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QUARTERLY TECHNICAL REPORT

July 1, 1952 thru September 30, 1952

It should be noted that the Quarterly Technical Reports of The University of Rochester Atomic Energy Project do not attempt to describe progress in all of the research programs but only in those in which some significant results have been achieved but which are not sufficiently complete to be written up as final reports.

Submitted by: Henry A. Blair
Director

Date of Report: 11/3/52

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RETICULOENDOTHELIAL FUNCTION IN THE X-IRRADIATED (LD_{50}) RABBIT AS MEASURED BY TOLERANCE TO PYROGENIC MATERIAL

by

R. W. Miller and R. Watson

ABSTRACT

9 rabbits were made tolerant to the daily intravenous administration of typhoid vaccine as measured by their febrile response. An LD_{50} of total body irradiation does not abolish this tolerance. The relationship of the reticuloendothelial system to this tolerance is briefly discussed.

* * * * *

Rabbits develop a tolerance to pyrogens as measured by body temperature. It has been suggested by Beeson (1) that this tolerance is a function of the reticuloendothelial system. He bases this concept on the fact that tolerance to intravenous typhoid vaccine is abolished by a Thorotrast blockade of the reticuloendothelial system. If Beeson's thesis is correct, then a functional disturbance of the r-e system produced by x-irradiation might be demonstrated by a loss of body temperature tolerance to typhoid vaccine.

Methods and Materials:

A. 6 healthy male albino stock rabbits were used. They were kept in individual cages in a room under constant temperature and humidity.

The animals were placed in wooden boxes for the periods when their temperatures were being recorded. The sliding top of the box had a semi-circular piece removed at its anterior end to hold the rabbit's head outside the box. The rear panel of the box flapped open on hinges, thus allowing the rectal temperature to be obtained with a minimum disturbance to the rabbit.

Pyrogen free glassware and needles were employed. These were checked from time to time by using them to inject pyrogen-free saline intravenously in control animals.

U. S. Public Health typhoid vaccine containing one billion organisms per ml was used as the pyrogenic material. The same lot was used throughout the experiment. This was kept under continual refrigeration and shaken vigorously before use. It was diluted 1:10 with physiologic saline (100 million organisms/ml) before injection.

The animals were placed in the wooden boxes for 4-6 hours daily for the two days prior to the first injection of typhoid vaccine. This was done to accustom them to the procedure. Baseline rectal temperature fluctuations were recorded during this time.

Each day after a baseline temperature had been recorded, each rabbit was given one cubic centimeter of typhoid vaccine into the marginal vein of the ear. Its rectal temperature was then recorded every half hour, until it returned to normal. The thermometers were inserted in the rectum for one minute by the clock for each recording. The same thermometer was used for all rabbits at all times.

Treatment schedule:

Day of experiment	1	2	3	4	5	6	7	8	9	10	11*	12	13	14	15	16
Typhoid vaccine injected	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Temperatures taken	X										X		X	X	X	X

* Total body irradiation after temperatures were recorded.

X-ray factors:

800 r 250 KV. Lead plano-convex filter, 1/2 inch at center, 1/4 inch at periphery. Ma: 15, TSD: 44 inches, Rate: 6.9 r.

B. 3 healthy adult albino rabbits were used under the same experimental circumstances, but the treatment schedule was altered:

Day of experiment	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Typhoid vaccine given	X	X	X	X	X	X	X	X	X	X	X	X				X	X
Temperatures taken	X											X				X	

Day of experiment	18	19	20	21	22	23	24	25	26*	27	28	29	30
Typhoid vaccine given	X	X	X	X	X	X	X	X	X				X
Temperatures taken									X				X

* Total body irradiation after temperatures were recorded.

Observations:

Part A. The rabbits developed a tolerance to pyrogen which was not altered by an LD_{50} of total body x-irradiation when the pyrogenic material was given daily except for the day after the x-ray exposure (Graph I).

Part B. The rabbits developed a tolerance to pyrogen which was not altered by a 3 day rest following x-irradiation. Thus, the tolerance was maintained even though a brief lapse in the pyrogenic stimulus was allowed.

Discussion:

Bloom (2) describes large amounts of lymphocytic debris in the phagocytes of rabbits 17 hours after total body x-irradiation. This suggests that the reticuloendothelial system may have been blockaded by the debris.

Thorotrast provides an effective blockade of the r-e system (3). Barrow et. al. showed that 16-18 hours after an intravenous injection of this drug no radioactive gold could be phagocytized. Following x-irradiation, on the other hand, the same method of testing showed no impairment of ability to phagocytize. This indicates that this function of the r-e system is not affected by x-irradiation.

Beeson showed that intravenous Thorotrast injection in rabbits abolishes their tolerance to pyrogens (1). However, Thorotrast disturbs the physiology in many ways (4). Therefore, Beeson's claim that the abolition of tolerance to pyrogens is the consequence of r-e blockade is based as yet on inconclusive evidence. However, if a reticuloendothelial blockade is solely responsible for this action when Thorotrast is administered, it must be assumed that a similar blockade does not occur when a rabbit is exposed to an LD_{50} of total body x-irradiation.

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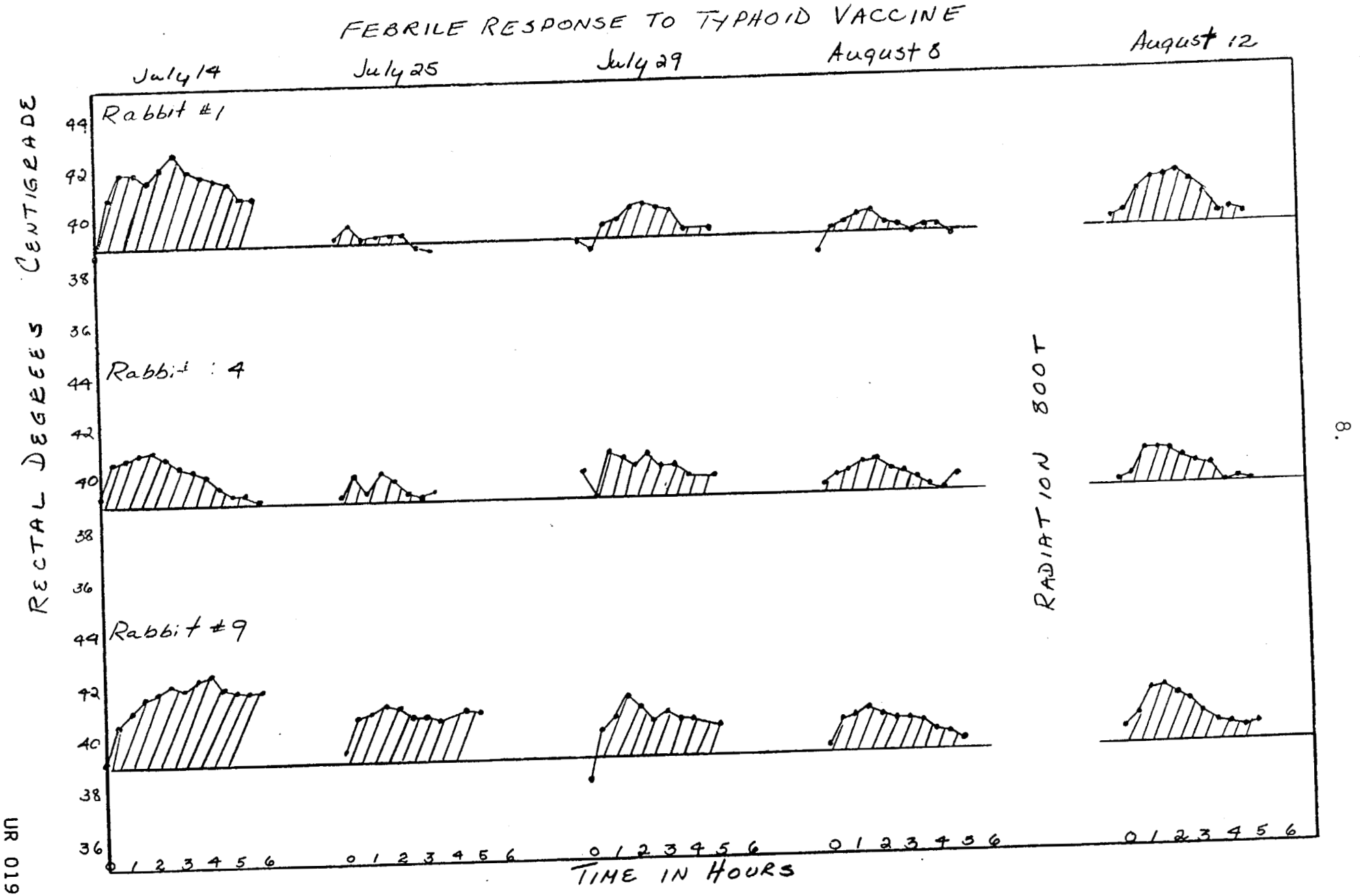

THE EFFECT OF WHOLE BLOOD TRANSFUSION ON DOGS RECEIVING AN LD_0 EXPOSURE TO IONIZING RADIATION

by

W. K. Cotton and R. W. Miller

ABSTRACT

Twenty mongrel dogs each received 300r of total-body x-irradiation. Ten of these animals served as controls, while the other ten received typed, cross-matched, compatible whole blood transfusions on a predetermined schedule during the post-irradiation test period.

There were no deaths in either group. It would seem, therefore, that the frequent administration of therapeutic amounts of whole blood is not detrimental to the survival of a dog that has received a non-lethal exposure to ionizing irradiation.

This experiment was done as consequence of a study by J. G. Allen, et al., whose results suggested a substantial increase in mortality resulting from the frequent administration of whole blood to dogs receiving an LD_0 exposure to ionizing irradiation.

* * * * *

Introduction: J. Garrott Allen and his associates have published a report on the effects of whole blood transfusion in the treatment and/or prevention of irradiation hemorrhage (1). Their results indicate that in the lower dosage levels of irradiation, whole blood transfusions increased the mortality of the recipient animals; since, at an LD_0 exposure 40% of the transfused dogs died, and at an LD_{40} dosage level the mortality was 20% greater among the transfused group. At higher dosage levels the mortality was essentially the same in both the control and the transfused groups.

It seemed appropriate to repeat a portion of this study in order to determine if the repeated administration of therapeutic quantities of whole blood is a primary hazard to a subject receiving a non-lethal exposure to ionizing radiation.

Methods: Twenty unanesthetized mongrel dogs were paired as closely as possible in respect to weight, sex, age, and blood type. Each animal was subjected to 300 r of whole-body x-irradiation from a 1 MEV machine. One of each pair following irradiation served as a control while the other received typed, cross-matched, compatible whole blood on a predetermined basis of three transfusions a week beginning on the 4th day post-irradiation for four weeks. The blood was drawn from donor animals in standard ACD solution 48-72 hours prior to its administration and stored at 4°C. It was transfused into the leg vein in the amount of 5 cc/kg. of body weight. Sufficient blood was withdrawn from each animal 3 x/weekly in order to follow its hematocrit, RBC, WBC and platelet counts.

A fourteen dog donor colony was maintained. Each donor and recipient animal was typed for the presence or absence of the dog "A" factor. A+ blood was given to A+ recipients and A- blood to A- recipients. The blood was cross-matched for major and minor incompatibility just prior to transfusion.

The diet of the donor colony was supplemented with daily feedings of horse meat and iron which maintained the donor hematocrits at approximately 95% of their control levels.

Results:

1. Mortality - None of the dogs succumbed during the 28 day experimental period.

2. Hematology - In both the control and transfused groups, the leucocytes and platelets fell off rapidly during the first ten days after irradiation, reaching a minimum level

by the fifteenth post-irradiation day. The average minimum for both groups, as shown in Graph I, was 2000 WBC/mm^3 and 20,000 platelets/mm^3 (Graph IV) although the platelet count in a few dogs reached zero, and a few control dogs had a WBC count of 400 for a two-day period. Graph III shows that the red cell count of the transfused group remained at the pre-radiation control level while the RBC's of the control group fell gradually throughout the experimental period. The hematocrits (Graph I) of both groups fell during the initial three day period until the first transfusion date when the hematocrit of the transfused group rose steadily to a level higher than its normal control value. This level was then maintained until the end of the test period. The hematocrits of the control group paralleled the RBC's by falling gradually and consistently throughout the four week period.

3. Blood transfusions - No clinical hemolytic or anaphylactoid transfusion reactions were noted.

Discussion: The results of our experiment under the stated conditions fail to corroborate the findings of J. G. Allen, et al., as given in the introduction. Since all of our animals survived, we cannot state that whole blood given to a dog which has been exposed to a non-lethal dose of x-irradiation is detrimental to his survival. Our results indicate no effect on mortality. The parallel fall in WBC's and platelets indicates a primary bone marrow defect as a result of irradiation which was not overcome by transfusing with whole blood.

In attempting to explain the varying results obtained from two basically

similar studies done by Allen and ourselves, an interpretation is offered in the differences existing between the dosage of radiation and the minimum leucocyte count. Allen's 175 r appears to be the highest dose of total body x-irradiation that can be given to a group of dogs in his laboratory without producing death. A corresponding effect in our laboratory, using different radiation factors, is produced by 300 r. The effects might be compared further by the leucopenia resulting from the irradiation in the two experiments, but Allen's data for this is not available in the literature.

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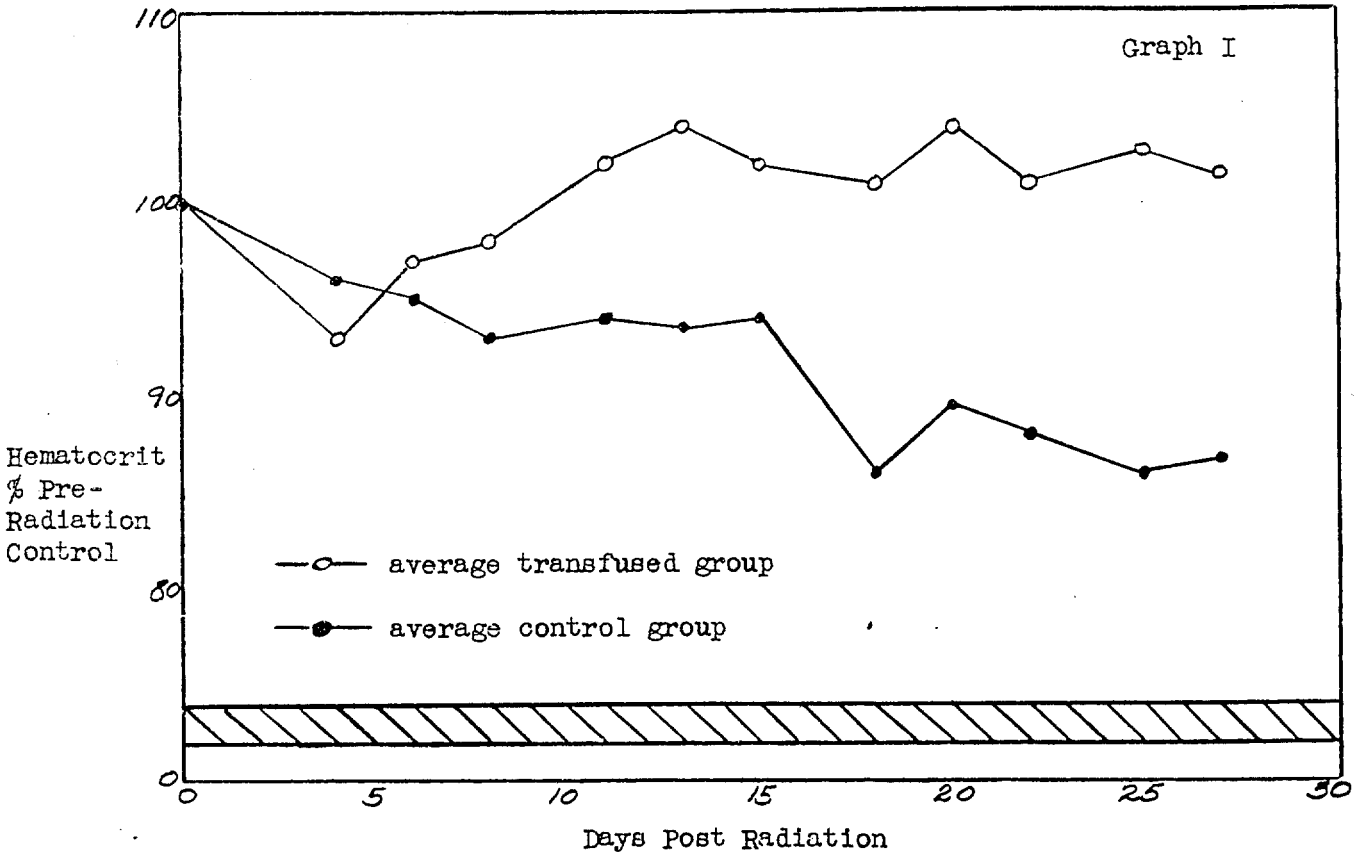
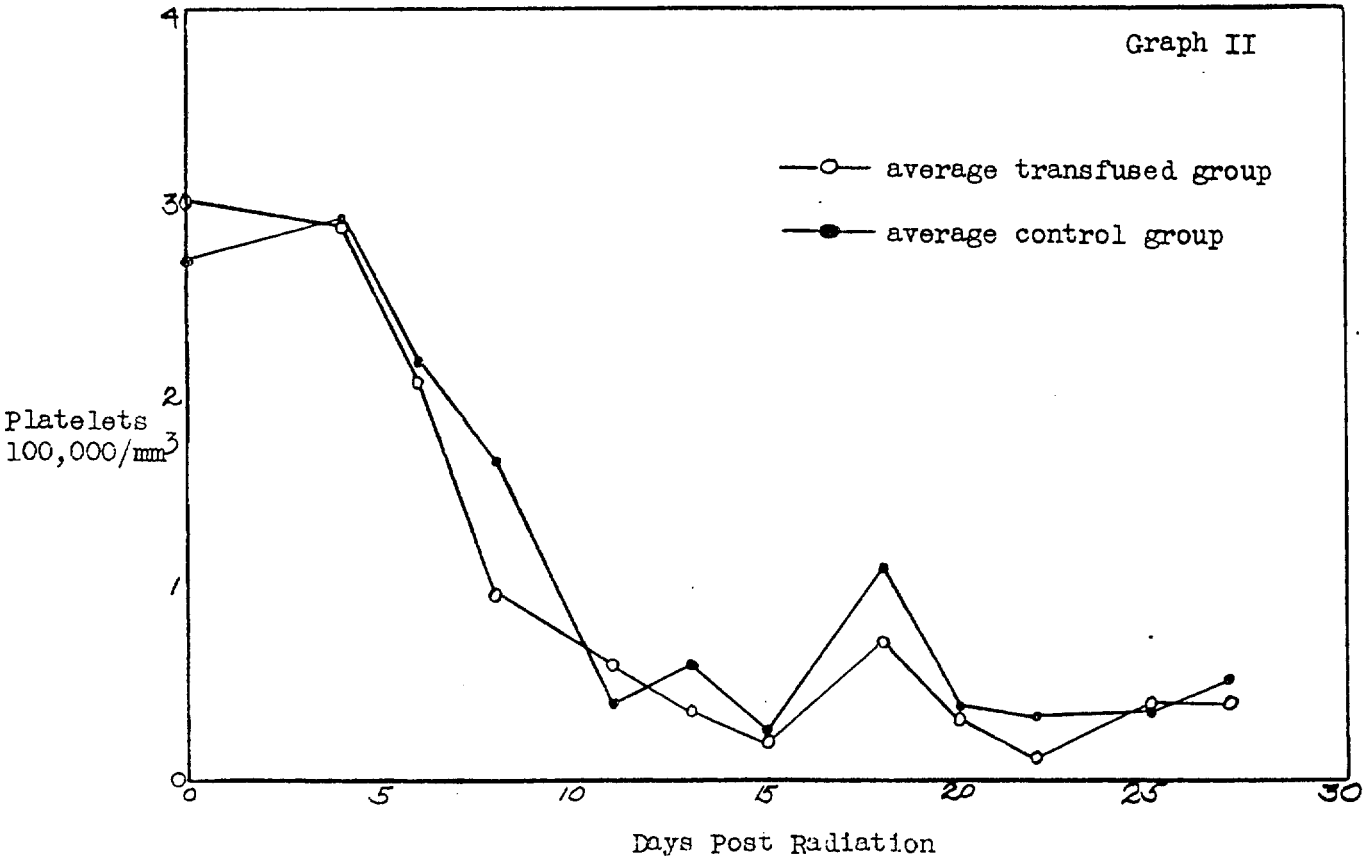
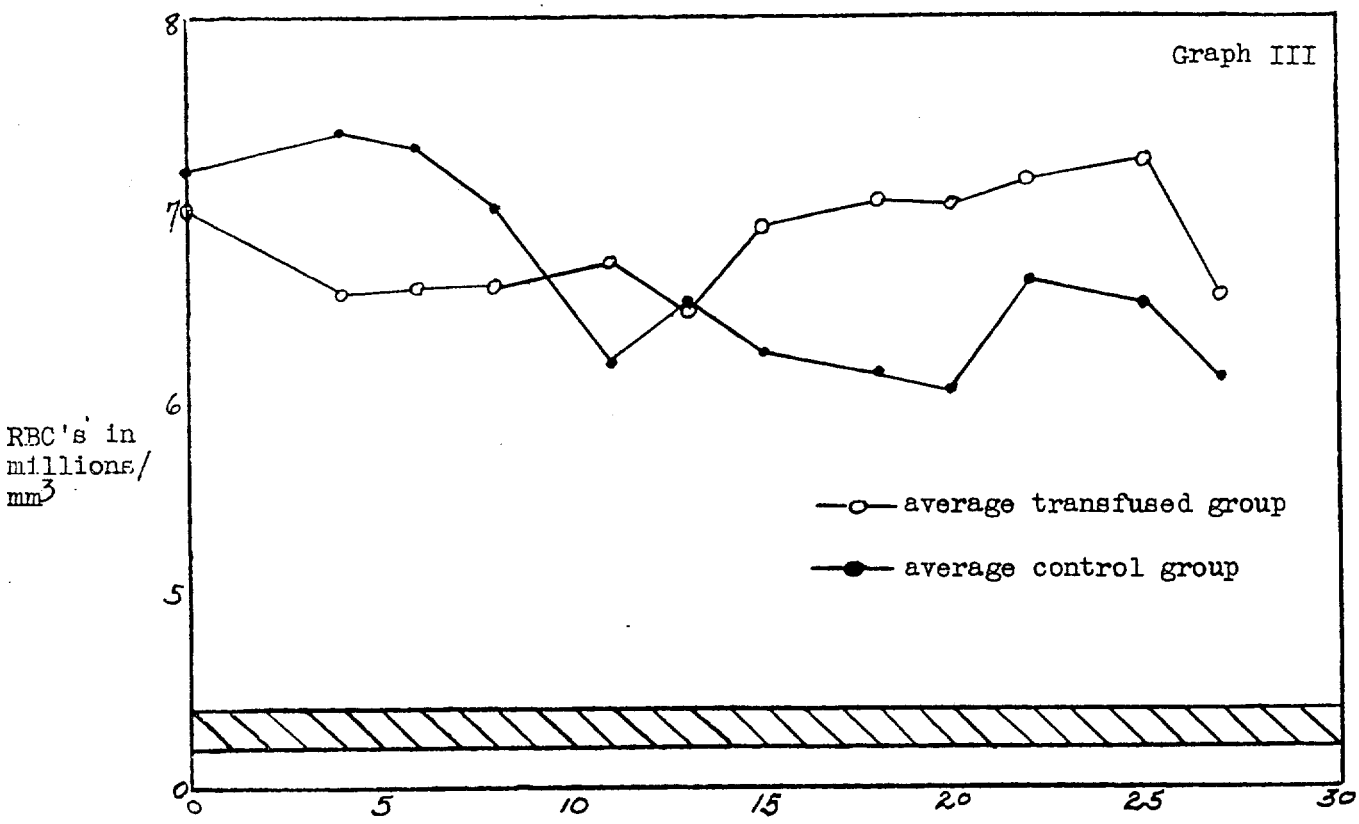
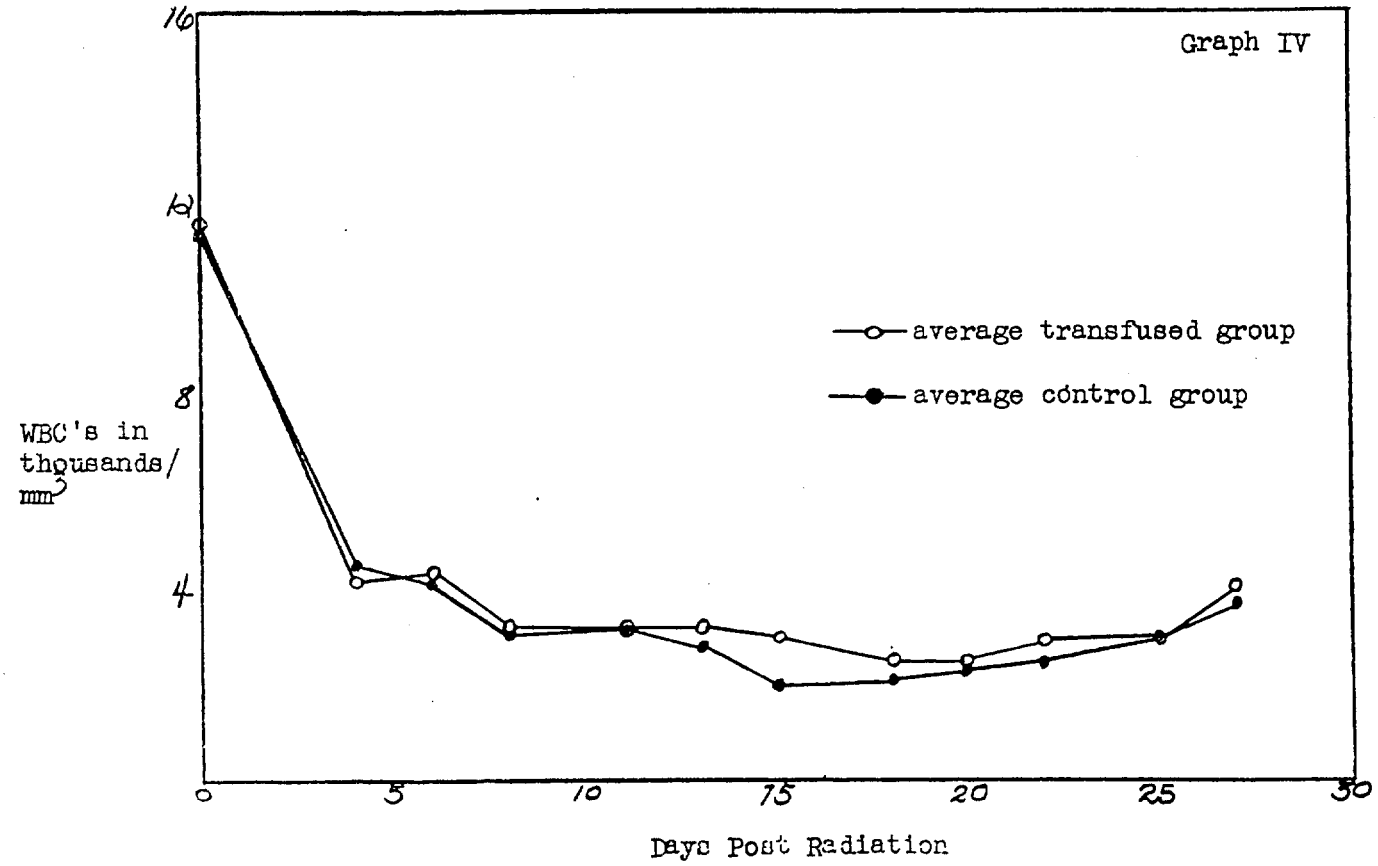

Graph I
110
100
90
80
0
Hematocrit
% Pre-
Radiation
Control
average transfused group
average control group
0
5
10
15
20
25
30
Days Post Radiation


Graph II
4
3
2
1
0
Platelets
100,000/mm3
average transfused group
average control group
0
5
10
15
20
25
30
Days Post Radiation


Graph III
RBC's in millions/ mm3
8
7
6
5
0
0
5
10
15
20
25
30
average transfused group
average control group
Days Post Radiation


Graph IV
WBC's in thousands/ mm3
16
12
8
4
0
5
10
15
20
25
30
average transfused group
average control group
Days Post Radiation

THE EFFECT OF CROSS-TRANSFUSIONS ON THE ACUTE RADIATION SYNDROME IN THE DOG

BY

John L. Grace, Joseph Seeger, and Robert W. Miller

ABSTRACT

12 dogs were given an LD_{80} of total body x-irradiation. 6 of these animals served as controls. 3 were cross-transfused daily from the 1-5th post-irradiation day, and 3 were so treated from the 7-11th post-irradiation day. Each cross-transfused dog received its transfusion from a compatible normal animal, the same donor being used throughout the five day period. This procedure did not diminish the mortality. No consistent major change in the hematology of the peripheral blood was detected.

* * * * *

The work of Salisbury, Rekers, et al (1) suggests that cross transfusion lowers the lethality of x-irradiation. Swisher and Furth (2) performed a small

1. X-irradiated control
2. X-irradiated and cross-transfused
3. Donor

6 groups of dogs were studied in this way. 500cc of blood were cross-transfused every day for five days. Three of the irradiated treated animals received their transfusions from the 1-5th day post-irradiation while the other three irradiated treated dogs were cross-transfused on the 7-11th days post-irradiation.

These animals had been immunized for distemper and given a vermifuge approximately six weeks before use. They were kept in separate cages and fed a diet of Purina dog chow with free access to water both before and during experiments.

Control determinations of hematocrit, red blood cell count, white blood cell count, platelet count and blood smear were made on each of 3 days of the week prior to irradiation. Following irradiation, these blood studies were made on week days for the first 21 days and three times for the next week until the 28th day. Peripheral blood studies were also made on some, but not all of the dogs after each cross transfusion. Standard laboratory methods were used for all these determinations.

The animals to be cross transfused were typed for presence of the canine "A" factor in their erythrocytes as described by Christian, et al. (4) and Young, et al. (5). Compatible donors and recipients were chosen so as to give A+ recipient dogs only A+ donor blood or A- recipient dogs A- blood. Donor's cells and recipient's serum, and recipient s cells and donor's serum were cross-matched.

Venipunctures were carried out using #13 needle inserted in either right or left jugular vein and a #190 polyethylene catheter placed into the vein for a distance from 10 to 15 cm. (depending on the size of the dog).

The catheters from the two dogs were attached to a three-way stopcock by means of Luer-Lok Couplers and a 20cc syringe was connected to the stopcock for exchanging the blood in 20cc quantities until 100cc had been cross transfused in each direction. All apparatus was lined with silicone previous to each cross transfusion.

The pairs of animals to be radiated, one of which served as the recipient and the other as a control, were exposed to 550r (approximately LD80) delivered from a 1000 KVP General Electric Industrial X-ray unit operated at 3 ma using a lead plano-convex filter $\frac{1}{2}$ inch thick in the center. Radiation was delivered at a rate of approximately 9r/minute as measured by a Victoreen chamber prior to exposure of each pair of animals. The target to skin distance was 35 inches.

Observations: Table I (Page 19) summarizes the treatment record, dog weights, estimated blood volumes, time required for the cross-transfusion, and day of death.

Mortality: Of the dogs cross-transfused early, 2 of 3 died (10th and 14th day after x-ray exposure), while 2 of 3 of their controls died (18th and 21st day post-irradiation). Of dogs cross-transfused during the second post-irradiation week, all 3 died (14, 14, and 15 days after x-ray), and all three controls died (12, 20, and 21 days after x-ray).

Hematology: Graphs' I-V (Page 20-24) are presented only to illustrate the lack of uniform hematologic effect on the donors and recipients brought about by the cross-transfusion.

Discussion: Daily cross-transfusion for five days during the first or second week post-irradiation did not reduce the mortality of dogs subjected to an LD80 of total body x-ray. No consistent major alteration in the hematologic studies on the peripheral blood were detected.

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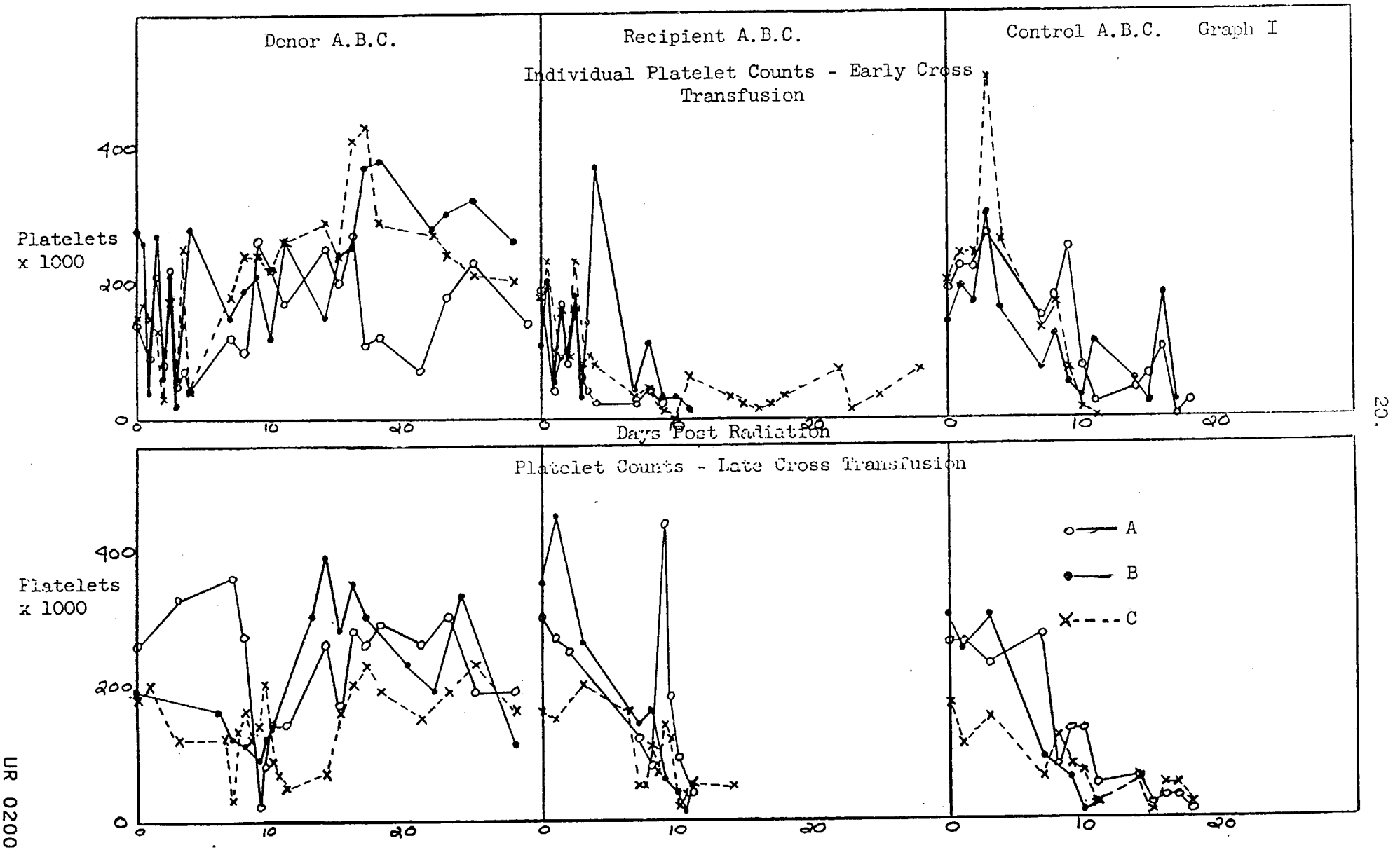
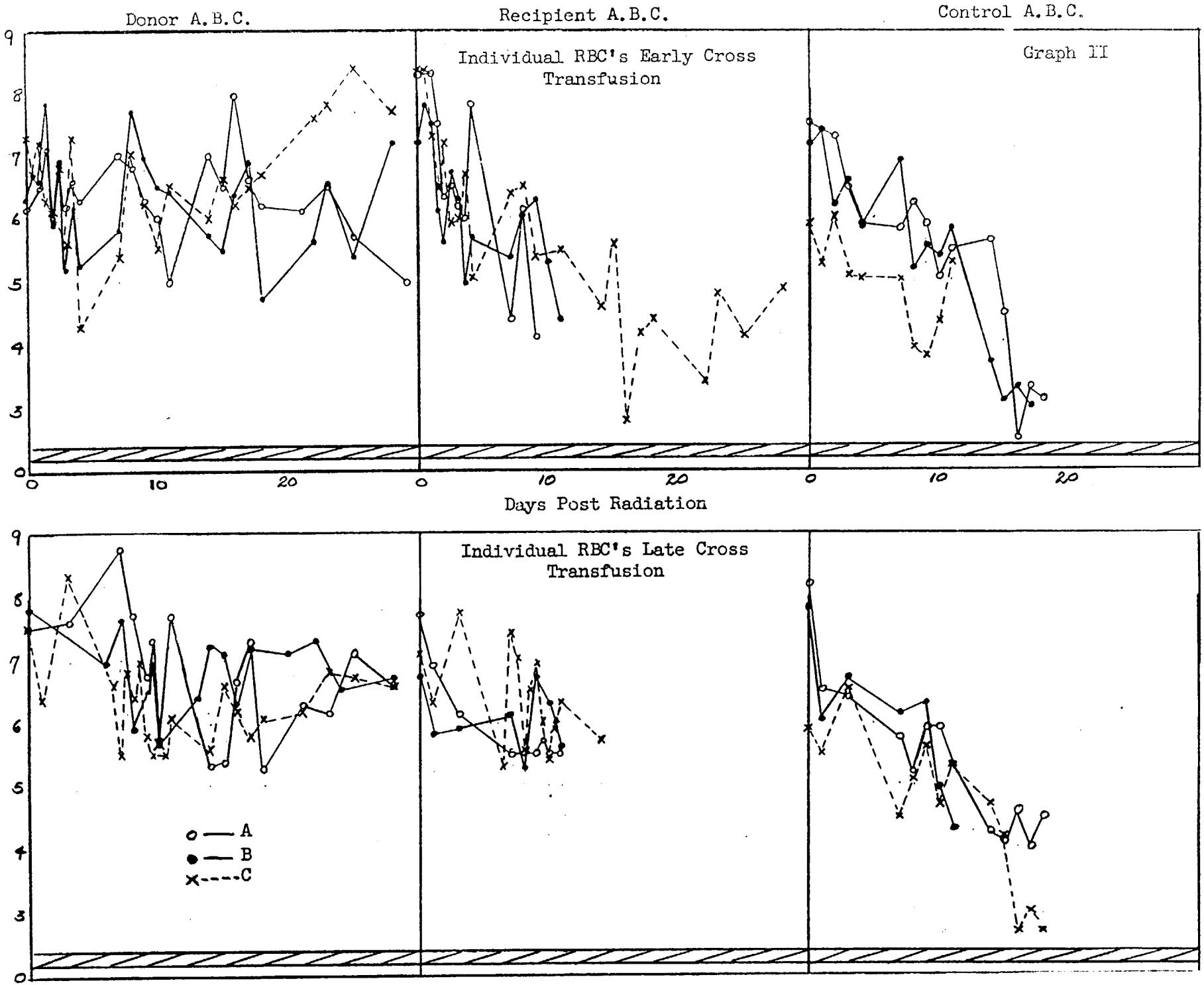
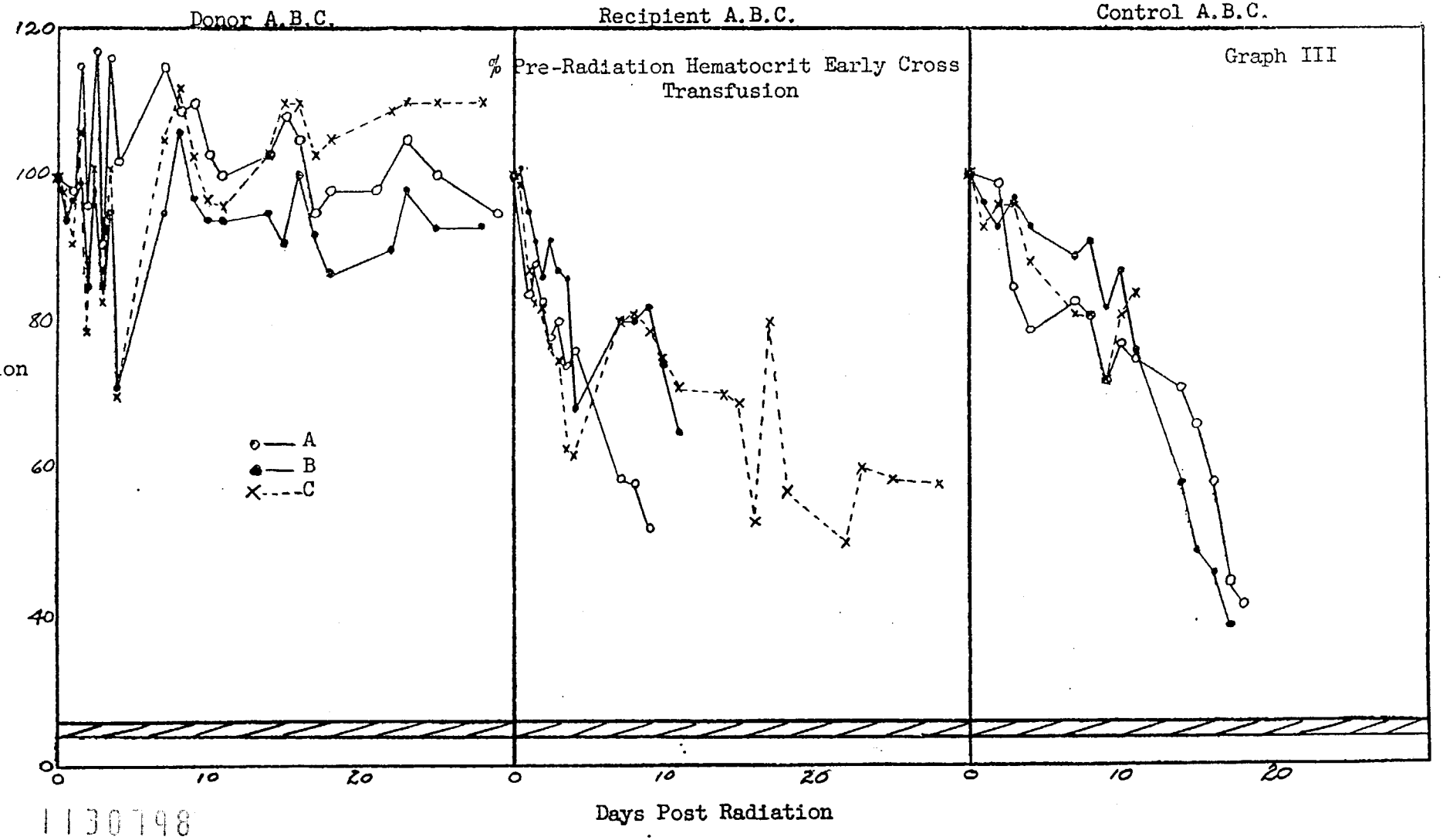
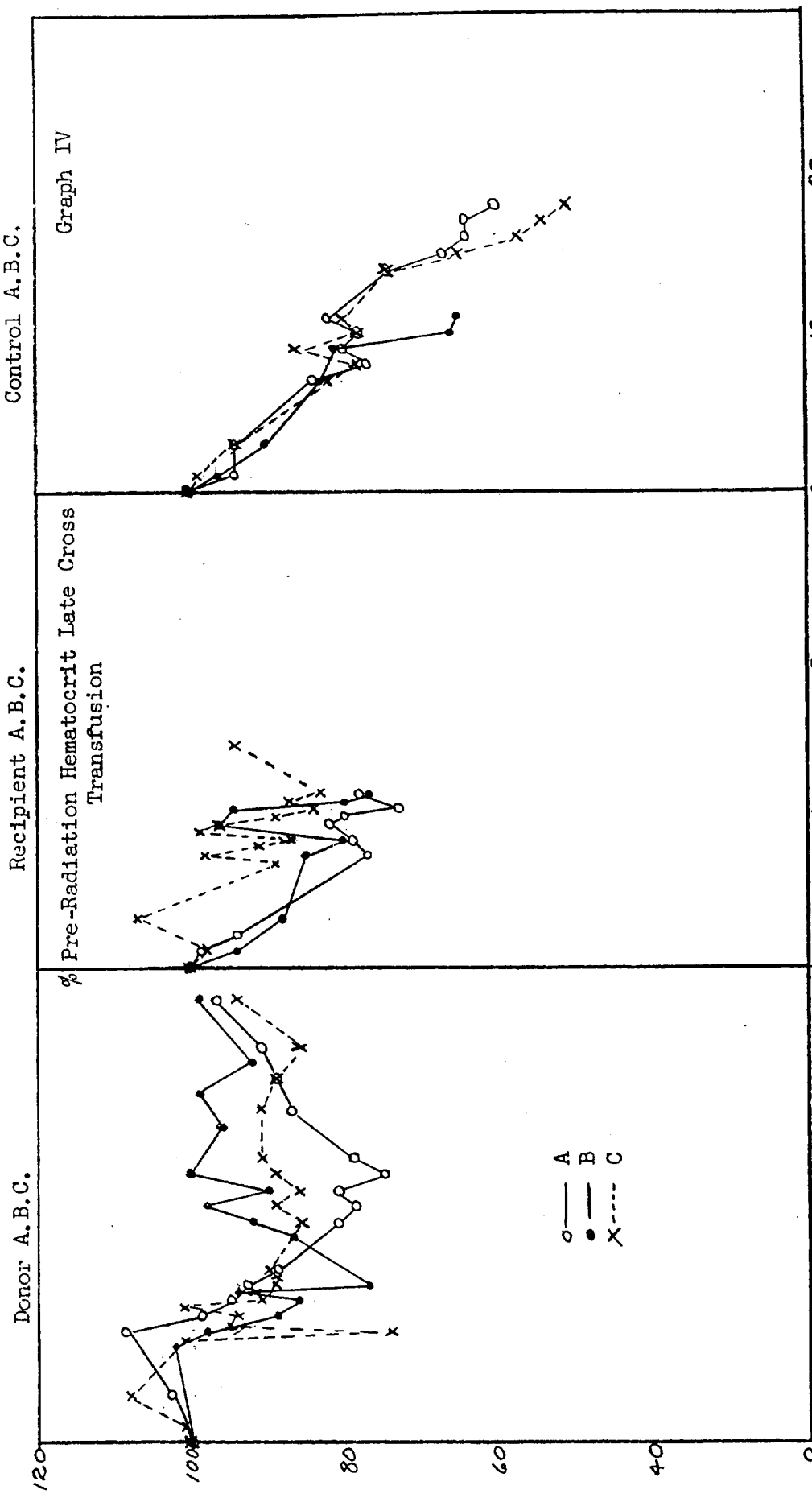
Table I

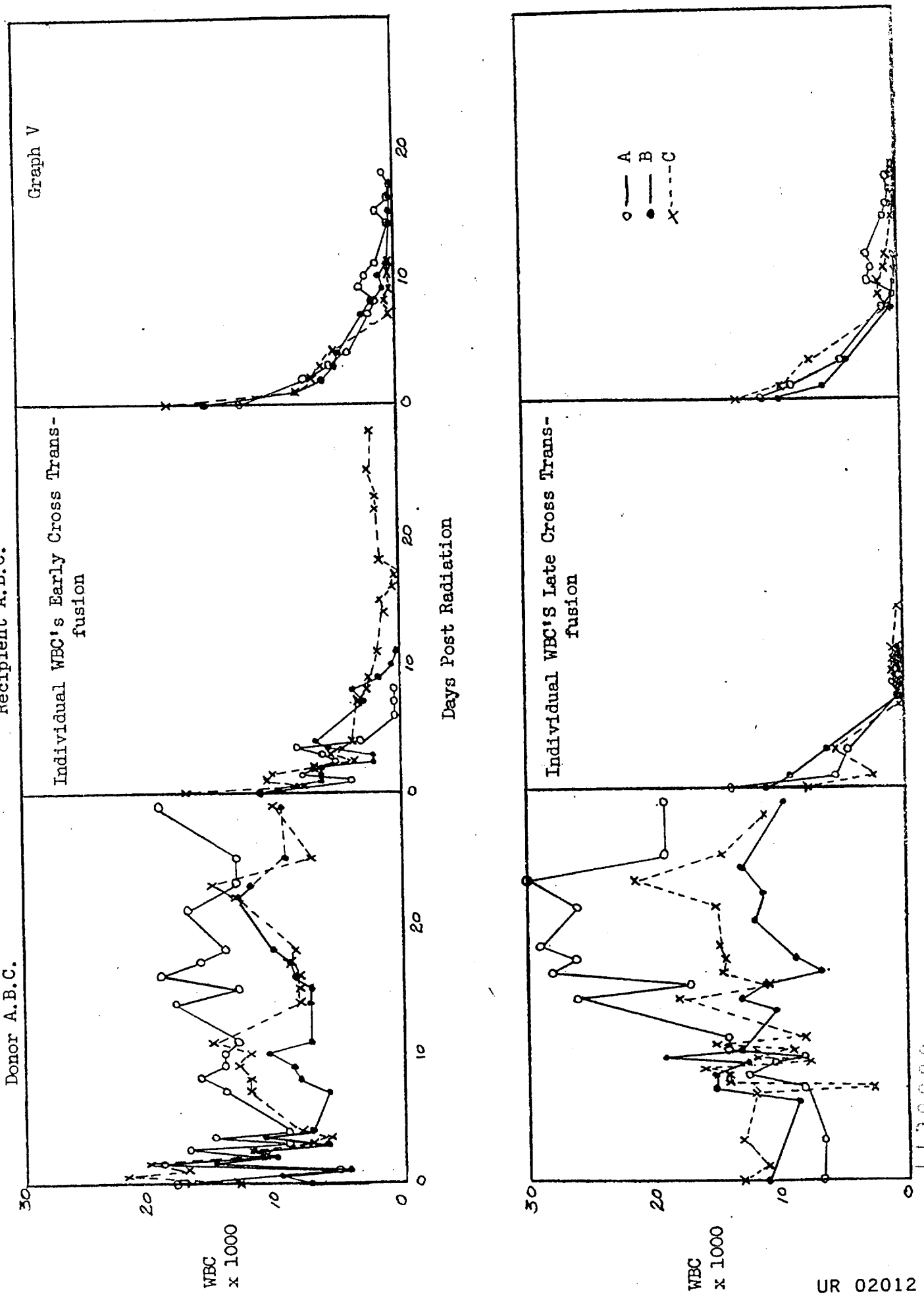
Dog #	Treatment	Dog wt. Kg.	Blood volume body wt.	Av. time of transfusion	Time died days post radiation
2581	41-A Control	19.21 Kg.	1630 cc		20 days
2400	41-A Recipient	16.4	1390	58 min.	14 days
2599	41-A Donor	22.0	1870		———
2615	41-B Control	9.65	820		12 days
2530	41-B Recipient	9.64	820	43 min	14 days
2196	41-B Donor	11.10	940		———
2389	41-C Control	13.85	1170		21 days
2596	41-C Recipient	12.25	1040	39 min	15 days
2216	41-C Donor	14.44	1230		———
2289	47-A Donor	11.43	970		———
2344	47-A Recipient	11.7	1000	42 min	10 days
2099	47-A Control	10.41	885		21 days
2588	47-B Donor	11.90	1020		———
2407	47-B Recipient	10.42	885	26 min	14 days
2417	47-B Control	10.00	850		18 days
2386	47-C Donor	9.20	780		———
2153	47-C Recipient	9.99	850	31 min	
2394	47-C Control	10.60	900		




Donor A.B.C.
Recipient A.B.C.
Control A.B.C.
Graph II
Individual RBC's Early Cross Transfusion
RBC x 10^6
Days Post Radiation
Individual RBC's Late Cross Transfusion
A
B
C







STUDIES RELATIVE TO THE EFFECT OF PIROMEN ON THE NUMBER AND THE PHAGOCYTIC ACTIVITY OF LEUKOCYTES OF IRRADIATED AND NORMAL DOGS, AND OF ONE MAN

by

M. Ingram, M. Adams, L. Coonan, G. Nielsen, D. Piatt, & G. Yettewich

ABSTRACT

Results of studies relative to the effect of Piromen therapy on the leukocyte picture and phagocytic activity of leukocytes in dogs and in one man are presented in table form and discussed briefly.

The dog experiments include final results of an experiment reported in an earlier Quarterly Report in which phagocytic activity was compared in two groups of dogs following whole body exposure to 300 r of 250 KVP x-ray. One of the groups received intravenous Piromen therapy throughout the post-exposure period. The results indicate that:

1. Irradiation with 300 r produced a decrease in phagocytic activity of leukocytes one week after exposure. This effect is not observed in Piromen treated dogs exposed to a like dose.
2. Phagocytic activity returns to normal before the beginning of hemapoietic recovery as indicated by leukocyte counts.
3. The magnitude and direction of post-exposure trends of leukocyte counts of irradiated dogs are not markedly affected by the intravenous administration of Piromen in the doses used in the experiment. There is perhaps a slight increase in absolute granulocyte counts of normal dogs treated with 4γ of Piromen i.v. 3 times a week.

Phagocytic activity increased gradually in the patient treated with intravenous Piromen for a period of approximately 7 months. There was no increase in the morning leukocyte or absolute granulocyte counts throughout this period.

* * * * *

The effect of exposure to 300 r of 250 KVP x-rays on the phagocytic activity of leukocytes has been reported in preliminary form in an earlier Quarterly Report.[1] The present report presents additional information obtained from the same studies and the results of serial observations on phagocytic activity of the leukocytes of a young man treated with Piromen*# for a period of approximately 7 months.

The dog studies consisted of two experiments. In the first, which was reported in the earlier Quarterly Report, 4 control blood studies and one phagocytosis determination were done on each of 4 dogs. Each dog then received a single whole body exposure to 300 r of 250 KVP x-rays. During the post-exposure period leukocyte counts (duplicate) and differential leukocyte counts were done 3 times a week, on Monday, Wednesday and Friday. On Wednesdays the red blood cell count, hemoglobin and hematocrit were also determined. Two of these irradiated dogs received 2 micrograms of Piromen intravenously each Monday, Wednesday and Friday, while the other two dogs served as controls and received no Piromen. Phagocytosis studies were done on each dogs blood once a week (Tuesday) for 4 weeks following exposure, and one final phagocytic study was run 6 weeks after exposure. The method used to study phagocytosis is presented in detail in the earlier Quarterly Report. The first experiment indicated that doses of two micrograms of Piromen 3 times a week did not affect the leukocyte picture. The second experiment was designed to determine whether or not larger doses of piromen might have some effect. Phagocytosis studies, however, were not carried out. Six dogs were studied in this second experiment. During the control period

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* The spelling of this trade name has only recently been changed from Pyromen to Piromen.

\# Kindly made available by the manufacturers, Travenol Laboratories.

each dog had eight blood studies consisting of erythrocyte counts, leukocyte counts, differential leukocyte counts, as well as determination of hemoglobin and hematocrit. Four of the six dogs were irradiated as in the first experiment and two of the irradiated dogs as well as two non-irradiated dogs received 12 micrograms of Piromen intravenously each week in 3 equal doses of 4 micrograms each. These doses were administered on Monday, Wednesday, and Friday for 6 weeks. Blood counts were done according to the schedule used in the first experiment.

Studies relative to the effect of Piromen on the phagocytic activity of human leukocytes were carried out on a 26 year old man, S.B. with amyotrophic lateral sclerosis.* Control phagocytosis studies were carried out on 3 consecutive days before the institution of Piromen therapy, and at irregular intervals thereafter. Throughout most of the 7 month treatment period, Piromen was administered intravenously in amounts of about 5 micrograms 3 times a week. From time to time, however, depending upon the clinical course of the patient as well as upon his response to medication, dosage was altered slightly, and for one 3 week period approximately midway in the course of therapy, Piromen was discontinued.

Results:

Survival: All dogs survived throughout the six weeks experimental period.

Leukocyte trends: The intravenous administration of Piromen in doses of 2 or 4 micrograms 3 times a week appears to have had no marked effect on the post-exposure trends of the leukocyte counts of irradiated dogs (Tables I, II, III and IV). It also appears to have had no marked effect on the leukocyte

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* The opportunity to study this patient stems from the interest and kind cooperation of the patient's family and of his attending physician, Dr. Paul Garvey.

picture of two normal dogs except for a possible increase in the total leukocytes and absolute granulocytes. Observed variations in the absolute eosinophil and absolute lymphocyte counts are of about the same magnitude as the variations observed during the control period.

In this respect it is also interesting to note that the administration of Piromen to the patient, S.B. did not increase the morning ("basal") leukocyte or absolute granulocyte count during the period of approximately 7 months covered by the present report.

Effect on phagocytosis: The phagocytic activity of leukocytes is measured by determining the percentage of granulocytes and monocytes which have actually phagocytised saccharated iron* after 40 minutes incubation with this material at 37.5° C, according to the procedure described in the earlier Quarterly Report.

Data obtained during the first four weeks of the first dog experiment were presented in preliminary form in the earlier Quarterly Report, at which time the examination of blood smears was not completed and it was stated that the figures presented were subject to revisions. The final results are presented at this time in Table V.

The data still appear to indicate a depression of leukocytic phagocytosis in irradiated dogs during the first post-exposure week. The Piromen treated dogs did not show this change. As noted in the previous report, the decrease in phagocytosis did not persist throughout the period of depression of the leukocyte count, but returned to normal two weeks after exposure. There is no ready explanation for the depression of phagocytic activity observed in both groups 6 weeks after exposure. It is expected that this

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* The commercial preparation Proferrin was used. This was supplied through the courtesy of the manufacturers, Sharp & Dohme, Inc.

will be studied further in the near future.

For the sake of comparison it may be noted that four phagocytosis studies on each of two normal litter mate dogs over a period of approximately one month show average deviations of 7.6 and 11.3 (average 9.5) when the average values are arbitrarily adjusted to 100, as were the control period values in the experimental groups.

Studies relative to the phagocytic activity of the leukocytes of patient S.B. indicate a slow but relatively steady increase in phagocytic activity throughout the course of Piromen therapy, reaching a relatively stable level after approximately 4 months of therapy. Discontinuing treatment for one 3 week period appears to have had little effect upon phagocytic activity (Table VI).

Discussion:

Although the procedure for determining the phagocytic activity of leukocytes is arbitrary and is currently in a state of development, observations presented here indicate that Piromen is capable of increasing the phagocytic activity of leukocytes.

In irradiated dogs the effect of Piromen therapy was that of maintaining phagocytic activity at about normal levels during a period when the phagocytic activity of leukocytes of non-treated dogs was depressed. How Piromen exerts this effect is not clear. It has been reported that Piromen has a specific effect on the reticuloendothelial system generally. This general concept, however, is difficult to define exactly as well as study experimentally. Studies designed to determine whether or not the observed effect represents a direct effect on leukocytes are expected to begin in this laboratory in the very near future. The relatively small difference between the Piromen treated and the non-treated irradiated dogs was observed on a regime of only 2γ 3 times a week. Phagocytosis was not studied in the second experiment, and should be

investigated when larger doses are administered to determine whether or not a greater effect could be achieved. Studies are now in progress to determine the effect of Piromen on leukocytic phagocytosis in normal dogs.

Leukocytic phagocytosis in the patient treated with Piromen over a period of 7 months shows a gradual increase apparently related to the cumulative dose. In this instance it is interesting that interruption of Piromen therapy for 3 weeks did not result in a depression of phagocytic activity. This long term effect of the drug has been noted in responses other than phagocytic activity. In fact, the characteristic pattern of the therapeutic response in, for example, allergic conditions, is said to consist of an initial beneficial effect requiring doses once or twice a week for a few weeks after which the initial gains are maintained with much less frequent doses - e.g. once a month.

The increase in peripheral blood granulocytes in normal dogs treated with Piromen is in agreement with reports of other investigators who have observed stimulation of myeloid hematopoiesis and extramedullary myelopoiesis in Piromen treated animals. The fact that no increase in granulocytopoiesis was observed in irradiated dogs treated with Piromen may simply reflect inability to respond to the granulocytopoietic stimulus of Piromen. One would expect that the markedly depressed leukocyte count per se would be a strong stimulus to make new leukocytes if the animals were able to do so. Studies using larger doses of Piromen will help determine whether heavily irradiated dogs are totally unable to respond further or whether the added stimulus in the experiments reported here was simply too small.

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Table I

Leukocyte Counts

(Average during control period adjusted to 100 for each dog)

	Irradiated only: No Piromen		Irradiation + Piromen		Piromen only:not Irrad.
	1st experiment (2 dogs)	2nd experiment (2 dogs)	1st experiment 2γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)
Pre-exposure	100	100	100	100	100
Average deviation	8.0	5.4	13.8	12.0	10.2
1 week post-exp.	59.4	38.3	52	55.2	96.7
2 weeks post-exp.	21.6	22.4	19	28.1	115.6
3 weeks post-exp.	28.7	18.3	18.1	18.6	114.6
4 weeks post-exp.	26	22.4	27.1	24.8	106.7
5 weeks post-exp.	27.4	40.6	41.9	45.9	115.6
6 weeks post-exp.	32.2	52.4	62.6	60.8	119.6

Table II

ABSOLUTE GRANULOCYTE COUNTS

(Average during control period adjusted to 100 for each dog)

	Irradiated Only: No Piromen		Irradiation + Piromen		Piromen Only Not Irradiated
	1st experiment (2 dogs)	2nd experiment (2 dogs)	1st experiment 2γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)
Pre-exposure	100	100	100	100	100
Average deviation	9.3	10.9	13.8	15.1	13.3
1 week post-exp.	65.2	40.7	54.0	65.5	94.6
2 weeks post-exp.	18.2	22.2	18.3	29.8	123.6
3 weeks post-exp.	14.7	17.8	16.5	15.8	125.8
4 weeks post-exp.	22.9	21.2	26.2	21.8	113.4
5 weeks post-exp.	45.9	42.9	43.2	48.2	126.4
6 weeks post-exp.	51.7	63.0	68.2	66.8	123.2

Table III

Absolute Eosinophiles

(Average during control period adjusted to 100 for each dog)

	Irradiated only: No Piromen		Irradiation + Piromen		Piromen only: not irrad.
	1st experiment (2 dogs)	2nd experiment (2 dogs)	1st experiment 2γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)
Pre-exposure	100	100	100	100	100
Average deviation	32.4	20.7	40.0	28.9	24.2
1 week post-exposure	42.0	65.6	44.6	42.6	109.4
2 weeks post-exposure	11.4	23.8	9.1	18.6	65.5
3 weeks post-exposure	8.0	12.3	4.8	12.2	134.8
4 weeks post-exposure	8.9	13.8	3.5	9.0	135.4
5 weeks post-exposure	15.6	29.0	10.9	26.0	147.0
6 weeks post-exposure	22.5	50.4	27.1	41.2	155.8

Table IV

Absolute Lymphocytes

(Average during control period adjusted to 100 for each dog)

	Irradiated only: No Piromen		Irradiation + Piromen		Piromen only: not irrad.
	1st experiment (2 dogs)	2nd experiment (2 dogs)	1st experiment 2γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)	2nd experiment 4γ 3 times/wk. (2 dogs)
Pre-exposure	100	100	100	100	100
Average deviation	21.4	19.9	12.8	17.6	19.5
1 week post-exp.	38.8	28.6	53.6	21.2	103.4
2 weeks post-exp.	21.6	23.6	28.4	21.6	92.6
3 weeks post-exp.	28.7	21.2	31.2	27.0	85.7
4 weeks post-exp.	26.0	28.0	30.1	39.4	87.6
5 weeks post-exp.	27.4	33.2	34.5	39.5	84.0
6 weeks post-exp.	32.2	34.0	38.5	41.3	107.9

Table V

Leukocyte Phagocytic Activity

(Pre-exposure value for each dog adjusted to 100)

	Pre-exposure	Post-exposure				
		1 week	2 weeks	3 weeks	4 weeks	6 weeks
Radiated (2 dogs	100	73	104	98	101	79
Radiated plus Piromen (2 dogs)	100	107	124	120	108	73

Table VI

EFFECT OF PIROMEN ON PHAGOCYTIC ACTIVITY OF HUMAN LEUKOCYTES (Patient S.B.)

Date	Cumulative Dose (micrograms)	Phagocytic Activity (average control value adjusted to 100)
3-4-52	0 (control)	94.6
3-5-52	0 (control)	102.0
3-6-52 (A.M.)	0 (control)	103.4
3-6-52 (P.M.)	2	148.7
3-12-52	14	95.1*
4-16-52	64	142.8
4-18-52	70	113.2
4-23-52	75	133.5
4-25-52	78	135.2
4-28-52	81	194.1
5-1-52	84	170.4
5-7-52	90	171.9
5-9-52	93	148.9
5-16-52	108	187.0
5-23-52	108 Off Piromen after dose on 5-16-52	160.9
6-6-52	108	172.4**
6-7-52	109 Piromen therapy started again	
6-20-52	126	199.0
6-30-52	134	191.9
7-3-52	147.2	196.3
7-11-52	171.3	227.4
9-30-52	350.4	209.5
10-9-52	371.9	214.2

* Patient receiving skin tests to determine sensitivity to certain hormones. One 4+ reaction. Phagocytosis studies discontinued until this variable eliminated.

** Average of 4 runs during day; average deviation 5%.

A NEW AND SIMPLE DIFFERENTIAL MORPHOLOGY STAIN FOR SPERMATOZOA

by
George W. Casarett

ABSTRACT

The formula, procedure, and staining results for a new, improved, simple, and rapid differential morphology stain for spermatozoa are given. This staining method has resulted consistently in clear, undistorted specimens with sharp differentiation of cytological structures. A single staining fluid is utilized and the procedure contains a minimum of steps. The method may be used with uniform success by personnel of little training. It has been used on over 2,000 samples of dog semen with consistently good results and gives equally good results with human specimens.

*****

Introduction: During the past three decades the importance of physiologic and morphologic study of spermatozoa in problems of infertility has become increasingly emphasized. Greater importance is being attached to the morphology of spermatozoa in the evaluation of semen and of the health of the spermatozoa. For such evaluations it is necessary that fixation and staining of spermatozoa result consistently in clear, undistorted specimens whose parts are distinctly differentiated from one another, preferably by differences in color as well as by differences in densities. A good differentiation of cell and nuclear membranes, nucleus and cytoplasm or acrosome, neck and neck granules, sheaths and body substance, should be obtained for routine morphologic study.

Mucus coating and other protein substances present problems in the staining of spermatozoa. Many dyes do not easily penetrate or stain spermatozoa intensely enough to differentiate structures satisfactorily. Another problem involves the fact that the mucus of the semen is stained by many dyes, resulting

in a cloudy background obscuring the visibility of spermatozoal structures. When this is the case, some investigators (e.g., Williams et al (1)) remove the mucus with a solution of chlorozene before staining, while others (Isenberg (2)) wash the spermatozoa with sodium bicarbonate and saline solutions. Other staining techniques leave the mucus unstained, however. Another problem is that of avoiding distortion of size and shape of morphologic structures by washing fluids and by unsuitable methods of fixation.

For routine study of sperm morphology in laboratory, clinic, or medical office it is desirable that the qualities of a good specimen be obtained consistently by means of a simple and rapid staining technique utilizing only one staining fluid and a minimum of procedural steps. The procedure described fulfils these criteria even when used by an inexperienced technician.

As a part of the preparation for a ten-year program of study of spermatozoa, this author experimented with the published techniques for staining spermatozoa. The results obtained with the simpler methods were variable and, on the whole, unsatisfactory for the problems at hand. The more satisfactory staining techniques were among the more complicated, lengthy or difficult procedures including those of Williams et al (1), Isenberg (2), Cary and Hotchkiss (3), Meaker (4), Gelarie (5), Holbert (6), and Pollak and Joel (7). The staining reactions in many of these methods are delicate and necessitate precision of technique in order to obtain invariable results. Since a simple and rapid technique giving uniform and excellent results was needed for the extensive research program at hand, the author entered upon a program of experimentation which led to the development of the following satisfactory differential staining fluid and technique. The technique is simple and rapid and gives uniformly a high degree of clear and sharp differentiation of morphologic characteristics with a minimum of distortion.

With the use of the stain as described below, the following differentiations are made in spermatozoa (see table 1).

TABLE 1

Stain Differentiation in Spermatozoal Structures

Sperm Structure	Stain Reaction
Galea capities	Pale bluish-gray; sharply outlined
Cell membrane	Bluish-gray; sharply outlined
Nuclear membrane (shell)	Bluish-gray; sharply outlined
Acrosome	Slate blue
Nucleus	Pink
Neck	Sharply outlined (dark blue); colorless inside
End knobs	Dark blue
Middle piece	Sheath dark blue; center dark pink
Axial filament	Dark blue
Tail	Dark blue

There is a tendency for abnormal forms of spermatozoa to stain more densely than the normal forms.

Formula and Preparation of Staining Fluid:

5% aqueous aniline blue (water soluble)	2 parts
5% aqueous eosin bluish (water and alcohol soluble)	1 part
1% aqueous solution of phenol	1 part

Prepare the above stock solutions of the dyes and phenol in distilled water and filter the dye solutions. Prepare staining fluid as needed according to the proportions given above and filter into dropping bottle. The staining

fluid is stable.

Procedure:

1. Prepare a thin, even smear of fresh semen on a clean, dry slide or coverslip and allow to dry in air. Since a high viscosity prevents thin spreading, the semen should be allowed to stand until it becomes liquid (30 to 60 minutes).
2. Fix for 3 minutes by flooding with 50-50 ethyl alcohol-ether solution. Dry in air.
3. Flood smear with staining fluid and stain for 5 to 7 minutes, preferably over a steam bath or a warming table.
4. Float and wash off staining fluid thoroughly with distilled water. Dry in air.
5. Mount and examine under oil immersion lens.

The staining fluid and procedure have been used in semen studies on over 2,000 samples of dog semen with uniform success. The method has been tested with human semen specimens and was found to give equally good results.

Summary: The formula, procedure, and staining results for a new, improved, simple, and rapid differential morphology stain for spermatozoa are given. This staining method has resulted consistently in clear, undistorted specimens with sharp differentiation of cytological structures. A single staining fluid is utilized and the procedure contains a minimum of steps. The method may be used with uniform success by personnel of little training. It has been used on over 2,000 samples of dog semen with consistently good results and gives equally good results with human specimens.

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STUDIES OF FLASH BURNS: THE INFLUENCE OF SPECTRAL QUALITIES OF THE CARBON ARC SOURCE (A PRELIMINARY REPORT)

by
Kelly M. Berkley, Herman E. Pearse and H. D. Kingsley

ABSTRACT

The physical, biological, histological, and statistical methods used to produce and evaluate high intensity, flash duration burns are briefly discussed. A modification of the spectral distribution of the source by Pyrex glass is used. This modification produced burns of less surface severity but approximately the same in depth of damage. This reaction is briefly discussed, and is felt to be due to the variability of absorption of energy of different wave lengths. The modifications covered by filters of other spectral characteristics are being studied and will be reported later.

Introduction: The physical factors affecting flash burns have been the primary consideration in this laboratory since 1947. Perkins, Pearse and Kingsley (1) studied the time-energy relationships of burns produced by the carbon arc source in pigs, demonstrating that surface appearance and depth could be correlated only at a constant exposure time. Our purpose is to determine the effect on the burn of removal of the ultraviolet portion of radiant energy, emitted by the carbon arc source.

Methods:

1. Physical: The physical equipment used to produce these lesions consists of an Army carbon arc searchlight, modified by an ellipsoidal mirror as described by Davis, Krolak and Blakney (2). The skin surface was exposed at the secondary focal point of the mirror through a transite shield with an

aperture of 1.8 cm. in diameter. Energy levels were varied by movement of open-type diaphragms along the optical axis.

The spectral characteristic of the energy was modified by the introduction of Pyrex glass, approximately 5 mm. in thickness, the plane face of which was placed at 68° to the optical axis, which is used as a part of a recently developed monitoring system (2).

2. Biological: As in previous studies in this laboratory (1, 3), Chester White pigs, anesthetized by dial-urethane, 75 mgm. per kg., administered intraperitoneally, were used. Only the flanks were used.

3. Histological: Biopsy specimens of the center of the lesion were fixed in Bouin's solution and stained with hematoxylin and eosin dyes.

4. Statistical Methods: Systematic randomization was employed to determine the site for any combination of factors used. By this method there is an equal probability of any combination falling in any position on the animal. Furthermore, every combination falls the same number of times on each pig. Evaluation was done without knowledge of the prevailing stimulus.

Experiment: Chester White pigs were chosen of weight between 10.6 and 16.6 kg. After anesthetization the hair was closely clipped and the skin washed and dried. Three rows of six burns each were produced on each side of four animals, producing 144 burns. Two burns were discarded for technical inaccuracy.

Three irradiance levels, 2.6, 9.6 and 18.8 calories per cm.^{2} per second were chosen. One-half second exposure times were used, thereby producing a radiant exposure of 1.3, 4.8 and 9.4 calories per cm.^{2}. One half of the burns were produced unmodified and the other half by the introduction of the Pyrex glass into the beam at each irradiance.

Burns were evaluated 24 hours after exposure. Only those lesions which showed visible signs of burning were examined microscopically. Only 17 biopsies were taken of erythematous burns, although 23 were produced. One hundred and nine burns were examined microscopically.

Results: The grading system, in which erythema is subclassified by intensity of color, coagulation by extent and intensity of whiteness, and the surface phenomenon of a steam bleb by surface extent is used (1, 3). On analysis burns are notably less severe when produced through a Pyrex glass plate which absorbs the ultraviolet portion of the spectrum. These results are shown in table 1.

The microscopic criterion used is depth of damage of collagen, expressed as percentage of total thickness of the dermis. A micrometer scale in the ocular of the microscope aided these determinations. In most instances the demarcation between damaged and undamaged tissue described by Hogg, Payne, and Pearse (4) could be determined within ten percent and in all instances within 20 percent. These results appear in table 2, which reveal that the depth of damage is not significantly changed by eliminating the ultraviolet portion.

Discussion: A change in the spectral qualities of radiant energy will vary its penetration into the skin. Ultraviolet radiation is largely absorbed in the epidermis, whereas with longer wave lengths transmission increases progressively (5). This varying distribution as a result of the differential transmission causes a change in the gross appearance of the burn lesion. The low distribution of energy in the superficial layers produced by removal of the ultraviolet portion of the spectrum by Pyrex glass causes a shift of the frequency curve to less severe burns at 1.3, 4.8 and 9.6 calories per cm.^{2}. At 1.3 calories per cm.^{2} the inclusion of ultraviolet yielded no burns. At 4.8 calories per cm.^{2} with ultraviolet,

60% of the burns produced were 2+ severe. At the same level, but without ultraviolet, no burns were that severe, and 80% were 2+ mild. At 9.6 calories per cm.^{2} with ultraviolet, almost one-half of the burns showed steam blebbing, but without ultraviolet no burns showed blebbing.

This change in the severity was not apparent microscopically for no difference in the depth of the burns was seen by the technique used.

It is doubtful that the delayed, faint erythema, produced by the unmodified carbon arc source can be reproduced easily by radiant energy of longer wave lengths obtained by use of the Pyrex glass plate which blocks the ultraviolet wave lengths in the range 2800 to 3200 A°.

Further studies are being done to observe the effect of other wave lengths of the carbon arc source on the thermally damaged skin.

Conclusions:

1. Placing a 5 mm. Pyrex glass plate in the beam of a carbon arc source removes much of the ultraviolet which produces a notable difference in the surface appearance of burns at radiant exposures of 1.3, 4.8, and 9.4 calories per cm.^{2} in 0.5 second.

2. This change in the spectral characteristics, however, does not alter the depth of the burn as determined by the histological technique used.

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TABLE 1

SUMMARY OF MACROSCOPIC RESULTS

			Erythema (1+)			Partial Coagulation (2+)			Total Coagulation (3+)			Steam Bleb (4++)			
	Radiant Exp cals.-cm.$^{-2}$	No Burn	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	No. of Exposures
Without Pyrex Glass Filter	1.3	0	22	1											23
	4.8					3	7	15							25
	9.4							1	8	4	1	3	0	7	24
With Pyrex Glass Filter	1.3	23													23
	4.8				4	18	1								23
	9.4							1	14	6	2	1			24

TABLE 2

SUMMARY OF MICROSCOPIC RESULTS

	Radiant Exposure cals. - cm.$^{-2}$	No Burn	Epidermal	Transepidermal	DERMAL							No. of Exposures	No. Examined Microscopically
					0-10%	10-20%	20-30%	30-40%	40-60%	60-90%	90 + %		
Without Pyrex Glass Filter	1.3	0	17									23	17
	4.8				13	9	1	0	1			25	24
	9.4					4	6	5	5	2	1	24	23
With Pyrex Glass Filter	1.3	23										23	0
	4.8			2	12	5	1	2				23	22
	9.4					1	10	5	4	2	1	24	23

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FIGURE I
THE MACROSCOPIC RESULTS OF BURNS PRODUCED WITH AND WITHOUT A PYREX GLASS FILTER

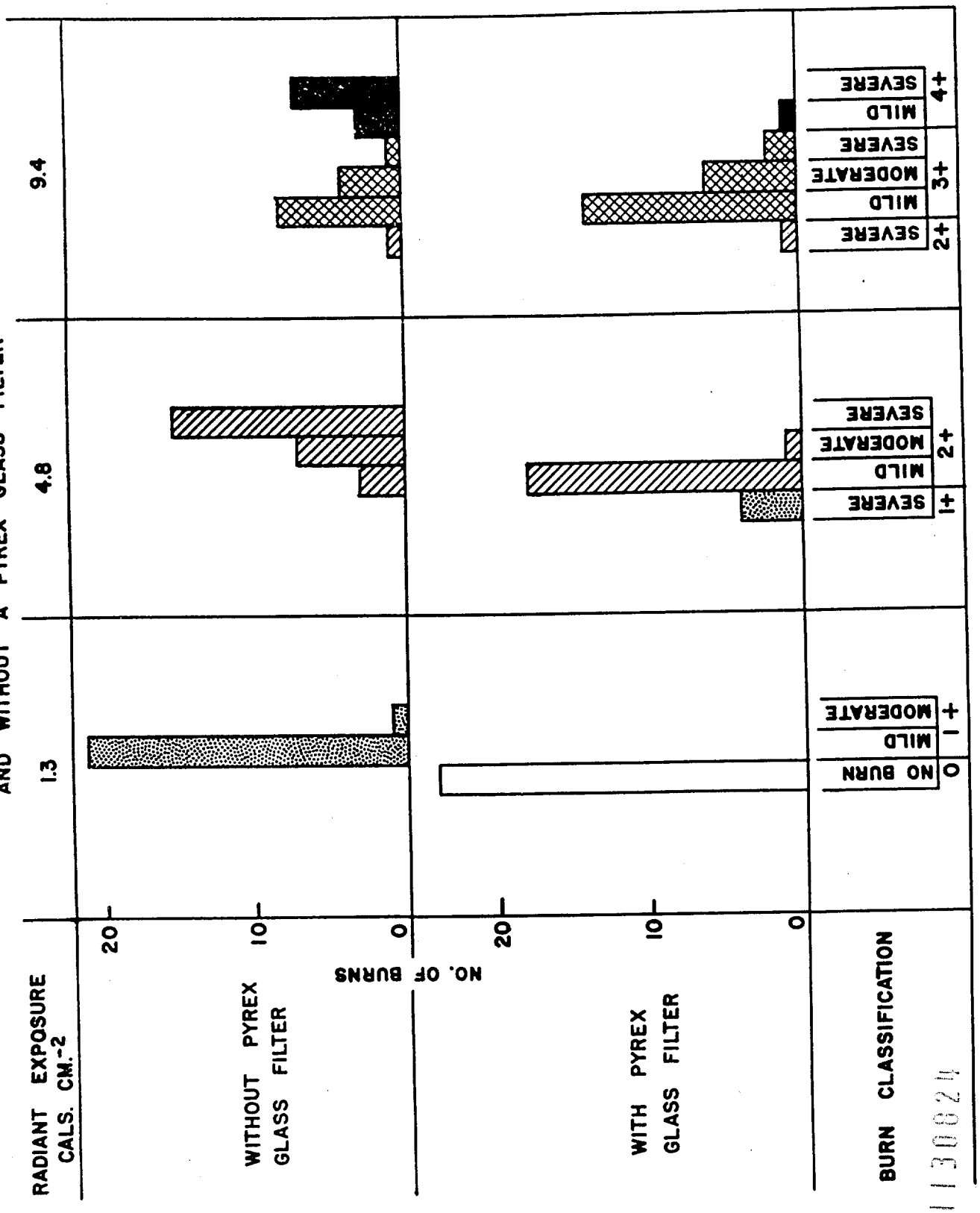
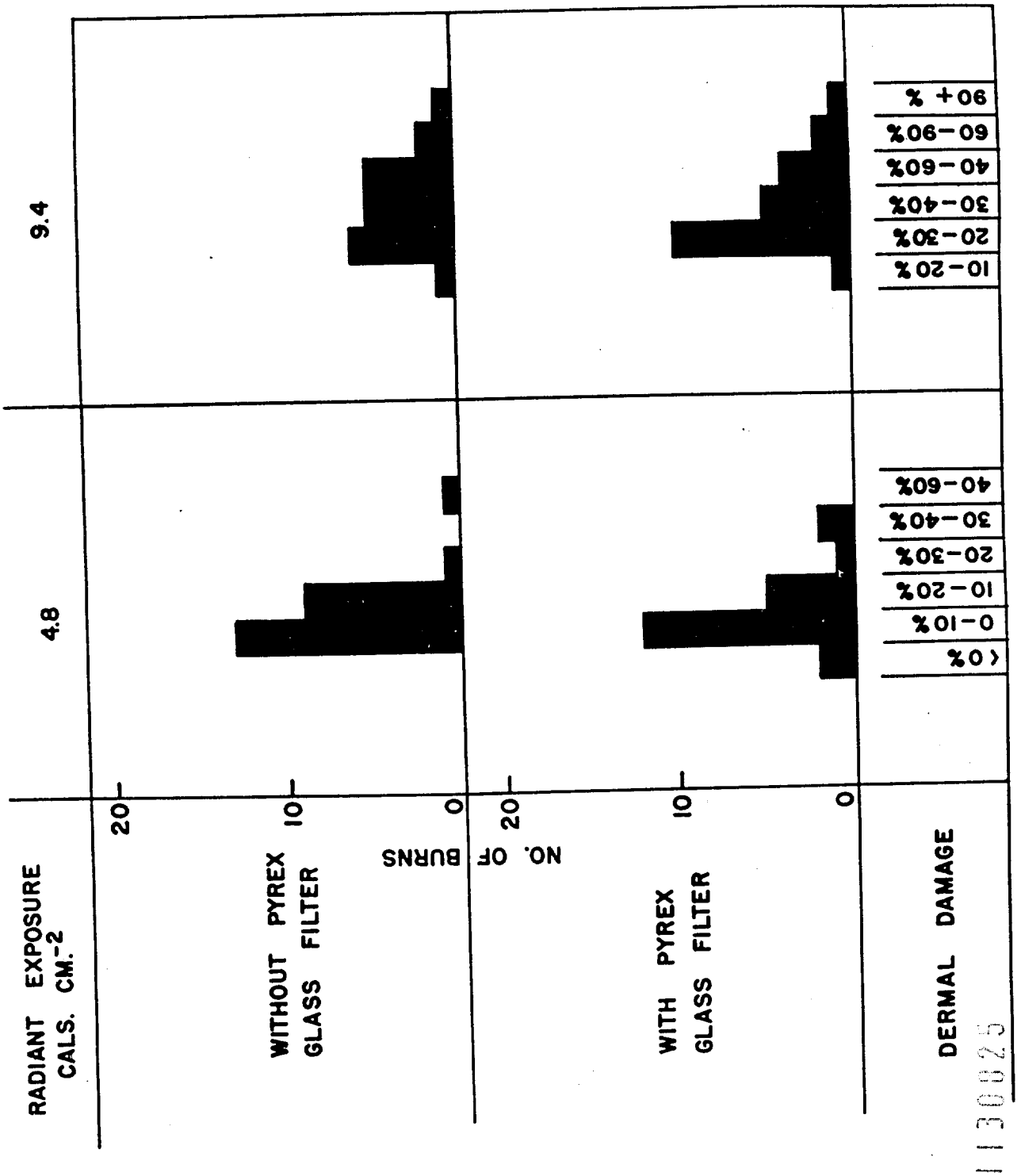


FIGURE 2

THE MICROSCOPIC RESULTS OF BURNS PRODUCED WITH AND WITHOUT A PYREX GLASS FILTER



Abstract of Paper Presented at the Biostatistics Conference - Iowa State College
Ames, Iowa June 16 - July 18, 1952

APPLICATION OF SOME MULTIVARIATE ANALYSIS TECHNIQUES TO DATA FROM RADIATION EXPERIMENTS

by
Arthur M. Dutton

Data from non-genetical radiation experiments often consist of successive measurements taken at intervals in time on each of several animals. The experimenter is primarily interested in whether or not there are treatment effects reflected by these measurements. This paper (1) reviews appropriate statistical methods for analyzing such data, (2) examines the assumptions involved in these analyses, and (3) exemplifies the calculations involved by applying the techniques to actual radiation data.

The most general method of analysis considered is that of the multivariate analysis of dispersion. The successive observations on an animal are considered to be a simple multivariate sample. The total sum of squares of each variate and the total sum of products for each pair of variates are divided into categories for treatments, error, etc., in a manner analogous to the well-known single variate analysis of variance. An appropriate criterion for testing the null hypothesis of no treatment effects is the ratio of two determinants. The approximate distribution of this criterion under the null hypothesis is indicated in the paper.

The model underlying this method of analysis is examined in detail in the paper.

The method of analysis is applied (1) to the data from a weight-loss experiment and (2) to the data from a wound-healing experiment. In the former experiment the data are successive weight losses of each of several rats subjected to two non-lethal radiation doses. In the latter experiment the data are successive wound areas of each of several rats subjected to a number of radiation treatments.

Abstract of Paper Presented at the Cincinnati Meeting of the American Industrial Hygiene Association April 24, 1952

BLOOD FLUORIDE CONCENTRATIONS IN DOGS EXPOSED TO HYDROGEN FLUORIDE

by

F. A. Smith, D. E. Gardner, J. DeVoldre and H. C. Hodge

A study of blood fluoride levels in dogs exposed 1 - 10 days to 20 mg HF/m^3 indicated that the level is increased 45-fold to a mean maximal value of 450 µg F/100 ml after four days of exposure. The concentration then drops, despite continuing exposure, to a mean value of 250 µg F/100 ml on the tenth exposure day. After termination of the exposure the concentration decreases rapidly during the first five days and then falls more slowly thereafter, until nearly normal concentrations are attained by the tenth post-exposure day.

Abstract of Paper Presented at the Cincinnati Meeting of the American Industrial Hygiene Association, April 24, 1952

SELECTED BLOOD AND URINE CHANGES IN EXPERIMENTAL BERYLLIUM POISONING

by
Charles J. Spiegl

Two clinical criteria offer promise as indicators of toxicity resulting from exposure to compounds of beryllium. The ratio of uric acid to creatinine in urine and the ratio of phospholipids to cholesterol in the red blood cells of dogs increased from control values to levels approximately two standard deviations outside the normal range. Although absolute concentrations of both uric acid and phospholipids were often erratic, the use of creatinine and cholesterol as relatively stable base-lines permitted the above observations to be made.

Increases in the two urine and blood ratios studied were observed in dogs subjected to BeF_2, and BeO, and $BeSO_4$ administered by injection or by inhalation. Injection of $BeSO_4$ into rabbits appeared to verify the red-cell phospholipid/creatinine change noted in dogs.

Abstract of Paper Presented at the Josiah Macy, Jr. Foundation, 4th Conference on Metabolic Interrelations, January 7-8, 1952, N.Y.

THE ION-BINDING PROPERTIES OF CARTILAGE

by
Eugene Boyd, William F. Neuman, and Isaac Feldman

Veal costal cartilage showed equal binding capacities for sodium, calcium, and barium. This capacity correlated closely with the sulfate content, indicating that chondroitin sulfate was responsible for the major portion of the binding. Phosphate was taken up from solution only by cartilage containing appreciable amounts of calcium. The binding of calcium by cartilage was shown to be an ion exchange reaction.

Abstract of the paper presented at the Northwestern New York Joint Meeting of the American Industrial Hygiene Association, Rochester, New York, December 2, 1951

PNEUMOTACHOGRAPHY IN THE STUDY OF RESPIRATORY DYSFUNCTIONS

by
Paul E. Morrow

Pneumotachography pertains to the measurement and analysis of respiratory airflow dynamics. In recent years, pneumotachography has been applied to the study of normal human respiration and has been helpful in such problems as the design of resuscitative devices, and respiratory protective devices. Many efforts have been made to ascertain the usefulness of pneumotachography in the detection of pulmonary dysfunctions. Its role in this regard is still not certain but appears valuable. More recent developments in the field of pneumotachography have indicated that this method may prove to be one of the more valuable tools in the study of respiration in laboratory animals, and it has indicated that respiratory kinetic measurements in man constitute a valuable supplement to existing lung function tests.

The modern pneumotachograph is generally an electronic assembly which possesses high sensitivity and operates with a minimum resistance to the respiration of the subject. Properly designed pneumotachographs provide accurate volumetric data also, and permit studies of ambulatory subjects or in situations where portable operation is necessary.

Abstract of Paper Presented to the American Society for Pharmacology and Experimental Therapeutics - Madison, Wisconsin, September 8-10, 1952

THE EFFECT OF URANIUM-PRODUCED NEPHROSIS IN THE RABBIT ON THE URINARY EXCRETION OF SODIUM FLUORIDE ADMINISTERED IN THE DRINKING WATER

by
H. C. Hodge, F. A. Smith, D. E. Gardner, W. L. Downs, and E. A. Maynard

Groups of 4 to 8 adult male albino rabbits were maintained on purina rabbit chow (42 ppm F) for forty days. The control group (8 rabbits) was given tap water (0.06 ppm F), the fluoride control group (4 rabbits) and the uranium-treated group (4 rabbits) were given drinking water containing 15 ppm F. The uranium-poisoned rabbits received 0.3 mg U/kg as uranyl nitrate subcutaneously after 14 days on the fluoride regimen. In the acute phase of uranium poisoning the water intake was reduced and a polyuria developed; both of these changes disappeared with the healing of the uranium injury. A marked proteinuria also appeared and there was a small increase in fluoride retention; both of these effects disappeared on recovery.

During the entire experimental period the total fluoride ingested by the control group was 246 mg per rabbit; of this about 30% was retained. Approximately 50% of the fluoride excreted was via the urine. The fluoride control group ingested 437 mg F per rabbit and retained about 45%. In the uranium-poinsoned group each rabbit ingested on the average 269 mg F and retained about 48% of it. Of the fluoride excreted in these two groups about 1/3 appeared in the urine.

Although fluoride retention was increased slightly during the period of acute uranium injury to the kidneys, the increase was not large. Moreover, during the entire experimental period which continued approximately 4 weeks after the administration of the uranium, the over-all fluoride retention was exactly the same as that of the fluoride control group.

Abstract of Paper Presented at the Annual Meeting
of the American Industrial Hygiene Association, Radiation Division,
Cincinnati, Ohio, April 21-24, 1952

CYCLOTRON HAZARDS AND THEIR MANAGEMENT

by
Herbert Mermagen

The radiation hazards discussed have been divided into two groups:

1. Those which will be produced during the operating periods of cyclotrons and which are due to accelerated particles, and

2. Those which stem from induced radioactivity of targets and other metal parts of the cyclotron tanks.

Illustrative tables are presented to familiarize the audience with two types of reactions giving rise to neutrons during the operation of the cyclotron, and also of induced activity which will be present after the shut-down of the cyclotron.

The physical locations of two cyclotrons are presented as a basis of discussion of shielding problems from the view point of radiation hazards to personnel outside of the cyclotron enclosures.

Methods of approach toward the elimination of potential hazards are discussed in a manner which is specific to the operation of the two Rochester cyclotrons.

1. The evalulation of the magnitude of the potential dangers from physical measurement by means of ionization chambers in terms of roentgen equivalent physical, and

2. Similar evaluations of biological investigations from data obtained on cyclotron operating and research personnel, as well as early experimental findings on animals exposed continuously to the prevailing radiations within the 130" cyclotron laboratory.

The material presented is applicable in a general way to most cyclotron installations.

No attempt is made to discuss in detail any technicalities, which after all might be too specific and also variable in their nature for other high-energy accelerators.

TECHNICAL REPORTS ISSUED FOR DISTRIBUTION

July 1, 1952 thru September 30, 1952

Report No.	Title	Authors	Subject Category
UR-201	Histopathology of Alpha Radiation from Internally Administered Polonium (UNCLASSIFIED) Issued: October 17, 1952	Casarett	Health and Biology
UR-207	A Formulation of the Injury, Life Span, Dose Relations for Ionizing Radiations. II. Application to the Guinea Pig, Rat and Dog (UNCLASSIFIED) Issued: July 29, 1952	Blair	Health and Biology
UR-211	The Occurence of Lymphocytes with Bilobed Nuclei in Cyclotron Personnel (UNCLASSIFIED) Issued: July 1, 1952	Ingram Adams et al	Health and Biology
UR-213	Quarterly Technical Report April 1, 1952 through June 30, 1952 (UNCLASSIFIED) Issued: August 12, 1952	Blair	Health and Biology
UR-214	The Relationship of the Cell Surface to Metabolism. VIII. The Stimulation of Fermentation by Extracellular Potassium (UNCLASSIFIED) Issued: August 12, 1952	Rothstein Demis	Health and Biology
UR-215	Calcium Complexes of ATP and ADP and their Significance in Calcification in Vitro (UNCLASSIFIED) Issued: August 15, 1952	DiStefano Neuman	Health and Biology