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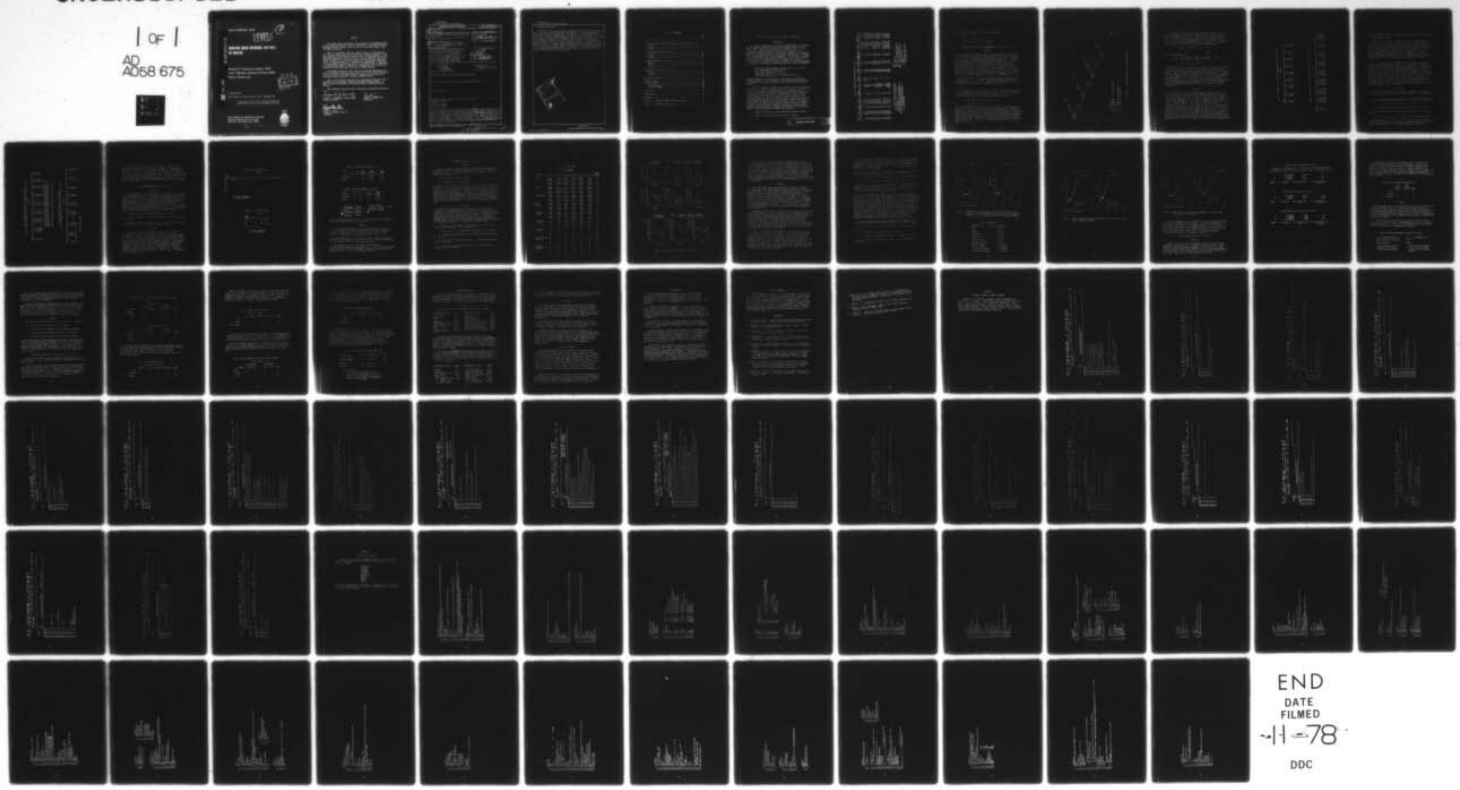

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LEVEL II

RADIATION EMESIS REPOSITORY (1971-1977): AN ANALYSIS

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September 1978

Final Report for Period January 1971 - December 1977

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USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
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NOTICES

This final report was submitted by personnel of the Weapons Effects Branch, Radiation Sciences Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 7757-05-18.

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The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act of 1970 and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources - National Research Council.

This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: SAM-TR-78-26	2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): RADIATION EMESIS REPOSITORY (1971-1977): AN ANALYSIS,	5. TYPE OF REPORT & PERIOD COVERED: Final Report, Jan 1971 - Dec 1977
6. PERFORMING ORG. REPORT NUMBER	
7. AUTHOR(s): Michael G. Yochmowitz, Captain, USAF; Joel L. Mattsson, Lieutenant Colonel, USAF; Vicky L. Bewley, B.S.	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS: USAF School of Aerospace Medicine (RZW), Aerospace Medical Division (AFSC), Brooks Air Force Base, Texas 78235	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: 62202F; 7757-05-18
11. CONTROLLING OFFICE NAME AND ADDRESS: USAF School of Aerospace Medicine (RZW), Aerospace Medical Division (AFSC), Brooks Air Force Base, Texas 78235	12. REPORT DATE: September 1978
	13. NUMBER OF PAGES: 77
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): 89 p.	15. SECURITY CLASS. (of this report): Unclassified
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Prodromal syndrome
Nausea
Radiation sickness
Ionizing radiation

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Emesis data collected from 21 ionizing radiation studies involving 210 rhesus (Macaca mulatta) monkeys has been examined. These studies contain a wide variety of experimental parameters prepared by investigators interested in unique situations. When proposed, they were viewed as pilot studies to determine the presence or the absence of radiation effects upon performance. This report examines the studies a posteriori grouping them as follows: Distribution Specification, ED_{50} Determinations, Dose Rates, Mixed Rates, and Descriptive.

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20. ABSTRACT (Continued)

Distribution specification studies found that the onset time of each episode had an exponential distribution, and the duration of each episode was either an exponential or Weibull distribution. The presence of similar distributions across many experiments suggests that the same mechanism is at work in each study and episode, differing only in intensity. ED_{50} studies found the effective dose for 50% emetic response to be 446 rads (Co^{60}, 20 rads/min), and that motion reduced the ED_{50} to 258 rads. Dose rate studies indicate a requirement for at least 10 animals per treatment group in making intergroup comparisons. Mixed rate and descriptive studies indicate the need for more systematic investigations. In an average rhesus monkey, if emesis occurred, the first episode occurred at 40 min postirradiation, followed in about 15 min by a second episode, and in another 15 min by a third and last episode.

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RADIATION EMESIS REPOSITORY (1971-1977): AN ANALYSIS

INTRODUCTION

This report summarizes the contents of the USAF School of Aerospace Medicine Radiation Sciences Division ionizing emetic repository from 1971 to 1977. This period includes the 21 studies listed in Table 1. As a group, the studies contain a wide variety of experimental parameters prepared by different investigators interested in unique and sometimes specified situations, and emesis data was collected incidental to the primary objectives of their experiment. Nevertheless, the emesis data can be viewed as pilot studies reflecting on this common syndrome, recognizing that the experiments were not designed for elaborate modeling efforts. With this in mind, we grouped the studies a posteriori on the basis of the analysis permitted by the data collected as follows:

Distribution specification (Studies 2, 18, 19, 27, 30, 33)
ED_{50} determinations (Studies 39, 41)
Dose rates (Studies 31.1, 31.2)
Mixed rates (Studies 36, 37, 38, 40)
Descriptive (Studies 3.1, 3.2, 26, 28, 32, 34, 35)

Computer programs used to examine this repository are documented to provide continuity to this data base. Brief explanations are given so nonprogrammers can access the data to update and/or pursue additional analysis.

We use the operational definition of emesis given by Fleischman and associates (4). That is, an emetic episode is defined as a "series of three or more reflexive movements consisting of coordinated mouth openings, opisthotonus, and maximal abdominal musculature contraction." Interepisode time is defined as "3 or more minutes between the last emetic movement of an episode and the first emetic movement of the subsequent episode." Note that this definition includes both productive and nonproductive episodes. This is necessary because monkeys have cheek pouches and can conceal or retain vomitus. Thus it is intended to indicate when the subjects are distressed beyond the stage of nausea. Appendix A illustrates this definition by graphically portraying the temporal nature of the emetic responses for subjects in the repository. Sources of variation evident in these figures include:

a. Whether or not a subject will experience an emetic episode.

b. Number of episodes experienced if there is emesis.

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TABLE 1. CONTENTS OF THE EMETIC REPOSITORY (1971-1977)

Study	Date	No. subjects	Weight kg	Hours observed	Task	Hours fasted	Exposure site	Type radiation	Neutron-gamma ratio	Delivery mode	Total mid-epigastric dose
2	3/72	16	2.0-3.1	15	D-	17	A&M	N/G	.72	2 Pulse Sep. by 10m	2160-2650
3.1	10/71	6	3.3-6.8	2	LAND	1,3,16	A&M	N/G	.5	1 Pulse	600-1000
3.2	10/71	6	3.2-6.8	2	LAND	1,16	A&M	N/G	.5	Steady rate	600-1000
18	7/71	11	3.2-4.1	22	PEP	1,14	AFRRI	N/G	.24	1 Pulse	1020-2920
19	3/72	9	2.3-3.7	22	PEP	1	A&M	N/G	.5	1 Pulse	2840-3350
26	8/72	9	3.0-5.0	2	PEP	17	A&M	N/G	.65	1 Pulse	283-2224
27	8/72	19	3.2-3.7	2	D-	17	A&M	N/G	.44	1 Pulse	2122-2365
28	3/73	10	3.2-4.3	2	PEP	1	A&M	N/G	.5	1 Pulse	170-1110
30	10/73	12	3.6-5.8	2	D-	1	SAM	X-ray	N/A	Steady rate	341-528
31.1	5/71	12	2.7-3.4	2	NAIVE	1,6	SAM	X-ray	N/A	Steady rate	517-580
31.2	5/71	12	2.8-3.5	2	NAIVE	1,6	SAM	X-ray	N/A	Steady rate	539-573
32	7/71	12	2.5-3.1	2	NAIVE	1	AFRRI	N/G	.24	1 Pulse	950-1130
33	9/71	4	3.0-3.4	2	NAIVE	1	SAM	X-ray	N/A	Steady rate	883-995
34	1/72	12	3.0-4.4	2	NAIVE	1,6	WSMR	N/G	5.0	1 Pulse	470-1000
35	3/74	10	?	2	PEP	1	A&M	N/G	?	?	250-500
36	12/75	8	2.95-4.32	12	D-	1	SAM	Co60	N/A	Mixed rates	300-300
37	12/75	7	2.95-4.32	12	D+	1	SAM	Co60	N/A	Mixed rates	300-300
38	12/76	4	4.3-5.7	72	PEP	1	SAM	Co60	N/A	Mixed rates	300-300
39	3/77	15	4.4-6.5	4	NAIVE	1	SAM	Co60	N/A	Steady rate	350-550
40	12/76	10	4.4-5.7	10	PEP/MART	1	SAM	Co60	N/A	Mixed rates	1440-1440
41	4/77	6	5.0-5.9	4*	SHAKE	1	SAM	Co60	N/A	Steady rate	200-300

D- = Lever pressing; Shock reinforcement
D+ = Lever pressing; Food reinforcement
LAND = Landolt
PEP = Primate equilibrium platform
NAIVE = No behavioral laboratory experience
PEP/MART = Primate equilibrium platform Multiple alternative reaction task
N/A = Not applicable

SHAKE = Motion
A&M = Texas A&M
N/G = Mixed neutron-gamma radiation
SAM = School of Aerospace Medicine
WSMR = White Sands Missile Range
AFRRI = Armed Forces Radiobiological Research Institute
? = Unknown
* = Observed until first episode; if no emesis, then 4 h

c. Kinds of episodes experienced (productive vs. nonproductive).

d. Duration of episodes.

e. Time of occurrence of each episode.

DISTRIBUTION SPECIFICATION (Studies 2, 18, 19, 27, 30, 33)

Methods

The approach used in modeling the prodromal syndrome is that used in the analysis of reliability and life data. The reliability of each subject is the infrequency with which he experiences emesis. Our goal was to estimate the probability of a failure--an emetic episode as well as the time until it occurs, and the duration of the episode. The decision tree in Figure 1 illustrates this approach. The origin represents immersion in the radiation field. The probability of experiencing a first episode is p_1; it takes t_1 minutes to occur, and will last d_1 minutes. The probability of a second episode is p_2; it occurs t_2 minutes following the first episode, and will last d_2 minutes. This process continues until the last episode when $p_{last+1}=0$. In this manner, the prodromal syndrome is viewed as a stochastic process.

For a given study, let n equal the total number of animals in the study and let x_i be the number of emetic responders during episode i. An estimate of p_i is $\hat{p}_i = x_i/n$.[1] Confidence intervals for p_i can be constructed from the binomial distribution (cf. ref. 12).

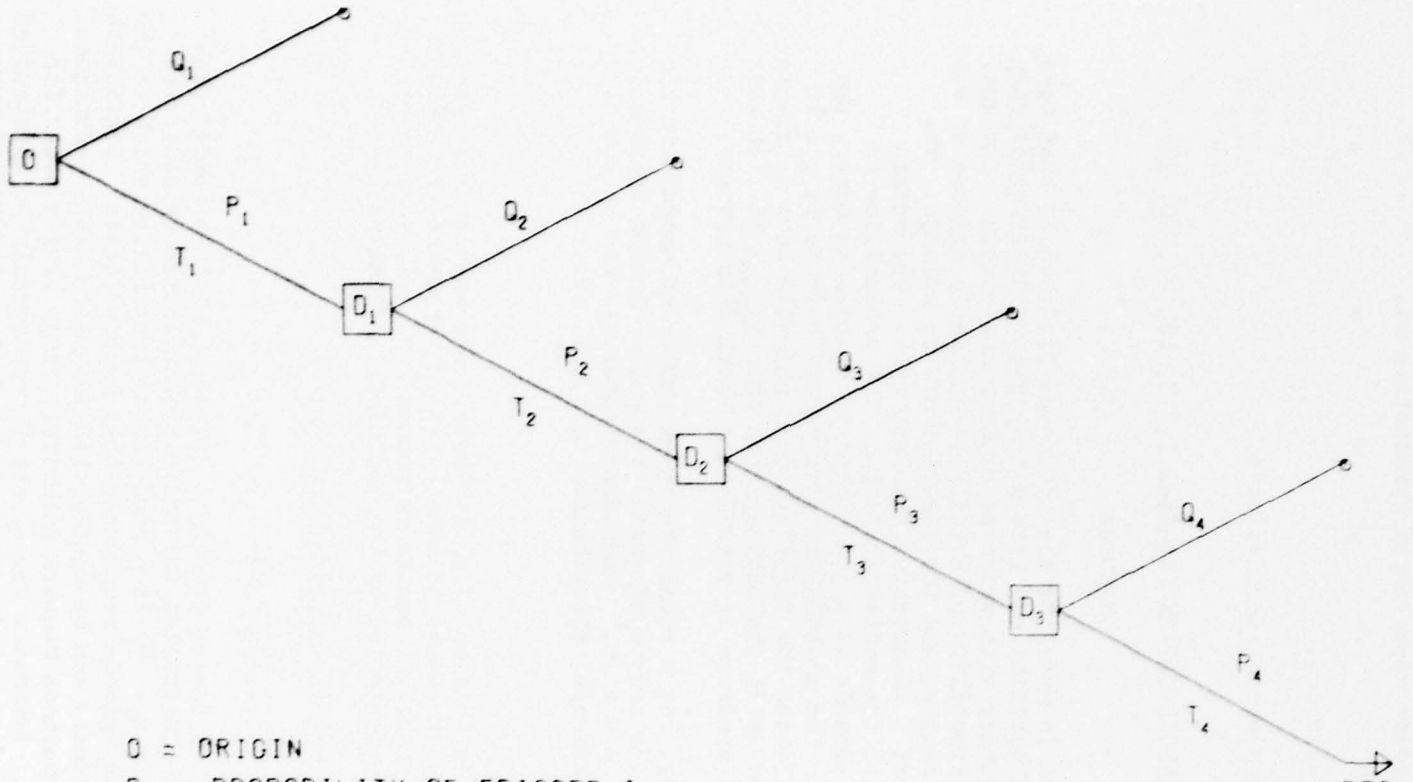
---

[1] As stated, the definition of p_i is vague. The modeler must decide upon the interpretation he wants to make. Let y_i represent the number of animals that have exactly i emetic responses. $y_i = x_i - x_{i+1}$. Related parameters are suggested by the additional estimates:

a. $\tilde{p}_i = y_i/n = (x_i - x_{i+1})/n$; $(x_0 = n)$

b. $\bar{p}_i = x_i/x_{i-1}$; $(x_0 = n)$.

$\tilde{p}_i$ is the probability of having exactly i episodes. Beta-binomial confidence limits can be constructed for these probabilities as described above with y_i replacing x_i. $\bar{p}_i$ is a conditional probability which is the proportion of previous episode responders that respond again. Confidence limits using this estimate can be constructed from life table techniques. Unfortunately, these methods require relatively large sample sizes for meaningful intervals. Estimates for $\tilde{p}_i$ and $\bar{p}_i$ can readily be constructed from estimates for $\hat{p}_i$ in Table 2. To avoid confusion, we limit future discussion to $\hat{p}_i$.



O = ORIGIN
P_I = PROBABILITY OF EPISODE I
Q_I = $1-P_I$
D_I = DURATION OF EPISODE I
T_I = TIME TO EPISODE I

Figure 1. Decision tree for the prodromal syndrome.

The approach to determining t_i and d_i was to consider them as random variables T_i and D_i whose distributions need specification. With small sample sizes, customary χ^2-goodness-of-fit tests are inappropriate for distribution determination as are the Kolmogorov-Smirnov (KS) tests which require a priori knowledge of parameters. We examined two of the most frequently occurring distributions in life testing--the exponential and the Weibull. These densities are given by:

$$f_X(x) = \frac{1}{\lambda} \exp\left(-\frac{1}{\lambda}x\right), \quad x > 0$$

$$= 0 \qquad\qquad x \leq 0$$

for the exponential, and

$$f_X(x) = \frac{\beta}{\delta}\left(\frac{x-\mu}{\delta}\right)^{\beta-1} \exp\left[-\left(\frac{x-\mu}{\delta}\right)^{\beta}\right], \quad x \geq \mu$$

$$= 0, \quad x < \mu; \ \beta, \delta > 0; \ \mu \geq 0$$

for the Weibull. With $\beta = 1$ and $\mu = 0$, one can see that the exponential is a special case of the Weibull. To test the adequacy of the exponential, we used a modified KS technique given by Lilliefors (5) for samples ≥ 3 and by Finklestein and Schafer (3) for samples = 2. A test derived by Mann, Scheuer, and Fertig (9) was used to test the adequacy of a two-parameter Weibull distribution ($\mu = 0$) when the exponential distribution failed. All testing was done at the $\alpha = .01$ level. Following selection of a distribution, maximum likelihood estimates were used to estimate exponential parameters; Mann's (7, 8) best linear invariant estimates were used for β and δ estimates in Weibull distributions.

Results

Tables 2 and 3 classify, respectively, by study and episode the proportion of emetic responders and the 95% confidence intervals for these proportions. The width of the confidence intervals in Table 3 is a function of the sample size and the α-level considered. Despite their width, meaningful data can still be gleaned by examining the end points of these intervals. For instance, the lower limits for p_1 in studies 2 and 27 indicate that at least 47% and 43% of those respectively exposed to such dose profiles (and associated experimental parameters) would experience the prodromal syndrome. Information of this nature could thus be used to make best-case inferences. By the same token upper limits for p_3 in study 30 indicate that, at most, 41% of those exposed to these experimental conditions would experience 3 episodes, while upper limits for p_4-p_8 indicate that a maximum of 23% will have 4 or more emetic episodes. Worst-case estimates can thus be made from these upper limits. Both best- and worst-case estimates from

TABLE 2. PROPORTION ($\hat{p}_i$) OF EMETIC RESPONDERS (PRODUCTIVE AND NONPRODUCTIVE)

	Episode							
Study	1	2	3	4	5	6	7	8
2	12/16	11/16	9/16	6/16	2/16	1/16	1/16	0/16
18	4/7	2/7	1/7	0/7	0/7	0/7	0/7	0/7
19	5/9	3/9	1/9	1/9	1/9	0/9	0/9	0/9
27	13/19	10/19	6/19	3/19	1/19	1/19	1/19	1/19
30	5/11	2/11	1/11	0/11	0/11	0/11	0/11	0/11
33	3/4	2/4	1/4	1/4	1/4	0/4	0/4	0/4

TABLE 3. PROBABILITY OF HAVING AN EMETIC RESPONSE (95% CONFIDENCE INTERVALS)

	Episode							
Study	1	2	3	4	5	6	7	8
2	(.47,.93)	(.41,.89)	(.29,.81)	(.15,.65)	(.01,.38)	(0.0,.30)	(0.0,.30)	(0.0,.27)
18	(.18,.90)	(.03,.71)	(0.0,.58)	(0.0,.35)	(0.0,.35)	(0.0,.35)	(0.0,.35)	(0.0,.35)
19	(.21,.86)	(.07,.70)	(0.0,.48)	(0.0,.48)	(0.0,.48)	(0.0,.28)	(0.0,.28)	(0.0,.28)
27	(.43,.87)	(.28,.76)	(.12,.57)	(.03,.40)	(0.0,.26)	(0.0,.26)	(0.0,.26)	(0.0,.26)
30	(.16,.77)	(.02,.52)	(0.0,.41)	(0.0,.23)	(0.0,.23)	(0.0,.23)	(0.0,.23)	(0.0,.23)
33	(.19,.99)	(.06,.93)	(0.0,.82)	(0.0,.81)	(0.0,.81)	(0.0,.53)	(0.0,.53)	(0.0,.53)

Table 3 are based upon 95% confidence limits. If one wanted to be less secure in these estimates, the confidence intervals could be shortened by increasing the α-level.

Tables 4 and 5 summarize by study and episode the distributions selected to describe T_i and D_i based upon $\alpha = .01$. In all (17 of 17) cases where the distributions could be identified, the distributions of time to failure (T_i) were exponentially distributed. This distribution suggests that when the prodromal syndrome occurs, one can characterize when it will happen as a function of λ which is dependent upon experimental conditions like hours fasted, radiation type, and the neutron-gamma ratio. Estimates of λ are informative, and they represent the mean time between failures. In all cases, we find that it takes longer for the first episode to occur than for successive episodes.

In 13 of 17 cases, the exponential distribution was an adequate descriptor of episode duration times at the .01 level. The Weibull was able to describe an additional 2 cases. The remaining 2 cases were neither Weibull nor exponential and are unknown. With $\mu = 0$, we can describe 15 of 17 cases of D_i's distribution as belonging to a two-parameter Weibull family. This characterization suggests that episode duration times can be described as functions of β and δ which depend upon experimental conditions. Thus, the same mechanism appears to be at work in each study and episode, but differing only in intensity. Estimates of λ (for the exponential subclass) are mean duration times for each episode. Study 2 with the greatest incidence, the most episodes, and the shortest time to the first episode appears to have the greatest duration times on the average.

Comments

The diversity of experimental parameters suggests a number of hypotheses to be tested. For a given dose, they include the hypothesis of

a. No difference between the same dose delivered as a single pulse vs. a double pulse, or a single pulse vs. a continuous dose rate, etc.

b. No difference between different dose rates.

c. No difference between fasting animals 17 h, 6 h, or 1 h.

d. No difference between behavioral tasks (PEP, D+, D-, Landolt, Naive).

e. No difference between .25, .50, or .75 neutron-gamma ratios.

With hindsight, one would like to test each of these hypotheses. Given the current situation, none can be examined because no two of the several studies differ in only a single independent variable.

TABLE 4. MEAN ONSET TIMES FOR EMETIC EPISODES IN MINUTES
(Distribution specification for T_i; $\alpha = .01$; λ = Mean time to onset in minutes)[a]

Study	Episode 1	2	3	4	5	6	7	8
2	λ =11.81[b]	λ =10.78	λ=11.13	λ=15.69	λ=11.5	N=1	N=1	N=0
18	λ =43.4	λ =27.25	N=1	N=0	N=0	N=0	N=0	N=0
19	λ =30.43	λ = 9.38	N=1	N=1	N=1	N=0	N=0	N=0
27	λ =28.92	λ=17.48	λ= 9.17	λ=10.31	N=1	N=1	N=1	N=1
30	λ =53.13	λ =12.02	N=1	N=0	N=0	N=0	N=0	N=0
33	λ =42.58	λ =18.56	N=1	N=1	N=1	N=0	N=0	N=0

[a] λ indicates an exponential distribution. δ and β indicate a Weibull distribution. N = 1 or N = 0 indicate sample sizes preventing distribution specification. Question marks (?) indicate that neither the Weibull nor the expoential could describe these cases with α = .01.

[b] Time since second pulse, which occurred 10 min after first pulse.

TABLE 5. DURATION OF EMETIC EPISODES IN MINUTES
(Distribution specification for D_i; $\alpha = .01$; λ = Mean duration time)[a]

Study	Episode 1	2	3	4	5	6	7	8
2	λ=3.24	?	λ=4.19	λ=3.3	λ=3.55	N=1	N=1	N=0
18	λ=2.58	λ= 4.1	N=1	N=0	N=0	N=0	N=0	N=0
19	λ= .48	λ= .39	N=1	N=1	N=1	N=0	N=0	N=0
27	λ=2.13	δ=3.62 β=13.40;	λ=1.86	λ=1.56	N=1	N=1	N=1	N=1
30	?	λ= .84	N=1	N=0	N=0	N=0	N=0	N=0
33	δ=2.45; β=71.78	λ=3.66	N=1	N=1	N=1	N=0	N=0	N=0

[a] See footnote a, Table 4.

Another consideration could be to shorten the range of total midepigastric doses for a given study. In study 18, 4 animals in the 1000-rad dose range were deleted from consideration in distribution specifications. This left 7 animals in the dose range of 2440-2990 rads. It is preferable to make inferences over narrow dose ranges, say 25-50 rads, rather than over a 550-rad range. This variability in dose ranges affects the precision of p_i, p_{ii}, p_{iii}, λ, δ, and β. Additionally, these estimates can be improved by increasing the sample sizes in each study.

ED_{50} DETERMINATIONS (Studies 39, 41)

Methods

The ED_{50} number is the effective dose for which 50% of a population will have an emetic episode. A literature search showed that estimates exist for humans, but none could be found for monkeys. We therefore sought to fill this void to aid in monkey-to-man extrapolations. The up-and-down method (1, 2) was selected over probit techniques because accurate estimates could be obtained with smaller samples. The procedure was to administer doses at equally spaced increments. If the primate vomited, the increment was lowered one unit. If the primate did not vomit, the dose was raised one unit. The increment selected was 50 rads. Assumptions upon which the procedure is based include:

a. Data is normally distributed with common variance.

b. Subjects that do not vomit would have vomited at a sufficiently higher dose.

Advantages of this procedure are that it concentrates testing near the mean and can save in the number of subjects tested.

Results

The ED_{50} for unrestrained man is reported to be 183 rads (log-normal distribution) or 214 rads (normal distribution) (6). Estimated ED_{50} for naive, stationary, chair-restrained rhesus monkeys was 446 rads. Naive monkeys that were oscillated forward and backward $\pm 5^{\circ}$ to 10° (pitch axis on the PEF) from horizontal had an ED_{50} of 258 rads. Dose rate was 20 rads/min to simulate common radiation therapy dose rates from which human ED_{50} estimates were derived. Experimental results are given in Tables 6 and 7. Large and small sample ED_{50} estimates are given in Tables 8 and 9. Note the close agreement of estimates by both large and small sample techniques. A comparison between stationary and motion groups is in order. This is accomplished via a large sample z-test.

TABLE 6. STATIONARY TREATMENT DATA

Dose (rads)	Subject 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
350	O[a]				O										
400		O		X[b]		O						O			
450			X				O				X		O		X
500								O		X				X	
550									X						

[a] O = emetic nonresponder
[b] X = emetic responder

TABLE 7. MOTION TREATMENT DATA

Dose (rads)	Subject 1	2	3	4	5	6
200					O[a]	
250		O		X[b]		O
300	X		X			

[a] O = emetic nonresponder
[b] X = emetic responder

TABLE 8. LARGE SAMPLE ESTIMATES (cf. ref. 1)

Group	N_0	N_x	d (rads)	ED_{50} (rads)	$S_{\bar{x}}$ (rads)
Stationary	8	7	50	446.43	27.04
Motion	3	3	50	258.33	18.64

TABLE 9. SMALL SAMPLE ESTIMATES (cf. ref. 2)

Group	N	N'	d (rads)	ED_{50} (rads)
Stationary	15	14	50	445.63
Motion	6	6	50	258.45

$$Z = \frac{\bar{X}_{stationary} - \bar{X}_{motion}}{\sqrt{\frac{S^2_{stationary}}{N_{stationary}} + \frac{S^2_{motion}}{N_{motion}}}} = \frac{446.43 - 258.33}{\sqrt{(27.04)^2 + (18.64)^2}} = 5.514$$

and is significant at the 5% level. We conclude that the presence of motior can trigger vomiting at lower doses.

Comments

The up-and-down technique uses substantially fewer monkeys than probit techniques, and should be considered in radiation studies designed to study effects of fasting on ED_{50} and/or the combined effects of radiation plus stressors other than motion.

Up-and-down step sizes should be about one standard deviation in magnitude, which approximates 70 rads for naive, stationary monkeys, and 30 rads for naive monkeys experiencing motion stress.

This monkey ED_{50} emesis data indicates a difference in radiosensitivity between man and monkey (ED_{50} = 183 rads for man and 446 rads for partially restrained monkeys). Monkey-man extrapolation is apparently not 1 to 1, and deserves further study.

DOSE RATES (Studies 31.1, 31.2)

Methods

Study 31 involves subjects receiving approximately the same total midepigastric dose at 1 of 6 different dose rates and 1 of 2 different fasting schedules. These fasting schedules were designed to test the null hypotheses that

(a) Fasting does not affect emesis.

(b) Dose rates do not affect emesis.

Midepigastric doses ranged from 517 to 573 rads. Table 10 summarizes the data collected from each of 9 separate variables. Onset is the time in minutes to the first episode, with time accumulating from the moment the x-ray machine was turned on. Offset is the time in minutes at the conclusion of the last episode. Total duration is the total time in minutes that the subject experienced both productive and nonproductive emetic episodes. The period between onset and offset times is defined as the subject's vulnerability period. The definitions of the remaining 5 variables are self explanatory. Figure 2 shows mean plots for this data.

Results

Hypothesis testing was accomplished by a two-factor analysis of variance. In all cases there were no significant dose rate x fasting interactions. Significant dose rate effects ($p<.1$) were identified for onset and offset times, duration time of productive episodes, as well as the number of productive and nonproductive episodes. Significant fasting effects ($p<.1$) were found for onset times and nonproductive duration times. Tukey's (cf. 11) multiple comparison procedure detected the following differences at the 10% level of significance.

a. Onset and offset times for 6 rads/min dose rate were longer than both the 50 rads/min and 175 rads/min rates.

b. Offset times at 12 rads/min were longer than at 175 rads/min.

c. Productive duration times for 12 rads/min were longer than at 25 rads/min.

d. The number of productive episodes at 12 rads/min were greater than at 25 rads/min.

e. The number of nonproductive episodes at 25 rads/min were greater than at 12 rads/min.

TABLE 10. DOSE RATE DATA

Variable	Dose rate (rads/min) 6	12	25	50	92	175	Hours fasted
Onset	86.17	144.07	92.72	32.70	107.00	71.35	1
	136.67	97.17	72.07	52.25	43.13	46.45	1
	103.42	50.58	81.63	51.62	63.73	30.00	6
	101.55	67.55	54.23	31.55	90.07	47.02	6
Offset	122.08	168.23	93.15	119.64	107.08	83.96	1
	140.97	105.37	121.15	82.55	121.60	48.07	1
	127.46	121.62	121.76	90.80	64.21	46.03	6
	164.93	143.05	66.95	35.32	93.45	50.24	6
Vulnerability	35.91	24.16	0.43	86.94	0.08	12.61	1
	24.04	71.04	40.13	39.18	0.48	16.03	1
	4.3	8.2	49.08	30.3	78.47	1.62	6
	63.38	75.5	12.72	3.77	3.38	3.22	6
Total duration	2.87	11.65	0.43	8.93	0.08	4.23	1
	4.30	5.13	0.82	3.14	8.63	1.62	1
	6.68	10.29	4.78	8.35	0.48	7.70	6
	12.82	3.40	3.95	3.77	3.38	3.22	6
Productive duration	2.87	11.65	0.0	8.25	0.0	4.23	1
	4.30	5.13	0.0	3.14	7.08	1.62	1
	6.68	9.36	0.60	8.35	0.0	3.52	6
	7.47	3.40	0.0	0.0	0.0	3.22	6
Nonproductive duration	0.0	0.0	0.43	0.68	0.08	0.0	1
	0.0	0.0	0.82	0.0	1.55	0.0	1
	0.0	0.93	4.18	0.0	0.48	4.18	6
	5.35	0.0	3.95	3.77	3.38	0.0	6
Total number episodes	4	3	1	5	1	2	1
	1	2	2	2	4	1	1
	3	6	4	3	1	3	6
	5	2	2	1	1	1	6
Number productive episodes	4	3	0	4	0	2	1
	1	2	0	2	2	1	1
	3	5	1	3	0	1	6
	3	2	0	0	0	1	6
Number nonproductive episodes	0	0	1	1	1	0	1
	0	0	2	0	2	0	1
	0	1	3	0	1	2	6
	2	0	2	1	1	0	6

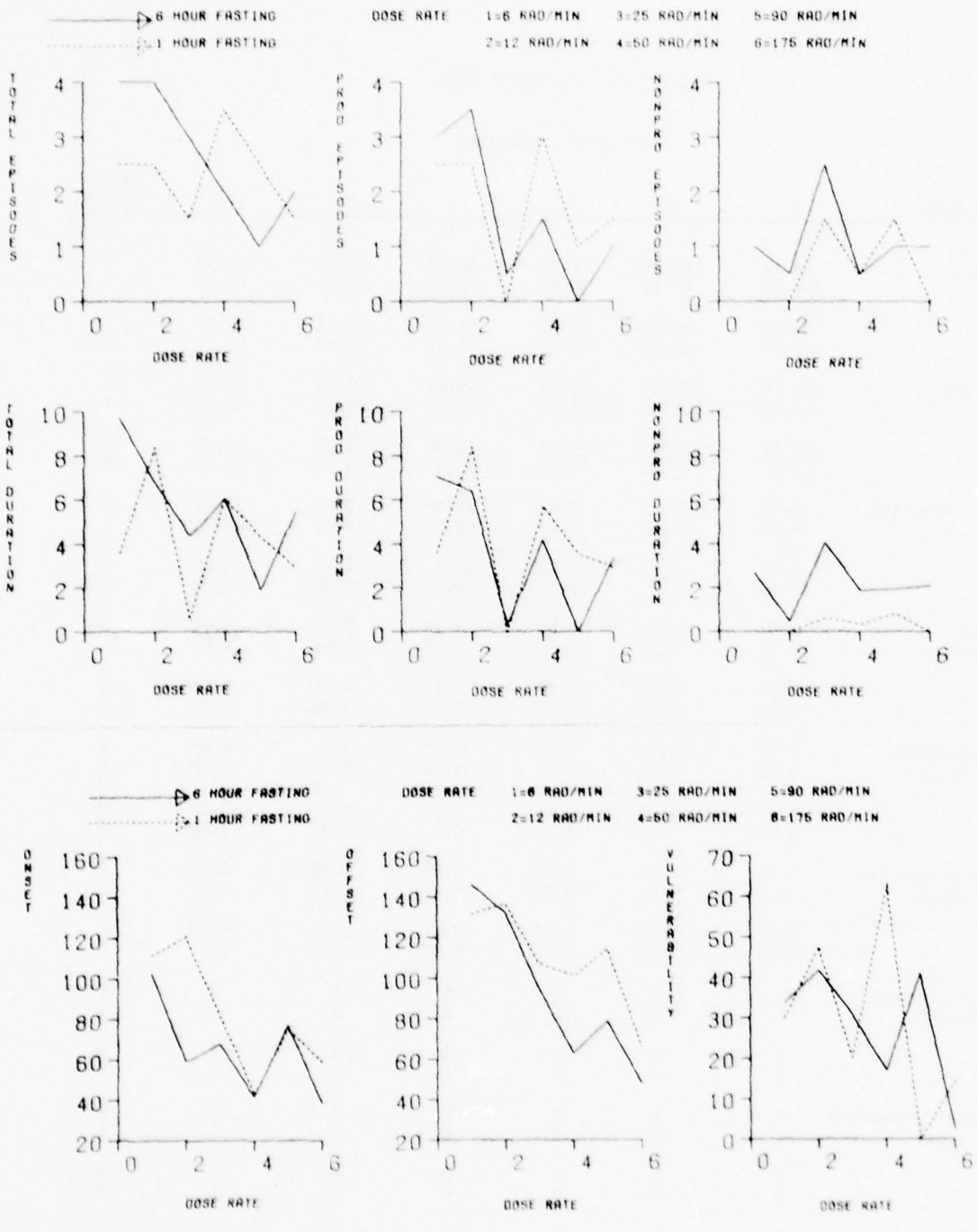


Figure 2. Mean scores for studies 31.1 and 31.2.

Note the lack of a clear-cut pattern in significant findings. For instance, if onset and offset times for 6 rads/min were significantly longer than both the 50 rads/min and 175 rads/min rates, one would have also expected them to be longer than the 92 rads/min rate. Similarly, if the number of nonproductive episodes at 25 rads/min were greater than at 12 rads/min, then one would have expected the number of nonproductive episodes at 50 rads/min, 92 rads/min, and 175 rads/min to be greater than the number of nonproductive episodes at the 12 rads/min rate. These inconsistencies can be attributed to the 2 replicates in each cell of the data matrices (see Table 10). Too many questions were asked with too little data.

Comments

Onset and offset times can be measured from three different starting points: when the machine is turned on, when it is turned off, or when some specific dose is delivered regardless of when the machine was turned on or off. When onset is measured from machine-on, a mechanical bias is introduced since lower dose rates take longer to deliver an effective dose of radiation to the subject. In the above data, if the time to deliver 446 rads (ED_{50} for emesis) is subtracted from all onset and offset times, then onset/offset times would measure the lag time between the delivery of an emetic dose and the time of appearance/disappearance of emesis. If dose rate has a physiological effect on onset/offset times, then these lag times should change at various dose rates.

Subtraction of the time to deliver 446 rads eliminated all evidence of dose rate effects on onset and offset times. For example, onset times measured from machine-on were 107.0 min at 6 rads/min and 48.7 min at 175 rads/min. These are statistically significant differences. Onset times measured from delivery of 446 rads were 32.6 min at 6 rads/min and 46.2 min at 175 rads/min and are not statistically different. This implies that the differences detected in study 31 were mechanical ones due to dose rate, and that the physiologically important event (between 6 rads/min and 175 rads/min) was not dose rate but the accumulation of an effective emetic dose.

Next, we use Type I (α) and Type II (β) errors to discuss the implications of testing 6 dose rates and 2 fasting schedules at once. Recall that a Type I error is the probability of rejecting the null hypothesis when it is true. For this data set, a Type I error is committed when we find either significant dose rate or fasting effects when there should be none. A Type II error is committed when one accepts the null hypothesis when it is false. For this data set, a Type II error is committed when one finds neither significant dose rate nor fasting effects when there should have been some. We believe this may be the case in the present situation.

An alternative to measuring Type II errors is to examine the power of the test where power is $1-\beta$. In hypothesis testing the investigator specifies the α-level he can tolerate and then chooses the sample size to maximize the power of his test. In this way one minimizes the probability of committing a Type II error. Figures 3-5, respectively, show power curves for testing:

a. Both the hypothesis of no dose rate effect among 6 dose rates and the hypothesis of no fasting effect among 2 fasting schedules.

b. The hypothesis of no fasting effect among 2 fasting schedules.

c. The hypothesis of no dose rate effect among 6 dose rates.

Delta (Δ) is the maximum difference between dose rates or fasting schedules that the investigator may wish to detect. Sigma (σ) is the estimated standard deviation for each variable. Such estimates (the $\sqrt{\text{MSE}}$ from the ANOVA's) are summarized in Table 11.

To illustrate the use of Figures 3-5, suppose an investigator wishes to detect 30-min onset time differences in dose rates and fasting schedules at the 5% level of significance. In such a case delta/sigma = 30/22.99 or 1.3. From Figure 3 we see that the probability of a correct decision (the power) is 10% for the experiment as it was implemented with 24 subjects. By increasing the sample size by a factor of five to 120 subjects, a more realistic power level of 64% results. If the investigator were willing to omit the question of dose rate effects and concentrate only on the question of fasting effects (with α = .05), the same 24 animals would yield a power level in excess of 90% (cf. Fig. 4). On the other hand, if one were willing to use 36 animals to test the hypothesis (α = .05) of effects among the 6 dose rates (while sacrificing an answer to the question of fasting effects), the probability of making a correct decision would be 34% (cf. Fig. 5).

Figures 3-5 and the above show that there are a number of ways to increase the probability of making a correct decision. They include:

a. A decrease in the α-level (an increase in the Type I error rate).

b. A decrease in the number of questions asked.

c. An increase in the maximum difference one wishes to detect.

d. An increase in the number of animals in each experimental combination.

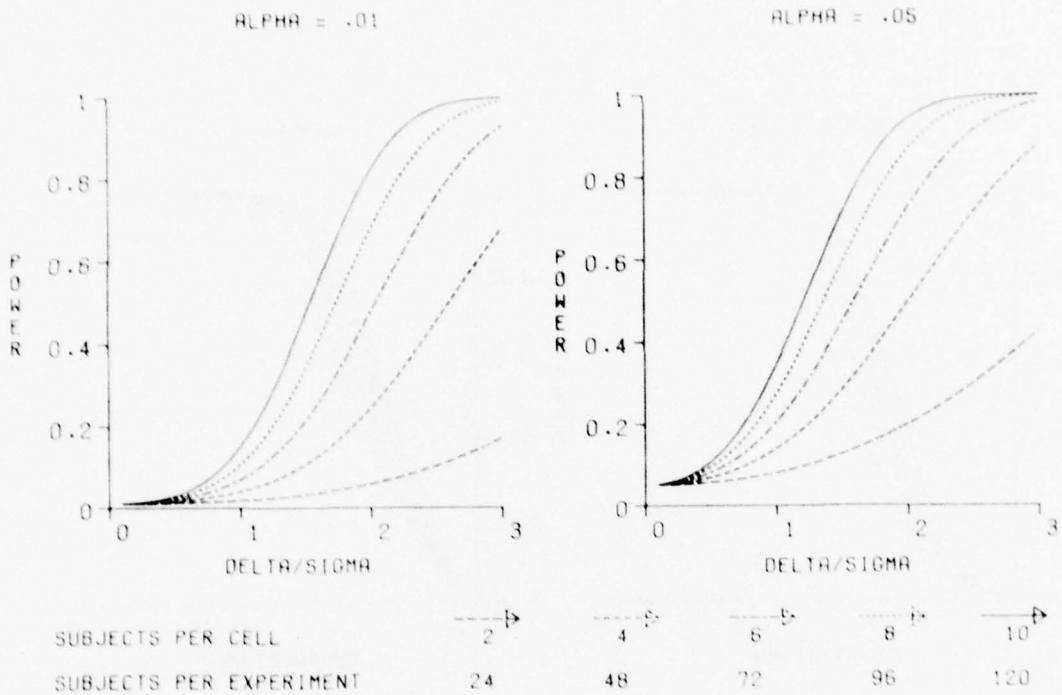


Figure 3. Minimal (worst case) power curves for testing both the hypothesis of no dose rate effect among 6 dose rates and the hypothesis of no fasting effect among 2 fasting schedules.

TABLE 11. ESTIMATES OF σ

Variable	Estimates
Onset	22.99 min
Offset	26.45 min
Vulnerability	26.49 min
Total duration	3.50 min
Productive duration	3.12 min
Nonproductive duration	1.74 min
Total No. episodes	1.61 episodes
No. productive episodes	1.26 episodes
No. nonproductive episodes	0.76 episodes

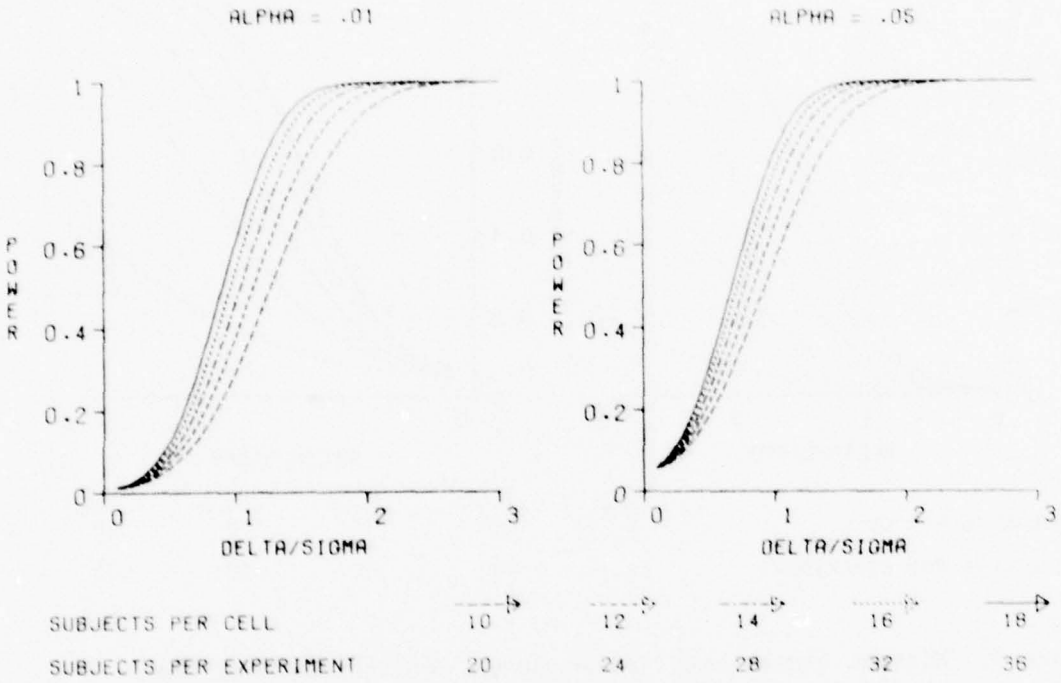


Figure 4. Power curves for testing the hypothesis of no fasting effect among 2 fasting schedules.

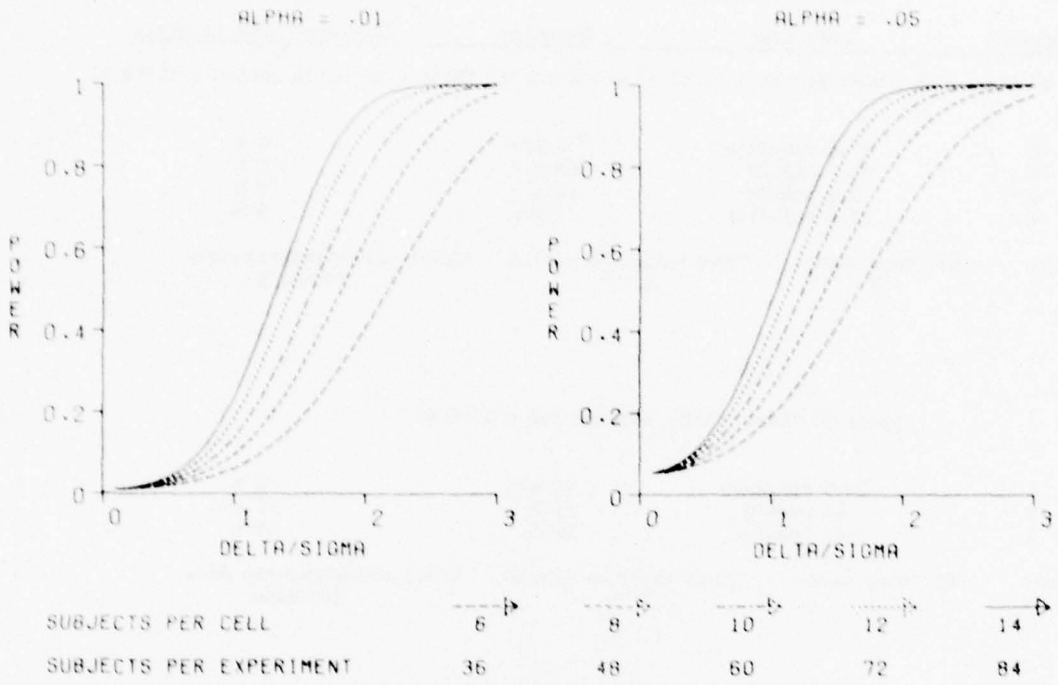


Figure 5. Power curves for testing the hypothesis of no dose rate effect among 6 dose rates.

Accurate estimates of σ are essential to ensure that operationally significant differences can be detected. In the above example 30 min represented a difference of 1.3 standard deviations in onset times. In real-world applications it might turn out that smaller differences in onset times (say 10 min) are relevant differences for detection. This would entail even larger sample sizes. We recommend at least 10 subjects/treatment group for intergroup comparisons.

MIXED RATES (Studies 36, 37, 38, 40)

Methods

Studies 36, 37, 38, and 40 represent a departure from previous experiments in that they call for scenario-specific profiles. Table 12 summarizes their experimental parameters. All four studies in this section use mixed dose rates protracted over relatively long exposure periods (0-72 h). These studies must be viewed as pilot studies due to their small sample sizes and their unique dose profiles.

TABLE 12. MIXED RATE EXPERIMENTAL PARAMETERS

Sequence	Dose rate	Duration	Time dose rate is given
Study 36 (Task = D-; work period = 11/12 h) and Study 37 (Task = D+; work period = 11/12 h)			
1	27.6 rads/min	2 min	0 h
2	97.8 rads/h	.62 h	1 h
3	9.9 rads/h	10 h	2 h
4	27.6 rads/min	3 min	9 h
Summary:	No. dose rates: 4	Total exposure period: 12 h	Total midepigastric dose: 302 rads
Study 38 (Task = PEP; work period = 9/72 h)			
1	13.5 rads/min	10 min	0 h
2	10 rads/h	10 h	10 min
3	1.05 rads/h	62 h	10 h
Summary:	No. dose rates: 3	Total exposure period: 72 h	Total midepigastric dose: 300 rads
Study 39 (Task = PEP + MART; work period = 10/10 h)			
1	50 rads/min	2 min	0 h
2	17.5 rads/min	2 min	1 h
3	7 rads/min	15 min	2 h
4	1000 rads/min	2 min	7.5 h
Summary:	No. dose rates: 4	Total exposure period: 10 h	Total midepigastric dose: 1440 rads

Studies 36 and 37 used the same profile to study the effects of both positive (D+) and negative (D-) reinforcement. Animals were trained to perform identical tasks with different rewards and were exposed to identical radiation profiles. One group received food pellets for a correct response. The other group received no food but a shock when they made an incorrect response--negative reinforcement. Table 13 shows the number of animals in each study that had at least one emetic episode.

TABLE 13. EMETIC RESPONSES IN STUDIES 36 AND 37

	Shock Study 36 D-	Food Study 37 D+	Total
Emesis	1	4	5
No emesis	7	3	10
No. of subjects	8	7	15

Results

Fisher's exact test (cf. 10) found no difference in the proportion of emetic responders between the two studies at the 10% level of significance. This finding is a result of the sample size selected. If no shock animals had vomited, Fisher's exact test would have found a significant difference between studies at the .05 level. Attention must be paid to the questions to be answered and the sample size selected to answer these questions.

It would be nice to compare study 38 with studies 36 and 37 as these studies involved 300-rad total midepigastric doses. However, as enumerated in Table 14, a number of differences between these studies are based solely on selected experimental parameters.

TABLE 14. EXPERIMENTAL PARAMETERS FOR STUDIES 36, 37, AND 38

Studies 36 and 37	Study 38
Discrete avoidance (lever pressing)	PEP
Stationary subjects	Motion
4 different dose rates, durations, and times of administration	3 different dose rates, durations, and times of administration
4 work sessions with 20-minute rest periods between sessions	9 1/2-h work sessions with rest periods of 1/2 h or 4 h between sessions

Even if the sample sizes were sufficiently large to permit valid numerical comparisons between these studies, one would be hard pressed to state the cause of any significant differences detected; should they be attributed to task differences, motion differences, dose-rate differences, or work-rest schedules.

In study 39, subjects were trained to perform two different tasks simultaneously--the continuous PEP (pitch axis only) and the discrete MART. The dose rates differed from the other studies in this section (see Table 12); in addition there were no rest periods. This study differed from other studies throughout the repository in that it is the only 2-task experiment that was implemented. Interstudy comparisons were not possible because of the variety of experimental parameters.

Comments

Mixed rate experiments may provide a practical area of research:

a. Testing for order effects in dose sequences.

b. Testing for time differences for the same dose sequence.

c. Testing for time differences for dose rate sequences.

d. Testing for task differences for the same dose profile.

Each of these areas can be systematically examined and thus provides a foundation upon which general statements can be made. The alternative is to continue looking at scenario-specific profiles which can only answer what might happen under a given set of conditions. Such an approach provides little or no information to field commanders, if the reality of their situation does not closely resemble the experimental scenario reported.

DESCRIPTIVE (Studies 3.1, 3.2, 26, 28, 32, 34, 35)

This section contains studies from the repository which could not be classified under any of the other headings. Similarly, they are also pilot studies.

Subjects in studies 3.1 and 3.2 were trained to perform the Landolt ring visual acuity task. Table 15 shows subjects in the two studies were exposed to 1 of 2 doses, 1 of 3 fasting schedules, 1 of 2 continued dose rates, and the same n:γ ratio. Multiple experimental parameters coupled with small sample sizes preclude the testing of hypotheses of differences between doses, dose-rates, and fasting schedules for this behavioral task and this neutron-gamma ratio.

TABLE 15. EMETIC RESPONSES AND FASTING SCHEDULE (h) IN STUDIES 3.1 AND 3.2

Study 3.1

Dose (Pulse, n:γ = .5)

	600 rads			1000 rads			
No. of subjects	1h	3h	16h	1h	3h	16h	Total
Emesis	1			1		1	3
No emesis	2	1					3
Total	3	1		1		1	6

Study 3.2

Dose (200 rads/min, n:γ = .5)

	600 rads			1000 rads			
No. of subjects	1h	3h	16h	1h	3h	16h	Total
Emesis	1			2		1	4
No emesis	2						2
Total	3			2		1	6

In Study 26 all subjects were on the same fasting schedule (17 h), dose rate (pulse), neutron-gamma ratio (.65), and task (PEP). They can be grouped into 4 dose ranges as shown in Table 16. Biologic variability and small sample sizes lead to a relatively flat dose-response curve. Emesis did not occur at the highest doses (2035 and 2224 rads) tested.

TABLE 16. EMETIC RESPONSES IN STUDY 26

Dose (rads) (Pulse, n:γ = .65)

	283-286	612-653	1092-1283	2035-2224	Total
Emesis	2	1	1	0	4
No emesis	1	1	1	2	5
No. of subjects	3	2	2	2	9

Study 28 was similar to study 26 in that the task (PEP), dose rate (pulse), neutron-gamma ratio (.5), and fasting schedule (1 h) were held constant for all subjects. The small sample size spread over many doses prevents definition of a dose-response curve (Table 17). This experiment did serve the purpose of dose ranging, by identifying the occurrence of emesis in the 540- to 1110-rad dose interval.

TABLE 17. EMETIC RESPONSES IN STUDY 28

	DOSE (rads) (Pulse, n:γ = .5)				
	<275	540-550	945-970	1010-1110	Total
Emesis	0	3	2	1	6
No emesis	3	0	0	1	4
No. of subjects	3	3	2	2	10

In study 32 all naive animals were subject to the same experimental parameters: fasting = 1 h; n:γ = 1/4; dose rate = pulse; dose range = 950 - 1130 rads. This study is unique in that only 1 of 12 subjects vomited in this relatively high dose range within the 2-h postexposure period.

Study 34 compared 2 doses (500 and 1000 rads) using naive animals exposed to a 5/1 neutron/gamma ratio. As shown in Table 18, the small sample sizes and different fasting schedules precluded the making of any rigid statements except that emesis can occur at either 500 or 1000 rads.

TABLE 18. EMETIC RESPONSES AND FASTING (h) SCHEDULE IN STUDY 34

	Dose (Pulse, n:γ = 5.0)					
	470-530 rads			950-1000 rads		
No. of subjects	1h	3h	6h	1h	3h	6h	Total
Emesis	1			1			2
No emesis	3		4	1		2	10
Total	4		4	2		2	12

Study 35 was another dose-ranging experiment involving 3 different doses where subjects were exposed to the same experimental parameters (a constant n:γ ratio; a 1-h fasting schedule; and the PEP pitch and roll task). Table 19 summarizes the occurrence of emesis at the various doses. Onset times were earlier, and the average number of episodes were greater for the 1000-rad dose.

TABLE 19. EMETIC RESPONSES IN STUDY 35

	Dose (Pulse, n:γ = ?)			
	250 rads	500 rads	1000 rads	Total
Emesis	3	1	4	8
No emesis	1	1	0	2
No. of subjects	4	2	4	10

The data from 10 studies (2, 3, 18, 19, 27, 28, 31, 33, 35, 39) were arbitrarily grouped together to provide a very gross description of the emetic response following radiation (Table 20). The group total was 89 monkeys representing all aspects of experimental variability such as different doses, dose rates, radiation quality (x, γ, n:γ), fasting times, and tasks. The objective is simply to provide future experimenters with rough statistical estimates to plan resource commitments, hopefully including fewer questions, more monkeys per treatment group, and longer observation periods.

TABLE 20. STATISTICAL SUMMARY OF GROUPED EMESIS DATA[a]

	$\bar{X}$	Range	S.D.
Onset delay (min)	40.4	1 to 106.9 (min)	18.2
Vulnerable period (min) (Syndrome duration)	31.4	.1 to 217 (min)	35.3
Episodes	2.9	1 to 14	2.1
% Productive	72%	38% to 85%	-

[a] 1. N=89 responders
2. Studies 2, 3, 18, 19, 27, 28, 31, 33, 35, 39
3. Since some observation periods were only 2 hours, there may be some data truncation.
4. Onset times for studies 31 and 39 were adjusted for low dose rate by subtracting the time necessary to deliver 450 rads (ED_{50} emesis).

COMPUTER PROGRAMS

This section briefly outlines the computer software used in the analysis of this repository. All programming was done in APL. Source listings of appropriate code are given in Appendix B. This section is not an APL tutorial. Its purpose is to indicate by name and function appropriate software tools so that the repository can be maintained.

Data Sets

Data set EMESIS.D770323 is organized by study as follows:

Description of data	Field	Description of data	Field
Study number	1-5	Animal type	43-48
Month	7-9	Number of males	50-55
Year	11-12	Number of females	57-61
Experimental site	14-18	Restraint used on subject	63-67
Type radiation used	20-24	Emesis data collected	69-74
Neutron/gamma ratio	26-29	Low dose (Midepigastric)	77-80
Task	31-34	High dose (Midepigastric)	83-86
Hours observed	36-37	Mode of dose administered	88-91
Number of animals	40-41		

The function REPOSITORY accesses this data set. It is user oriented and permits the novice to examine the experimental parameters in all studies currently cataloged in the computer repository. This function can produce tables similar to Table 1 as well as subtables of any of the experimental parameters selected. For example, one can obtain a listing of all PEP experiments or all experiments conducted at White Sands Missile Range.

The data set ALL.EMESIS.D770420, organized by subject and study, contains additional experimental parameters on each animal such as fasting schedule and dose rate as well as what happened on exposure day: the number of emetic episodes, onset and duration times, and the classification of episodes as productive or nonproductive. This data is structured as follows:

Description of data	Field	Description of data	Field
Subject ID	1-5	Pulse size (min)	24-26
Study No.	7-10	Dose rate (rads/min)	28-31
Dose (Midepigastric)	12-15	Number of episodes	33-34
Hours fasted	17-20	Onset time (xxx.xxmin)	36-41
Radiation mode	22	Duration time "	43-47
(0 = steady or mixed rates)		Kind of emesis	49
(1 = single pulse)		(1 = productive; 2 = nonprod)	
(2 = double pulse)		No. of contractions	51-53

The pattern starting in column 36 for onset times, duration times, kinds of emesis, and number of contractions repeats itself (starting in column 55) as many times as is necessary until all episodes have been described.

Plot Routines

The graphs in Appendix A were created by the function PLOTEME. This function obtains its data from the ALL.EMESIS.D770420 data set. When called, this function will ask the user to define the study he wishes to draw. The function will automatically draw dose profiles for continuous- and single-pulse experiments. The user must write his own software to draw more complicated dose profiles. DRA33, DRA36, DRA37, and DRA38 are such examples for studies 33, 36, 37, and 38, respectively.

The power and the dose rate curves were drawn by the functions SETUPMOD following correct definition of X and Y variables. These APL functions are general in nature and permit the user to draw as many coordinate axes with as many variables as one specifies.

A graphics DIRECTORY has been created which stores all the illustrations created in this technical report. To display any item in the directory one merely needs to type the word DISPLAY followed by the name of the file to be displayed in quotes. This system will save dollars and time in not having to recreate these illustrations for a second time. A second advantage of this system is that it allows graphic overlays so that different studies can be examined simultaneously.

Analysis Programs

Analysis programs developed in this report include LILLYEX X, WEIBULL X, ANOVA X, TUKE2, and DSTAT X. These routines are user oriented and will prompt the user for necessary information. LILLYEX X and WEIBULL X, respectively, test to see if data X has exponential or Weibull distributions. ANOVA X is used to perform a two-factor analysis of variance on a three-dimensional data matrix X where the first dimension represents replicates, levels of the B factor are the second dimension, and the levels of the A factor are the third dimension. TUKE2 will take the output of ANOVA X and perform Tukey's multiple comparison procedures on each factor. DSTAT X will compute means, standard deviations, and other descriptive statistics on the data vector X.

Again, we repeat that the purpose of this section and Appendix B is not to serve as a "how to" guide. Their inclusion is to indicate which tools are currently available in support of this repository. There is no substitute for computer terminal experience and a reading of the RTW Emetic Repository Log Book to better learn how to use these tools.

CONCLUSIONS

Data on ionizing radiation emesis, collected from 21 studies involving 210 rhesus monkeys, has been examined. These studies contained a wide variety of experimental parameters prepared by investigators interested in unique situations. The studies were grouped a posteriori on the basis of the analysis permitted by the data collected.

In several studies the distribution of emesis onset times and episode durations could be determined. In these instances, the onset time of each episode had an exponential distribution, and the duration of each episode was either an exponential or Weibull distribution. The presence of similar distributions across many experiments suggests that the same mechanism is at work in each study and episode, differing only in intensity.

One study found the ED_{50} for radiation emesis to be 446 rads (Co^{60}, 20 rads/min), and that motion reduced the ED_{50} to 258 rads. Another study (No. 31) demonstrated 100% incidence of emesis at 550 rads (X-ray, 6 to 175 rads/min).

Although designed to answer other research questions, these studies are good emesis syndrome pilot studies in that they refine experimental techniques, permit the training of personnel and the development of SOPs, and provide experience for contingency plans. They provide the opportunity to operationally define what is to be measured; they facilitate the selection of competing metrics, and suggest how long the measurement process should occur.

The effects of such factors as dose rate, fasting time, radiation quality, and performance tasks on the radiation emesis syndrome are still undetermined. The present studies provide estimates of σ for planning fully developed emesis experiments so understanding of the interrelationships between α-levels, number of questions to be answered, operationally relevant differences to be detected, and the sample size selected can result in cost-effective experiments with a high payoff in valid findings. As a rule of thumb, we recommend at least 10 subjects per treatment group in making intergroup comparisons.

ACKNOWLEDGMENTS

We wish to thank Lt. Col. Dan J. Craig, Mr. Donald J. Barnes, and Mr. G. Carroll Brown for sharing the emetic data they collected (Table 1). Thanks are also due Mr. Kenneth A. Hardy and Mr. Stewart J. Allen for the dosimetry support rendered in the original studies. We are grateful to Mr. Donald Cosgrove for use of his power function programs, to Capt. Carl R. Efird for advice in the development of computer software for Appendix A, and to Mr. Bruce Montague for computer software permitting an interface between a CRT and a Calcomp plotter. Finally, we are grateful to Ms. Maria Luisa Valdez for the data collation involved in this effort.

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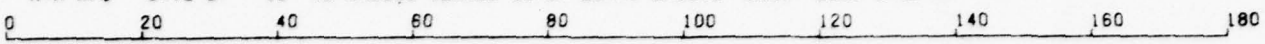
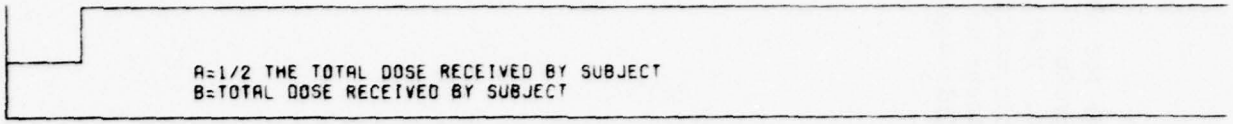
APPENDIX A

PICTORIAL SUMMARY OF EMETIC FINDINGS

Appendix A is a graphical summary of emetic findings for the studies listed in Table 1. Bars 2 units high indicate productive episodes. Bars 1 unit high indicate nonproductive episodes. Width of bars indicate episode duration. Flat lines show no emetic activity between emetic episodes. Absence of bars and lines indicate no emetic signs during the observation period given in Table 1. This appendix is organized by study numbers presented in Table 1.

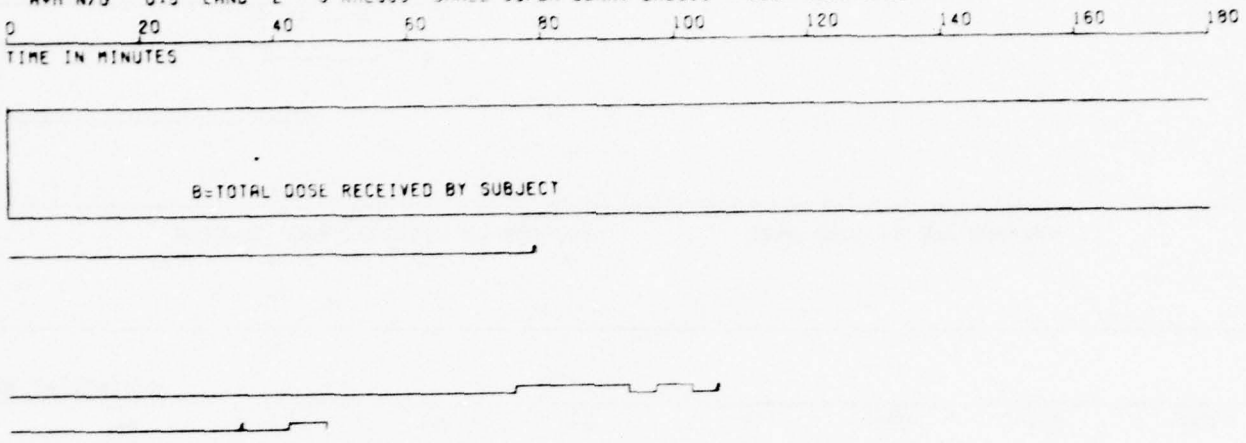
STUDY NO.	DATE	SITE TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
2	MAR 72	A+M	N/G	0.72 D-	15	16	RHESUS	16MALE 0DFEM	BEHAV	EMESIS	2160	2650	2PUL





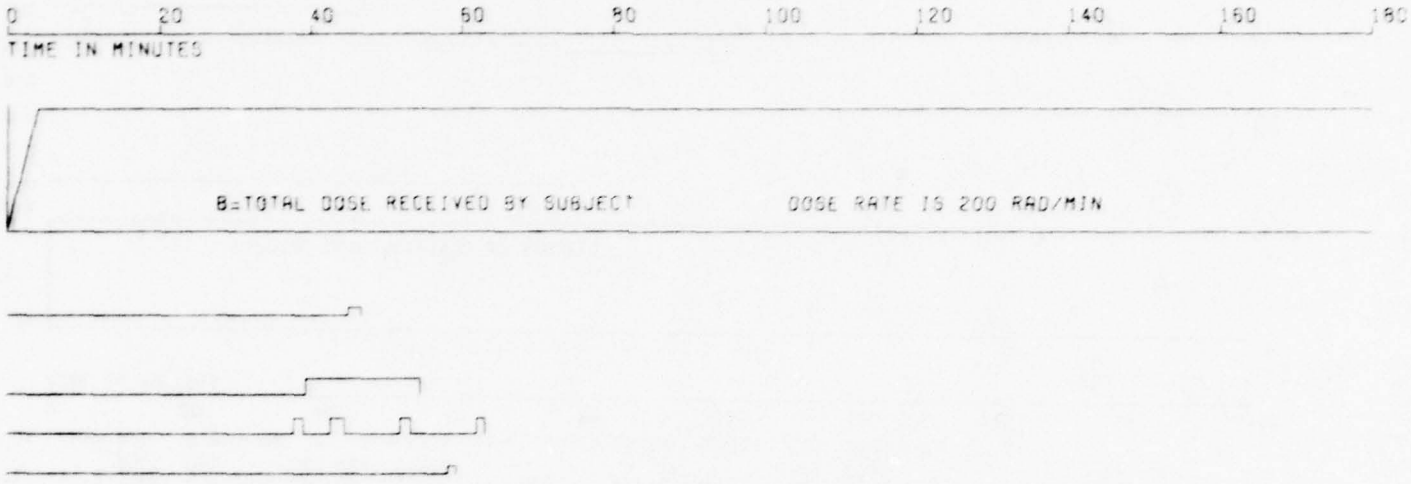
ID	DOSE	HRFD
28	2160	17.0
34	2190	17.0
24	2410	17.0
36	2430	17.0
32	2490	17.0
22	2520	17.0
23	2520	17.0
26	2530	17.0
33	2530	17.0
27	2580	17.0
35	2590	17.0
25	2600	17.0
21	2620	17.0
30	2620	17.0
31	2630	17.0
29	2650	17.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
3-1	OCT 71	A+M	N/G	0.5	LAND	2	6	RHESUS	6MALE 0OFEM	BEHAV	EMESIS	600	1000	1PUL

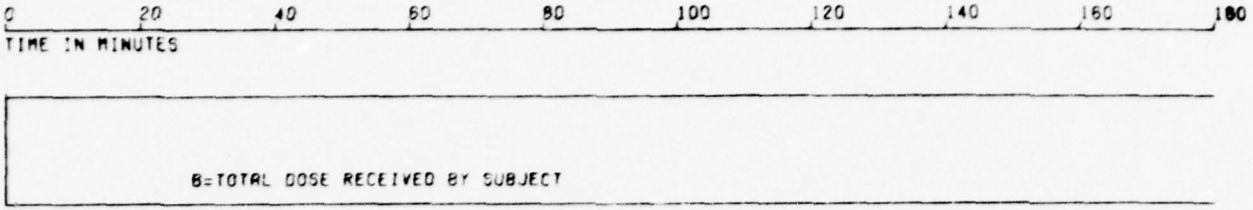


ID	DOSE	HRFD
38	600	1.0
39	600	1.0
40	600	1.0
43	600	3.0
41	1000	16.0
42	1000	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
3-2	OCT 71	A+M	N/G	0.5	LAND	2	6	RHESUS	6MALE OOFEM	BEHAV	EMESIS	600	1000	CTED

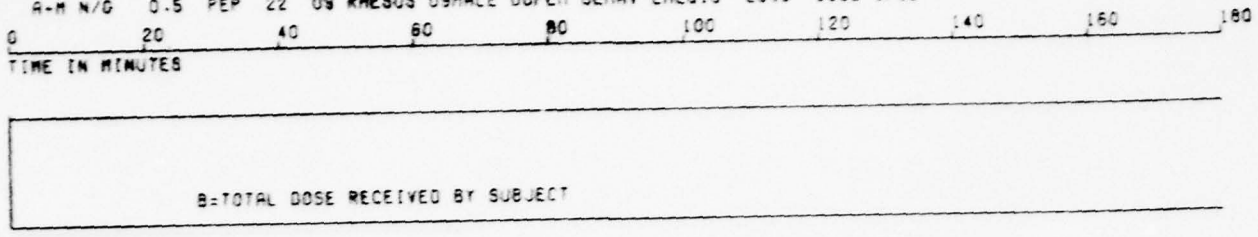


STUDY NO.	DATE	SITE	TYPE RAD.	N/C RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
18	JUL 71	AFRRI	N/C	0.24	PEP	22	11	RHESUS	11MALE 00FEM	BEHAV	EMESIS	1020	2920	IPUL



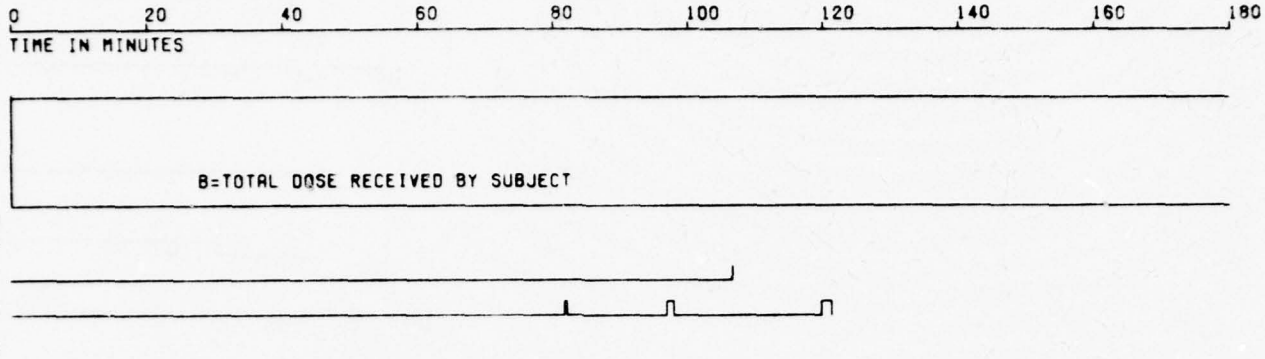
ID	DOSE	HRFD
284	1020	1.0
283	1050	1.0
281	1080	1.0
282	1130	1.0
277	2440	14.0
278	2580	14.0
273	2600	14.0
275	2740	14.0
276	2780	14.0
279	2890	14.0
280	2920	14.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
	19 MAR 72	A-M	N/G	0.5	PEP	22	08	RHESUS	08MALE 00FEM	BEHAV	EMESIS	2840	3380	1PUL



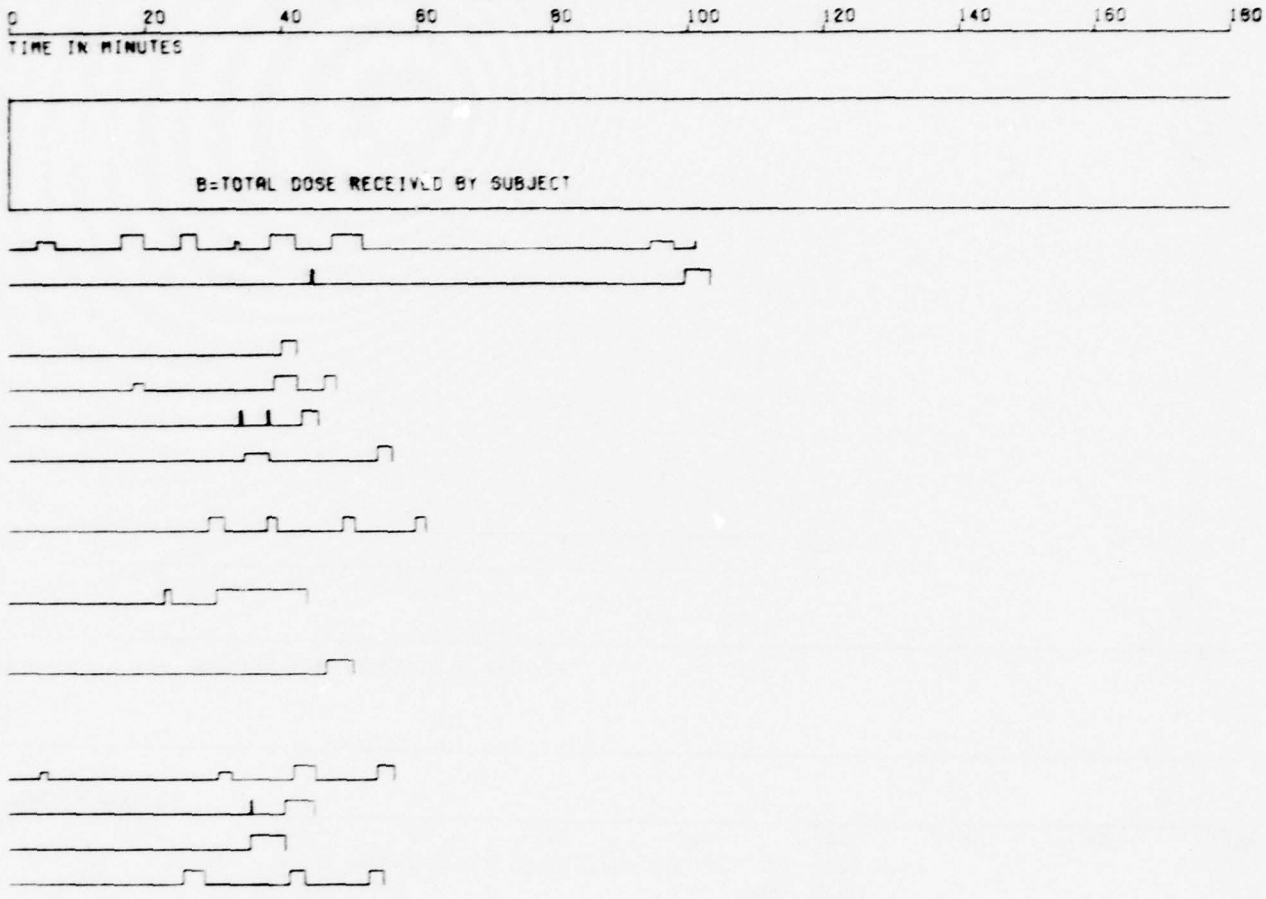
ID	DOSE	HRFD
293	2840	1.0
290	3045	1.0
288	3070	1.0
286	3090	1.0
287	3100	1.0
285	3180	1.0
292	3220	1.0
291	3240	1.0
37	3380	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
26	AUG 72	A+M	N/G	0.65	PEP	2	09	RHESUS	09MALE 00FEM	BEHAV	EMESIS	283	2224	1PUL



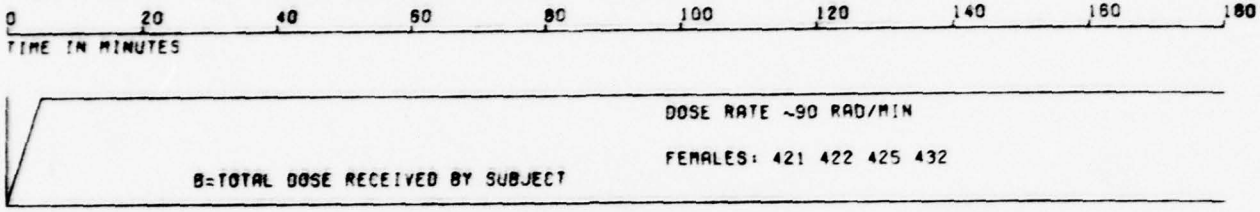
ID	DOSE	HRFD
371	283	17.0
370	286	17.0
372	286	17.0
368	612	17.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
	27 AUG 72	A+M	N/G	0.44	D-	2	19	RHESUS	19MALE 00FEM	BEHAV	EMESIS	2122	2365	IPUL



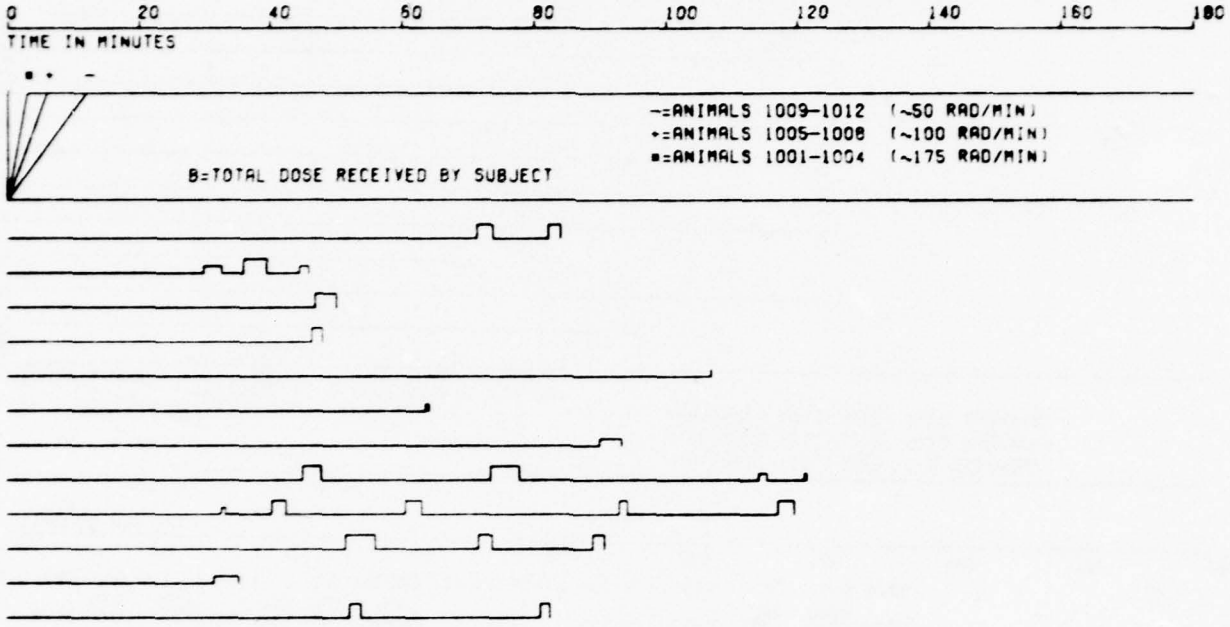
STUDY NO.
DATE
SITE
TYPE RAD.
N/G RAT
TASK
HRS OBS
NO. ANS
ANIMAL TYPE
SEX
RESTR
EMESIS
LOW DOSE
HIGH DOSE
MODE
28 MAR 73
A-M
N/G
0.6
PEP
2
10
RHESUS
MALE
OPEN
BEHAV
EMESIS
170
1110
IPUL
0
20
40
60
80
100
120
140
160
180
TIME IN MINUTES
B
RADS
B=TOTAL DOSE RECEIVED BY SUBJECT
ID DOSE HRFD
397 170 1.0
405 250 1.0
402 275 1.0
403 540 1.0
399 550 1.0
400 550 1.0
396 945 1.0
398 970 1.0
404 1010 1.0
401 1110 1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/C RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
	30 OCT 73	SAM	X-RAY		D-	2	12	RHESUS	08MALE 04FEM	PHYSI	EMESIS	341	528	STED



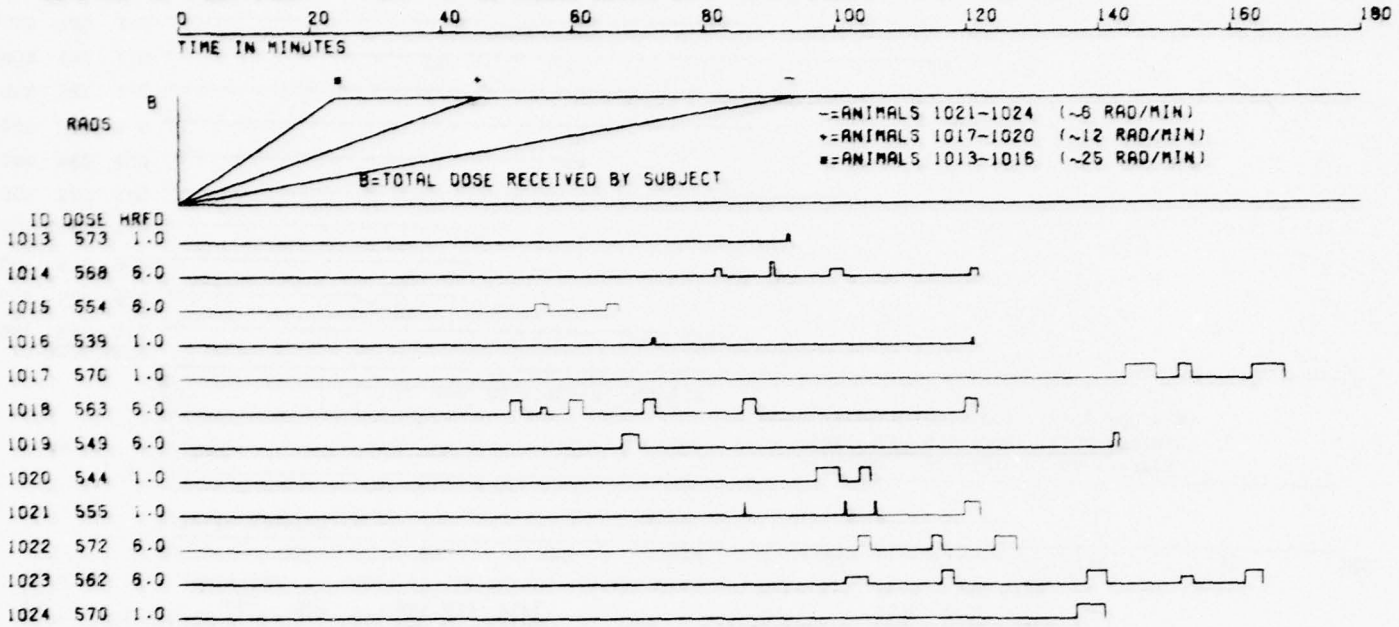
ID	DOSE	HRFD
428	341	.0
425	513	.0
423	515	.0
429	515	.0
430	515	.0
422	518	.0
432	516	.0
421	523	.0
427	523	.0
424	525	.0
426	525	.0
431	528	.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/C RAY	TASK OBS	HRS ANS	NO.	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
31.1	MAY 71	SAM	X-RAY		NAIV	2	12	RHESUS	12MALE 00FEM	NAIVE	EMESIS	517	580	STED



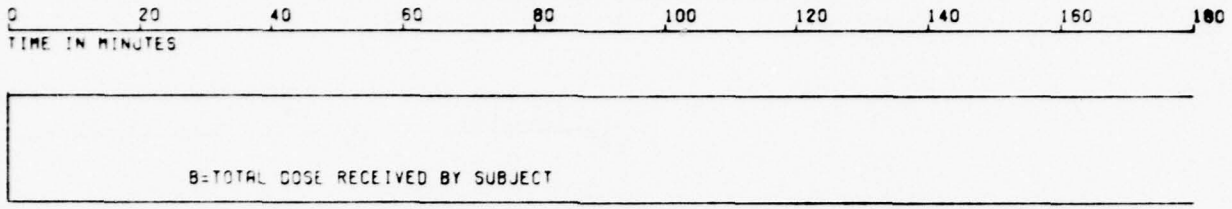
ID	DOSE	MRFD
1001	542	1.0
1002	525	6.0
1003	537	6.0
1004	517	1.0
1005	550	1.0
1006	552	6.0
1007	563	6.0
1008	562	1.0
1009	580	1.0
1010	580	6.0
1011	580	6.0
1012	575	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
31.2	MAY 71	SAM	X-RAY		NAIV	2	12	RHESUS	12MALE 00FEM	NAIVE	EMESIS	539	573	STED



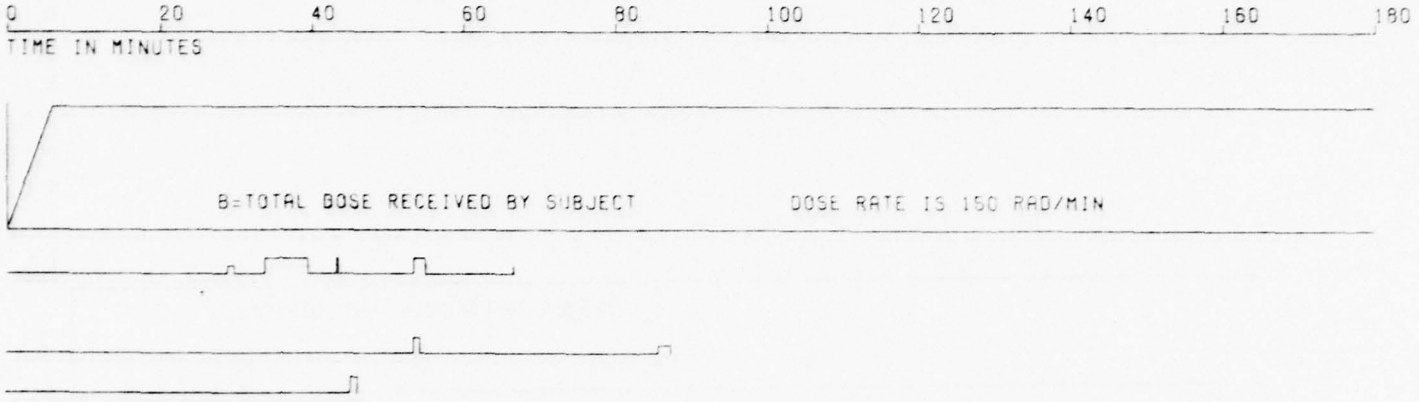
ID	DOSE	HRFD
1013	573	1.0
1014	568	6.0
1015	554	6.0
1016	539	1.0
1017	570	1.0
1018	563	6.0
1019	543	6.0
1020	544	1.0
1021	555	1.0
1022	572	6.0
1023	562	6.0
1024	570	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
32	JUL 71	AFRRI	N/G	0-24	NAIV	2	12	RHESUS	12MALE 00FEM	BEHAV	EMESIS	950	1130	1PUL



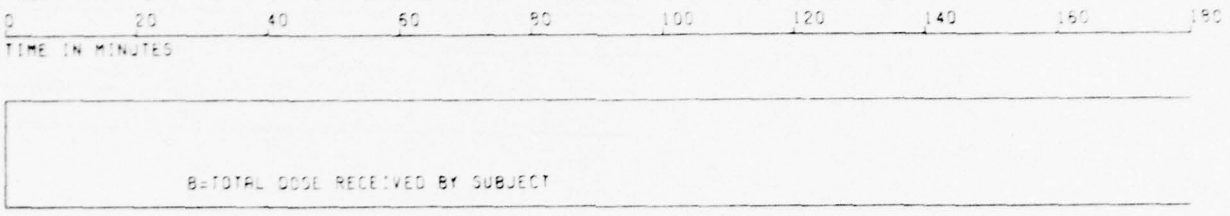
ID	DOSE	HRFD
1031	950	1.0
1035	960	1.0
1030	970	1.0
1034	970	1.0
1032	980	1.0
1029	990	1.0
1027	1000	1.0
1033	1000	1.0
1036	1000	1.0
1028	1080	1.0
1025	1100	1.0
1026	1130	1.0

STUDY NO.	DATE	SITE TYPE RAD.	N/G RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
33	SEP 71	SAM X-RAY		NAIV	2	04	RHESUS	04MALE 00FEM	BEHAV	EMESIS	883	955	STED



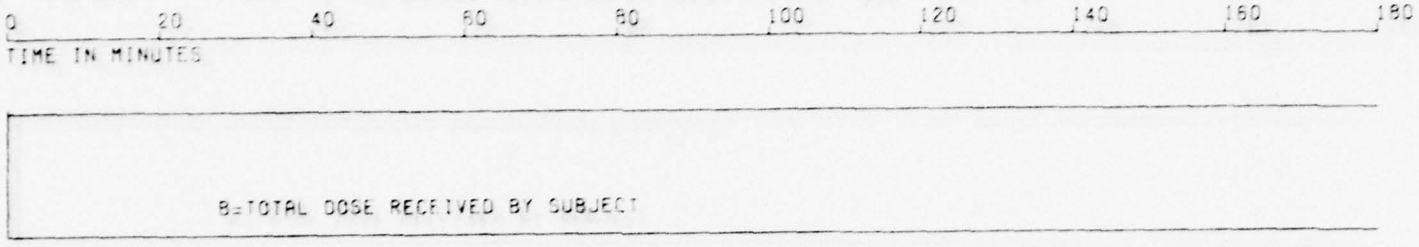
ID	DOSE	HR-D
1038	883	1.0
1040	883	1.0
1037	915	1.0
1039	955	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	TYPE RAT	N/C	TASK	HRS OBS	NO. ANO	ANIMAL TYPE	SEX	REGTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
	24 JAN 72	WSMR	N/C	5.0	NAIV	2	12	RHESUS	12MALE 00FEM		BEHAV	EMESIS	470	1000	IPUL



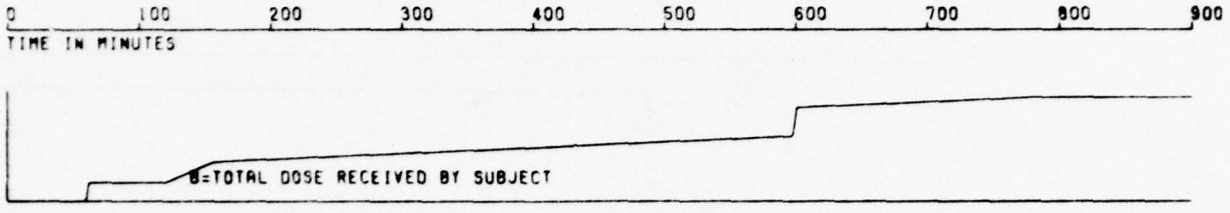
ID	DOSE	HRFD
1043	470	1.0
1046	470	6.0
1044	480	1.0
1045	480	6.0
1041	490	1.0
1042	490	1.0
1047	510	6.0
1048	530	6.0
1049	950	1.0
1050	970	1.0
1052	980	6.0
1051	1000	6.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/C RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
35	MAR 74	A-M	N/C		PEP	2	10	RHESUS	10MALE 00FEM	BEHAV	EMESIS	250	1000	1PUL



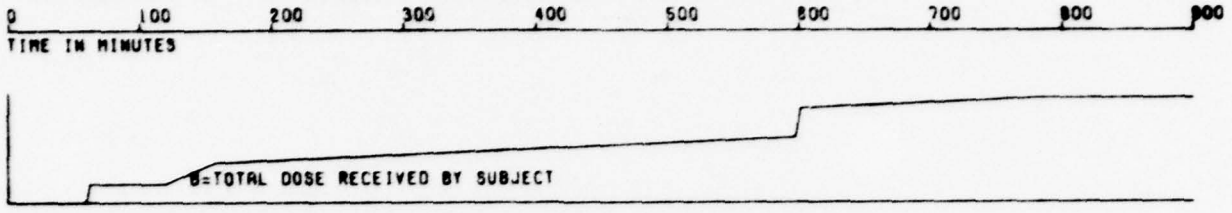
ID	DOSE	HRFD
1053	250	1.0
1054	250	1.0
1055	250	1.0
1056	250	1.0
1057	500	1.0
1058	500	1.0
1059	1000	1.0
1060	1000	1.0
1061	1000	1.0
1062	1000	1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/C RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
36	DEC 75	SAM	COL60	N/A	D-	12	08	RHESUS	08MALE 00FEM	BEHAV	EMESIS	300	300	STED

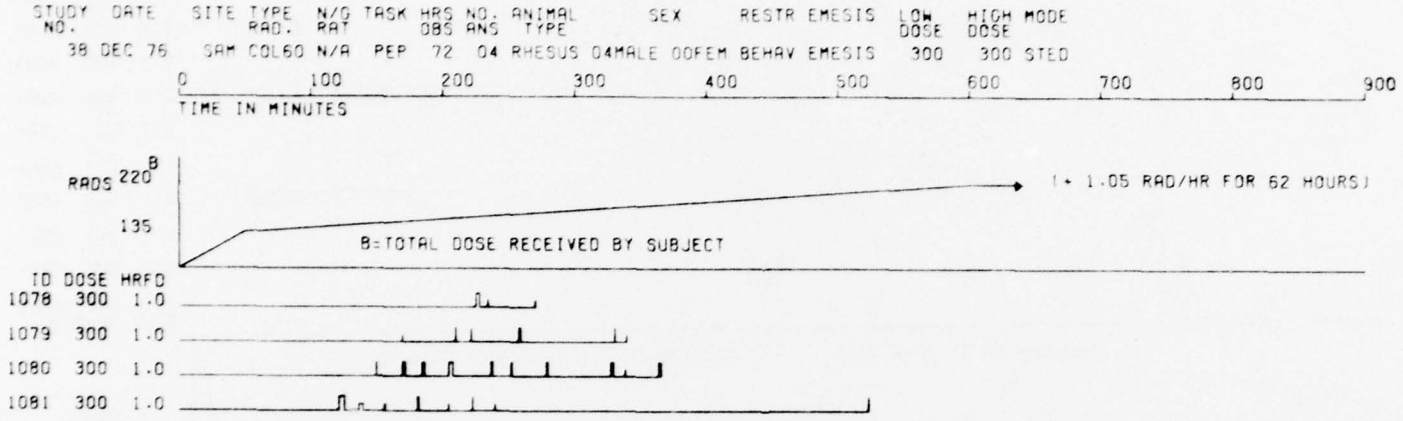


ID	DOSE	HRFD
1063	300	1.0
1064	300	1.0
1065	300	1.0
1066	300	1.0
1067	300	1.0
1068	300	1.0
1069	300	1.0
1070	300	1.0

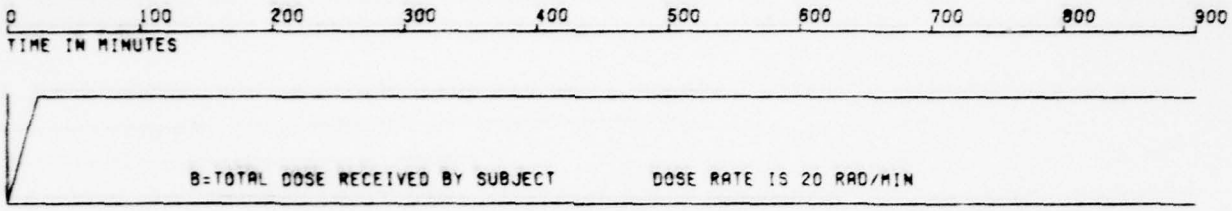
STUDY NO.	DATE	SITE	TYPE RAD.	M/C RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
37	DEC 75	SAM	COL60	M/A	D+	12	07	RHESUS	07MALE 00FEM	BEHAV	EMESIS	300	300	STEQ



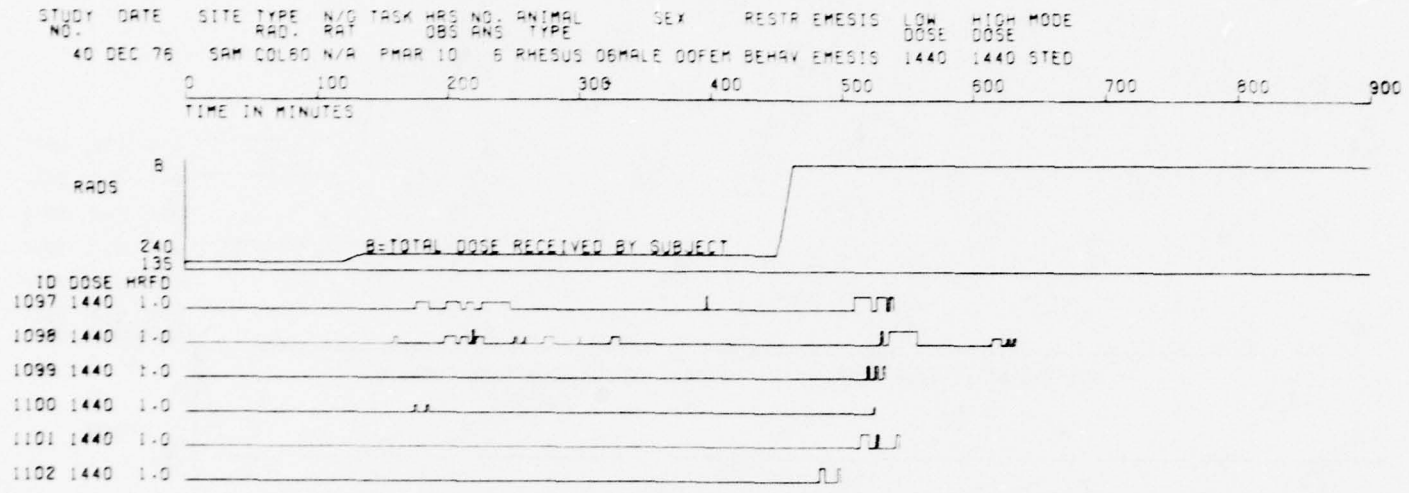
ID	DOSE	HRFD
1071	300	1.0
1072	300	1.0
1073	300	1.0
1074	300	1.0
1075	300	1.0
1076	300	1.0
1077	300	1.0


STUDY NO.
DATE
SITE TYPE RAD.
N/O RAT
TASK
HRS OBS
NO. ANS
ANIMAL TYPE
SEX
RESTR
EMESIS
LOW DOSE
HIGH DOSE
MODE
38 DEC 76 SAM COL60 N/A PEP 72 04 RHESUS 04MALE 00FEM BEHAV EMESIS 300 300 STED
0 100 200 300 400 500 600 700 800 900
TIME IN MINUTES
RADS
220
B
135
(+ 1.05 RAD/HR FOR 62 HOURS)
B=TOTAL DOSE RECEIVED BY SUBJECT
ID DOSE HRFD
1078 300 1.0
1079 300 1.0
1080 300 1.0
1081 300 1.0

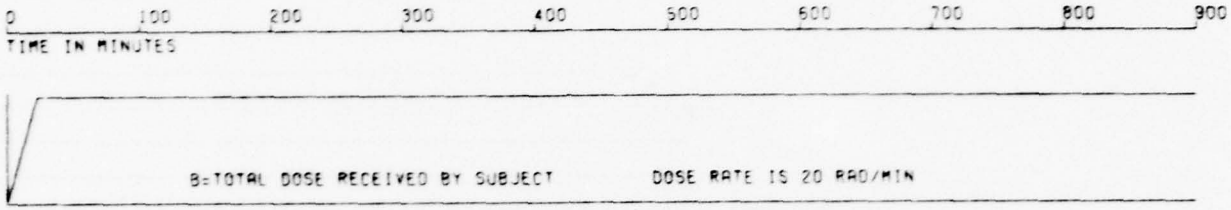
STUDY NO.	DATE	SITE	TYPE RAD.	N/O RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
39	MAR 77	SAM	COL60	N/A	NAIV	4	15	RHESUS	15MALE 00FEM	CHAIR	EMESIS	350	550	STED



ID	DOSE	HRFD
1082	350	1.4
1086	350	1.0
1083	400	1.3
1085	400	1.0
1087	400	1.3
1093	400	1.5
1084	450	1.0
1088	450	1.3
1092	450	1.6
1094	450	1.0
1096	450	1.5
1089	500	1.5
1091	500	2.2
1095	500	1.0
1090	550	1.3


STUDY NO. DATE SITE TYPE REQ. N/O RAT TASK OBS HRS ANS NO. ANIMAL TYPE SEX RESTR EMESIS LOW DOSE HIGH DOSE MODE
40 DEC 76 SAM COLSO N/A PMAR 10 6 RHESUS OBMALE OOFEM BEHAV EMESIS 1440 1440 STED
0 100 200 300 400 500 600 700 800 900
TIME IN MINUTES
B
RADS
240
135
B=TOTAL DOSE RECEIVED BY SUBJECT
ID DOSE HRFD
1097 1440 1.0
1098 1440 1.0
1099 1440 1.0
1100 1440 1.0
1101 1440 1.0
1102 1440 1.0

STUDY NO.	DATE	SITE	TYPE RAD.	N/O RAT	TASK	HRS OBS	NO. ANS	ANIMAL TYPE	SEX	RESTR	EMESIS	LOW DOSE	HIGH DOSE	MODE
41	APR 77	SAM	COLBO	N/A	SHAM	4	8	RHESUS	OMALE	OOFEM	CHAIR	EMESIS	200	300	STEP



ID	DOSE	HRFD
1107	200	1.0
1104	250	1.0
1106	250	1.0
1108	250	1.0
1103	300	1.0
1105	300	1.0

APPENDIX B

COMPUTER SCURCE CODES

Appendix B is a listing of computer source codes from which the present repository analysis and maintenance was possible. The major functions include:

REPOSITORY
PLOTEME
SETUPMOD
DIRECTORY
LILLYEX X
WEIBULL X
ANOVA X
TUKE2
DSTAT X

Appropriate subroutines are also listed. The inclusion of this appendix is to identify computer tools presently in support of this repository. It is not a "how to" guide.

```
      ∇REPOSITORY[□]∇
    ∇ REPOSITORY;□IO;DATA;LR;R;KEY;T;I;NR
[1]   'THIS PROGRAM WILL ALLOW THE USER TO DIVIDE THE SUMMARY TABLE OF STUDIES BY THE ASPECTS OF THE STUDIES'
[2]   'PLEASE WAIT WHILE FILE IS BEING LOCATED'
[3]   □IO←1
[4]   DATA←LOADEMECIS
[5]   LR←1↑⍴DATA
[6]   →('YES' ASK 'DO YOU WANT TO SEE A SUMMARY TABLE OF THE STUDIES?')/YES
[7]   →L2
[8]  YES:RHEADER
[9]   DATA
[10] L2:→('YES' ASK 'DO YOU NEED AN EXPLANATION OF HOW TO SUBDIVIDE THE SUMMARY TABLE?')/YESA
[11]  →NOA
[12] YESA:TEX 3
[13]  'YOU WILL BE ASKED IF YOU WANT TO SUBDIVIDE THE SUMMARY TABLE.  IF YOU ANSWER NO THE PROGRAM WILL TERMINATE.'
[14]  'IF YOU ANSWER YES YOU WILL BE ASKED TO TYPE IN A KEYWORD FROM THE TABLE OF ABBREVIATIONS.'
[15]  'YOU CAN CONTINUE THIS PROCESS UNTIL YOU NO LONGER WANT TO SUBDIVIDE.'
[16]  'THE ABBREVIATION TABLE FOLLOWS:'
[17]  ' '
[18]  DD
[19] NOA:' '
[20] RESTART:R←(0,LR)⍴' '
[21]  →('YES' ASK 'DO YOU WANT TO SUBDIVIDE THE SUMMARY TABLE?')/YESB
[22]  →NOB
[23] YESB:KEY←'' ASK 'TYPE IN THE KEYWORD YOU WANT THE TABLE TO BE SUBDIVIDED BY'
[24]  I←0
[25]  NR←1↑⍴DATA
[26] LP:→(NR<I←I+1)/OUT
[27]  →(0=⍴DATA[I;] PATTERN KEY)/LP
[28]  R←R,[1] DATA[I;]
[29]  →LP
[30] OUT:→('YES' ASK 'DO YOU WANT TO SUBDIVIDE THE NEW TABLE AGAIN?')/YESC
[31]  →NOC
```

```
      ∇REPOSITORY[□32]∇
[32] YESC:'TYPE IN THE KEYWORD THAT YOU WANT TO SUBDIVIDE BY'
[33]  KEY←□
[34]  I←0
[35]  T←(0,LR)ρ' '
[36]  NR←1↑ρR
[37] LP2:→(NR<I←I+1)/OUT2
[38]  →(0=ρR[I;] PATTERN KEY)/LP2
[39]  T←T,[1] R[I;]
[40]  →LP2
[41] OUT2:R←T
[42]  →OUT
[43] NOC:TEK 3
[44]  RHEADER
[45]  R
[46]  ' '
[47] NOB:→('YES' ASK 'DO YOU WANT TO GO THROUGH THIS PROCESS AGAIN USING DIFFERENT KEYWORDS?')/RESTART
```

```
      ∇LOADEMESIS[□]∇
    ∇ R←LOADEMESIS;□IO;SHRI;LR;L;I
[1]   □IO←1
[2]   I←□EX 'SHRI'
[3]   '' CHK 'SHRI' TRY 'SP DSN=EB.A3H01.Z652007.EMESIS.D770420,DISP=SHR,UNIT=3330,VOL=000062,CODE=A'
[4]   □IO←1
[5]   LR←0
[6]  LP:L←SHRI
[7]   →(0=ρL)/END
[8]   →(0<LR)/GO
[9]   LR←ρL
[10]  R←(0,LR)ρ' '
[11] GO:R←R,[1] L
[12]  →LP
[13] END:I←□EX 'SHRI'
    ∇
```

```
      ∇ASK[□]∇
    ∇ R←ANS ASK TEXT;NA;NT
[1]   NT←1+⍴,TEXT
[2]  LP:R←NT↑□,⍞,⍨←TEXT,' '
[3]   →(0=⍴R)/LP
[4]   →(0=NA←⍴ANS)/0
[5]   R←ANS[⍳NA]←R
      ∇

      ∇DD[□]∇
    ∇ DD
[1]   'ABBREVIATION     USEAGE       MEANING'
[2]   ' '
[3]   'EMESIS           EMESIS       COLLECTED EMESIS DATA'
[4]   ' '
[5]   'A+M              LOCATION     TEXAS A+M UNIVERSITY'
[6]   'AFRRI            LOCATION     ARMED FORCES RAD. RESEARCH INSTITUTE'
[7]   'NSL              LOCATION     NORTHROP SPACE LABORATORIES'
[8]   'SAM              LOCATION     SCHOOL OF AEROSPACE MED.'
[9]   'TREES            LOCATION     TRANSIENT RAD. EFFECTS'
[10]  'WSMR             LOCATION     WHITE SANDS MISSILE RANGE'
[11]  ' '
[12]  'UNRES            RESTRAINT    UNRESTRAINED'
[13]  'BEHAV            RESTRAINT    BEHAVIORAL CHAIR'
[14]  'PHYSI            RESTRAINT    PHYSIOLOGICAL RECORDING CHAIR'
[15]  ' '
[16]  'N/G              RADIATION    MIXED NEUTRON/GAMMA'
[17]  'X-RAY            RADIATION    LINAC X-RAY'
[18]  'NEUT             RADIATION    NEUTRON,PURE'
[19]  'FLASH            RADIATION    FLASH X-RAY'
[20]  'COB60            RADIATION    COBALT 60 GAMMA'
```

```
      ∇DD[⎕21]∇
[21]  'LASER          RADIATION    LASER'
[22]  'MICRO          RADIATION    MICROWAVE'
[23]  'HIGHZ          RADIATION    HIGH-Z--HEAVY ION'
[24]  ' '
[25]  'CMTS           TASK'
[26]  'D-             TASK         DISCRETE AVOIDANCE PROGRAM-NEGATIVE REINPORCEMENT'
[27]  'D+             TASK         DISCRETE AVOIDANCE PROGRAM-POSITIVE REINPORCEMENT'
[28]  'DMTS           TASK         DELAYED MATCH-TO-SAMPLE'
[29]  'DRL            TASK'
[30]  'LAND           TASK'
[31]  'MAP            TASK         MULTIPLE AVOIDANCE PROGRAM'
[32]  'NAIV           TASK'
[33]  'PEP            TASK         PRIMATE EQUILIBRIUM PLATPORM'
[34]  'PMAR           TASK         PEP-MART'
[35]  'VTT            TASK         VISUAL TRACKING TASK'
[36]  ' '
```

```
      ∇PATTERN[⎕]∇
    ∇ R←S PATTERN P;I;LP
[1]   I←0
[2]   R←⍳0
[3]   LP←(⍴S)⍴1
[4]  LOOP:→(0=⍴P)/END
[5]   LP←LP∧((I+S)=1↑P),I↓0
[6]   P←1↓P
[7]   I←I+1
[8]   →LOOP
[9]  END:R←LP/⍳⍴S
      ∇
```

```
      ∇PLOTEME[□]∇
    ∇ PLOTEME;ST;□IO;N
[1]   □IO←1
[2]   USING CENTIMETERS,4015,FOCUS,BUFFERED
[3]   SET CHARSIZE TO 3
[4]   SET SCALE TO 0.18 0.18
[5]   ANMODE
[6]   ERASE
[7]   EMEINP
[8]  OLP:'THE VARIABLE AVAILABLE FOR COMPARISON OPERATIONS IS "STUDY" '
[9]   COMPO←'' ASK 'ENTER THE COMPARISON OPERATION '
[10]  INDX←((⍷COMPO)/⍳⍴STUDY)-1
[11]  J←1
[12]  →(0=⍴INDX)/NOGO
[13]  ERASE
[14]  HEAD
[15]  PL← 0 20
[16]  STRING 'TIME IN MINUTES' AT 5 25
[17]  STRING '   ID DOSE HRFD' AT 0 20.5
[18]  MOVE TO 5 25.5
[19]  I←0
[20]  SCAL←1
[21]  →(36>⍷(6+COMPO))/SCL
[22]  SCL2
[23]  SCAL←1+5
[24]  →RDLP
[25] SCL:SV←SVSTAT
[26]  DRAW 0 1
[27]  MOVE 0 0.5
[28]  STRING▼I
[29]  RESTAT SV
[30]  →(180<I←I+20)/RDLP
```

```
      ∇PLOTEMB[□31]∇
[31]  DRAW 20 0
[32]  →SCL
[33] RDLP:RDEMB INDX
[34]  →('DOSE'∧.=4↑COMPO)/LP
[35]  DRDOS
[36] LP:ONS←RDONS
[37]  →(∧/0=ρONS)/GO
[38]  STRING(5 0 ▼ID,DOS),(5 1 ▼EPF) AT PL
[39]  PL[1]←PL[1]+5
[40]  MOVE TO PL
[41]  N←1↑ρONS
[42]  I←0
[43]  DP←0
[44] ILP:→(N<I←I+1)/OUT
[45]  DP←ONS[I;1]-DP
[46]  PROD
[47]  DP←+/ONS[I; 1 2]
[48]  →ILP
[49] OUT:PL←0,PL[2]-0.9
[50]  →LP
[51] GO:MOVE TO PL
[52]  ANMODE
[53]  →('NO' ASK 'HARD COPY ?')/GO1
[54]  HDCOPY 1
[55]  ' '
[56]  →GO1
[57] NOGO:'NO DATA CONFORMS TO YOUR SPECIFICATIONS'
[58] GO1:→('NO' ASK 'CONTINUE ?')/END
[59]  ERASE
[60]  →OLP
[61] END:ENDIOPLT
```

```
      ∇EMEINP[□]∇
    ∇ EMEINP;A
[1]   A←□EX 2 4 ρ'PTR BUFF'
[2]   BUFF←⍳0
[3]   '' CHK(2 4 ρ'PTR BUFF') TRY 'IR DSN=HB.A3H01.Z652007.ALL.EMESIC.D770420,DISP=OLD,CODE=A'
      ∇
```

```
      ∇HEAD[□]∇
    ∇ HEAD;I;N;COMP;□IO
[1]   □IO←1
[2]   USING DIRECT
[3]   →('STUDY='∧.=6↑COMPO)/END
[4]   COMP←6↑COMPO
[5]   N←1↑ρSUMMARY
[6]   I←0
[7]  LP:→(N<I←I+1)/END
[8]   →(SUMMARY[I;⍳5]∨.≠6↑⊂COMP)/LP
[9]   STRING(RHEADER[1;]) AT 1 27.5
[10]  STRING(RHEADER[2;]) AT 1 27.1
[11]  STRING(SUMMARY[I;]) AT 1 26.5
[12]  →0
[13] END:STRING COMPO AT 1 27.5
      ∇
```

```
      ∇RDEME[□]∇
    ∇ RDEME INDX;□IO
[1]   □IO←1
[2]   S← 0 319 ρ' '
[3]  LP:→(0=ρINDX)/END
[4]   PTR←0,1+INDX
[5]   '' CHK PTR
[6]   INDX←1+INDX
[7]   S←S,[1] BUFF
[8]   P←⍎S[1;22]
[9]   PS←⍎S[1; 24 25 26]
[10]  →LP
```

```
      ∇RDEME[□11]∇
[11] END:STU←⍎S[1; 7 8 9 10]
[12]  →((STU=31.1)∨(STU=31.2))/SORTST
[13]  BUFF← 12 13 14 15 CSORT S
[14]  →0
[15] SORTST:BUFF← 2 3 4 5 CSORT S
```

```
      ∇RDONS[□]∇
    ∇ R←RDONS;□IO
[1]   □IO←1
[2]   R←⍳0
[3]   →(J>1↑ρBUFF)/0
[4]   R←BUFF[J;]
[5]   J←J+1
[6]   ID←⍎R[1+⍳4]
[7]   DOS←⍎R[11+⍳4]
[8]   HRP←0
[9]   →(∧/' '=R[16+⍳4])/NOST
[10]  HRP←⍎R[16+⍳4]
[11] NOST:→(∧/' '=R←35↓R)/END
[12]  →((R[10]='.')∧(R[18]≠' '))/OK
[13]  R[18]←'0'
[14] OK:R←(((ρR)↑4),4)ρR←⍎R
[15]  →0
[16] END:R← 0 4 ρ0
      ∇
```

```
      ∇CSORT[□]∇
    ∇ R←N CSORT D
[1]   →(0=⍴N)/□LC+2
[2]   →□LC+2
[3]   N←⍳¯1↑⍴D
[4]   D←D[⍋(' ',□AV)⍳,D[;¯1↓N];]
[5]   N←¯1↓N
[6]   →(0<⍴N)/□LC-2
[7]   R←D
    ∇
```

```
      ∇PROD[□]∇
    ∇ PROD
[1]   →(ONS[I;3]=1)/DRA1
[2]   DRAW(DP×SCAL),0,0,1,(ONS[I;2]×SCAL),0,0,¯1
[3]   →0
[4]  DRA1:DRAW(DP×SCAL),0,0,2,(ONS[I;2]×SCAL),0,0,¯2
    ∇
```

```
      ∇DPDOS[□]∇
    ∇ DPDOS
[1]   I←0
[2]   MOVE TO 5 21
[3]   SV←SVSTAT
[4]   DRAW 0 16
[5]   RESTAT SV
[6]   DRAW 180 0
[7]   RESTAT SV
[8]   →(P=1)/OU
[9]   →(P≠0)/LP
[10]  COMPO[('.'=COMPO)/⍳⍴COMPO]←'0'
[11]  ⍎('DRA',(6↓COMPO))
[12]  →STR
[13] LP:→(P=I←I+1)/LP1
[14]  DPAW 0,(15.57×1↑P),(PS),0
[15]  →LP
[16] LP1:DPAW 0,(15.57×1↑P),(180-PS↑I 1),0
[17]  STRING 'A' AT 4.2 22.25
[18]  STRING 'A=1/2 THE TOTAL DOSE RECEIVED BY SUBJECT ' AT 10 22
[19]  →STR
[20] OU:DRAW 0 15.57 180 0
[21] STR:STRING 'B' AT 4.2 23.57
[22]  STRING 'B=TOTAL DOSE RECEIVED BY SUBJECT' AT 10 21.5
[23]  STRING 'RADS' AT 2 23
    ∇

      ∇SCL2[□]∇
    ∇ SCL2
[1]  SCL:SV←SVSTAT
[2]   DRAW 0 1
[3]   MOVE 0 0.5
[4]   STRING▼I
[5]   RESTAT SV
[6]   →(900<I←I+100)/0
[7]   DPAW 20 0
[8]   →SCL
    ∇
```

```
      ∇ENDIOPLT[□]∇
    ∇ ENDIOPLT;A
[1]   A←⎕EX 2 4 ρ'PTR BUFF'
    ∇
```

```
      ∇DRA33[□]∇
    ∇ DRA33
[1]   DRAW 6 15.57 174 0
[2]   STRING 'DOSE RATE IS 150 RAD/MIN' AT 23.59 21.5
    ∇
```

```
      ∇DRA36[□]∇
    ∇ DRA36
[1]   DRAW 12 0 0.4 2.75 11.6 0 7.6 3.1 88 3.65 0.6 4.15 36 1.5 23.8 0
[2]   STRING '55' AT 3.5 21.4
[3]   STRING '117' AT 3.5 22
[4]   STRING '190' AT 3.5 22.6
[5]   STRING '273' AT 3.5 23.2
    ∇
```

```
      ∇DRA37[□]∇
    ∇ DRA37
[1]   DRAW 12 0 0.4 2.75 11.6 0 7.6 3.1 88 3.65 0.6 4.15 36 1.5 23.8 0
[2]   STRING '55' AT 3.5 21.4
[3]   STRING '117' AT 3.5 22
[4]   STRING '190' AT 3.5 22.6
[5]   STRING '273' AT 3.5 23.2
    ∇
```

```
      ∇DRA38[□]∇
    ∇ DRA38
[1]   DRAW 10 5.3 110 7 8 0 ¯1 0.7 0 ¯1.4 1 0.7
[2]   STRING '(+ 1.05 RAD/HR FOR 62 HOURS)' AT 27.94 23.21
[3]   STRING '220' AT 3.39 23.21
[4]   STRING '135' AT 3.39 21.92
    ∇
```

```
     ∇SETUPMOD[□]∇
    ∇ SETUPMOD;□IO;NPLOTS;S;C;XL;YL;DATA
[1]   □IO←1
[2]   ANMODE
[3]   SET CHARSIZE TO 3
[4]   NPLOTS←⍎'' ASK 'ENTER NUMBER OF PLOTS:'
[5]   YLIMIT←S←C←⍳0
[6]   XL←YL← 0 20 ⍴⍳0
[7]   DATA← 0 80 ⍴I←0
[8]  LOOP:→(NPLOTS<I←I+1)/OUT
[9]   'PLOT ',▼I
[10]  C←C,⍎0 ASK 'ENTER ORIGIN LOCATION IN INCHES:'
[11]  S←S,⍎0 ASK 'ENTER AXES LENGTHS IN INCHES: '
[12]  YLIMIT←YLIMIT,⍎0 ASK 'ENTER Y LIMITS'
[13]  XL←XL,[1] 20 ASK 'ENTER X-AXIS LABEL'
[14]  YL←YL,[1] 20 ASK 'ENTER Y-AXIS LABEL'
[15]  DATA←DATA,[1] 80 ASK 'ENTER DATA SET TO BE PLOTTED:'
[16]  →LOOP
[17] OUT:II←0
[18]  TEK 2
[19]  USING SCREEN
[20]  SET ROTATION TO 0
[21]  C←(⍉2,(⍴C)÷2)⍴C
[22]  S←(⍉2,(⍴S)÷2)⍴S
[23]  YLIMIT←(⍉2,(⍴YLIMIT)÷2)⍴YLIMIT
[24] PLOT:→(NPLOTS<II←II+1)/END
[25]  C[II;] CONVERT S[II;]
[26]  YLIM←YLIMIT[II;]
[27]  SET VIEWPORT CORNER TO CORNER,SIZE TO SIZE
[28]  '' EGMPLOTMOD▲DATA[II;]
[29]  XL[II;] LABEL YL[II;]
[30]  →PLOT
[31] END:LEN3
[32]  LENTO
    ∇
```

```
      ∇CONVERT[□]∇
    ∇ C CONVERT S
[1]   C[1]←C[1]×273
[2]   CORNER←C[1],C[2]←C[2]×283.6
[3]   S[1]←S[1]×273
[4]   SIZE←S[1],S[2]←S[2]×283.6
    ∇
```

```
      ∇EGMPLOTMOD[□]∇
    ∇ WIN EGMPLOTMOD DATA
[1]   →OK×⍳1≠⍴⍴DATA
[2]   DATA←DATA VS⍳⍴DATA
[3]  OK:USING SCREEN,BUFFERED
[4]   →SKIP×⍳0=⍴,WIN
[5]   SET VIEWPORT CORNER TO 600 400 ,SIZE TO(⌽2⍴WIN)×,CSZ[CHARSIZE DEFN;]
[6]  SKIP:((⌊/DATA[;1]),⌈/DATA[;1]) EGMAXIS YLIM
[7]   I←2
[8]  LOOP:→DATA[1;1] WITH DATA[1;I]
[9]   ΔV2S
[10]  MOVE TO DEFN
[11]  →(1↓DATA[;1]) WITH 1↓DATA[;I]
[12]  →(1 4 5 6 7)[1+5|⁻2+I] ΔR2A TO DEFN
[13]  ΔV2S
[14]  ΔDRW
[15]  →((1+⍴DATA)≥I←I+1)/LOOP
[16]  ANMODE
    ∇
```

```
      ∇LABEL[□]∇
    ∇ XLAB LABEL YLAB;I;J
[1]   USING SCREEN
[2]   I←VIEWPORT DEFN
[3]   SET CHARSIZE TO 2
[4]   STRING XLAB AT 1↓CURSOR
[5]   J←0
[6]   MOVE TO 1↓CURSOR
[7]   USING CHARACTERS
[8]  LOOP:→XIT×⍳J≥⍴YLAB
[9]   STRING YLAB[J←J+1]
[10]  MOVE 0 1
[11]  →LOOP
[12] XIT:ANMODE
    ∇
```

```
      ∇DIR[□]∇
    ∇ DIR
[1]   'DO YOU WANT:'
[2]   ' 1) ALL PLOTS CREATED USING THIS APL ACCOUNT?(1)'
[3]   ' 2) ALL PLOTS WITH A GIVEN QUALIFIER?(2)'
[4]   'RESPOND 1 OR 2'
[5]   ANS←□
[6]   →(ANS=1)/A
[7]   'QUALIFIER?'
[8]   QUAL←¯9↑□
[9]   →C
[10] A:ACC←⍕1↑□AI
[11] ⍝---TO GET ANOTHER ACCOUNT-- REPLACE ABOVE
[12] C:'' CHK 'SVW' TRY 'SR DSN=HB.Δ3H01.P379021.APL.GRAPHICS.DIR,UNIT=3330,VOL=000062'
[13]  'ACCNT  QUAL     PLOT NAME'
[14] LP:REC←SVW
[15]  →(REC=0)/0
[16]  →(ANS=2)/B
[17]  →(ACC≠4↑REC)/LP
[18]  REC
[19]  →LP
[20] B:→(QUAL≠4+13↑REC)/LP
[21]  REC
[22]  →LP
    ∇
```

```
      ∇DISPLAY[□]∇
    ∇ DISPLAY
[1]   DS←'SR UNIT=3330,VOL=000062,DSN='
[2]   '' CHK 'SVC' TRY DS,SETDSN 0
[3]  LP:→(0=ρREC←SVC)/0
[4]   □ARBO REC
[5]   →LP
    ∇
```

```
      ∇CHK[□]∇
    ∇ Δ←R CHK Q
[1]   →(0=ρ,R)/L0
[2]   Δ←R=1↑Q
[3]  L0:→(∨/Q<0,R)/0
[4]   Δ←(⍳30)⍳1↑Q
[5]   ⍎ 18 ¯21[□IO+2=□NC 'QLR']+'''TSIO ERROR '',(⍕Q),'' '',,QLR[□IO+Δ;]'
[6]   ⍎(0≤L/Q)↑'→'
[7]   •
    ∇
```

```
     ∇SETDSN[⎕]∇
    ∇ DSN←SETDSN DIPPG
[1]   ACC←'HB.Δ3H01.A',(▼1+⎕AI),'.'
[2]   A--CHANCE TO WORK ANOTHERS PLOTS
[3]   'LIMIT RESPONSES TO ≤8 CHARACTERS.'
[4]   ''
[5]   'PLOT QUALIFIER NAME?'
[6]   'GIVE A QUALIFIER IF YOU WANT ONE, ELSE HIT CARRIAGE RETURN.'
[7]   QUAL←⍞
[8]   'PLOT NAME?'
[9]   NAME←⍞
[10]  →(0≠⍴QUAL)/A
[11]  DSN←ACC,NAME
[12]  →END
[13] A:DSN←ACC,QUAL,'.',NAME
[14] END:→(DIPPG=0)/0
[15]  '' CHK 'SVG' TRY 'SW DSN=HB.Δ3H01.P379021.APL.GRAPHICS.DIP,UNIT=3330,VOL=000062,DISP=MOD '
[16]  SVG←(▼1+⎕AI),(¯9+QUAL),' ',NAME
[17]  '' CHK SVG
[18]  SVG←''
[19]  '' CHK SVG
    ∇
```

```
      ∇TRY[□]∇
    ∇ A←B TRY C;D;E
[1]   →(2=□NC 'PID')/L0
[2]   PID←''⍴□,⍴□←'PID← ?'
[3]  L0:B←(¯2+ 1 1 ,⍴B)⍴B
[4]   E←B[□IO;]
[5]   E←((1+⍴B),4)⍴' CTL DAT'
[6]   →(D←0=PID □SVO B,D,(⍴B)⍴E)/L2
[7]   ⍞←E,'←;0'
[8]   A← 1 0 1 0 □SVC E
[9]   →(0=A←⍴⍞←E,'←C')/0
[10]  →((0,D)=1+A←⍞←E)/0
[11]  →(1 2 ∧.≠1+A)/L1
[12]  (¯1+A)+'∨'
[13]  E
[14] L1:D←□SVR B
[15]  '' CHK A
[16] L2:(,' ',D,'¯',B,'¯'),' SHAPE OFFER FAILED'
      ∇
```

```
      ∇ANOVA[□]∇
    ∇ ANOVA D;□IO
[1]   □IO←1
[2]   TEK 4
[3]   'SOURCE          DF        SS          MS          F-FIXED'
[4]   ' '
[5]   N←(⍴DIM←⍴D)-1
[6]   T←((R←(2*N)+2×K←(REPS←DIM[1])≥2),4)⍴0
[7]   CT←((N+1)⍴0) SS D
[8]   T[R; 2 3]←(⍳(×/DIM)-1),((N+1)⍴1) SS D
[9]   →(REPS=1)/REP
[10]  T[1; 2 3]←(REPS-1),((⍳(N+1))≤1) SS D
[11] REP:D←+/[1] D
[12]  SUMS←D
[13]  DIV←DIM
[14]  DIM←1↓DIM
[15]  V←⌊((2*(N+1)-⍳N)∘.|⍳S)÷(2*N-⍳N)∘.×⍳S←(2*N)-1⍴1
[16]  V[;⍳(2*N)-1]←V[;(+/(X∘.>X)+((⍳⍴X)∘.≥⍳⍴X)∧X∘.=X)⍳⍳⍴X←+/[1] V]
[17]  I←1
[18] CALC:T[I+K; 2 3]←(×/((V[;I]=1)/DIM-1)),(V[;I] SS D)÷REPS
[19]  →((2*N)>I←I+1)/CALC
[20]  T[;3]←T[;3]-CT
[21]  →(N=1)/ONE
[22]  I←2
[23] CONT:DV←(K⍴0),(X←(~(~CT)∨.∧S)∧(CT←V[;I])∨.∧S←V[;⍳I-1]),(R-(I+K-1))⍴0
[24]  T[I+K;3]←T[I+K;3]-+/T[;3]×DV
[25]  →((2*N)>I←I+1)/CONT
[26] ONE:→(REPS=1)/REPON
[27]  T[R-1;2]←T[R;2]-+/[1] T[⍳(R-2);2]
[28]  T[R-1;3]←T[R;3]-+/[1] T[⍳(R-2);3]
[29] REPON:T[⍳(R-1);4]←T[⍳(R-1);3]÷T[⍳(R-1);2]
[30]  I←1
[31] PRNT:T[I+K;1]←10⊥V[;I]
[32]  →((2*N)>I←I+1)/PRNT
```

```
      ∇ANOVA[⎕33]∇
[33]  L2←0=¯2↓T[;1]
[34]  L←L2/2 10⍴'ERROR     TOTAL     '
[35]  V←((-+/L2),0)+V←ASORT T[;1]
[36]  V←V,[1] L
[37]  N←1↑⍴T
[38]  N←N-1
[39]  →(0=T[1;1])/OUT
[40]  T[N;1+⍳2]←T[1;1+⍳2]+.×T[N;1+⍳2]
[41]  T[N;4]←T[N;3]÷T[N;2]
[42]  →(0=T[N;4])/MSG
[43]  F←T[;4]÷T[N;4]
[44]  T←T,F
[45]  T←1 1↓T
[46]  (1 0↓V),(9 0 ,12 4 ,12 4 ,12 4)⍕T
[47]  →MEANS
[48] OUT:F←T[;4]÷T[N;4]
[49]  T←(0 1↓T),F
[50]  V,(9 0 ,12 4 ,12 4 ,12 4)⍕T
[51] MEANS:→((⍴⍴D)=2)/END
[52]  →0
[53] END:TWOWAY
[54]  →(1=1↑DIV)/R2
[55]  R1←3
[56]  →COMP
[57] R2:R1←4
[58]  ' '
[59]  ' '
[60] COMP:'ENTER MULTIPLE COMPARISON PROCEDURE'
[61]  'CHOICES ARE: '
[62]  'TUKEY SCHEFL SCHEFC BONFL BONFC'
[63]  →0
[64] MSG:'ERROR SUMS OF SQUARES IS 0'
```

```
      ∇SS[□]∇
    ∇ S←Y SS R;DIM;K;ZEROS;ONES
[1]   →(K=ONES←K-⍴ZEROS←(Y=0)/⍳K←⍴DIM←⍴R)/4
[2]   R←+/[(⍳0)⍴ZEROS[⍴ZEROS]] R
[3]   →(0≠⍴ZEROS←¯1↓ZEROS)/2
[4]   R←R*2
[5]   R←+/R
[6]   →(0<ONES←ONES-1)/5
[7]   S←R+×/(Y=0)/DIM
    ∇


      ∇ASORT[□]∇
    ∇ R←ASORT X;□IO;I
[1]   □IO←1
[2]   R← 0 10 ⍴' '
[3]   →(0 1 ≠⍴⍴X)/SC,VEC
[4]   'CAN NOT DO MATRICES'
[5]   →
[6]  SC:X←1↓X
[7]  VEC:I←0
[8]   →((⍴X)<I←I+1)/0
[9]   R←R,[1] 10↑⍕((26⍴10)⊤X[I])/⍕'ABCDEFGHIJKLMNOPQRSTUVWXYZ'
[10]  →VEC+1
    ∇


      ∇TWOMN[□]∇
    ∇ TWOMN
[1]   MEANA←(+/[1] SUMS)÷×/(¯1↓DIV)
[2]   MEANB←(+/SUMS)÷×/(1↓DIV),(¯1↓DIV)
    ∇
```

```
      ∇TUKE2[□]∇
    ∇ TUKE2;Q;DF;MSUB;LB;UB;DELTA;DELTB
[1]   ' '
[2]   '***TUKEY***'
[3]   ' '

[4]   DF←(DIV[3],T[(R1);1])
[5]   '   FACTOR A'
[6]   Q←⍎'' ASK 'ENTER Q AT THE 1-α LEVEL WITH DF ',(⍕DF),' : '
[7]   ' '
[8]   DELTA←Q×(T[(R1);3]÷(×/(2÷DIV)))÷0.5
[9]   LAYOUT DIV[3]
[10]  MSUB←MENA[COL1]-MENA[COL2]
[11]  LB←MSUB-DELTA
[12]  UB←MSUB+DELTA
[13]  '           T           T''  LOWER LIMIT   UPPER LIMIT'
[14]  (12 0 , 12 0 , 12 4 , 14 4)⍕COL1,COL2,LB,UB
[15]  ' '
[16]  '   FACTOR B'
[17]  DF←(DIV[2],T[(R1);1])
[18]  Q←⍎'' ASK 'ENTER Q AT THE 1-α LEVEL WITH DF ',(⍕DF),' : '
[19]  DELTB←Q×(T[(R1);3]÷(×/DIV[1,3]))÷0.5
[20]  LAYOUT DIV[2]
[21]  MSUB←MENB[COL1]-MENB[COL2]
[22]  LB←MSUB-DELTB
[23]  UB←MSUB+DELTB
[24]  ' '
[25]  '           T           T''  LOWER LIMIT   UPPER LIMIT'
[26]  (12 0 , 12 0 , 12 4 , 14 4)⍕COL1,COL2,LB,UB
      ∇
```

```
      ∇LAYOUT[□]∇
    ∇ LAYOUT T;I;S
[1]   COL1←COL2←⍳0
[2]   I←0
[3]  LP:→(T=I←I+1)/OUT
[4]   S←(T-I)⍴I
[5]   COL1←COL1,S
[6]   S←I+⍳T
[7]   COL2←COL2,S
[8]   →LP
[9]  OUT:COL1←((⍴COL1),1)⍴COL1
[10]  COL2←((⍴COL2),1)⍴COL2
      ∇
```

```
      ∇DSTAT[□]∇
    ∇ DSTAT X;R;MAX;MIN;N;MEAN;VAR;SD;MD;MED;MODE;V;M
[1]   R←(MAX←X[⌈ρX])-MIN←(X←X[⍋X])[1]
[2]   SD←(VAR←(+/(X-MEAN←(+/X)÷N)*2)÷(N←ρX)-1)*0.5
[3]   MD←(+/|X-MEAN)÷N
[4]   MED←0.5×+/X[(⌈N÷2),1+⌊N÷2]
[5]   →(N>ρMODE←((ρV)ρ(⍳M)≤1)/V←X[(V=M←⌈/V←+/X∘.=X)/⍳ρX])/7
[6]   MODE←⍬
[7]   'SAMPLE SIZE          ';N
[8]   'MAXIMUM              ';MAX
[9]   'MINIMUM              ';MIN
[10]  'RANGE                ';R
[11]  'MEAN                 ';MEAN
[12]  'VARIANCE             ';VAR
[13]  'STANDARD DEVIATION   ';SD
[14]  'MEAN DEVIATION       ';MD
[15]  'MEDIAN               ';MED
[16]  'MODE                 ';MODE
      ∇
```

```
      ∇LILLYEX[□]∇
    ∇ LILLYEX X;□IO;M;F;DELTA;D;DLILLY;SSTAR;R1;R2;S;A;B;Q;DF
[1]   □IO←1
[2]   M←(+/X)÷ρX
[3]   F←(1-*-X[⍋X]÷M)
[4]   DELTA←(((⍳ρX)÷ρX)-F),F-((⍳ρX)-1)÷ρX
[5]   D←⌈/⍉(2,ρX)ρDELTA
[6]   DLILLY←⌈/DELTA
[7]   SSTAR←+/|D
[8]   ' '
[9]   '   LILLIEFORS KS TEST FOR EXPONENTIAL DISTRIBUTION WITH UNKNOWN MEAN'
[10]  '   D* = ';▼DLILLY;' N= ';ρX
[11]  '   SEE JASA 64:387-389 FOR TABLES'
[12]  ' '
[13]  '   FINKLESTEIN AND SCHAFER S< TEST FOR EXPONENTIAL DIST. WITH UNKNOWN MEAN'
[14]  '   S* = ';SSTAR;'  N= ';ρX
[15]  '   SEE MANN, SCHAFER, SINGPURWALLA, METHODS FOR STASTISTICAL ANALYSIS OF RELIABILITY AND LIFE DATA  PAGE 337 FOR S* TABLE'
[16]  R1←⌊(ρX)÷2
[17]  R2←(ρX)-R1
[18]  S←(⍳ρX)×X[⍋X]-(0,¯1↓X[⍋X])
[19]  A←(+/R1↑S)÷R1
[20]  B←(+/R1↓S)÷R2
[21]  Q←A÷B
[22]  ' '
[23]  '   THE FERCHO-RINGER-GWEDENKO Q-STATISTIC IS'
[24]  '   Q= ';Q
[25]  DF←(2×R1),(2×R2)
[26]  '   TO BE COMPARED WITH F WITH ';DF;' DF AT THE 1-(α÷2) LEVEL'
    ∇
```

```
      ∇WEIBULL[□]∇
    ∇ WEIBULL X;□IO;I;N;K;D;L;C;S
[1]   □IO←1
[2]   'ZEIBULL TEST OF FIT'
[3]   ' '
[4]   'CONSTANTS K AND PERCENTILES FOR S CAN BE FOUND '
[5]   '   IN MANN, SCHAFER, AND SINGPURWALLA PAGES 342-347'
[6]   ' '
[7]   I←0
[8]   N←⍴X
[9]   K←⍳10
[10]  X←X[⍋X]
[11]  D←(1+X)-(¯1+X)
[12] LP:→(N=I←I+1)/OUT
[13]  K←K,⍎'' ASK 'ENTER K WITH N= ',(⍕N),' AND I= ',⍕I
[14]  →LP
[15] OUT:L←D÷K
[16]  C←1+L(N+2)
[17]  C←(C-1)÷L
[18]  S←(+/C)÷(+/L)
[19]  ' '
[20]  'S= ';S
    ∇
```