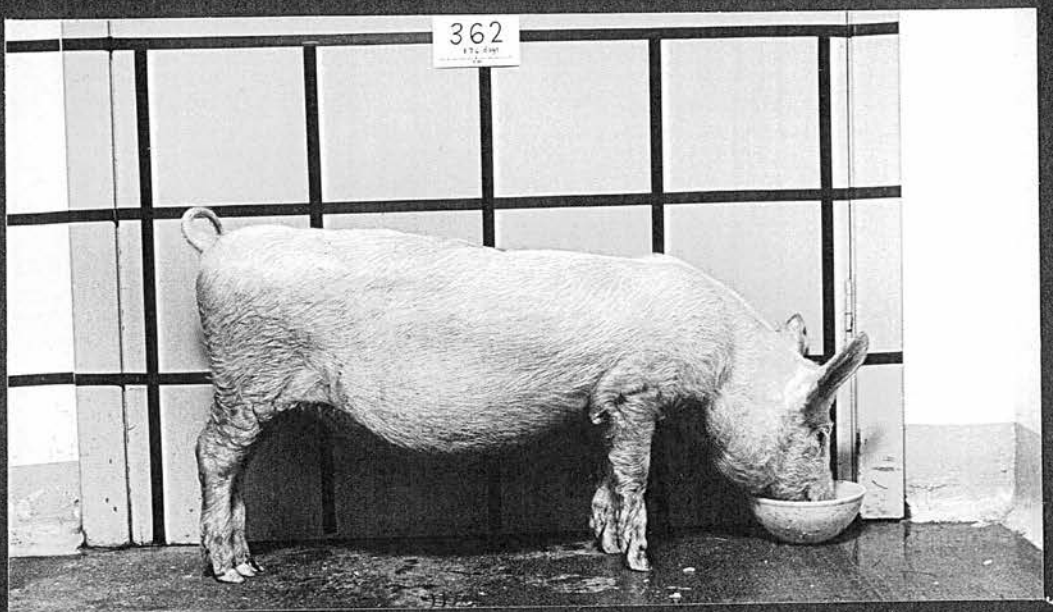
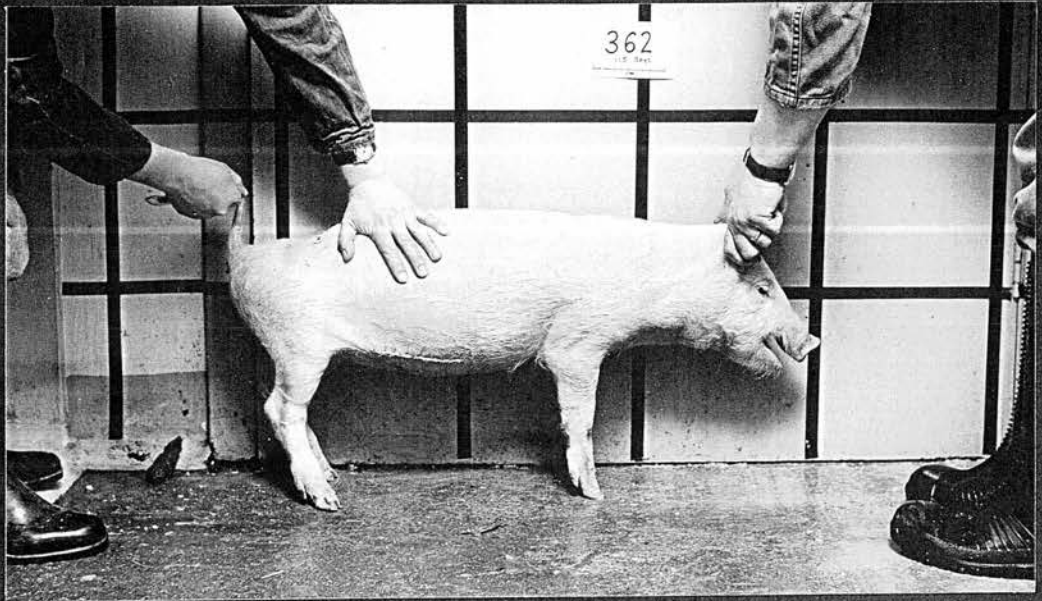


PLATE 21 Inguinal lymph nodes of 362 before treatment.

PLATE 22 Nodes of 362 at the end of cyclophosphamide treatment.

PLATE 23 Nodes of pig 362 in relapse.

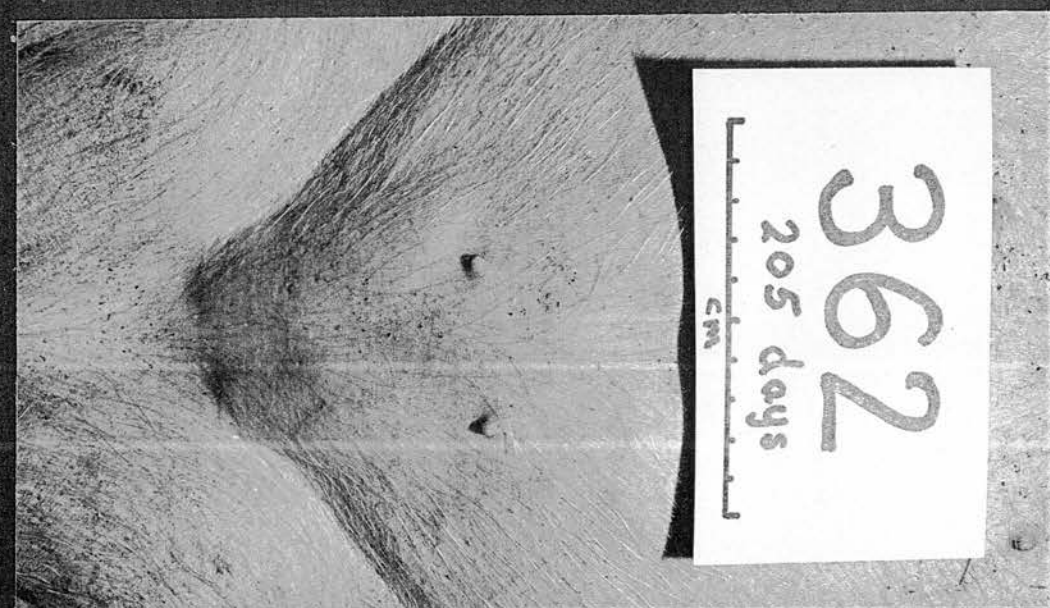
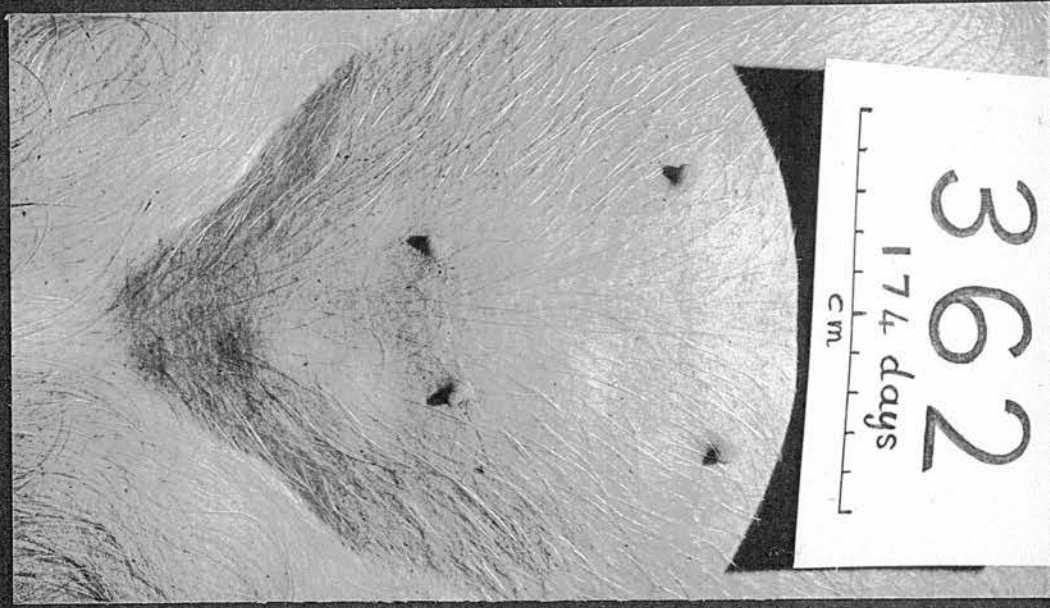
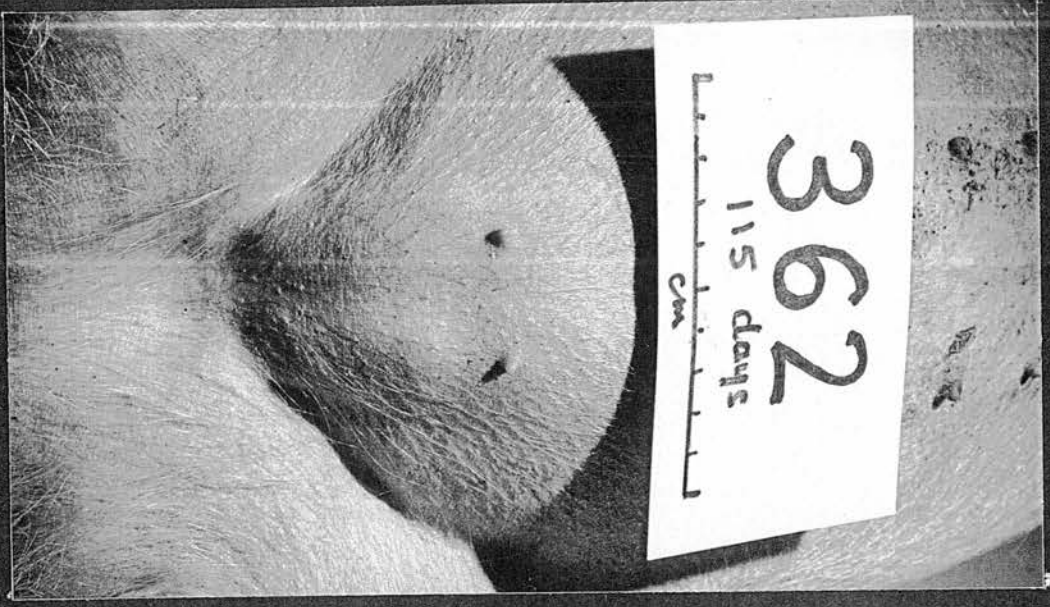
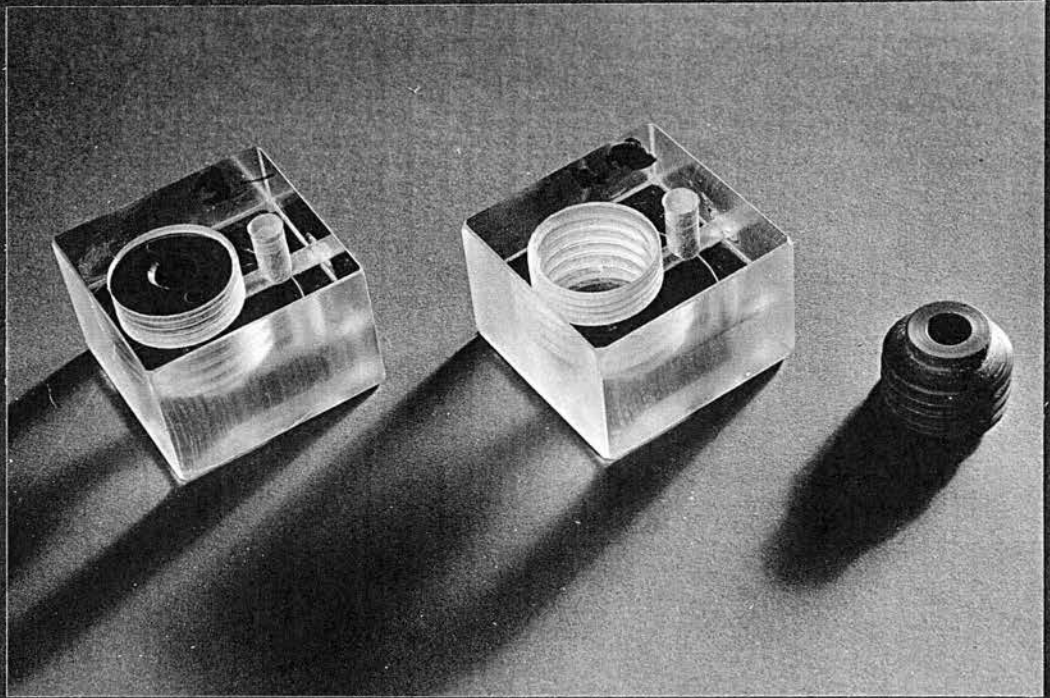


PLATE 24

Chemotaxis chambers.



APPENDIX I.

APPENDIX I

TABLE I

PREDNISOLONE: NORMAL PIGS - CLINICAL RECORDS

Fig No. 2 - SALINE TREATED CONTROL

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	13	++	+++	-	
-1	13	++	+++	+	
Start of Dosing					
1	15	+++	+++	-	
2	16	++	+++	-	thinner
3	17	+++	+++	-	
4	18	+++	+++	-	
5	20	++	+++	-	
6	22	+++	+++	-	

DESTROYED - END OF TREATMENT

APPENDIX I

TABLE 2

FIG NO. 4 - SALINE - TREATED CONTROL

WEEKS	BODY WT. (Kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	16	+++	+++	-	
-1	16	+++	+++	-	
Start of Dosing					
1	20.5	+++	+++	-	
2	21	++	+++	-	
3	23.5	+++	+++	-	
4	26	+++	+++	-	
5	28.5	+++	+++	-	
6	30.5	+++	+++	-	
End of Treatment					
7	33	+++	+++	-	
8	39	+++	+++	-	
9	42	+++	+++	-	
10	45	+++	+++	-	
11	48.5	+++	+++	-	
At autopsy	49	DESTROYED	+++	-	

APPENDIX I

TABLE 3

FIG NO. 1 - 2mg/kg/day prednisolone

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	15	+++	+++	-	
-1	17	+++	+++	-	
Start of Dosing					
1	19.5	+++	+++	-	
2	20.5	++	+++	-	drinking more
3	22	+++	+++	-	pendulous abdomen
4	25	+++	+++	-	
5	26.5	+++	+++	-	
6	27	+++	+++	-	

DESTROYED - END OF TREATMENT

APPENDIX I

TABLE 4

PIG No. 6 - 2mg/kg/day prednisolone

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	12	+++	+++	-	
-1	13	+++	+++	-	
Start of Dosing					
1	14.5	+++	+++	-	
2	15	+++	+++	-	Drinking more, thinner
3	17	+++	+++	-	
4	18.5	+++	+++	-	
5	21	+++	+++	-	
6	22	+++	+++	-	
End of Treatment					
7	25	+++	+++	-	
8	29	+++	+++	-	
9	32	+++	+++	-	
10	34.5	+++	+++	-	
11	37	+++	+++	-	
At autopsy	40	DESTROYED			

APPENDIX I

TABLE 5

Pig No. 5 - 4mg/kg/day prednisolone

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	16	+++	+++	-	
-1	18	+++	+++	-	
Start of Dosing					
1	21	+++	+++	-	drinking more
2	22	+++	+++	-	very pendulous abdomen urine scalding
3	23	+++	+++	-	rectal eversion
4	25.5	+++	+++	-	rectal eversion more pronounced
5	27	+++	+++	-	
6	29	+++	+++	-	

DESTROYED - END OF TREATMENT.

APPENDIX I

TABLE 6

Pig No. 8 - 4mg/kg/day prednisolone

WEEKS	BODY WT (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	18	+++	+++	-	
-1	21	+++	+++	-	
Start of Dosing					
1	23	+++	+++	-	
2	24	+++	+++	-	Drinking more
3	25.5	+++	+++	-	Pendulous abdomen
4	29	+++	+++	-	
5	32	+++	+++	-	Rectal Eversion
6	33	+++	+++	-	
End of Treatment					
7	34.5	+++	+++	-	
8	40	+++	+++	-	
9	44.5	+++	+++	-	
10	46.5	+++	+++	-	
11	49	+++	+++	-	
At Autopsy	52.5	DESTROYED			

APPENDIX I

TABLE 7

Pig No. 3 - 6mg/kg/day prednisolone

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	15	+++	+++	-	
-1	17	+++	+++	-	
Start of Dosing					
1	19	+++	+++	-	
2	21	+++	+++	-	Drinking more
3	22	+++	+++	-	Pendulous abdomen
4	24.5	+++	+++	-	Slight rectal eversion
5	24.5	+++	+++	-	
6	25.5	+++	+++	-	
End of Treatment					
7	28	+++	+++	-	
8	32	+++	+++	-	
9	36.5	+++	+++	-	
10	37.5	+++	+++	-	
11	40	+++	+++	-	
At Autopsy	40	DESTROYED			

APPENDIX I

TABLE 8

Fig No. 7 - 6mg/kg/day prednisolone

WEEKS	BODY WT. (kg)	FITNESS	APPETITE	DIARRHOEA	OTHER
-2	15	+++	+++	-	
-1	16	+++	+++	-	
Start of Dosing					
1	19	+++	+++	-	Drinking more
2	20	+++	+++	-	Pendulous abdomen
3	21.5	+++	+++	-	
4	24.5	+++	+++	-	
5	23	+++	+++	-	
6	23.5	+++	+++	-	

DESTROYED - END OF TREATMENT

APPENDIX I

TABLE 9

PREDNISOLONE : NORMAL PIGS - PIG N° 2 - SALINE - TREATED CONTROL
 WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	28.6	44	49	6	0	1	0
- 5	35.0	36	51	13	0	0	0
0	37.9	61	30	7	0	1	1
Start of Dosing							
7	37.9	55	28	15.5	0	0.5	1
14	38.5	58.5	29	12	0	0	0.5
21	42.4	61	27.5	11	0	0.5	0
28	36.8	59.5	30.5	10	0	0	0
35	28.4	56	36	8	0	0	0
	Destroyed						

TABLE 10

PREDNISOLONE : NORMAL PIGS - PIG N° 4 - SALINE - TREATED CONTROL
 WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	27.2	36	61	3	0	0	0
- 5	22.0	38	59	2	0	1	0
0	23.6	39	53	6	1	1	0
Start of Dosing							
7	24.5	41.5	51.5	6.5	0	0.5	0
14	26.9	36	56.5	6	0	1.5	0
21	20.7	40	48.5	9.5	0	1.5	0.5
28	19.5	38	52.5	7.5	0	1	1
35	20.4	35	50.5	12	0.5	2	0
End of Dosing							
42	18.9	40.5	49.5	8.5	0.5	1	0
49	21.7	42	45	9.5	0	3	0.5
56	20.4	47.5	44	7.5	0	1	0
63	15.4	38.5	53.5	5	0	3	0
70	18.9	34.5	56	6.5	0	2.5	0.5
76	Destroyed						

APPENDIX I

TABLE 11

PREDNISOLONE : NORMAL PIGS - PIG N° 1 - 2mg/kg INTRAMUSCULARLY - 5 DAYS/WEEK
 WHITE BLOOD CELLS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	28.8	58	36	5	0	0	1
- 5	37.2	62	32	6	0	0	0
0	36.2	61	34	4	0	1	0
Start of Dosing							
7	31.4	60.5	32.5	5.5	0	0.5	1
14	30.2	58.5	32	8	0.5	1	0
21	26.1	42.5	45	10	0	2	0.5
28	19.9	41.5	39.5	15	1	3	0
35	19.7	37	47	12.5	0.5	3	0
	Destroyed						

TABLE 12

PREDNISOLONE : NORMAL PIGS - PIG N° 6 - 2mg/kg INTRAMUSCULARLY - 5 DAYS/WEEK

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	24.3	51	43	6	0	0	0
- 5	31.1	54	38	7	0	0	1
0	35.6	54	34	11	0	0	1
Start of Dosing							
7	30.0	52.5	43.5	3.5	0	0.5	0
14	26.4	61	32.5	5.5	0	1	0
21	28.2	52	34.5	11.5	0	2	0
28	21.7	53.5	38.5	6	0	2	0
35	21.5	47	43	8.5	0.5	0.5	0.5
End of Dosing							
42	17.8	42.5	45.5	10.5	0.5	0.5	0.5
49	18.8	42.5	47	8.5	0	2	0
56	14.3	36.5	53	8	0	2	0.5
63	14.4	45	40	13.5	0	1	0.5
70	15.1	44.5	43	9	0	3	0.5
76	Destroyed						

APPENDIX I

TABLE 13

PREDNISOLONE : NORMAL PIGS - PIG N° 5 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	30.1	52	42	2	0	4	0
- 5	25.6	33	54	11	0	1	1
0	21.2	32	59	9	0	0	0
Start of Dosing							
7	26.1	42.5	47.5	9.5	0	0	0.5
14	24.3	36	55	7	0.5	1.5	0
21	23.4	36	53.5	8	0.5	1.5	0.5
28	18.6	35.5	50.5	9	0	5	0
35	18.8	35	48	11.5	0.5	5	0
	Destroyed						

TABLE 14

PREDNISOLONE : NORMAL PIGS - PIG N° 8 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	35.9	58	40	2	0	0	0
- 5	32.0	44	51	5	0	0	0
0	31.4	36	53	10	0	1	0
Start of Dosing							
7	30.6	39.5	52	7.5	0	0	1
14	29.3	52	39.5	7	0	1.5	0
21	23.9	29.5	57.5	11.5	0	0.5	1
28	21.9	34	58.5	7	0	0.5	0
35	18.4	26.5	59.5	13	0.5	0.5	0
End of Dosing							
42	15.1	46	46	6	0	2	0
49	20.0	39.5	51	9	0	0.5	0
56	17.6	51	43	4.5	0.5	1	0
63	17.8	39	49.5	8	0	3	0.5
70	15.1	36.5	53.5	7.5	0	2.5	0
76	Destroyed						

APPENDIX I

TABLE 15

PREDNISOLONE : NORMAL PIGS - PIG N° 7 - 6 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	44.7	60	34	4	0	1	1
- 5	46.0	69	26	4	0	1	0
0	36.4	62	28	8	0	2	0
Start of Dosing							
7	36.0	52.5	37.5	9	0.5	0.5	0
14	34.8	57.5	37.5	4.5	0	0.5	0
21	31.8	51.5	35.5	9.5	0	2.5	1
28	26.5	44	45.5	5.5	0	4	1
35	22.7	51	31	11	0	6	1
	Destroyed						

TABLE 16

PREDNISOLONE : NORMAL PIGS - PIG N° 3 - 6 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 12	23.4	47	49	4	0	0	0
- 5	24.0	47	47	5	0	1	0
0	23.7	36	54	7	1	1	1
Start of Dosing							
7	22.6	44.5	44.5	10	0.5	0	0.5
14	25.8	45	44.5	9	0	1.5	0
21	22.9	40.5	47.5	9.5	0	2.5	0
28	16.8	39	47.5	10.5	0	1.5	1.5
35	13.7	39.5	45	11.5	0	2	2
End of Dosing							
42	13.2	46	41	12	0	1	0
49	16.1	54.5	36	7.5	0	2	0
56	12.0	43	44.5	12	0	0.5	0
63	11.6	39.5	44.5	12.5	1	2.5	0
70	11.5	44	43.5	11	0	1.5	0
76	Destroyed						

APPENDIX I

TABLE 17

PREDNISOLONE : NORMAL PIGS - PIG N° 2 - SALINE - TREATED CONTROL

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	6.73	0.315	11.1	46.8	35.2	16.5	473
- 5	6.25	0.315	10.4	50.4	33.0	16.6	738
0	6.85	0.28	9.6	40.9	34.3	14.0	908
Start of Dosing							
7	6.95	0.33	9.1	47.5	27.6	13.1	752
14	6.97	0.26	9.2	37.3	35.4	13.2	509
21	6.95	0.30	9.6	43.2	32.0	13.8	683
28	6.72	0.30	9.5	44.6	31.7	14.1	513
35	7.02	0.32	10.3	45.6	32.2	14.7	568
	Destroyed						

TABLE 18

PREDNISOLONE : NORMAL PIGS - PIG N° 4 - SALINE - TREATED CONTROL

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	6.48	0.335	11.4	51.7	34.0	17.6	127
- 5	5.49	0.32	10.0	58.3	31.3	18.2	482
0	7.22	0.335	11.3	46.4	33.7	15.7	368
Start of Dosing							
7	7.18	0.325	10.9	45.3	33.5	15.2	408
14	7.38	0.33	11.0	44.7	33.3	14.9	367
21	6.70	0.32	10.0	47.8	31.3	14.9	350
28	7.68	0.33	10.9	43.0	33.0	14.2	324
35	6.97	0.33	10.9	47.4	33.0	15.6	435
End of Dosing							
42	7.20	0.32	11.2	44.4	35.0	15.6	297
49	7.12	0.32	11.0	44.9	34.4	15.5	315
56	7.23	0.33	11.4	45.6	34.6	15.8	321
63	7.13	0.34	12.1	47.7	35.6	17.0	261
70	7.57	0.36	12.4	47.6	34.4	16.4	252
76	Destroyed						

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TABLE 19

PREDNISOLONE : NORMAL PIGS - PIG N° 1 - 2mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	7.28	0.34	11.6	46.7	34.1	15.9	321
- 5	6.32	0.345	11.5	54.6	33.3	18.2	514
0	7.82	0.34	11.6	43.5	34.1	14.8	514
Start of Dosing							
7	7.75	0.34	11.4	43.9	33.5	14.7	554
14	7.52	0.34	11.2	45.2	32.9	14.9	400
21	7.15	0.33	11.0	46.2	33.3	15.4	553
28	7.84	0.36	11.8	45.9	32.8	15.1	224
35	8.78	0.37	12.3	42.1	33.2	14.0	380
	Destroyed						

TABLE 20

PREDNISOLONE : NORMAL PIGS - PIG N° 6 - 2mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	6.13	0.27	9.0	44.1	33.3	14.7	374
- 5	6.39	0.31	10.1	48.5	32.6	15.8	510
0	7.10	0.33	10.4	46.5	31.5	14.7	545
Start of Dosing							
7	7.46	0.31	10.2	41.6	32.9	13.7	812
14	7.36	0.31	10.3	42.1	33.2	14.0	672
21	7.47	0.30	10.4	40.2	34.7	13.9	626
28	7.69	0.34	10.9	44.2	32.1	14.2	263
35	7.56	0.34	11.5	45.0	33.8	15.2	312
End of Dosing							
42	7.48	0.35	11.4	46.8	32.6	15.2	391
49	7.94	0.32	11.0	40.3	34.4	13.9	479
56	7.26	0.32	10.6	44.1	33.1	14.6	450
63	7.32	0.33	11.2	45.6	33.9	15.5	388
70	7.53	0.36	11.5	47.8	31.9	15.3	390
76	Destroyed						

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TABLE 21

PREDNISOLONE : NORMAL PIGS - PIG N° 5 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	7.07	0.33	11.2	46.7	33.9	15.8	275
- 5	6.64	0.315	12.5	47.4	39.7	18.8	412
0	7.24	0.30	10.8	41.4	36.0	14.9	548
Start of Dosing							
7	7.37	0.30	10.7	40.7	35.7	14.5	614
14	7.78	0.32	11.1	41.1	34.7	14.3	518
21	7.96	0.35	11.3	44.0	32.3	14.2	528
28	7.47	0.33	10.8	44.2	32.7	14.5	158
35	7.35	0.35	11.2	47.6	32.0	15.2	448
	Destroyed						

TABLE 22

PREDNISOLONE : NORMAL PIGS - PIG N° 8 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	7.25	0.34	11.6	46.9	34.1	16.0	293
- 5	6.72	0.325	12.2	48.4	37.5	18.2	719
0	6.80	0.325	11.4	47.8	35.1	16.8	561
Start of Dosing							
7	7.66	0.35	11.8	45.7	33.7	15.4	659
14	7.91	0.35	11.7	44.3	33.4	14.8	544
21	7.79	0.34	12.0	43.7	35.3	15.4	453
28	7.84	0.35	11.7	44.6	33.4	14.9	234
35	7.87	0.36	12.0	45.7	33.3	15.3	487
End of Dosing							
42	8.07	0.35	12.3	43.4	35.1	15.2	470
49	7.87	0.36	11.6	45.7	32.2	14.7	365
56	7.47	0.32	10.9	42.8	34.1	14.6	459
63	7.90	0.35	11.6	44.3	33.1	14.7	405
70	7.81	0.35	11.9	44.8	34.0	15.2	383
76	Destroyed						

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TABLE 23

PREDNISOLONE : NORMAL PIGS - PIG NO 7 - 6mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	7.16	0.33	11.0	46.1	33.3	15.4	208
- 5	6.32	0.32	10.7	50.6	33.4	16.9	534
0	6.82	0.315	10.1	46.2	32.1	14.8	559
Start of Dosing							
7	7.09	0.315	10.5	44.4	33.3	14.8	514
14	7.45	0.34	11.1	45.6	32.7	14.9	488
21	6.92	0.32	10.7	46.2	33.4	15.5	400
28	7.62	0.345	11.4	45.3	33.0	15.0	230
35	7.99	0.34	11.4	42.6	33.5	14.3	359
	Destroyed						

TABLE 24

PREDNISOLONE : NORMAL PIGS - PIG NO 3 - 6mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 12	6.75	0.33	11.2	48.9	33.9	16.6	314
- 5	6.49	0.315	11.0	48.5	34.9	17.0	541
0	7.20	0.32	10.6	44.4	33.1	14.7	480
Start of Dosing							
7	7.39	0.33	10.7	44.7	32.4	14.5	591
14	7.42	0.32	10.6	43.1	33.1	14.3	466
21	7.69	0.335	10.8	43.6	32.2	14.0	555
28	7.48	0.34	10.8	45.5	31.8	14.4	296
35	7.56	0.36	11.3	47.6	31.4	15.0	415
End of Dosing							
42	7.58	0.36	11.3	47.5	31.4	14.9	364
49	7.87	0.32	11.2	40.7	35.0	14.2	309
56	7.56	0.34	11.4	45.0	33.5	15.1	380
63	7.52	0.335	10.7	44.6	31.9	14.2	312
70	7.48	0.32	11.0	42.8	34.4	14.7	251
76	Destroyed						

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TABLE 25

PREDNISOLONE : NORMAL PIGS - PIG NO 2 - SALINE TREATED CONTROL
SERUM ELECTROLYTES - MMOL/Litre

Days from Start Of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	157	6.0	93	2.63	0.99	3.13
14	138	5.8	99	2.50	0.95	3.07
21	136	6.3	96	2.50	1.03	2.36
28	148	5.5	99	2.63	1.07	3.13
35	141	5.5	101	2.73	1.03	2.58
	Destroyed					

TABLE 26

PREDNISOLONE : NORMAL PIGS - PIG NO 4 - SALINE TREATED CONTROL
SERUM ELECTROLYTES - MMOL/Litre

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	148	5.3	94	2.75	0.99	2.49
14	137	+	101	3.00	0.99	+
21	133	5.1	96	2.63	1.03	2.58
28	146	5.8	95	2.70	0.99	2.71
35	145	4.9	97	2.95	1.05	2.45
End of Dosing						
42	130	4.6	97	2.55	1.03	2.36
49	146	4.7	99	2.98	1.07	2.33
56	141	4.9	97	2.65	0.95	2.65
63	146	4.2	98	2.80	0.99	2.03
70	142	4.1	97	3.03	0.95	2.36
76	Destroyed					

+ Insufficient sample

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TABLE 27

PREDNISOLONE : NORMAL PIGS - FIG NO 1 - 2mg/kg INTRAMUSCULARLY 5 DAYS/WEEK
SERUM ELECTROLYTES - MMOL./Litre

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	150	6.2	97	3.00	0.90	2.42
14	140	6.2	102	2.75	0.95	2.81
21	136	6.6	99	2.80	1.15	2.23
28	142	6.0	93	2.70	1.07	2.62
35	133	4.9	96	3.05	1.03	2.16
	Destroyed					

TABLE 28

PREDNISOLONE : NORMAL PIGS - FIG NO 6 - 2mg/kg INTRAMUSCULARLY 5 DAYS/WEEK
SERUM ELECTROLYTES - MMOL./Litre

Days from Start Of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	154	4.5	93	2.63	0.90	2.16
14	138	6.8	99	3.00	0.90	2.65
21	133	6.6	94	2.63	1.15	2.16
28	149	5.3	101	2.63	1.07	2.65
35	136	5.2	99	2.78	0.99	2.65
End of Dosing						
42	140	4.9	97	2.65	1.11	2.49
49	150	4.5	99	2.93	1.07	1.94
56	141	4.8	94	2.65	0.90	2.62
63	150	4.8	97	2.88	1.07	2.33
70	150	4.9	101	3.13	0.90	2.55
76	Destroyed					

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TABLE 29

PREDNISOLONE : NORMAL PIGS - PIG NO 5 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES MMOL/Litre

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	158	6.3	94	2.75	0.99	2.81
14	142	5.4	110	2.75	0.95	3.33
21	133	6.2	97	2.63	1.11	2.26
28	147	5.8	97	2.63	0.99	2.20
35	144	5.6	99	3.05	1.03	2.39
	Destroyed					

TABLE 30

PREDNISOLONE : NORMAL PIGS - PIG NO 8 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/Litre

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	152	5.3	93	3.00	1.07	3.07
14	142	5.4	99	2.75	0.99	3.17
21	130	5.8	92	2.65	1.15	2.20
28	142	6.1	90	2.65	1.03	2.55
35	133	6.2	94	2.95	1.03	2.39
End of Dosing						
42	136	5.1	97	2.73	1.11	2.75
49	147	4.7	97	2.83	1.03	2.07
56	144	4.7	96	2.78	1.03	2.91
63	150	5.0	96	2.93	1.07	2.78
70	141	5.0	101	3.03	0.99	2.29
76	Destroyed					

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TABLE 31

PREDNISOLONE : NORMAL PIGS - PIG NO 7 - 6mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/Litre

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	150	5.3	90	3.0	0.99	2.29
14	137	6.8	100	2.75	0.99	3.00
21	131	5.7	91	2.50	0.99	1.84
28	143	5.6	97	2.63	1.07	2.52
35	142	5.6	97	2.88	0.99	2.03
	Destroyed					

TABLE 32

PREDNISOLONE : NORMAL PIGS - PIG NO 3 - 6mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

Days from Start of Dosing	Sodium	Potassium	Chloride	Calcium	Magnesium	Phosphate
7	157	5.6	94	2.75	0.99	2.71
14	137	6.6	102	2.75	0.99	+
21	139	6.2	96	2.80	1.15	2.26
28	146	5.6	93	2.70	1.07	2.65
35	144	4.8	90	2.88	0.95	2.23
End of Dosing						
42	131	5.0	98	2.05	1.03	2.49
49	148	5.2	103	2.83	1.07	1.97
56	139	5.4	100	2.65	0.95	2.71
63	150	4.7	98	2.93	0.95	2.39
70	140	3.7	78	2.95	1.11	2.36
76	Destroyed					

+ Insufficient sample.

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TABLE 33

PREDNISOLONE : NORMAL PIGS
SERUM TOTAL PROTEIN - g/litre

Days from Start of Dosing	Group D - Controls		Group A - 2mg/kg		Group B - 4mg/kg		Group C - 6mg/kg	
	2	4	1	6	5	8	3	7
7	50	59	69	57	57	63	55	59
14	51	58	58	56	53	60	53	58
21	57	66	64	58	47	59	51	55
28	54	68	62	60	58	64	54	62
35	62	67	61	70	64	67	62	58
End of Dosing	Dead		Dead		Dead			Dead
42		52	Dead	53	Dead	65	58	
49		57		62		60	60	
56		52		54		54	54	
63		55		63		57	59	
70		60		57		53	67	

TABLE 34

PREDNISOLONE : NORMAL PIGS
SERUM ALBUMIN - g/litre

Days from Start of Dosing	Group D - Controls		Group A - 2mg/kg		Group B - 4mg/kg		Group C - 6mg/kg	
	2	4	1	6	5	8	3	7
7	14	28	29	25	28	25	27	24
14	14	22	25	20	25	27	26	24
21	20	30	32	25	34	34	33	31
28	20	34	37	37	35	36	33	33
35	24	29	34	32	37	36	35	34
End of Dosing	Dead		Dead		Dead			Dead
42		30	Dead	30	Dead	33	23	
49		25		26		30	28	
56		28		25		27	28	
63		28		27		30	28	
70		37		34		39	32	

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TABLE 35

PREDNISOLONE : NORMAL PIGS - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

Dose Level	Saline Controls		2mg/kg		4mg/kg		6mg/kg	
	Pig No	4	1+	6	5+	8	7+	3
Submandibular LN	2.60	4.44	2.10	3.17	2.64	4.59	2.00	2.49
Parotid LN	1.60	2.08	1.67	1.97	2.64	1.93	1.22	1.92
Retropharyngeal LN	0.65	1.20	0.89	1.29	1.20	1.79	1.13	0.60
Cervical LN	1.60	4.07	2.58	4.80	2.20	2.40	1.26	3.52
Prescapular LN	0.70	1.42	0.40	1.81	1.85	1.65	1.00	2.00
Left Bronchial LN	2.00	3.60	2.88	1.89	2.00	2.44	1.15	3.39
Mid Bronchial LN	0.13	0.26	0.52	0.24	0.03	0.63	0.30	0.39
Apical Bronchial LN	0.21	0.49	0.22	0.85	0.31	0.40	0.25	0.39
Right Bronchial LN	0.13	0.32	NF	0.19	0.15	0.10	0.17	0.13
External Iliac LN	1.47	3.53	1.75	2.85	1.70	3.55	1.53	2.09
Internal Iliac LN	0.29	0.58	0.87	0.92	0.14	0.46	0.13	0.35
Inguinal LN	3.43	6.03	3.15	3.92	3.82	5.34	2.00	4.09
Mesenteric and Colonic LN	115.2	200	91.8	130	93.76	130	87.80	110
Gastric LN	6.75	13.24	6.99	12.70	6.89	16.65	5.30	11.84
Splenic LN	0.58	1.83	0.48	0.96	0.45	1.99	0.41	0.76
Preauricular LN	0.82	1.19	0.84	1.31	0.85	1.15	0.41	1.00
Popliteal LN	0.35	NF	0.49	0.51	0.26	0.42	0.09	0.33
Liver	770	1620	1010	1330	1120	1420	760	1230
Kidney (mean)	55	82	70	70	70	95	47	75
Adrenal (mean)	1.21	2.20	1.75	2.33	1.56	2.30	1.32	2.21
Thymus	19.96	62.60	18.5	80.57	10.94	95.55	5.96	84.23
Spleen	50	60	50	50	35	45	50	55

+ Killed at end of treatment NF - Not found

APPENDIX I
TABLE 36

CLINICAL RECORDS - PIG No 3630 - 4 mg/kg PREDNISOLONE INTRAMUSCULARLY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP (Range in °C)	FITNESS	APPETITE	R. Ing	L. Ing	R. Prec	L. Prec (mm)	OTHER
- 4	34.5	-	-	++	++	-	-	-	-	
- 3	34	-	-	++	++	-	-	-	-	
- 2	35.5	-	-	++	++	-	-	-	-	
- 1	35	86	38.3 - 40.0	++	++	54 x 26	64 x 30	55 x 26	51 x 32	
0	34	88	38.8 - 39.6	++	++	65 x 29	73 x 26	45 x 25	48 x 20	
Start of										
Dosing										
1	34.5	89	39.0 - 39.7	++	+++	58 x 24	60 x 24	32 x 20	32 x 20	
2	35	90	38.6 - 39.1	++	++	44 x 22	54 x 23	32 x 16	34 x 18	Swollen neck Penicillin
3	34	90	38.5 - 39.5	++	++	41 x 17	46 x 20	24 x 11	28 x 15	
4	38	93	38.0 - 39.5	+	++	52 x 24	52 x 20	Too Small	Too Small	Trembling lg KCl in treacle
5	40	88	38.9 - 39.6	+++	+++	Too Small	Too Small	Too Small	Too Small	
6	36		38.7 - 39.0	+++	+++		Destroyed			

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TABLE 40

CLINICAL RECORDS		PIG No 67		- 4 mg/kg		PREDNISOLONE		ORALLY											
WEEK	BODY WT (Kg)	ABDOMEN (cm)	RECTAL TEMP (°C)	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec (mm)	OTHER									
0	27	84	39.6	++	++	50 x 26	50 x 25	36 x 20	32 x 17										
Start of																			
Dosing																			
1	31.5	84	40.0	++	+	50 x 29	46 x 29	32 x 16	28 x 14	Severe diarrhoea									
2	34.5	83	39.2	++	++	46 x 28	44 x 24	30 x 15	29 x 13	Improved									
3	37	82	39.2	+++	+++	42 x 25	40 x 22	25 x 13	28 x 14	Normal faeces									
4	38	88	39.4	+++	+++	40 x 23	40 x 22	Too	Small	Diarrhoea									
5	39	88	39.2	++	+	34 x 20	38 x 22	Too	Small	Diarrhoea Improved									
				+++	+++														
6	36.5	89	39.9	++	+	29 x 22	32 x 18	Too	Small	Diarrhoea									
Destroyed																			

APPENDIX I
TABLE 41

CLINICAL RECORDS		PIG No 141 - 4 mg/kg		PREDNISOLONE		ORALLY													
WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP (°C)	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec. (mm)	OTHER									
0	28	86	39.9	+	++	62 x 32	57 x 33	37 x 20	34 x 22										
Start of																			
Dosing																			
1	34.5	84	39.1	+++	+++	48 x 23	46 x 24	29 x 15	26 x 14	Severe									
2	36.5	87	39.2	++	+	48 x 27	44 x 22	24 x 14	24 x 14	Diarrhoea									
3	33	84	39.4	++	++	38 x 24	38 x 24	28 x 14	25 x 14	Improved									
4	37	88	39.3	+++	++	38 x 23	32 x 20	Too	Small	Severe									
5	40	87	37.4	+++	+++	40 x 22	38 x 22	Too	Small	Diarrhoea									
6	40	90.5	38.6	+++	+++	33 x 20	36 x 20	Too	Small	Faeces									
End of																			
Dosing																			
7	45	89	38.3	+++	+++	38 x 22	34 x 21	Too	Small	Normal									
8	48.5	88	39.1	+++	++	43 x 26	42 x 24	Too	Small										
9	52	Not Measured		++	++														
10	53.5	93	39.3	++	++	54 x 24	51 x 28	Too	Small										
11	54.5	95	39.9	++	+	60 x 32	61 x 32	43 x 20	44 x 20										
12	57	96	38.8	++	-	64 x 33	64 x 30	46 x 24	50 x 26	Diarrhoea									
Destroyed																			

APPENDIX I
TABLE 42

PREDNISOLONE THERAPY - PIG NO 3630 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONO%	BASO%	EOSINO%	OTHER
- 25	29.9	25	75	0	0	0
- 19	36.5	21.5	77.5	1	0	0
- 12	30.2	18.5	81.5	0	0	0
- 5	33.4	40.5	59	0	0.5	0
Start of Dosing -0						
2	21.8	33	66	0	1	0
9	14.9	31	67.5	0.5	1	0
16	22.1	71	27.5	0.5	1	0
23	13.3	64.5	34.5	0.5	0.5	0
30	17.4	75	25	0	0	0
37	15.5	66.5	32	1.5	0	0
	Destroyed					

TABLE 43

PREDNISOLONE THERAPY - PIG No 3656 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONO%	BASO%	EOSINO%	OTHER%
- 25	34.0	47	53	0	0	0
- 19	23.0	47.5	52.5	0	0	0
- 12	24.9	51.5	48.5	0	0	0
- 5	33.4	45	55	0	0	0
Start of Dosing -0						
2	32.4	62	38	0	0	0
9	20.2	30	67	1	2	0
16	17.5	63.5	36.5	0	0	0
23	11.2	54	44.5	0.5	1	0
30	21.0	79.5	20.5	0	0	0
37	22.2	49.5	46	2	2.5	0
	Destroyed					

APPENDIX I
TABLE 44

PREDNISOLONE THERAPY - PIG No 3637 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONO%	BASO%	EOSINO%	OTHER
- 25	28.6	10	90	0	0	0
- 19	26.4	7	92.5	0	0.5	0
- 12	30.6	10	88	1	1	0
- 5	31.7	9.5	90	0	0.5	0
Start of Dosing						
2	26.7	17.5	82.5	0	0	0
9	18.4	22	76.5	0	1.5	0
16	14.0	39	59.5	0.5	1	0
23	18.3	56	42	0	2	0
30	21.9	85	15	0	0	0
37	17.4	51.5	43.5	0.5	4.5	0
End of Dosing						
44	14.4	49	48.5	0	2.5	0
51	18.0	42	51	2	5	0
58	19.9	31	65	1	3	0
65	19.9	21	76.5	0	2.5	0
72	26.3	12.5	86.5	0.5	0.5	0
	Destroyed					

TABLE 45

PREDNISOLONE THERAPY - PIG No 3652 - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	MEUTR%	MONO%	BASO%	EOSINO%	OTHER
- 25	44.5	60	40	0	0	0
- 19	33.5	47.5	52.5	0	0	0
- 12	25.8	30	69.5	0.5	0	0
- 5	18.4	29.5	70	0	0.5	0
Start of Dosing -0						
2	19.1	33	66	0	1	0
9	16.8	59.5	39.5	1	0	0
16	17.5	58.5	41	0	0.5	0
23	16.3	66	32.5	0.5	1	0
30	18.4	76	23.5	0	0.5	0
37	15.2	51.5	45	1.5	2	0
Ene of Dosing						
44	15.4	50	47.5	2	0.5	0
51	17.3	48.5	49	1	1.5	0
58	21.5	43	57	0	0	0
65	24.4	20	79	0.5	0.5	0
72	25.5	15	84.5	0	0.5	0
	Destroyed					

APPENDIX I
TABLE 46

PREDNISOLONE THERAPY - PIG No 67 - 4 mg/kg ORALLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONO%	BASO%	EOSINO%	OTHER
- 5	35.3	15.5	84	0.5	0	0
0	26.7	13	86.5	0.5	0	0
Start of Dosing						
7	13.8	57.5	41	0	1.5	0
14	23.4	51	46.5	0	2	0.5
21	16.7	61	34	2	3	0
28	18.9	60	37	0	3	0
35	17.5	76	24	0	0	0
42	29.7	70	25	0	5	0
	Destroyed					

TABLE 47

PREDNISOLONE THERAPY - PIG No 141 - 4 mg/kg ORALLY 5 DAYS/WEEK

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONO%	BASO%	EOSINO%	OTHER
- 5	37.6	11	89	0	0	0
0	27.3	6	94	0	0	0
Start of Dosing						
7	24.1	71	29	0	0	0
14	24.0	75.5	24.5	0	0	0
21	20.9	79	20	1	0	0
28	18.3	52	46	1	1	0
35	28.1	72	26	0	2	0
42	26.5	81	19	0	0	0
End of Dosing						
49	16.1	22	75	1	2	0
56	19.4	23	77	0	0	0
63	23.2	14	84	0	2	0
70	27.4	18	82	0	0	0
77	27.1	22	76	1	1	0
86	38.1	12	88	0	0	0
	Destroyed					

APPENDIX I
TABLE 48

PREDNISOLONE THERAPY - PIG No 3630 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 25	4.24	0.255	7.9	60.1	31.0	18.6	175
- 19	4.38	0.24	8.2	54.8	34.2	18.7	251
- 12	4.68	0.23	8.4	49.2	36.5	18.0	72
- 5	4.66	0.27	9.1	57.9	33.7	19.5	129
Start of Dosing -0							
2	4.98	0.275	9.3	55.2	33.8	18.7	184
9	5.09	0.27	9.2	53.1	34.1	18.1	236
16	5.66	0.30	10.3	53.0	34.3	18.2	149
23	6.06	0.31	9.7	51.2	31.3	16.0	344
30	5.03	0.30	9.8	59.6	32.7	19.5	368
37	5.00	0.28	9.2	56.0	32.9	18.4	258
	Destroyed						

TABLE 49

PREDNISOLONE THERAPY - PIG No 3656 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 25	5.48	0.305	9.3	55.7	30.5	17.0	160
- 19	5.77	0.27	8.8	46.8	32.6	15.3	243
- 12	4.78	0.25	8.5	52.3	34.0	17.8	99
- 5	4.91	0.27	9.1	55.0	33.7	18.5	250
Start of Dosing -0							
2	5.12	0.28	9.7	54.7	34.6	19.0	202
9	5.90	0.31	10.4	52.6	33.6	17.6	229
16	5.89	0.32	10.6	54.3	33.1	18.0	156
23	5.39	0.325	9.3	60.3	28.6	17.3	310
30	5.92	0.33	10.9	55.7	33.0	18.4	380
37	6.14	0.34	11.8	55.4	34.7	19.2	305
	Destroyed						

APPENDIX I
TABLE 50

PREDNISOLONE THERAPY - PIG No 3637 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 25	4.92	0.28	8.9	56.9	31.8	18.1	125
- 19	4.65	0.27	8.8	58.1	32.6	18.9	184
- 12	4.86	0.27	9.0	55.6	33.3	18.5	118
- 5	4.56	0.26	8.4	57.0	32.3	18.4	155
Start of Dosing							
2	4.49	0.265	8.6	59.0	32.5	19.2	156
9	4.23	0.27	8.3	63.8	30.7	19.6	213
16	4.65	0.30	9.8	64.5	32.7	21.1	116
23	4.95	0.285	9.5	57.6	33.3	19.2	337
30	4.26	0.28	9.5	65.7	33.9	22.3	337
37	5.34	0.30	10.0	56.2	33.3	18.7	348
End of Dosing							
44	5.61	0.28	10.4	49.9	37.1	18.5	287
51	6.06	0.33	11.3	54.5	34.2	18.7	382
58	5.52	0.31	10.0	56.2	32.3	18.1	416
65	5.25	0.30	9.8	57.1	32.7	18.7	226
72	4.78	0.265	8.7	55.4	32.8	18.2	248
	Destroyed						

TABLE 51

PREDNISOLONE THERAPY - PIG No 3652 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	THROMB
- 25	5.20	0.255	8.9	49.0	34.9	17.1	363
- 19	4.61	0.23	7.9	49.9	34.4	17.1	139
- 12	4.63	0.23	7.7	49.7	33.5	16.6	107
- 5	4.21	0.24	7.6	57.0	31.7	18.1	145
Start of Dosing							
2	4.70	0.235	8.0	50.00	34.0	17.0	190
9	4.40	0.245	8.0	55.7	32.7	18.2	286
16	5.05	0.28	9.0	55.5	32.1	17.8	223
23	5.28	0.29	9.1	54.9	31.4	17.2	341
30	5.18	0.28	9.1	54.1	32.5	17.6	350
37	5.35	0.28	9.3	52.3	33.2	17.4	220
End of Dosing							
44	5.75	0.30	10.0	52.2	33.3	17.4	156
51	6.51	0.28	9.9	43.0	35.4	15.2	333
58	5.34	0.25	9.0	46.8	36.0	16.9	244
65	4.06	0.245	7.7	60.3	31.4	19.0	145
72	3.51	0.22	6.8	62.7	30.9	19.4	242
	Destroyed						

APPENDIX I
TABLE 52

PREDNISOLONE THERAPY - PIG No 67 - 4 mg/kg ORALLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD	
							UREA	THROMB
- 5	3.64	0.22	7.5	60.4	34.1	20.6	6.76	152
0	3.45	0.20	7.1	58.0	35.5	20.6	5.45	154
Start of Dosing								
7	3.39	0.21	7.1	61.9	33.8	20.9	6.11	371
14	4.39	0.26	9.3	59.2	35.8	21.2	5.89	404
21	4.39	0.28	9.5	63.8	33.9	21.6	7.60	324
28	4.79	0.29	9.9	60.5	34.1	20.7	6.80	363
35	4.79	0.32	9.3	66.8	29.1	19.4	8.22	339
42	4.85	0.30	9.9	61.9	33.0	20.4	8.57	374
	Destroyed							

TABLE 53

PREDNISOLONE THERAPY - PIG No 141 - 4mg/kg ORALLY

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD	
							UREA	THROMB
- 5	3.78	0.21	7.0	55.6	33.3	18.5	9.19	65
0	3.72	0.215	7.5	57.8	34.9	20.2	6.81	+
Start of Dosing								
7	4.81	0.30	10.1	62.4	33.7	21.0	4.26	198
14	5.15	0.32	11.1	62.1	34.7	21.6	5.47	273
21	4.69	0.30	10.5	64.0	35.0	22.4	8.40	304
28	5.10	0.34	11.1	66.7	32.6	21.8	6.00	562
35	5.05	0.32	10.3	63.4	32.2	20.4	6.70	143
42	6.04	0.37	12.9	61.3	34.9	21.4	7.44	274
End of Dosing								
49	6.24	0.38	12.6	60.9	33.2	20.2	6.15	193
56	5.83	0.33	11.1	56.6	33.6	19.0	3.52	227
63	5.41	0.32	10.2	59.1	31.9	18.9	5.46	179
70	5.26	0.29	9.8	55.1	33.8	18.6	5.40	+
77	4.55	0.26	8.9	57.1	34.2	19.6	6.92	101
86	4.21	0.27	8.3	64.1	30.7	19.7	5.05	119
	Destroyed							

+ Partially
clotted
sample

APPENDIX I
TABLE 54

PREDNISOLONE THERAPY - PIG No 3630 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/LITRE

DAYS FROM START OF DOSING	SODIUM	POTASSIUM	CHLORIDE	CALCIUM	MAGNESIUM	PHOSPHATE
- 25	137	5.5	91	2.60	0.82	2.10
- 19	131	5.8	90	2.66	0.86	2.25
- 12	141	4.4	91	2.66	0.82	1.68
- 5	132	4.3	87	2.70	0.74	1.81
Start of Dosing -0						
2	148	4.0	89	2.46	0.99	2.26
9	135	4.1	94	2.65	0.82	1.83
16	140	3.5	98	2.54	0.90	1.90
23	142	5.2	87	2.73	0.86	1.39
30	149	4.8	92	2.45	0.90	1.78
37	144	6.1	91	2.70	0.95	1.30
	Destroyed					

TABLE 55

PREDNISOLONE THERAPY - PIG No 3656 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/LITRE

DAYS FROM START OF DOSING	SODIUM	POTASSIUM	CHLORIDE	CALCIUM	MAGNESIUM	PHOSPHATE
- 25	133	4.9	90	2.53	0.90	2.42
- 19	136	4.9	90	2.73	0.95	2.25
- 12	142	4.6	91	2.58	0.90	1.62
- 5	141	4.1	93	2.62	0.90	2.33
Start of Dosing -0						
2	148	4.8	93	2.85	0.90	2.39
9	135	5.8	93	2.88	0.86	2.30
16	138	4.5	91	2.70	0.99	2.24
23	146	6.2	86	2.88	0.99	2.03
30	152	7.2	90	2.90	0.95	1.98
37	144	4.7	95	2.53	0.90	1.83
	Destroyed					

APPENDIX I
TABLE 56

PREDNISOLONE THERAPY - PIG No 3637 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/LITRE

DAYS FROM START OF DOSING	SODIUM	POTASSIUM	CHLORIDE	CALCIUM	MAGNESIUM	PHOSPHATE
- 25	125	5.1	90	2.73	0.78	2.33
- 19	139	5.3	91	2.62	0.78	2.20
- 12	145	4.8	93	2.73	0.82	1.55
- 5	136	4.9	93	2.81	0.86	2.53
Start of Dosing -0						
2	148	4.7	91	2.42	0.90	2.91
9	136	4.4	96	2.85	0.82	2.06
16	136	4.5	99	2.58	0.90	2.00
23	147	5.7	90	2.95	0.90	2.07
30	144	4.3	89	2.53	0.78	1.55
37	144	4.6	96	2.70	0.82	1.98
End of Dosing						
44	150	4.5	95	2.73	0.75	2.53
51	154	4.5	96	2.68	0.71	2.45
58	149	5.4	95	2.81	0.72	2.63
65	148	5.3	95	2.89	0.72	2.69
72	154	4.5	93	2.70	0.67	2.20
Destroyed						

TABLE 57

PREDNISOLONE THERAPY - PIG No 3652 - 4mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM ELECTROLYTES - MMOL/LITRE

DAYS FROM START OF DOSING	SODIUM	POTASSIUM	CHLORIDE	CALCIUM	MAGNESIUM	PHOSPHATE
- 25	137	4.5	86	2.33	0.86	2.23
- 19	136	4.9	93	2.62	0.86	2.14
- 12	145	4.9	89	2.50	0.82	1.52
- 5	140	4.6	89	2.46	0.82	1.94
Start of Dosing -0						
2	148	4.3	93	2.62	1.03	2.16
9	132	4.6	94	2.58	0.86	2.18
16	138	4.5	98	2.62	0.90	2.27
23	148	4.7	101	3.58	1.15	2.10
30	148	4.3	88	2.40	0.82	1.77
37	134	4.7	83	2.63	0.90	2.03
End of Dosing						
44	145	4.7	94	2.68	0.75	2.15
51	148	4.5	96	2.68	0.70	1.87
58	144	5.6	91	2.81	0.70	2.19
65	140	5.5	98	2.81	0.70	2.42
72	146	4.4	91	2.60	0.78	2.20
Destroyed						

APPENDIX I
TABLE 58

PREDNISOLONE THERAPY - 4 mg/kg INTRAMUSCULARLY 5 DAYS/WEEK

SERUM PROTEINS (g/l)

DAYS FROM START OF DOSING	TOTAL PROTEIN				ALBUMIN			
	3630	3637	3652	3656	3630	3637	3652	3656
- 25	55	63	59	65	19	29	21	23
- 19	72	72	74	78	27	28	17	21
- 12	65	70	72	72	26	30	20	21
- 5	61	59	63	67	26	27	23	19
Start of Dosing								
2	70	63	72	72	28	27	27	24
9	59	57	65	76	33	31	33	35
16	64	70	66	70	33	35	41	39
23	72	56	76	64	47	42	51	44
30	75	66	66	66	39	38	36	41
37	59	53	64	72	33	38	33	46
End of Dosing								
44	Dead	61	72	Dead	Dead	38	37	Dead
51		62	72			36	38	
58		59	57			33	32	
65		60	66			28	32	
72		63	70			30	32	

APPENDIX I
TABLE 59

PREDNISOLONE THERAPY - 4 mg/kg ORALLY 5 DAYS/WEEK

DAYS FROM START OF DOSING	SERUM PROTEINS (g/l)							
	TOTAL PROTEIN		ALBUMIN		GLOBULINS		A/G RATIO	
	67	141	67	141	67	141	67	141
- 5	51.7	57.5	14.4	20.7	37.3	36.8	0.39	0.56
0	48.6	64.1	19.9	24.2	28.7	39.9	0.69	0.61
Start of Dosing								
7	54.3	62.1	31.3	41.2	23.0	20.9	1.36	1.97
14	55.5	57.5	36.8	34.3	18.7	23.2	1.97	1.48
21	63.4	44.1	42.9	26.7	20.5	17.4	2.09	1.53
28	65.4	54.9	41.9	31.8	23.5	23.1	1.78	1.38
35	60.7	57.0	40.0	26.9	20.7	30.1	1.93	0.89
42	51.1	64.9	33.8	38.4	17.3	26.5	1.95	1.45
End of Dosing								
49	Dead		Dead		Dead		Dead	
56		60.3		30.0		30.3		0.99
63		57.3		24.5		32.8		0.75
70		59.4		23.3		36.1		0.65
77		59.8		22.9		36.9		0.62
86		68.3		25.3		43.0		0.59

APPENDIX I
TABLE 60

PREDNISOLONE THERAPY - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

THERAPY	PREDNISOLONE INTRAMUSCULARLY 4mg/kg				ORALLY 4 mg/kg	
PIG NUMBER	3630 ⁺	3637	3652	3656 ⁺	67 ⁺	141
Submandibular LN	10.35	20.00	22.23	4.66	5.25	25.72
Parotid LN	3.66	14.66	29.00	7.11	3.45	22.76
Retropharyngeal LN	1.48	4.47	6.40	3.46	1.42	6.54
Cervical Ln	6.48	15.12	14.53	4.11	5.84	25.30
Prescapular LN	1.77	4.47	4.55	1.24	1.10	3.76
Left Bronchial LN	5.43	16.85	16.19	3.29	3.62	45.41
Mid Bronchial LN	0.70	3.86	4.31	0.48	1.32	8.54
Apical Bronchial LN	1.51	4.48	2.82	2.00	0.35	7.22
Right Bronchial LN	1.26	4.13	2.19	1.31	1.40	6.60
External Iliac LN	4.00	2.19	19.60	3.00	3.01	14.71
Internal Iliac LN	0.55	12.33	3.30	0.37	0.68	2.99
Inguinal LN	8.95	17.80	19.39	6.13	6.10	24.24
Mesenteric and Colonic LN	275 77.80	2040 620	865 300	175 93.52	365 45.00	2090 600
Gastric LN	4.98	21	39.93	10.27	4.00	40.71
Splenic LN	4.55	10.28	10.74	2.27	2.75	9.99
Precurral LN	1.19	2.19	8.00	1.00	1.00	4.94
Popliteal LN	1825	1790	1710	1300	2003	2710
Liver						
Kidney (mean)	117	100	80	65	111	160
Adrenal (mean)	1.48	2.66	1.38	1.14	2.20	2.82
Thymus	11.14	25.27	12.68	6.36	12.40	77.42
Spleen	180	475	365	75	180	1210

⁺ Killed at end of treatment

APPENDIX II

APPENDIX II
TABLE 1

CLINICAL RECORDS - PIG No 39 (SALINE - TREATED CONTROL)

WEEKS	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	6.5	38.9	++	+++	-	Runt infected navel
- 2	7.0	39.4	++	+++	-	
-10	8.5	39.7	++	+++	-	
1st Dose						
1	9.75	38.5	++	+++	-	
2	10.0	38.5	++	+++	-	
3	10.5	38.7	++	+++	-	
2nd Dose						
4	12.0	38.7	++	+++	-	
5	14.0	38.9	++	+++	-	
6	14.5	37.9	+++	+++	-	Condition improved
3rd Dose						
7	15.5	38.8	+++	+++	-	
8	19.5	38.5	+++	+++	-	
9	20.0	39.2	+++	+++	-	
4th Dose						
10	21.0	38.3	+++	+++	-	
11	21.0	38.4	+++	+++	-	
12	23.5	38.4	+++	+++	-	
5th Dose						
13	24.0	38.7	+++	+++	-	
14	25.5	38.6	+++	+++	-	
15	27.0	39.3	+++	+++	-	
6th Dose						
16	29.5	39.2	+++	+++	-	
17	32.0	39.1	+++	+++	-	

End of treatment

Detailed clinical examinations discontinued - remained well

Weight at euthanasia - 42kg

APPENDIX II
TABLE 2

CLINICAL RECORDS - PIG No 42 - (SALINE - TREATED CONTROL)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	14.75	39.3	+++	+++	-	
- 2	16.5	39.3	+++	+++	-	
- 1	18.5	39.2	+++	+++	-	
1st Dose						
1	20.5	38.6	+++	+++	-	
2	20.75	39.0	+++	+++	-	
3	21.5	39.1	+++	+++	-	
2nd Dose						
4	23.0	39.3	+++	+++	-	
5	27.0	38.7	+++	+++	-	
6	26.5	38.7	+++	+++	-	
3rd Dose						
7	28.0	39.0	+++	+++	-	
8	33.0	38.5	+++	+++	-	
9	32.25	39.1	+++	+++	-	Bursitis on hocks
4th Dose						
10	35.0	38.4	+++	+++	-	
11	36.5	38.3	+++	+++	-	
12	38.0	39.0	+++	+++	-	
5th Dose						
13	38.5	38.9	+++	+++	-	
14	40.0	38.5	+++	+++	-	
15	42.75	39.2	+++	+++	-	
6th Dose						
16	45.5	39.0	+++	+++	-	
17	52.0	40.2	++	+++	-	Badly mauled about neck and shoulders by other pigs
Destroyed - end of treatment						

APPENDIX II
TABLE 3

CLINICAL RECORDS - PIG No 43 - (SALINE - TREATED CONTROL)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	20.5	37.9	+++	+++	-	
- 2	20.0	39.4	+++	+++	-	
- 1	22.5	38.7	+++	+++	-	
1st Dose						
1	24.5	38.3	+++	+++	-	
2	25.0	38.4	+++	+++	-	
3	25.5	38.4	+++	+++	-	
2nd Dose						
4	29.5	38.6	+++	+++	-	
5	33.0	38.9	+++	+++	-	
6	33.5	38.1	+++	+++	-	
3rd Dose						
7	37.0	38.7	+++	+++	-	
8	43.0	39.0	+++	+++	-	
9	43.0	38.8	+++	+++	-	
4th Dose						
10	44.5	39.0	+++	+++	-	
11	47.0	38.8	+++	+++	-	
12	49.0	38.0	+++	+++	-	
5th Dose						
13	48.5	38.4	+++	+++	-	
14	51.0	38.4	+++	+++	-	
15	53.0	38.9	+++	+++	-	
6th Dose						
16	58.5	39.1	+++	+++	-	
17	64.0					
Destroyed end of treatment						

APPENDIX II
TABLE 4

CLINICAL RECORDS - PIG No 46 - (SALINE - TREATED CONTROL)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	17.5	39.6	+++	+++	-	
- 2	19.5	39.3	+++	+++	-	
- 1	21.75	38.6	+++	+++	-	
1st Dose						
1	22.75	39.2	+++	+++	-	
2	24.5	38.7	+++	+++	-	
3	25.0	38.9	+++	+++	-	
2nd Dose						
4	28.0	38.8	+++	+++	-	
5	30.5	38.3	+++	+++	-	
6	31.25	38.0	+++	+++	-	
3rd Dose						
7	34.0	39.0	+++	+++	-	
8	39.0	39.0	+++	+++	-	
9	41.0	38.9	+++	+++	-	
4th Dose						
10	42.0	38.7	+++	+++	-	
11	42.0	38.3	+++	+++	-	
12	44.5	38.4	+++	+++	-	
5th Dose						
13	44.5	37.7	+++	+++	-	
14	47.5	37.8	+++	+++	-	
15	48.0	39.0	+++	+++	-	
6th Dose						
16	54.0	38.9	+++	+++	-	
17	57.5	39.3	+++	+++	-	

End of treatment - detailed clinical examinations discontinued -
remained well.

Weight at euthanasia 74.5kg

APPENDIX II
TABLE 5

CLINICAL RECORDS - PIG No 40 - (1mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	20.5	39.1	+++	+++	-	
- 2	21.0	38.4	+++	+++	-	
- 1	24.5	38.8	+++	+++	-	
1st Dose						
1	25.5	39.6	+++	+++	-	
2	26.0	38.7	+++	+++	-	
3	27.5	38.5	+++	+++	-	
2nd Dose						
4	28.5	38.9	+++	+++	-	
5	32.0	38.6	+++	+++	-	
6	34.0	38.6	+++	+++	-	
3rd Dose						
7	35.5	38.7	+++	+++	-	
8	40.0	38.7	+++	+++	-	
9	41.0	39.1	+++	+++	-	
4th Dose						
10	41.5	38.8	+++	+++	-	
11	43.5	38.7	+++	+++	-	
12	46.0	38.5	+++	+++	-	
5th Dose						
13	47.5	37.6	+++	+++	-	
14	50.0	39.0	+++	+++	-	
15	51.5	39.3	+++	+++	-	
6th Dose						
16	54.5	39.4	+++	+++	-	
17	60.5	39.5	+++	+++	-	

End of treatment

Clinical examinations discontinued - remained well

Weight at euthanasia - 74kg

APPENDIX II
TABLE 6

CLINICAL RECORDS - PIG No 45 (1mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	14.5	38.4	+++	+++	-	
- 2	14.5	38.9	+++	+++	-	
- 1	15.75	39.9	+++	+++	-	
1st Dose						
1	17.25	38.3	+++	+++	-	
2	17.5	38.7	+++	+++	-	
3	16.5	38.6	+++	+++	-	
2nd Dose						
4	17.5	38.7	+++	+++	-	
5	19.5	38.8	+++	+++	-	
6	20.0	38.1	+++	+++	-	
3rd Dose						
7	21.0	38.1	+++	+++	-	
8	24.0	39.2	+++	+++	-	
9	23.5	38.4	+++	+++	-	
4th Dose						
10	25.0	38.2	+++	+++	-	
11	24.5	37.8	+++	+++	-	
12	26.0	38.7	+++	+++	-	
5th Dose						
13	27.0	38.1	+++	+++	-	Large ulcer on gum and lower lip below incisor teeth
14	28.0	38.0	++	+++	-	Ulcer healing - irregular cardiac rhythm
15	29.0	39.0	+++	+++	-	Irregular cardiac rhythm
6th Dose						
16	30.0	38.7	+++	+++	-	New larger ulcer in same position as above
17	36.0					

Destroyed - end of treatment

APPENDIX II
TABLE 7

CLINICAL RECORDS - PIG No 47 (2mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	11	39.1	+++	+++	-	
- 2	11.5	38.7	+++	+++	-	
- 1	12.25	39.7	+++	+++	-	Rather thin
1st Dose						
1	14.0	38.3	+++	+++	-	
2	13.5	38.4	+++	+++	-	
3	15.0	38.4	+++	+++	-	
2nd Dose						
4	16.25	38.9	+++	+++	-	
5	18.5	38.5	+++	+++	-	
6	19.25	38.3	+++	+++	-	Listless
3rd Dose						
7	19.0	38.7	++	+++	-	Listless
8	22.5	39.6	++	+++	-	Listless, mild skin rash
9	21.75	38.6	++	+++	-	Listless
4th Dose						
10	22.5	38.1	++	+++	-	Listless, patchy hair loss
11	24.0	38.2	+++	+++	-	
12	25.5	37.8	+++	+++	-	Partial alopecia
5th Dose						
13	25.0	38.8	+++	+++	-	Irregular cardiac rhythm
14	26.5	37.8	+++	+++	-	
15	28.0	38.0	++	++	-	Listless, very thin
6th Dose						
16	Not weighed	39.4	++	++	-	Irregular cardiac rhythm
16.5			+	-	Very severe haemorrhagic	Tachycardia Individual heart sounds unrecognisable

Found dead - Weight 22.3kg

APPENDIX II
TABLE 8

CLINICAL RECORDS - PIG No 49 (2mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	15.0	39.4	+++	+++	-	
- 2	16.0	39.1	+++	+++	-	
- 1	18.5	39.3	+++	+++	-	Rather thin
1st Dose						
1	19.5	38.5	+++	+++	-	
2	20.0	38.7	+++	+++	-	
3	20.0	38.8	+++	+++	-	
2nd Dose						
4	21.25	39.5	+++	+++	-	
5	23.0	39.0	+++	+++	-	Blotchy appearance of skin
6	23.5	38.0	++	+++	-	
3rd Dose						
7	24.5	38.7	++	+++	-	Listless, irregular cardiac rhythm
8	27.5	39.2	++	+++	-	Heart more regular
9	26.5	39.4	+++	+++	-	
4th Dose						
10	26.5	37.9	++	+++	-	Listless, patchy hair loss
11	29.0	38.0	++	+++	-	Listless, cardiac irregularity very pronounced
12	29.0	38.4	++	+++	-	As above, partial alopecia
5th Dose						
13	28.5	38.6	++	+++	-	As above
14	29.5	37.2	++	+++	-	As above
15	31.5	38.9	++	++	-	Heartbeat extremely irregular, though not increased in rate individual heart sounds unrecognisable
6th Dose						
16	Not weighed	38.8	++	++	-	Buccal ulceration heart as above

Found dead - Weight 30.5kg

APPENDIX II
TABLE 9

CLINICAL RECORDS - PIG No 41 (4mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	17.0	39.1	+++	+++	-	
- 2	17.5	38.9	+++	+++	-	
- 1	19.0	39.0	+++	+++	-	
1st Dose						
1	20.0	38.6	+++	+++	-	
2	?	39.9	+	++	-	Purpura on abdomen, ears and limbs ulcers in mouth

Sudden death - Weight - 20.0 kg

TABLE 10

CLINICAL RECORDS - PIG No 48 (4mg/kg ADRIAMYCIN EVERY 3 WEEKS)

WEEK	BODY WT (kg)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	OTHER
- 3	18.5	39.2	+++	+++	-	
- 2	19.75	39.1	+++	+++	-	
- 1	22.0	38.7	+++	+++	-	
1st Dose						
1	21.0	38.6	+++	+++	-	
2	20.5	38.9	+++	+++	Slight	
3	20.5	38.8	+++	+++	-	
2nd Dose						
4	20.0	38.5	++	+++	Slight	
5	22.5	38.8	++	+++	Slight	Right inguinal lymph node enlarged. Marks resembling purpura on abdomen, trembling
6	22.0	38.8	++	+++	Moderate	
3rd Dose						
7	21.0	37.5	++	++	-	Listless, slight generalised alopecia large mouth ulcers pale mucous membranes hooves dark coloured
8	21.0	39.8 40.7	+ +	+ -	Severe	Dehydration - definite hair loss with skin lesions. Unsteady, shivering. Large mouth ulcers Tachycardia (>200/min) enlarged lymph nodes, hooves separating at coronary bands - walls underrun polydipsia

Destroyed in extremis. Weight 20.0kg

APPENDIX II
TABLE 11

ADRIAMYCIN : NORMAL PIGS - PIG No 39 (SALINE - TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	29.8	77.5	15	7	0	0	0
- 15	26.5	68	26	5	0	0	1
- 8	24.7	65	31	4	0	0	0
- 1	13.1	48.5	45.5	5	0	1	0
Dose 1 - 0							
+ 6	24.6	49	40	7	0	2	2
13	28.8	41	51	7	0	0	1
20	26.3	59	33	7	0	0	1
Dose 2 - 21							
27	19.1	52	39	6	0	2	1
30	19.7	46.5	50	3.5	0	0	0
34	20.7	39.5	48.5	9.5	0.5	1.5	0.5
41	12.8	34.5	58.5	6.5	0.5	0	0
Dose 3 - 42							
48	21.2	42	48.5	9	0	0.5	0
51	18.8	44.5	50.5	3.5	0.5	0.5	0.5
55	17.8	39.5	48.5	9	0.5	2	0.5
62	13.0	37.5	54.5	6.5	0	1	0.5
Dose 4 - 63							
69	18.3	42.5	51	4.5	0	1.5	0.5
72	16.9	45	49.5	3	1	1.5	0
76	17.3	39.5	54	4.5	0	2	0
84	16.8	53.5	39	5	0	2.5	0
Dose 5 - 84							
90	17.1	45	47	5.5	0	2.5	0
93	16.8	49.5	41	6.5	0.5	2.5	0
97	16.5	49	46	3	1	1	0
104	18.0	38	58	3.5	0.5	0	0
Dose 6 - 105							
111	16.3	46	41.5	10.5	0.5	1.5	0
114	19.3	35.5	55.5	7	0	1.5	0.5
118	18.7	40	47.5	12	0	0.5	0
End of treatment							
126	15.5	45	48	5	0	1	1
132	18.4	42.5	50	5	0	2.5	0
139	23.3	53.5	39	5	0	1	1.5
146	19.4	58.5	37.5	3	0	1	0
153	18.8	47	43	7	0	3	0
160	18.5	49.5	42	7	0	1.5	0

APPENDIX II
TABLE 12

ADRIAMYCIN : NORMAL PIGS - PIG No 42 (SALINE - TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	25.2	60.5	31.5	7.5	0	0.5	0
- 15	19.9	28	70	2	0	0	0
- 8	19.1	35	60	4	0	1	0
- 1	22.4	39.5	54.4	4.5	0	1.5	0
Dose 1 - 0							
+ 6	23.5	34	59	4	0	3	0
13	18.1	20	74	4	0	2	0
20	22.7	32	62	4	0	2	0
Dose 2 - 21							
27	25.5	39	57	2	0	2	0
30	23.0	34.5	57	5.5	0	3	0
34	17.5	33.5	59.5	6	0	1	0
41	20.6	38	58.5	3.5	0	0	0
Dose 3 - 42							
48	26.1	34	59.5	6.5	0	0	0
51	26.8	32	60.5	7.5	0	0	0
55	22.6	20	71	7	0	2	0
62	20.4	29	65	3.5	0	2.5	0
Dose 4 - 63							
69	24.0	45.5	49	5	0	0.5	0
72	22.1	27	66.5	4	0.5	2	0
76	20.6	26.5	67.5	4.5	0	1.5	0
84	20.7	37.5	60	2	0	0.5	0
Dose 5 - 84							
90	21.0	33	64	3	0	0	0
93	20.1	37.5	54	3	0	5	0.5
97	21.8	35	55.5	7.5	0	2	0
104	21.9	42	54.5	3	0	0.5	0
Dose 6 - 105							
111	8.0	33	56	10.5	0	0	0.5
113	Destroyed						

APPENDIX II
TABLE 13

ADRIAMYCIN : NORMAL PIGS - PIG No 43 (SALINE - TREATED CONTROL)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	25.4	56.5	36	7	0	0	0.5
- 15	28.9	33	61	6	0	0	0
- 8	25.7	59	31	8	0	2	0
- 1	20.9	40	53	6	0	0.5	0.5
Dose 1 - 0							
+ 6	27.5	38	52	7	0	3	0
13	26.7	41	46	9	1	3	0
20	27.7	40	58	2	0	0	0
Dose 2 - 21							
27	23.3	37	52	5	0	6	0
30	22.4	42	55.5	2.5	0	0	0
34	18.2	33	59.5	7	0.5	0	0
41	15.9	34	61.5	1.5	1	2	0
Dose 3 - 42							
48	21.7	35	58	6	0	0.5	0.5
51	23.3	34	56	7	0	3	0
55	18.9	23	67.5	6	0.5	3	0
62	19.2	41	53	4.5	0	1.5	0
Dose 4 - 63							
69	19.1	41.5	56.5	1.5	0	0.5	0
72	17.1	30.5	61	6.5	0	2	0
76	17.0	36	56.5	3.5	0	4	0
84	19.8	29	62.5	6	0	2	0.5
Dose 5 - 84							
90	18.2	30.5	60	5.5	0.5	3	0.5
93	18.8	35.5	56	4.5	1	3	0
97	28.4	55.5	38	4	1	1.5	0
104	19.6	40.5	48.5	6.5	0	4.5	0
Dose 6 - 105							
111	16.9	31.5	56.5	6.5	1.5	4	0
113	Destroyed						

APPENDIX II
TABLE 14

ADRIAMYCIN : NORMAL PIGS - PIG No 46 (SALINE - TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	21.6	40.5	50.5	8.5	0	0	0.5
- 15	21.2	41	47	10	1	1	0
- 8	22.7	45	51	3	0	1	0
- 1	25.2	45.5	49	4.5	0	1	0
Dose 1 - 0							
+ 6	18.0	36	58	2	0	4	0
13	24.7	37	57	4	0	2	0
20	23.1	39	57	3	0	1	0
Dose 2 - 21							
27	22.1	40	55	4	0	1	0
30	21.7	42.5	51.5	4	0	2	0
34	27.1	45	49	5	0	1	0
41	13.5	46	50	3	0	1	0
Dose 3 - 42							
48	19.3	33.5	62	3	0	1.5	0
51	20.9	35.5	59.5	3.5	0.5	1	0
55	18.4	28	62.5	8	0	1.5	0
62	13.2	26.5	66.5	4	0.5	2	0.5
Dose 4 - 63							
69	17.4	36.5	58	4.5	0	1	0
72	13.9	36	58	5	0	1	0
76	15.9	39	55.5	4	0	1.5	0
84	15.2	36	51.5	10.5	0.5	1	0.5
Dose 5 - 84							
90	15.8	32	62	3	0	3	0
93	15.4	44	48.5	5	0	2.5	0
97	14.3	34	59	3.5	0	3.5	0
104	17.7	35	57	6	0	2	0
Dose 6 - 105							
111	12.0	34	56	6.5	0	3	0.5
114	20.5	29.5	61.5	7	0.5	1.5	0
118	16.1	35.5	54	9.5	0	1	0
End of treatment							
126	14.7	33	59	5	0	2	1
132	14.2	28.5	61.5	6.5	0.5	3	0
139	21.6	39.5	54.5	3.5	0.5	2	0
146	17.1	37	56.5	3	0	3.5	0
153	13.4	39.5	45	13	0	2.5	0
160	12.4	42.5	53	3.5	0.5	0.5	0

APPENDIX II
TABLE 15

ADRIAMYCIN : NORMAL PIGS - PIG No 40 (1 mg/kg ADRIAMYCIN INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	23.3	45	46	8	0	1	0
- 15	23.0	45	50	4	0	1	0
- 8	21.8	48	44	7	0	1	0
- 1	20.3	38.5	56	4	0	1	0.5
Dose 1 - 0							
+ 6	17.9	20	74	3	0	2	1
13	22.5	34	58	1	1	6	0
20	22.6	34	58	7	0	1	0
Dose 2 - 21							
27	20.3	33	55	8	0	3	1
30	19.1	39.5	53	7	0	0.5	0
34	12.0	45	45	8.5	0	1	0.5
41	17.2	38.5	57	2.5	0	2	0
Dose 3 - 42							
48	13.7	33.5	59.5	6	0	0.5	0.5
51	15.0	35.5	49.5	14	0	1	0
55	16.1	33.5	58	6.5	0	1.5	0.5
62	12.1	34.5	57.5	4	1	3	0
Dose 4 - 63							
69	15.1	35	59	3.5	0	2.5	0
72	16.3	36	57.5	4.5	0	1.5	0.5
76	15.0	43.5	46	8	0	2.5	0
84	16.2	37.5	54	5	0	3.5	0
Dose 5 - 84							
90	15.0	37.5	56.5	4	0	2	0
93	14.6	45.5	42.5	8.5	0	3.5	0
97	14.4	39.5	52.5	3	0	5	0
104	17.4	49	38	10	0.5	2.5	0
Dose 6 - 105							
111	10.2	29	60.5	3.5	0	6.5	0.5
114	19.2	34	56	8	0	2	0
118	14.1	45.5	44.5	8	0	1.5	0.5
End of treatment							
126	13.7	31	60	9	0	0	0
132	13.1	34.5	53.5	8.5	0	3.5	0
139	18.0	50	42	5.5	0	2	0.5
146	17.5	39.5	48.5	7.5	0	4.5	0
153	16.8	41.5	43	9	0	6.5	0
160	14.8	40.5	49.5	6	0	2.5	1.5

APPENDIX II
TABLE 16

ADRIAMYCIN : NORMAL PIGS - PIG No 45 (1 mg/kg ADRIAMYCIN INTRAVENOUSLY)
WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	28.6	62.5	26	10	0	0.5	1
- 15	33.9	58	40	2	0	0	0
- 8	29.6	59	34	6	0	1	0
- 1	24.7	54	38	6.5	0	1	0.5
Dose 1 - 0							
+ 6	21.0	54	39	4	0	3	0
13	24.4	42	44	11	0	3	0
20	22.1	44	50	5	0	1	0
Dose 2 - 21							
27	22.3	55	33	10	0	2	0
30	23.4	61	27.5	10	0	1.5	0
34	21.7	52	33.5	12.5	0	2	0
41	14.6	66	24	6.5	0	3.5	0
Dose 3 - 42							
48	10.9	48	40.5	8	0.5	3	0
51	14.2	52	38.5	7	0	2.5	0
55	15.7	49	40	6	0	5	0
62	12.6	48	46.5	2	1	2.5	0
Dose 4 - 63							
69	12.7	48	43	5.5	0	3.5	0
72	12.0	44.5	48.5	5	0.5	1.5	0
76	12.7	53.5	37.5	4	0	3.5	1.5
84	14.1	53	37.5	7	0	2.5	0
Dose 5 - 84							
90	10.4	39.5	53	5.5	0	2	0
93	11.3	47	41	9	0.5	2.5	0
97	10.8	53	37.5	6.5	0.5	2.5	0
104	14.1	47.5	43	6	0	3.5	0
Dose 6 - 105							
111	10.7	55	34.5	8	0.5	1.5	0.5
113	Destroyed						

APPENDIX II
TABLE 17

ADRIAMYCIN : NORMAL PIGS - PIG No 47 (2mg/kg ADRIAMYCIN INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	⁺ NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	23.6	60.5	29.5	7.5	0	2.5	0
- 15	28.2	62	31	6	0	1	0
- 8	19.1	47	48	4	0	1	0
- 1	15.0	50.5	42.5	6.5	0	0	0.5
Dose 1 - 0							
+ 6	8.4	37	53	9	0	0	1
13	15.6	38	53	9	0	0	0
20	17.2	43	51	6	0	0	0
Dose 2 - 21							
27	11.8	51	40	7	0	2	0
30	11.1	52	37	10	0	0.5	0.5
34	22.2	45	37.5	15.5	0	1.5	0.5
41	9.9	51	42	7	0	0	0
Dose 3 - 42							
48	7.4	54(22)	37	8	0	1	0
51	7.2	67	21	10	1	1	0
55	13.6	59.5	32	7.5	0	1	0
62	13.2	56.5	38	4.5	0	0.5	0.5
Dose 4 - 63							
69	11.2	68.5	27	4	0	0.5	0
72	10.1	54	39.5	5.5	0	1	0
76	12.7	60	35	4	0	1	0
84	12.3	62.5	30	5	1	1	0.5
Dose 5 - 84							
90	10.8	64.5	30	5.5	0	0	0
93	12.2	55	33	12	0	0	0
97	12.3	60.5	32	6	0	1.5	0
104	15.6	69	22.5	7.5	0	1	0
Dose 6 - 105							
110	Died						

⁺Non-Lob. Neutr. shown where >10%
in parentheses

APPENDIX II
TABLE 18

ADRIAMYCIN : NORMAL PIGS - PIG No 49 (2 mg/kg ADRIAMYCIN INTRAVENOUSLY)
WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	⁺ NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	31.1	53	36	8.5	0	2	0.5
- 15	26.2	42	52	3	0	3	0
- 8	18.6	51	44	5	0	0	0
- 1	19.8	20.5	68.5	8.5	0.5	1	1
Dose 1 - 0							
+ 6	13.0	9	75	14	0	1	1
13	20.9	31	61	7	0	0	1
20	25.0	42	51	6	0	1	0
Dose 2 - 21							
27	18.8	59	33	8	0	0	0
30	20.0	47.5	36	16	0	0.5	0
34	12.2	50.5	40.5	8	0	0.5	0.5
41	18.6	52.5	38.5	6.5	0	2.5	0
Dose 3 - 42							
48	10.1	52.5(39)	40	7.5	0	0	0
51	8.3	23	59	15	0	0	3
55	15.2	52	41.5	6.5	0	0	0
62	15.4	54.5	36.5	6.5	0.5	1.5	0.5
Dose 4 - 63							
69	11.9	41	52	6.5	0.5	0	0
72	11.4	43	46.5	9.5	0	0.5	0.5
76	15.8	71.5	24	4	0	0.5	0
84	14.9	54.5	38.5	5.5	0	0	1.5
Dose 5 - 84							
90	8.8	45.5	46	5.5	0	2	1
93	8.6	38	46	15	0	1	0
97	12.1	59.5	27	13	0	0.5	0
104	14.2	60.5	32.5	6	0	1	0
Dose 6 - 105							
109	Died						

⁺Non-Lob. Neutr. shown where >10%.

APPENDIX II
TABLE 19

ADRIAMYCIN : NORMAL PIGS - PIG No 48 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)
WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	+ NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	25.6	45.5	43	8.5	0	3	0
- 15	28.0	45	47	7	0	0	1
- 8	25.1	38	51	9	0	1	1
- 1	18.7	22.5	64.5	10.5	0	1	1.5
Dose 1 - 0							
+ 6	8.8	24	68	8	0	0	0
9	16.1	44(32)	44	12	0	0	0
13	19.8	56(14)	35	9	0	0	0
20	22.0	43	51	6	0	0	0
Dose 2 - 21							
27	13.4	41	45	12	0	2	0
30	14.4	51	31.5	17	0	0.5	0
34	18.4	72	18.5	9	0.5	0	0
41	21.8	59	32.5	6.5	0	2	0
Dose 3 - 42							
48	3.9	34	60	4	0	0	2
51	6.8	38(19)	41	21	0	0	0
55	6.7	63(30.5)	23.5	13.5	0	0	0
58	Died						

(+ Non-Lob. Neutr. shown where >10%)

TABLE 20

ADRIAMYCIN : NORMAL PIGS - PIG No 41 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)
WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	+ NEUTR%	LYMPH%	MONO%	BASO%	EOSINO%	OTHER%
- 22	15.8	43.5	46.5	8.5	0	1.5	0
- 15	19.8	58	35	7	0	0	0
- 8	14.4	37	51	9	0	1	2
- 1	12.4	42.5	50.5	6	0	1	0
Dose 1 - 0							
+ 6	4.0	23(11)	73	4	0	0	0
9	5.5	37(31)	52	11	0	0	0
10	Died						

(+ Non-Lob. Neutr. shown where >10%)

APPENDIX II
TABLE 21

ADRIAMYCIN : NORMAL PIGS - PIG No 48 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)

ABSOLUTE WHITE BLOOD CELLS - COUNTS $\times 10^9$ /LITRE

DAYS FROM START OF DOSING	WBC	T.NEUTR.	LYMPH	MONO	BASO	EOSINO%	OTHER
- 22	25.6	11.6	11.0	2.2	0	0.8	0
- 15	28.0	12.6	13.2	2.0	0	0	0.2
- 8	25.1	9.5	12.8	2.3	0	0.3	0.2
- 1	18.7	4.2	12.1	2.0	0	0.2	0.2
Dose 1 - 0							
+ 6	8.8	2.1	6.0	0.7	0	0	0
9	16.1	7.1	7.1	1.9	0	0	0
13	19.8	11.1	6.9	1.8	0	0	0
20	22.0	9.5	11.2	1.3	0	0	0
Dose 2 - 21							
27	13.4	5.5	6.0	1.6	0	0.3	0
30	14.4	7.3	4.5	2.4	0	0.1	0.1
34	18.4	13.2	3.4	1.7	0	0.1	0
41	21.8	12.9	7.1	1.4	0	0.4	0
Dose 3 - 42							
48	3.9	1.3	2.3	0.2	0	0	0.1
51	6.8	2.6	2.8	1.4	0	0	0
55	6.7	4.2	1.6	0.9	0	0	0
58	Died						

TABLE 22

ADRIAMYCIN : NORMAL PIGS - PIG NO 41 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)

ABSOLUTE WHITE BLOOD CELLS - COUNTS $\times 10^9$ /LITRE

DAYS FROM START OF DOSING	WBC	T.NEUTR.	LYMPH	MONO	BASO	EOSINO%	OTHER
- 22	15.8	6.9	7.4	1.3	0	0.2	0
- 15	19.8	11.5	6.9	1.4	0	0	0
- 8	14.4	5.3	7.4	1.3	0	0.1	0.3
- 1	12.4	5.3	6.3	0.7	0	0.1	0
Dose 1 - 0							
+ 6	4.0	0.9	2.9	0.2	0	0	0
9	5.5	2.0	2.9	0.6	0	0	0
10	Died						

APPENDIX II
TABLE 23

ADRIAMYCIN : NORMAL PIGS - PIG No 39 (SALINE - TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	6.38	0.30	9.5	47.0	31.7	14.9	5.94	404
- 15	6.48	0.30	9.4	46.3	31.3	14.5	7.76	504
- 8	6.66	0.29	9.4	43.5	32.4	14.1	8.00	480
- 1	5.88	0.26	8.4	44.2	32.3	14.3	5.94	457
Dose 1 - 0								
+ 6	5.67	0.25	8.3	44.1	33.2	14.6	7.25	842
13	6.01	0.26	8.3	43.3	31.9	13.8	9.14	691
20	6.32	0.28	8.6	44.3	30.7	13.6	5.65	605
Dose 2 - 21								
27	5.84	0.315	8.9	53.9	28.2	15.2	9.51	529
30	6.21	0.27	8.9	43.5	33.0	14.3	7.53	434
34	6.05	0.29	9.4	47.9	32.4	15.5	10.67	459
41	6.17	0.28	9.5	45.4	33.9	15.4	8.00	1008
Dose 3 - 42								
48	5.90	0.305	9.7	51.7	31.8	16.4	8.75	516
51	5.92	0.29	9.3	49.0	32.1	15.7	7.35	534
55	6.22	0.305	9.7	49.0	31.8	15.6	9.21	563
62	6.26	0.31	10.0	49.5	32.3	16.0	6.0	474
Dose 4 - 63								
69	7.39	0.33	11.6	44.7	35.2	15.7	7.56	392
72	6.57	0.34	10.8	51.8	31.8	16.4	6.67	380
76	6.67	0.32	10.8	48.0	33.8	16.2	6.86	316
84	6.91	0.335	11.2	48.5	33.4	16.2	7.98	294
Dose 5 - 84								
90	7.55	0.355	12.3	47.0	34.6	16.3	7.79	272
93	7.08	0.34	11.9	48.02	35.0	16.81	6.67	222
97	7.61	0.355	12.1	46.6	34.1	15.9	8.24	340
104	7.76	0.37	12.5	47.7	33.8	16.1	7.04	269
Dose 6 - 105								
111	7.62	0.35	13.1	45.9	37.4	17.2	9.78	215
114	7.11	0.35	11.8	49.2	33.7	16.6	7.62	372
118	7.26	0.385	12.0	53.0	31.2	16.5	6.92	264
End of treatment								
126	7.47	0.36	12.4	48.2	34.4	16.6	6.65	291
132	7.40	0.37	12.5	50.0	33.8	16.9	7.40	253
139	7.60	0.34	12.3	44.7	36.2	16.2	6.32	210
146	7.55	0.36	12.9	47.7	35.8	17.1	7.53	267
153	7.93	0.395	13.8	49.8	34.9	17.4	6.48	168
160	7.46	0.385	13.3	51.6	34.5	17.8	8.47	261

APPENDIX II
TABLE 24

ADRIAMYCIN : NORMAL PIGS - PIG No 42 (SALINE - TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.23	0.35	11.5	48.4	32.9	15.9	6.40	400
- 15	7.00	0.335	11.2	47.9	33.4	16.0	7.76	448
- 8	7.35	0.325	11.4	44.2	35.1	15.5	6.35	425
- 1	6.82	0.32	10.9	46.9	34.1	16.0	6.40	341
Dose 1 - 0								
+ 6	7.11	0.32	10.9	45.0	34.1	15.3	6.75	521
13	6.77	0.29	10.5	42.8	36.2	15.5	7.31	475
20	6.01	0.27	9.5	44.9	35.1	15.8	6.59	418
Dose 2 - 21								
27	6.81	0.29	10.3	42.6	35.5	15.1	5.62	431
30	6.93	0.30	10.2	43.3	34.0	14.7	7.06	468
34	6.33	0.30	9.8	47.4	32.7	15.5	8.53	392
41	6.45	0.29	10.4	45.0	35.9	16.1	6.59	533
Dose 3 - 42								
48	6.71	0.32	11.1	47.7	34.7	16.5	8.75	511
51	5.99	0.305	9.9	50.9	32.5	16.5	7.78	503
55	6.51	0.31	10.4	47.6	33.5	16.0	8.48	600
62	6.40	0.31	10.3	48.4	33.2	16.1	6.0	469
Dose 4 - 63								
69	7.18	0.35	11.2	48.7	32.0	15.6	6.72	400
72	7.08	0.345	11.4	48.7	33.0	16.1	6.22	392
76	6.97	0.33	11.3	47.3	34.2	16.2	6.86	311
84	8.02	0.355	12.1	44.3	34.1	15.1	5.70	260
Dose 5 - 84								
90	7.21	0.36	12.1	49.9	33.6	16.8	6.36	340
93	7.37	0.35	12.1	47.5	34.6	16.4	5.33	301
97	7.51	0.355	12.4	47.3	34.9	16.5	6.06	379
104	7.89	0.38	13.2	48.2	34.7	16.7	5.92	272
Dose 6 - 105								
111	7.21	0.34	12.0	47.2	35.3	16.6	11.11	316
113	Destroyed							

APPENDIX II
TABLE 25

ADRIAMYCIN : NORMAL PIGS - PIG NO 43 (SALINE - TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.57	0.365	12.2	48.2	33.4	16.1	5.48	436
- 15	7.25	0.37	11.9	51.0	32.2	16.4	6.55	381
- 8	7.55	0.335	11.8	44.4	35.2	15.6	6.35	407
- 1	6.76	0.315	10.6	46.6	33.7	15.7	6.63	413
Dose 1 - 0								
+ 6	7.52	0.32	10.8	42.6	34.0	14.4	6.00	414
13	7.26	0.34	11.0	43.0	35.0	15.3	7.77	614
20	6.81	0.315	10.4	46.3	33.0	15.3	6.59	455
Dose 2 - 21								
27	7.14	0.30	10.8	42.0	36.0	15.1	5.84	375
30	6.81	0.31	10.5	45.5	33.9	15.4	6.35	292
34	6.79	0.32	10.7	47.1	33.4	15.8	8.00	372
41	6.68	0.31	10.8	46.4	34.8	16.2	5.41	765
Dose 3 - 42								
48	6.80	0.33	10.9	47.1	33.8	15.9	9.00	414
51	6.41	0.32	10.6	49.9	33.1	16.5	5.62	390
55	6.90	0.33	11.1	47.8	33.6	16.1	7.52	353
62	6.77	0.34	11.5	50.2	33.8	17.0	6.22	344
Dose 4 - 63								
69	7.31	0.34	12.0	46.5	35.3	16.4	6.09	262
72	6.96	0.345	11.7	49.6	33.9	16.8	5.72	307
76	6.98	0.345	11.7	49.4	33.9	16.8	6.86	262
84	7.63	0.36	13.0	47.2	36.1	17.0	5.32	213
Dose 5 - 84								
90	7.63	0.375	13.1	49.1	34.9	17.2	5.74	284
93	7.70	0.38	12.9	49.4	33.9	16.8	5.56	224
97	7.75	0.385	13.1	49.7	34.0	16.9	5.58	197
104	7.85	0.37	12.5	47.1	33.8	15.9	5.12	261
Dose 6 - 105								
111	7.67	0.35	12.9	45.6	36.9	16.8	8.44	266
113	Destroyed							

APPENDIX II
TABLE 26

ADRIAMYCIN : NORMAL PIGS - PIG No 46 (SALINE - TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.05	0.36	11.5	51.1	31.9	16.3	5.48	401
- 15	6.93	0.34	11.0	49.1	32.4	15.9	6.06	339
- 8	7.25	0.33	11.1	45.5	33.6	15.3	8.00	478
- 1	6.49	0.31	10.2	47.8	32.9	15.7	5.26	420
Dose 1 - 0								
+ 6	5.86	0.27	9.0	46.1	33.3	15.4	8.00	408
13	6.28	0.28	9.2	44.6	32.9	14.6	7.31	588
20	6.80	0.28	10.0	41.2	35.7	14.7	6.35	808
Dose 2 - 21								
27	7.11	0.30	9.8	42.2	32.3	13.8	5.62	461
30	6.52	0.30	9.9	46.0	33.0	15.2	7.06	452
34	6.51	0.30	9.9	46.1	33.0	15.2	8.27	453
41	6.29	0.29	9.8	46.1	33.8	15.6	4.24	414
Dose 3 - 42								
48	6.65	0.315	10.6	47.4	33.7	15.9	8.75	535
51	6.28	0.32	10.3	51.0	32.2	16.4	7.14	521
55	6.43	0.30	10.2	46.7	34.0	15.9	8.00	691
62	6.33	0.32	10.4	50.6	32.5	16.4	6.67	503
Dose 4 - 63								
69	6.83	0.34	10.8	49.8	31.8	15.8	6.72	319
72	6.71	0.335	10.6	49.9	31.6	15.8	6.44	410
76	6.70	0.315	10.6	47.0	33.7	15.8	8.69	388
84	7.33	0.34	11.6	46.4	34.1	15.8	6.84	281
Dose 5 - 84								
90	7.07	0.33	11.3	46.7	34.2	16.0	6.77	340
93	7.31	0.365	12.1	49.9	33.2	16.6	6.22	300
97	7.61	0.36	12.4	47.3	34.4	16.3	6.29	244
104	7.63	0.35	12.1	45.9	34.6	15.9	5.92	424
Dose 6 - 105								
111	8.18	0.35	13.5	42.8	38.6	16.5	7.55	270
114	7.44	0.31	12.2	41.7	39.4	16.4	7.24	417
118	7.03	0.315	11.4	44.8	36.2	16.2	6.70	269
End of treatment								
126	7.39	0.35	11.9	47.4	34.0	16.1	6.65	331
132	7.51	0.355	12.3	47.3	34.6	16.4	6.80	303
139	7.88	0.36	12.9	45.7	35.8	16.4	4.32	273
146	8.02	0.38	13.1	47.4	34.5	16.3	6.59	309
153	8.12	0.36	13.5	44.3	37.5	16.6	6.48	220
160	7.41	0.35	12.6	47.2	36.0	17.0	6.82	285

APPENDIX II
TABLE 27

ADRIAMYCIN : NORMAL PIGS - PIG No 40 (1 mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.64	0.38	12.7	49.7	33.4	16.6	6.40	442
- 15	7.40	0.37	12.2	50.0	33.0	16.5	7.76	408
- 8	7.62	0.36	12.3	47.2	34.2	16.1	6.82	428
- 1	6.87	0.33	11.0	48.0	33.3	16.0	6.86	381
Dose 1 - 0								
+ 6	6.60	0.28	10.1	42.4	36.1	15.3	5.75	329
13	6.63	0.29	9.7	43.7	33.5	14.6	6.40	671
20	5.96	0.29	10.1	48.7	34.8	16.9	6.59	500
Dose 2 - 21								
27	6.76	0.32	10.9	47.3	34.1	16.1	5.62	586
30	6.46	0.30	10.8	46.4	36.0	16.7	7.53	433
34	6.14	0.30	10.2	48.9	34.0	16.6	8.00	406
41	6.65	0.33	11.1	49.6	33.6	16.7	7.06	764
Dose 3 - 42								
48	6.40	0.325	11.1	50.8	34.2	17.3	7.50	459
51	5.88	0.30	10.0	51.0	33.3	17.0	7.35	437
55	6.57	0.335	11.1	51.0	33.1	16.9	8.24	528
62	6.65	0.335	11.3	50.4	33.7	17.0	6.00	401
Dose 4 - 63								
69	7.00	0.34	12.3	48.6	36.2	17.6	6.51	315
72	6.82	0.33	11.9	48.4	36.1	17.4	6.00	292
76	6.95	0.335	11.9	48.2	35.5	17.1	6.63	302
84	7.41	0.365	12.5	49.3	34.2	16.9	7.22	285
Dose 5 - 84								
90	7.23	0.365	12.7	50.5	34.8	17.6	8.00	306
93	7.39	0.36	12.8	48.7	35.6	17.3	6.89	289
97	7.28	0.36	12.8	49.5	35.6	17.6	6.79	245
104	7.84	0.37	13.0	47.2	35.1	16.6	6.24	276
Dose 6 - 105								
111	7.75	0.36	13.5	46.5	37.5	17.4	8.44	230
114	7.10	0.34	12.7	47.9	37.4	17.9	6.86	401
118	7.02	0.33	12.2	47.0	37.0	17.4	8.43	244
End of treatment								
126	7.51	0.37	13.5	49.3	36.5	18.0	7.06	261
132	7.38	0.375	13.2	50.8	35.2	17.9	7.80	273
139	7.38	0.38	13.3	51.5	35.0	18.0	6.74	208
146	7.73	0.39	13.5	50.5	34.6	17.5	7.29	231
153	7.87	0.35	14.0	44.5	40.0	17.7	6.10	238
160	7.17	0.315	12.9	48.8	36.0	17.6	7.53	-

APPENDIX II

TABLE 28

ADRIAMYCIN : NORMAL PIGS - PIG No 45 (1 mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	6.93	0.35	11.7	50.5	33.4	16.9	6.17	504
- 15	6.85	0.34	11.3	49.6	33.2	16.5	6.79	398
- 8	6.89	0.335	11.4	48.6	34.0	16.5	6.59	595
- 1	6.83	0.32	10.7	46.9	33.4	15.7	5.49	361
Dose 1 - 0								
+ 6	5.80	0.25	8.9	43.1	35.6	15.3	5.00	298
13	5.93	0.26	9.1	43.8	35.0	15.3	5.94	750
20	6.27	0.29	10.1	46.3	34.8	16.1	6.35	453
Dose 2 - 21								
27	6.39	0.30	10.1	46.9	32.7	15.3	5.19	521
30	6.63	0.30	10.4	45.2	34.7	15.7	5.18	+
34	6.14	0.28	10.1	45.6	36.1	16.5	7.20	530
41	6.37	0.32	11.1	50.2	34.7	17.4	4.24	392
Dose 3 - 42								
48	6.28	0.32	10.8	51.0	33.8	17.2	7.50	403
51	5.79	0.30	10.1	51.8	33.7	17.4	7.35	416
55	5.99	0.31	10.3	51.8	33.2	17.2	7.27	553
62	6.08	0.32	10.6	52.6	33.1	17.4	6.44	479
Dose 4 - 63								
69	6.52	0.335	11.1	51.4	33.1	17.0	6.72	293
72	6.32	0.335	11.1	53.0	33.1	17.6	5.78	244
76	6.31	0.32	11.3	50.7	35.3	17.9	6.40	360
84	7.21	0.345	12.0	47.9	34.8	16.6	6.08	302
Dose 5 - 84								
90	6.83	0.355	12.3	52.0	34.6	18.0	5.95	280
93	6.81	0.345	11.9	50.7	34.5	17.5	5.33	238
97	6.91	0.34	11.9	49.2	35.0	17.2	5.33	292
104	7.14	0.365	12.6	51.1	34.5	17.6	6.24	275
Dose 6 - 105								
111	7.00	0.33	12.1	47.1	36.7	17.3	8.00	197
113	Destroyed							

+ Partially clotted sample

APPENDIX II

TBALE 29

ADRIAMYCIN : NORMAL PIGS - PIG No. 47 (2 mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.12	0.33	10.8	46.3	32.7	15.2	4.57	472
15	6.62	0.33	10.7	49.8	32.4	16.2	3.39	482
- 8	7.05	0.315	10.4	44.7	33.0	14.8	5.65	440
- 1	6.30	0.265	9.3	42.1	35.1	14.8	6.40	477
Dose 1 - 0								
+ 6	5.45	0.235	8.7	43.1	37.0	16.0	5.25	224
13	5.84	0.27	8.6	46.2	31.9	14.7	6.86	583
20	5.94	0.265	8.6	44.6	32.5	14.5	6.12	455
Dose 2 - 21								
27	6.02	0.24	8.5	39.9	35.4	14.1	5.40	311
30	5.70	0.24	7.9	42.1	32.9	13.9	7.53	218
34	5.21	0.25	8.4	48.0	33.6	16.1	10.13	447
41	5.74	0.285	9.2	49.7	32.3	16.0	6.59	118
Dose 3 - 42								
48	5.80	0.31	9.7	53.4	31.3	16.7	8.00	272
51	5.27	0.26	8.7	49.3	33.5	16.5	5.62	209
55	5.08	0.25	8.4	49.2	33.6	16.5	8.73	272
62	5.78	0.295	9.7	51.0	32.9	16.8	5.78	445
Dose 4 - 63								
69	6.69	0.35	10.9	52.3	31.1	16.3	6.51	250
72	6.10	0.30	10.2	49.2	34.0	16.7	7.78	223
76	6.00	0.30	10.3	50.0	34.3	17.2	7.77	201
84	6.73	0.35	11.1	52.0	31.7	16.5	6.46	193
Dose 5 - 84								
90	6.65	0.33	11.4	49.6	34.5	17.1	6.97	182
93	6.46	0.32	11.0	49.5	34.4	17.0	5.33	111
97	6.18	0.31	10.7	50.2	34.5	17.3	8.24	283
104	7.36	0.325	11.4	44.2	35.1	15.5	7.04	223
Dose 6 - 105								
110	Died							

APPENDIX II

TABLE 30

ADRIAMYCIN : NORMAL PIGS - PIG No 49 (2mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 22	7.56	0.38	12.7	50.3	33.4	16.8	5.94	458
- 15	7.08	0.38	12.0	53.7	31.6	16.9	5.33	464
- 8	7.32	0.335	11.8	45.8	35.2	16.1	7.71	209
- 1	6.28	0.31	10.1	49.4	32.6	16.1	6.63	357
Dose 1 - 0								
+ 6	5.99	0.28	9.5	46.7	33.9	15.9	6.00	217
13	6.40	0.27	9.6	42.2	35.6	15.0	6.17	472
20	6.44	0.30	10.3	46.6	34.3	16.0	5.88	501
Dose 2 - 21								
27	6.50	0.285	9.7	43.8	34.0	14.9	6.05	412
30	6.14	0.30	9.7	48.9	32.3	15.8	5.65	336
34	6.03	0.30	10.0	49.8	33.3	16.6	7.47	357
41	6.22	0.32	10.4	51.4	32.5	16.7	4.24	395
Dose 3 - 42								
48	5.96	0.31	10.6	52.0	34.2	17.8	7.00	289
51	5.60	0.28	9.6	50.0	34.3	17.1	4.76	129
55	5.42	0.27	9.1	49.8	33.7	16.8	6.79	262
62	6.15	0.31	10.5	50.4	33.9	17.1	6.22	373
Dose 4 - 63								
69	6.59	0.33	10.9	50.1	33.0	16.5	6.72	203
72	6.19	0.32	10.7	51.7	33.4	17.3	6.00	162
76	6.21	0.315	10.9	50.7	34.6	17.6	5.49	201
84	6.76	0.345	11.5	51.0	33.3	17.0	4.56	338
Dose 5 - 84								
90	6.67	0.345	11.7	51.7	33.9	17.5	5.13	179
93	6.42	0.31	11.1	48.3	35.8	17.3	6.00	106
97	6.71	0.325	11.4	48.4	35.1	17.0	5.39	198
104	6.89	0.36	11.9	52.2	33.1	17.3	5.92	202
Dose 6 - 105								
109	Died							

APPENDIX II
TABLE 31

ADRIAMYCIN : NORMAL PIGS - PIG No 48 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	UREA	THROMB
- 22	7.60	0.37	12.3	48.7	33.2	16.2	6.17	342
- 15	6.98	0.35	11.7	50.1	33.4	16.8	5.82	119 *
- 8	7.44	0.34	11.5	45.7	33.8	15.5	6.82	346
- 1	6.60	0.305	10.3	46.2	33.8	15.6	6.86	304
Dose 1 - 0								
+ 6	6.29	0.30	9.9	47.7	33.0	15.7	4.25	95
9	-	-	9.3	-	-	-	-	72
13	4.89	0.22	7.2	45.0	32.7	14.7	6.17	55
20	5.48	0.26	8.5	47.4	32.7	15.5	7.06	528
Dose 2 - 21								
27	6.08	0.27	9.7	44.4	35.9	16.0	5.84	225
30	5.98	0.25	8.9	41.8	35.6	14.9	5.88	106
34	4.49	0.24	7.9	53.5	32.9	17.6	6.97	223
41	5.62	0.31	10.3	55.2	33.2	18.3	4.47	439
Dose 3 - 42								
48	6.02	0.345	11.5	57.3	33.3	19.1	6.25	137
51	5.72	0.315	10.3	55.1	32.7	18.0	4.11	22
55	4.16	0.22	7.6	52.9	34.5	18.3	6.79	22
58	Died							

* Partially clotted sample

TABLE 32

ADRIAMYCIN : NORMAL PIGS - PIG No 41 (4 mg/kg ADRIAMYCIN INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	UREA	THROMB
- 22	7.06	0.36	12.0	51.0	33.3	17.0	6.47	427
- 15	6.94	0.35	11.8	50.4	33.7	17.0	5.33	342
- 8	7.65	0.35	12.2	45.8	34.9	15.9	6.12	327
- 1	7.19	0.345	11.3	48.0	32.8	15.7	6.40	340
Dose 1 - 0								
+ 6	7.00	0.32	10.9	45.7	34.1	15.6	6.25	106
9	-	-	6.1	-	-	-	-	57
10	Died							

APPENDIX II

TABLE 33

ADRIAMYCIN : NORMAL PIGS

SERUM ALKALINE PHOSPHATASE - (**iu**/l)

DAYS FROM START OF DOSING	GROUP D - CONTROLS				GROUP A (1 mg/kg)		GROUP B (2 mg/kg)		GROUP C (4 mg/kg)	
	39	42	43	46	40	45	47	49	41	48
- 22	93	161	125	204	156	139	120	120	157	135
- 15	116	126	123	161	120	101	41	112	127	146
- 8	70	107	65	142	88	65	78	98	103	112
- 1	121	141	106	158	111	89	111	107	144	136
Dose 1 - 0										
6	89	120	85	123	82	87	65	69	143	34
13	148	149	108	146	93	47	102	61	Dead	27
20	100	74	123	136	93	81	105	87		36
Dose 2 - 21										
27	150	132	115	94	115	92	130	81		64
30	140	120	109	166	120	66	87	108		45
34	143	131	118	144	98	78	109	88		38
41	145	95	102	126	100	78	132	70		45
Dose 3 - 42										
48	159	130	121	137	110	87	82	60		44
51	81	104	155	109	108	116	61	45		22
55	180	117	105	148	128	102	88	72		27
62	145	117	109	157	102	111	130	120		Dead
Dose 4 - 63										
69	110	75	77	110	63	61	96	80		
72	127	108	86	136	72	60	138	90		
76	MEASUREMENTS			DISCONTINUED						

APPENDIX II

TABLE 34

ADRIAMYCIN : NORMAL PIGS

SERUM GLUTAMIC OXALOACETATE TRANSAMINASE (SGOT) (iu/l)

DAYS FROM START OF DOSING	GROUP D - CONTROL				GROUP A (1mg/kg)		GROUP B (2 mg/kg)		GROUP C (4 mg/kg)	
	39	42	43	46	40	45	47	49	41	48
- 22	24.2	16.5	21.6	19.5	16.9	16.9	18.0	25.2	22.6	20.0
- 15	22.6	20.6	23.6	18.5	21.6	22.6	12.3	18.0	19.5	36.0
- 8	19.5	15.4	17.5	17.5	18.5	16.4	24.7	28.8	17.5	50.4
- 1	67.5	12.4	30.4	10.8	18.5	11.8	9.8	16.5	14.9	29.9
Dose 1 - 0										
6	55.6	20.0	30.9	124.1	238.0	148.7	67.4	46.3	147.2	12.8
13	28.8	20.6	16.9	14.9	11.3	12.3	26.2	17.5	Dead	14.4
20	22.6	29.8	20.6	17.5	18.5	14.4	13.9	16.9		13.3
Dose 2 - 21										
27	20.6	16.4	14.4	13.3	14.4	14.4	15.4	17.5		10.3
30	13.3	15.9	16.4	18.5	12.8	8.2	4.6	16.9		10.3
34	19.0	14.4	13.4	24.2	20.6	16.4	14.4	13.3		21.6
41	26.0	15.5	21.0	23.0	18.0	24.0	19.0	44.0		24.0
Dose 3 - 42										
48	38.6	29.3	53.5	24.2	28.8	48.4	33.4	49.4		15.4
51	22.1	24.7	28.3	39.6	21.6	61.2	21.1	7.0		9.0
55	21.0	20.0	26.7	16.0	17.0	11.0	19.5	19.0		48.5
62	13.4	23.0	14.4	7.2	14.9	21.6	17.0	56.7		Dead
Dose 4 - 63										
69	19.0	17.0	24.0	17.0	29.0	22.0	26.0	23.0		
72	11.0	19.5	24.2	17.5	21.6	18.0	14.0	13.4		
76										

MEASUREMENTS

DISCONTINUED

APPENDIX II
TABLE 35

ADRIAMYCIN : NORMAL PIGS • ORGAN AND LYMPH NODE WEIGHTS, IN GRAMS

DOSE LEVEL PIG NO	SALINE CONTROLS									
	39	42	43	46	40	45	47	49	41	48
	1 mg/kg									
	2 mg/kg									
	4 mg/kg									
Submandibular LN	3.31	6.14	6.00	6.26	5.00	3.48	2.96	4.57	2.72	2.00
Parotid LN	4.91	4.70	5.44	8.10	6.38	3.17	2.37	5.79	2.48	4.64
Retropharyngeal LN	2.14	2.85	2.80	1.99	2.48	1.61	2.09	3.51	0.95	0.71
Cervical LN	4.42	6.80	6.85	5.77	6.23	4.61	2.00	4.51	3.20	5.30
Prescapular LN	2.71	8.82	2.60	3.68	3.48	2.83	1.54	1.07	2.17	2.70
Left Bronchial LN	2.43	3.35	3.95	4.81	5.55	2.33	1.82	2.44	3.05	4.00
Mid Bronchial LN	0.27	0.65	0.66	0.81	0.57	0.60	0.66	0.44	0.35	0.34
Apical Bronchial LN	0.65	1.25	0.50	0.63	0.70	0.56	0.32	0.59	0.65	0.41
Right Bronchial LN	0.70	0.80	0.68	NF	0.83	0.31	0.59	0.61	0.50	0.34
Internal Iliac LN	0.72	0.58	0.36	1.00	0.85	1.02	0.46	0.65	0.74	0.69
External Iliac LN	3.00	7.90	4.54	6.79	6.13	4.44	4.31	4.21	2.50	3.94
Inguinal LN	5.30	9.30	6.85	6.67	6.76	6.19	9.62	6.18	3.78	5.76
Mesenteric and Colonic LN	135.00	107.00	192.00	200.00	190.00	87.00	85.15	140.00	95.00	100.00
Gastric LN	10.76	14.23	19.95	11.60	11.13	10.00	9.68	12.34	7.93	10.49
Splenic LN	1.73	2.12	1.92	1.64	1.55	0.64	1.12	1.44	0.59	0.64
Precrural LN	1.23	2.75	2.95	1.75	1.19	2.15	1.13	1.91	1.27	1.58
Popliteal LN	NF	1.40	0.69	0.84	NF	0.69	0.17	0.91	NF	1.22
Liver	1140.00	1320.00	1780.00	1780.00	1910.00	1090.00	756.00	862.00	710.00	874.00
Kidney (mean of 2)	65.00	105.00	110.00	137.00	125.00	65.00	70.00	76.00	50.00	81.00
Adrenal (mean of 2)	2.84	3.55	4.20	4.5	3.78	1.85	3.0	3.25	1.76	3.20
Thymus	56.13	43.15	70.86	69.33	78.16	19.70	2.67	10.29	8.00	2.40
Spleen	160.00	175.00	160.00	320.00	230.00	90.00	28.00	25.00	19.00	21.50

APPENDIX II
TABLE 36

ADRIAMYCIN THERAPY - PIG No 3785 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS
WHITE BLOOD CELL COUNTS X 10⁹/LITRE + DIFFERENTIAL COUNTS (%)

DAYS FROM START OF DOSING	WBC	TOTAL NEUTROPHILS %	MONONUCLEARS %	BASO %	EOSINO% %	OTHER %
- 28	19.8	28.5	70.5	1.0	0	0
- 22	22.3	29.5	68.5	2.0	0	0
- 15	23.8	23.5	75.5	0	1.0	0
- 9	26.6	18.5	80.0	0.5	1.0	0
Prednisolone						
- 1	15.6	28.5	69.0	1.0	1.5	0
Dose 1 - 0						
6	12.5	37.0	63.0	0	0	0
9	11.7	29.0	68.0	0	3.0	0
13	14.5	35.0	61.0	2.0	2.0	0
21	15.9	37.0	59.5	3.5	0	0
Dose 2 - 23						
27	10.4	42.0	51.0	4.0	3.0	0
30	12.3	46.0	51.5	0.5	2.0	0
34	15.9	42.5	57.0	0	0.5	0
41	14.5	24.5	74.0	0	1.5	0
Dose 3 - 44						
48	11.6	55.5	41.0	3.5	0	0
51	21.7	59.0	41.0	0	0	0
55	20.3	67.5	32.5	0	0	0
56	Destroyed					

TBALE 37

ADRIAMYCIN THERAPY - PIG No 3786 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS

DAYS FROM START OF DOSING	WBC	TOTAL NEUTROPHILS %	MONONUCLEARS %	BASO %	EOSINO %	OTHER %
- 28	20.1	19.5	78.5	1.0	1.0	0
- 22	17.0	25.0	72.5	2.0	0.5	0
- 15	19.6	29.5	70.0	0	0.5	0
- 9	21.6	8.5	91.0	0.5	0	0
Prednisolone						
- 1	16.9	32.0	64.5	0.5	3.0	0
Dose 1 - 0						
6	15.2	37.0	62.0	1.0	0	0
9	12.7	16.0	79.0	4.0	1.0	0
13	17.9	56.5	41.5	1.5	0.5	0
21	21.8	35.0	61.0	3.0	1.0	0
Dose 2 - 23						
27	10.8	34.5	61.5	3.0	1.0	0
30	14.0	42.0	50.5	3.0	4.5	0
34	16.2	41.5	56.5	2.0	0	0
40	Died					

APPENDIX II

TABLE 38

ADRIAMYCIN THERAPY - PIG No 192 - 1 mg/kg ADRIAMYCIN EVERY 3 WEEKS
 WHITE BLOOD CELL COUNTS X 10⁹/LITRE + DIFFERENTIAL COUNTS (%).

DAYS FROM START OF DOSING	WBC	TOTAL NEUTROPHILS %	MONONUCLEARS %	BASO %	EOSINO %	OTHER %
- 16	19.7	35	63	0	2	0
- 9	18.0	35	65	0	0	0
- 2	19.1	17	83	0	0	0
Dose 1 - 0						
7	13.1	27	73	0	0	0
12	18.9	19	81	0	0	0
19	21.0	19	81	0	0	0
Dose 2 - 21						
26	12.9	17	83	0	0	0
33	19.1	29	71	0	0	0
40	18.2	21	78	1	0	0
Dose 3 - 42						
47	11.1	23	76	0	1	0
54	13.5	26	72	2	0	0
61	19.0	37	62	1	0	0
Dose 4 - 63						
68	15.2	38	60	0	2	0
75	19.8	32	68	0	0	0
82	15.3	14	85	0	1	0
Dose 5 - 84						
89	14.8	19	79	1	1	0
96	18.5	23	76	0	1	0
103	17.1	24	73	2	1	0
Dose 6 - 105						
110	9.5	16	80	1	3	0
117	13.4	29	70	0	1	0
125	16.8	28	72	0	0	0
Dose 7 - 126						
131	9.6	25	73	1	1	0
138	14.3	22	77	0	1	0
145	23.0	26	72	1	0	1
Dose 8 - 147						
152	8.4	9	89	2	0	0
159	17.3	21	78	0	1	0
161	Destroyed					

APPENDIX II

TABLE 39

ADRIAMYCIN THERAPY - PIG No 194 - 1 mg/kg ADRIAMYCIN EVERY 3 WEEKS
 WHITE BLOOD CELL COUNTS X 10⁹/LITRE + DIFFERENTIAL COUNTS (%)

DAYS FROM START OF DOSING	WBC	TOTAL NEUTROPHILS	MONONUCLEARS	BASO	EOSINO	OTHER
		%	%	%	%	%
- 16	20.8	25	75	0	0	0
- 9	23.5	28	72	0	0	0
- 2	24.7	15	85	0	0	0
Dose 1 - 0						
7	20.4	27	70	3	0	0
12	27.1	22	76	1	1	0
19	21.3	17	81	1	1	0
Dose 2 - 21						
26	26.0	21	78	1	0	0
33	30.5	13	86	1	0	0
40	41.3	9	89	2	0	0
Dose 3 - 42						
47	21.1	14	84	1	1	0
54	25.7	12	87	1	0	0
61	43.9	16	84	0	0	0
Dose 4 - 63						
68	23.4	14	83	1	2	0
75	23.5	5	95	0	0	0
82	35.2	11	88	0	1	0
Dose 5 - 84						
89	25.2	49	50	0	1	0
96	23.3	25	73	1	1	0
103	31.6	11	88	0	1	0
Dose 6 - 105						
110	9.2	9	89	1	1	0
117	10.6	14	86	0	0	0
125	23.8	16	81	1	1	1
Dose 7 - 126						
131	10.3	17	79	1	3	0
138	16.6	22	78	0	0	0
145	25.5	16	81	2	1	0
Dose 8 - 147						
152	13.6	23	73	4	0	0
159	15.5	15	82	3	0	0
173	28.1	12	87	0	1	0
180	29.1	17	80	1	2	0
187	31.9	13	86	0	1	0
195	18.0	24	75	0	1	0
197	Destroyed					

APPENDIX II
TABLE 40

ADRIAMYCIN THERAPY - PIG No 3785 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	4.83	0.24	8.7	49.7	36.3	18.0	12.40	133
- 22	4.55	0.24	8.5	52.8	35.4	18.7	10.80	424 ⁺
- 15	4.22	0.25	8.4	59.2	33.6	19.9	11.50	49 ⁺
- 9	3.93	0.22	7.5	56.0	34.1	19.1	9.08	80
Prednisolone								
- 1	4.88	0.285	9.7	58.4	34.0	19.9	12.00	188
Dose 1 - 0								
6	4.69	0.27	10.4	57.6	38.5	22.2	8.40	138
9	5.16	0.27	9.7	52.3	35.9	18.8	8.44	213
13	5.11	0.27	9.8	52.8	36.3	19.2	8.46	124
21	5.29	0.305	9.8	57.7	32.1	18.5	9.12	89
Dose 2 - 23								
27	5.37	0.275	9.9	51.2	34.9	17.9	5.74	237 ⁺
30	5.39	0.28	9.6	52.0	34.3	17.8	6.67	86 ⁺
34	4.99	0.26	9.0	52.1	34.6	18.0	6.79	127
41	5.66	0.33	10.7	58.3	32.4	18.9	7.84	149
Dose 3 - 44								
48	6.84	0.38	13.4	55.6	35.3	19.6	12.66	162
51	7.06	0.40	13.7	56.7	34.3	19.4	9.90	188
55	6.58	0.34	12.5	51.7	36.8	19.0	9.08	170
56	Destroyed							

TABLE 41

ADRIAMYCIN THERAPY - PIG No 3786 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	3.87	0.22	7.6	56.9	34.6	19.6	9.80	106
- 22	3.70	0.22	7.3	59.5	33.2	19.7	10.80	85
- 15	3.47	0.235	7.6	67.7	32.3	21.9	8.25	91
- 9	3.19	0.205	6.6	64.3	32.2	20.7	7.78	81
Prednisolone								
- 1	4.11	0.27	8.8	65.7	32.6	21.4	8.44	181
Dose 1 - 0								
6	4.55	0.26	9.2	57.1	35.4	20.2	6.30	160
9	4.28	0.26	8.7	60.8	33.5	20.3	6.22	192
13	4.58	0.275	9.4	60.0	34.2	20.5	6.63	204
21	4.76	0.28	9.0	58.8	32.1	18.9	7.22	164
Dose 2 - 23								
27	4.71	0.255	9.2	54.1	36.1	19.5	4.92	239
30	4.91	0.28	9.6	57.0	34.3	19.6	7.11	178
34	4.91	0.27	9.3	55.0	34.4	18.9	6.79	149
40	Died							

APPENDIX II
TABLE 42

ADRIAMYCIN THERAPY - PIG No 192 - 1 mg/kg ADRIAMYCIN EVERY 3 WEEKS

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 16	5.36	0.265	9.1	49.4	34.3	17.0	5.07	350
- 9	5.35	0.30	10.5	56.1	35.0	19.6	6.00	+
- 2	6.15	0.33	11.2	53.7	33.9	18.2	7.36	+
Dose 1 - 0								
7	5.90	0.33	11.1	55.9	33.6	18.8	6.32	225 ⁺
12	5.62	0.315	10.8	56.1	34.3	19.2	6.88	121 ⁺
19	4.93	0.29	9.8	58.8	33.8	19.9	6.88	248
Dose 2 - 21								
26	6.79	0.33	10.8	48.6	32.7	15.9	6.17	193
33	6.20	0.32	10.6	51.6	33.1	17.1	8.96	330
40	5.81	0.335	10.4	57.7	31.0	17.9	6.64	298
Dose 3 - 42								
47	6.34	0.34	11.7	53.6	34.4	18.5	-	289
54	5.87	0.34	10.6	57.9	31.2	18.1	7.62	183
61	6.36	0.33	11.0	51.9	33.3	17.3	6.08	300
Dose 4 - 63								
68	6.62	0.35	12.1	52.9	34.6	18.3	5.76	201
75	6.27	0.335	11.4	53.4	34.0	18.2	7.74	317
82	5.89	0.315	10.5	53.5	33.3	17.8	7.84	295
Dose 5 - 84								
89	6.08	0.34	11.4	55.9	33.5	18.8	6.22	230
96	6.00	0.31	11.2	51.7	36.1	18.7	-	191
103	6.04	0.335	11.2	55.5	33.4	18.5	7.58	170
Dose 6 - 105								
110	6.76	0.33	12.2	48.8	37.0	18.0	5.25	+
117	6.56	0.38	12.5	57.9	32.9	19.1	-	96 ⁺
125	6.00	0.325	10.9	54.2	33.5	18.2	-	92 ⁺
Dose 7 - 120								
131	5.58	0.305	10.5	54.7	34.4	18.8	-	68 ⁺
138	5.70	0.33	10.8	57.9	32.7	18.9	8.33	114
145	6.24	0.33	11.2	52.9	33.9	17.9	8.47	184
Dose 8 - 147								
152	5.71	0.30	10.6	52.5	35.3	18.6	7.00	78
159	5.44	0.30	10.9	55.1	36.3	20.0	6.36	112
161	Destroyed							

APPENDIX II

TABLE 43

ADRIAMYCIN THERAPY - PIG No 194 - 1 mg/kg ADRIAMYCIN EVERY 3 WEEKS

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 16	5.67	0.31	10.0	54.7	32.3	17.6	5.07	445
- 9	5.99	0.35	11.1	58.4	31.7	18.5	5.60	194
- 2	6.19	0.31	10.7	50.1	34.5	17.3	7.84	217
Dose 1 - 0								
7	5.64	0.315	10.2	55.9	32.4	18.1	5.89	263
12	5.73	0.315	10.2	55.0	32.4	17.8	7.20	336
19	5.53	0.31	10.8	56.1	34.8	19.5	6.88	355
Dose 2 - 21								
26	6.94	0.33	10.9	47.6	33.0	15.7	7.78	200 ⁺
33	6.49	0.32	10.6	49.3	33.1	16.3	8.32	90 ⁺
40	7.84	0.37	13.9	47.2	37.6	17.7	5.89	50 ⁺
Dose 3 - 42								
47	5.38	0.31	9.8	57.6	31.6	18.2	-	+
54	5.52	0.31	10.3	56.2	33.2	18.7	7.04	+
61	5.53	0.30	10.3	54.3	34.3	18.6	5.12	81 ⁺
Dose 4 - 63								
68	5.55	0.315	11.1	56.8	35.2	20.0	5.60	67 ⁺
75	5.39	0.30	10.5	55.7	35.0	19.5	7.26	175
82	4.76	0.275	9.8	57.8	35.6	20.6	7.36	158
Dose 5 - 84								
89	4.51	0.265	9.2	58.8	34.7	20.4	6.00	246 ⁺
96	4.90	0.28	10.1	57.1	36.1	20.6	-	+
103	5.21	0.295	10.8	56.6	36.6	20.7	8.00	87 ⁺
Dose 6 - 105								
110	4.97	0.265	10.1	53.3	38.1	20.3	4.25	+
117	5.38	0.30	11.0	55.8	36.7	20.4	-	+
125	5.80	0.31	11.2	53.4	36.1	19.3	-	98 ⁺
Dose 7 - 126								
131	5.17	0.27	10.5	52.2	38.9	20.3	-	85 ⁺
138	6.37	0.35	12.2	54.9	34.9	19.2	6.67	112 ⁺
145	6.23	0.325	11.7	52.2	36.0	18.8	4.71	+
Dose 8 - 147								
152	6.43	0.32	12.6	49.8	39.4	19.6	4.50	88 ⁺
159	6.14	0.30	12.2	48.9	40.7	19.9	3.27	82
173	5.39	0.27	11.0	50.1	40.7	20.4	4.00	140
180	5.47	0.30	11.1	54.8	37.0	20.3	5.68	159
187	5.19	0.28	10.8	54.0	38.6	20.8	-	131
195	4.80	0.275	10.4	57.3	37.9	21.7	5.67	172
197	Destroyed							

APPENDIX II

TABLE 44

ADRIAMYCIN THERAPY - PIGS 3785 and 3786 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS
 SGOT (iu/l) AND SERUM BILIRUBIN (mol/l)

DAYS FROM START OF DOSING	SGOT		SERUM BILIRUBIN TOTAL		FREE	CONJUGATED
	3785	3786	3785	3786	3785 only	3785 only
- 28	40.6	35.5				
- 22	18.0	13.0				
- 15	93.2	87.0	not	not	not	not
- 9	74.5	58.5				
Prednisolone						
- 1	19.1	13.9	measured	measured	measured	measured
Dose 1 - 0						
6	28.0	22.0				
9	18.5	17.0				
Dose 2 - 23						
34	119.4	25.0	Serum Yellow			
41	210.0	Dead	1.37	2.85		
Dose 3 - 44			73.9	Dead	35.6	38.3
48	149.3		208.0		39.9	168.1
51	127.7		251.3		89.9	161.4
55	181.0		279.0		110.0	169.0

TABLE 45

ADRIAMYCIN THERAPY - PIGS 3785 and 3786 - 2 mg/kg ADRIAMYCIN EVERY 3 WEEKS
 SERUM PROTEINS (g/l)

DAYS FROM START OF DOSING	TOTAL PROTEIN		ALBUMIN		GLOBULINS		A/G RATIO	
	3785	3786	3785	3786	3785	3786	3785	3786
- 15	57.3	57.8	27.6	27.0	29.7	30.8	0.93	0.88
Dose 1 - 0								
9	59.4	57.3	33.6	30.4	25.8	26.9	1.30	1.13
Dose 2 - 23								
27	58.7	57.7	31.2	27.2	27.5	30.5	1.13	0.89
30	58.9	61.0	34.1	32.5	24.8	28.5	1.38	1.14
34	54.2	61.0	28.4	32.4	25.8	28.6	1.10	1.13
41	50.3	Dead	24.4	Dead	25.9	Dead	0.94	Dead
Dose 3 - 44								
48	51.3		21.7		29.6		0.73	
51	58.3		21.0		37.3		0.56	
55	53.0		18.6		34.4		0.54	

APPENDIX II

TABLE 46

ADRIAMYCIN THERAPY - PIG NO 192 and 194 1 mg/kg ADRIAMYCIN EVERY 3 WEEKS
 SERUM PROTEINS (g/l)

DAYS FROM START OF DOSING	TOTAL PROTEIN		ALBUMIN		GLOBULINS		A/G RATIO	
	192	194	192	194	192	194	192	194
- 16	53.8	60.7	23.0	22.2	30.8	38.5	0.75	0.58
- 9	52.3	53.0	25.6	26.9	26.7	26.1	0.96	0.80
- 2	56.3	55.1	25.8	24.8	30.5	30.3	0.84	0.82
Dose 1 - 0								
7	64.2	57.7	26.9	22.9	37.3	34.8	0.72	0.66
12	53.2	58.5	23.0	24.4	30.2	34.1	0.76	0.72
19	-	61.7	-	26.2	-	35.5	-	0.74
Dose 2 - 21								
26	68.8	63.3	26.9	30.1	41.9	33.2	0.64	0.91
33	66.9	63.1	31.2	31.8	35.7	31.3	0.87	1.02
40	66.2	59.0	28.8	31.9	37.4	27.1	0.77	1.18
Dose 3 - 42								
47	74.9	73.8	33.2	34.8	41.7	39.0	0.80	0.89
54	70.9	72.9	32.6	34.6	38.3	38.3	0.85	0.90
61	60.1	72.2	29.8	36.4	30.3	35.8	0.98	1.02
Dose 4 - 63								
68	73.6	69.6	30.5	33.7	43.1	35.9	0.71	0.94
75	66.6	79.3	30.5	36.9	36.1	42.4	0.84	0.87
82	65.3	66.5	29.6	30.6	35.7	35.9	0.83	0.85
Dose 5 - 84								
89	69.3	75.1	30.7	29.3	38.6	45.8	0.80	0.64
96	62.9	76.4	33.0	35.2	29.9	41.2	1.10	0.85
103	-	-	-	-	-	-	-	-
Dose 6 - 105								
110	78.9	79.1	38.1	38.5	40.8	40.6	0.93	0.95
117	71.6	75.9	40.1	39.9	31.5	36.0	1.27	1.11
125	66.6	75.5	34.1	39.1	32.5	36.4	1.04	1.07
Dose 7 - 126								
131	71.3	74.3	37.0	39.8	34.3	34.5	1.08	1.15
138	61.5	74.4	36.3	44.5	25.2	29.9	1.44	1.49
145	73.8	74.7	35.7	43.9	38.1	30.8	0.94	1.43
Dose 8 - 147								
152	67.7	74.8	39.3	42.3	28.4	32.5	1.38	1.30
159	66.8	71.6	32.2	49.4	34.6	22.2	0.93	2.23
173	Dead	67.4	Dead	41.7	Dead	25.7	Dead	1.62
180		74.9		39.6		35.3		1.12
187		-		-		-		-
195		79.2		32.2		47.0		0.69
197		Dead		Dead		Dead		Dead

APPENDIX II

TABLE 47

ADRIAMYCIN THERAPY - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

DOSE LEVEL PIG NUMBER	2mg/kg 3785	2mg/kg 3786	1mg/kg 192	1mg/kg 194
Submandibular LN	8.46	20.63	79.00	33.11
Parotid LN	7.50	14.97	15.50	20.45
Retropharyngeal LN	3.05	5.45	10.50	16.77
Cervical LN	7.89	22.39	9.95	11.30
Prescapular LN	3.83	5.82	1.68	2.50
Left Bronchial LN	5.65	21.24	48.50	41.25
Mid Bronchial LN	0.64	2.35	1.90	3.00
Apical Bronchial LN	2.17	4.41	10.50	11.50
Right Bronchial LN	2.45	5.88	7.70	12.20
Internal Iliac LN	1.07	1.52	2.65	3.00
External Iliac LN	9.66	10.00	17.30	34.40
Inguinal LN	10.91	16.39	10.00	30.00
Mesenteric and Colonic LN	430.00	1486.00	1700.00	1970.00
Gastric LN	149.78	418.00	1160.00	1560.00
Splenic LN	25.60	17.25	65.70	51.60
Precrural LN	3.74	9.40	4.10	8.50
Popliteal LN	1.54	7.02	1.95	4.20
Liver	2628.00	1926.00	2950.00	4140.00
Kidney (mean of 2)	113.00	132.00	160.00	205.00
Adrenal (mean of 2)	5.54	4.70	5.00	6.00
Thymus	3.90	11.86	50.15	26.00
Spleen	206.00	288.00	1615.00	1700.00

APPENDIX II
TABLE 48

CLINICAL RECORDS PIG No 3785 M L/S - 2 mg/kg ADRIAMYCIN INTRAVENOUSLY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	R. Ing.	L. Ing.	R. Prec.	L. Prec.	OTHER
- 4	33.5	80	39.3	++	++	-	59 x 35	60 x 38	50 x 25	47 x 26	Poor body condition
- 3	33.0	84	38.9	++	++	-	54 x 30	57 x 30	36 x 21	33 x 22	
- 2	35.5	92	38.9	++	++	-	64 x 30	64 x 33	44 x 23	41 x 22	
- 1	42.0	92	38.6	++	++	Slight	57 x 30	56 x 33	38 x 20	38 x 21	Prednisolone
0	40.0	82.5	38.5	+++	+++	-	51 x 28	53 x 31	30 x 16	33 x 21	
1st Dose											
1	40.0	83.5	38.6	+++	+++	-	50 x 24	49 x 27	28 x 18	31 x 18	
2	41.5	82	38.4	+++	+++	-	45 x 23	48 x 24	31 x 16	31 x 16	
3	41.5	84	38.5	+++	+++	-	56 x 28	55 x 26	37 x 20	40 x 22	
2nd Dose											
4	44.5	84	37.3	+++	+++	-	48 x 25	46 x 24	28 x 16	28 x 18	Listless
5	45	86	39.9	++	++	-	49 x 25	56 x 29	31 x 17	31 x 18	Listless catarrhal discharge from eyes. Mucous membranes slightly yellow
3rd Dose											
7	35.0	69	38.3	++	+	-	39 x 25	43 x 24	Impossible to measure accurately		Very listless severely jaundiced very poor being bulged
8	30.5	-	-	+	+						
9	28.5										Destroyed in extremis

APPENDIX II
TABLE 49

CLINICAL RECORDS PIG No 3786 M L/S - 2 mg/kg ADRIAMYCIN INTRAVENOUSLY													
WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	R. Ing. (mm)	L. Ing.	R. Prec.	L. Prec.	OTHER		
- 4	30.0	83	39	++	++	-	60 x 28	62 x 22	49 x 20	44 x 20			Poor body condition
- 3	28.5	85	37.5	++	++	-	58 x 25	60 x 25	44 x 20	39 x 18			
- 2	30.5	87.5	40.3	++	++	-	60 x 28	58 x 24	38 x 22	38 x 20			
- 1	35.0	85.5	39.1	++	++	Slight	52 x 22	54 x 28	38 x 15	38 x 17			Prednisolone
0	32.3	77	38.4	+++	++	-	49 x 24	48 x 28	32 x 14	31 x 16			
1st Dose													
1	35.0	76.5	38.9	+++	+++	-	50 x 24	46 x 24	28 x 16	32 x 18			
2	34.0	79	38.7	+++	+++	-	52 x 24	52 x 25	30 x 18	28 x 18			
3	34.0	85	38.5	+++	+++	-	58 x 27	55 x 28	40 x 16	36 x 18			
2nd Dose													
4	34.5	79	37.8	+++	+++	-	53 x 26	52 x 27	36 x 16	32 x 17			
5	35.5	83	39.4	+++	+++	-	50 x 28	52 x 28	38 x 18	38 x 20			
6	34.5		40.0	+									Very depressed constipated

Died Suddenly

APPENDIX II
TABLE 50

CLINICAL RECORDS - PIG No 192 F L/S - 1 mg/kg ADRIAMYCIN INTRAVENOUSLY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	R.Ing. (mm)	L.Ing.	R.Prec.	L.Prec.	Other
-3	14.5	61	39.8 40.8 40.3	++ + +	++ + +	- - -	38 x 17	34 x 16	23 x 10	24 x 10	No cough, Abnormal lung sounds
- 2	17.5	66	40.1 40.1 40.6 41.1	+ + + +	+ + + +	- - - -	46 x 17	45 x 15	Unmeasurable		nasal discharge - ampicillin - improving
- 1	20.5	66	39.5	++	++	-	42 x 16	42 x 17	"		
0	21.5	68	39.9	++	++	-	45 x 20	44 x 20	"		
1st Dose											
1	23	65	39.6	+++	+++	-	41 x 19	41 x 20	"		
2	28	73	39.9	+++	+++	-	48 x 21	47 x 20	"		
3	31	75	39.8	+++	+++	-	48 x 24	52 x 23	"		
2nd Dose											
4	32.5	73.5	39.6	+++	+++	-	44 x 15	43 x 15	"		
5	34	77.5	39.6	+++	+++	-	48 x 19	48 x 19	"		
6	38	80.5	39.6	+++	+++	-	46 x 21	46 x 21	"		
3rd Dose											
7	39.5	79	38.8	+++	+++	-	46 x 19	40 x 16	"		
8	43	78.5	41.9 40.8 39.2 38.2	+ ++ ++ +++	- + ++ +++	- - - -	50 x 25	48 x 22	"		Vomited once Erysipelas Penicillin
9	42.5	77.5	38.2	+++	+++	-	30 x 15	26 x 12	"		
4th Dose											
10	42.5	81	38.8	+++	+++	-	41 x 20	35 x 20	"		
11	45	83.5	Not recorded	+++	+++	-	40 x 19	44 x 18	"		Azaperone
12	49	85	39.8	++	++	-	43 x 21	34 x 18	"		
5th Dose											
13	53.5	86	39.5	+++	+++	-	46 x 20	41 x 20	"		Accidental intra- arterial injection, ear swollen and mottled
14	56	84	39.9	+++ +	+++ ++	- -	Nodes Unmeasurable		"		Edge of pinna curling and blistered, fell - injured back. Improved rapidly without treatment
15	60	89	39.8	+++	+++	-	Too heavy to turn over				
6th Dose											
16	59	-	39.8	+++	+++	-	-	-	-	-	Ear healed but edge curled and pruritic
17	62	-	39.5 38.7	+++ +	+++ -	- -	-	-	-	-	Heart strong - 120/min Sudden collapse laboured respiration heart strong but rapid recovered without treatment
18	67	-	39.5	++	++	-	-	-	-	-	
7th Dose											
19	70	-	39.5	++	++	-	-	-	-	-	
20	73	-	39.7	+++	+++	-	-	-	-	-	
21	75	-	39.1	+++	+++	-	-	-	-	-	
8th Dose											
22	76	-	39.1	++	++	-	-	-	-	-	ECG Taken
23	77	-	Not recorded	++	++	-	-	-	-	-	
Destroyed end of treatment											

APPENDIX II
TABLE 51

CLINICAL RECORDS - PIG No 194 M - 1 mg/kg ADRIAMYCIN INTRAVENOUSLY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	DIARRHOEA	R.Ing. (mm)	L.Ing.	R.Prec.	L.Prec.	OTHER
- 3	20.5	Not recorded	41.4 40.6 40.2 39.6	+	- + ++ ++	- - - -	Not		Recorded		Rapid noisy respiration nasal discharge, abnormal lung sounds particularly on left side. Ampicillin for 6 days (no cough) Improving
- 2	20.5	72	39.5 40.2 39.9 39.6	++	++ ++ ++ +++	- - - -	50 x 28	50 x 29	Unmeasurable		Still upper respiratory noise. High pitched whistling & wheezing noises in lungs. No fluid sounds
- 1	25	72.5	39.9	++	++	-	51 x 28	53 x 28	-		
0	26.5	75	40.5	++	+	-	56 x 29	53 x 31	-		Still abnormal lung sounds on left side especially
1st Dose											
1	27	71	39.5	+++	+++	-	42 x 25	44 x 25	-		
2	32	81	39.6	+++	+++	-	52 x 24	48 x 28	-		
3	37.5	78	39.3	+++	+++	-	57 x 33	56 x 30	-		
2nd Dose											
4	40	81.5	39.6	+++	+++	-	52 x 24	49 x 22	-		
5	44	81	39.5	+++	+++	-	60 x 32	59 x 29	-		
6	47	84	39.1	+++	+++	-	56 x 32	50 x 34	-		
3rd Dose											
7	47	82.5	39.2	+++	+++	-	54 x 36	53 x 29	-		
8	53	86	39.5	++	+++	-	61 x 36	56 x 31	-		Lungs still abnormal dyspnoeic - penicillin for 3 days
9	53	86	39.1	+++	+++	-	65 x 29	52 x 26			
4th Dose											
10	53.5	87	39.1	+++	+++	-	56 x 28	60 x 32			Lungs difficult to assess because of upper respiratory noise
11	55	92	Not recorded	+++	+++	-	65 x 29	61 x 30			Small ulcers round base of lower incisors
12	63.5	95.5	39.9	+++	+++	-	61 x 39	59 x 30			Ulcers healed
5th Dose											
13	63.5	101	40.6 40.0 39.5 39.2 40.9	++ ++ ++ +++ ++	- ++ ++ +++ ++	- - - - -	56 x 32	57 x 34			Dyspnoeic - 1/m chloramphenicol for 3 days
14	73	-	39.2	+++	+++	-	Too heavy to turn over				Noisy breathing - trimethoprim/sulphonamide in food for 6 days -
15	80	-	40.9	++	++	-					but still noisy, lungs improved, heart rate 120/min, regular
6th Dose											
16	82	-	39.1	+++	+++	-					Noisy breathing - trimethoprim/sulphonamide in food for 6 days (Prophylactic)
17	86	-	39.5	+++	+++	-					
18	95	-	40.2	+++	+++	-					
7th Dose											
19	96	-	39.8	+++	+++	-					
20	101	-	39.5	+++	+++	-					
21	104	-	39.5	+++	+++	-					
8th Dose											
22	112	-	39.2	++	++	-					
23	114.5	-	39.3	++	++	-					
24	123	-	39.3	++	++	-					Slight cough
25	117	-	40.2	+++	+++	-					Unilateral castration performed
26	123	-	39.8	++	++	-					Difficulty in breathing
27	123	-	40.2	++	++	-					Vomited once
28	119	-	40.7	+	+	-					Breathing difficult

Destroyed - end of experiment

APPENDIX III.

APPENDIX III

TABLE 1

CLINICAL RECORDS - PIG No. 405 (Saline-Treated Control)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	17.5		+++	+++	-	
-2	18	39.4	+++	+++	-	
-1	18.5	39.0	+++	+++	-	
1st Dose						
1	19.5	38.6	+++	+++	-	
2	20	38.7	+++	+++	-	
3	21.5	38.3	+++	+++	-	Severe bursitis both tarsi
2nd Dose						
4	25	38.6	+++	+++	-	
5	26	37.1	+++	+++	-	
6	28	38.7	+++	+++	-	
7	30		+++	+++	-	

DESTROYED.

APPENDIX III

Pig No. 409 - (Saline-Treated Control)

TABLE 2

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	19.5		+++	+++	-	
-2	20	39.1	+++	+++	-	
-1	20.5	39.6	+++	+++	-	
1st Dose						
1	22	38.6	+++	+++	-	
2	23.5	39.0	+++	+++	-	
3	25	38.9	+++	+++	-	
2nd Dose						
4	26.5	DESTROYED				

APPENDIX III

TABLE 3

CLINICAL RECORDS - Pig No. 411 (Saline - Treated Control)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	19		+++	+++	-	
-2	20	38.9	+++	+++	-	swollen left hind leg - 1/M Penicillin
-1	21	39.8	+++	+++	-	
1st Dose						
1	22	39.1	+++	+++	-	
2	23.5	38.3	+++	+++	-	swollen lower lip
3	25	39.3	+++	+++	-	
2nd Dose						
4	26	DESTROYED				

APPENDIX III

TABLE 4

Pig No. 414 - (Saline - Treated Control)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	16		+++	+++	-	
-2	17	39.1	+++	+++	-	
-1	17	39.4	+++	+++	-	
1st Dose						
1	18	38.4	+++	+++	-	
2	19.5	38.4	+++	+++	-	
3	21	39.2	+++	+++	-	
2nd Dose						
4	29	39.4	+++	+++	-	
5	29	38.4	+++	+++	-	
6	31.5	38.4	+++	+++	-	
7	32	DESTROYED				

APPENDIX III

TABLE 5

CLINICAL RECORDS - Pig No. 407 (20 and 40 mg/kg CYCLOPHOSPHAMIDE)

WEEKS	BODY WT. (kg)	RECTAL TEMP (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	19		+++	+++	-	
-2	20	39.7	+++	+++	-	loud systolic heart murmur
-1	20.5	40.0	+++	+++	-	
1st Dose						
1	22	38.1	+++	+++	-	
2	24	39.3	+++	+++	-	
3	26	39.4	+++	+++	-	
2nd Dose						
4	27.5	DESTROYED				

APPENDIX III

TABLE 6

Pig No. 415 (20 and 40 mg/kg CYCLOPHOSPHAMIDE)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	18.5		+++	+++	-	
-2	19.5	39.4	+++	+++	-	Bruised abdomen
-1	20.5	39.2	+++	+++	-	Damaged Hoof
1st Dose						
1	21.5	37.8	+++	+++	-	
2	23	38.3	+++	+++	-	
3	24	39.0	+++	+++	-	
2nd Dose						
4	29	39.6	+++	+++	-	
5	31.5	38.0	+++	+++	-	
6	34.5	39.0	+++	+++	-	
7	36	DESTROYED				

APPENDIX III
TABLE 8

FIG No. 416 (30 and 60 mg/kg CYCLOPHOSPHAMIDE)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	19		+++	+++	-	
-2	20	39.0	+++	+++	-	
-1	20	39.1	+++	+++	-	
1st Dose						
1	21.5	39.3	+++	+++	-	
2	23	38.5	+++	+++	-	bitten tail
3	25	38.1	+++	+++	-	
2nd Dose						
4	26	DESTROYED				

APPENDIX III

TABLE 9

CLINICAL RECORDS - Pig No. 402 (40 and 80 mg/kg CYCLOPHOSPHAMIDE)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	18.5		+++	+++	-	
-2	20	39.4	+++	+++	-	
-1	21	39.4	+++	+++	-	
1st Dose						
1	22	37.9	+++	+++	-	
2	23	39.7	+++	+++	-	
3	24	39.7	+++	+++	-	Severe busitis-- right tarsus
2nd Dose						
4	24	DESTROYED				

APPENDIX III
TABLE 10
FIG NO. 412 (40 and 80 mg/kg CYCLOPHOSPHAMIDE)

WEEKS	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	17		+++	+++	-	
-2	18	38.7	+++	+++	-	
-1	19	39.7	+++	+++	-	
1st Dose						
1	20	38.6	+++	+++	-	
2	20	39.0	+++	+++	-	
3	21	39.6	+++	+++	-	
2nd Dose						
4	24	39.2	+++	+++	-	
5	25.5	38.5	+++	+++	-	
6	28	38.7	+++	+++	-	Skin and mucous membranes pale
7	28.5	39.2	+++	+++	-	
DESTROYED						

APPENDIX III
TABLE 11

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 414 (SALINE TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	29.8	40	55	5	0	0	0
- 7	19.9	53	43	3	0	1	0
0	20.7	49	43	7	0	1	0
Dose 1 - 0							
1	25.3	41	54	4	0	0	1
2	26.4	52	43	5	0	0	0
3	23.3	44	51	4	0	1	0
4	25.1	43	51	6	0	0	0
5	26.3	49	46	4	0	0	1
6	24.8	40	55	4	0	1	0
7	21.2	43	49	7	0	0	1
14	25.7	49	46	3	0	1	1
Dose 2 - 18							
21	22.7	46	48	4	0	1	1
22	20.1	37	57	6	0	0	0
23	24.8	53	42	5	0	0	0
24	26.0	53	42	3	1	1	0
28	20.4	35	59	6	0	0	0
35	15.8	28	58	12	0	2	0
42	14.4	36	57	6	0	1	0
44	Destroyed						

APPENDIX III
TABLE 12

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 405 (SALINE TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM FROM START OF DOSING	WBC	* NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	24.5	47	48	4	1	0	0
- 7	19.7	44	52	4	0	0	0
0	19.3	62	33	3	0	1	1
Dose 1 - 0							
1	28.7	43	47	9	0	1	0
2	23.9	37	51	9	0	3	0
3	25.1	46	49	4	0	1	0
4	23.9	50	45	4	0	0	1
5	24.9	45	42	5	1	7	0
6	32.8	54(10)	39	5	0	2	0
7	21.6	44	51	3	1	1	0
14	22.5	48	47	4	0	1	0
Dose 2 - 18							
21	18.8	40	43	14	0	3	0
22	15.6	38	51	6	0	5	0
23	15.2	39	49	7	0	5	0
24	17.7	42	50	7	0	1	0
28	12.8	39	46	8	0	7	0
35	13.1	39	54	6	0	1	0
42	15.9	54	37	6	0	3	0
44	Destroyed						

APPENDIX III

TABLE 13

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 411 (SALINE TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	23.7	35	56	6	3	0	0
- 7	21.7	34	49	7	6	4	0
0	17.9	42	47	7	2	2	0
Dose							
1 - 0							
1	23.4	37	45	7	2	9	0
2	29.9	35	57	3	3	2	0
3	39.9	11.5	85	1.5	1.5	0.5	0
4	26.7	18	67	9	3	2	1
5	25.5	18	72	3	6	1	0
6	31.2	16	75	2	4	1	2
7	19.1	34	54	5	5	2	0
14	24.6	34	49	8	7	6	0
Dose							
2 - 18							
21	22.2	24	58	5	8	5	0
22	20.7	31	57	5	4	3	0
23	Destroyed						

APPENDIX III

TABLE 14

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 409 (SALINE TREATED CONTROL)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	25.1	45	45	6	1	3	0
- 7	22.9	38	51	6	3	2	0
0	16.9	40	50	7	0	3	0
Dose							
1 - 0							
1	22.9	39	52	6	0	3	0
2	23.5	46	51	1	2	0	0
3	20.4	43	51	4	1	1	0
4	22.1	37	55	7	0	1	0
5	22.1	36	55	9	0	0	0
6	24.4	44	50	4	0	2	0
7	21.5	37	57	5	0	0	1
14	23.0	47	49	3	0	0	1
Dose							
2 - 18							
21	19.7	41	48	9	0	2	0
22	19.2	39	55	4	1	1	0
23	Destroyed						

APPENDIX III
TABLE 15

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 415 (20 and 40 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	26.3	60	28	10	0	2	0
- 7	23.6	48	49	1	1	1	0
0	27.1	73	23	1	1	2	0
Dose 1 - 0							
1	29.6	58	36	3	0	3	0
2	14.0	39	57	4	0	0	0
3	16.7	50	48	1	0	1	0
4	10.6	23	67	10	0	0	0
5	13.3	4	79	17	0	0	0
6	15.2	33	60	7	0	0	0
7	17.4	44	51	5	0	0	0
14	25.6	56	41	3	0	0	0
Dose 2 - 18							
21	15.2	70	27	2	0	1	0
22	6.3	30	63	5	0	1	1
23	4.9	3	90	5	1	0	1
24	8.1	8	73	17	0	0	2
28	17.6	63	31	6	0	0	0
35	19.5	50	38	7	0	5	0
42	19.6	58	36	2	0	3	1
44	Destroyed						

APPENDIX III
TABLE 16

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 407 (20 and 40 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	25.6	58	37	5	0	0	0
- 7	22.0	40	55	3	1	0	1
0	19.1	46	50	4	0	0	0
Dose 1 - 0							
1	18.5	47	49	2	1	1	0
2	14.0	39	57	4	0	0	0
3	16.7	50	48	1	0	1	0
4	10.6	23	67	10	0	0	0
5	13.3	4	79	17	0	0	0
6	12.8	23	71	6	0	0	0
7	15.3	36	55	9	0	0	0
14	24.3	51	46	3	0	0	0
Dose 2 - 18							
21	10.2	65	33	2	0	0	0
22	4.8	15	80	4	0	0	1
23	4.2	3	87	10	0	0	0
24	8.6	5	54	40	0	0	1
25	Destroyed						

APPENDIX III
TABLE 17

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 404 (30 and 60 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	*NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	24.0	49	42	8	0	1	0
- 7	27.3	43	51	5	1	0	0
0	22.7	51	44	3	2	0	0
Dose 1 - 0							
1	24.2	50	49	1	0	0	0
2	19.0	56	42	0	1	1	0
3	18.5	75	22	2	0	1	0
4	9.2	15	78	7	0	0	0
5	8.6	5	70	24	0	0	1
6	14.5	24(13)	58	18	0	0	0
7	17.0	36	46	18	0	0	0
14	32.0	56	41	3	0	0	0
Dose 2 - 18							
21	10.2	75	25	0	0	0	0
22	3.5	12	84	4	0	0	0
23	2.3	0	89	8	0	0	3
24	5.1	(11)	62	27	0	0	0
28	12.6	41	50	9	0	0	0
35	20.9	65	30	4	0	1	0
42	16.0	55	39	3	0	2	1
45	Destroyed						

* NON-LOB NEUTR SHOWN IN PARENTHESES WHEN >10% OF TOTAL

APPENDIX III
TABLE 18

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 416 (30 and 60 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	*NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	27.3	47	46	5	0	2	0
- 7	23.4	51	41	7	1	0	0
0	21.6	35	59	5	0	1	0
Dose 1 - 0							
1	18.2	35	58	6	0	1	0
2	32.8	71	27	1	0	1	0
3	18.5	47	47	3	1	0	2
4	11.3	20	67	12	0	0	1
5	15.5	10	77	12	0	0	1
6	14.2	25	62	13	0	0	0
7	16.6	33	53	12	0	0	2
14	35.5	56	41	3	0	0	0
Dose 2 - 18							
21	12.0	80	19	0	1	0	0
22	3.5	13	81	1	1	1	3
23	2.8	3	84	12	0	0	1
24	Destroyed						

APPENDIX III
TABLE 19

CYCLPPHOSPHAMIDE : NORMAL PIGS - PIG NO 412 (40 and 80 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	*NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	27.7	47	42	9	0	2	0
- 7	23.5	29	64	5	1	1	0
0	25.8	64	21	11	0	4	0
Dose 1 - 0							
1	16.0	55	34	5	0	6	0
2	30.1	76	22	0	0	2	0
3	8.7	32	63	2	2	1	0
4	5.4	0	82	14	3	0	1
5	8.0	10	55	32	2	0	1
6	14.2	17	62	21	0	0	0
7	16.9	33	60	6	0	0	1
14	29.3	51	42	6	0	1	0
Dose 2 - 18							
21	3.8	40	46	3	3	8	0
22	1.9	0	96	2	1	0	1
23	2.2	(12)	74	14	0	0	0
24	4.1	25(19)	43	31	0	0	1
28	10.9	47(10)	45	5	0	0	3
35	17.4	58	30	9	0	3	0
42	20.4	58	30	8	0	3	1
45	Destroyed						

* NON-LOB NEUTR SHOWN IN PARENTHESES WHEN > 10% OF TOTAL

APPENDIX III
TABLE 20

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 402 (40 and 80 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	*NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER
- 14	29.1	41	56	3	0	0	0
- 7	24.8	41	53	5	0	1	0
0	17.5	42	52	5	0	1	0
Dose 1 - 0							
1	16.5	44	53	2	0	1	0
2	17.9	60	36	3	1	0	0
3	13.3	57	43	0	0	0	0
4	12.7	9	85	4	1	0	1
5	4.7	0	92	8	0	0	0
6	10.2	11(10)	74	15	0	0	0
7	15.0	26(14)	54	19	0	0	1
14	28.4	43	52	3	0	0	2
Dose 2 - 18							
21	7.3	72	22	4	1	1	0
22	2.4	4	91	2	2	0	1
23	2.0	0	98	2	0	0	0
24	Destroyed						

* NON-LOB NEUTR SHOWN IN PARENTHESES WHEN > 10% OF TOTAL

APPENDIX III

TABLE 21

CYCLOSPHOSPHAMIDE : NORMAL PIGS - PIG NO 414 (SALINE - TREATED CONTROL)

DAYS FROM START OF DOSINGS	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.64	0.39	13.2	51.0	33.8	17.3	4.76	417
- 7	7.24	0.345	12.4	47.7	35.9	17.1	5.89	354
0	7.17	0.35	12.4	48.8	35.4	17.3	6.97	262
Dose								
1 - 0								
1	-	0.35	-	-	-	-	-	-
2	-	0.38	-	-	-	-	-	-
3	-	0.36	-	-	-	-	-	-
4	-	0.35	-	-	-	-	-	-
5	-	0.365	-	-	-	-	-	-
6	-	0.335	-	-	-	-	-	-
7	7.72	0.36	12.6	46.6	35.0	16.3	8.41	286
14	7.95	0.385	12.9	48.4	33.5	16.2	6.11	315
Dose								
2 - 18								
21	7.96	0.37	12.6	46.5	34.1	15.8	6.44	336
23	-	0.36	-	-	-	-	-	-
24	-	0.32	-	-	-	-	-	-
28	6.70	0.33	11.6	49.3	35.2	17.3	4.11	342
35	7.49	0.36	12.4	48.1	34.4	16.6	5.05	306
42	7.14	0.35	12.0	53.2	33.9	18.1	5.05	236
44	Destroyed							

APPENDIX III
TABLE 22

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 405 (SALINE TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.89	0.375	12.6	47.5	33.6	16.0	4.19	372
- 7	8.08	0.36	12.4	44.6	34.4	15.3	4.63	377
0	7.20	0.35	11.2	48.6	32.0	15.6	5.13	229
Dose								
1 - 0								
1	-	0.35	-	-	-	-	-	-
2	-	0.36	-	-	-	-	-	-
3	-	0.365	-	-	-	-	-	-
4	-	0.375	-	-	-	-	-	-
5	-	0.36	-	-	-	-	-	-
6	-	0.355	-	-	-	-	-	-
7	8.10	0.35	12.2	43.2	34.9	15.1	6.15	274
14	8.37	0.37	12.4	44.2	33.5	14.8	4.84	259
Dose								
2 - 18								
21	8.46	0.385	13.0	45.5	33.8	15.4	4.89	333
23	-	0.365	-	-	-	-	-	-
24	-	0.345	-	-	-	-	-	-
28	7.84	0.36	12.4	45.9	34.4	15.8	2.74	307
35	7.89	0.395	13.0	50.1	32.9	16.5	2.95	265
42	8.07	0.38	12.9	47.1	33.9	16.0	3.58	201
44	Destroyed							

APPENDIX III
TABLE 23

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 411 (SALINE TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.89	0.38	13.2	48.2	34.7	16.7	3.81	325
- 7	7.92	0.37	13.3	46.7	35.9	16.8	4.63	324
0	7.34	0.35	12.2	47.7	34.9	16.6	4.92	385
Dose								
1 - 0								
1	-	0.35	-	-	-	-	-	-
2	-	0.375	-	-	-	-	-	-
3	-	0.37	-	-	-	-	-	-
4	-	0.38	-	-	-	-	-	-
5	-	0.35	-	-	-	-	-	-
6	-	0.365	-	-	-	-	-	-
7	7.35	0.35	12.4	47.6	35.4	16.9	5.33	448
14	8.32	0.375	13.1	45.6	34.9	15.9	5.47	353
Dose								
2 - 18								
21	8.14	0.38	13.1	46.7	34.5	16.1	5.33	357
23	Destroyed							

APPENDIX III
TABLE 24

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 409 (SALINE TREATED CONTROL)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.83	0.37	12.4	47.3	33.5	15.8	4.19	333
- 7	7.67	0.36	12.6	46.9	35.0	16.4	5.68	412
0	7.17	0.35	11.7	48.8	33.4	16.3	6.15	306
Dose								
1 - 0								
1	-	0.345	-	-	-	-	-	-
2	-	0.35	-	-	-	-	-	-
3	-	0.35	-	-	-	-	-	-
4	-	0.35	-	-	-	-	-	-
5	-	0.35	-	-	-	-	-	-
6	-	0.345	-	-	-	-	-	-
7	7.60	0.35	12.4	46.1	35.4	16.3	8.00	316
14	7.67	0.38	12.3	49.5	32.4	16.0	6.74	335
Dose								
2 - 18								
21	8.16	0.36	12.9	44.1	35.8	15.8	6.67	391
23	Destroyed							

APPENDIX III
TABLE 25

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 415 (20 and 40mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.93	0.375	12.6	47.3	33.6	15.9	4.57	263
- 7	7.98	0.375	12.7	47.5	33.9	16.1	4.84	317
0	7.60	0.35	12.1	46.0	34.6	15.9	6.15	274
Dose								
1 - 0								
1	-	0.355	-	-	-	-	-	-
2	-	0.375	-	-	-	-	-	-
3	-	0.355	-	-	-	-	-	-
4	-	0.35	-	-	-	-	-	-
5	-	0.34	-	-	-	-	-	-
6	-	0.33	-	-	-	-	-	-
7	7.98	0.365	12.4	45.7	34.0	15.5	9.03	232
14	7.95	0.38	12.7	47.8	33.4	16.0	7.58	294
Dose								
2 - 18								
21	7.58	0.35	11.9	46.2	34.0	15.7	6.22	213
23	-	0.34	-	-	-	-	-	-
24	-	0.33	-	-	-	-	-	-
28	7.24	0.33	11.5	45.6	34.8	15.9	4.11	213
35	7.32	0.36	12.3	49.2	34.2	16.8	4.21	335
42	7.87	0.38	12.9	48.3	33.9	16.4	3.79	219
44	Destroyed							

APPENDIX III
TABLE 26

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 407 (20 and 40mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.43	0.36	12.5	48.5	34.7	16.8	4.57	297
- 7	7.37	0.35	12.4	47.5	35.4	16.8	5.89	651
0	6.90	0.345	12.0	50.0	34.8	17.4	5.74	273
Dose 1 - 0								
1	-	0.35	-	-	-	-	-	-
2	-	0.36	-	-	-	-	-	-
3	-	0.315	-	-	-	-	-	-
4	-	0.36	-	-	-	-	-	-
5	-	0.32	-	-	-	-	-	-
6	-	0.315	-	-	-	-	-	-
7	6.73	0.33	11.4	49.0	34.5	16.9	6.77	222
14	7.01	0.33	11.2	47.1	33.9	16.0	5.47	272
Dose 2 - 18								
21	6.62	0.32	11.0	48.3	34.4	16.6	5.78	265
23	-	0.30	-	-	-	-	-	-
24	-	0.30	-	-	-	-	-	-
25	Destroyed							

APPENDIX III
TABLE 27

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 404 (30 and 60 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THOMB
- 14	6.60	0.365	11.8	55.3	32.3	17.9	6.10	295
- 7	7.07	0.35	12.4	49.5	35.4	17.5	3.79	400
0	6.91	0.335	11.7	48.5	34.9	16.9	5.33	366
Dose 1 - 0								
1	-	0.35	-	-	-	-	-	-
2	-	0.35	-	-	-	-	-	-
3	-	0.34	-	-	-	-	-	-
4	-	0.33	-	-	-	-	-	-
5	-	0.31	-	-	-	-	-	-
6	-	0.315	-	-	-	-	-	-
7	6.79	0.32	11.2	47.1	35.0	16.5	7.38	224
14	7.21	0.335	11.7	46.5	34.9	16.2	7.16	409
Dose 2 - 18								
21	6.74	0.33	11.2	49.0	33.9	16.6	5.78	254
23	-	0.30	-	-	-	-	-	-
24	-	0.37	-	-	-	-	-	-
28	6.18	0.29	9.9	46.9	34.1	16.0	4.34	175
35	6.99	0.345	11.5	49.4	33.3	16.5	4.42	340
42	6.86	0.33	11.5	48.1	34.8	16.8	4.84	305
45	Destroyed							

APPENDIX III
TABLE 28

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 416 (30 and 60 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.03	0.355	11.9	50.5	33.5	16.9	4.38	375
- 7	7.69	0.36	12.4	46.8	34.4	16.1	5.05	334
0	7.34	0.345	12.2	47.0	35.4	16.6	6.36	296
Dose 1 - 0								
1	-	0.34	-	-	-	-	-	-
2	-	0.36	-	-	-	-	-	-
3	-	0.355	-	-	-	-	-	-
4	-	0.33	-	-	-	-	-	-
5	-	0.33	-	-	-	-	-	-
6	-	0.32	-	-	-	-	-	-
7	7.18	0.335	11.4	46.7	34.0	15.9	6.56	276
14	7.70	0.36	12.7	46.8	35.3	16.5	6.74	313
Dose 2 - 18								
21	7.46	0.34	11.4	45.6	33.5	15.3	4.89	352
23	-	0.32	-	-	-	-	-	-
24	Destroyed							

APPENDIX III
TABLE 29

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 412 (40 and 80 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.98	0.38	13.2	47.6	34.7	16.5	4.95	317
- 7	7.86	0.385	13.5	49.0	35.1	17.2	5.05	247
0	7.17	0.35	12.4	48.8	34.9	17.0	6.15	255
Dose 1 - 0								
1	-	0.345	-	-	-	-	-	-
2	-	0.40	-	-	-	-	-	-
3	-	0.345	-	-	-	-	-	-
4	-	0.33	-	-	-	-	-	-
5	-	0.33	-	-	-	-	-	-
6	-	0.32	-	-	-	-	-	-
7	6.80	0.33	11.8	48.5	35.8	17.4	6.56	250
14	7.41	0.35	11.8	47.2	33.7	15.9	6.32	352
Dose 2 - 18								
21	7.16	0.34	11.4	47.5	33.5	15.9	5.11	248
23	-	0.30	-	-	-	-	-	-
24	-	0.27	-	-	-	-	-	-
28	5.58	0.28	9.7	50.2	34.6	17.4	2.74	262
35	6.14	0.345	11.4	56.2	33.0	18.6	5.05	360
42	6.75	0.35	11.9	51.9	34.0	17.6	4.42	310
45	Destroyed							

APPENDIX III

TABLE 30

CYCLOPHOSPHAMIDE : NORMAL PIGS - PIG NO 402 (40 and 80 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 14	7.59	0.385	13.0	50.7	33.8	17.1	4.19	303
- 7	7.21	0.355	12.2	49.2	34.4	16.9	4.42	285
0	6.96	0.345	12.1	49.6	35.1	17.4	5.74	215
Dose								
1 - 0								
1	-	0.34	-	-	-	-	-	-
2	-	0.365	-	-	-	-	-	-
3	-	0.34	-	-	-	-	-	-
4	-	0.35	-	-	-	-	-	-
5	-	0.33	-	-	-	-	-	-
6	-	0.30	-	-	-	-	-	-
7	6.48	0.30	10.6	46.3	35.3	16.4	8.62	111
14	7.15	0.34	11.2	47.6	32.9	15.7	5.47	380
Dose								
2 - 18								
21	6.73	0.33	11.3	49.0	34.2	16.8	4.22	202
23	-	0.33	-	-	-	-	-	-
24	Destroyed							

APPENDIX III

TABLE 31

CYCLOPHOSPHAMIDE : NORMAL PIGS

SERUM TOTAL PROTEIN - g/litre

DAYS FROM START OF DOSING	GROUP D - CONTROLS				GROUP A - LOW DOSE		GROUP B - MEDIUM DOSE		GROUP C - HIGH DOSE	
	405	409	411	414	407	415	404	416	402	412
- 7	61.6	59.4	58.3	60.6	57.6	54.9	63.6	60.0	60.4	58.5
0	56.7	61.5	53.9	57.8	58.8	55.0	58.0	58.8	58.9	58.2
Dose 1 - 0										
7	61.6	64.2	62.2	58.4	60.7	67.4	61.2	65.4	63.7	62.2
14	59.2	56.3	55.2	58.5	51.2	56.1	59.0	59.4	62.6	57.9
Dose 2 - 18										
21	66.8	56.1	62.3	61.5	53.5	49.1	59.8	59.0	57.5	56.5
28	61.8	dead	dead	53.4	dead	50.2	50.9	dead	dead	51.6
35	62.9			58.6		54.0	56.6			57.5
42	61.1			50.8		55.9	53.2			51.2

TABLE 32

SERUM ALBUMIN - g/litre

DAYS FROM START OF DOSING	GROUP D - CONTROLS				GROUP A - LOW DOSE		GROUP B - MEDIUM DOSE		GROUP C - HIGH DOSE	
	405	409	411	414	407	415	404	416	402	412
- 7	30.5	32.8	29.1	31.5	33.7	27.1	36.6	31.8	34.7	31.3
0	28.2	28.5	27.2	31.5	31.6	27.9	32.0	31.2	34.7	29.0
Dose 1 - 0										
7	37.8	30.8	25.4	35.1	35.1	35.2	36.8	36.3	34.4	31.2
14	34.4	30.8	29.1	32.0	28.4	31.0	34.6	33.8	27.0	24.7
Dose 2 - 18										
21	27.4	28.6	23.9	26.8	22.1	21.8	16.2	24.9	17.6	22.3
28	29.9	dead	dead	26.3	dead	22.1	26.6	dead	dead	24.6
35	27.2			27.3		24.3	24.0			22.1
42	28.1			26.6		25.9	23.3			21.9

APPENDIX III

TABLE 33

CYCLOPHOSPHAMIDE : NORMAL PIGS

SERUM ALKALINE PHOSPHATASE - (iu/l)

DAYS FROM START OF DOSING	GROUP D - CONTROLS				GROUP A - LOW DOSE		GROUP B - MEDIUM DOSE		GROUP C - HIGH DOSE	
	405	409	411	414	407	415	404	416	402	412
- 7	81	119	94	77	139	95	128	68	112	89
0	76	99	97	69	146	97	123	80	116	86
Dose 1 - 0										
1	86	102	102	84	162	93	136	89	155	84
2	69	128	59	80	148	88	158	84	138	78
14	86	97	91	76	151	110	126	83	100	62
Dose 2 - 18										
21	42	67	49	54	109	47	63	43	72	30
28	91	dead	dead	84	dead	79	89	dead	dead	47
35	113			95		123	144			64
42	98			97		113	147			89

APPENDIX III
TABLE 34

CYCLOPHOSPHAMIDE : NORMAL PIGS - ABSOLUTE ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

DOSE PIG NO	CONTROL 409+	CONTROL 411+	CONTROL 405	CONTROL 414	CONTROL 414	LOW 407+	LOW 415	MEDIUM 416+	MEDIUM 404	HIGH 402+	HIGH 412
Head LN	8.43	8.76	8.52	8.51	10.01	10.64	7.11	8.50	6.32	11.81	
Prescapular LN	0.62	0.57	1.04	0.68	1.87	1.30	1.17	1.00	1.00	1.78	
Bronchial LN	4.16	7.90	2.87	3.60	3.79	2.89	5.07	3.03	2.46	4.39	
Iliac LN	1.70	1.79	2.56	2.93	2.16	2.38	1.26	2.19	1.80	2.65	
Inguinal LN	2.80	4.50	2.67	3.10	3.01	3.90	2.19	3.65	3.25	3.24	
Mesenteric LN											
and Colonic Gastric LN	100.00	85.00	90.00	100.00	80.00	100.00	100.00	112.00	80.00	90.00	
and Splenic Preaural LN	14.45	11.09	9.20	15.22	6.84	9.74	7.53	8.07	9.74	12.00	
Popliteal LN	1.00	1.31	0.86	0.90	0.69	0.89	0.55	0.86	1.02	0.78	
	0.75	0.42	0.48	0.79	0.17	0.68	0.27	0.19	0.31	0.33	
Liver	1040.00	985.00	750.00	930.00	1000.00	830.00	865.00	940.00	825.00	990.00	
Kidney	60.00	75.00	55.00	62.50	72.00	60.00	70.00	65.00	62.00	60.00	
Adrenal	1.55	1.45	1.63	1.81	1.77	1.45	1.50	1.38	2.02	1.70	
Thymus	30.00	44.44	30.62	43.91	25.9	25.18	24.00	50.25	20.67	63.00	
Spleen	75.00	85.00	90.00	70.00	50.00	70.00	90.00	85.00	90.00	100.00	

+ Killed at end of treatment

APPENDIX III

TABLE 35

CYCLOPHOSPHAMIDE THERAPY - PIG NO 357 (20 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	⁺ NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER %
- 21	50.4	59(16)	41	0	0	0
- 14	40.8	74	24	1	1	0
- 7	36.4	56	42	0	2	0
0	25.0	45	54	0	1	0
Dose 1 - 0						
1	16.2	40	56	1	3	0
2	14.3	51	46	1	3	0
3	18.7	28	70	2	0	0
4	13.2	3	97	0	0	0
5	16.3	0	99	0	0	1
6	19.8	9	89	2	0	0
7	22.6	29	71	0	0	0
14	23.2	32	67	0	1	0
Dose 2 - 17						
21	9.0	11	88	1	0	0
22	10.3	6	92	1	1	0
27	17.4	40	59	0	1	0
34	30.8	25	73	2	0	0
Dose 3 - 37						
41	11.7	3	96	1	0	0
42	12.3	10	89	1	0	0
	Destroyed					

+

Non - lob neutr. shown in parentheses
where >10% of total

APPENDIX III

TABLE 36

CYCLOPHOSPHAMIDE THERAPY - PIG NO 420 (20 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER %
- 21	20.5	24	76	0	0	0
- 14	19.0	27	73	0	0	0
- 7	36.6	45	54	0	1	0
0	25.7	34	66	0	0	0
Dose 1 - 0						
1	17.2	63	36	0	1	0
2	15.2	58	42	0	0	0
3	17.2	42	58	0	0	0
4	9.4	10	87	1	1	1
5	10.0	6	94	0	0	0
6	15.4	8	92	0	0	0
7	19.4	11	88	1	0	0
14	39.9	38	62	0	0	0
Dose 2 - 17						
21	8.3	3	95	1	1	0
22	11.1	8	92	0	0	0
27	25.9	30	69	0	1	0
34	27.8	20	79	1	0	0
Dose 3 - 37						
41	7.3	26	74	0	0	0
42	5.4	1	99	0	0	0
	Destroyed					

APPENDIX III

TABLE 37

CYCLOPHOSPHAMIDE THERAPY - PIG NO 359 (20 mg/kg INTRAVENOUSLY)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR%	MONONUCL %	BASO %	EOSINO %	OTHER %
- 21	43.2	50	49	1	0	0
- 14	36.0	31	66	2	1	0
- 7	35.8	26	73	1	0	0
0	33.3	20	79	0	1	0
Dose 1 - 0						
1	39.0	36	63	1	0	0
2	35.5	52	48	0	0	0
3	18.6	8	91	1	0	0
4	17.0	2	98	0	0	0
5	19.3	9	91	0	0	0
6	32.0	21	79	0	0	0
7	28.0	19	79	1	1	0
14	25.7	11	89	0	0	0
Dose 2 - 17						
21	7.0	0	99	1	0	0
22	10.7	8	92	0	0	0
27	15.9	26	73	0	1	0
34	38.8	50	48	2	0	0
Dose 3 - 37						
41	24.5	31	68	1	0	0
42	13.9	0	99	1	0	0
43	12.0	2	97	1	0	0
49	27.4	45	55	0	0	0
51	Destroyed in extremis					

APPENDIX III
TABLE 38

CYCLOPHOSPHAMIDE THERAPY - PIG NO 362 (20 mg/kg INTRAVENOUSLY)
WHITE BLOOD CELLS $\times 10^9/l$ AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	+ NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER %
- 21	18.9	36	62	2	0	0
- 14	18.9	42	57	1	0	0
- 7	14.0	38	61	1	0	0
0	12.2	24	75	0	1	0
Dose 1 - 0						
1	9.0	33	66	1	0	0
2	7.3	29	71	0	0	0
3	17.1	3	97	0	0	0
4	8.8	0	100	0	0	0
5	11.8	8	91	1	0	0
6	12.2	10	87	3	0	0
7	13.0	19	81	0	0	0
14	25.4	19	77	1	3	0
Dose 2 - 17						
21	6.4	1	99	0	0	0
22	8.7	12(10)	87	1	0	0
27	17.6	28	72	0	0	0
34	23.8	26	73	1	0	0
Dose 3 - 37						
41	11.5	42	57	1	0	0
42	11.0	1	96	2	1	0
43	9.2	3	95	1	0	1
49	17.6	31	67	2	0	0
55	23.1	20	78	2	0	0
63	23.9	18	82	0	0	0
69	20.7	12	86	0	2	0
76	24.1	12	88	0	0	0
84	24.6	4	96	0	0	0
90	32.6	3	97	0	0	0
92	Destroyed					

+ Non-lob neutr. shown in parentheses where > 10% of total

APPENDIX III

TABLE 39

CYCLOPHOSPHAMIDE THERAPY - PIG NO 357 (20 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 21	6.04	0.30	10.3	49.7	34.3	17.1	-	510
- 14	5.77	0.315	10.5	54.6	33.3	18.2	10.00	737
- 7	5.43	0.27	9.1	49.7	33.7	16.8	4.65	433
0	5.00	0.235	8.0	47.0	34.0	16.0	6.38	230
Dose 1 - 0								
1	-	0.26	-	-	-	-	-	-
2	-	0.25	-	-	-	-	-	-
3	-	0.26	-	-	-	-	-	-
4	-	0.265	-	-	-	-	-	-
5	-	0.275	-	-	-	-	-	-
6	-	0.285	-	-	-	-	-	-
7	5.81	0.30	10.2	51.6	34.0	17.6	5.20	Clumped
14	7.12	0.38	12.1	53.4	31.8	17.0	4.42	383
Dose 2 - 17								
21	5.10	0.27	9.3	52.9	34.4	18.2	5.62	342
22	-	0.27	-	-	-	-	-	-
27	5.63	0.31	10.6	55.1	34.2	18.8	4.11	281
34	6.19	0.32	11.4	51.7	35.6	18.4	4.00	301
Dose 3 - 37								
41	5.44	0.29	9.8	53.3	33.8	18.0	2.53	295
42	-	0.30	-	-	-	-	-	-
	Destroyed							

APPENDIX III

TABLE 40

CYCLOPHOSPHAMIDE THERAPY - PIG NO 420 (20 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 21	5.79	0.305	10.3	52.7	33.8	17.8	-	220
- 14	6.27	0.30	11.4	47.8	38.0	18.2	4.20	257
- 7	6.59	0.33	11.2	50.1	33.9	17.0	3.53	298
0	6.18	0.265	9.1	42.9	34.3	14.7	5.97	181
Dose 1 - 0								
1	-	0.28	-	-	-	-	-	-
2	-	0.275	-	-	-	-	-	-
3	-	0.27	-	-	-	-	-	-
4	-	0.255	-	-	-	-	-	-
5	-	0.26	-	-	-	-	-	-
6	-	0.27	-	-	-	-	-	-
7	5.34	0.26	8.7	48.7	33.5	16.3	5.40	243
14	5.89	0.28	9.9	47.5	35.4	16.8	5.68	244
Dose 2 - 17								
21	4.77	0.25	8.3	52.4	33.2	17.4	6.05	228
22	-	0.235	-	-	-	-	-	-
27	4.67	0.255	8.7	54.6	34.1	18.6	5.49	275
34	4.46	0.27	9.1	60.5	33.7	20.4	5.89	153
Dose 3 - 37								
41	4.08	0.23	7.9	56.4	34.3	19.4	4.63	192
42	-	0.225	-	-	-	-	-	-
	Destroyed							

APPENDIX III

TABLE 41

CYCLOPHOSPHAMIDE THERAPY - PIG NO 359 (20 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 21	6.32	0.32	10.5	50.6	32.8	16.6	-	200
- 14	5.74	0.26	8.8	45.3	33.8	15.3	6.00	110
- 7	6.00	0.32	10.6	53.3	33.1	17.7	4.84	227
0	5.41	0.27	9.0	49.9	33.3	16.6	5.58	227
Dose 1 - 0								
1	-	0.255	-	-	-	-	-	-
2	-	0.285	-	-	-	-	-	-
3	-	0.265	-	-	-	-	-	-
4	-	0.27	-	-	-	-	-	-
5	-	0.26	-	-	-	-	-	-
6	-	0.30	-	-	-	-	-	-
7	4.91	0.265	8.7	54.0	32.8	17.7	4.40	255
14	6.50	0.37	11.7	56.9	31.6	18.0	4.21	Clumped
Dose 2 - 17								
21	5.29	0.29	10.0	54.8	34.5	18.9	4.76	278
22	-	0.30	-	-	-	-	-	-
27	6.08	0.36	12.5	59.2	34.7	20.6	4.57	417
34	5.18	0.31	10.6	59.8	34.2	20.5	6.11	185
Dose 3 - 37								
41	5.60	0.31	10.8	55.4	34.8	19.3	3.37	219
42	-	0.31	-	-	-	-	-	-
43	-	0.29	-	-	-	-	-	-
49	7.09	0.42	13.4	59.2	31.9	18.9	11.24	131
51	Destroyed							

APPENDIX III

TABLE 42

CYCLOPHOSPHAMIDE THERAPY - PIG NO 362 (20 mg/kg INTRAVENOUSLY)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 21	5.88	0.265	8.5	45.1	32.1	14.5	-	237
- 14	6.25	0.29	10.1	46.4	34.8	16.2	8.60	193
- 7	5.92	0.27	9.2	45.6	34.1	15.5	5.58	324
0	5.44	0.24	8.3	44.1	34.6	15.3	7.07	217
Dose 1 - 0								
1	-	0.275	-	-	-	-	-	-
2	-	0.28	-	-	-	-	-	-
3	-	0.27	-	-	-	-	-	-
4	-	0.27	-	-	-	-	-	-
5	-	0.28	-	-	-	-	-	-
6	-	0.27	-	-	-	-	-	-
7	5.12	0.245	8.1	47.9	33.1	15.8	5.20	293
14	7.07	0.365	12.0	51.6	32.9	17.0	4.63	186
Dose 2 - 17								
21	5.89	0.30	9.9	50.9	33.0	16.8	5.62	263
22	-	0.275	-	-	-	-	-	-
27	6.16	0.335	11.6	54.4	34.6	18.8	5.49	249
34	6.61	0.355	12.5	53.7	35.2	18.9	6.74	201
Dose 3 - 37								
41	6.47	0.32	11.3	49.5	35.3	17.5	5.47	202
42	-	0.33	-	-	-	-	-	-
43	-	0.325	-	-	-	-	-	-
49	6.55	0.33	11.2	50.4	33.9	17.1	6.05	263
55	6.97	0.33	11.5	47.3	34.8	16.5	6.74	316
63	6.12	0.32	10.5	52.3	32.8	17.2	7.27	249
69	5.51	0.285	11.1	51.7	38.9	20.1	6.86	181
76	5.08	0.27	9.0	53.1	33.3	17.7	8.24	169
84	5.09	0.29	9.8	57.0	33.8	19.3	6.86	171
90	4.49	0.275	9.3	61.2	33.8	20.7	9.81	91
92	Destroyed							

APPENDIX III

TABLE 43

CYCLOPHOSPHAMIDE THERAPY

SERUM ALKALINE PHOSPHATASE iu/litre

DAYS FROM START OF DOSING	PIG NUMBER			
	357	420	359	362
- 14	34	70	93	78
- 7	47	50	113	102
0	78	77	88	76
Dose				
1 - 0				
1	101	74	201	106
2	131	75	150	112
7	88	No sample	61	71
14	98	65	107	113
Dose				
2 - 17				
21	90	61	85	96
27	55	47	93	71
34	68	57	98	65
Dose				
3 - 37				
41	31	58	73	88
49	Dead	Dead	73	94
55			Dead	82
63				48
69				42
76				55
84				43
90				31

APPENDIX III

TABLE 44

CYCLOPHOSPHAMIDE THERAPY

SERUM PROTEINS (g/l)

DAYS FROM START OF DOSING	TOTAL PROTEIN				ALBUMIN			
	357	420	359	362	357	420	359	362
- 14	35.9	60.4	53.6	53.7	11.5	24.0	16.9	19.9
- 7	75.6	78.0	59.3	55.9	17.8	28.2	18.0	17.6
0	48.6	57.1	52.9	44.6	17.5	25.3	18.2	15.7
Dose 1 - 0		No				No		
7	48.8	sample	54.2	50.1	30.0	Sample	31.3	32.6
14	63.0	58.0	66.4	63.4	31.0	30.8	26.6	27.9
Dose 2 - 17								
21	62.1	62.7	64.0	57.6	24.3	19.2	21.6	23.6
27	59.1	55.0	61.6	55.9	25.9	20.7	22.6	24.9
34	63.7	61.1	59.1	62.2	26.8	18.8	23.0	26.4
Dose 3 - 37								
41	56.5	53.7	58.5	56.5	21.4	20.0	23.7	24.0
49	Dead	Dead	75.7	59.0	Dead	Dead	31.6	24.3
55			Dead	69.1			Dead	25.4
63				60.6				19.7
69				59.5				19.3
76				60.8				18.6
84				68.8				25.9
90				78.0				23.8

APPENDIX III

TABLE 45

CYCLOPHOSPHAMIDE THERAPY - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

PIG NUMBER	357	420	359	362
Submandibular LN	11.02	13.97	10.78	67.00
Parotid LN	8.11	7.60	2.82	10.32
Retropharyngeal LN	3.78	2.80	1.54	13.40
Cervical LN	3.66	4.35	4.08	16.12
Prescapular LN	1.74	1.36	0.39	2.27
Left Bronchial LN	9.63	12.54	9.08	71.79
Mid Bronchial LN	0.87	6.02	0.83	21.38
Apical Bronchial LN	2.13	3.18	1.22	26.36
Right Bronchial LN	1.31	3.81	1.22	16.46
Internal Iliac LN	0.68	0.62	0.58	2.10
External Iliac LN	2.48	8.96	1.95	8.92
Inguinal LN	4.06	10.92	2.58	17.68
Mesenteric and				
Colonic LN	330.00	555.00	290.00	2975.00
Gastric and				
Splenic LN	120.48	157.66	108.53	1050.00
Preocrural LN	2.08	4.97	1.32	9.44
Popliteal LN	0.59	2.42	0.03	4.66
Liver	1035.00	1200.00	940.00	2770.00
Kidney (Mean of 2)	75.00	67.00	80.00	120.00
Adrenal (Mean)	2.55	1.11	4.50	2.79
Thymus	18.25	21.70	NF	34.69
Spleen	175.00	305.00	156.00	1150.00

APPENDIX III
TABLE 46

CLINICAL RECORDS - PIG No 357 - (20 mg/kg CYCLOPHOSPHAMIDE)												
WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec. (mm)	OTHER		
- 3	14	-	39.2	++	+	Not	Measured			Diarrhoea - Laparotomy very weak, severe diarrhoea with blood clots and necrotic debris		
- 2	12	-	38.6	+	+	"	"					
- 1	16	-	39.1	++	++	"	"					
0	18.5	64	39.3	+++	+++	34 x 20	36 x 18	Not	Measured			
1st Dose												
1	23	67	38.1	+++	+++	35 x 20	36 x 18	Not	Measured			Conjunctivitis
2	25.5	70	39.9	+++	+++	40 x 21	41 x 24	Not	Measured			
3	27.5	67	36.7	+++	+++	41 x 19	40 x 20	Not	Measured			
2nd Dose												
4	30	70.5	38.9	+++	+++	35 x 14	41 x 21	30 x 14	36 x 17			
5	31.5	69	38.5	+++	+++	39 x 20	44 x 20	33 x 15	36 x 18			
6	28.5	76	37.9	++	+	44 x 18	46 x 19	34 x 16	32 x 18			
3rd Dose												
7	Destroyed			++	+					Severe diarrhoea Improved		

APPENDIX III
TABLE 47

CLINICAL RECORDS - PIG No 359 (20 mg/kg CYCLOPHOSPHAMIDE)

WEEK	BODY WT (kg)	ABDOMEN (CM)	RECTAL TEMP °C	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec. (mm)	OTHER
- 3	16.5			++	++	Not	Measured			Laparotomy
- 2	19	63.5	40.2	++	++	46 x 22	42 x 22	30 x 13	30 x 13	
- 1	22.5	65	39.1	++	++	46 x 20	44 x 22	26 x 17	26 x 15	Wound healed
0	25	69	39.5	+++	+++	50 x 29	56 x 28	30 x 18	30 x 17	
1st Dose										
1	27	67	38.9	+++	+++	41 x 22	45 x 22	28 x 15	27 x 15	
2	29.5	72	39.5	+++	+++	45 x 22	43 x 24	27 x 16	27 x 16	
3	31	70	38.7	+++	+++	43 x 22	50 x 23	23 x 11	22 x 11	
2nd Dose										
4	32	70.5	39.5	+++	+++	48 x 21	42 x 22	29 x 13	32 x 14	
5	34.5	71	39.4	+++	+++	48 x 20	49 x 22	34 x 14	32 x 14	
6	35	77	39.0	+++	++	49 x 26	53 x 26	34 x 15	32 x 14	
3rd Dose										
7	Not weighed	69	39.8	+++	+++	44 x 21	51 x 19	Not Measured	Measured	Laparotomy
			37.8	++	+					Vomiting, drinking
			37.5	+	-					Dehydrated
8	28	Destroyed	in	extremis						Very weak, further operation failed to reveal site of obstruction

Laparotomy
Vomiting, drinking
Dehydrated
Very weak, further operation failed to reveal site of obstruction

APPENDIX IV.

APPENDIX IV
TABLE 1

CYTARABINE: NORMAL PIGS

CLINICAL RECORDS - Pig No. 298 (25mg x 2 and 45mg x 2 daily)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	19.5	Not recorded	+++	+++	-	Tarsal bursitis
-2	21	" "	+++	+++	-	LN Biopsy
-1	22	39.4	+++	+++	-	Some Oedema
0	25	39.0	+++	+++	-	
Start of Dosing						
1	23.5	38.6	+++	+++	-	Healing
2	24	38.6	+++	+++	-	Healed
3	24	39.5	+++	+++	-	LN Biopsy
End of Dosing						
4	26	39.5	+++	+++	-	Wound leaking
5	28.5	38.9	+++	+++	-	Wound broken down
6	33	38.2	+++	+++	-	Infected
7	34	39.9	+++	+++	-	
	DESTROYED					

APPENDIX IV
TABLE 2

CYTARABINE: NORMAL PIGS
PIG NO. 306 - (25mg x 2 and 45mg x 2 Daily)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	17	Not Recorded	+++	+++	-	
-2	18	" "	+++	+++	-	
-1	17.5	39.4	+++	+++	-	LN Biopsy
0	20.5	39.8	+++	+++	-	Little oedema
Start of Dosing						
1	20	39.3	+++	+++	-	Wound leaking
2	21.5	38.5	+++	+++	-	Infected
3	19	39.7	+++	+++	-	Not quite healed
DESTROYED						

APPENDIX IV

TABLE 3

CYTARABINE: NORMAL PIGS

CLINICAL RECORDS - Pig No. 300 (25mg x 2 and 35mg x 2 daily)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	17	Not Recorded	+++	+++	-	
-2	18	" "	+++	+++	-	
-1	19	38.3	+++	+++	-	LN Biopsy
0	20.5	39.2	+++	+++	-	Some oedema
Start of Dosing						
1	19.5	38.8	+++	+++	-	Wound Leaking
2	21	38.2	+++	+++	-	Infected
3	20	39.4	+++	+++	-	Not Quite healed
						LN Biopsy
End Of Dosing						
4	24	39.2	+++	+++	-	Little oedema
5	25.5	39.0	+++	+++	-	Healing
6	28.5	39.1	+++	+++	-	Healed
7	32	39.7	+++	+++	-	
DESTROYED						

APPENDIX IV

TABLE 4

CYTARABINE: NORMAL PIGS
Pig No. 310 (25mg x 2 and 35mg x 2 daily)

<u>WEEK</u>	<u>BODY WT. (kg)</u>	<u>RECTAL TEMP. (°C)</u>	<u>FITNESS</u>	<u>APPETITE</u>	<u>DIARRHOEA</u>	<u>OTHER</u>
-3	16.5	Not Recorded	+++	+++	-	
-2	16.5	" "	+++	+++	-	
-1	18.5	38.6	+++	+++	-	LN Biopsy
0	20	38.8	+++	+++	-	Some oedema
<u>Start of Dosing</u>						
1	18.5	38.6	+++	+++	-	Infected
2	20.5	37.9	+++	+++	-	Improved
3	19.5	38.8	+++	+++	-	Almost healed
<u>DESTROYED</u>						

APPENDIX IV

TABLE 5

CYTARABINE: NORMAL PIGS

CLINICAL RECORDS - Pig No. 307 (25mg x 2 daily)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	20.5	Not Recorded	+++	+++	-	
-2	21.5	" "	+++	+++	-	
-1	22	38.7	+++	+++	-	LN Biopsy
0	23	39.8	+++	+++	-	Little oedema
Start of Dosing						
1	22.5	39.2	+++	+++	-	Healing
2	24	39.1	+++	+++	-	Healed
3	24	38.9	+++	+++	-	LN Biopsy
End of Dosing						
4	26	38.3	+++	+++	-	Wound leaking
5	28.5	39.1	+++	+++	-	Healing
6	33	39.0	+++	+++	-	Healed
7	36.5	39.8				

DESTROYED

APPENDIX IV

TABLE 6

CYTARABINE: NORMAL PIGS

PIG No. 312 (25mg x 2 daily)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	20	Not recorded	+++	+++	-	
-2	21	Not recorded	+++	+++	-	
-1	21.5	39.1	+++	+++	-	LN biopsy
0	25	39.0	+++	+++	-	Some oedema
Start of Dosing						
1	23.5	38.7	+++	+++	-	Infected
2	26	38.2	+++	+++	-	Infected
3	27	39.2	+++	+++	-	Healed
DESTROYED						

APPENDIX IV

TABLE 7

CYTARABINE: NORMAL PIGS

CLINICAL RECORDS Pig No. 304 (SALINE - TREATED CONTROL)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	18	Not Recorded	+++	+++	-	
-2	19.5	Not Recorded	+++	+++	-	
-1	22	38.9	+++	+++	-	LN Biopsy
0	24	39.6	+++	+++	-	Severe oedema
Start of Dosing						
1	22.5	39.6	+++	+++	-	Incision healing
2	25	39.6	+++	+++	-	Infected
3	28.5	39.5	+++	+++	-	Healed LN Biopsy
End of Dosing						
4	33	38.0	+++	+++	-	Severe oedema
5	36	38.9	+++	+++	-	Wound Infected
6	39	38.9	+++	+++	-	Infected
7	39	39.6	+++	+++	-	
DESTROYED						

APPENDIX IV
TABLE 8

CYTARABINE: NORMAL PIGS
Pig No. 305 (SALINE - TREATED CONTROL)

WEEK	BODY WT. (Kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	15.5	Not Recorded	+++	+++	-	
-2	16.5	Not Recorded	+++	+++	-	
-1	17	39.2	+++	+++	-	LN Biopsy
0	19.5	39.5	+++	+++	-	Little oedema
Start of Dosing						
1	19	39.1	+++	+++	-	Healing
2	20.5	39.0	+++	+++	-	Healed
3	25	39.5	+++	+++	-	
DESTROYED						

APPENDIX IV

TABLE 9

CYTARABINE: NORMAL PIGS

CLINICAL RECORDS Pig No. 308 (SALINE - TREATED CONTROL)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	18	Not Recorded	+++	+++	-	
-2	18.5	Not Recorded	+++	+++	-	
-1	20.5	38.8	+++	+++	-	LN BIOPSY
0	21.5	39.8	+++	+++	-	Extensive Oedema
Start of Dosing						
1	25	39.1	+++	+++	-	Healing
2	21	38.1	+++	+++	-	Healed
3	22.5	38.5	+++	+++	-	LN BIOPSY
End of Dosing						
4	24	40	+++	+++	-	Some Oedema
5	27.5	39.1	+++	+++	-	Healed
6	29.5	38.7	+++	+++	-	
7	34	39.6	+++	+++	-	
DESTROYED						

APPENDIX IV
TABLE 10

CYTARABINE: NORMAL PIGS
PIG No. 309 (SALINE-TREATED CONTROL)

WEEK	BODY WT. (kg)	RECTAL TEMP. (°C)	FITNESS	APPETITE	DIARRHOEA	OTHER
-3	13	Not Recorded	+++	+++	-	
-2	13.5	Not Recorded	+++	+++	-	LN Biopsy
-1	14	39.6	+++	+++	-	Little Oedema
0	15.5	39.3	+++	+++	-	Wound leaking
Start of Dosing						
1	15	39.6	+++	+++	-	Infected
2	17.5	38.8	+++	+++	-	Infected
3	17.5	39.3	+++	+++	-	Still not healed
DESTROYED						

APPENDIX IV
TABLE 11

CYTARABINE : NORMAL PIGS - PIG N° 306 (25mg x 2 and 45mg x 2 daily)

WHITE BLOOD CELL COUNTS X 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER%
- 28	26.8	53	40	6	0	1	0
- 21	27.7	45	50	3	0	2	0
- 14	27.2	49	45	4	0	2	0
- 7	30.1	52	44	4	0	0	0
0	22.9	39	57	4	0	0	0
Start of Dosing							
1	24.6	51	43	5	0	1	0
2	29.8	53	39	7	0	1	0
3	21.5	43	50	7	0	0	0
4	16.9	38	58	2	1	1	0
7	17.7	43	47	7	0	2	1
8	19.0	27	60	10	0	3	0
9	17.0	32	59	8	0	1	0
10	16.5	36	56	7	0	1	0
11	18.2	40	56	3	1	0	0
Dose Increased							
14	12.8	35	60	5	0	0	0
15	11.8	47	48	4	1	0	0
16	9.5	18	76	5	0	1	0
17	11.0	24	73	3	0	0	0
18	9.8	16	80	3	0	1	0
Destroyed							

APPENDIX IV

TABLE 12

CYTARABINE : NORMAL PIGS - PIG NO 298 (25mg x 2 daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days From Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO.%	BASO %	EOSINO %	OTHER %
- 28	27.5	50	37	11	0	2	0
- 21	28.3	48	45	7	0	0	0
- 14	26.9	47	46	5	0	2	0
- 7	30.1	48	46	5	0	1	0
0	20.7	29	64	5	0	2	0
Start of Dosing							
1	20.7	39	51	6	1	3	0
2	17.7	40	58	0	0	2	0
3	18.6	36	57	3	0	4	0
4	14.2	29	59	10	0	2	0
7	16.0	34	58	5	0	2	1
8	16.4	44	50	5	0	1	0
9	14.6	30	62	6	0	2	0
10	14.2	31	62	6	0	0	1
11	16.1	42	54	4	0	0	0
Dose Increased							
14	13.3	36	51	12	1	0	0
15	12.0	36	60	3	1	0	0
16	15.5	51	42	7	0	0	0
17	13.5	22	70	8	0	0	0
18	9.1	27	67	6	0	0	0
End of Dosing							
21	10.5	27	67	4	1	0	1
23	12.0	9	80	9	0	0	2
25	13.6	9	77	13	0	0	1
28	20.5	39	55	5	1	0	0
31	28.7	57	40	2	1	0	0
35	25.6	42	50	5	1	2	0
38	23.5	35	55	4	0	6	0
42	20.3	42	45	10	0	3	0
45	14.3	24	71	2	0	3	0

Destroyed

APPENDIX IV

TABLE 13

CYTARABINE : NORMAL PIGS - PIG NO 310 (25mg x 2 and 35mg x 2 daily)
 WHITE BLOOD CELL COUNTS x 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days From Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	35.8	47	45	6	0	2	0
- 21	31.2	33	57	6	1	3	0
- 14	36.8	26	59	13	0	2	0
- 7	27.1	39	48	10	1	2	0
0	23.0	36	53	6	0	5	0
Start of Dosing							
1	21.3	36	60	1	0	3	0
2	19.7	34	56	7	1	2	0
3	19.4	43	48	6	1	2	0
4	17.6	39	56	4	0	1	0
7	17.6	38	52	9	0	1	0
8	15.8	32	58	9	1	0	0
9	13.8	32	60	7	0	1	0
10	13.4	33	57	8	0	2	0
11	11.5	28	69	2	0	0	1
Dose Increased							
14	9.9	27	68	2	1	1	1
15	11.0	20	72	7	1	0	0
16	11.9	34	57	9	0	0	0
17	10.9	24	69	7	0	0	0
18	5.1	18	75	7	0	0	0

Destroyed

APPENDIX IV

TABLE 14

CYTARABINE : NORMAL PIGS - PIG NO 300 (25mg x 2 and 25mg x 2 daily)

WHITE BLOOD CELL COUNTS x 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days From Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	29.8	61	31	6	0	2	0
- 21	19.7	48	43	8	0	1	0
- 14	22.9	49	43	5	0	3	0
- 7	31.1	58	29	10	0	2	1
0	19.4	34	57	4	0	5	0
Start of Dosing							
1	21.6	40	53	5	0	2	0
2	17.1	44	45	7	0	4	0
3	17.4	55	39	5	0	1	0
4	14.2	38	49	10	0	3	0
7	13.1	47	40	12	0	1	0
8	12.7	39	57	4	0	0	0
9	11.9	34	55	11	0	0	0
10	12.4	41	49	9	0	1	0
11	10.9	37	55	8	0	0	0
Dose Increased							
14	11.3	36	57	7	0	0	0
15	9.1	20	73	7	0	0	0
16	8.5	14	75	7	3	0	1
17	8.0	22	71	6	0	0	1
18	6.7	23	69	8	0	0	0
End of Dosing							
21	9.9	30	60	8	1	0	1
23	9.4	11	74	12	1	0	2
25	11.0	4	78	16	0	0	2
28	15.7	33	63	4	0	0	0
31	21.7	46	51	2	0	1	0
35	16.6	42	51	7	0	0	0
38	23.3	55	35	10	0	0	0
42	18.2	39	47	10	0	3	1
45	15.0	29	65	2	0	3	1
	Destroyed						

APPENDIX IV

TABLE 15

CYTARABINE : NORMAL PIGS - PIG NO 312 (25mg x 2 daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days from Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO.%	BASO %	EOSINO %	OTHER %
- 28	27.9	52	41	5	1	1	0
- 21	31.6	51	39	8	1	1	0
- 14	34.4	55	39	5	0	0	1
- 7	33.8	59	33	6	0	2	0
0	26.4	25	67	2	0	6	0
Start of Dosing							
1	28.0	42	50	4	0	4	0
2	24.7	55	39	5	0	1	0
3	21.4	54	40	3	0	2	1
4	17.3	32	58	9	0	1	0
7	18.6	38	48	9	0	5	0
8	16.8	31	54	12	1	2	0
9	18.8	33	56	10	1	0	0
10	27.2	76	18	6	0	0	0
11	21.8	53	35	10	0	2	0
14	16.0	37	57	6	0	0	0
15	13.4	29	64	4	0	0	3
16	23.1	53	45	1	0	0	1
17	18.8	44	50	5	1	0	0
18	15.3	48	45	7	0	0	0
	Destroyed						

APPENDIX IV

TABLE 16

CYTARABINE : NORMAL PIGS - PIG NO 307 (25mg x 2 daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days From Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	30.5	53	32	8	1	6	0
- 21	23.8	41	53	5	0	1	0
- 14	28.8	41	47	11	0	1	0
- 7	31.1	55	40	4	0	1	0
0	22.2	39	57	4	0	0	0
Start of Dosing							
1	23.5	55	40	4	0	1	0
2	18.2	45	51	4	0	0	0
3	16.2	43	47	5	3	2	0
4	16.2	29	57	11	0	3	0
7	16.3	42	51	5	0	1	1
8	19.6	50	37	13	0	0	0
9	15.7	38	53	9	0	0	0
10	11.8	33	61	5	1	0	0
11	10.9	40	53	7	0	0	0
14	9.9	36	62	1	1	0	0
15	11.2	27	69	3	1	0	0
16	9.7	33	62	4	1	0	0
17	9.9	31	62	4	3	0	0
18	6.6	27	67	5	1	0	0
End of Dosing							
21	8.3	10	81	4	3	0	2
23	13.3	16	69	10	2	0	3
25	16.0	32	59	8	0	0	1
28	22.3	52	43	5	0	0	0
31	28.0	55	41	4	0	0	0
35	21.6	39	54	3	0	4	0
38	24.0	57	36	5	0	2	0
42	19.4	47	45	6	1	1	0
45	14.3	30	60	7	0	2	1

APPENDIX IV
TABLE 17

CYTARABINE : NORMAL PIGS - PIG NO 305 (Saline x 2 daily)
WHITE BLOOD CELL COUNTS x 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days from Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	23.5	43	47	9	0	1	0
- 21	32.7	70	28	2	0	0	0
- 14	31.9	46	49	4	0	1	0
- 7	43.5	73	25	1	0	0	1
0	20.1	39	53	5	0	3	0
Start of Dosing							
1	25.1	52	43	2	0	3	0
2	24.1	56	35	7	0	2	0
3	22.8	38	56	5	0	0	1
4	26.9	51	38	9	0	2	0
7	24.4	38	58	4	0	0	0
8	23.7	36	57	6	0	0	1
9	21.1	37	53	10	0	0	0
10	34.6	26	68	6	0	0	0
11	22.4	29	65	3	0	2	1
14	20.9	36	55	7	0	1	1
15	21.2	40	49	8	0	1	2
16	21.3	37	56	5	0	1	1
17	25.8	28	64	7	0	1	0
18	Destroyed						

APPENDIX IV
TABLE 18

CYTARABINE : NORMAL PIGS - PIG NO 309 (Saline x 2 daily)
WHITE BLOOD CELL COUNTS x 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days from Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	24.3	25	69	5	0	1	0
- 21	25.9	48	44	7	0	1	0
- 14	27.9	34	64	2	0	0	0
- 7	28.7	39	54	7	0	0	0
0	22.1	36	53	6	0	5	0
Start of Dosing							
1	25.5	40	54	4	0	0	2
2	25.2	43	48	8	0	1	0
3	24.0	32	61	5	1	0	1
4	21.9	31	59	7	0	3	0
7	24.9	32	59	7	1	1	0
8	24.2	27	65	8	0	0	0
9	31.5	40	52	8	0	0	0
10	24.2	42	52	6	0	0	0
11	23.3	34	56	7	0	1	2
14	23.6	33	59	5	0	2	1
15	25.7	36	57	4	2	1	0
16	25.5	37	52	8	1	2	0
17	29.6	32	61	6	0	1	0
18	Destroyed						

APPENDIX IV

TABLE 19

CYTARABINE : NORMAL PIGS - PIG NO 304 (Saline x 2 daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

Days From Start of Dosing	WBC	NEUTR.%	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	30.5	55	39	4	1	1	0
- 21	24.1	55	44	1	0	0	0
- 14	29.3	39	55	5	0	1	0
- 7	29.7	61	32	7	0	0	0
0	20.0	31	64	4	1	0	0
Start of Dosing							
1	25.7	40	53	5	0	2	0
2	25.9	59	30	10	0	1	0
3	26.2	53	41	3	0	1	2
4	22.7	38	51	7	0	0	4
7	18.9	33	57	6	0	3	1
8	23.7	37	54	4	0	2	0
9	23.3	44	49	3	0	3	1
10	23.7	39	52	6	0	3	0
11	23.1	31	63	4	0	2	0
14	24.1	38	58	2	0	1	1
15	22.2	39	53	4	0	2	2
16	23.2	31	59	7	0	3	0
17	24.7	37	57	5	0	1	0
18	22.6	38	58	4	0	0	0
End of Dosing							
21	19.0	35	52	8	0	5	0
23	17.4	34	53	9	1	3	0
25	18.5	40	50	9	0	1	0
28	28.8	56	43	1	0	0	0
31	28.3	62	29	6	0	3	0
35	22.3	39	51	8	0	2	0
38	26.5	41	52	4	0	2	1
42	20.8	32	61	6	0	1	0
45	16.6	24	62	11	0	8	1

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TABLE 20

CYTARABINE : NORMAL PIGS - PIG N° 308 (Saline x 2 Daily)

WHITE BLOOD CELL COUNTS x 10⁹/LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	LYMPH %	MONO %	BASO %	EOSINO %	OTHER %
- 28	35.7	46	46	8	0	0	0
- 21	23.9	32	57	9	1	1	0
- 14	25.6	46	49	4	0	1	0
- 7	27.9	46	41	10	0	1	2
- 0	29.5	45	50	4	0	1	0
Start of Dosing							
1	36.0	33	62	5	0	0	0
2	28.4	44	47	9	0	0	0
3	29.7	38	53	5	1	2	1
4	31.0	36	52	10	0	2	0
7	32.7	37	58	4	1	0	0
8	25.9	35	56	7	0	1	1
9	28.1	34	57	8	0	1	0
10	22.6	35	51	11	0	2	1
11	22.3	39	54	6	0	1	0
14	20.6	43	51	4	0	0	2
15	25.0	44	50	5	0	1	0
16	27.4	30	60	5	1	2	2
17	27.0	37	53	10	0	0	0
18	24.2	34	56	5	0	4	1
End of Dosing							
21	11.1	27	62	10	0	1	0
23	24.4	27	70	3	0	0	0
25	18.7	40	49	8	1	1	1
28	27.0	34	59	5	0	2	0
31	24.7	40	50	9	0	1	0
35	25.5	38	54	6	0	2	0
38	24.4	27	64	8	0	1	0
42	20.6	33	53	11	1	2	0
45	18.6	34	57	7	0	2	0

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TABLE 22

CYTARABINE : NORMAL PIGS - PIG N° 298 (25mg x 2 and 45mg x 2 daily)

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	6.74	0.33	11.2	49.0	33.9	16.6	3.52	432
- 21	7.15	0.36	11.9	50.4	33.1	16.6	5.94	251
- 14	7.27	0.355	11.6	48.8	32.7	16.0	4.63	270
- 7	7.51	0.35	11.7	46.6	33.4	15.6	4.45	335
0	7.37	0.36	11.7	48.8	32.5	15.9	3.20	355
Start of Dosing								
1	7.86	0.355	11.6	45.2	32.7	14.8	-	291
2	7.43	0.34	11.7	45.8	34.4	15.7	-	373
3	7.60	0.35	11.6	46.1	33.1	15.3	-	354
4	7.32	0.35	11.3	47.8	32.9	15.4	5.33	355
7	7.22	0.33	10.8	45.7	32.7	15.0	-	302
8	7.04	0.33	10.7	46.9	32.4	15.2	-	233
9	7.07	0.32	10.5	45.3	32.8	14.9	-	261
10	7.07	0.31	10.3	43.8	33.2	14.6	-	297
11	6.88	0.30	10.2	43.6	34.0	14.8	3.50	262
Dose Increased								
14	6.46	0.28	9.5	43.3	33.9	14.7	-	194
15	6.78	0.295	9.8	43.5	33.2	14.5	-	138
16	6.51	0.30	9.6	46.1	32.0	14.7	-	165
17	6.32	0.27	9.3	42.7	34.4	14.7	-	157
18	6.18	0.265	9.0	42.9	34.0	14.6	4.24	209
End of Dosing								
21	5.56	0.27	9.0	48.6	33.3	16.2	-	54
23	5.90	0.29	9.2	49.2	31.7	15.6	-	167
25	6.35	0.32	10.1	50.4	31.6	15.9	1.66	247
28	6.85	0.345	11.3	50.4	32.8	16.5	-	220
31	6.98	0.35	11.8	50.1	33.7	16.9	-	236
35	6.95	0.355	12.0	51.1	33.8	17.3	-	229
38	6.77	0.32	11.0	47.3	34.4	16.2	5.52	263
42	6.51	0.33	10.7	50.7	32.4	16.4	6.00	321
45	7.05	0.36	11.9	51.1	33.1	16.9	-	252

APPENDIX IV

TABLE 24

CYTARABINE : NORMAL PIGS - PIG NO 300 (26mg x 2 and 35mg x 2 daily)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	7.22	0.33	11.6	45.7	35.2	16.1	4.32	220
- 21	6.89	0.355	11.0	51.5	31.0	16.0	5.68	311
- 14	7.05	0.34	11.1	48.2	32.6	15.7	5.05	391
- 7	7.52	0.32	11.2	42.6	35.0	14.9	5.76	342
0	7.02	0.33	11.1	47.0	33.6	15.8	3.66	369
Start of Dosing								
1	7.24	0.335	11.2	46.3	33.4	15.5	-	311
2	6.79	0.32	10.5	47.1	32.8	15.5	-	408
3	7.55	0.34	11.4	45.0	33.5	15.1	-	431
4	7.30	0.34	11.2	46.6	32.9	15.3	4.57	375
7	6.70	0.305	10.3	45.5	33.8	15.4	-	299
8	7.01	0.31	10.4	44.2	33.5	14.8	-	300
9	7.01	0.29	10.1	41.4	34.8	14.4	-	362
10	6.77	0.28	9.7	41.4	34.6	14.3	-	321
11	6.47	0.28	9.5	43.3	33.9	14.7	5.25	246
Dose Increased								
14	6.76	0.29	9.4	42.9	32.4	13.9	-	226
15	6.65	0.275	9.5	41.4	34.5	14.3	-	187
16	6.49	0.285	9.2	43.9	32.3	14.2	-	190
17	5.94	0.26	9.0	43.8	34.6	15.2	-	208
18	5.90	0.25	8.5	42.4	34.0	14.4	5.18	212
End of Dosing								
21	5.37	0.23	7.8	42.8	33.9	14.5	-	81
23	5.20	0.235	7.8	45.2	33.2	15.0	-	248
25	5.63	0.275	8.6	48.8	31.3	15.3	3.31	359
28	5.97	0.32	9.9	53.6	30.9	16.6	-	269
31	6.27	0.31	10.2	49.4	32.9	16.3	-	191
35	6.13	0.305	10.0	49.8	32.8	16.3	-	329
38	6.28	0.30	9.7	47.8	32.3	15.4	5.24	245
42	6.24	0.30	9.6	48.1	32.0	15.4	7.33	465
45	6.60	0.335	10.5	50.8	31.3	15.9	-	346

APPENDIX IV

TABLE 25

CYTARABINE : NORMAL PIGS - PIG NO 312 (25mg x 2 daily)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	7.57	0.36	12.4	47.6	34.4	16.4	5.76	306
- 21	7.69	0.38	12.8	49.4	33.7	16.6	9.55	338
- 14	8.23	0.385	13.1	46.8	34.0	15.9	8.84	253
- 7	7.74	0.355	12.1	45.9	34.1	15.6	8.48	360
0	7.86	0.37	12.6	47.1	34.1	16.0	6.86	325
Start of Dosing								
1	8.90	0.36	12.6	40.4	35.0	14.2	-	350
2	7.46	0.345	11.9	46.2	34.5	16.0	-	271
3	7.48	0.355	11.5	47.5	32.4	15.4	-	359
4	8.00	0.35	12.4	43.8	35.4	15.5	5.33	386
7	6.82	0.33	11.0	48.4	33.3	16.1	-	303
8	7.09	0.31	10.8	43.7	34.8	15.2	-	250
9	6.87	0.29	10.4	42.2	35.9	15.1	-	190
10	6.69	0.30	10.1	44.8	33.7	15.1	-	218
11	6.67	0.295	10.2	44.2	34.6	15.3	6.00	299
14	6.52	0.31	10.0	47.5	32.3	15.3	-	217
15	6.47	0.29	9.6	44.8	33.1	14.8	-	126
16	6.18	0.28	9.6	45.3	34.3	15.5	-	114
17	6.30	0.285	9.7	45.2	34.0	15.4	-	197
18	6.33	0.26	9.6	41.1	36.9	15.2	4.47	330
	Destroyed							

APPENDIX IV

TABLE 26

CYTARABINE : NORMAL PIGS - PIG NO 307 (25mg x 2 daily)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	7.66	0.38	12.6	49.6	33.2	16.4	5.28	192
- 21	7.60	0.38	12.9	50.0	33.9	17.0	8.26	327
- 14	7.61	0.375	12.8	49.3	34.1	16.8	6.32	283
- 7	7.41	0.345	12.5	46.6	36.2	16.9	4.96	217
0	7.26	0.35	11.9	48.2	34.0	16.4	4.11	334
Start of Dosing								
1	7.86	0.37	12.7	47.1	34.3	16.2	-	250
2	7.60	0.34	12.0	44.7	35.3	15.8	-	325
3	7.48	0.355	12.1	47.5	34.1	16.2	-	232
4	7.88	0.35	12.6	44.4	36.0	16.0	6.86	347
7	6.90	0.325	10.9	47.1	33.5	15.8	-	288
8	7.31	0.335	11.3	45.8	33.7	15.5	-	207
9	6.95	0.31	10.8	44.6	34.8	15.5	-	190
10	6.78	0.31	10.5	45.7	33.9	15.5	-	187
11	6.43	0.295	10.4	45.9	35.3	16.2	7.50	196
14	6.71	0.30	10.4	44.7	34.7	15.5	-	96
15	6.91	0.31	10.4	44.9	33.5	15.1	-	80
16	6.31	0.27	9.5	42.8	35.2	15.1	-	96
17	6.63	0.28	10.0	42.2	35.7	15.1	-	110
18	5.94	0.255	9.1	42.9	35.7	15.3	4.71	156
End of Dosing								
21	5.34	0.25	8.3	46.8	33.2	15.5	-	29
23	4.84	0.22	7.7	45.5	35.0	15.9	-	194
25	5.41	0.265	8.5	49.0	32.1	15.7	1.38	396
28	6.24	0.325	10.3	52.1	31.7	16.5	-	237
31	6.78	0.34	11.8	50.1	34.7	17.4	-	249
35	7.03	0.365	12.2	51.9	33.4	17.4	-	164
38	6.43	0.335	10.9	52.1	32.5	17.0	5.52	198
42	6.90	0.35	11.5	50.7	32.9	16.7	7.33	316
45	7.06	0.37	12.0	52.4	32.4	17.0	-	394

APPENDIX IV
TABLE 27

CYTARABINE : NORMAL PIGS - PIG NO 305 (Saline x 2 daily)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB.
- 28	7.48	0.35	12.0	46.8	34.3	16.0	4.32	4.42
- 21	7.28	0.36	11.9	49.5	33.1	16.3	8.26	343
- 14	7.25	0.345	11.4	47.6	33.0	15.7	6.32	340
- 7	7.74	0.33	11.7	42.6	35.5	15.1	5.28	322
0	7.42	0.35	11.7	47.2	33.4	15.8	3.66	322
Start of Dosing								
1	7.99	0.35	12.0	43.8	34.3	15.0	-	303
2	7.40	0.33	11.7	44.6	35.5	15.8	-	315
3	7.34	0.34	11.1	46.3	32.6	15.1	-	328
4	7.50	0.34	11.8	45.3	34.7	15.7	6.86	371
7	7.50	0.335	11.6	44.7	34.6	15.5	-	371
8	6.91	0.31	10.8	44.9	34.8	15.6	-	368
9	7.25	0.32	11.0	44.1	34.4	15.2	-	381
10	7.45	0.33	11.3	44.3	34.2	15.2	-	336
11	7.54	0.345	11.3	45.8	32.8	15.0	6.00	385
14	7.84	0.36	11.9	45.9	33.1	15.2	-	337
15	7.84	0.355	11.8	45.3	33.2	15.1	-	265
16	7.60	0.35	11.8	46.1	33.7	15.5	-	278
17	8.29	0.39	12.5	47.0	32.1	15.1	5.71	348
18	Destroyed							

APPENDIX IV
TABLE 28

CYTARABINE : NORMAL PIGS - PIG NO 309 (Saline x 2 daily)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB.
- 28	7.42	0.385	12.8	51.9	33.2	17.3	5.28	432
- 21	7.00	0.36	12.1	51.4	33.6	17.3	7.48	234
- 14	7.10	0.34	11.8	47.9	34.7	16.6	5.05	259
- 7	7.42	0.36	12.1	48.5	33.6	16.3	4.00	318
0	6.99	0.35	11.2	50.1	32.0	16.0	4.57	313
Start of Dosing								
1	7.72	0.35	12.1	45.3	34.6	15.7	-	368
2	7.10	0.32	11.5	45.1	35.9	16.2	-	322
3	7.71	0.355	12.1	46.0	34.1	15.7	-	392
4	7.56	0.36	12.2	47.6	33.9	16.1	5.71	398
7	7.35	0.335	11.6	45.6	34.6	15.8	-	364
8	7.38	0.35	11.8	47.4	33.7	16.0	-	433
9	7.65	0.335	12.2	43.8	36.4	15.9	-	463
10	7.53	0.33	10.9	43.8	33.0	14.5	-	341
11	7.36	0.33	11.2	44.8	33.9	15.2	7.50	418
14	7.60	0.34	11.6	44.7	34.1	15.3	-	411
15	7.66	0.34	11.5	44.4	33.8	15.0	-	343
16	7.30	0.34	11.5	46.6	33.8	15.8	-	363
17	7.43	0.36	11.9	48.5	33.1	16.0	5.33	300
18	Destroyed							

APPENDIX IV

TABLE 29

CYTARABINE : NORMAL PIGS - PIG N° 304 (Saline x 2 daily S/Cut)

Days From Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	6.90	0.34	11.6	49.3	34.1	16.8	4.64	542
- 21	6.68	0.34	11.4	50.9	33.5	17.1	6.97	359
- 14	7.14	0.35	11.9	49.0	34.0	16.7	6.11	466
- 7	7.43	0.35	12.0	47.1	34.3	16.2	6.88	236
0	7.12	0.34	11.9	47.8	35.0	16.7	4.80	346
Start of Dosing								
1	7.28	0.33	11.9	45.3	36.1	16.3	-	294
2	7.17	0.35	11.9	48.8	34.0	16.6	-	354
3	7.29	0.35	11.6	48.0	33.1	15.9	-	387
4	7.00	0.34	11.8	48.6	34.7	16.9	6.86	397
7	7.08	0.345	11.5	48.7	33.3	16.2	-	341
8	7.61	0.36	11.2	47.3	31.1	14.7	-	397
9	7.09	0.33	11.4	44.5	34.5	16.1	-	340
10	7.40	0.35	11.7	47.3	33.4	15.8	-	319
11	6.92	0.32	10.9	46.2	34.1	15.8	7.00	334
14	7.22	0.35	11.8	48.5	33.7	16.3	-	368
15	7.34	0.33	11.4	45.0	34.5	15.5	-	312
16	7.00	0.35	11.5	50.0	32.9	16.4	-	341
17	7.16	0.33	11.4	46.1	34.5	15.9	-	330
18	7.20	0.33	11.6	45.8	35.2	16.1	5.18	323
End of Dosing								
21	6.36	0.305	10.2	48.0	33.4	16.0	-	59
23	6.46	0.31	10.6	48.0	34.2	16.4	-	263
25	6.35	0.30	10.1	47.2	33.7	15.9	1.66	393
28	6.83	0.325	11.1	47.6	34.2	16.3	-	423
31	5.97	0.27	9.8	45.2	36.3	16.4	-	314
35	5.98	0.30	10.0	51.0	33.3	17.0	-	457
38	6.47	0.315	10.2	48.7	32.4	15.8	6.34	319
42	6.30	0.33	10.4	52.4	31.5	16.5	7.33	390
45	7.03	0.35	11.2	49.8	32.0	15.9	-	305

APPENDIX IV

TABLE 30

CYTARABINE : NORMAL PIGS - PIG N° 308 (Saline x 2 daily S/Cut)

Days from Start of Dosing	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 28	7.52	0.355	12.1	47.2	34.1	16.1	3.68	473
- 21	7.33	0.37	12.1	50.5	32.7	16.5	6.19	298
- 14	7.57	0.355	11.9	46.9	33.5	15.7	5.05	333
- 7	7.86	0.35	12.1	44.5	34.6	15.4	4.00	269
0	7.51	0.35	11.7	46.6	33.4	15.6	5.49	327
Start of Dosing								
1	7.66	0.35	11.8	45.7	33.7	15.4	-	298
2	7.67	0.345	11.4	45.0	33.0	14.9	-	278
3	7.46	0.34	11.4	45.6	33.5	15.3	-	370
4	7.80	0.35	12.0	44.9	34.3	15.4	6.10	343
7	7.47	0.365	11.4	48.9	31.2	15.3	-	341
8	7.68	0.37	11.7	44.2	31.6	15.2	-	296
9	7.81	0.36	11.7	46.1	32.5	15.0	-	244
10	7.65	0.35	11.4	45.8	32.6	14.9	-	292
11	7.53	0.345	11.1	45.8	32.2	14.7	4.00	309
14	7.63	0.34	11.6	44.6	34.1	15.2	-	355
15	7.64	0.345	11.5	45.2	33.3	15.1	-	244
16	7.88	0.38	11.8	48.2	31.1	15.0	-	318
17	8.02	0.38	12.2	47.4	32.1	15.2	-	218
18	7.92	0.35	12.0	44.2	34.3	15.2	3.76	357
End of Dosing								
21	7.52	0.35	11.1	46.5	31.7	14.8	-	297
23	7.69	0.345	11.8	44.9	33.3	15.0	-	336
25	7.65	0.345	11.5	45.1	33.3	15.0	1.93	286
28	7.68	0.345	11.7	44.9	33.9	15.2	-	277
31	7.74	0.36	13.0	46.5	36.1	16.8	-	261
35	7.76	0.375	12.5	48.3	33.3	16.1	-	226
38	7.42	0.33	11.3	44.5	34.2	15.2	4.97	271
42	6.99	0.32	10.6	45.8	33.1	15.2	6.00	274
45	6.96	0.34	11.1	48.9	32.6	15.9	-	225

APPENDIX IV

TABLE 31

CYTARABINE : NORMAL PIGS

SERUM TOTAL PROTEIN - g/litre

DAYS FROM START OF DOSING	GROUP D - CONTROLS						TREATED GROUP			
	304	305	308	309	307	312	300	310	298	306
- 28	63.7	62.6	56.9	49.0	60.8	56.4	60.2	57.7	64.1	59.7
- 21	60.6	56.2	54.5	63.0	54.2	55.8	56.9	58.4	59.1	61.5
- 14	58.2	52.7	50.3	49.8	55.6	58.2	60.6	55.3	56.0	55.9
- 7	63.0	58.5	57.8	54.4	69.9	57.5	60.5	57.5	53.7	62.5
0	66.6	65.9	59.2	59.3	69.0	54.5	62.2	57.4	61.9	60.0
Start of Dosing										
4	55.5	55.0	52.7	59.2	61.9	56.9	55.2	56.2	52.5	55.5
11	60.4	62.3	56.6	57.3	62.6	60.1	57.5	60.2	58.2	59.7
					Group A - Low Dose		Group B - Medium Dose		Group C - High Dose	
18	59.2	65.3	62.4	56.8	58.3	61.3	60.7	62.4	59.1	60.3
End of Dosing										
25	57.5	dead	54.9	dead	56.2	dead	56.9	dead	55.4	dead
31	55.7		60.5		61.6		58.3		56.4	
38	57.2		55.6		56.1		60.2		53.9	
45	65.3		58.7		59.6		57.7		62.4	

TABLE 32

SERUM ALBUMIN g/litre

DAYS FROM START OF DOSING	GROUP D - CONTROLS						TREATED GROUP			
	304	305	308	309	307	312	300	310	298	306
- 28	34.2	36.8	34.7	28.2	37.3	33.0	31.5	35.5	33.1	33.5
- 21	34.3	32.8	34.7	31.0	34.8	33.0	33.4	31.8	32.5	35.0
- 14	34.2	32.0	32.7	39.4	34.8	31.9	33.0	32.4	32.6	33.4
- 7	32.1	29.8	32.9	30.6	36.0	29.9	31.9	32.0	27.9	39.6
0	36.0	36.8	29.6	30.5	35.8	31.5	31.6	32.6	31.0	32.1
Start of Dosing										
4	35.2	33.2	32.4	33.9	42.3	36.2	37.4	37.0	33.7	35.9
11	34.5	32.6	31.0	40.0	45.1	35.3	37.2	40.2	34.2	35.1
					Group A - Low Dose		Group B - Medium Dose		Group C - High Dose	
18	32.5	35.0	33.5	32.8	42.7	33.9	38.1	39.9	35.1	36.7
End of Dosing										
25	25.5	dead	26.8	dead	28.4	dead	29.6	dead	28.4	dead
31	25.0		31.4		32.5		32.1		28.2	
38	33.5		27.1		25.5		28.0		25.8	
45	25.5		27.2		28.9		26.2		28.9	

APPENDIX IV

TABLE 33

CYTARABINE : NORMAL PIGS

SERUM GLUTAMIC OXALOACETATE TRANSAMINASE (SGOT)(iu/l)

DAYS FROM START OF DOSING	GROUP D - CONTROLS						TREATED GROUP			
	304	305	308	309	307	312	300	310	298	306
0 Start of Dosing	30.9	25.7	27.7	27.7	20.6	30.9	30.9	27.7	41.2	20.6
4	31.9	29.9	19.6	17.5	16.5	11.3	26.8	14.4	13.4	13.9
11	31.9	30.9	24.7	28.8	20.6	18.5	30.9	26.8	27.8	28.8
					Group A - Low Dose		Group B - Medium Dose		Group C - High Dose	
18 End of Dosing	12.3	24.7	19.5	19.9	10.3	11.3	15.4	17.5	26.7	12.8
25	37.1	dead	25.7	dead	12.3	dead	12.3	dead	18.5	dead
31	12.4		21.6		27.7		26.7		34.0	
38	28.8		14.9		24.2		27.8		21.6	
45	15.0		15.0		15.0		20.0		15.0	

TABLE 34

SERUM ALKALINE PHOSPHATASE. (iu/l)

DAYS FROM START OF DOSING	GROUP D - CONTROLS						TREATED GROUP			
	304	305	308	309	307	312	300	310	298	306
0 Start of Dosing	92	118	55	64	54	65	67	50	58	86
4	142	157	114	75	103	91	97	78	88	97
11	150	124	145	91	92	119	126	101	93	125
					Group A - Low Dose		Group B - Medium Dose		Group C - High Dose	
18 End of Dosing	143	146	81	131	60	86	73	66	74	83
25	108	dead	86	dead	35	dead	66	dead	89	dead
31	83		111		97		114		113	
38	103		76		95		144		122	
45	98		60		70		74		94	

APPENDIX IV
TABLE 35

CYTARABINE : NORMAL PIGS - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS

DOSE LEVEL	SALINE CONTROLS										LOW DOSE		MEDIUM DOSE		HIGH DOSE		
	PIG NO	304	305 ⁺	308	309 ⁺	307	312 ⁺	300	310 ⁺	298	306 ⁺						
Submandibular LN	3.00	2.53	2.51	2.28	2.44	3.03	2.51	1.71	3.06	1.90							
Parotid LN	2.63	2.33	1.85	2.10	3.39	2.33	2.75	1.56	3.59	2.14							
Retropharyngeal LN	1.86	0.86	0.86	0.48	1.14	0.91	1.16	0.63	1.48	1.69							
Cervical LN	5.03	1.99	5.77	1.48	3.19	1.48	1.98	2.05	2.99	2.10							
Prescapular LN	2.12	1.83	1.26	0.68	1.20	0.90	1.71	0.83	1.86	0.63							
Left Bronchial LN	3.33	2.09	3.06	1.56	3.91	3.30	2.97	2.65	4.87	3.04							
Mid Bronchial LN	0.60	0.39	1.23	0.56	0.82	1.17	0.11	0.66	1.21	0.27							
Apical Bronchial LN	0.60	0.39	0.84	0.31	0.60	0.56	0.64	0.63	0.54	0.57							
Right Bronchial LN	0.60	0.39	1.59	0.56	0.55	0.81	0.24	0.28	1.57	0.43							
External Iliac LN	2.48	1.24	2.82	1.10	2.92	2.10	3.80	1.45	2.50	1.65							
Internal Iliac LN	0.64	0.56	0.65	0.38	0.47	0.25	0.28	0.26	0.66	0.40							
Inguinal LN	-	4.90	-	3.60	-	5.30	-	8.00	-	4.20							
Mesenteric and Colonic LN	150.00	81.67	130.00	56.78	135.00	85.58	100.00	54.70	120.00	68.21							
Gastric LN	16.43	5.63	19.91	6.59	13.27	10.20	15.04	6.19	18.77	6.90							
Splenic LN	1.42	0.43	1.59	0.69	1.46	0.38	0.79	0.51	1.20	0.90							
Precrural LN	2.00	0.74	1.71	0.54	1.99	0.87	1.35	0.81	1.84	0.72							
Popliteal LN	0.60	0.39	0.40	0.23	0.43	1.54	0.39	0.20	0.93	0.57							
Liver	1230.00	610.00	1130.00	535.00	1050.00	870.00	980.00	570.00	1280.00	540.00							
Kidney (mean)	90.00	45.00	85.00	35.00	95.00	67.00	75.00	47.00	100.00	40.00							
Adrenal (mean)	2.00	1.19	1.59	0.76	1.83	1.47	1.85	1.05	2.08	1.22							
Thymus	55.00	31.35	48.81	34.30	39.56	11.41	36.31	4.38	32.09	10.27							
Spleen	80.00	50.00	110.00	50.00	125.00	70.00	80.00	65.00	100.00	45.00							

+ Killed at end of treatment

APPENDIX II V

TABLE 36

CYTARABINE THERAPY - PIG N° 4243 (50 and 100mg daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER
-20	18.5	26	74	0	0	0
-14	28.8	26	70	1	3	0
- 7	33.4	27	71	1	1	0
0	15.6	22	77	1	0	0
Start of Dosing						
1	13.8	23	76	1	0	0
2	13.2	34	64	1	1	0
3	11.7	34	65	1	0	0
4	12.1	17	83	0	0	0
7	23.6	22	77	0	1	0
8	18.7	24	76	0	0	0
9	18.2	21	79	0	0	0
10	13.1	34	64	1	1	0
11	15.8	37	58	2	3	0
Dose Increased						
14	16.5	25	71	0	4	0
15	14.2	34	64	2	0	0
16	14.7	33	63	3	1	0
17	13.8	19	76	3	2	0
18	21.2	8	87	5	0	0
Destroyed						

APPENDIX IV

TABLE 37

CYTARABINE THERAPY - PIG N° 318 (50 and 100mg daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	+ NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER
-20	26.8	63	37	0	0	0
-14	23.8	39	61	0	0	0
- 7	29.7	16	82	0	2	0
0	40.7	24	76	0	0	0
Start of Dosing						
1	37.7	29	71	0	0	0
2	33.4	21	79	0	0	0
3	25.9	24	76	0	0	0
4	25.9	13	87	0	0	0
7	28.7	18	82	0	0	0
8	21.2	15	85	0	0	0
9	25.7	12	88	0	0	0
10	12.6	27(26)	73	0	0	0
11	15.8	24 (20)	75	0	1	0
Dose Increased						
14	20.3	25	75	0	0	0
15	14.8	20	78	2	0	0
16	16.3	17	82	1	0	0
17	14.9	29	68	3	0	0
18	12.4	20	79	1	0	0
Destroyed						

+ numbers of immature neutrophils in parentheses
when greater than 10% of WBC count

APPENDIX IV

TABLE 38

CYTARABINE THERAPY - PIG N° 317 (50 and 100mg daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER
- 20	14.7	21	79	0	0	0
- 14	33.1	27	73	0	0	0
- 7	25.6	14	86	0	0	0
0	26.3	30	70	0	0	0
Start of Dosing						
1	22.6	34	65	1	0	0
2	28.3	24	75	1	0	0
3	24.8	24	75	1	0	0
4	28.3	16	84	0	0	0
7	27.0	12	88	0	0	0
8	23.6	15	85	0	0	0
9	24.3	6	94	0	0	0
10	26.0	8	92	0	0	0
11	25.4	15	85	0	0	0
Dose Increased						
14	29.2	18	82	0	0	0
15	20.1	3	97	0	0	0
16	19.8	7	93	0	0	0
17	13.7	1	99	0	0	0
18	14.1	5	94	1	0	0
End of Dosing						
21	14.1	15	84	1	0	0
23	16.5	41	59	0	0	0
25	24.5	38	61	0	1	0
28	22.1	34	66	0	0	0
30	29.1	41	57	0	2	0
32	22.0	31	69	0	0	0
35	21.6	23	76	1	0	0
37	21.5	36	64	0	0	0
39	30.0	18	82	0	0	0
42	18.6	12	88	0	0	0
44	22.6	20	78	1	1	0
46	23.4	22	77	1	0	0

APPENDIX IV

TABLE 39

CYTARABINE THERAPY - PIG N° 4248 (50 and 100mg daily)

WHITE BLOOD CELL COUNTS $\times 10^9$ /LITRE AND DIFFERENTIAL COUNT PERCENTAGES

DAYS FROM START OF DOSING	WBC	NEUTR %	MONONUCL %	BASO %	EOSINO %	OTHER %
- 20	22.6	25	75	0	0	0
- 14	23.7	23	77	0	0	0
- 7	35.0	9	89	1	1	0
0	21.4	25	74	0	1	0
Start of Dosing						
1	17.9	23	75	2	0	0
2	16.8	15	83	1	1	0
3	19.7	47	52	0	1	0
4	22.8	54	44	1	1	0
7	21.8	23	75	1	1	0
8	18.1	38	61	1	0	0
9	17.7	25	74	1	0	0
10	15.0	41	59	0	0	0
11	17.3	28	71	1	0	0
Dose Increased						
14	20.8	11	89	0	0	0
15	18.1	21	78	1	0	0
16	16.6	25	75	0	0	0
17	17.9	12	84	4	0	0
18	22.6	24	76	0	0	0
End of Dosing						
21	28.4	25	75	0	0	0
23	33.3	32/28	62	0	0	0
25	23.4	46	54	0	0	0
28	32.9	54	44	1	1	0
30	26.0	24	74	1	1	0
32	22.5	36	63	1	0	0
35	26.2	24	74	1	1	0
37	27.1	34	65	0	1	0
39	29.9	26	73	0	1	0
42	26.9	21	78	1	0	0
44	28.0	23	75	1	1	0
46	28.7	17	83	0	0	0

APPENDIX IV

TABLE 40

CYTARABINE THERAPY - PIG N° 318 - 50 and 100mg DAILY

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 20	4.16	0.28	8.9	67.3	31.8	21.4	3.61	171
- 14	4.73	0.28	10.8	59.2	38.6	22.8	6.05	226
- 7	3.96	0.28	9.6	70.0	34.3	24.2	4.33	109
0	3.50	0.23	7.7	65.7	33.5	22.0	8.00	139
Start of Dosing								
1	3.49	0.21	7.1	60.2	33.8	20.3	-	119
2	3.25	0.21	6.9	64.6	32.9	21.2	-	148
3	3.22	0.195	6.1	60.6	31.3	18.9	-	110
4	3.21	0.19	6.7	59.2	35.3	20.9	6.10	214
7	3.16	0.205	6.9	64.9	33.7	21.8	5.12	84
8	2.79	0.185	5.8	66.3	31.4	20.8	-	92
9	2.90	0.19	6.7	65.5	35.3	23.1	-	149
10	2.39	0.15	5.2	62.8	34.7	21.8	-	226
11	2.93	0.185	6.4	63.1	34.6	21.8	7.57	130
Dose Increased								
14	3.17	0.20	6.9	63.1	34.5	21.8	8.44	170
15	2.81	0.185	6.4	65.8	34.6	22.8	-	162
16	2.84	0.18	6.5	63.4	36.1	22.9	-	206
17	2.78	0.18	6.0	64.7	33.3	21.6	-	159
18	2.62	0.17	5.6	64.9	32.9	21.4	5.18	279
Destroyed								

APPENDIX IV

TABLE 41

CYTARABINE THERAPY - PIG N° 4243 - 50 and 100mg daily

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 20	4.89	0.28	9.2	57.3	32.9	18.8	3.61	+
- 14	5.71	0.31	11.0	54.3	35.5	19.3	7.78	82
- 7	5.64	0.285	10.1	50.5	35.4	17.9	6.83	+
0	3.90	0.21	7.4	53.8	35.2	19.0	7.53	+
Start of Dosing								
1	3.58	0.18	6.5	50.3	36.1	18.2	-	+
2	3.19	0.17	6.1	53.3	35.9	19.1	-	79
3	3.38	0.24	6.6	71.0	27.5	19.5	-	+
4	3.18	0.185	6.3	58.2	34.1	19.8	4.96	119
7	4.30	0.27	9.1	62.8	33.7	21.2	7.04	70+
8	4.70	0.26	9.5	55.3	36.5	20.2	-	89+
9	4.27	0.23	9.5	53.9	41.3	22.2	-	182
10	4.56	0.22	9.4	48.2	42.7	20.6	-	+
11	4.43	0.26	8.7	58.7	33.5	19.6	5.19	94+
Dose Increased								
14	5.36	0.275	10.7	51.3	38.9	20.0	7.11	63+
15	5.34	0.32	10.7	59.9	33.4	20.0	-	258
16	4.95	0.30	10.3	60.6	34.3	20.8	-	130
17	5.47	0.32	11.0	58.5	34.4	20.1	-	93+
18	5.02	0.32	10.2	63.7	31.9	20.3	5.18	127
Destroyed								

+ Clumped Thromb.

APPENDIX IV

TABLE 42

CYTARABINE THERAPY - FIG N° 317 - 50 AND 100 mg DAILY

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 20	5.57	0.29	9.7	52.1	33.4	17.4	3.87	141
- 14	6.05	0.305	10.6	50.4	34.8	17.5	6.49	171
- 7	5.96	0.28	9.6	47.0	34.3	16.1	5.33	119
0	5.48	0.27	9.5	49.3	35.2	17.3	8.00	150
Start of Dosing								
1	4.91	0.245	8.3	49.9	33.9	16.9	-	97
2	5.28	0.25	8.9	47.3	35.6	16.9	-	124
3	4.89	0.25	7.8	51.1	31.2	16.0	-	118
4	4.80	0.24	8.2	50.0	34.2	17.1	5.28	94
7	4.55	0.24	8.2	52.7	34.2	18.0	4.64	155
8	4.50	0.245	7.9	54.4	32.2	17.6	-	81
9	4.27	0.23	7.8	53.9	33.9	18.3	-	128
10	4.56	0.245	8.3	53.7	33.9	18.2	-	146
11	4.44	0.22	8.1	49.6	36.8	18.2	3.89	120
Dose Increased								
14	4.60	0.23	8.1	50.0	35.2	17.6	6.22	136
15	4.24	0.235	7.8	55.4	33.2	18.4	-	205
16	4.35	0.23	8.0	52.9	34.8	18.4	-	193
17	3.01	0.15	5.3	49.8	35.3	17.6	-	60
18	3.96	0.22	7.2	55.6	32.3	17.9	11.29	126
End of Dosing								
21	3.88	0.215	7.1	55.4	33.0	18.3	7.76	124
23	4.37	0.23	7.8	52.6	33.9	17.8	-	138
25	4.60	0.26	8.2	56.5	31.5	17.8	4.94	162
28	4.97	0.26	8.7	52.3	33.5	17.5	5.65	163
30	4.82	0.26	8.6	53.9	33.1	17.8	-	140
32	4.54	0.25	8.0	55.1	32.0	17.6	6.12	116
35	4.67	0.235	7.8	50.3	33.2	16.7	6.97	90
37	4.07	0.225	7.1	55.3	31.6	17.4	-	65
39	4.05	0.21	7.2	51.9	34.3	17.8	7.48	128
42	3.61	0.20	6.7	55.4	33.5	18.6	6.86	121
44	3.37	0.19	6.1	56.4	32.1	18.1	-	98
46	3.71	0.20	6.6	53.9	33.0	17.8	5.33	78

APPENDIX IV

TABLE 43

CYTARABINE THERAPY - PIG N° 4248 - 50 and 100mg DAILY

DAYS FROM START OF DOSING	RBC	PCV	Hb	MCV	MCHC	MCH	BLOOD UREA	THROMB
- 20	5.09	0.27	9.3	53.0	34.4	18.3	4.65	188
- 14	4.51	0.24	8.2	53.2	34.2	18.2	5.41	158
- 7	5.27	0.275	9.1	52.2	33.1	17.3	9.67	112
0	4.93	0.255	8.8	51.7	34.5	17.9	7.06	149
Start of Dosing								
1	5.20	0.26	8.3	50.0	31.9	16.0	-	200
2	5.26	0.285	9.6	54.2	33.3	18.1	-	326
3	5.50	0.275	9.5	50.0	34.5	17.3	-	172
4	5.51	0.295	10.0	53.5	33.9	18.1	5.28	252
7	5.28	0.29	10.0	54.9	34.5	18.9	5.76	152
8	5.15	0.26	9.4	50.5	36.2	18.3	-	171
9	5.17	0.25	9.6	48.4	38.4	18.6	-	161
10	4.39	0.27	8.9	61.5	33.0	20.3	-	123
11	4.64	0.255	8.8	55.0	34.5	19.0	3.89	125
Dose Increased								
14	5.37	0.27	9.8	50.3	36.3	18.3	7.33	179
15	4.78	0.275	9.3	57.5	33.8	19.5	-	167
16	4.80	0.29	9.2	60.4	31.7	19.2	-	231
17	4.93	0.31	9.2	62.9	29.7	18.7	-	134
18	4.68	0.30	9.0	64.1	30.0	19.2	9.88	127
End of Dosing								
21	5.14	0.28	9.8	54.5	35.0	19.1	6.12	187
23	5.59	0.32	10.5	57.2	32.8	18.8	-	162
25	6.11	0.38	13.0	62.2	34.2	21.3	10.35	270
28	5.44	0.315	10.2	57.9	32.4	18.8	3.53	283
30	5.24	0.29	9.7	55.3	33.4	18.5	-	260
32	5.83	0.29	10.0	49.7	34.5	17.2	7.06	300
35	5.95	0.30	10.5	50.4	35.0	17.6	7.79	192
37	5.31	0.29	9.3	54.6	32.1	17.5	-	160
39	5.87	0.30	9.7	51.1	32.3	16.5	6.65	191
42	5.50	0.295	9.8	53.6	33.2	17.8	6.86	211
44	5.42	0.275	9.4	50.7	34.2	17.3	-	204
46	4.96	0.26	8.8	52.4	33.8	17.7	6.67	151

APPENDIX IV

TABLE 44

CYTARABINE THERAPY

SERUM ALKALINE PHOSPHATASE(SAP) SERUM GLUTAMIC OXALOACETATE TRANSAMINASE (SGOT) iu/l

DAYS FROM START OF DOSING	SAP				SGOT			
	4243	4248	317	318	4243	4248	317	318
- 20	26.0	13.0	43.0	23.0	6.7	7.7	7.2	8.7
- 14	47.0	34.0	63.0	61.0	18.5	20.1	14.4	20.1
- 7	51.2	40.6	56.0	97.0	32.9	27.0	18.5	17.5
0	22.0	18.0	34.0	44.0	64.0	28.0	25.0	43.0
Start of Dosing								
4	32.0	27.6	43.0	34.0	21.6	27.2	16.4	12.3
7	16.0	25.0	27.0	26.0	38.0	18.0	15.0	20.0
11	33.0	45.0	28.0	29.0	15.4	20.1	12.3	20.0
Dose Increased								
14	43.0	70.0	33.0	19.0	5.2	26.8	4.1	6.2
18	53.0	56.0	26.0	52.0	17.5	25.7	16.5	13.4
End of Dosing								
21	Dead	26.0	23.0	Dead	Dead	11.3	16.5	Dead
25		23.0	16.0			19.6	12.9	
28		12.0	22.0			12.9	9.3	
32		35.0	No sample			26.2	No sample	
35		37.0	33.0			19.0	11.8	
39		44.0	32.0			20.6	9.8	
42		44.0	22.0			30.9	13.4	

APPENDIX IV
TABLE 45

CYTARABINE THERAPY
SERUM PROTEINS (g/l)

DAYS FROM START OF DOSING	TOTAL PROTEIN				ALBUMIN			
	4243	4248	317	318	4243	4248	317	318
- 20	64.3	79.2	68.7	58.7	21.4	17.5	17.0	18.4
- 14	70.1	67.6	72.0	65.0	29.4	19.0	22.1	23.0
- 7	66.7	74.2	73.9	57.7	20.4	17.5	23.6	19.8
0	77.8	72.1	79.4	60.2	28.2	20.0	24.6	20.8
Start of Dosing								
4	77.0	64.4	57.6	71.0	19.5	21.5	16.7	19.7
7	67.9	80.7	69.5	64.0	24.0	19.0	21.0	19.0
11	61.4	68.7	63.5	53.0	27.7	20.7	16.3	18.2
Dose Increased								
14	65.1	55.2	68.7	49.5	30.6	18.4	18.5	17.1
18	76.3	70.6	71.0	72.4	25.7	15.8	18.6	14.1
End of Dosing								
21	Dead	71.3	68.7	Dead	Dead	20.8	22.1	Dead
25		79.6	58.0			23.9	23.2	
28		65.2	71.8			21.4	24.6	
32		69.1	No sample			23.3	No sample	
35		72.6	68.2			23.3	18.3	
39		65.1	65.6			25.8	23.8	
42		67.6	55.6			28.4	16.8	

TABLE 46

CYTARABINE THERAPY
SERUM PROTEINS CONTINUED (g/l)

DAYS FROM START OF DOSING	GLOBULINS (BY DIFFERENCE)				A/G RATIO			
	4243	4248	317	318	4243	4248	317	318
- 20	42.9	61.7	51.7	40.3	0.50	0.28	0.33	0.46
- 14	40.7	48.6	49.9	42.0	0.72	0.39	0.44	0.55
- 7	46.3	56.7	50.3	37.9	0.44	0.31	0.47	0.52
0	49.6	52.1	54.8	39.4	0.57	0.38	0.45	0.53
Start of Dosing								
4	57.5	39.9	40.9	51.3	0.34	0.54	0.41	0.38
7	43.9	61.7	48.5	45.0	0.55	0.31	0.43	0.42
11	33.7	48.0	47.2	34.8	0.82	0.43	0.35	0.52
Dose Increased								
14	34.5	36.8	50.2	32.4	0.89	0.50	0.37	0.53
18	50.6	54.8	52.4	58.3	0.51	0.29	0.35	0.24
End of Dosing								
21	Dead	50.5	46.6	Dead	Dead	0.41	0.47	Dead
25		55.7	34.8			0.43	0.67	
28		43.8	47.2			0.49	0.52	
32		46.8	No sample			0.48	No sample	
35		49.3	49.9			0.47	0.37	
39		39.3	41.8			0.66	0.57	
42		39.2	38.8			0.72	0.43	

APPENDIX IV

TABLE 47

CYTARABINE THERAPY - ORGAN AND LYMPH NODE WEIGHTS IN GRAMS
OF PIGS KILLED AT THE END OF TREATMENT

PIG NUMBER	4243	318
Submandibular LN	23.42	16.60
Parotid LN	10.56	5.21
Retropharyngeal LN	4.52	2.50
Cervical LN	14.76	8.70
Prescapular LN	5.61	1.48
Left Bronchial LN	29.77	8.35
Mid Bronchial LN	6.63	2.36
Apical Bronchial LN	8.70	1.20
Right Bronchial LN	8.09	2.40
Internal Iliac LN	1.51	1.86
External Iliac LN	9.39	5.34
Inguinal LN	14.93	11.12
Mesenteric and Colonic LN	720.00	1070.00
Gastric and Splenic LN	569.44	462.49
Precural LN	7.41	3.34
Popliteal LN	0.78	0.94
Liver	1850.00	1740.00
Kidney (Mean of 2)	140.00	120.00
Adrenal (Mean)	2.90	2.27
Thymus	5.78	4.10
Spleen	1000.00	765.00

APPENDIX IV
TABLE 50

CLINICAL RECORDS - PIG No 4248 - 50 and 100mg CYTARABINE DAILY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec. (mm)	OTHER
- 1	46	92.5	40.9 39.6 38.9	+	-	70 x 40	77 x 43	45 x 22	46 x 22	Listless, harsh dry lung sounds, 1/m penicillin, improved
0	44.5	97	39.9	++	+	68 x 40	72 x 34	39 x 18	43 x 20	Lung sounds still abnormal
Start of Dosing										
1	45.5	96	39.6	++	++	69 x 33	69 x 31	37 x 17	34 x 16	
2	47	95	39.3	++	+	61 x 35	62 x 37	44 x 19	41 x 18	
3	50.5	92	39.6	+++	+++	58 x 30	58 x 29	33 x 15	36 x 16	
End of Dosing										
4	44.5	88	39.6 39.3	+	-	67 x 28	65 x 25	35 x 16	35 x 15	Listless 1/m ampicillin Diarrhoea Oral neomycin for 5 day Improved
5	44	90	39.0 38.8	++	++	66 x 32	64 x 31	38 x 17	36 x 16	
6	48	88	39.6	++	+++	67 x 36	56 x 32	39 x 17	38 x 18	Weak, crossing legs when standing
7	52.5	99.5	40.2	++	++	73 x 38	73 x 40	45 x 20	42 x 21	

APPENDIX IV
TABLE 51

CLINICAL RECORDS - PIG No 317 - 50 and 100 mg CYTARABINE DAILY

WEEK	BODY WT (kg)	ABDOMEN (cm)	RECTAL TEMP °C	FITNESS	APPETITE	R. Ing.	L. Ing.	R. Prec.	L. Prec. (mm)	OTHER
- 1	32.5	85.5	39.6	++	+++	57 x 34	64 x 35	40 x 18	39 x 17	
0	38.5	87.5	40.0	++	++	58 x 35	59 x 34	39 x 17	44 x 18	
Start of Dosing										
1	41	88	40.6	++	++	54 x 30	64 x 35	43 x 19	39 x 18	Diarrhoea - oral neomycin for 5 days Improved
2	41.5	90.5	40.0	++	++	59 x 30	63 x 33	43 x 19	38 x 18	
3	41.5	89.5	40.0	++	++	55 x 34	58 x 33	30 x 15	34 x 16	
End of Dosing										
4	33.5	Surgery 81	39.7	+	-	46 x 26	50 x 30	32 x 16	34 x 16	Diarrhoea - 1/m ampicillin for 3 days
			39.6	++	+					
			39.3	++	++					
5	37	81.5	39.6	+++	+++	58 x 34	62 x 32	40 x 18	38 x 17	
6	41	93	39.6	++	+	60 x 35	64 x 33	38 x 18	37 x 16	Rather weak, faeces soft 1/m ampicillin for 3 days
			40.8	++	-					
7	41.5	90.5	39.3	++	+	59 x 31	66 x 34	39 x 18	35 x 19	

APPENDIX V.

The Effects of Prednisolone on Normal Pigs*

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Abstract—Prednisolone at doses of 0, 2, 4 and 6 mg/kg was given daily 5 days/week for 5½ weeks to 4 pairs of normal Large White sibling pigs. One of each pair was then killed. Treatment caused a dose-related reduction in the size of the thymus with “overshoot” on recovery. A similar but less spectacular reduction, without “overshoot”, on recovery, occurred in the lymph nodes and blood lymphocyte counts. There was also a reduction in serum total globulin levels and a complementary increase in serum albumin during treatment. Treated pigs showed a reduced contact sensitivity to DNFB during the last week of treatment. No changes attributable to treatment were observed in blood neutrophil and platelet counts nor in the red cell pictures.

It is concluded that the pig falls in the “corticosteroid-resistant” group of species which includes man.

INTRODUCTION

THE EXISTENCE of a hereditary form of lymphoma in Large White Pigs was first reported by McTaggart *et al.* [1]. The clinical, haematological and pathological features of 53 cases were described by Head *et al.* [2]. The condition has been shown to be transmitted in association with an autosomal recessive gene. Diagnosis may be made as early as 4 weeks of age but more commonly at 2-3 months. Clinical features include marked stunting of growth, lymphadenopathy, muscle wasting and the development of a pot belly. No affected pig has yet reached functional sexual maturity (normally reached at about 6 months) despite the fact they may live to the age of 15 months. As the disease is now known to be predictable in its course, it seemed appropriate to use the herd for evaluation of new cytotoxic drugs. The tumour has marked similarities to poorly differentiated lymphocytic lymphoma in man and may prove a more predictable system than established small laboratory animal lymphomas. The suitability of the pig as a model was examined by testing with a selection of drugs already in common use.

Prednisolone was chosen as the first drug for assessment as it is known in several experimental models to be a useful cytolytic agent for lymphocytes [3]. It induces a limited temporary remission in acute lymphatic leukaemia in children, although it has a much enhanced effect when combined with vincristine. It also has beneficial effects in B lymphocyte tumours such as some of the non-Hodgkin lymphomas, myeloma and macroglobulinaemia [4].

This paper will describe the methods used in toxicity testing with particular reference to the monitoring of the effects of different levels of prednisolone on non-lymphomatous Large White pigs. The effects of prednisolone on pig lymphoma cases and of other steroids and cytotoxic drugs will be reported later.

MATERIAL AND METHODS

Animals

A litter of 8 normal Large White pigs (5 females, 3 castrated males) was used. These animals were of the lymphoma strain but were of non-carrier parentage. They were weaned at 8 weeks and housed in the same pen. Monitoring was commenced 2 weeks later. Animals were fed on “Breeder’s Cubes” (SAI Ltd.) with water *ad libitum*. At weekly intervals from 3 weeks before treatment commenced the animals were weighed and blood samples were taken from the anterior vena cava [5]. An EDTA sample was taken for

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routine haematology and a clotted sample for calcium, magnesium, inorganic phosphate, sodium, potassium, chloride, total protein and protein fraction estimations. Animals were also sensitised with dinitro-fluorobenzene (DNFB) so that recall to this antigen could be tested at later periods throughout treatment. Four groups of 2 pigs selected by lot were treated with 2, 4 or 6 mg/kg of prednisolone sodium phosphate solution (Codelsol, MSD, 16 mg/ml) or with normal saline corresponding to the volume of the 4 mg/kg injection. The dose was given i/m daily for 5 days each week. Clinical observations were undertaken each day. After 5½ weeks of treatment a bone marrow core biopsy was taken from the crest of the ileum, using an 11 gauge Jamshidi needle (Kormed Inc.). One pig from each pair was then killed by intravenous pentobarbitone overdose and an immediate autopsy carried out. Treatment of the remaining animals continued during the week, being reduced to half, quarter and one-eighth during the last 3 days before being finally discontinued. Five weeks later, when it was considered that the visible effects of the drug had disappeared, a bone marrow core biopsy was taken and the animals were slaughtered.

Haematology

Red and white cells were counted using an electronic counter (Coulter Electronics Ltd., Model ZF). Platelets were counted using a white cell pipette, an Improved Neubauer haemocytometer and Baar's diluting fluid without brilliant cresyl blue. White cell differential counts were based on 200 cells counted in Leishman-stained smears. Haemoglobin was estimated by the cyanmethaemoglobin method using a Coulter haemoglobinometer, and packed cell volume (PCV) using a Gelman Hawksley microhaematocrit centrifuge. Mean cell volume (MCV), mean cell haemoglobin concentration (MCHC) and mean cell haemoglobin (MCH) were obtained by calculation.

Biochemistry

Serum sodium and potassium were measured by flame emission and calcium and magnesium by atomic absorption spectrophotometry (Shandon Southern, Model A3400). Serum chloride was measured in an EEL chloride meter (Evans Electro Selenium Ltd.) and inorganic phosphate by the method of Fiske and Subbarow [6]. Total protein was estimated by the biuret method of Henry *et al.* [7] and albumin by the bromocresol green dye-binding method described by Dumas *et al.*

[8]. On selected occasions a more detailed analysis of protein fractions was carried out by electrophoresis on Millipore cellulose acetate strip (Phoroslide) at 100 V for 20 min. Proteins were stained with Ponceau S, decolourized with 5% acetic acid, dehydrated in ethyl alcohol for 5 min, cleared in acetic acid-ethyl acetate for 1 min and dried in a warm oven. Protein fraction readings and a permanent trace were obtained for each sample using a Millipore Phoroscope densitometer.

Cell-mediated response

Delayed hypersensitivity reactions were measured by contact sensitivity to DNFB in equal volumes of acetone and dimethylsulphoxide (DMSO) [9]. An area of skin between the shoulder blades or the iliac crests was prepared by removing the hair with scissors and cleaning with spirit. On each occasion 5 µl DNFB solution was applied with an automatic micropipette and spread within an area of 14 mm in diameter with the flattened end of a glass rod. Pigs were sensitized with 10% DNFB. A preliminary test 20 days later with 1% DNFB indicated that this concentration was too weak (Table 1). Subsequent tests were carried out during and after the course of prednisolone treatment, using 5 or 10% DNFB, readings being made at 24 hr and, sometimes, at 48 hr. An interval of at least 7 days was allowed to elapse between tests.

Pathology

The autopsy examination was started immediately after an animal had been killed so that the tissues selected for fixation were placed in buffered neutral formol saline within a few minutes and never more than 20 min after death. These tissues were processed to paraffin wax, sectioned at 6 µm and stained with haematoxylin and eosin. Certain sections were also stained with Gordon and Sweet's stain for reticulin fibres, Martius scarlet blue, periodic acid-Schiff reaction, Perls' prussian blue method for haemosiderin and Leishman's stain.

In the course of the autopsy the lymph nodes throughout the body, thymus, spleen, kidney, liver and adrenal glands were dissected out and weighed. In the case of bilateral organs, mean values were obtained for kidneys and adrenals but only one of a pair of lymph nodes, always from the same side, was weighed. The absolute weights were then expressed as relative weights in centigrams per kilogram of body weight. The relative

Table 1. Effect of prednisolone on skin reactions of individual pigs to dinitrofluorobenzene (DNFB)

Days from primary sensitization	0	20	27	35	42	43	67	68	81	82
% DNFB applied	10	1	10	10	5		5		10	
Prednisolone dose—Control	0	0	2	4	4	4	—	—	—	—
	4	0	3	3	3	3	0	0	3	4
2 mg	3	0	3	3	0	0	—	—	—	—
	3	0	2	3	1	3	2	1	3	4
4 mg	0	0	1	3	1	1	—	—	—	—
	4	0	3	3	3	2	0	0	4	4
6 mg	1	0	2	2	0	0	—	—	—	—
	3	0	3	3	0	1	1	0	3	4

0, negative; 1, slight erythema; 2, erythema and swelling; 3, small ulcerations; 4, large ulcerations. Treatment with prednisolone commenced on the 11th day and ceased or was tailed off from the 44th day after sensitization.

weights of the "bronchial", "head" and "iliac" groups of nodes represent the totals for the various nodes in each of these regions.

The biopsy core samples of bone marrow were initially fixed in buffered neutral formol saline and then post-fixed in Bouin's fluid for 48 hr and decalcified in EDTA. In addition, the bone marrow of the body of the first lumbar vertebra and the wing of the ileum including the crest were taken as 5 mm slices cut with a saw and decalcified in formic formol before processing to paraffin wax. These latter samples were used to assess the value of the biopsy method.

To facilitate comparison between samples during the histological examination groups of sections were ranked in degree of change using a split-field comparator microscope. Where a structure could be drawn in outline (e.g. liver lobule, hepatic cell, white pulp pattern of spleen or thymic lobule), a microscope fitted with a Wild drawing tube was employed to demonstrate the degree of change present.

RESULTS

Clinical observations

Throughout the experiment, all pigs were bright and active. Prednisolone did not appear to depress interest in food but as individual intakes could not be measured the effect on appetite could not be assessed. Rectal temperatures fluctuated from day to day within the normal range for pigs of this age. All pigs on prednisolone, irrespective of dose, were noted to have marked polydipsia and polyuria. At the higher dose levels, they became pot-bellied. After 3 weeks of treatment, the 2 pigs receiving 4 mg/kg doses showed rectal

eversion but this corrected itself spontaneously. The mean weight gain during the 5 weeks of treatment (Table 2) was lower in the 6 mg dose group (5.5 kg) than in any other group (controls, 8.5 kg; 2 mg dose, 7.5 kg; 4 mg dose, 9.0 kg). Similarly, during the post-treatment period, weight gain was lowest in the 6 mg dosed pig (14.5 kg as against 18.5, 18.0 and 19.0 kg respectively), despite the fact that its commencing weight was average for the litter.

Haematology

There was a steady decline in mean absolute lymphocyte counts in all groups during the treatment period. This decline was dose-related, being least in the controls and greatest in the 6 mg dosed group (Table 3, $r=0.75$, $df=6$, $P<0.05$, >0.02 ; $y=1835+564x$). The percentage drops in lymphocyte counts in the 4 groups were 5.8, 23.8, 31.5 and 42.6 respectively. During the posttreatment period the absolute lymphocyte counts remained more or less static.

Eosinophil counts showed a mean decrease in the control group during the treatment period whereas the treated groups all showed increases (Table 3).

Neutrophil counts showed a mean decrease in all groups during the treatment period (Table 3) but, as in the case of platelet counts and red cell pictures, there were no differences between groups which could be attributed to the treatments.

Biochemistry

Observations based on electrophoresis indicated that serum albumin levels increased in all groups during the treatment period (Table 4). This increase was exaggerated in

Table 2. Effect of prednisolone on body weight (kg) and on relative weights of organs (cg/kg body weight) of individual pigs

Prednisolone dose	Pigs killed at end of treatment				Pigs killed at end of experiment			
	Control	2 mg	4 mg	6 mg	Control	2 mg	4 mg	6 mg
Body weight:								
Before treatment	15	19.5	21	19	20.5	14.5	23	19
At end of treatment	22	27	29	23.5	30.5	22	33	25.5
At end of experiment	—	—	—	—	49	40	52	40
Lymph nodes:								
Mesenteric and colonic	523	341	324	374	408	325	250	275
Gastric and splenic	33	28	25	24	31	34	32	32
Bronchial group	11	13	9	8	10	8	7	11
Total splanchnic	567	382	358	406	449	367	289	318
Head group	30	27	30	24	24	28	21	21
Iliac group	8	10	6	7	8	10	8	6
Prescapular	3	2	7	4	3	5	3	5
Precrural	4	3	3	2	2	3	2	3
Inguinal	15	12	13	9	12	10	10	10
Popliteal	2	2	1	0.4	N.F.	1	1	1
Total superficial	62	56	60	46	49	57	45	46
Thymus	91	69	38	26	133	203	185	210
Spleen	227	185	121	212	122	125	87	138
Liver	3500	3741	3862	3234	3306	3325	2731	3075
Kidney	250	259	241	200	167	175	183	188
Adrenal	5	7	6	6	4	6	4	6

In the case of bilateral organs only one side was weighed except adrenal and kidney which are mean values. N.F. = not found.

Table 3. Effect of prednisolone on mean absolute white cell counts ($\times 10^9/l \pm S.D.$) of pairs of pigs, A: before treatment; B: at end of treatment; Diff: rise or fall during treatment; % percentage change

Prednisolone dose	Lymphocytes	Neutrophils	Eosinophils	
Control	A	12.0 \pm 0.8	16.2 \pm 9.8	0.3 \pm 0.1
	B	10.3 \pm 0.1	11.5 \pm 6.2	0.2 \pm 0.3
	Diff	-0.7 \pm 0.8	-4.7 \pm 3.7	-0.1 \pm 0.4
	%	-5.8	-29.0	-33.3
2 mg	A	12.2 \pm 0.1	20.7 \pm 2.0	0.2 \pm 0.3
	B	9.3 \pm 0.1	8.7 \pm 2.0	0.4 \pm 0.3
	Diff	-2.9 \pm 0.1	-12.0 \pm 4.0	+0.2 \pm 0.1
	%	-23.8	-58.0	+100.0
4 mg	A	14.6 \pm 2.9	9.0 \pm 3.2	0.2 \pm 0.2
	B	10.0 \pm 1.3	5.7 \pm 1.2	0.5 \pm 0.6
	Diff	-4.6 \pm 1.6	-3.3 \pm 4.4	+0.3 \pm 0.8
	%	-31.5	-36.7	+150.0
6 mg	A	11.5 \pm 1.8	15.6 \pm 9.9	0.5 \pm 0.4
	B	6.6 \pm 0.6	8.5 \pm 4.4	0.8 \pm 0.7
	Diff	-4.9 \pm 2.5	-7.1 \pm 5.6	0.3 \pm 0.4
	%	-42.6	-45.5	+60.0

the control group because one pig had a pretreatment value of only 10.7 g/l compared with a mean of $24.1 \pm S.D. 2.2$ g/l for the other 7 pigs. If this latter figure is taken as a more acceptable pre-treatment value for the control group, then it is found that, whereas the control and 2 mg dosed groups

showed mean increases in albumin of only 1.7 g/l (+7.05%) and 1.2 g/l (+4.8%) respectively, the 4 mg and 6 mg dosed groups showed mean increases of 9.0 g/l (+36.9%) and 7.8 g/l (+36.1%) respectively.

Table 4 also indicates that whereas the control group showed increases in mean total

Table 4. Effect of prednisolone on electrophoresis-derived mean serum protein values (g/l \pm S.D.) of pairs of pigs, A: before treatment; B: at end of treatment; Diff: rise or fall during treatment; %: percentage change

Prednisolone dose	Serum albumin	Serum globulins			
		α	β	γ	Total
Control A	18.6 \pm 11.1*	12.0 \pm 4.5	6.5 \pm 0.4	5.6 \pm 1.7	24.0 \pm 2.3
B	25.5 \pm 3.7	17.5 \pm 2.8	12.3 \pm 2.6	9.2 \pm 5.4	39.0 \pm 0.1
Diff	+6.9 \pm 7.4*	+5.5 \pm 7.2	+5.8 \pm 2.1	+3.6 \pm 7.1	+15.0 \pm 2.1
%	+37.1*	+45.8	+89.2	+64.3	+62.5
2 mg A	25.1 \pm 1.8	15.9 \pm 3.0	12.6 \pm 2.9	8.8 \pm 2.3	37.3 \pm 8.1
B	26.3 \pm 4.4	16.8 \pm 2.1	12.2 \pm 1.6	10.4 \pm 1.8	39.4 \pm 2.0
Diff	+1.2 \pm 6.2	+0.9 \pm 5.0	-0.4 \pm 4.5	+1.6 \pm 0.5	+2.1 \pm 10.1
%	+4.8	+5.7	-3.2	+18.2	+5.6
4 mg A	24.4 \pm 2.0	16.6 \pm 0.7	10.5 \pm 1.1	8.4 \pm 1.0	35.5 \pm 0.8
B	33.4 \pm 0.9	13.5 \pm 1.1	10.1 \pm 3.7	8.5 \pm 0.4	32.1 \pm 3.0
Diff	+9.0 \pm 1.1	-3.1 \pm 1.8	-0.4 \pm 2.6	+0.1 \pm 1.3	-3.4 \pm 2.2
%	+36.9	-18.7	-3.8	+1.2	-9.6
6 mg A	21.6 \pm 1.0	13.8 \pm 0.7	8.4 \pm 1.1	6.4 \pm 0.3	28.5 \pm 2.1
B	29.4 \pm 2.3	13.8 \pm 0.2	9.3 \pm 0.9	7.6 \pm 1.6	30.6 \pm 0.6
Diff	+7.8 \pm 1.3	0.0 \pm 0.5	+0.9 \pm 0.3	+1.2 \pm 1.9	+2.1 \pm 2.7
%	+36.1	Nil	+10.7	+18.8	+7.4

*See Text.

globulin values and in all globulin fractions during the treatment period, the treated groups showed much smaller increases or even decreases in the corresponding values.

Since alpha-1 and alpha-2 globulins were not always distinguishable on the Phoroscope trace, it is not possible to give separate figures for these sub-fractions.

Total serum globulin values obtained by differences from chemical analysis of total proteins and albumin (but unconfirmed by the electrophoretic method because of inadequate samples) suggest that in the 4 mg and 6 mg treated groups the total globulins reached a nadir of about 20 g/l during the 4th week of treatment. A similar effect was noted in the 2 mg treated group but the nadir was not so low (*ca.* 24 g/l) and did not appear until a week later.

None of the serum inorganic elements showed any differences between groups which could be attributed to the treatments. In particular, there was no evidence of sodium retention nor of potassium or calcium depletion in the treated groups.

Cell-mediated response

It appears from Table 1 that during the last week of prednisolone treatment (42-43 days after sensitization) there is an anergy in the prednisolone-treated pigs as compared with the controls. There is a tendency for this anergy to be reversed in the 3 treated pigs

after withdrawal of the drug, i.e. 81-82 days after sensitization.

Post mortem and histological findings

The most spectacular finding was in the thymus. At the end of the treatment period there was a dose-related reduction in relative weight of the thymuses of the treated pigs (Table 2, $r = -0.99$, $df = 2$, $P = 0.01$; $y = 90 - 11.3x$). When compared with the control, the reduction amounted to 24, 58 and 72% in the 2, 4 and 6 mg dosed pigs respectively. As the thymus of this control was more involuted than would be expected in a normal pig of this age, these percentage reductions are probably underestimated. Histologically, the thymus lobule size of the treated pigs was reduced, the cortex being more involuted than the medulla, but the density of the cell population of both cortex and medulla was normal. The lymphoid involution was paralleled by a relative widening of the fat and connective tissue interlobular septa (Fig. 1).

In those pigs killed 5 weeks after treatment was discontinued, the relative thymus weights represented 156, 142 and 165% respectively of the corresponding control value. Despite this "overshoot", all were histologically normal (Fig. 2).

A less spectacular reduction in relative weights was found in the lymph nodes of

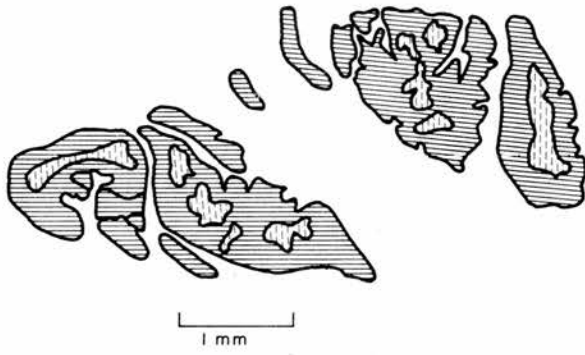


Fig. 1. Drawing of transverse section of whole thymus gland of pig receiving 6 mg/kg prednisolone and killed at end of 5 weeks' treatment.

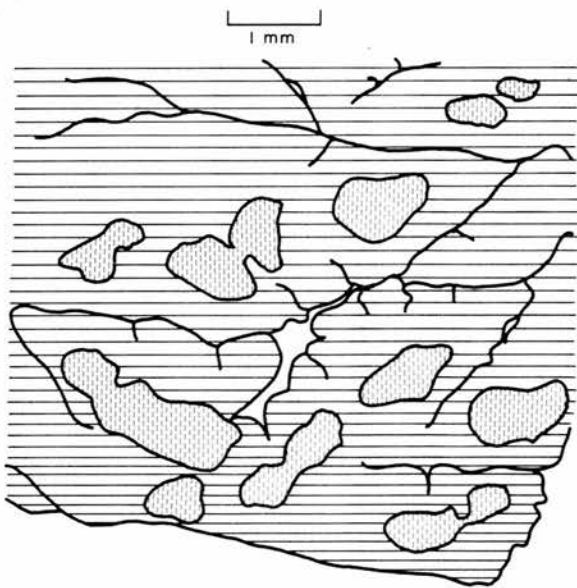


Fig. 2. Drawing of approximately half of cross section of thymus of control pig killed at end of experiment.

the treated pigs slaughtered at the end of treatment (Table 2). This was not dose-related but averaged 23% in the splanchnic nodes and 13% in the superficial nodes.

Histologically, the lymph nodes of the 6 mg dosed pig killed at the end of treatment, were distinctive in several respects. In contrast to the control and other treated pigs killed at the same time, (1) the submandibular node showed many "blast" cells with numerous mitotic figures both in the reaction centres and in some of the paracortical regions where there was a reduction in small lymphocytes (Figs. 3 and 4); (2) the prescapular node had virtually no lymphocytes in the cortex (Figs. 5 and 6); (3) the medulla of the mesenteric lymph node was reduced in size and the paracortical zone was more extensive than usual (Figs. 7 and 8); (4) the external iliac

node showed more foci of megakaryocytes and normoblasts in the medulla; (5) the Peyer's patches were the smallest in the series and the cells in the open centre were inactive (Figs. 9 and 10). This animal had similar amounts of adipose tissue to the others, its poor weight gain being attributable to poor bone and muscle development.

There was no evidence of "overshoot" in the relative lymph node weights of the pigs killed 6 weeks later; indeed, although the superficial nodes were now comparable in relative weight to the control nodes, the splanchnic nodes averaged only 72% of the relative weight of the control nodes. Histologically, the external iliac lymph nodes of all pigs killed at this time showed more extramedullary haemopoiesis than in any of those killed earlier. In addition, the ratio of cortex to medulla was reversed from 1:3 to 3:1, this being attributable to an increase in size of both the reaction centres and the paracortical zone.

There was some variation in the relative weights and in the histological appearances of the white pulp of all 8 spleens, but these were not correlated with dose of prednisolone nor timing of death; nor were the variations in the white pulp related to the weight of the organ.

Lung, liver, kidney, adrenal and stomach were normal and similar in all cases. No pig showed any evidence of ascites or osteoporosis.

The bone marrow samples showed only differences that were attributable to age and growth rate. The core biopsies were comparable to the post mortem specimens.

The only evidence of intercurrent disease was in the second control pig which had a mild inflammation of the caecum associated with spirochaetes.

DISCUSSION

The extent and rate of development of the lytic effects of prednisolone on the lymphoreticular system of the pigs, in particular the thymus, the lymph nodes and the blood lymphocytes, clearly place them in the corticosteroid-resistant group of species which includes man, ferret and guinea pig, as opposed to the corticosteroid-sensitive mouse, rat, hamster and rabbit, in which the lytic effects are much more severe and rapid at comparable dosage [3].

The reduction in size of the thymus during treatment and its recovery with "overshoot" after withdrawal of treatment is a phenomenon



Fig. 3. Submandibular lymph node of pig killed at end of treatment with 6 mg/kg prednisolone. Note large "blast" cells in the nodule and in the paracortical zone where there are fewer small lymphocytes than in Fig. 4. H & E \times 250.

Fig. 4. Submandibular lymph node of control pig. Compare with Fig. 3. H & E \times 250.

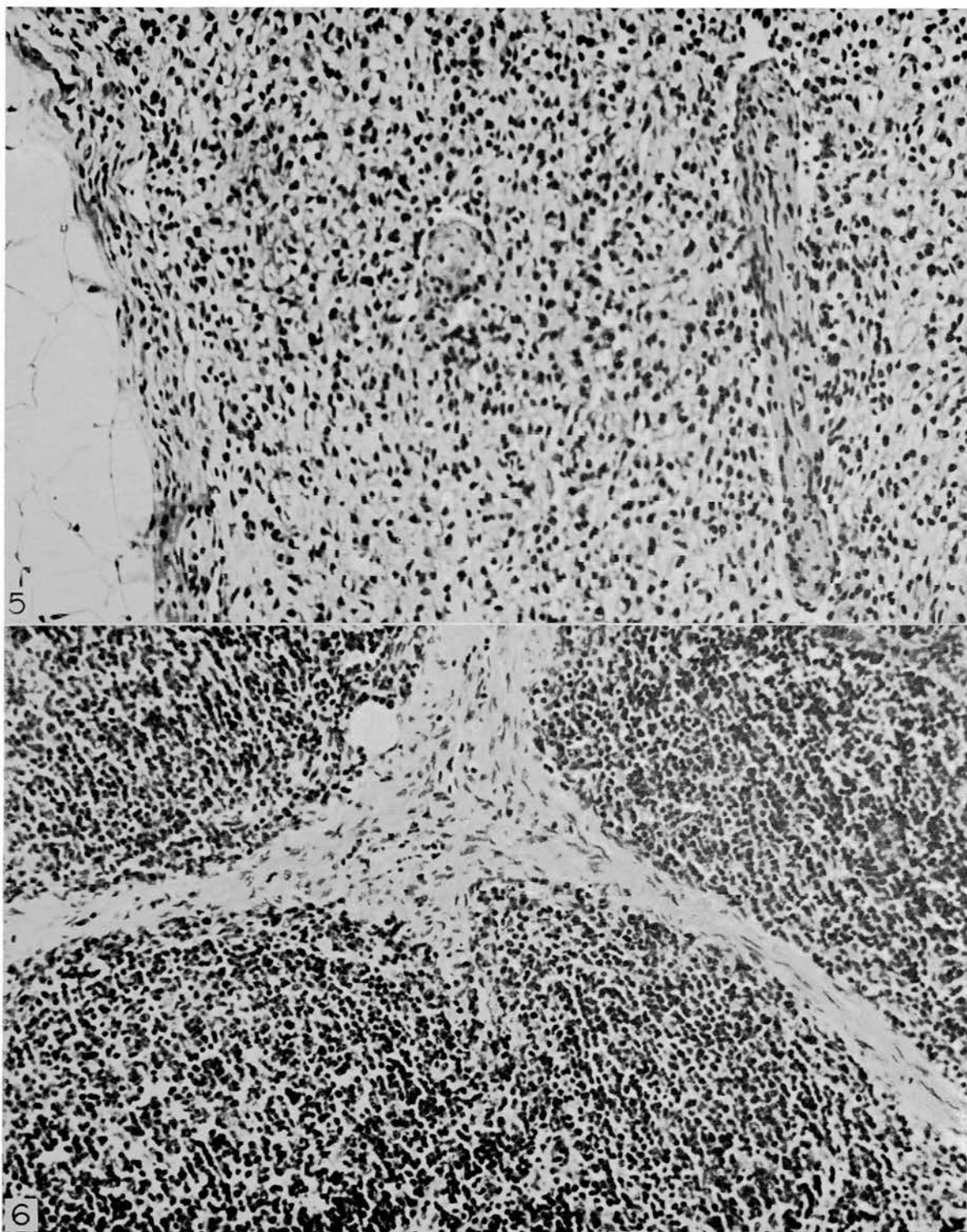


Fig. 5. Prescapular lymph node of same pig as Fig. 3. Note no lymphocytes round trabecula. There is no difference in the fixed histiocyte meshwork of cortex and medulla. H & E \times 250.

Fig. 6. Prescapular lymph node of pig killed at the end of treatment with 2 mg/kg prednisolone. Note modules and paracortical zone round trabeculae. Compare with Fig. 5. H & E \times 250.

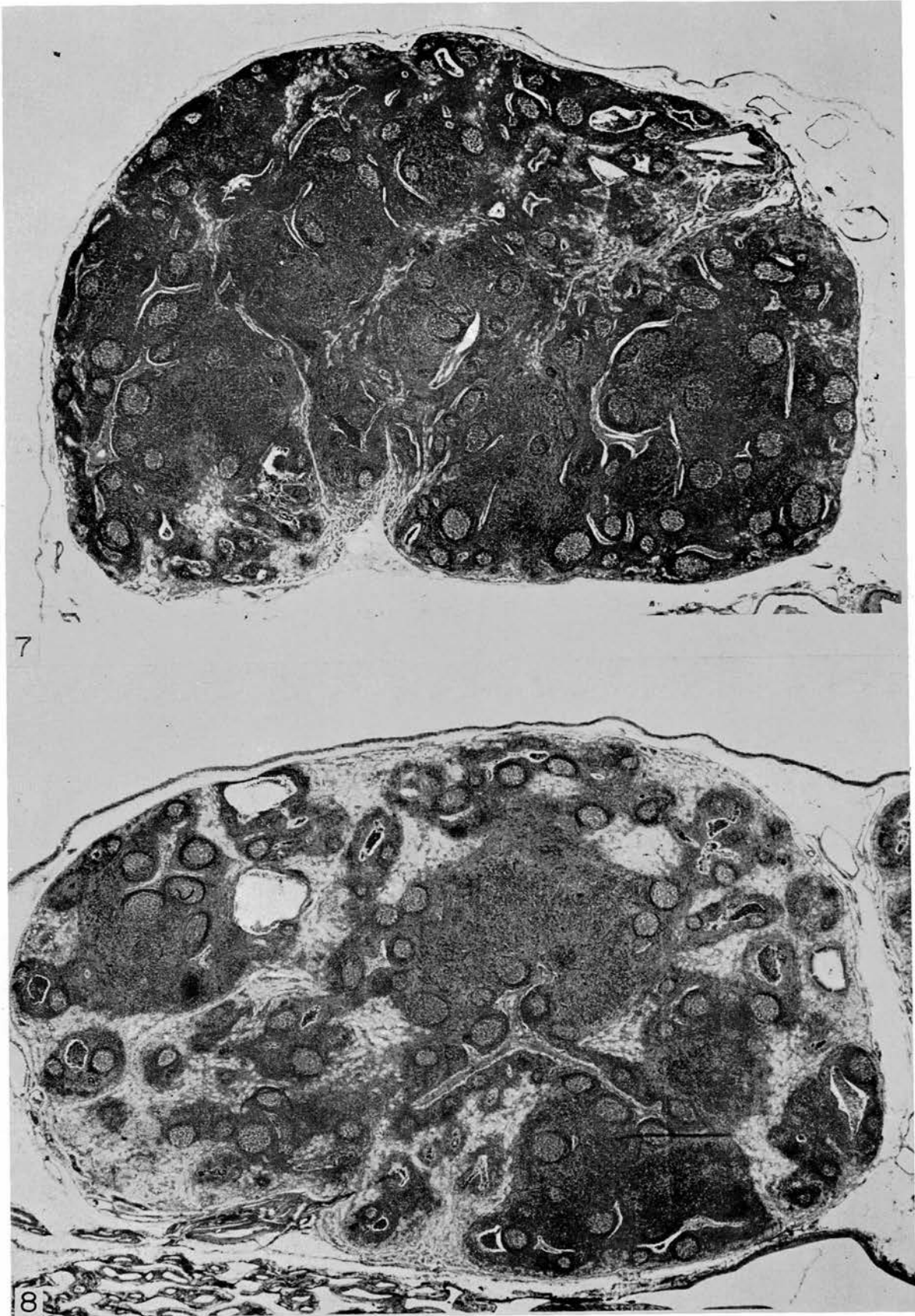


Fig. 7. Mesenteric lymph node of same pig as Figs. 3 and 5. Note small size of medulla and increased size of paracortical zone. H & E $\times 14$.

Fig. 8. Mesenteric lymph node of control pig. Compare with Fig. 7. H & E $\times 14$.

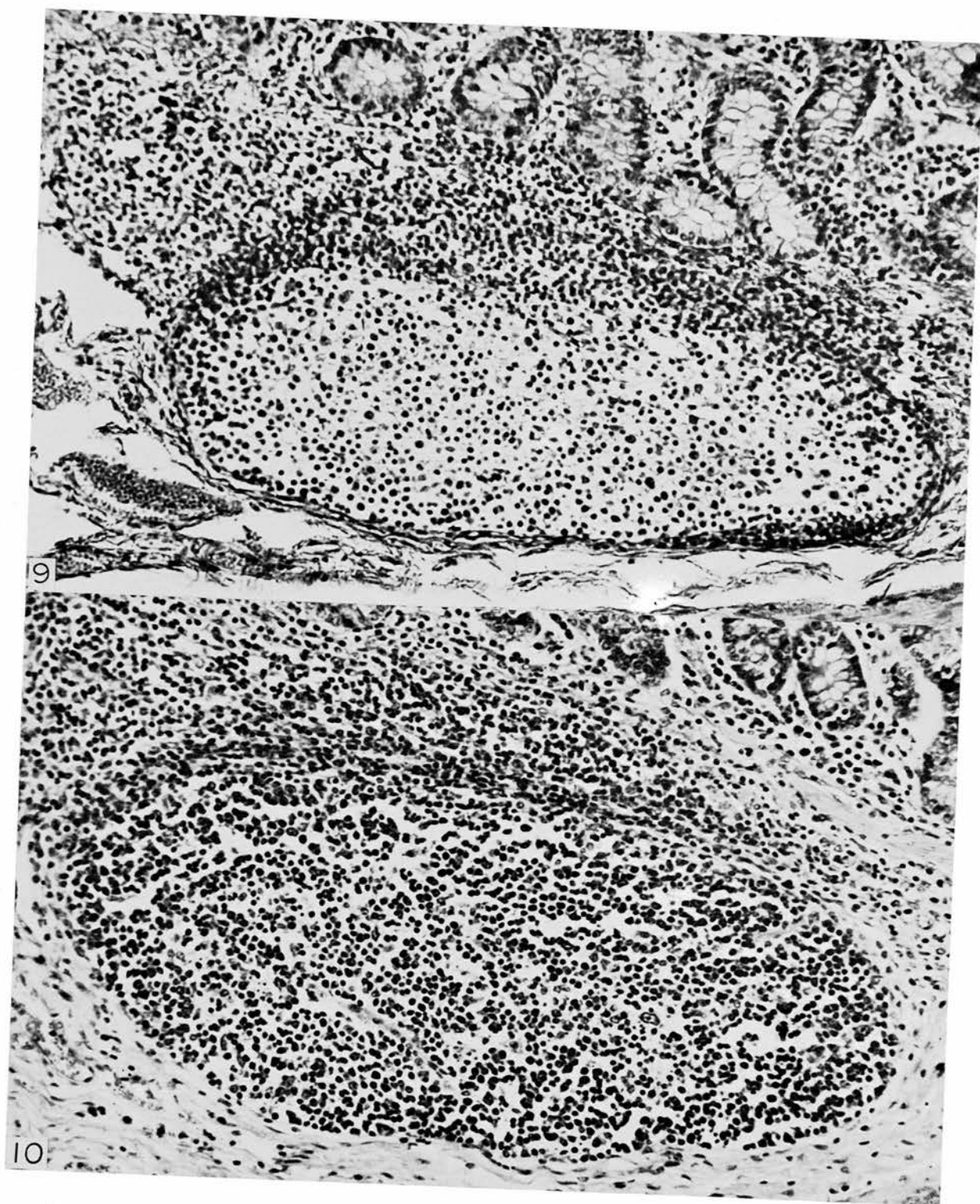


Fig. 9. Peyer's patch on the ileum of same pig as Figs. 3, 5 and 7. Note depleted "inactive" nodule. H & E $\times 250$.

Fig. 10. Peyer's patch from the ileum of control pig. Compare with Fig. 9. H & E $\times 250$.

which has been described in non-lymphomatous children treated with prednisone or triamcinolone [10]. The growth retardation observed in the 6 mg dosed pigs has also been encountered in corticosteroid-treated children [11]. The latter usually show a rapid increase in growth after treatment is discontinued but this effect was not observed in any treated pigs during the 5 weeks post-treatment period. The growth retardation observed suggested that a dose of 4 mg/kg/day might be more suitable than 6 mg/kg/day for the therapeutic study which followed.

In the absence of any evidence of ascites, the pot belly observed at the two higher levels was presumed to be attributable to muscle relaxation. This was supported by the fact that the apparent distension disappeared when an affected animal was laid on its back.

The observed depression of serum globulin and increase in serum albumin levels associated with treatment have also been observed in man but mostly in relation to corticosteroid therapy of chronic diseases. It is popularly believed that corticosteroids affect especially the γ -globulin fraction but Bernfeld *et al.* [12] demonstrated that in ACTH-treated patients the beta fraction was mainly affected.

In our own experiments, the effects of prednisolone treatment on serum proteins were more obvious in lymphoma cases than in normal pigs. For this reason these effects will be discussed more fully in a later paper.

With respect to corticosteroid suppression of cell-mediated immunity, the pigs again fell within the steroid-resistant group of species

since it has been shown that, although corticosteroids can suppress skin sensitivity reactions in that group, large doses or prolonged treatment are required. In man, for example, prednisone given orally in 40 mg/day doses had to be administered on average for 13.6 days to negate the effects of the PPD tuberculin test [13].

The immediate neutrophilia and eosinopenia which are to be expected in man receiving over 10 mg prednisone per day and which persist while treatment lasts [11] were not observed even transiently in any of the treated pigs. We have, however, observed neutrophilia in pigs treated with corticosteroids in another connection.

It is thus evident that the reactions of normal pigs to prednisolone show promising similarities to those occurring in man. Further, no laboratory animal in common use is also comparable to man both in size and in being omnivorous. Young pigs are relatively easily handled and yet are large enough to permit sizeable samples of blood and biopsy materials being taken repeatedly without ill effect. As will be emphasised in a later paper, the survival time of lymphomatous pigs is much closer to that of children than is that of small rodents. All these features point to the practicability and advantages of using the pig as a model for the testing of cytotoxic drugs.

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Prednisolone Treatment of Hereditary Pig Lymphoma

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Abstract—Two age-matched pairs of pigs with hereditary lymphoma were treated with prednisolone sodium phosphate in daily intramuscular doses of 4 mg/kg on 5 days/week for 5.5 weeks. One of each pair was then killed and autopsied, the other 5 weeks later.

Treatment resulted in marked reductions in blood mononuclear cell count, serum globulin (chiefly gamma) levels and lymph node, thymus and adrenal size. Increases in PCV (haematocrit), platelet counts and in serum albumin and magnesium levels occurred. The red cell picture continued to improve until two weeks after treatment ceased. All these changes reversed rapidly during the post-treatment period. Neutrophilia occurred only during the fifth week of treatment.

Serum Na, K, Ca, chloride and inorganic phosphate levels showed no treatment-related changes.

The skin hypersensitivity reaction to DNFB, absent before treatment, became positive during and after prednisolone treatment but was never as marked as in sensitised normal pigs.

INTRODUCTION

FOLLOWING the establishment of 4 mg/kg as a suitable dose of prednisolone for pigs [1], an experiment was set up to determine the effects of the drug on cases of hereditary lymphoma of pigs [2] and to establish whether these effects were comparable to those occurring in lymphoid neoplasia of man.

MATERIALS AND METHODS

Two pairs of pigs numbered 30, 37 and 52, 56, which were 6 and 5 months old respectively at the start of the experiment, were used. The latter pair were littermates. All were female and affected with lymphoma which had been diagnosed between 8 and 10 weeks of age.

The same monitoring methods were used as in the corresponding experiment on normal

pigs [1] except that all four pigs received the same dose of prednisolone sodium phosphate (Codelsol, M.S.D.), namely 4 mg/kg administered intramuscularly once daily 5 days/week for 5.5 weeks. In addition, a bone marrow core biopsy sample was taken from the wing of the ileum before treatment commenced as well as prior to slaughter. The expiratory girth at the level of the umbilicus and the length and breadth of the inguinal and pre-crucial lymph nodes were measured once weekly. The lymph node measurements were taken with ball-pointed calipers without compressing the node and without lifting it into a fold of skin.

Since it is not always easy to differentiate the various types of mononuclear cells in routine smears from lymphoma cases, differential counts were based on "total mononuclear cells".

All pigs were given supportive therapy throughout the experiment with a vitamin-mineral feed supplement (Nutrequin, Berk). During prednisolone treatment, they also received framycetin sulphate (Feed Additive, C. Vet.) at prophylactic dose level.

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At the end of 5.5 weeks treatment, one pig of each age pair was killed (Group I, pigs 30 and 56). Treatment of the survivors (Group II, pigs 37 and 52) was tailed off during the succeeding three days and they were killed 5 weeks later.

Pig 54, an unaffected littermate of the younger age pair, whose only abnormality was a congenital right deviation of the nasal bones and nasal septum, was killed as an untreated control two days after its Group I sibling.

Further autopsy controls were provided by the use of data from 17 untreated lymphoma cases which had died or had been killed at comparable ages to the treated pigs.

RESULTS

Clinical observations

Before the commencement of treatment, all four pigs ate fairly well, but they were less active and easier to handle than normal pigs of similar size. Weight gains were poor.

Within a few days of starting treatment, there was a marked improvement in appetite and general fitness and the pigs became much more lively. Weight gains were not improved during treatment (Table 1). All pigs showed polydipsia and polyuria but had normal faeces. Rectal temperatures varied within the normal range (37.5–39.7°C) apart from a period of febrile response (up to 40.1°C) in two pigs associated with infected abrasions and bite wounds.

During prednisolone treatment, the lymph nodes decreased in size. The length of the left inguinal node was taken as representative since both lengths and breadths of the other nodes showed similar changes. Its mean length in the 4 pigs was $66 \pm \text{S.D. } 5.7$ mm before treatment. After 4 weeks of treatment, it was 45.5 ± 4.7 mm, a decrease of 31%. During the rest of the treatment period, the glands were too soft to be accurately measured. Five weeks after treatment was withdrawn, the mean measurement in the two remaining pigs was 64.5 ± 6.7 mm, an increase of 41.8%, these measurements being compar-

Table 1. *Body weights (kg) and relative weights of organs (cg/kg body weight) of individual lymphomatous pigs treated with prednisolone compared with an untreated normal (non-lymphomatous) littermate of two of them and 17 untreated lymphoma cases of the same age-group.*

	Normal		Lymphoma cases			
	Untreated		Treated		Untreated	
	Group I		Group II		Mean (range) of 17 pigs	
	Pig No. 54	Pig No. 30	Pig No. 56	Pig no. 37	Pig No. 52	
Age at death (days)	221	237	219	272	244	231 (200 to 280)
Body weight (kg):						
Pretreatment	75.0	34.0	25.0	28.5	22.0	41 (23 to 83)
End of treatment	—	36.0	31.0	29.0	24.5	—
End of experiment	—	—	—	38.0	30.5	—
Lymph nodes:						
Mesenteric and colonic	267	764	565	5368	2836	4177 (646 to 9906)
Gastric and splenic	28	230	336	1687	1115	1960 (740 to 3210)
Bronchial group	7	25	23	77	84	217 (38 to 919)
Total splanchnic	302	1019	924	7132	4035	6261 (1662 to 12670)
Head group	25	61	62	143	237	163 (45 to 286)
Iliac group	7	13	11	38	75	36 (11 to 67)
Prescapular	2	5	4	12	15	15 (4 to 47)
Precurral	3	13	7	27	35	23 (7 to 39)
Inguinal	8	25	20	47	64	51 (18 to 156)
Popliteal	1	3	3	6	26	11 (2 to 16)
Total superficial	46	120	107	273	452	290 (93 to 476)
Thymus	100	31	21	67	42	18 (0 to 67)
Spleen	373	500	242	1250	1197	2156 (1030 to 7800)
Liver	2193	5069	4194	4711	5607	6288 (3120 to 9270)
Kidney	167	325	209	263	262	331 (180 to 443)
Adrenal	3	4	4	7	5	11 (5 to 28)

In the case of bilateral organs only one side was weighed, except kidney and adrenal which are mean values.

ble to those at the beginning of the experiment. The pot-bellied appearance associated with the disease increased during the treatment period, despite the fact that girth measurements made while the animals lay on their backs remained fairly steady in three pigs and actually decreased progressively from 880 to 800 mm in the fourth (pig 37). There was no clinical evidence of ascites; in particular, little or no fluid could be detected by paracentesis abdominis. During the post-treatment period, the two surviving pigs showed increases of 110 mm (pig 37) and 100 mm (pig 52) in girth measurement which were associated with increases in body weight (Table 1).

Haematology

The most spectacular haematological effect was on the mononuclear cells (Fig. 1) whose value dropped from an overall pretreatment mean of $20.5 \pm 5.6 \times 10^9/l$ to a nadir of $4.1 \pm 0.5 \times 10^9/l$ during the fifth week of treatment when no recognisable tumour cells were observed in the peripheral blood. By the end of treatment, the mononuclear cells had risen to $7.4 \pm 2.2 \times 10^9/l$. During the next five weeks, the mononuclear counts of the two surviving pigs rose progressively to approximately pretreatment levels.

During the pretreatment period, absolute neutrophil counts fluctuated widely in individual pigs, with an overall mean of $9.7 \pm 6.7 \times 10^9/l$ (Fig. 1). During the second

week of treatment, this dropped to $6.2 \pm 2.7 \times 10^9/l$, rising to $15.6 \pm 2.5 \times 10^9/l$ during the fifth week and falling again to $9.5 \pm 1.4 \times 10^9/l$ at the end of treatment. This fall continued in the two Group II pigs during the post-treatment period, reaching $3.6 \pm 0.4 \times 10^9/l$ 5 weeks after treatment ceased.

Two weeks before treatment started, all four pigs had low thrombocyte counts (mean $99 \pm 20 \times 10^9/l$ (Fig. 1). By the fifth week of treatment, the mean had risen to $359 \pm 19 \times 10^9/l$. During the last week, it fell to $283 \pm 56 \times 10^9/l$. Four weeks later, the 2 surviving pigs had a mean count of $206 \pm 86 \times 10^9/l$.

Eosinophil counts remained at a low level throughout the experiment in all pigs except No. 37 (Group II) in which they fluctuated considerably.

The packed cell volume (Fig. 2) tended to fall during the pretreatment period but rose rapidly from a mean of 0.26 ± 0.01 at the commencement of treatment to 0.30 ± 0.02 three weeks later, remaining at about this level until the second week after treatment ceased. During the last three weeks of the experiment there was a rapid fall to 0.24 ± 0.03 . RBC and haemoglobin showed similar changes.

The only discernible treatment-related effects on the derived red cell indices were in Group II where, during the post-treatment period, the mean cell volume rose from 51.0 ± 1.6 fl to 59.1 ± 5.1 fl and the mean cell haemoglobin concentration dropped from 35.2 ± 2.7 to 31.9 ± 1.4 g/dl.

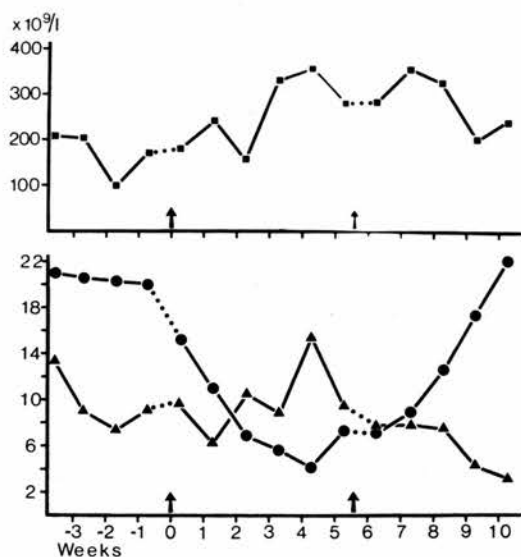


Fig. 1. Mean absolute counts of total mononuclear cells (●—●), neutrophil granulocytes (▲—▲) and platelets (■—■) of lymphomatous pigs before, during and after treatment with prednisolone. Arrows indicate beginning and end of treatment.

Serum biochemistry

The mean serum magnesium concentration, which had remained fairly steady at an overall mean of 0.84 ± 0.05 mmole/l during the pretreatment period, showed upward fluctuation

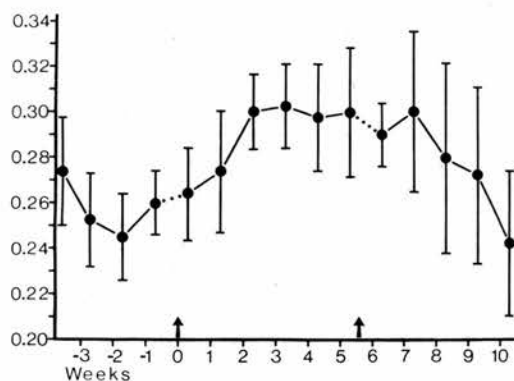


Fig. 2. Packed cell volume (mean \pm 1 S.D.) of lymphomatous pigs before, during and after treatment with prednisolone. Arrows indicate beginning and end of treatment.

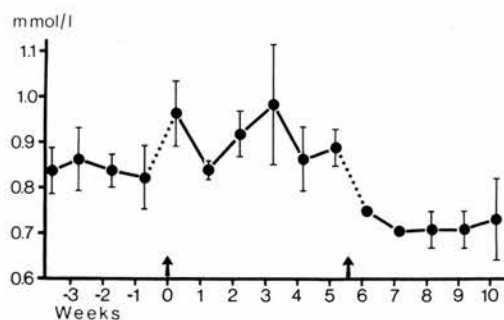


Fig. 3. Serum magnesium (mean \pm 1 S.D.) of lymphomatous pigs before, during and after treatment with prednisolone. Arrows represent beginning and end of treatment.

tuations during treatment (Fig. 3) but remained within the normal range for the pig (0.8–1.25 mmole/l). After treatment ceased, it fell immediately in the two surviving pigs to 0.75 mmole/l and remained below that level during the rest of the experiment. No signs of hypomagnesaemic tetany were observed.

The mean serum potassium concentration remained unchanged throughout the experiment (Table 2). The mean serum sodium, calcium, chloride and inorganic phosphate concentrations all showed small progressive increases during the course of the experiment (Table 2).

The total serum globulin level (Fig. 4) fluctuated considerably before treatment having an overall mean of 43.1 ± 7.9 g/l. During treatment it fell sharply, reaching a nadir with a mean of 21.0 ± 5.2 g/l during the fourth week. From then on it tended to rise again but within the period of observation, never reached the pretreatment level.

The mean serum albumin level (Fig. 4) remained relatively steady before treatment with an overall value of 23.6 ± 4.0 g/l. During treatment it showed changes more or less

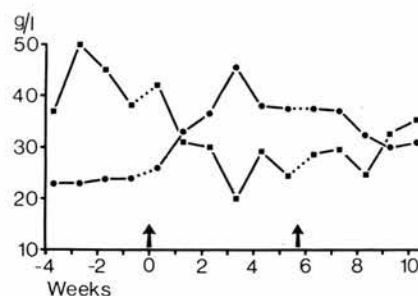


Fig. 4. Serum albumin (●-●) and serum globulin (■-■) of lymphomatous pigs before, during and after treatment with prednisolone. Arrows represent beginning and end of treatment.

complementary to those in globulin. At its peak during the fourth week it had a mean of 46.0 ± 3.9 g/l.

These effects were exaggerated when the albumin/globulin ratio was calculated. Before treatment this had an overall mean of 0.57 ± 0.17 . The ratio increased rapidly during treatment reaching a peak during the fourth week with a mean of 2.28 ± 0.5 . Thereafter it fell again but remained above unity until the last two weeks of the experiment.

Electrophoretic analysis showed that the drop in globulin during treatment was attributable essentially to a 50% reduction in the gamma fraction (Table 3).

Cell-mediated immunity

Before therapy began, the skin hypersensitivity reaction to 10% DNFB was minimal or absent in all four lymphomatous pigs. During and after therapy, a response of score 2 (erythema and swelling) was apparent (Table 4). The reaction of the untreated non-lymphomatous pig was much more severe (large ulcerations, score 4).

Table 2. Serum inorganic elements (mmole/l) of lymphoma cases treated with prednisolone

	A	B	C
Number of pigs	4	4	2
Mg	0.84 ± 0.05	0.91 ± 0.04	0.72 ± 0.01
K	4.84 ± 0.20	4.84 ± 0.46	4.89 ± 0.07
Na	137.25 ± 1.88	142.65 ± 1.05	147.80 ± 4.50
Cl	90.44 ± 1.14	92.37 ± 0.98	94.40 ± 0.60
Ca	2.62 ± 0.10	2.70 ± 0.09	2.74 ± 0.03
PO ₄	2.07 ± 0.10	2.02 ± 0.18	2.34 ± 0.23

Mean and S.D. were calculated for all samples taken during A: pre-treatment; B: treatment, and C: post-treatment periods.

Table 3. Mean \pm S.D. (g/l) of serum globulin fractions obtained by electrophoresis from lymphoma cases treated with prednisolone.

	A	B	C	D
Number of pigs	4	2*	4	2
α_1	0.9 \pm 0.7	0.45 \pm 0.2	0.9 \pm 0.4	12.5 \pm 1.1
α_2	10.1 \pm 2.4	9.10 \pm 0.3	9.5 \pm 1.1	
β	9.3 \pm 2.4	8.75 \pm 2.1	10.5 \pm 2.4	
γ	15.7 \pm 3.3	7.40 \pm 0.6	7.2 \pm 1.7	13.4 \pm 1.9

A: at commencement of treatment; B; during fourth week of treatment when total globulin value was at its lowest; C: at end of treatment; and D: five weeks later.

*2 samples lost.

Table 4. Skin hypersensitivity reactions of individual lymphomatous pigs to 10% DNFB before, during and after treatment with prednisolone, compared with the reaction of an untreated normal (non-lymphomatous) littermate of two of them

	Pig No.	At sensitisation	Pretreatment	During last week of treatment	1 month post-treatment
Group I	30	3	0	2	—
	56	1	0	2	—
Group II	37	0	0	2	2
	52	1	1	2	2
Normal	54	1	4	—	—

0, negative; 1, slight erythema; 2, erythema and swelling; 3, small ulcerations; 4, large ulcerations.

Post-mortem and histological findings

Group I pigs resembled normal animals except that the lymph nodes were slightly enlarged. As in untreated lymphoma, the cortex and medulla were not distinguishable on the cut surface but, unlike such cases, the nodes were firm not soft.

Group II pigs showed lesions typical of advanced, untreated cases of the disease as described by Head *et al.* [2], except for the thymus and alimentary tract (q.v. below).

The relative weights of organs are summarised in Table 1. In Group I, treatment had reduced the relative weights of the splanchnic lymph nodes to well below the minimum value of the 17 untreated cases, but they were still about three times greater than those of the untreated normal pig. In Group II, the withdrawal of treatment resulted in marked recrudescence so that the splanchnic nodes were nearly 6 times larger than in Group I and approximated to the mean value of the untreated cases. The increase in relative weight was greatest in the mesenteric and colonic nodes and least in the bronchial group.

Similar, but less spectacular effects were observed in the superficial nodes both individually and as a group.

On histological examination, treatment in Group I had caused a depletion of cells in the paracortical region of the lymph nodes and the few nodules found had reverted to primary small structures (Figs. 5, 6 and 7). The increase in size of the nodes was due to paracortical tissue in which a few probable tumour cells were seen, but none in mitosis. This area in the gastric and mesenteric nodes had much fibrin deposition. Regrowth of tumour in Group II nodes resulted in replacement of normal structure almost completely by tumour cells and some small lymphocytes, except for a few small nodules (Figs. 5 and 8).

The inguinal nodes of Group I were unique in that one pole showed lymphoid depletion described above but the other pole was replaced by tumour so that it resembled a Group II node.

The relative weight of the thymus was about twice as great in Group II as in Group I. All were above the average for the un-

treated cases but none was as high as the untreated normal pig. Histologically, the thymuses of Group I pigs were reduced to lobules of adipose tissue with occasional epithelial cells and groups of up to 50 lymphocytes. The recovery of normal cortical and medullary structure when treatment was stopped resembled that seen in prednisolone treated normal pigs [1], but the more rapidly regrowing tumour had caused some thymus suppression in pig 52.

The effects on the splenic relative weights were similar to those on the lymph nodes, so that histologically the Group I white pulp showed no nodules and the red pulp, though large, was depleted of cells (Fig. 9). Five weeks without treatment allowed tumour to regrow, nodules to reform and extramedullary haemopoiesis to develop in Group II so that the spleen resembled that of a typical late stage untreated lymphosarcoma (Fig. 10).

When bone marrow biopsies were taken immediately prior to slaughter, they were found to be representative of the picture in the decalcified bone sections. The pretreatment biopsies all showed tumour tissue but in the post-treatment samples no tumour cell masses were found, although there were more haemopoietic cells and less adipose tissue than normal. In the Group II post-mortem samples, there seemed to be an increase in normoblast foci, a reduction in megakaryocytes and large islands of tumour cells. Whereas the decalcified lumbar vertebral body and wing of the ilium are normal sites of haemopoiesis, the marrow of the femoral shaft is a fat store in this age of pig. It is noteworthy, therefore, that it was haemopoietic in Group I and both haemopoietic and neoplastic in Group II pigs.

In contrast to other lymphoid sites, the Group I pigs showed large reaction centres in the stomach, Peyer's patches and caecum, particularly in pig 56. Moreover, in the sites occupied by tumour in Group II pigs, there was a sparsely cellular zone with no obvious tumour cells in mitosis.

In some organs, e.g. the ovarian stroma and the adventitia of both the arcuate vessels of the kidney and the blood vessels of the fat of the vertebral canal, a tumour lymphocyte infiltrate was present in Group II but absent in Group I. In other organs of Group I some foci of small lymphocytes were present, whereas they were absent (e.g. periportal) or smaller (e.g. peribronchial) in normal pigs. These areas in Group II animals were occupied by large proliferating tumour masses.

DISCUSSION

There are three main areas of interest in these results: firstly the effect on the marrow in which tumour was reduced but haemopoiesis was stimulated; secondly the effect on serum biochemistry, in particular the changes in albumin/globulin ratio and in magnesium levels; thirdly the differential sensitivity of tumour cells in different organs.

The percentage reduction in circulating mononuclear cells was twice as great as that observed even at the highest dose level of 6 mg/kg in normal pigs [1]. This is in keeping with the observation of Schrek [3] that in man leukaemic lymphocytes were more sensitive to steroids than were normal lymphocytes.

The observed reduction in total serum globulin and increase in serum albumin during treatment was to be anticipated from the observation in man that control of symptoms by corticosteroid therapy is usually associated with such an effect [4]. The reduction in globulin may have resulted from steroid lympholysis primarily of tumour cells which were producing an excess of gamma globulin. However, we have not been able to demonstrate that the high level of gamma globulin found in lymphoma pigs is produced by the tumour cells. Indeed, these appear to be neither T nor B cells since the percentage of cells forming rosettes with sheep RBC and of cells showing fluorescence for immunoglobulin is very low compared with normal pigs (unpublished data). It may be that the gamma globulin came from normal B cells in response to the presence of the tumour. These cells were then involved in the steroid lympholysis or reduced their production of globulin as the tumour disappeared, or both.

The increase in serum albumin levels during treatment appears to result from an osmotic mechanism acting through the hepatic interstitial fluid so that the production of albumin by the liver is inversely related to the globulin concentration [5]. Increased albumin production would be helped by prednisolone-induced improvement in appetite, resulting in increased protein uptake and improved utilisation following reduced interference with organ function by the tumour or its products.

The suspicion that in normal pigs prednisolone produced a nadir in total serum globulin values before the end of treatment [1] was borne out in the lymphoma pigs in which it was accompanied by a peak in the serum albumin. These effects and the nadir in

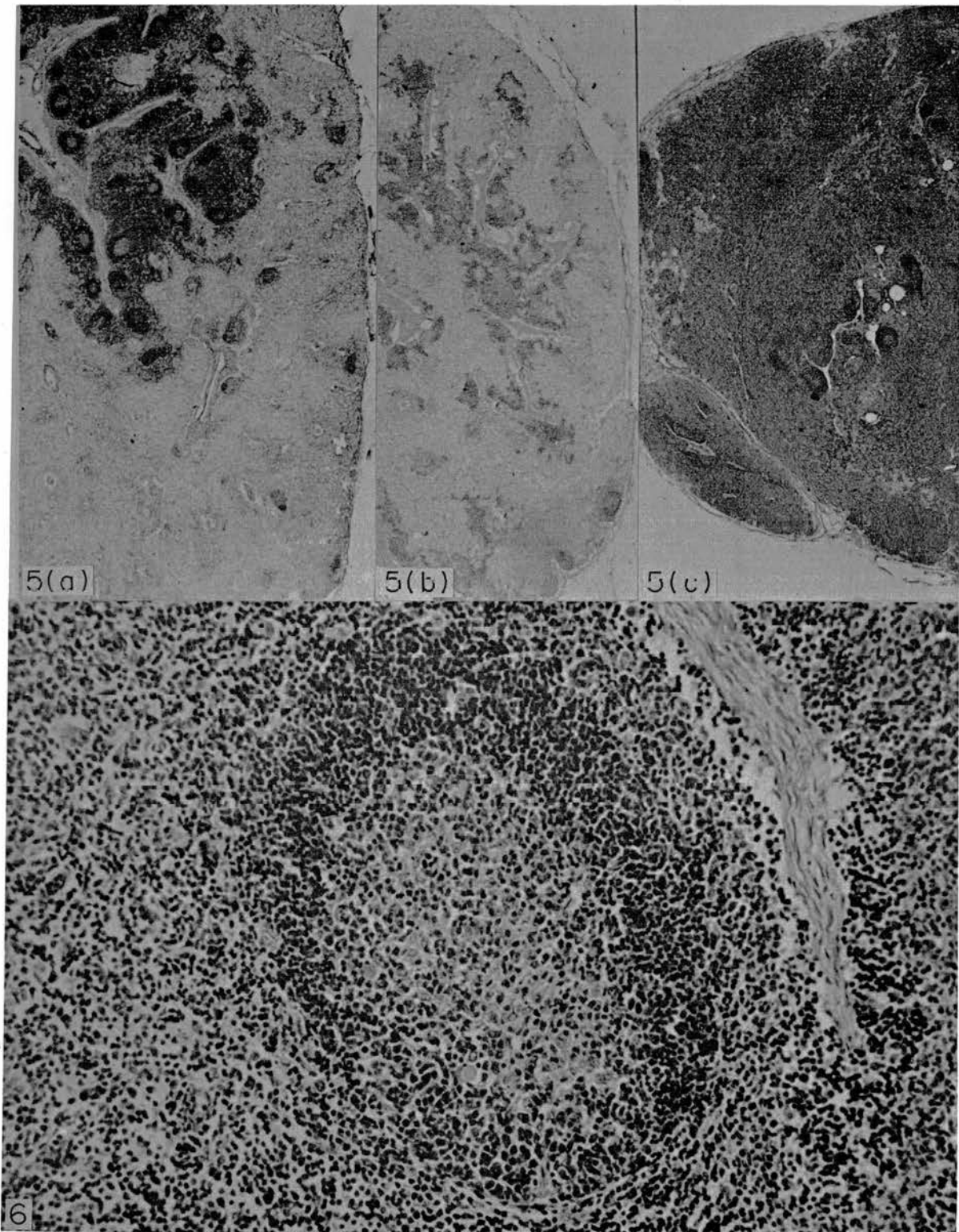


Fig. 5. Prescapular lymph nodes. a, pig 54 normal control; b, lymphoma pig 30 at the end of treatment; c, lymphoma pig 37 at the end of the post-treatment period. Note reduction in the number of cortical nodules and density of paracortical zone in b. In c the medulla is virtually obliterated but some cortical nodules have reappeared. H&E $\times 10$.

Fig. 6. Mesenteric lymph node from pig 54, normal control. Note trabecula on right with surrounding sinus, secondary cortical nodule with reaction centre in the middle and paracortical zone on the left. Compare with Figs. 7 and 8. H&E $\times 10$.

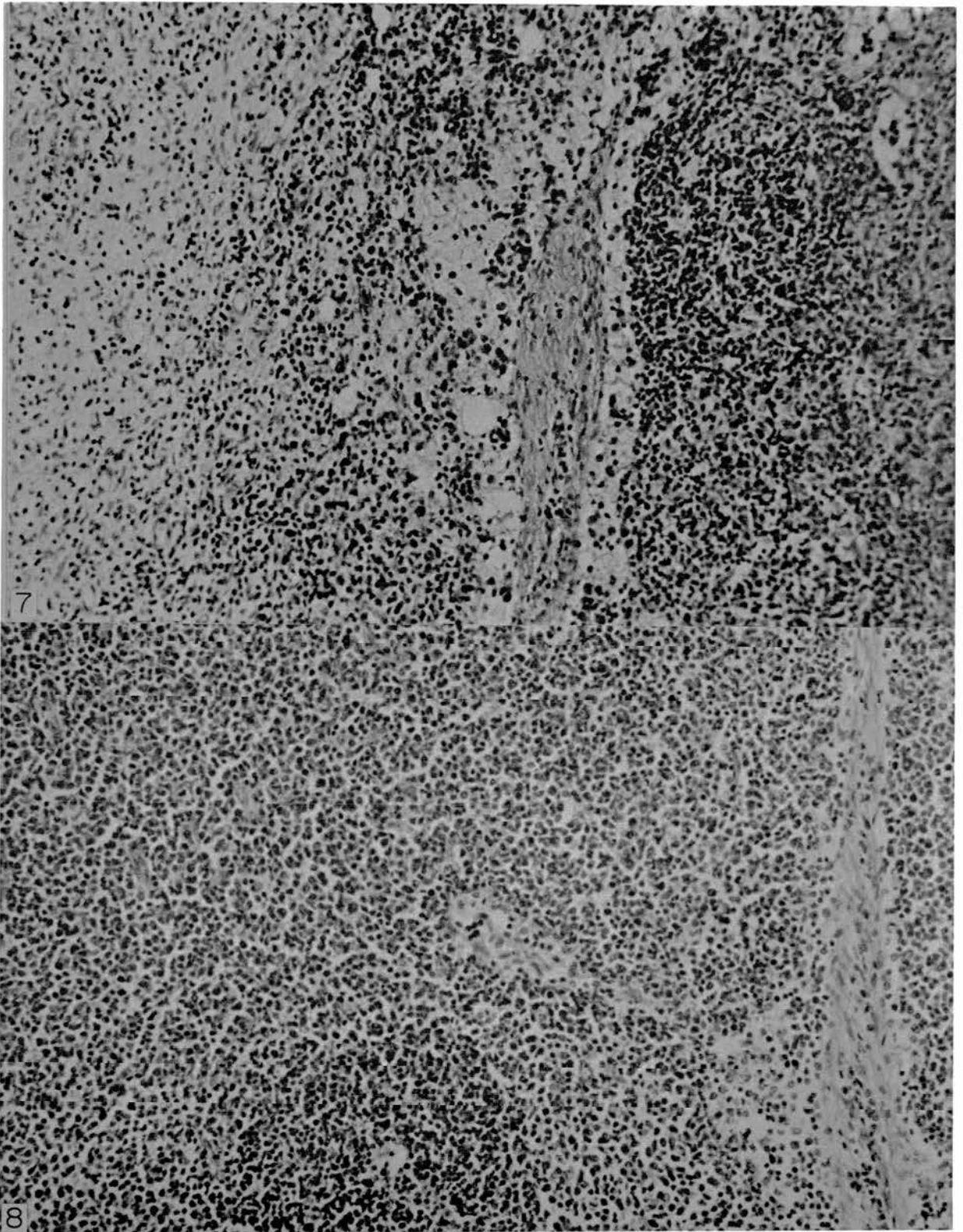


Fig. 7. Mesenteric lymph node from lymphoma pig 30 at the end of treatment. Note trabecula in centre surrounded by dilated sinus, poorly defined primary cortical nodules on right and depleted paracortex on the left. Compare with Figs. 6 and 8. H&E $\times 500$.

Fig. 8. Mesenteric lymph node from lymphoma pig 52 at the end of the post-treatment period. Note that tumour recrudescence replaces most of the normal architecture but a trabecula is visible on the right and a poorly defined primary nodule at the bottom centre. Compare with Figs. 6 and 7. H&E $\times 500$.

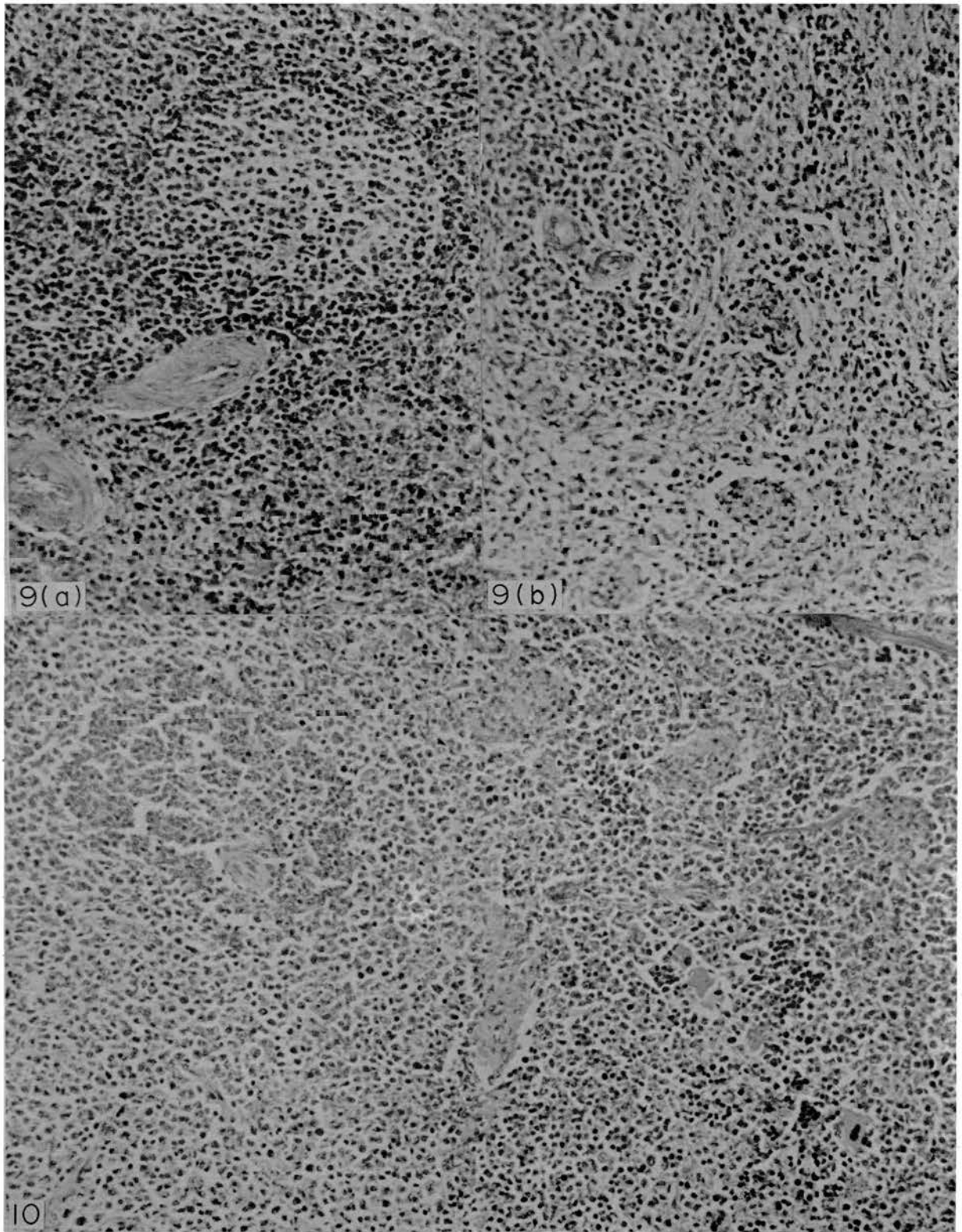


Fig. 9. Spleens from a, pig 54, normal control and b, lymphoma pig 56 at the end of treatment. Note the disappearance of secondary nodule and depletion of both red and white pulp in the treated case. Compare with Fig. 10. H&E $\times 500$.

Fig. 10. Spleen from lymphoma pig 52 at the end of the post-treatment period. Note regenerating white pulp top left surrounded by tumour tissue; on the right small dark nuclei of normoblasts and some megakaryocytes can be seen. Compare with Fig. 9. H&E $\times 500$.

mononuclear cells and peaks in neutrophils and platelets during the fifth week of treatment suggest that thereafter the effects of the treatment began to decline. Shaw *et al.* [6] observed that the effects of prednisolone on chronic lymphocytic leukaemia of man were transient and Rosenthal *et al.* [7] reported that remissions obtained in lymphocytic leukaemias of children and other lymphoid neoplasia with ACTH or cortisone were of short duration. This waning of effect may be due to suppression of the hypothalamic-pituitary-adrenal axis [8]. Certainly, the mean relative weight of the adrenals of Group I pigs at the end of treatment was only two-thirds that of Group II 5 weeks after withdrawal and only one-third that of the 17 untreated lymphoma cases (Table 1).

The continued improvement in the red cell picture into the second week after treatment was discontinued might be due to a stimulating effect of prednisolone on early red cell precursors in the marrow so that the resulting increased population of maturing cells in the "pipeline" continued to appear in the peripheral blood for some time.

Increased levels of serum magnesium (up to 1.85 mmole/l which is within the cardiotoxic range) have been observed during treatment of human patients with leukaemia and have been attributed to the release of the element from damaged malignant cells [9]. The reduction to subnormal levels observed in our lymphoma pigs once treatment was withdrawn may be associated with increased uptake of the element from the blood stream by the rapidly regrowing tumour.

Such a mechanism would be expected to affect serum potassium levels similarly [10], but these remained unchanged throughout the experiment. Potassium and calcium loss only result from high dosage or prolonged treatment with corticosteroids [9].

Although the average skin hypersensitivity reaction score of 2 was not as high as that observed in the normal untreated pig, it was higher than that observed in untreated lymphoma pigs (unpublished data). These reactions show that prednisolone had a slightly beneficial effect on the cell-mediated response of the treated lymphoma pigs. This response is unlike that observed in normal pigs receiving prednisolone, where the effect was to suppress the hypersensitivity reaction [1].

The absence of increases in body weight during treatment and the increases observed in Group II after its withdrawal are in keeping with the known growth-depressive effects

of prednisolone [11]. It is not clear, however, to what extent these effects are attributable in lymphomatous pigs to changes in tumour mass as reflected in the superficial lymph node measurements and post-mortem findings.

The problem of identifying isolated non-dividing tumour cells sparsely scattered through a population of other lymphoid cells remains unsolved. It is, therefore, difficult to state whether treatment destroyed all the tumour cells in an area or reduced their number and mitotic rate so that they were not detectable by conventional histology. It is clear from our results, however, that tumour growth was suppressed to different degrees in different sites in the body, e.g. completely in the kidney but not in the gastro-intestinal tract. Even in a single organ only localised suppression was sometimes achieved, e.g. the inguinal lymph node.

In the early drug-induced remission period, one might expect to see the supporting connective tissue stroma of the tumour now depleted of tumour cells. The gastric and splenic lymph nodes, which are the organs most enlarged in the untreated case, certainly showed a zone of fibres and blood vessels between the paracortical area and the medulla which would fit this concept. This, and comparable areas in other lymphoid organs, often showed fibrin deposition, suggesting some defect in the integrity of the blood vascular system. In these areas, large "blast" cells were seen which may have been unmasked reticuloendothelial cells or possibly tumour cells prevented from progressing through mitosis.

It is clear from the foregoing discussion that hereditary lymphoma of pigs is a good model for comparison with the human. In addition to changes associated with prednisolone treatment that were predicted from previous work (e.g. red and white cell parameters, albumin/globulin ratio and weight gain) new features have come to light such as magnesium fluctuations, differential tumour sensitivities and correction of anergy. These open up new avenues of research and may lead to changes in our fundamental thinking about lymphoid neoplasia.

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