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723990

PERSONAL AND CONFIDENTIAL

October 3, 1969

TO: FILE

FROM: S. M. SANDERS *SMS*

EVALUATION OF BIOASSAY DATA FROM EMPLOYEE ACCIDENTALLY INJECTED WITH ^{238}Pu

Plutonium-238 nitrate was accidentally injected above the posterior aspect of the proximal interphalangeal joint of the right index finger of an employee on November 29, 1968. Evaluation of the bioassay data indicates that his plutonium body burden (excluding that in the finger and blood) rose to a maximum of 53 nCi on the 18th day following injection. This was reduced to 37 nCi by the use of DTPA over the next 66-day period. Little change is believed to have occurred in the body burden over the remainder of the period.

The plutonium-238 content of the employee's body was estimated by a material balance using data supplied in two letters(1,2). The first step was to estimate the amount of plutonium initially taken up by the employee's body by comparing data from blood analyses contained in Table 1 made within a few days of the accident with data from patients injected with Pu(IV) citrate by Langham's group(3). A least squares fit of Langham's data gave a line of regression defined by

$$Y = 22.5\ X^{-1.2} \qquad (i)$$

where X = the days after injection, and
Y = the percent of injected Pu(IV) citrate in the total blood volume.

A least squares fit of the plutonium concentration in the employee's blood during the first five days was then made. These data were selected for they represented a period before the plutonium concentrations in the blood could be greatly influenced by additional contributions of plutonium to the body from the wound site. A comparison of blood samples collected at various times after DTPA administration indicated little if any influence of this drug on the concentration of plutonium in the blood. Thus the use of DTPA was not considered when selecting blood data. The line of regression was restrained so that the slope equaled that calculated from data from Langham's group. This gave a line defined by

$$Y = 2.04\ X^{-1.2} \qquad \text{(ii)}$$

where Y = the Pu concentration in d/m/ml of blood.

This was multiplied by 5370 ml, estimated to be the volume of the employee's blood[1], to obtain the total amount of plutonium in his blood. An estimate of the initial quantity of plutonium injected into the employee's body was then obtained by dividing equation (ii) by equation (i). This amounted to 48,673 d/m.

The first sample of blood taken two and three-quarters hours after injection contained 4.2 d/m of plutonium per ml. Multiplying this by the blood volume or 5370 ml gave 22,554 d/m of plutonium in the blood. This plutonium, however, is included in amount injected. Therefore the quantity initially in the body, excluding the blood stream and finger, was 26,119 d/m or about 12 nCi.

The next step was to determine the total quantity of plutonium which must be considered here. This does not include plutonium excised initially or that found on dressings and other materials external to the body. The quantity of plutonium which remained in the injured finger after the first excision was estimated using data obtained from measurements with the wound monitor[2]. This was a 5-inch diameter by 1-mm thick sodium iodide scintillation crystal operated inside the whole body counter shield. These data, which are contained in Table 2 and plotted in Figure 1, were adjusted to account for an estimated 1/16-inch tissue absorption. The quantity of plutonium in the injured finger during the first 18 days after the accident can be represented by the equation

$$Y = 180{,}000\ \exp\left(-\frac{.693X}{5}\right) \qquad \text{(iii)}$$

where Y = the amount of Pu in d/m, and
X = the days after the injury.

From this, the quantity of plutonium initially available to the body from the injured finger was estimated to be 180,000 d/m.

Thus the sum of the plutonium initially injected into the blood and body or 48,673 d/m and that available for later incorporation into the body from the wound site or 180,000 d/m is 228,673 d/m or 103 nCi. There is the possibility that some plutonium may have been injected deep into the knuckle capsule where it could not be measured by the wound monitor. However the trend in the blood data thus far indicates that, if this is the case, it does not represent a major source of plutonium to the body.

The amount of plutonium in the body itself on day X was next calculated as the difference between 103 nCi and the following measured quantities:

- plutonium in the finger on day X
- plutonium in the blood on day X
- total plutonium excreted in urine by day X

- total plutonium excreted in feces by day X
- total plutonium excised by day X.

A second excision was made on the 18th day. An estimate of the plutonium removed by this operation was made as follows:

- the amount of plutonium remaining in the injured finger on the 18th day was calculated to be 14,844 d/m using equation (iii).
- the three wound monitor measurements following the second excision (see Figure, 1) can be represented by

$$Y = 14{,}000 \exp\left(- \frac{.693X}{26.5}\right). \qquad \text{(iv)}$$

From this relationship, the amount of plutonium remaining after the excision was calculated to be 8,743 d/m.

The amount of plutonium excised, which is the difference between the above two figures, was thus 6,101 d/m. This value may be high by a factor of two, for only 3,068 d/m could be found by counting the excised tissue and gauze. However, some plutonium may have been lost during the operation.

The blood concentrations used in the material balance were obtained from a least squaresfit of the data in Table 1 and Figure 2. This gave a line of regression (the straight line in figure 2) of

$$Y = .61\ X^{-.82} \qquad \text{(v)}$$

where Y = the plutonium concentration in d/m/ml of blood.

Because there seemed to be little influence by DTPA on blood concentration, all data were used. (The lack of response in blood concentration to DTPA was probably due to the fact that, in all but three cases, blood samples were collected just prior to DTPA injection. However on days 36, 39 and 40 the blood samples were taken just after DTPA injections and these data do not appear to be out of line with the others.) The concentrations calculated from equation (v) were multiplied by the volume of blood or 5370 ml to obtain the total amount of plutonium in blood on day X. These values, expressed in nCi, are given for 25 different times after the accident in Table 3.

The total quantities of plutonium excreted via urine and feces from the time of the accident until day X are given with the raw data on this case[1]. These are also given in Table 3.

The quantities of plutonium in the finger on day X were taken from Figure 1. These along with the calculated body burdens are given in Table 3. The body burdens at different times are also plotted in Figure 3.

Thus it is estimated that the employee's body accumulated a maximum of 53 nCi of plutonium during the first 18 days with the amount dropping to about 37 nCi after 84 days. Since this drop was principally due to the action of DTPA, it can be credited with the reduction of the body burden by about 30%.

The daily excretion of plutonium in urine, given in Table 4 and plotted in Figure 4, could not be related to body content. An attempt was made using the equation

$$Y = 61200 \sum_{T=0}^{18} \exp\left(-\frac{.693T}{5}\right)(X-T)^{-2.2}. \qquad \text{(vi)}$$

This is the upper curve in Figure 4. It is based on the concept that plutonium leaves the finger for the body at a rate

$$R = A \exp\left(-\frac{.693T}{5}\right) \qquad \text{(vii)}$$

for 18 days. Each day, T, this quantity is fixed in the body and excreted as an independent acute assimilation

$$Y = R\,(X-T)^{-2.2}. \qquad \text{(viii)}$$

The excretion on any day, X, is then the sum of these 18 independent assimilations. Assuming the same fraction of assimilated plutonium is excreted as in cases reported by Langham's group,

$$\frac{61200}{.0023} \sum_{T=0}^{18} \exp\left(-\frac{.693T}{5}\right) = 1.89 \times 10^{8} \text{ d/m} \qquad \text{(ix)}$$

or 8.5×10^{4} nCi would have to be assimilated to give these results.

From this it is evident that plutonium in a wound site has a more direct influence on the urinary excretion than previously supposed. A base line represented by

$$Y = \begin{cases} 3333\, X^{-0.426}, & X \leq 18 \\ 708748\, X^{-2.28}, & X \geq 18 \end{cases} \qquad \text{(x)}$$

was fitted to the data to aid in analysis. Values for Y are given in Table 4 and plotted as the lower curve in Figure 4. As a test of the fit of this curve and an indication of the effect of DTPA, the ratio of the actual excretion rate to Y is also given in Table 4 and plotted in Figure 5. An indication that the influence of the plutonium in the wound on the urinary excretion rate overshadows that of the plutonium in the rest of the body is the high negative power of the time function. Here 2.28 was needed to fit the date while data from Langham's group(3) gave a range of from 0.46 to 1.31(4). Integrating the area under this curve from 85 days to infinity gave a total amount of plutonium yet to be excreted of 2858 d/m or 1.29 nCi, which is slightly more than the plutonium in the finger at that time.

A possible explanation of this influence may lie in the chemical form of the plutonium leaving the wound site. If this form is readily cleared from the blood by the kidney while that from the rest of the body is not, the blood will reflect the plutonium content of the bone and liver while the urine will reflect the plutonium leaving the wound. This could also explain why DTPA seemed to have little effect on the level of plutonium in the blood.

Of all the data, the excretion of plutonium in the feces, given in Table 5 and Figure 6 is the most difficult to interpret. There seems to be little correlation between the administration of DTPA and the excretion rate. The excretion rate is lower than one would expect from the urine data. The ratio of the fecal to the urinary excretion rates obtained by Langham's group ranged from 3.13 on the first day to 0.69 on the 76th day. It is interesting, however, that the ratios in 8 of the 22 samples ranged between .05 and .06.

A least squares analysis of the fecal data gave a line of regression represented by the solid line in Figure 6 and equation

$$Y = 3487\, X^{-1.15} \qquad \text{(xi)}$$

where Y = the daily fecal excretion of plutonium expressed as d/m/day.

This compares with the line of regression obtained by Langham's group[3] of

$$Y = 0.63\, X^{-1.09} \qquad \text{(xii)}$$

where Y = the daily fecal excretion of plutonium expressed as percent of the injected dose.

Assuming that the higher values in Figure 6 probably were due to the influence of DTPA, a least squares fit of the four lowest values was made. The line of regression obtained was restrained so that the slope was the same as that in equation (xii). This is represented by the dashed line in Figure 6 and the equation

$$Y = 1053\, X^{-1.09} \qquad \text{(xiii)}$$

where Y = the daily fecal excretion of plutonium expressed as d/m/day.

By dividing equation (xiii) by (xii), a body burden of plutonium of 167,222 d/m or 75 nCi was obtained. This is about 43% higher than the amount predicted by the material balance method, which could be the result of the influence of plutonium from the wound site.

Additional fecal samples collected when there is no influence from DTPA are needed to better evaluate the meaning of the fecal data. These have been requested.

Thus all data with the exception of those from urinalyses indicate a quantity of plutonium-238 in the employee's body which reached a maximum of about 132% of the MPBB. This has since been reduced to about 92% of the MPBB. The urine data, however, have brought to light some interesting aspects of plutonium metabolism which could be studied further.

Summary

The plutonium-238 content of the employee's body was estimated by a material balance outlined in Figure 7. The plutonium remaining in the finger and body (including blood) after the first excision was estimated to be 103 nCi. This included 22 nCi removed from the wound site immediately and 81 nCi which remained in the finger. The estimate of the plutonium removed from the wound site was based on a comparison of blood analyses during the first five days with those from patients injected with known amounts of plutonium (IV) citrate. 10 nCi of this was calculated to be initially in the blood by taking the product of the blood concentration and volume. The plutonium initially in the wound site was estimated by extrapolating wound monitor measurements back to time 0.

If this total of 103 nCi is correct, then the amount of plutonium in the body is the difference between it and all other measurable quantities including plutonium in the blood and finger, plutonium excreted in the urine and feces, and excised plutonium. These calculations indicate that the employee's body burden rose to 53 nCi (1.32 MPBB) just before the second excision on the 18th day. During this period 92 percent of the plutonium in the finger was released. Of this amount, 58 percent was excreted. Had this gone to the body first and then been excreted, only about 3 percent would have been eliminated. Thus the use of DTPA may have caused the excretion of 55 percent of the plutonium released from the finger.

The level of plutonium fixed in the body usually remains fairly constant. Thus a reduction to 37 nCi (.92 MPBB) over the next 66 days indicates that DTPA given during this period was probably responsible for removing about 30 percent of the plutonium from the body.

Only 3.4 percent of the plutonium was removed from the finger by the second excision. This was due to the lateness of the operation. Actually 41 percent of the plutonium present at the time of the operation was excised.

The material balance can not be extended beyond the 84th day with any accuracy. It is estimated that 1.5 nCi was excreted in the urine and feces between the 84th and 259th days. Some of this probably came from the finger. Thus at the end of this period the employee's body probably contained between 36 and 37 nCi.

Oct. 3, 1969

References:

1. Plutonium-238 Assimilation, Savannah River Plant, November 29, 1969. (June 3, 1969)

2. Letters from C. M. Patterson to W. H. Langham and W. S. Snyder (July 23, 1969).

3. W. H. Langham et al., Distribution and Excretion of Plutonium Administered Intravenously to Man, LA-1151 (Sept. 20, 1950).

4. E. L. Geiger and S. M. Sanders, Jr., Acute Uptake of Plutonium and Uranium Following Wound Contamination, Proceeding of the Health Physics Society (June 1956).

SMS:hp

TABLE 1

PLUTONIUM CONCENTRATION IN THE BLOOD

Days After Accident	Blood Conc. (d/m/ml)	Days After Accident	Blood Conc. (d/m/ml)	Days After Accident	Blood Conc. (d/m/ml)
0.115	4.2	32	.039	67	.033
1.15	1.3	34	.050	68	.005
2.15	.27	36	.033	70	.022
2.90	.12	39	.033	71	.021
3.92	.17	40	.024	74	.037
4.94	.24	41	.026	75	.015
6	.062	43	.024	77	.020
8	.27	46	.038	78	.016
10	.19	47	.031	81	.016
11	.071	50	.023	82	.013
13	.034	54	.037	87	.027
14	.044	57	.027	102	.020
18	.025	60	.031	116	.014
20	.034	61	.035	130	.007
21	.051	63	.017	144	.012
31	.076	64	.009		

TABLE 2

WOUND MONITOR DATA

Days After Accident	Pu in Finger (d/m)	Days After Accident	Pu in Finger (d/m)
3	119,000	40	4,930
6	69,000	48	4,420
13	33,300	57	3,740
17	17,000	64	3,540
21	8,040	76	3,280
31	6,270	84	2,380

TABLE 3

MATERIAL BALANCE OF PLUTONIUM

Days After Accident	Pu in Finger (nCi)	Pu in Blood (nCi)	Pu in Excreted Urine (nCi)	Pu in Excreted Feces (nCi)	Pu Excised (nCi)	Pu in Body (nCi)
0	81.08	10.16				11.76
1	70.59	1.48	1.50			29.44
2	61.45	.84	4.85	.62		35.25
3	53.49	.60	11.24	.99		36.68
4	46.57	.48	12.74	2.32		40.89
5	40.54	.39	13.50	2.60		45.98
6	35.29	.34	18.67	2.91		45.79
7	30.72	.30	21.45	3.21		47.32
8	26.75	.27	24.89	3.27		47.83
9	23.28	.24	26.45	3.59		49.44
10	20.27	.22	28.08	3.62		50.81
12	15.36	.19	32.89	3.76		50.79
14	11.64	.17	34.84	3.86		52.49
16	8.82	.15	37.50	4.01		52.52
18	3.94	.14	39.38	4.10	2.75	52.70
20	3.74	.13	41.14	4.18	2.75	51.07
31	2.80	.09	45.32	4.43	2.75	47.62
35	2.52	.08	48.64	4.52	2.75	44.49
40	2.21	.07	50.67	4.59	2.75	42.71
45	2.04	.06	52.03	4.66	2.75	41.46
50	1.88	.06	52.99	4.88	2.75	40.45
60	1.64	.05	53.76	5.30	2.75	39.51
70	1.52	.05	55.49	5.37	2.75	37.83
80	1.42	.04	56.55	5.48	2.75	36.77
84	1.07	.04	56.88	5.52	2.75	36.74

TABLE 4

URINARY EXCRETION

Days After Accident X	Days After DTPA	Urinary Excretion U (d/m/day)	Y (d/m/day)	$\frac{U}{Y}$	Days After Accident X	Days After DTPA	Urinary Excretion U (d/m/day)	Y (d/m/day)	$\frac{U}{Y}$
1	-	3,333	3,333	1.00	60	1	740	62.4	11.85
2	1	7,441	2,480	3.00	61	1	660	60.1	10.98
3	1	14,178	2,087	6.79	62	2	177	57.9	3.06
4	1	3,330	1,846	1.80	63	1	585	55.9	10.47
5	2	1,680	1,679	1.00	64	1	550	53.9	10.21
6	1	11,486	1,553	7.40	65	2	170	52.0	3.27
7	2	6,180	1,454	4.25	66	3	157	50.2	3.13
8	1	7,622	1,374	5.55	67	1	590	48.5	12.15
9	2	3,461	1,307	2.65	68	1	400	46.9	8.52
10	3	3,621	1,249	2.90	69	2	185	45.4	4.08
11	1	5,770	1,199	4.81	70	1	350	43.9	7.97
12	1	4,922	1,156	4.26	71	1	290	42.5	6.82
13	2	982	1,117	.88	72	2	180	41.2	4.34
14	1	3,342	1,082	3.09	73	3	97	39.9	2.43
15	1	4,589	1,051	4.37	74	1	460	38.7	11.89
16	2	1,320	1,022	1.29	75	1	305	37.5	8.13
18	1	3,980	972	4.09	76	2	165	36.4	4.53
19	1	2,955	860	3.48	77	1	340	35.3	9.62
20	2	950	765	1.24	78	1	295	34.3	8.60
21	3	2,763	684	4.04	79	2	130	33.3	3.90
32	1	3,297	262	12.59	80	3	97	32.4	2.99
33	1	2,271	244	9.30	81	1	265	31.5	8.42
34	2	741	228	3.25	82	1	265	30.6	8.65
35	1	1,080	213	5.06	83	2	112	29.8	3.76
36	1	1,557	200	7.78	84	3	82	29.0	2.83
37	2	498	188	2.65	85	4	48	28.2	1.70
38	3	208	177	1.18	86	5	51	27.5	1.86
39	1	1,348	167	8.08	87	6	41	26.8	1.53
40	1	890	157	5.65	95	14	24	21.9	1.10
41	2	520	149	3.50	102	21	16	18.6	.86
42	1	1,117	141	7.93	109	27	16	16.0	1.00
43	1	775	133	5.81	110	29	7.8	15.7	.50
44	2	336	127	2.65	116	35	11	13.9	.79
45	3	270	120	2.24	117	36	13	13.6	.95
46	1	810	114	7.08	118	37	11	13.4	.82
47	1	690	109	6.33	130	49	6.0	10.7	.56
48	2	255	104	2.46	131	50	8.6	10.5	.82
49	3	205	99.1	2.07	132	51	6.9	10.3	.67
50	4	165	94.6	1.74	137	56	8.1	9.50	.85
51	5	155	90.4	1.71	138	57	7.6	9.34	.81
52	6	100	86.5	1.16	144	63	5.9	8.48	.70
53	7	87	82.8	1.05	145	64	5.0	8.35	.60
54	8	115	79.4	1.45	146	65	6.4	8.22	.78
55	9	80	76.1	1.05	151	70	7.4	7.61	.97
56	10	97	73.1	1.33	152	71	6.6	7.50	.88
57	11	73	70.2	1.04	158	77	7.7	6.86	1.12
58	12	119	67.4	1.76	159	78	5.6	6.76	.83
59	13	156	64.9	2.40	160	79	5.6	6.67	.84

[illegible]

URINARY EXCRETION

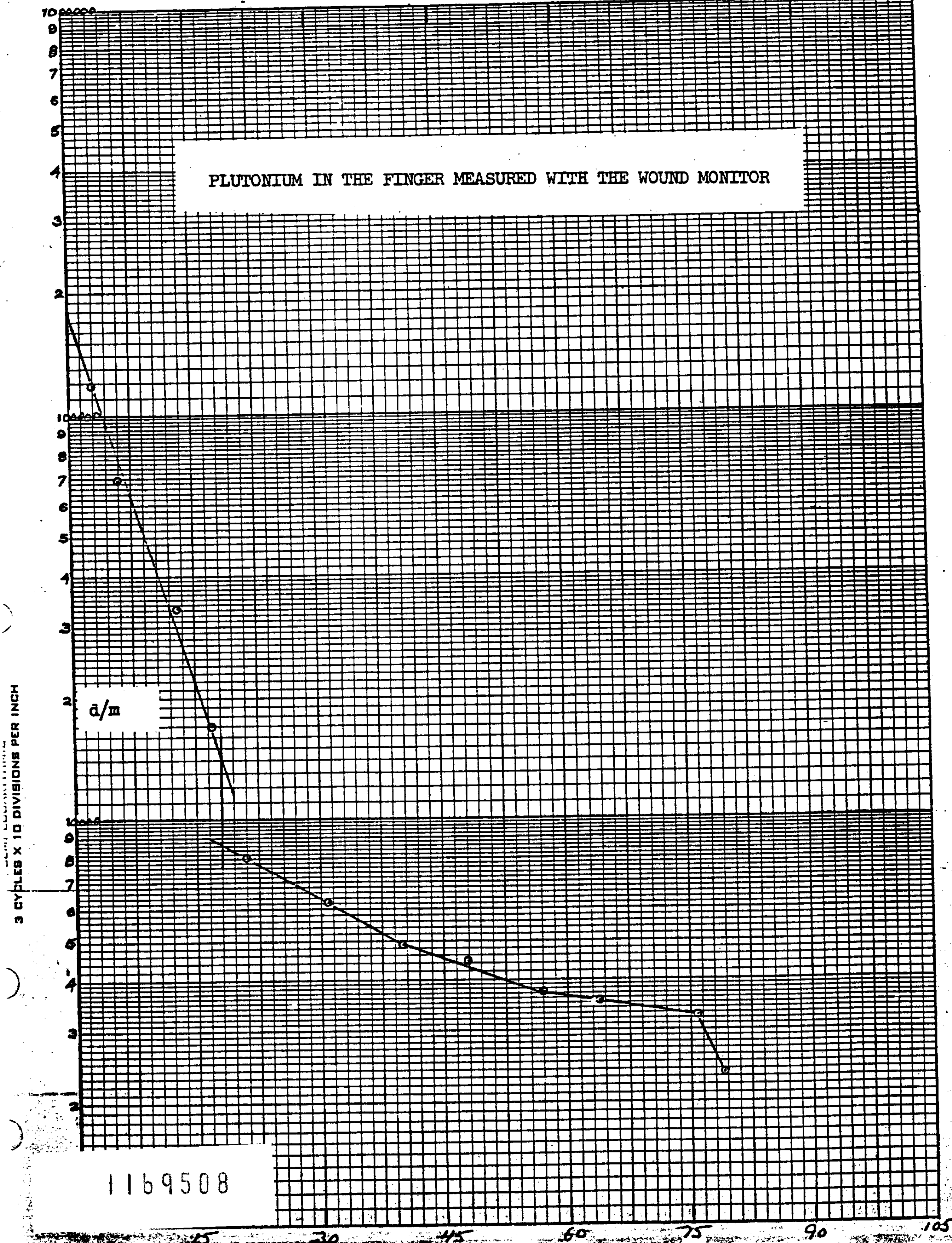
Days After Accident X	Days After DTPA	Urinary Excretion U (d/m/day)	Y (d/m/day)	U/Y
172	91	5.4	5.65	.96
173	92	5.2	5.58	.93
190	109	4.2	4.51	.93
191	110	4.9	4.45	1.10
202	121	2.7	3.92	.69
203	122	6.3	3.87	1.63
218	137	2.7	3.29	.82
219	138	3.6	3.26	1.10
230	149	3.5	2.91	1.20
231	150	4.0	2.89	1.39
246	165	2.5	2.50	1.00
247	166	2.3	2.48	.93
258	177	2.8	2.24	1.25
259	178	2.6	2.22	1.17

TABLE 5

FECAL EXCRETION

Days After Accident	Days After DTPA	Fecal Excretion F (d/m)	Urinary Excretion U (d/m)	F/U
2	1	1,374	7,441	.19
3	1	826	14,178	.06
4	1	2,950	3,330	.89
5	2	615	1,680	.37
6	1	700	11,486	.06
7	2	665	6,180	.11
8	1	127	7,622	.02
9	2	710	3,461	.21
10	3	69	3,621	.02
11	1	80	5,770	.01
12	1	250	4,922	.05
13	2	60	982	.06
14	1	150	3,342	.05
15	1	230	4,539	.05
31	9	79	-	-
34	2	25	741	.03
41	2	30	520	.06
49	3	76	205	.37
55	8	92	80	1.15
62	2	55	177	.31
70	1	21	350	.06
76	2	22	165	.13

FIGURE 1



PLUTONIUM IN THE FINGER MEASURED WITH THE WOUND MONITOR

FIGURE 2

THE CONCENTRATION OF PLUTONIUM IN BLOOD

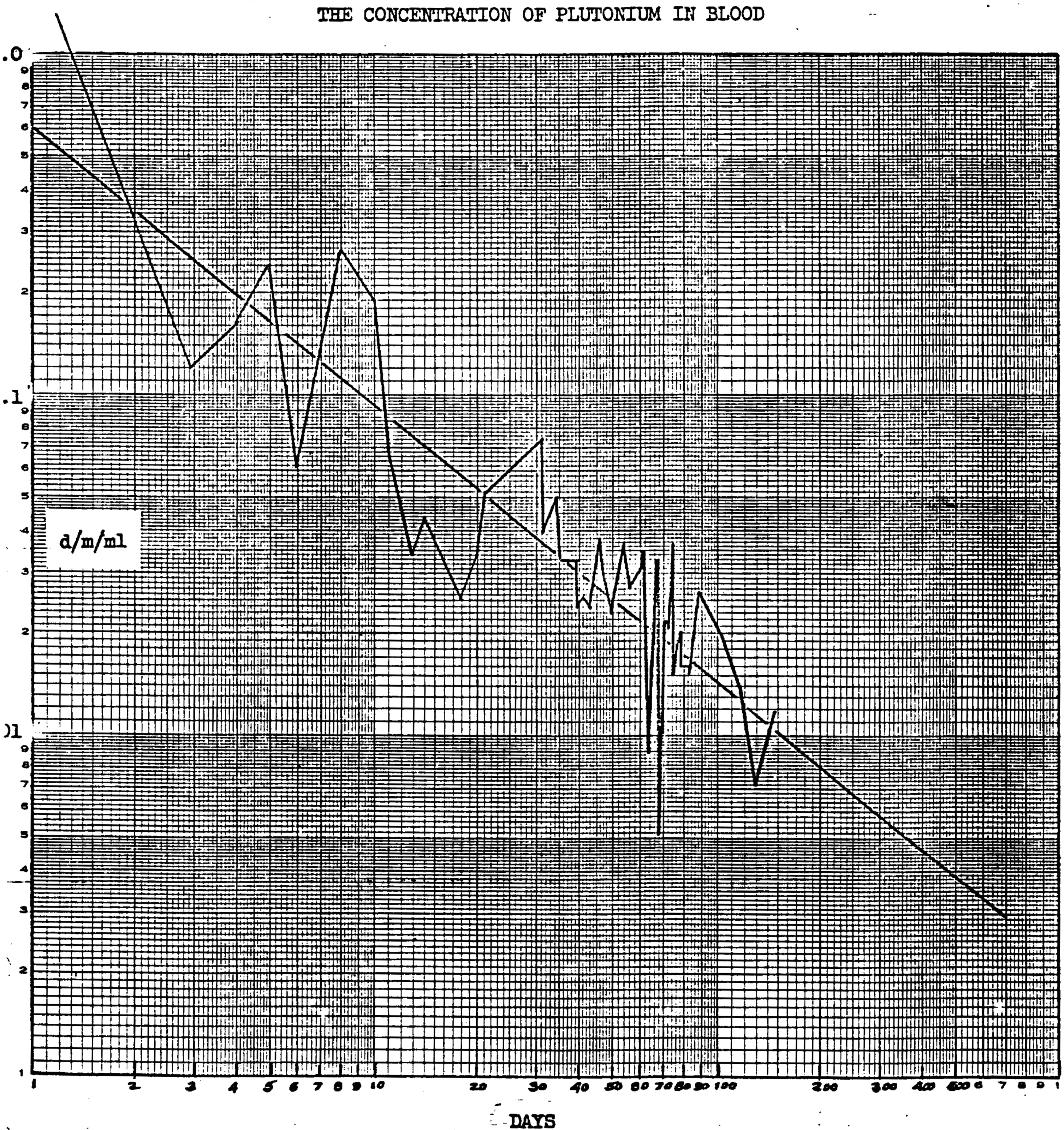


FIGURE 3

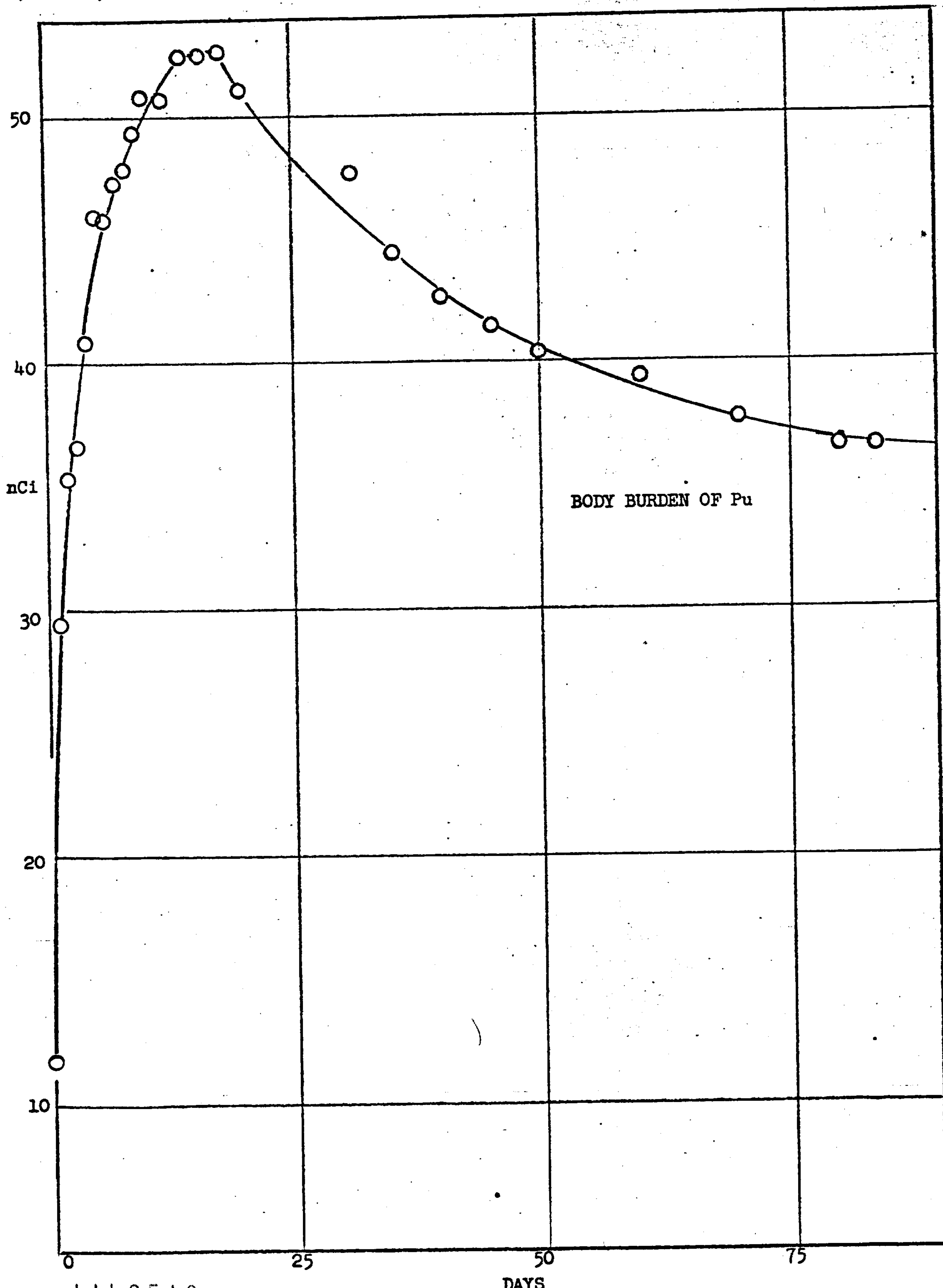


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FIGURE 4

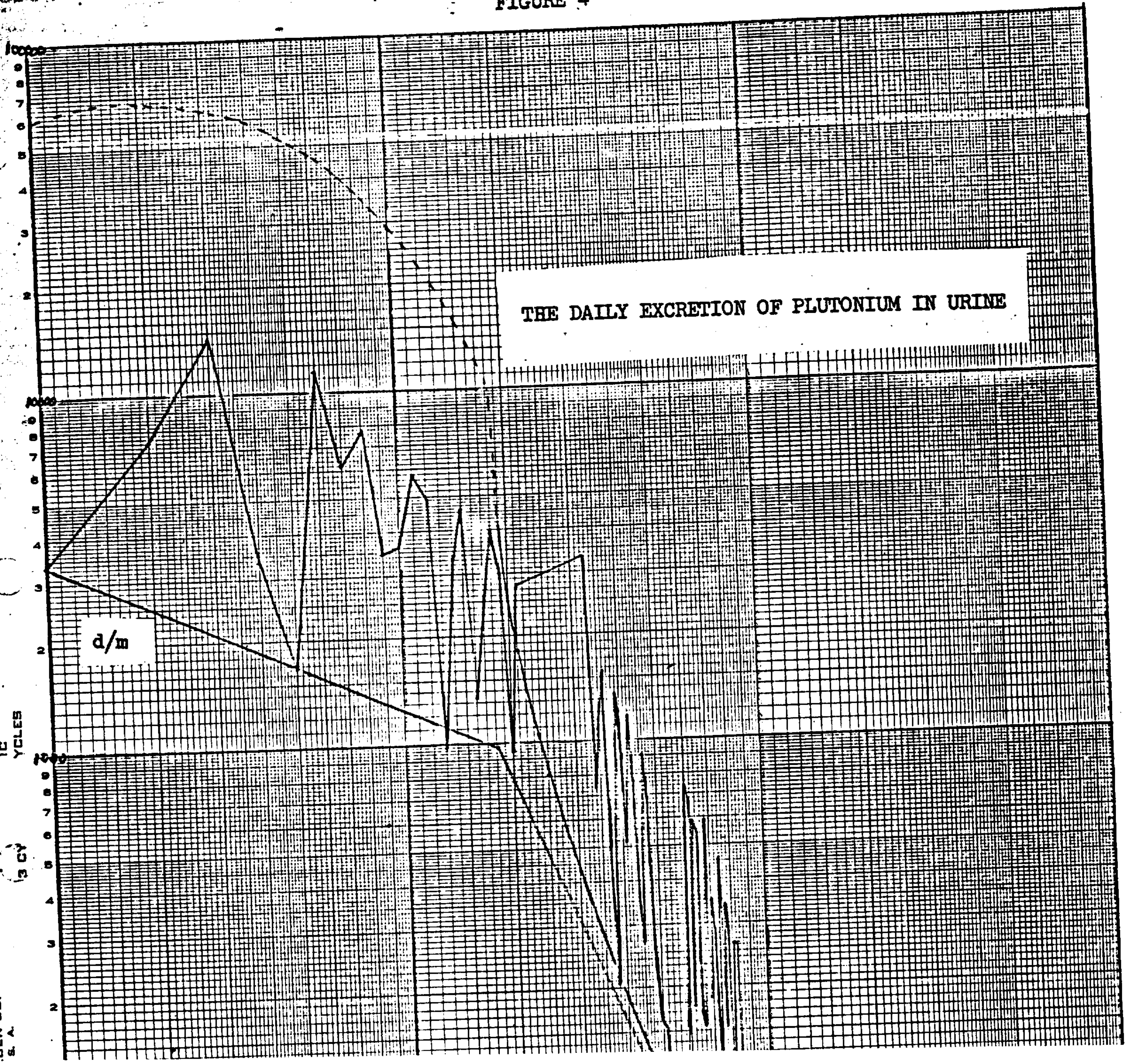

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FIGURE 5

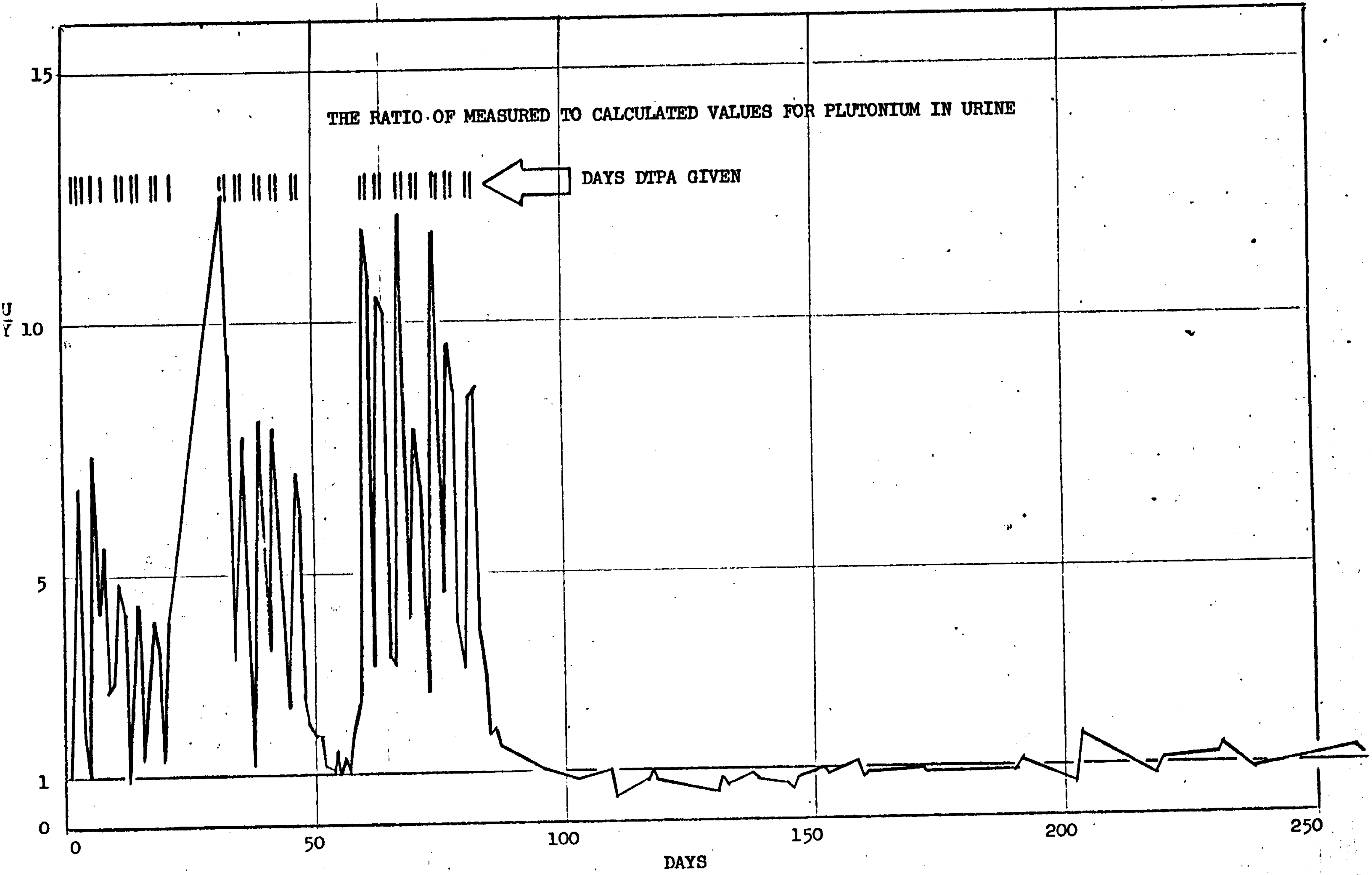
THE RATIO OF MEASURED TO CALCULATED VALUES FOR PLUTONIUM IN URINE
DAYS DTPA GIVEN
U/Y
15
10
5
1
0
0
50
100
150
200
250
DAYS

FIGURE 6

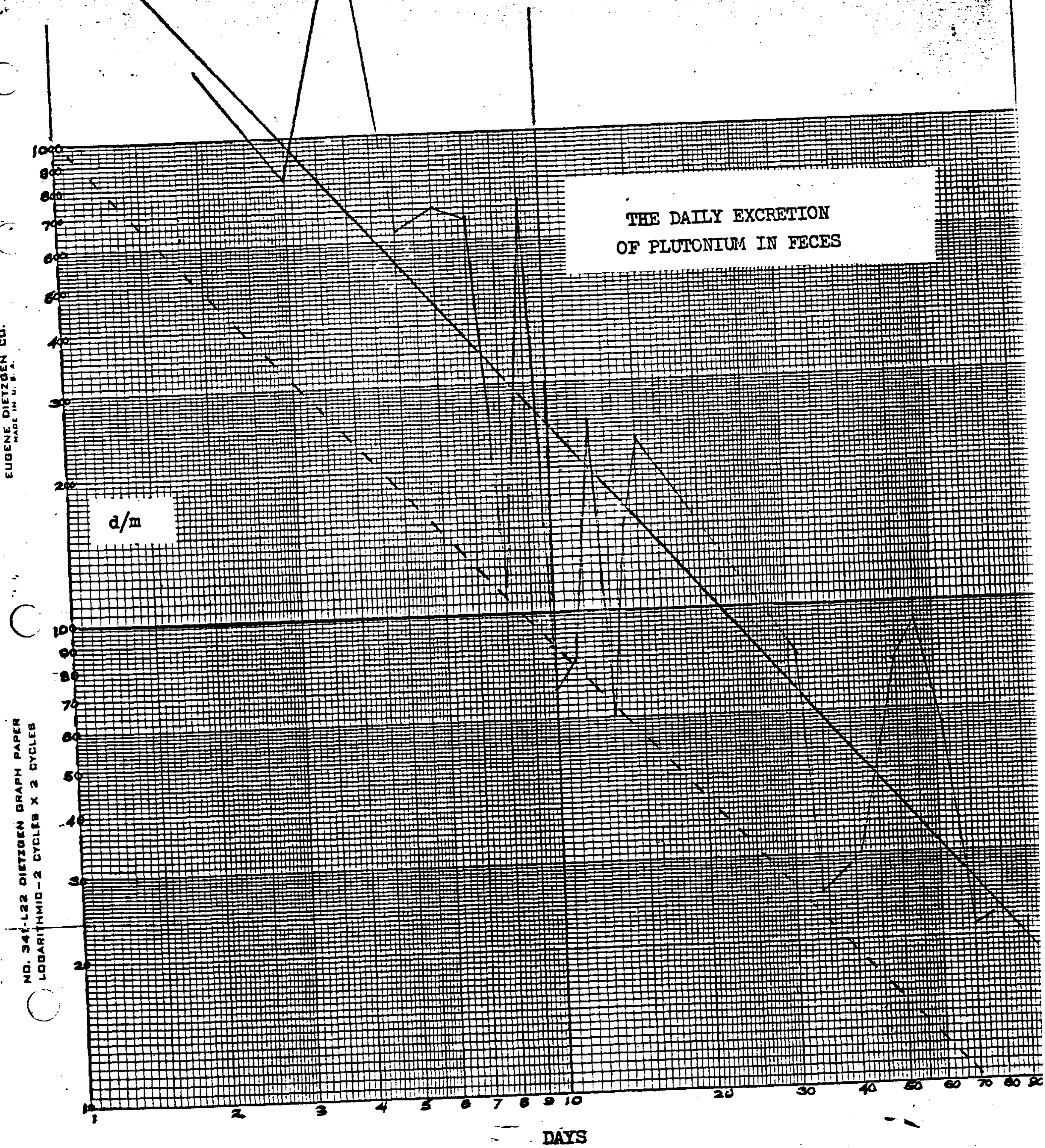

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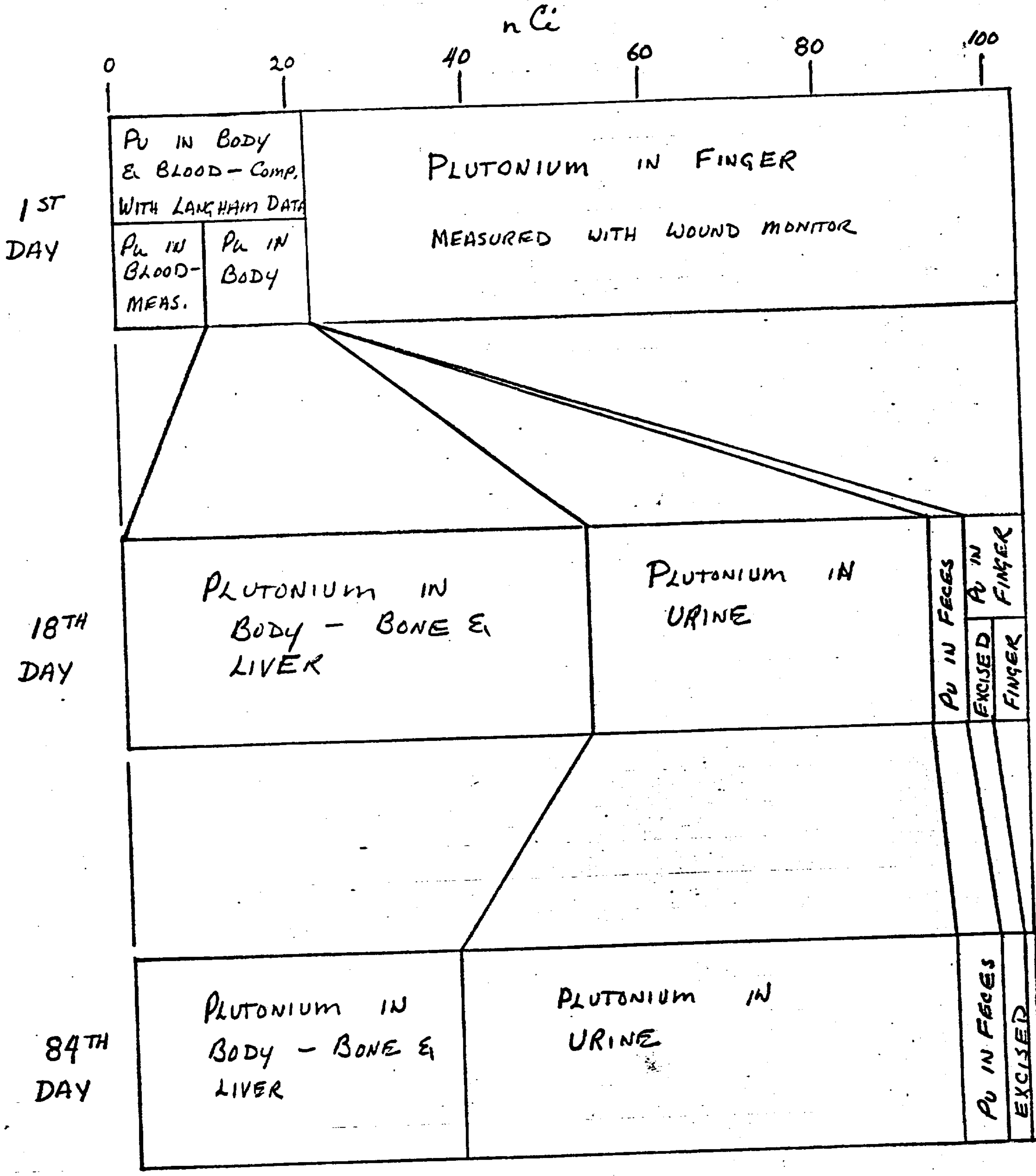
FIGURE 7

OUTLINE OF MATERIAL BALANCE OF PLUTONIUM



UNIVERSITY OF CALIFORNIA
LOS ALAMOS SCIENTIFIC LABORATORY
(CONTRACT W-7405-ENG-36)
P. O. Box 1663
Los Alamos, New Mexico 87544

IN REPLY
REFER TO:

H-4

September 2, 1969

SEP 4 1969

Walter S. Snyder, Ph.D.
Health Physics Division
Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830

Dear Walter:

Enclosed are Healy's and Lawrence's contributions on the Savannah River Case. Treat it as privileged information as Patterson seems to want it that way. I hope you, Healy and Lawrence can get together during your forthcoming visit to Los Alamos.

I am about out of the exposure prediction business and have given the responsibility to them.

Sincerely,

Wright H. Langham
Biomedical Research Group

WHL:gm
Encl. 2 Memorandums

1169515

LOS ALAMOS SCIENTIFIC LABORATORY
UNIVERSITY OF CALIFORNIA
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OFFICE MEMORANDUM

TO : James N.P. Lawrence, Assoc. Group Leader, H-1

DATE: July 24, 1969

FROM : J. W. Healy, H-1

SUBJECT: SAVANNAH RIVER DATA

SYMBOL : H-1

I have reviewed the bioassay data from Savannah River and have attempted an independent appraisal. This is a very complicated situation due to the possible presence of a pool of plutonium in the wound, possibly feeding into the blood, a probable immediate uptake and the unknown effects on excretion rate of the chelating agents used. I would consider the following analysis a very preliminary look since there are other possibilities which could be tried, particularly with respect to the possible uptake from the wound over a period of time.

Wound Counter: The data from the wound counter are plotted in Fig. 1. A second excision was made on the 18th day which coincides with the end of the sudden drop which started on the 12th day. However only 2400 dis/min were measured on the excised sample. It is, therefore, unknown whether this shape is due to an artifact in the data, the plutonium was lost by surface cleaning or some 10^5 dis/min were absorbed from the site between the 12th and 18th day. It seems unlikely that the material would remain for 12 days and then suddenly slough off or absorb. If this curve could be explained, it could be helpful in a more detailed examination of the data.

Urine Data: A plot of the urine data shows a wide scatter in the initial portion up to 30-40 days, a rapid drop at about 46 days when chelation was discontinued for a short period, a recovery when chelation was resumed, and a second drop when chelation was finally stopped (Fig. 2). Incidentally, I have proceeded on the assumption that these data represent the full excretion although there are some periods where no sample is given. For example, from 2:15 p.m. on 11/29 to 12 noon on 11/30 (16-17 hours) or from 6:00 p.m. on 12/2 to 1:30 p.m. on 12/3 (19-20 hours). Another feature of the curve is the apparent curvature in the period from 50-80 days. I have plotted a $t^{-0.74}$ line on this curve to indicate the deviation.

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For purposes of analysis, it was assumed that the chelating agents increased the excretion rate in the urine by a factor "a". It was further assumed that the excretion rate of the amount remaining in the body was given by $0.002aBt^{-0.74}$ where B is the body burden remaining at time t. In other words, Langham's equations were assumed to apply with the enhanced excretion rate but corrected for the amount remaining in the body. The body burden was then computed assuming the loss to be only in the urine. This was justified for this preliminary analysis by noting that the cumulative excretion in the feces was only about 10% of that in the urine. The body burden can then be computed from:

$$dB = -\ 0.002aBt^{-0.74dt}$$

using the condition that $B=B_o$ when t=1 day.

Several values of a were assumed based upon Thompson's writeup in the Plutonium Handbook. The simplest was that a was constant during the period of administration. Under these conditions B is given by:

$$\ln \frac{B}{B_o} = -\ \frac{0.002a}{0.26}\ [t^{0.26}-1]$$

Since there is also some indication that the effectiveness of DTPA decreases with time, factors of the form a = b-ct were tried. Under these conditions the body burden is given by:

$$\ln \frac{B}{B_o} = -\ \left(\frac{0.002b}{0.26}\ [t^{0.26}-1]\ -\ \frac{0.002c}{1.26}\ [t^{1.26}-1]\right)$$

The excretion rate is then given by Langham's equation corrected for the enhancement and for the decreased body burden due to prior excretion.

During the period of no chelation the excretion rate drops rapidly and the change in body burden is much slower. The data for the period following the cessation of chelation at 82 days is given in Fig. 3. The dotted line represents a $t^{-0.24}$ slope fitted to the points past 130 days while the other curves represent exponentials obtained by successive subtractions. In other words, at 82 days, the effect of the DTPA decreases with about 70% represented by a 1.5 day half-life and about 30% by an 11 day half-life. I hold no special brief for these numbers except that they were used to represent the fall-off of the DTPA effect. Note that the plot indicates an enhancement of excretion by about a factor of ten at 82 days. This did influence my choice of c in the equation for a.

For the period following chelation, the excretion rate can be related to the excretion rate before chelation stops by:

$$E = E_Q\, B\left[0.7e^{-0.462(t-Q)} + 0.3e^{-0.063(t-Q)}\right] + 0.002\, Bt^{-0.74}$$

where Q is the time that chelation is stopped and E_Q is the excretion rate at this time. Although the change in body burden is not significant, the body burden related to the body burden at the time chelation is stopped (B_Q) can be written as:

$$\ln \frac{B}{B_Q} = -E_o\left[\frac{0.7}{0.426}\left(1-e^{-0.462[t-Q]}\right) + \frac{0.3}{0.063}\left(1-e^{-0.063[t-Q]}\right)\right]$$

$$+ \frac{0.002b}{0.26}\left[t^{0.26} - Q^{0.26}\right]$$

These equations were used to estimate body burden and excretion rates during the periods of no chelation.

The values of a chosen for trial were a=100, a=100-t, a=100-0.8t, and a=200-2t. At 82 days these relations would give an enhancement of the DTPA in urine excretion of 100, 18, 34, and 36. The functions chosen are entirely arbitrary as a part of an iteration process to see which would fit the data best.

The calculated curves are plotted against the urine data in Figs. 4 to 7 with the curve normalized to the data at an excretion rate of 6.3 dis/min at 150 days. The poorest fit seems to be the a=200-2t function with a=100 next. There is little to choose between the other two although the 100-0.8t seems a little better in the 60 to 82 day period. None of the calculated curves indicate as much of a drop in the 46 to 59 day period of no chelation as the actual data. This may indicate that the short component of the effectiveness decay curve is of more importance at this earlier time.

As another measure of the curve fit, I have plotted the cumulative excretion rate against the cumulative excretion predicted by the differences in calculated body burden (Fig. 8). The cumulative excretion at 150 days was taken as the base and the points represent the total excretion from the time given to 150 days. The curves were normalized at 100 days.

In each case, the calculated curve seems to be somewhat high at the early times. This may well be due to a continued movement from material in the wound into the bloodstream over the first few days. This would give a different result from the simple model used here where the administration is considered to be entirely at time zero and the calculations are based on the body burden at one day. Some effort was expended in attempting to compute typical curves for this effect but the equations need more study to see if an analytical solution can be found to avoid the numerical analyses. It was, therefore, considered that for this preliminary analysis the effect would be small and have little influence over the shape of the curve at longer times.

The estimate of the quantity of plutonium in the body can be made for each of these values of a from the excretion rates and the calculated values. If one assumes that Langham's equation holds after the period of chelation to represent the amount remaining in the body, an additional estimate can be made. All estimates were based on an excretion rate of 6.3 dis/min at 150 days.

Method	Body Burden at 150 days (μCi)	Extrapolated Burden at One Day (μCi)
Langham	0.058	0.12*
a=100	0.035	0.16
a=100-t	0.052	0.17
2=100-0.8t	0.047	0.17
a=200-2t	0.047	0.50

*Obtained by summing body burden at 150 days and total excretion.

Blood: The blood data are plotted in Fig. 9. Although the data on humans available for comparison covers only a period of about 30 days, it has earlier been fitted to a power function to give $0.0029t^{-1.3}$ as the content of the administered dose in the total blood volume. The line in Fig. 9 has been fitted with this slope to a concentration of 0.01 dis/min/mliter at 130 days. The data after chelation would not contradict such a fit although the amount of scatter makes it difficult to conclude that a fit exists.

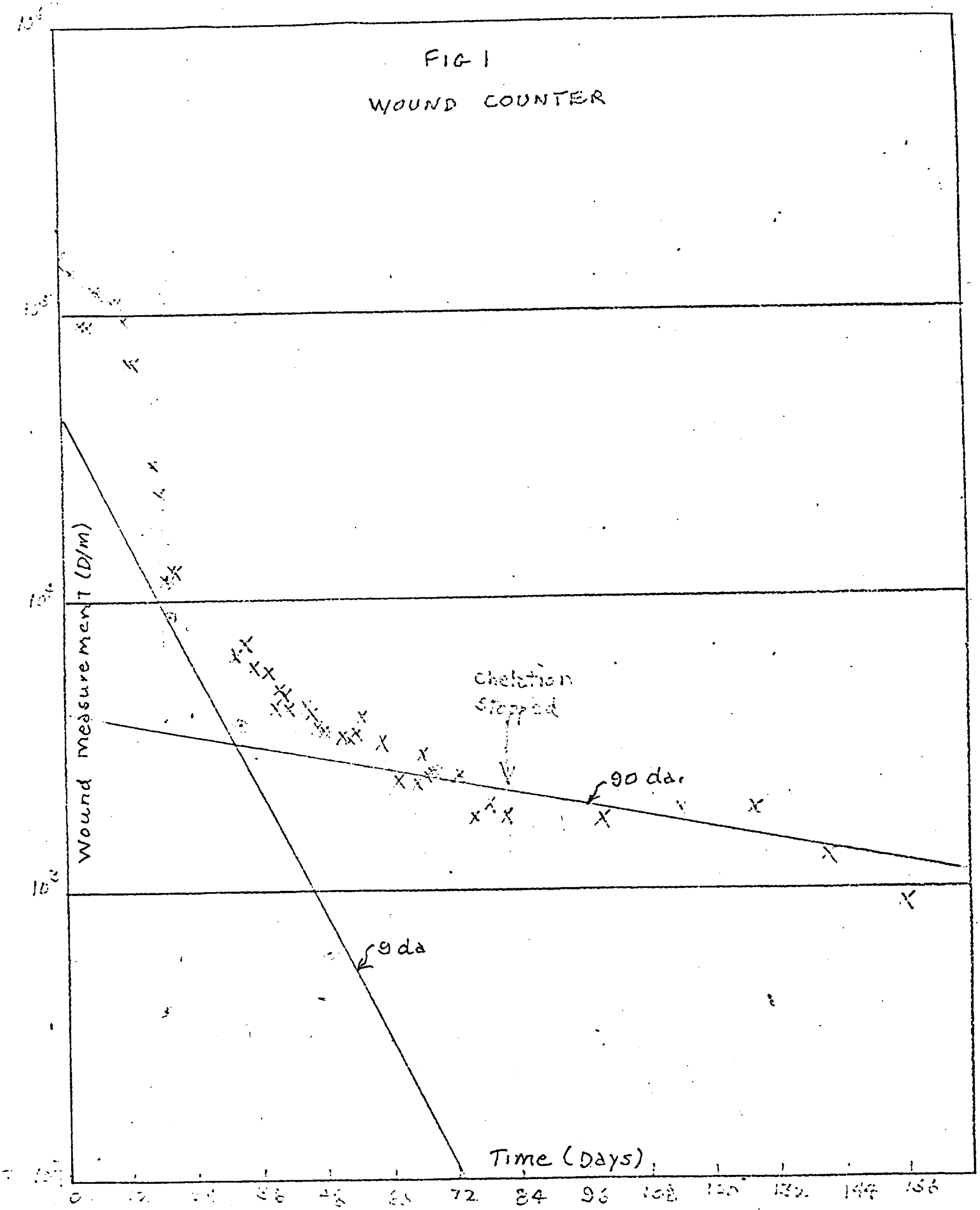
Using the above relation and a blood volume of 5370 mliters, a concentration of 0.01 dis/min/mliter at 130 days would be equivalent to a body burden of 0.05 μCi, a value in remarkable, but possibly fortuitous, agreement with the urine data. If this treatment of the data is accepted, the lower values of blood concentration for the first several weeks may be of significance in the effect of DTPA.

Feces: The fecal excretion is plotted in Fig. 10. The dotted line represents a slope of $t^{-1.09}$ as given by Langham. To show the effect of the change in body burden due to DTPA, each point was corrected for time by the Langham function and for the change in body burden using the a=100-0.8t function. The average of all points was computed and the solid line represents the fecal excretion for this quantity. No conclusions can be drawn by eye as to the fit, but the curve is not inconsistent with the data.

The estimated body burden at one day from the above treatment is 0.59 μCi or, since the function used predicts a body burden of about 28% of this at 150 days, about 0.17 μCi following chelation. This is considerably higher than the blood or urine estimate and may indicate an enhancement of fecal excretion by about a factor of three.

Conclusions: The present preliminary analysis would indicate that at least a portion of the excretion curve can be explained by the significant decrease of the body burden due to the DTPA treatment. Only a few of the possible pertubations which could be attributed to the effect of DTPA have been examined with no real attempt to find the best fit. There are some anomolies which could be studied further, as, for example, the possibility that the DTPA effectiveness returns to a higher value after the period of no use about the 50th day. Further work on the possibility of plutonium moving to the bloodstream during the first few days would be warranted to see if a better fit could be obtained. Careful study of data such as these could be useful in giving more information on the effectiveness of DTPA as well as a basis for interpretation of data from future cases where DTPA is used.

This preliminary estimate would indicate that the body burden at 150 days is in the range 0.05 to 0.06 μCi. The upper value may be somewhat better since the possible effect of continued administration from the wound has not been made.



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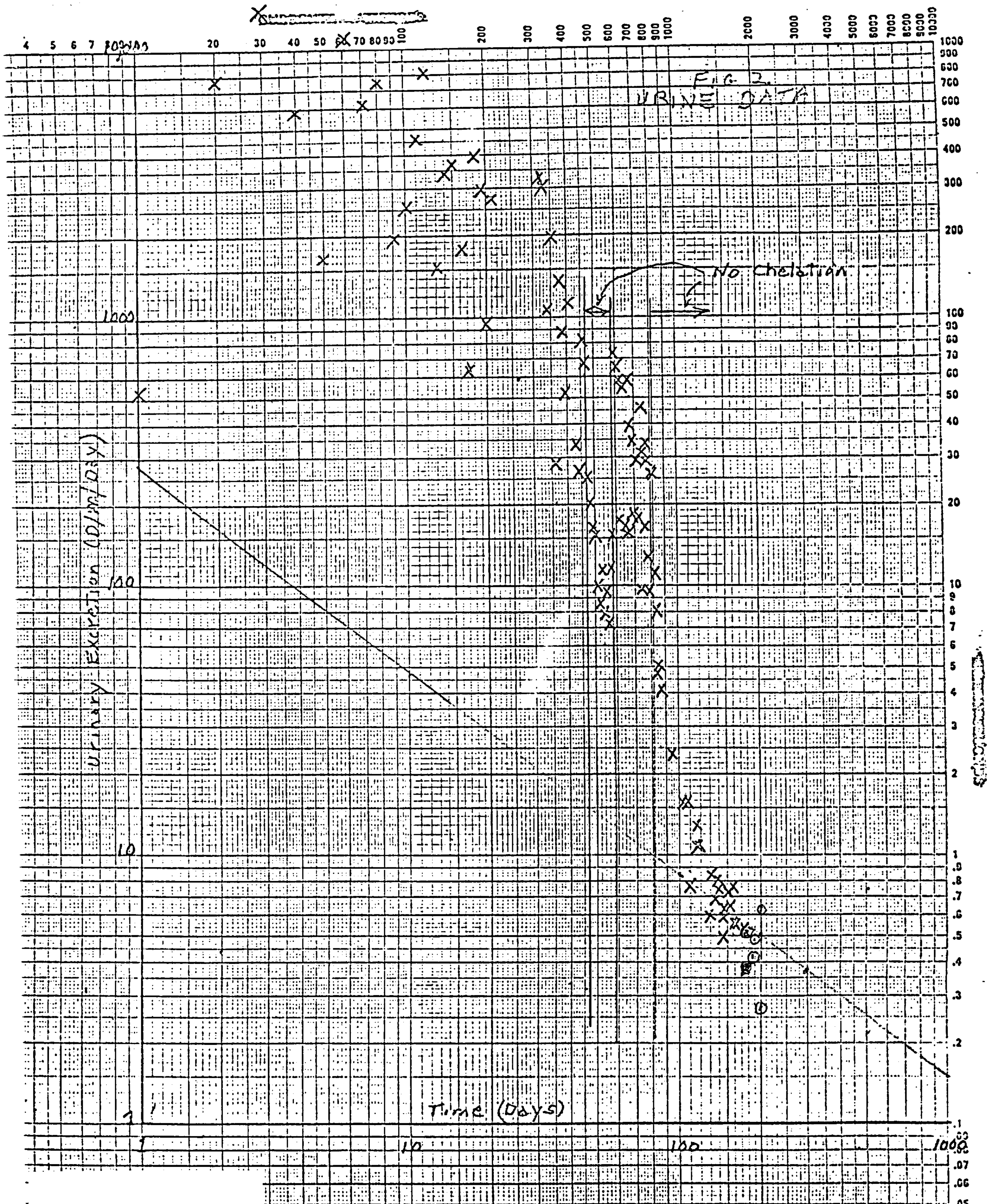
FIG 2.
URINE DATA
No Chelation
Urinary Excretion (D/m/Day)
Time (Days)
1000
100
10
1
10
100
1000

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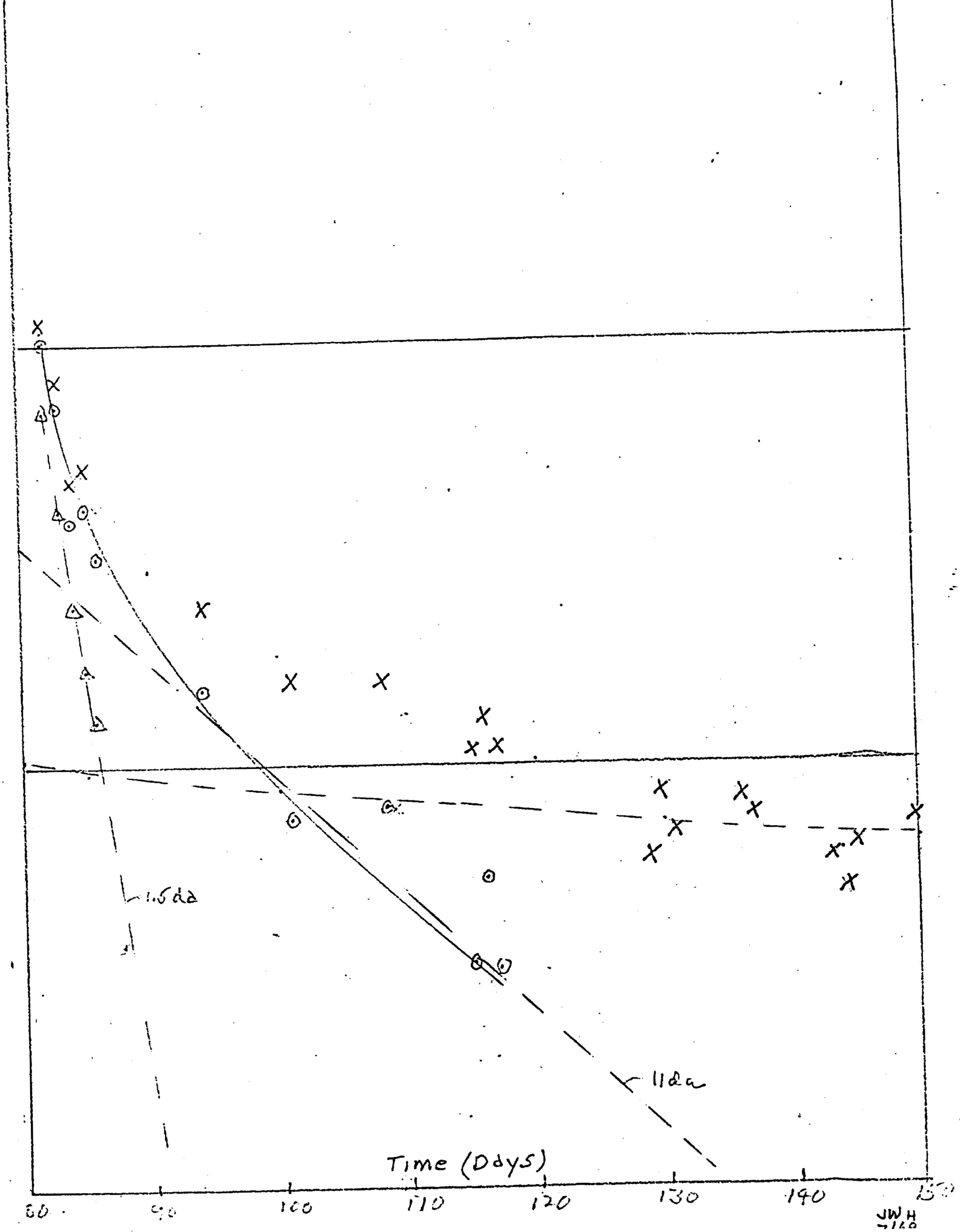
FIG 3
EXCRETION AFTER CHELATION



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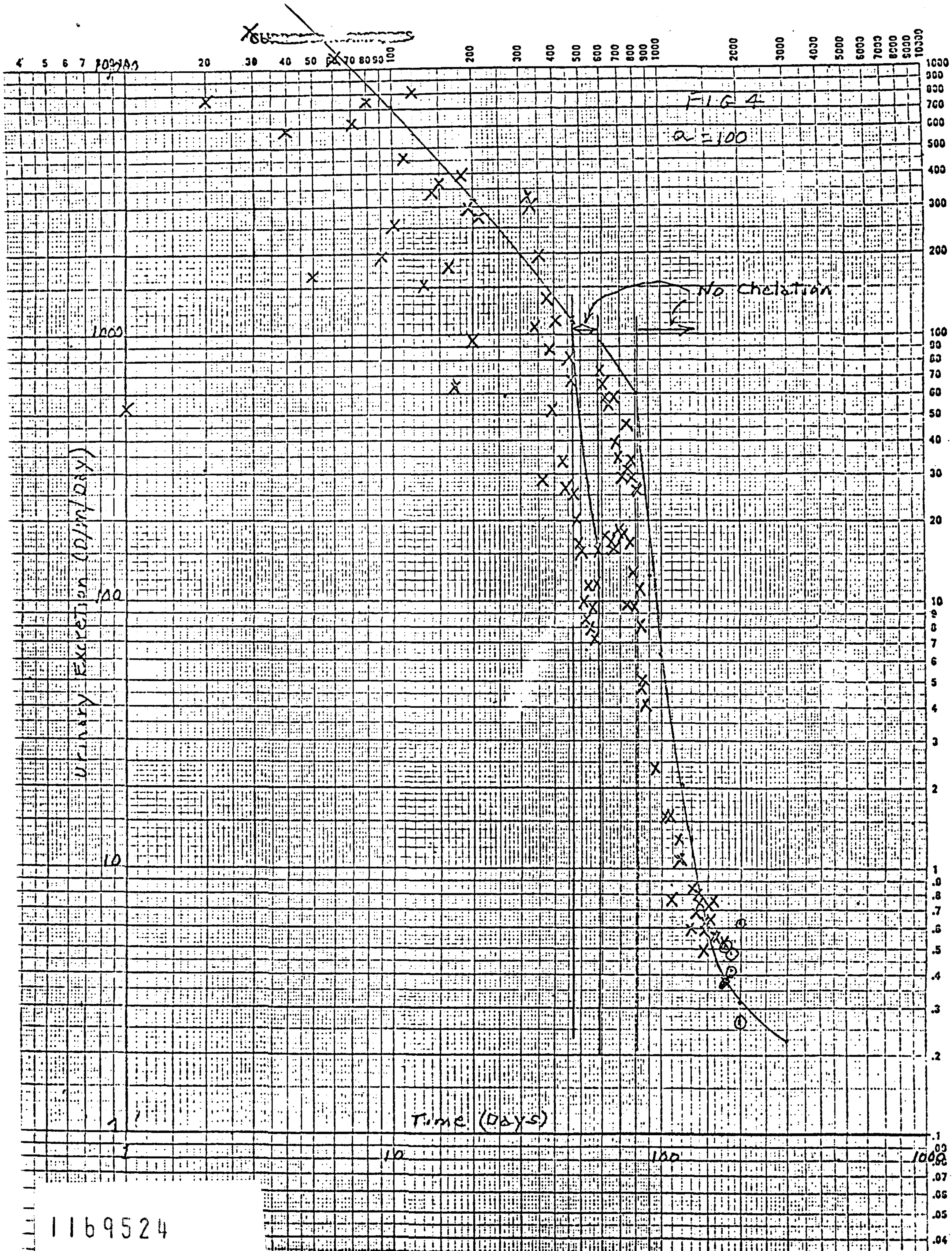

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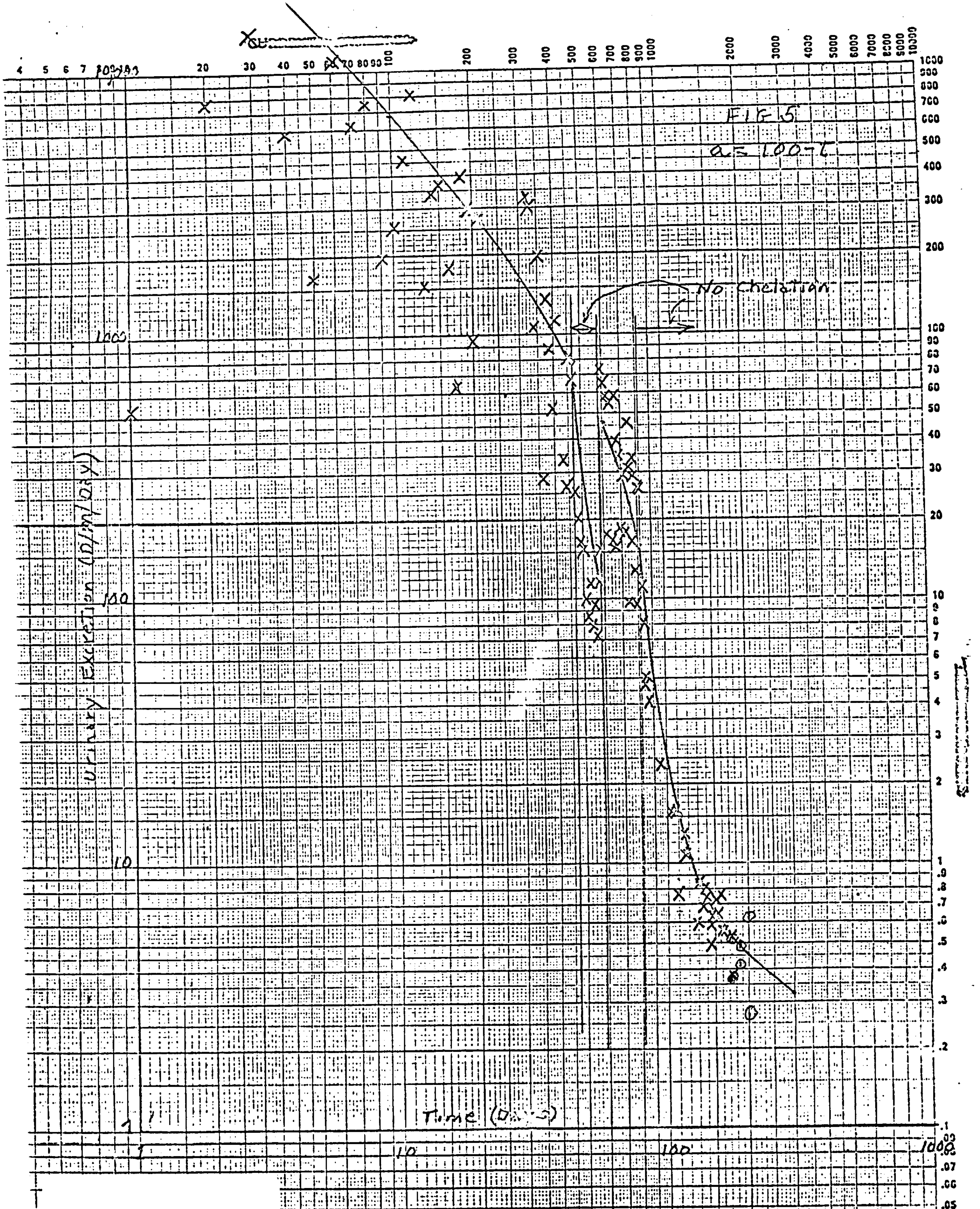

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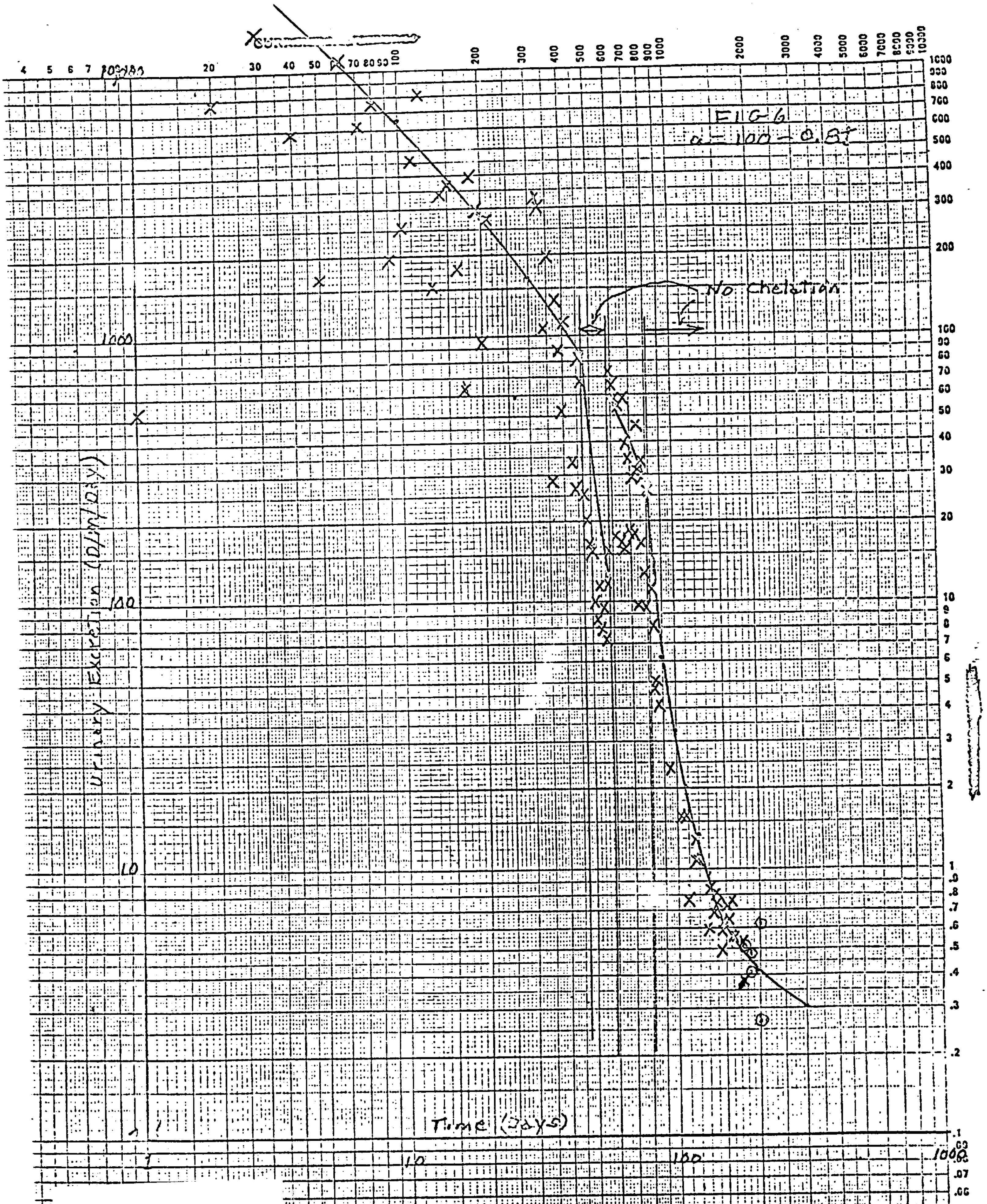
FIG 6
a = 100 - 0.8t
No Chelation
Urinary Excretion (DPM/DAY)
Time (Days)

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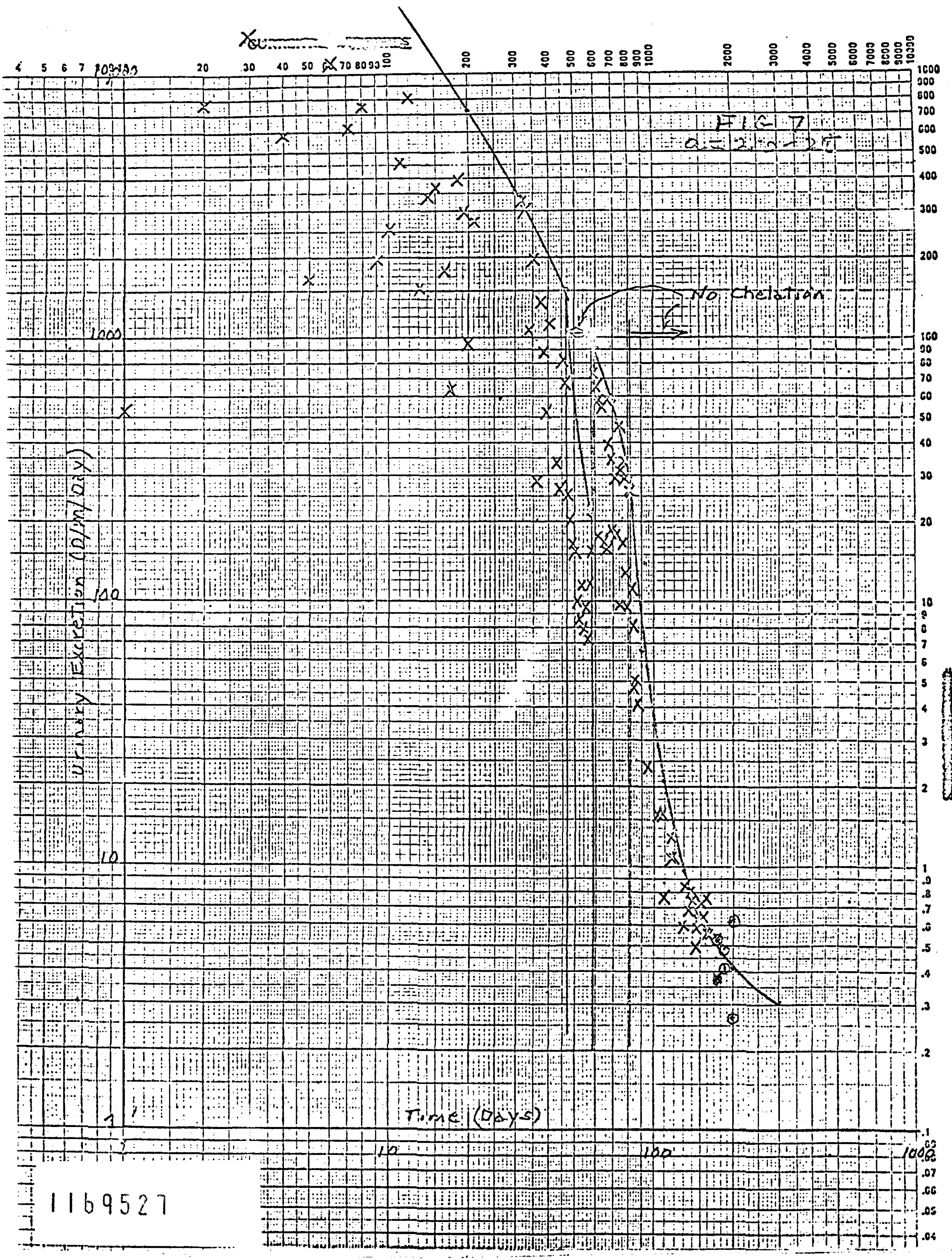

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OFFICE MEMORANDUM

TO : Wright Langham, Group Leader, H-4 DATE: June 30, 1969

FROM : James N.P. Lawrence, Assoc. Group Leader, H-1

SUBJECT: SVR PLUTONIUM ACCIDENT CASE

SYMBOL : H-1

According to the Monitoring and Bioassay Data Sheets for the 24-hour period following the accident, the total urinary excretion was 3333 dis/min. This was prior to the first administration of DTPA. Using this figure and Langham's equation $D_E = 500\ Ut^{0.74}$ for t = 1, the body burden (D_E) would have been $\sim$1.7 × 10^6 dis/min (0.75 μCi), PUQFUA calculation of the amount remaining on July 1, 1969 is 1.57 × 10^6 dis/min.

On the attached chart are plotted the observed urinary excretion per 24-hour period (noon til noon) for the entire set of data. The double-line curve represents the "expected" excretion according to Langham's equation. It is obvious that the DTPA treatments had a marked effect on the urinary excretion. I know of no way to incorporate the data during the DTPA treatments into a calculation of body burden.

How to use the urinary excretion data for these periods when DTPA was <u>not</u> administered is not at all certain. Before plotting the "expected" excretion curve, I examined the plot of the urinary data, and decided that the data on 11/30/68, 1/19-25/69, and from 3/3/69 through 5/20/69 appeared to be relatively free of DTPA effects. From this data, I devised five sets (described below) and feed the information into the PUQFUA computer code with the results indicated.

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Set Identification	Dates of Samples Included	PUQFUA Body Burden (μCi)	
SVR-1	11/30/68, 1/19-25/69 3/3 thru 5/20/69	0.04	Samples on 11/30/68 and 1/19/69 were judged invalid by computer code and code calculated the initial exposure date to be 1/20/69.
SVR-2	11/30/68	0.71	Based on one sample only.
SVR-3	1/19-25/69, 3/3 thru 5/20/69	0.04	Initial sample not included in original data. Accident programed to occur 51 days before the 1/19/69 sample. Since sample on 1/19/69 was judged invalid by computer code, code calculated the initial exposure date to be 1/20/69.
SVR-4	1/19 -25/69	0.03	Initial sample not included in origianl data. Accident programed to occur 51 days before the 1/19/69 sample. Since sample on 1/19/69 was judged invalid by computer code, the code calculated the initial exposure to occur on 1/20/69.
SVR-5	3/3 thru 5/20/69	0.02	Accident programed to occur 94 days before the 3/3/69 sample. Since computer code judged sample on 3/3/69 to be invalid, the code calculated the initial exposure to have occurred on 3/7/69.

Since the urinary data fluctuated adversely insofar as the PUQFUA code was concerned (causing invalidation of initial sample in all groupings of data except SVR-2), and thereby causing the actual accident data to be ignored, I have concluded that PUQFUA in its present form is incapable of a reasonable estimation of the body burden after the DTPA treatments.

At this point, I plotted the "expected" excretion assuming the sample on 11/30/69 to be a valid sample. By examining the data after 2/19/69 when the DTPA treatments was discontinued, it appears (to me) that the effects of the DTPA have not worn off until 3/19/69 or later. I made this judgment on the observation that the slope of the excretion rate observed and "expected" are about the same at this time interval after the accident. The ratio of the observed to the expected is about 1/12th. Thus, in the absence of DTPA, a sample on 11/30/69 of $\frac{3333}{12} \cong 280$ dis/min would have given the observed data after

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3/19/69. The indicated systemic body burden from the data after 3/19/69 is about 0.06 μCi. In regard to the critical organ for the calculated systemic burden, I would not hazard a guess.

Since the conversion from counts/min to dis/min for plutonium wound monitoring varies ~~too~~ markedly with the depth of plutonium in the tissue (data which not known), I can not venture an intelligent guess as to the quantity remaining at the wound site.

Jim:

I put the newer data on the curves as the circles. They do not make any difference in my look.

JWH

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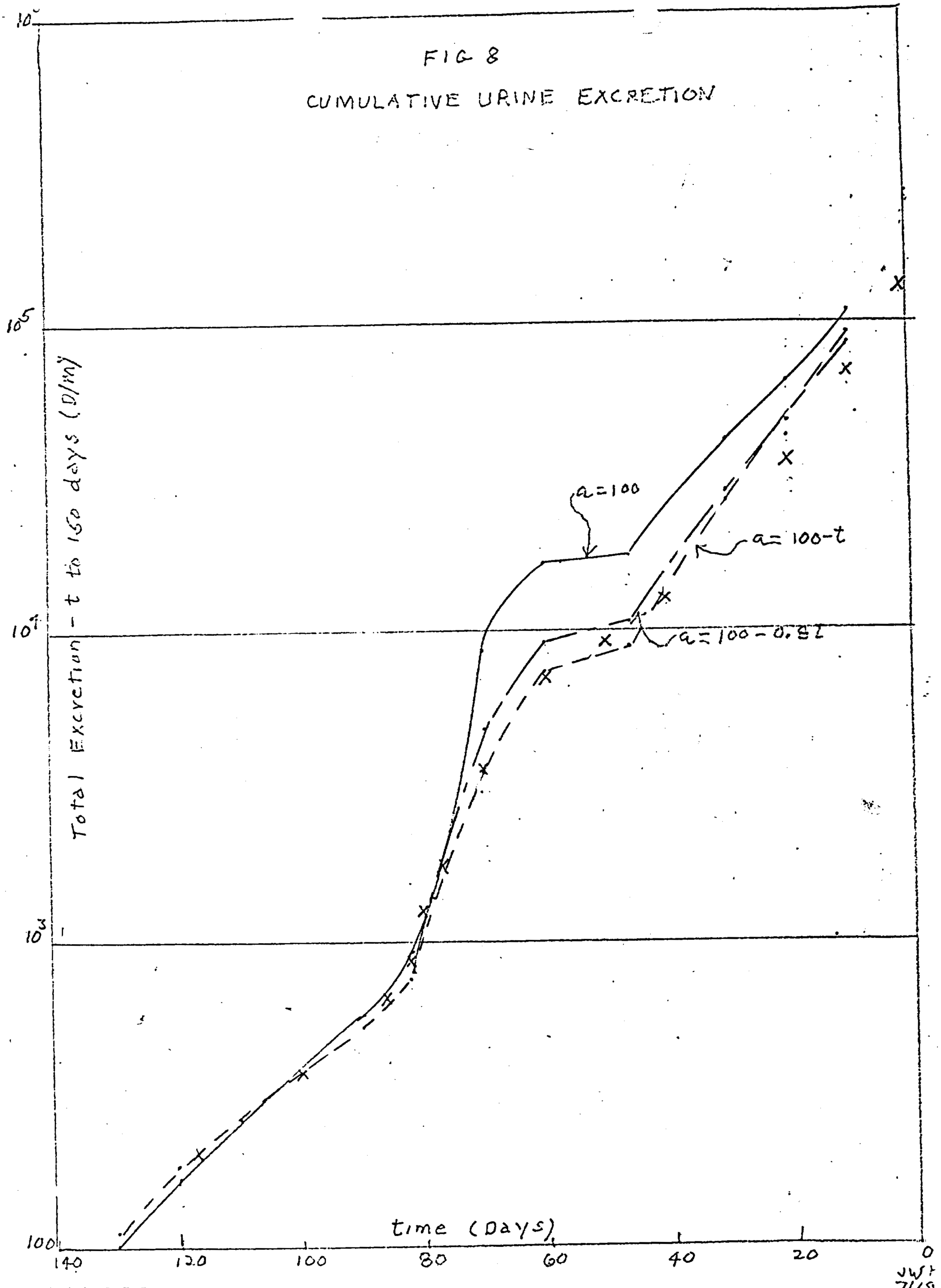
FIG 8
CUMULATIVE URINE EXCRETION
Total Excretion - t to 150 days (D/M)
time (DAYS)
a=100
a= 100-t
a=100-0.5t
10⁵
10⁴
10³
100
140
120
100
80
60
40
20
0
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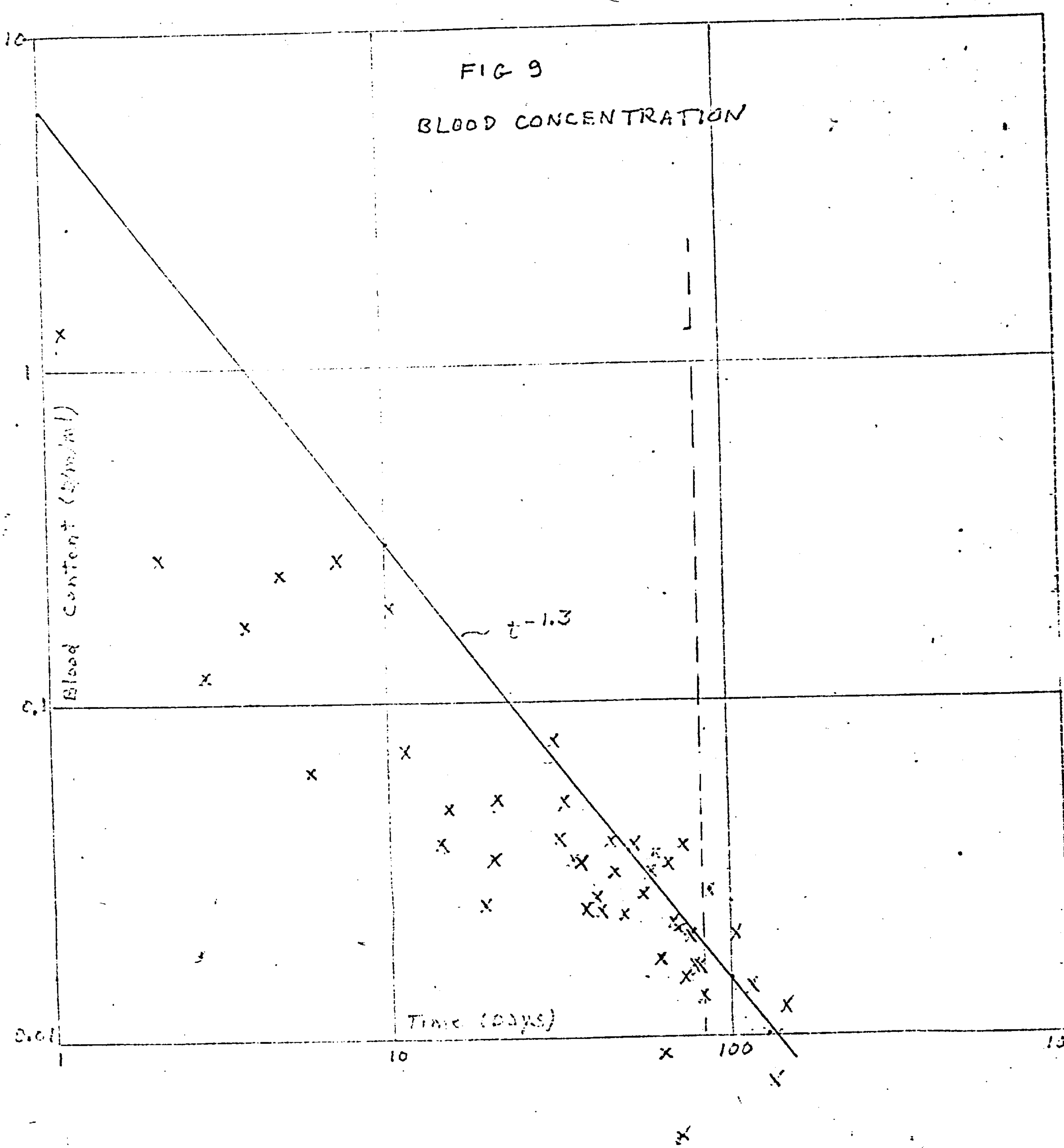
FIG 9
BLOOD CONCENTRATION
$t^{-1.3}$
Blood Content
Time (Days)
10
1
0.1
0.01
1
10
100

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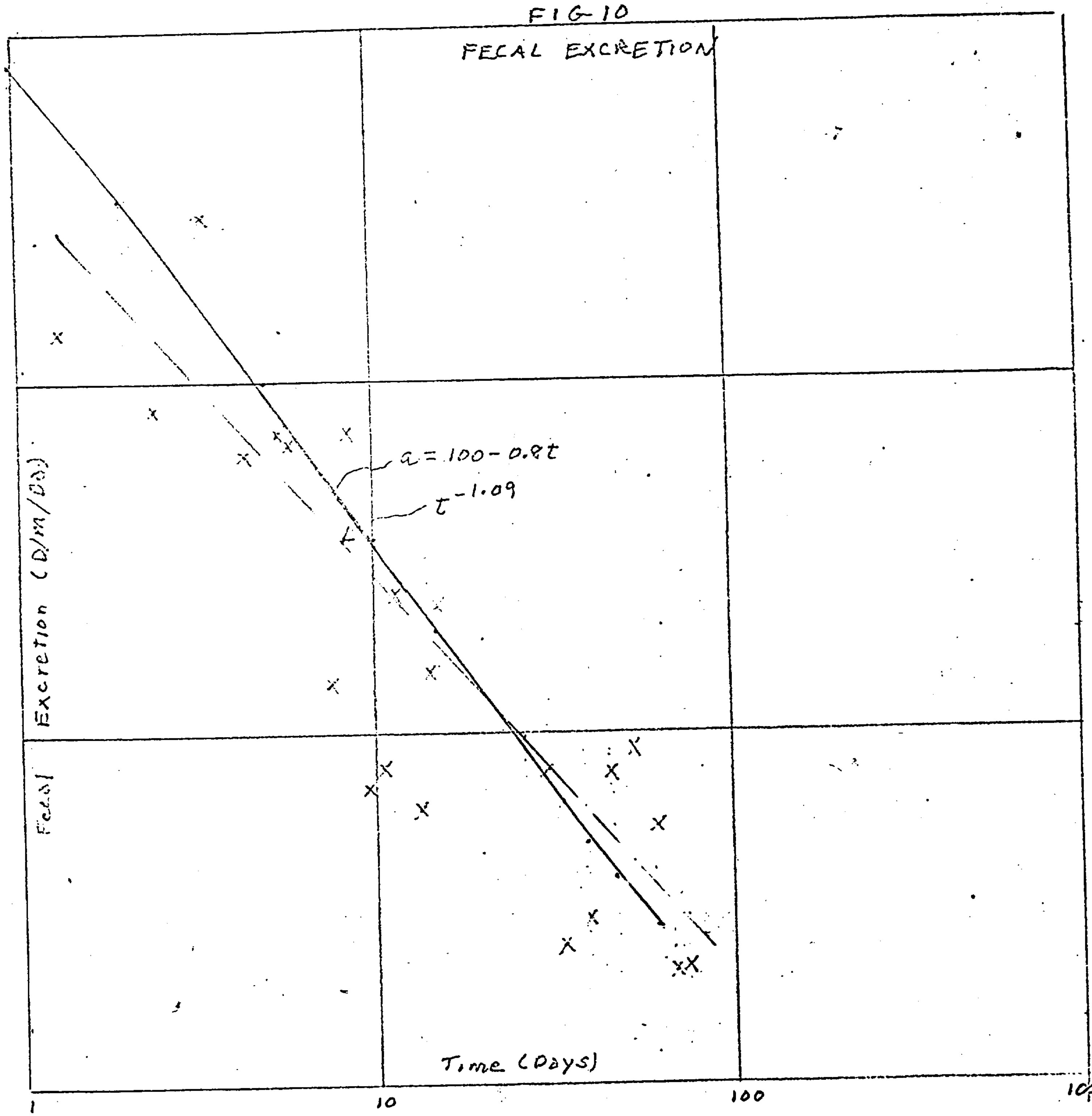
FIG 10
FECAL EXCRETION
a = 100 - 0.8t
t^-1.09
Fecal Excretion (D/M/Day)
Time (Days)
1
10
100
100

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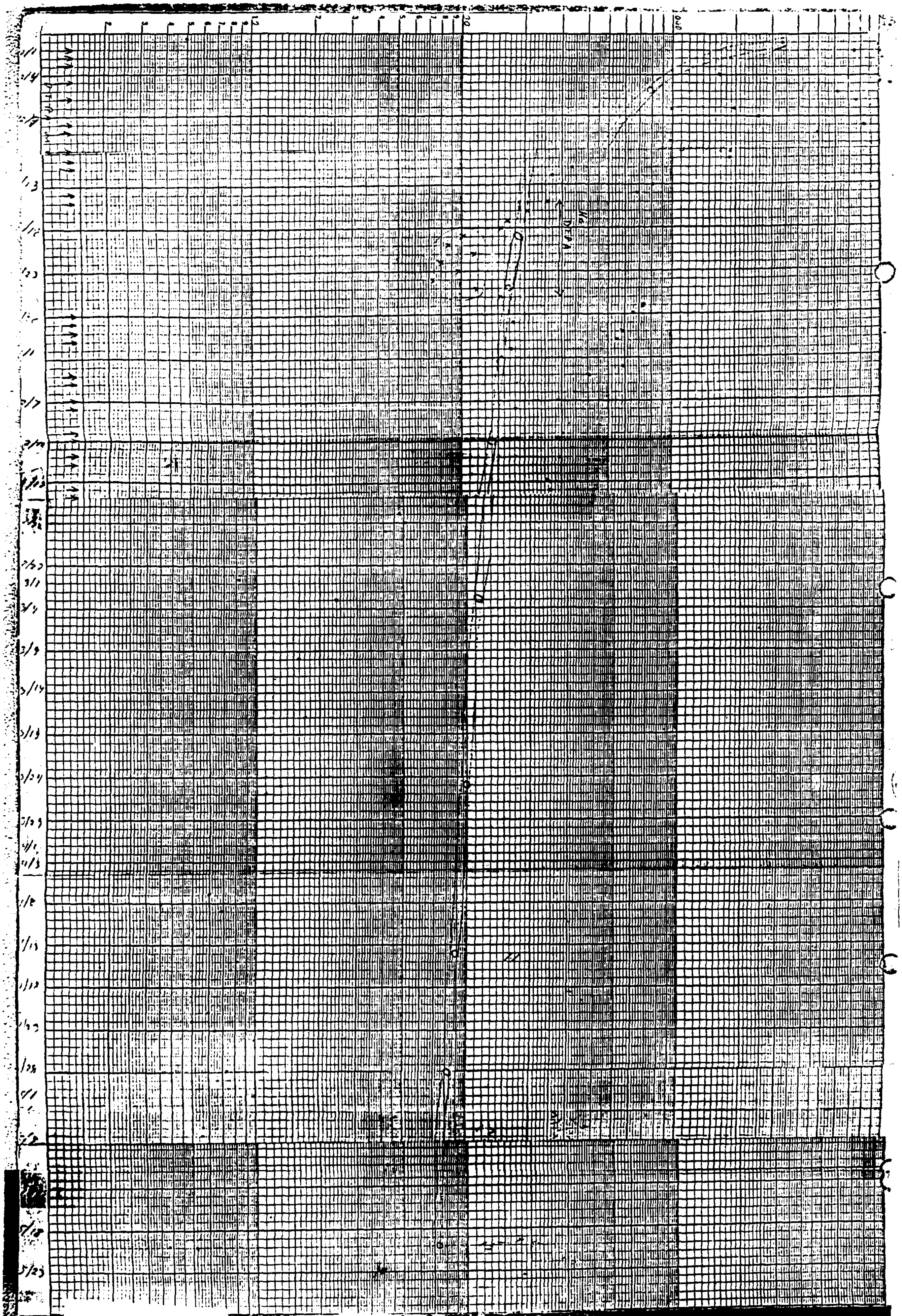

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