

CHAPTER III

RESULTS



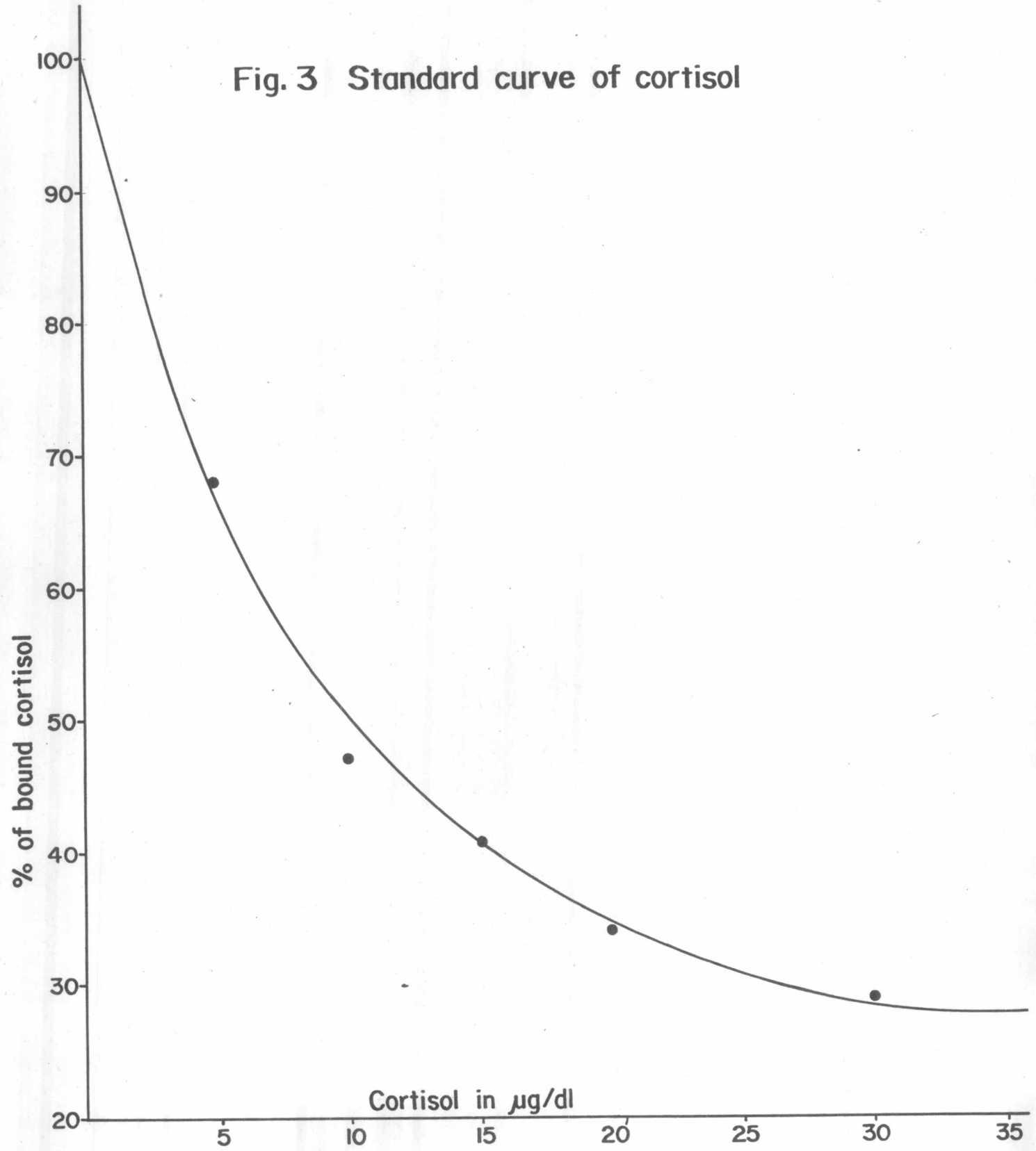
1. Standard curve of cortisol

Typical standard curve of cortisol is shown in Fig. 3. The results of the assay of the standard cortisol were calculated as percentages of H^3 -F bound to CBG ($\frac{\text{cpm of supernate}}{\text{total count}} \times 100$) and were plotted against dose of standard cortisol.

2. Normal value of plasma cortisol

Blood samples from 14 normal subjects (male:female=1:1) ages ranging from 8 to 13 years were measured for plasma cortisol levels at 2 different times of the day, i.e. the morning period (7-9 a.m.) and the afternoon period (3-4 p.m.). None of these subjects suffered from chronic illness, malnutrition, nor definite psychological factors. The results are shown in Table 1. The mean morning value \pm S.D. was 10.31 ± 1.42 with the range of 8.0 to 12.0 $\mu\text{g/dl}$. In the afternoon period the mean value \pm S.D. was 7.16 ± 1.32 with the range of 4.8 to 9.2 $\mu\text{g/dl}$.

Fig. 3 Standard curve of cortisol



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Table 1. Normal values of plasma cortisol by competitive protein binding assay .

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Plasma cortisol levels	
					morning value ($\mu\text{g/dl}$)	afternoon value ($\mu\text{g/dl}$)
1	M	13	34.8	146	12.0	8.0
2	M	13	35	148.2	11.8	7.8
3	M	10	24.6	130	9.5	6.4
4	F	10	24	132	8.0	6.6
5	M	11	27.3	130.9	9.5	5.0
6	F	11	26	132.8	9.0	6.6
7	F	11	26	132	12.0	9.2
8	F	12	30	140	10.4	9.0
9	M	13	35.2	148	12.0	8.4
10	F	14	37	147	11.0	7.4
11	F	8	20.6	120.5	8.5	6.4
12	M	13	34.5	147	11.6	7.8
13	M	10	24	132	10.0	4.8
14	M	11	27	130	9.0	6.8
N					14	14
Mean					10.31	7.16
S.D.					1.42	1.32
S.E.M.					0.38	0.35
Range					8.0-12.0	4.8-9.2

3. Plasma cortisol determination in patients with nephrotic syndrome

Plasma cortisol levels in the morning and in the afternoon in 10 nephrotic syndrome patients who received oral prednisolone 2 mg/kg/day as single daily dose are shown in Table 2. The study had been carried out after 2 months of therapy in all patients. The mean values \pm S.D. of plasma cortisol levels in the morning were 4.24 ± 1.00 $\mu\text{g/dl}$ and 3.75 ± 0.94 $\mu\text{g/dl}$ in the afternoon, and ranged from 2.8 to 5.5 $\mu\text{g/dl}$ and 2.4 to 5.0 $\mu\text{g/dl}$, respectively.

Plasma cortisol levels in the morning and in the afternoon in 23 nephrotic syndrome patients who received oral prednisolone 4 mg/kg/day once every other day are shown in Table 3. The study had been carried out after 2 months of therapy in all patients. The mean values \pm S.D. of plasma cortisol levels in the morning were 5.50 ± 1.11 $\mu\text{g/dl}$ and 4.95 ± 1.16 $\mu\text{g/dl}$ in the afternoon, and ranged from 3.4 to 7.4 $\mu\text{g/dl}$ and 3.0 to 6.8 $\mu\text{g/dl}$, respectively.

Table 2. Plasma cortisol levels in patients with nephrotic syndrome receiving oral prednisolone 2 mg/kg/day as single daily dose. The study had been carried out after 2 months of therapy in all patients.

No	Sex	Age (yr)	Weight (.kg)	Height (cm)	Plasma cortisol levels	
					morning value ($\mu\text{g}/\text{dl}$)	afternoon value ($\mu\text{g}/\text{dl}$)
1	F	6	17.5	107	3.4	3.0
2	M	7	24	120	4.0	3.6
3	M	8	27	130	4.8	4.0
4	M	9	32	132	5.0	4.6
5	M	6	30	140	3.6	3.2
6	M	13	42	150	5.5	5.0
7	M	13	40.7	156	5.4	4.9
8	M	6	20	114	2.8	2.4
9	M	10	34	140	4.9	4.2
10	M	6	21	115	3.0	2.6
N					10	10
Mean					4.24	3.75
S.D.					1.00	0.94
S.E.M.					0.32	0.30
Range					2.8 - 5.5	2.4 - 5.0

Table 3. Plasma cortisol levels in patients with nephrotic syndrome receiving oral prednisolone 4 mg/kg/day once every other day. (or the average dose of 2 mg/kg/day.) The study had been carried out after 2 months of therapy in all patients.

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Plasma cortisol levels	
					morning value ($\mu\text{g/dl}$)	afternoon value ($\mu\text{g/dl}$)
1	F	6	20	99.5	5.9	5.2
2	M	6	21.5	117	5.4	4.8
3	M	8	26	123	6.3	5.8
4	M	6	19	100	5.6	5.0
5	M	8	37	120	6.0	5.6
6	M	9	35	138	6.9	6.2
7	M	6	19	132	5.3	4.9
8	M	6	21.1	114	5.6	4.8
9	F	2	9	88	3.9	3.2
10	F	2	10.5	68	3.7	3.0
11	F	2	8	107	3.6	3.2
12	F	2	11	66	3.9	3.0
13	F	2	10	75	3.4	3.0
14	M	13	40	140	7.1	6.6
15	M	15	44	140	7.4	6.8
16	M	8	27	124	6.2	5.8
17	M	7	23	123	6.0	5.0
18	M	6	22	102	5.6	5.0
19	M	6	22	120	5.4	4.9
20	M	5	18	110	5.2	4.6
21	M	9	30	134	6.2	5.9
22	F	6	20	110	5.8	5.2
23	F	8	29	130	6.0	5.8
N					23	23
Mean					5.50	4.95
S.D.					1.11	1.16
S.E.M.					0.23	0.24
Range					3.4-7.4	3.0-6.8

4. Plasma cortisol determination in patients with rheumatic heart disease

Plasma cortisol levels in the morning and in the afternoon in 14 rheumatic heart disease treated with different doses interpreted as times of the physiologic doses are shown in Table 4. All patients received oral prednisolone every day in 3-4 divided doses for 30 days.

There were significantly reversed relationships between the doses of prednisolone and plasma cortisol levels in the morning ($p < 0.001$) and in the afternoon ($p < 0.005$) as illustrated in Figures 4 and 5.

Table 4 The correlation between doses of the steroid and plasma cortisol levels in 14 patients with rheumatic heart disease treated with different doses interpreted as times of the physiologic doses. All patients received oral prednisolone every day in 3-4 divided doses for 30 days.

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Doses related to physiologic dose*	Plasma cortisol levels	
						morning value ($\mu\text{g/dl}$)	afternoon value ($\mu\text{g/dl}$)
1	M	9	31	143	x 3 times	9.4	7.4
2	M	7	24	131.5	x 3 times	8.6	6.4
3	M	6	22.6	130	x 3 times	8.2	3.6
4	F	7	23	124	x 7.5 times	3.4	2.4
5	M	8	28	127	x 7.5 times	3.2	2.3
6	M	5	15	107	x 7.5 times	3.2	2.2
7	M	6	20	110	x 7.5 times	3.6	2.6
8	M	9	31	134	x 10 times	3.0	2.6
9	F	7	24	121	x 10 times	3.0	2.8
10	F	8	28	125	x 12.5 times	2.1	1.9
11	F	8	29	129	x 12.5 times	2.0	0.9
12	M	9	30	134	x 12.5 times	1.9	0.9
13	F	5	16	105	x 15 times	0.8	0.6
14	F	13	36	144	x 15 times	0.6	0.4
Mean \pm S.D. of 3 times						8.7 \pm 0.61	5.8 \pm 1.97
Mean \pm S.D. of 7.5 times						3.35 \pm 0.91	2.38 \pm 0.17
Mean \pm S.D. of 10 times						3.0 \pm 0	2.7 \pm 0.14
Mean \pm S.D. of 12 times						2.0 \pm 0.1	1.23 \pm 0.58
Mean \pm S.D. of 15 times						0.7 \pm 0.14	0.5 \pm 0.14

* The physiologic dose of cortisol is $15-20 \text{ mg/m}^2/24\text{hr}$ (or $3-4 \text{ mg}$ of prednisolone/ $\text{m}^2/24\text{hr}$)

Fig. 4 Correlation between the doses of prednisolone and plasma cortisol levels in the morning

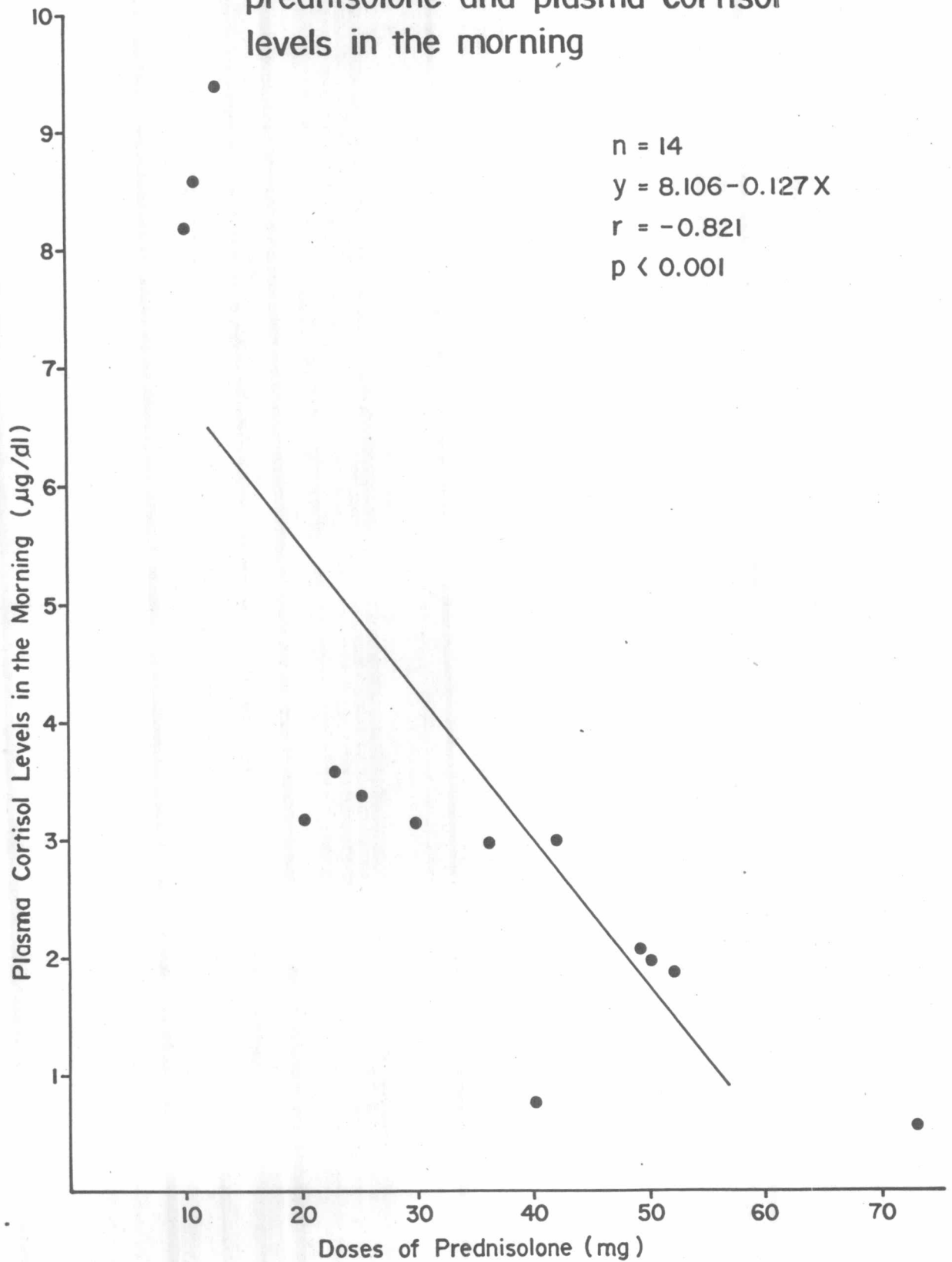
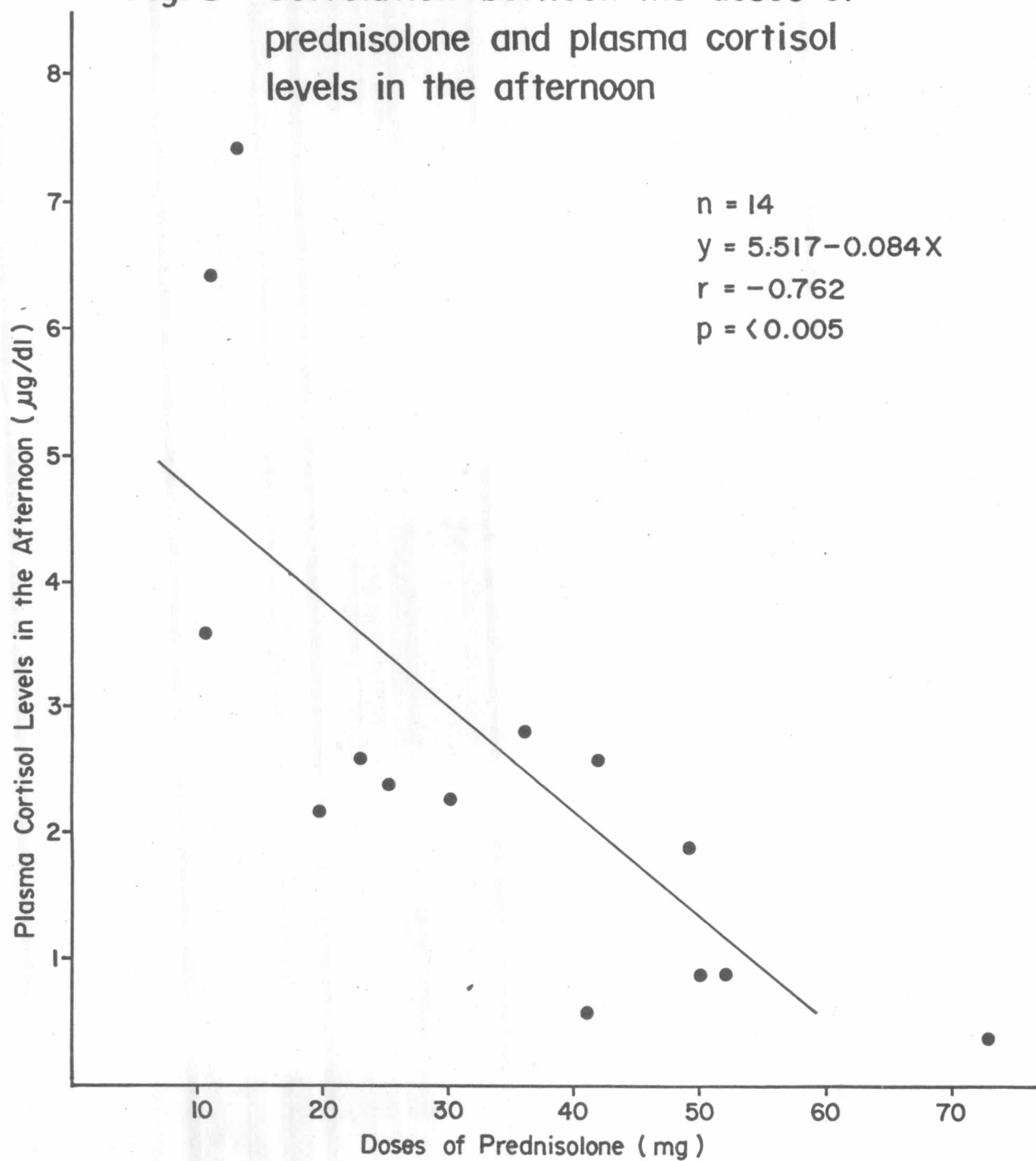


Fig. 5 Correlation between the doses of prednisolone and plasma cortisol levels in the afternoon



5. Plasma cortisol determination in patients with rheumatoid arthritis

Plasma cortisol levels in the morning and in the afternoon in 10 rheumatoid arthritis receiving oral prednisolone approximately 5 times of the physiologic doses every day in 3-4 divided doses with various durations of therapy are shown in Table 5.

There were significantly reversed relationships between the duration of therapy and plasma cortisol levels in the morning ($p < 0.001$) and in the afternoon ($p < 0.001$) as illustrated in Figures 6 and 7.

Table 5. Plasma cortisol determination in patients with rheumatoid arthritis receiving oral prednisolone approximately 5 times of the physiologic doses every day in 3-4 divided doses with various durations of therapy.

No	Sex	Age (yr)	Duration (mo)	Weight (kg)	Height (cm)	Plasma cortisol levels.	
						morning value ($\mu\text{g}/\text{dl}$)	afternoon value($\mu\text{g}/\text{dl}$)
1	M	6	5	20	115	3.3	2.9
2	M	9	5	29	134	2.6	2.3
3	M	6	5	19	110	2.4	2.0
4	F	13	9	36	144	2.0	1.7
5	M	6	9	19	110	1.9	1.5
6	F	7	9	23	120	1.7	1.2
7	F	9	12	29	136	1.5	0.9
8	F	10	12	32	137	1.4	0.7
9	F	13	12	36	144	0.7	0.5
10	M	9	12	30	130	0.4	0.2
Mean \pm S.D. of 5 months						2.77 \pm 0.47	2.4 \pm 0.46
Mean \pm S.D. of 9 months						1.87 \pm 0.15	1.47 \pm 0.25
Mean \pm S.D. of 12 months						1.0 \pm 0.54	0.58 \pm 0.30

Fig. 6 Correlation between the duration of therapy and plasma cortisol levels in the morning

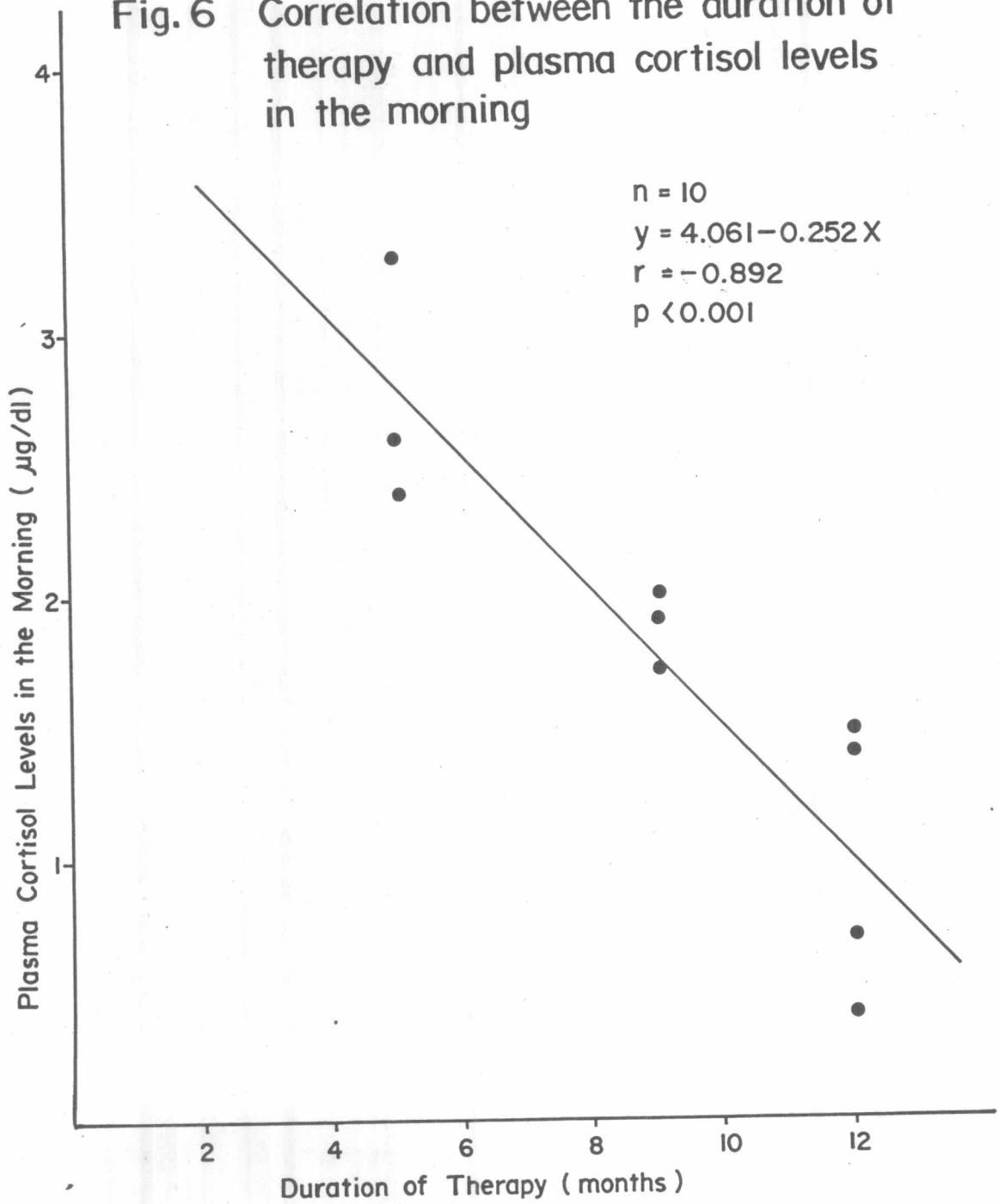
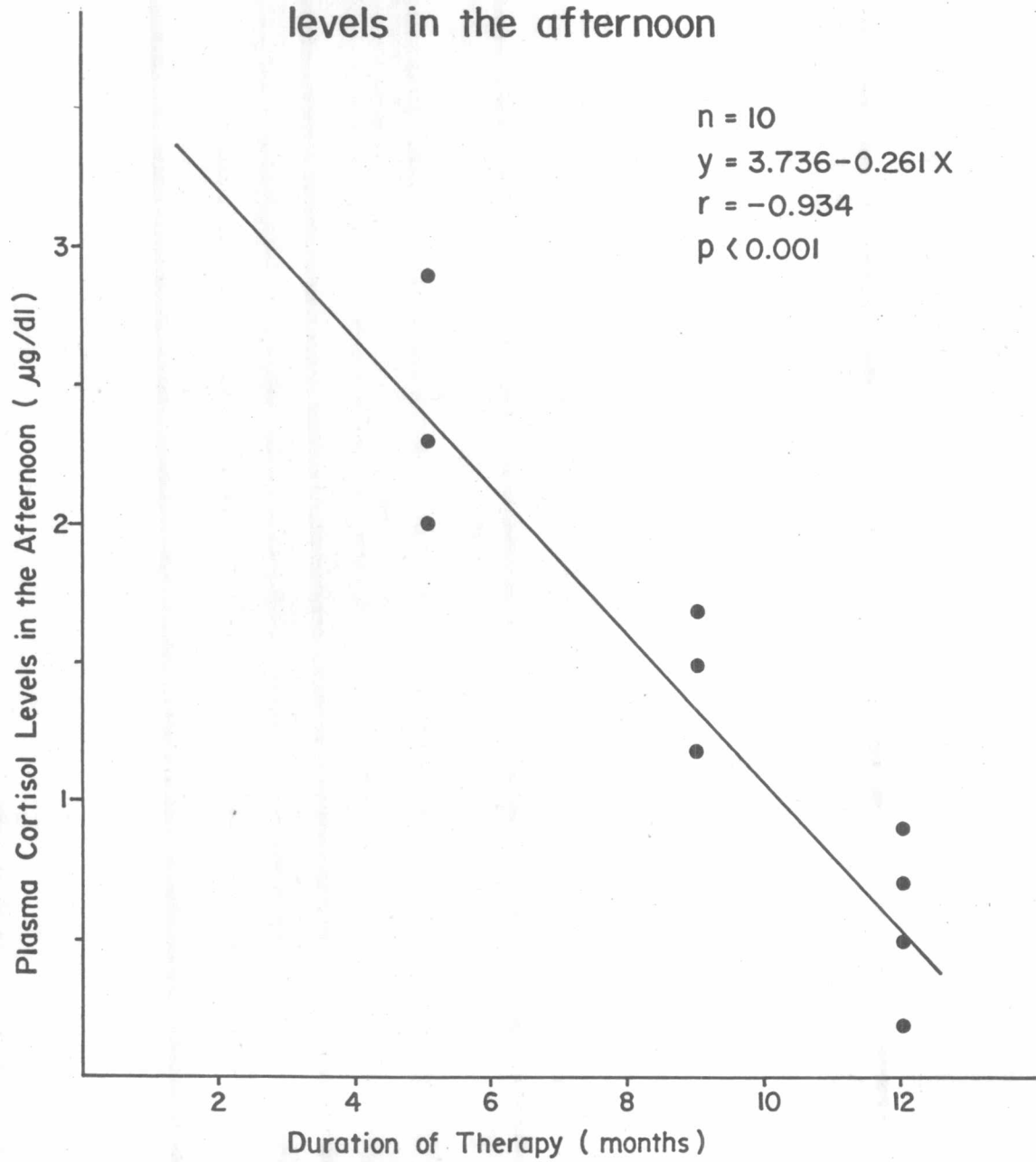


Fig.7 Correlation between duration of therapy and plasma cortisol levels in the afternoon



6. Normal distribution of urinary 17-hydroxycorticosteroids and 17-ketosteroids

Normal distribution of 17-hydroxycorticosteroids and 17-ketosteroids from 10 normal subjects are presented in Table 6. The mean value \pm S.D. of 17-hydroxycorticosteroids was 8.19 ± 1.75 mg/m²/24hr and of 17-ketosteroid was 10.86 ± 2.25 mg/m²/24hr with the range from 5.6 to 10.2 mg/m²/24hr and 7.8 to 14.9 mg/m²/24hr respectively.

Table 6 Normal distribution of urinary 17-hydroxycorticosteroids and 17-ketosteroids

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Surface area (in ²)	17-OHCS (mg/24hr)	17-OHCS (mg/m ² /24hr)	17-KS (mg/24hr)	17-KS (mg/m ² /24hr)
1	M	13	34.8	146	1.18	12.0	10.2	15.6	13.2
2	M	13	35	148.2	1.20	12.0	10.0	13.1	10.9
3	M	10	24.6	130	0.94	7.7	8.2	9.0	9.6
4	F	10	24	132	0.92	6.4	6.9	8.2	8.9
5	M	11	27.3	130.9	0.98	7.3	7.4	11.8	12.0
6	F	11	26	132.8	0.98	6.9	7.0	7.6	7.8
7	F	11	26	132	0.98	6.4	6.5	8.4	8.6
8	F	12	30	140	1.06	5.9	5.6	10.9	10.3
9	M	13	35.2	148	1.20	12.0	10.0	14.9	12.4
10	F	14	37	147	1.22	12.3	10.1	18.2	14.9
N							10		10
Mean							8.19		10.86
S.D.							1.75		2.25
S.E.M.							0.55		0.71
Range							5.6-10.2		7.8-14.9

7. Urinary 17-hydroxycorticosteroids and 17-ketosteroids in patients with nephrotic syndrome

Urinary 17-hydroxycorticosteroids and 17-ketosteroids in 10 nephrotic syndrome patients who received oral prednisolone 2 mg/kg/day as single daily dose are shown in Table 7. The study had been carried out after 2 months of therapy in all patients. The mean value \pm S.D. of 17-hydroxycorticosteroids was 2.61 ± 0.44 mg/m²/24hr and of 17-ketosteroids was 4.79 ± 0.50 mg/m²/24hr, with the range from 1.9 to 3.3 mg/m²/24hr and 4.0 to 5.4 mg/m²/24hr, respectively.

Urinary 17-hydroxycorticosteroids and 17-ketosteroids in 22 nephrotic syndrome patients who received oral prednisolone 4 mg/kg/day once every other day are shown in Table 8. The study had been carried out after 2 months of therapy in all patients. The mean value \pm S.D. of 17-hydroxycorticosteroids was 5.34 ± 0.89 mg/m²/24hr and of 17-ketosteroids was 7.25 ± 1.31 mg/m²/24hr, with the range from 4.4 to 7.7 mg/m²/24hr, and 5.3 to 10.0 mg/m²/24hr, respectively.

Table 7. Urinary 17-OHCS and 17-KS in patients with nephrotic syndrome

receiving oral prednisolone 2 mg/kg/day as single daily dose.

The study had been carried out after 2 months of therapy in all patients.

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Surface area(m ²)	17-OHCS (mg/24hr)	17-OHCS (mg/m ² /24hr)	17-KS (mg/24hr)	17-KS (mg/m ² /24hr)	
1	F	6	17.5	107	0.72	2.4	3.3	3.8	5.3	
2	M	7	24	120	0.90	2.6	2.9	4.5	5.0	
3	M	8	27	130	0.98	2.9	3.0	4.7	4.8	
4	M	9	32	132	1.06	2.6	2.5	5.1	4.8	
5	M	6	30	140	1.06	2.5	2.4	4.9	4.6	
6	M	13	42	150	1.31	2.8	2.1	5.2	4.0	
7	M	13	40.7	156	1.31	3.2	2.4	5.4	4.1	
8	M	6	20	114	0.80	2.4	3.0	4.3	5.4	
9	M	10	34	140	1.15	2.2	1.9	5.2	4.5	
10	M	6	21	115	0.82	2.1	2.6	4.4	5.4	
N							10		10	
Mean								2.61		4.79
S.D.								0.44		0.50
S.E.M.								0.14		0.16
Range								1.9- 3.3		4.0-5.4

Table 8. Urinary 17-OHCS and 17-KS in patients with nephrotic syndrome receiving oral prednisolone 4 mg/kg/day once every other day. (or the average doses of 2 mg/kg/day) The study had been carried out after 2 months of therapy in all patients.

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Surface area(m ²)	17-OHCS (mg/24hr)	17-OHCS (mg/m ² /24hr)	17-KS (mg/24hr)	17-KS (mg/m ² /24hr)
1	F	6	20	99.5	0.76	4.1	5.4	6.2	8.2
2	M	6	21.5	117	0.83	4.3	5.2	6.4	7.7
3	M	8	26	123	0.94	4.7	5.0	6.6	7.0
4	M	6	19	100	0.74	3.8	5.1	6.0	8.1
5	M	8	37	120	1.15	5.2	4.5	6.9	6.0
6	M	9	35	138	1.15	5.4	4.7	6.7	5.8
7	M	6	19	132	0.82	4.2	5.1	5.8	7.1
8	M	6	21.1	114	0.82	4.3	5.2	5.6	6.8
9	F	2	9	88	0.47	3.6	7.7	4.7	10.0
10	F	2	10.5	68	0.47	3.4	7.2	4.2	8.9
11	F	2	8	107	0.47	3.0	6.4	4.5	9.6
12	F	2	11	66	0.47	3.2	6.8	4.3	9.1
13*	-	-	-	-	-	-	-	-	-
14	M	13	40	140	1.25	5.6	4.5	6.9	5.5
15	M	15	44	140	1.33	5.9	4.4	7.0	5.3
16	M	8	27	124	0.96	4.6	4.8	6.4	6.7
17	M	7	23	123	0.84	4.5	5.4	5.9	7.0
18	M	6	22	102	0.82	4.3	5.2	5.7	7.0
19	M	6	22	120	0.85	4.4	5.2	6.0	7.1
20	M	5	18	110	0.74	3.6	4.9	4.8	6.5
21	M	9	30	134	1.04	4.9	4.7	6.5	6.3
22	F	6	20	110	0.78	4.1	5.3	6.1	7.8
23	F	8	29	130	1.00	4.8	4.8	5.9	5.9
N							22		22
Mean							5.34		7.25
S.D.							0.89		1.31
S.E.M.							0.19		0.28
Range							4.4-7.7		5.3-10.0

* No. 13 died

8. Urinary 17-hydroxycorticosteroids and 17-ketosteroids in patients with rheumatic heart disease

Urinary 17-hydroxycorticosteroids and 17-ketosteroids in 14 rheumatic heart disease treated with different doses interpreted as times of the physiologic doses are shown in Table 9. All patients received prednisolone every day in 3-4 divided doses for 30 days.

There were significantly reversed relationships between the doses of prednisolone and 17-hydroxycorticosteroids ($p < 0.001$) and 17-ketosteroids ($p < 0.001$) as shown in Figures 8 and 9.

Table 9. The correlation between doses of the steroid and urinary 17-OHCS and 17-KS in 14 patients with rheumatic heart disease treated with different doses interpreted as times of the physiologic doses. All patients received oral prednisolone every day in 3-4 divided doses for 30 days.

No	Sex	Age (yr)	Weight (kg)	Height (cm)	Surface area(m ²)	Doses related to physiologic doses*	17-OHCS (mg/24hr)	17-OHCS (mg/m ² /24hr)	17-KS (mg/24hr)	17-KS (mg/m ² /24hr)
1	M	9	31	143	1.08	x 3 times	4.5	4.2	7.7	7.1
2	M	7	24	131.5	0.92	x 3 times	3.3	3.6	6.3	6.9
3	M	6	22.6	130	0.88	x 3 times	2.8	3.2	5.8	6.6
4	F	7	23	124	0.84	x 7.5 times	2.2	2.6	4.9	5.8
5	M	8	28	127	1.00	x 7.5 times	2.5	2.5	5.2	5.2
6	M	5	15	107	0.66	x 7.5 times	1.5	2.3	3.7	5.6
7	M	6	20	110	0.78	x 7.5 times	2.1	2.7	4.2	5.4
8	M	9	31	134	1.06	x 10 times	1.8	1.7	3.6	3.4
9	F	7	24	121	0.90	x 10 times	1.6	1.8	3.2	3.6
10	F	8	28	125	0.98	x 12.5 times	1.2	1.2	2.5	2.5
11	F	8	29	129	1.00	x 12.5 times	1.0	1.0	2.6	2.6
12	M	9	30	134	1.04	x 12.5 times	1.3	1.3	2.2	2.1
13	F	5	16	105	0.68	x 15 times	0.6	0.9	1.1	1.6
14	F	13	36	144	1.22	x 15 times	0.4	0.3	1.6	1.3
Mean \pm S.D. of 3 times								3.67 \pm 0.50		6.87 \pm 0.25
Mean \pm S.D. of 7.5 times								2.53 \pm 0.17		5.5 \pm 0.26
Mean \pm S.D. of 10 times								1.75 \pm 0.07		3.5 \pm 0.14
Mean \pm S.D. of 12.5 times								1.17 \pm 0.15		2.4 \pm 0.26
Mean \pm S.D. of 15 times								0.6 \pm 0.42		1.45 \pm 0.21

* The physiologic dose of cortisol is 15-20 mg/m²/24hr (or 3-4 mg of prednisolone/m²/24hr)

Fig. 8 Correlation between the doses of prednisolone and urinary 17-OHCS

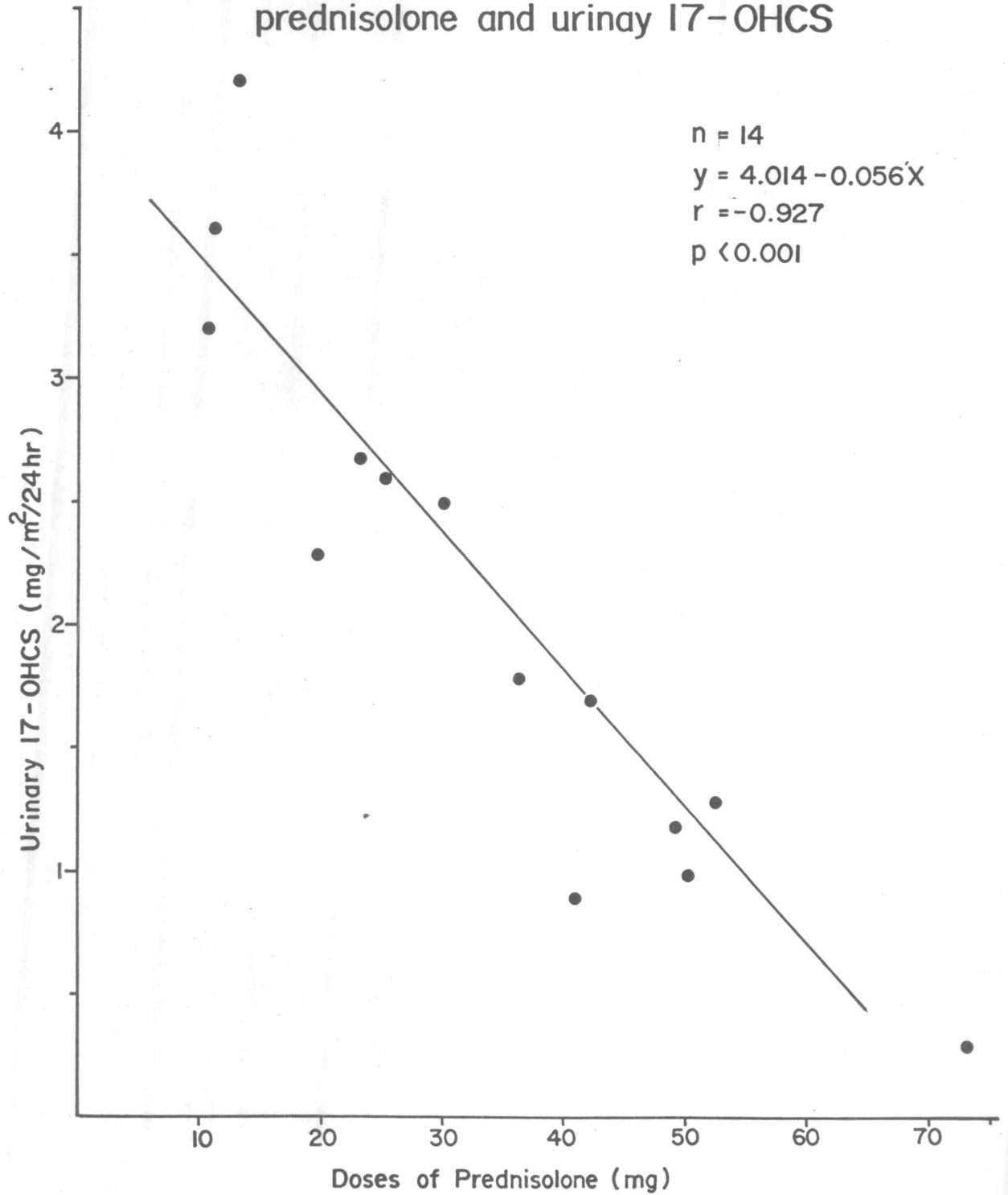
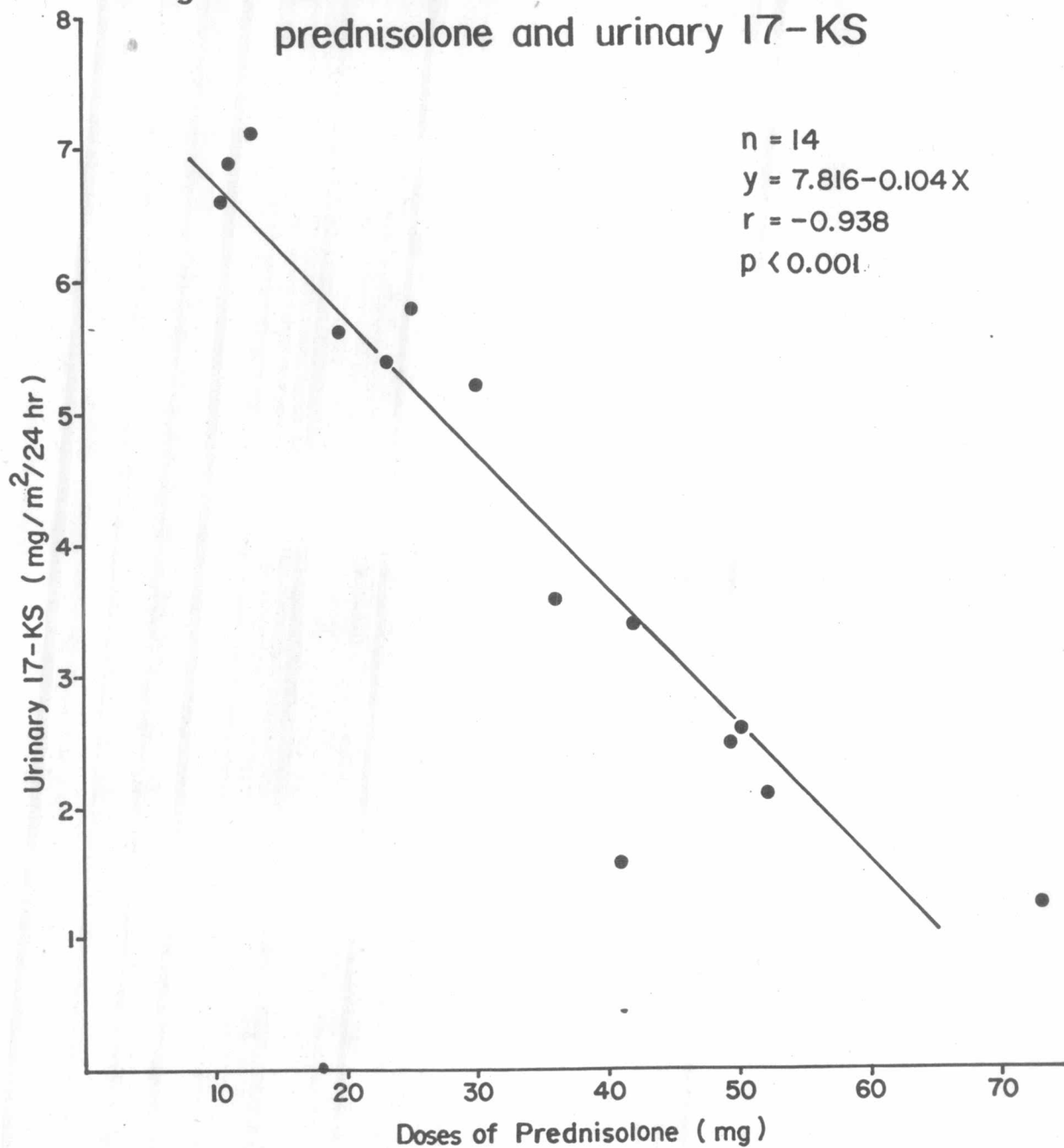


Fig. 9 Correlation between the doses of prednisolone and urinary 17-KS



9. Urinary 17-hydroxycorticosteroids and 17-ketosteroids in patients with rheumatoid arthritis

Urinary 17-hydroxycorticosteroids and 17-ketosteroids in 10 rheumatoid arthritis receiving oral prednisolone approximately 5 times of the physiologic doses every day in 3-4 divided doses with various durations of therapy are shown in Table 10.

There were significantly reversed relationships between the duration of therapy and urinary 17-hydroxycorticosteroids ($p < 0.001$) and 17-ketosteroids ($p < 0.001$) as illustrated in Figures 10 and 11.

Table 10. Urinary 17-OHCS and 17-KS in patients with rheumatoid arthritis receiving oral prednisolone approximately 5 times of the physiologic doses every day in 3-4 divided doses with various durations of therapy.

No	Sex	Age (yr)	Duration (mo)	Weight (kg)	Height (cm)	Surface area(m ²)	17-OHCS (mg/24hr)	17-OHCS (mg/m ² /24hr)	17-KS (mg/24hr)	17-KS (mg/m ² /24hr)
1	M	6	5	20	115	0.80	2.9	3.6	3.9	4.9
2	M	9	5	29	134	1.20	2.7	2.3	5.0	4.2
3	M	6	5	19	110	0.76	2.2	2.9	3.0	4.0
4	F	13	9	36	144	1.22	1.8	1.5	4.4	3.6
5	M	6	9	19	110	0.78	1.4	1.8	3.0	3.8
6	F	7	9	23	120	0.88	1.4	1.6	2.8	3.2
7	F	9	12	29	136	1.03	0.9	0.9	2.6	2.5
8	F	10	12	32	137	1.10	0.7	0.6	2.5	2.3
9	F	13	12	36	144	1.22	0.4	0.3	2.3	1.9
10	M	9	12	30	130	1.04	0.2	0.2	1.8	1.7
Mean \pm S.D. of 5 months							2.93 \pm 0.65		4.37 \pm 0.47	
Mean \pm S.D. of 9 months							1.63 \pm 0.15		3.53 \pm 0.31	
Mean \pm S.D. of 12 months							0.5 \pm 0.32		2.1 \pm 0.37	

Fig. 10 Correlation between the duration of therapy and urinary 17-OHCS

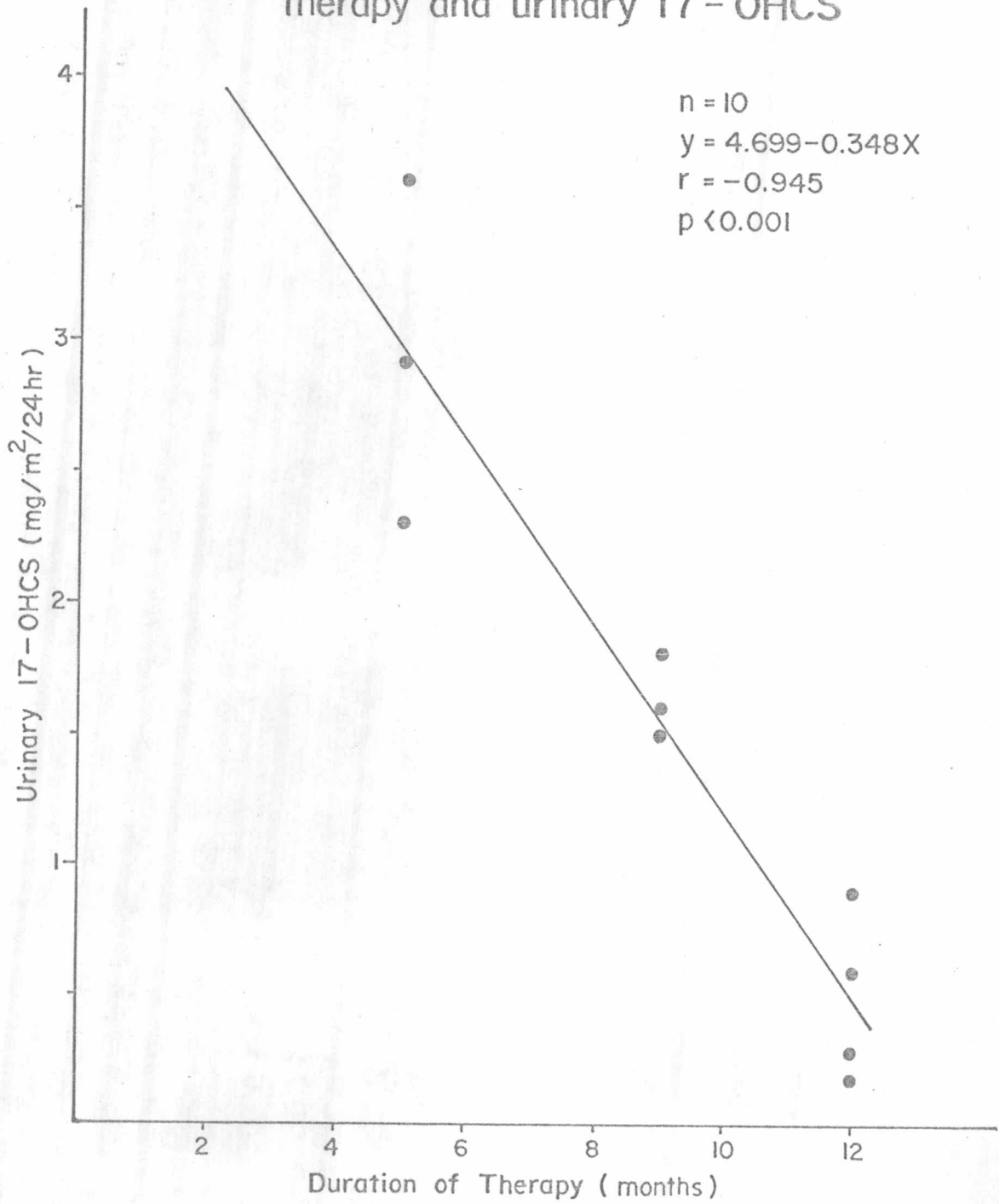


Fig. II Correlation between the duration of therapy and urinary 17-KS

