THE CHANGES IN THE BLOOD OF HUMANS CHRONICALLY EXPOSED TO LOW LEVEL GAMMA RADIATION.*

Norman P. Knowlton, Jr.

L A D C # 587

(Contribution from the Los Alamos Scientific Laboratory of the University of California, Los Alamos, New Mexico.)

*This document is based on work performed under contract No. 7405-eng-36 for the Atomic Energy Commission.

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At the Los Alamos Scientific Laboratory a number of individuals are exposed continually to small amounts of ionizing radiation. Although it is well known that small doses of radiation (0.1 to 10 r.) in single acute exposures cause no change in the peripheral blood picture, it is possible that if a large enough group of individuals with such exposures are studied over a long period of time one might obtain changes in the average blood counts which are statistically significant.

In view of this possibility, ten individuals who had daily film badge exposure records and weekly blood counts over a seventy-seven week period were selected for study. The following is a statistical study of the changes in the total white blood count and the absolute neutrophil and lymphocyte counts for these ten individuals.

A group of 24 individuals have been used as controls in this study and, although they do not have blood studies as frequently as the exposed group, the large number of individuals tends to correct this deficiency.

A. INDIVIDUALS STUDIED:

Exposed Group: These ten individuals (all males) received an average of 16.21 roentgens of gamma rays per man over a 77 week period (0.211 roentgens per week). The extremes of dosage varied from 13.06 to 24.20 roentgens. Table II shows the exact dosage received by each man. The number of blood counts done on each individual during this 77 week period varied from 37 to

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74 with an average of 64 blood counts per man. The number of counts obtained on each man are tabulated in Table IV. During this study period all 10 men carried out a similar experiment involving materials which emit gamma rays. In general, the radiation was received uniformly over the 77 week period with perhaps double the average amount during the periods between 11 and 21, and weeks 25 and 32. The radiation delivered during a week period was received in the five day work week and usually they received approximately one-half of their weekly dosage during one of the five days. One of the individuals had been working on this particular experiment for 14 months before this blood study was begun (Case 4); one for 7 months (Case 6) and one individual (Case 7), who is included in the study, began work seven weeks after the study began. The other seven individuals began working on this operation 0 to 20 weeks before the study period. None of the ten individuals had significant exposure to ionizing radiation before starting on this experiment.

Control Group: This group consists of 24 individuals (23 males and 1 female), who were picked for study specifically because their jobs involved no appreciable exposure to neutrons, beta, gamma or X-radiation. They had slight exposure to alpha radiation, but this is not considered an external hazard because of its low penetrating power in tissues (approximately 50 microns) and the alpha exposure was such that inhalation or ingestion was unlikely. These 24 individuals have had no known exposure to other toxic materials, such as dusts, organic solvent vapors, etc. The blood counts of these persons were studied over approximately the same time period as those of the exposed group. The number of blood counts done on each individual during this period varied from three to nineteen, with an average of ten blood counts per individual.

B. METHODS OF STATISTICAL STUDY:

Exposed Group: This group was studied during a period of 77 weeks from December 1946 to June 1948. This period was divided into two time periods of

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of 38 and 39 weeks. In the second, 39 week period, there was one week during which no blood examinations were made (the December holiday season 1947) and so the two periods are considered as equal in length. The analysis of the hematological data consists of an attempt to demonstrate a difference in the blood picture of the individuals between the two 38 week periods. This was done by two methods:

(1) To compare the weekly average of the blood counts of the ten men during the first and second thirty-eight week periods.

(2) To study the difference between the blood counts of each individual during the 1st and 2nd 38 week periods.

Control Group: Since there were fewer counts per individual in this group the hematological data was considered as an average of all individuals and individual changes were studied only in the case of the total white blood count. The data includes all blood studies from May 1946 to July 1948 on these individuals. This period was divided into two approximately equal periods - May 1946 to June 1947 and July 1947 to July 1948. It should be mentioned that no blood counts were excluded from the data on any of the 24 control cases or the 10 exposed individuals over the time periods studied.

C. RESULTS:

Exposed Group: Table I shows the difference in the total white blood count between the first and second 38 week time periods. In this data the average counts of all ten men for each week are considered, thereby reducing the variation of the counts from the mean in comparison to the variation present if each individual is considered separately. The mean WBC in the first 38 weeks is 7892 and for the second period 6945 - a drop of 12.0%.

Table II shows the change of the total white blood count of each of the ten

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individuals for two 26 week periods from December 1946 to May 1947 and from December 1947 to May 1947 to rule out possible seasonal effects on the blood count. The drop in total white blood count is from 7770 to 6720 cells per cubic millimeter - a drop of 13.5 per cent. The individual drops vary from 5.6 to 17.1 per cent with an average of 12.4 per cent. Table II also gives the exposure record of the ten individuals.

Table III shows the difference in the absolute neutrophil counts in the first and second time periods. The average weekly counts of all ten men were used for the statistical test. There is a drop from 4881 to 4366 neutrophils per cubic millimeter - a decrease of 10.5 per cent.

Table IV shows the changes in the absolute neutrophil counts of each individual. Nine out of ten of the men show a drop and one shows a rise of 2.5 per cent. The changes vary from minus 13.4 to plus 2.5 per cent with an average decrease of 10.4 per cent.

Table V shows the difference in the absolute lymphocyte counts in the two 38 week time periods. These figures are obtained from the average absolute lymphocyte counts of all ten individuals for each week. There is a drop from 1920 to 1611 lymphocytes per cubic millimeter of blood - a decrease of 16.1 per cent.

Table VI demonstrates the changes in the absolute lymphocyte counts of each of the ten individuals. All ten show a decrease with a range from minus 1.7 to minus 26.6 per cent. The average drop is 16.6 per cent.

Figure I shows the average weekly blood counts of the exposed group and a graphic representation of their exposure record.

<u>Control Group</u>: The analysis of the total white blood counts of the control group of 24 individuals is shown in Table VII. There are 11 decreases, 12 rises, and one count that is constant during the period studied. The change

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in the WBC varies from plus 20 to minus 28 per cent with an average of minus 1.0 per cent. The means of the average WBC for each individual show a change of minus 1.3 per cent, while the average of the sum of all counts for each time period shows a change of plus 0.4 per cent.

The comparison of the neutrophils and lymphocytes in the two time periods has been done on the basis of the average percent of these blood cells in the differential count since the total white blood count has remained approximately constant. Table VIII shows the average percent neutrophils and lymphocytes in the first and second part of the study period. It is evident that there is no drop in the percent neutrophils and a small (3.1%) drop in the per cent lymphocytes.

D. DISCUSSION:

The statistical analyses for changes in the total white blood count and the absolute neutrophil and lymphocyte counts in ten individuals exposed to approximately 0.2 roentgens of gamm rays per week over a 77 week period show highly significant decreases in all three of these blood elements. There appear to be no significant changes in the blood of twenty-four individuals who received no known exposure to beta, gamma, X-rays or neutrons. The exposed group showed a 12-13 per cent decrease in the total white blood count, a 10-11 per cent fall in the absolute neutrophil count, and a 16-17 per cent drop in the absolute lymphocyte count. The control group showed a drop of 0-1 per cent in the total white blood count, no change in the per cent neutrophils, and a decrease of 3 per cent in the per cent lymphocytes.

It would appear that this group of 10 individuals exposed to doses of gamma radiation which is considered below tolerance have had significant changes in their peripheral blood. These changes which are relatively small are only recognized when blood examinations are made frequently over a long period of time. It must be emphasized that, although no other agents which might cause these changes have been uncovered, it is quite possible that they existed. Such factors as

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the altitude at Los Alamos (7,400 feet above sea level), dietary changes, previous exposure to ionizing radiation, illnesses, unmeasured gamma radiation, and the remote possibility of inhalation or ingestion of radioactive materials have been investigated and, although they appear to be negligible, it is always a possibility that one or more of them might have been casual agents.

It is improbable, but not beyond the realm of possibility, that such dosage levels would give changes in the blood picture. With dosages as low as 20 to 30 roentgens in a single acute exposure, it is possible to show a significant decrease in the lymphocytes of the peripheral blood of a single animal. At a dosage of 30 roentgens this decrease may be twice the drop seen in this study. Although it is known that a certain amount of ionizing radiation given in an acute exposure causes a greater effect than if the same amount is gigen over a long period of time, there must be a definite relationship between the two. It is evident in animal experiments that this factor is not a one to one ratio, but that it probably takes at least ten times the amount of total radiation in chronic exposures to obtain the drops seen in single acute exposures. This is quite a reasonable phenomenon for there is constant repair during chronic irradiation, but with an acute dose the entire damage is done during a brief period before effective repair has been instigated. The ratio between dosages giving a similar depression in acute and chronic exposures would be closer to one to one if one considers what dosage in an acute exposure will give a residual depression of bone marrow or lymphoid activity months after exposure. In such a case the time for repair could be made equal to that present in a chronic exposure study.

In view of these findings, it is important that hematological and exposure data at various other laboratories be analyzed to determine whether or not these are real changes. If confirmatory results are subsequently obtained, the present concept of tolerance doses should be carefully reviewed.

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E. SUMMARY:

A group of ten individuals exposed to 0.2 roentgens of gamma radiation per week showed a significant fall in the total white blood count and the absolute neutrophil and lymphocyte counts during a 77-week period. The degree of fall would not have been predicted from experimental irradiation in animals and other unknown factors might have also been casual agents. It is suggested that hematological and exposure data in other laboratories be analyzed statistically to confirm or disprove the effect of such low dosages of ionizing radiation on humans.

TABLE I

EXPOSED GROUP

STATISTICAL ANALYSIS OF CHANGE IN WBC:

$\bar{x}$ = Average of first 38 weeks

$\bar{y}$ = Average of second 38 weeks

$\bar{x}$ =	7892	$\bar{y}$ =	6945
n_x =	38	n_y =	38
σ_x =	543	σ_y =	565

$\bar{x} - \bar{y}$ = 947 = 12.0 per cent drop

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t = 7.5

PROBABILITY = approx. 10^{-8}

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TABLE II

EXPOSED GROUP

Individual Changes in WBC

CASE NO.	WBC WEEKS 1-26	WBC WEEKS 53-77	% DROP	ROENTGENS WEEKS 1-26	ROENTGENS WEEKS 27-52	ROENTGENS WEEKS 53-77	TOTAL
1	8250	7455	10.5	6.30	6.15	1.39	13.84
2	7712	6510	15.6	7.23	9.74	7.23	24.20
3	6312	5527	12.4	5.77	5.30	2.76	13.83
4	6657	5767	13.4	7.21	4.17	2.25	13.63
5	6445	5412	16.0	8.34	8.04	3.23	19.61
6	7925	6750	14.8	9.61	4.53	4.02	18.16
7	7457	6582	11.7	4.66	7.46	3.80	15.92
8	9292	7705	17.1	5.39	4.80	2.87	13.06
9	10,702	8932	16.5	4.78	6.12	2.78	13.68
10	6945	6555	5.6	6.25	6.62	3.31	16.18
AVERAGE	7770	6720	12.4				16.21

Difference between the two means = 1050 = 13.5% drop

TABLE III

EXPOSED GROUP

STATISTICAL ANALYSIS OF CHANGE IN NEUTROPHIL COUNT

$\bar{x} = 4881$ $\bar{y} = 4366$

$n_x = 38$ $n_y = 38$

$\sigma_x = 393$ $\sigma_y = 499$

$\bar{x} - \bar{y} = 515$ = 10.5 per cent drop

$t = 4.93$

PROBABILITY = approx. 10^{-6}

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TABLE IV

EXPOSED GROUP

INDIVIDUAL CHANGES IN NEUTROPHIL COUNTS

CASE NO.	NEUTROPHILS PER MM^3, AVERAGE # Counts	Wks. 1-38	#Counts	Wks.39-77	% CHANGE
1	34	5367	28	4668	- 13.0
2	36	5131	36	4553	- 11.3
3	38	4022	26	3781	- 6.0
4	24	4212	13	3662	- 13.1
5	38	3776	36	3270	- 13.4
6	33	4276	28	3711	- 13.2
7	29	3953	36	3471	- 12.2
8	38	4844	31	4263	- 12.0
9	38	7908	34	6953	- 12.1
10	33	4668	31	4785	+ 2.5
AVERAGE		4816		4312	- 10.4

Difference between the two means = 504 = 10.5% drop

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TABLE V

EXPOSED GROUP

STATISTICAL ANALYSIS OF CHANGE IN LYMPHOCYTE COUNT

$\bar{x} = 1920$	$\bar{y} = 1611$
$n_x = 38$	$n_y = 38$
$\sigma_x = 260$	$\sigma_y = 220$

$\bar{x} - \bar{y} = 309 = 16.1\%$ drop

$t = 4.93$

PROBABILITY = approx. 10^{-7}

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TABLE VI

EXPOSED GROUP

INDIVIDUAL CHANGES IN LYMPHOCYTE COUNTS

CASE NO.	LYMPHOCYTES PER MM^3, AVERAGE Weeks 1-38	Weeks 39-77	% CHANGE
1	1749	1720	- 1.7
2	1863	1410	- 24.3
3	1664	1308	- 21.4
4	1385	1121	- 19.1
5	1727	1455	- 15.8
6	2331	1835	- 21.3
7	2019	1948	- 3.5
8	2786	2066	- 25.8
9	1706	1589	- 6.9
10	1603	1177	- 26.6
AVERAGE	1883	1563	- 16.6

Difference between the two means - 320 = 17.0% drop

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T A B L E VII
Control Group

TOTAL WHITE BLOOD COUNT

Case No.	FIRST TIME PERIOD No. Counts	Sum of WBC's	Average WBC	SECOND TIME PERIOD No. Counts	Sum of WBC's	Average WBC	% Change
11	7	46375	6625	4	27400	6850	+ 3
12	3	26550	8850	4	28000	7000	- 21
13	6	42150	7025	4	23700	5925	- 16
14	9	79425	8825	10	83500	8350	- 5
15	8	54000	6750	11	79750	7250	+ 7
16	9	74250	8250	9	73125	8125	- 2
17	6	53100	8850	6	63600	10600	+ 20
18	7	57225	8175	7	58450	8350	+ 2
19	6	43500	7250	6	36750	6125	- 16
20	5	35250	7050	4	20200	5050	- 28
21	7	47075	6725	5	37250	7450	+ 11
22	6	37950	6325	4	30400	7600	+ 20
23	3	25050	8350	4	34200	8550	+ 2
24	6	47850	7975	5	41250	8250	+ 3
25	7	42875	6125	5	27000	5400	- 12
26	1	6950	6950	2	15400	7700	+ 11
27	1	8450	8450	3	25425	8475	0
28	5	37625	7525	2	15950	7975	+ 6
29	4	35600	8900	3	24675	8225	- 8
30	4	19400	4850	3	15075	5025	+ 8
31	4	40400	10100	3	29400	9800	- 3
32	3	37125	12375	4	48100	12025	- 3
33	3	28200	9400	3	30675	10225	+ 9
34	5	51000	10200	2	17950	8975	- 12
TOTAL	125	977375	191900	113	887225	189300	- 24
		÷ 125	÷ 24		÷ 113	÷ 24	÷ 24
AVERAGE		7820	7995		7852	7887	- 1.0%

Average of All WBCs 7852 - 7820 = + 32 = 0.4%

Average of Case Averages 7887- 7995 = -108 = 1.3%

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TABLE VIII

CONTROL GROUP

PER CENT NEUTROPHILS AND LYMPHOCYTES

NEUTROPHILS:

	No. Counts	Average %	% Change
1st Year	125	58.39	0.0%
2nd Year	113	58.43	

LYMPHOCYTES:

	No. Counts	Average %	% Change
1st Year	125	29.3	- 3.1%
2nd Year	113	28.4	

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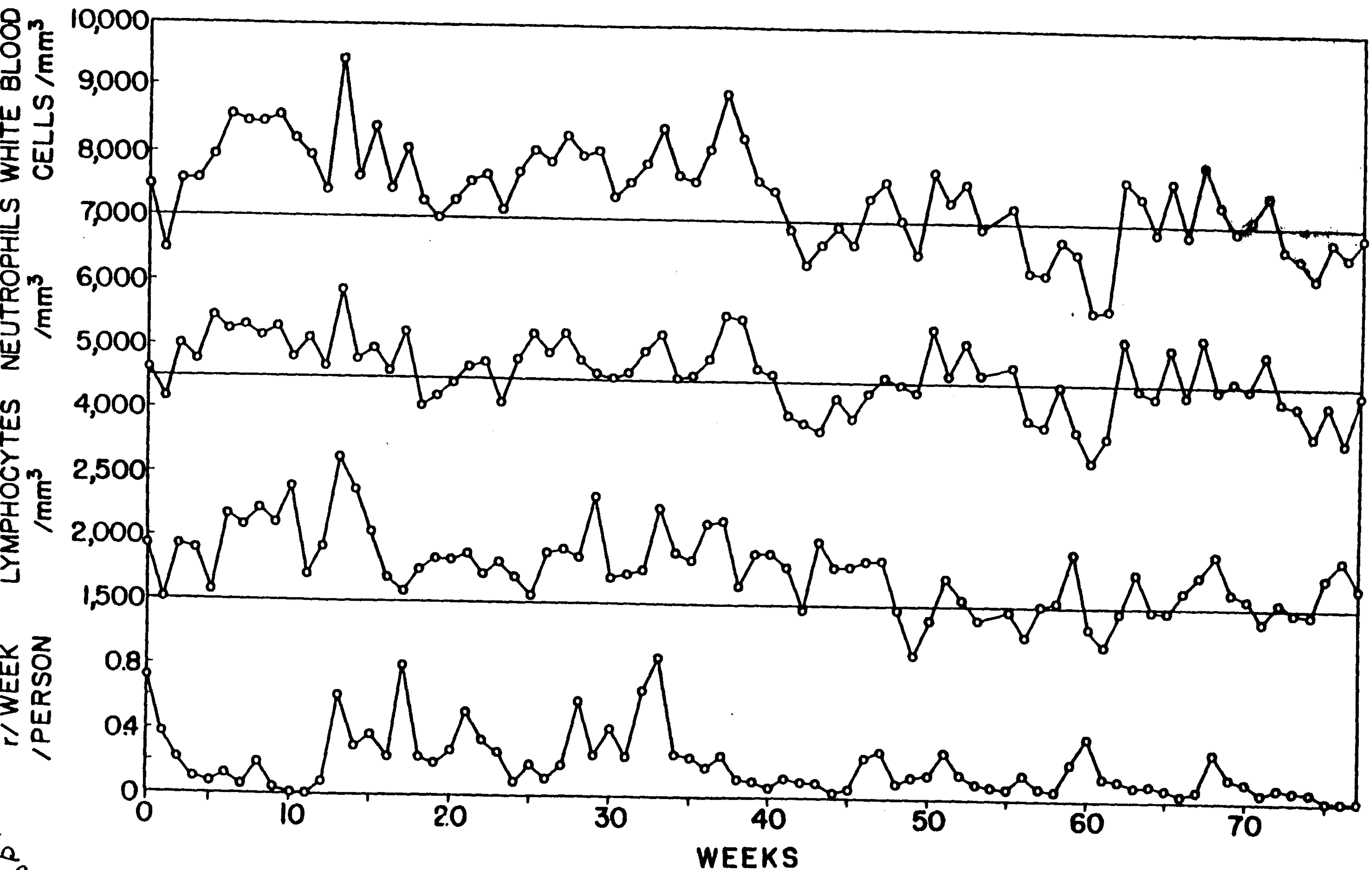
BLOOD CHANGES FOLLOWING CHRONIC EXPOSURE TO GAMMA RAYS



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June 19, 1945

To: Mr. Joseph Hoffman

From: T/4 Ralph C. Steinhardt, Jr.

Subject: Summary Report on Health Conditions in RaLa Program

It is the purpose of this report to describe the activities in the RaLa program which are related to health matters, to indicate hazards which are involved in the program, and to summarize the activities of Group A-6 in controlling and eliminating these hazards.

Part I - RaLa Chemistry Group (CM-14):

Group CM-14 is primarily engaged in the preparation of high intensity (100 - 1000 c) radio-lanthanum (La^{140}, T = 40 hrs) sources for use in the RaLa program. The method of preparation of these sources consists in separating the lanthanum, primarily by remote control procedures, from an equilibrium mixture with radio-barium (Ba^{140}, T = 300 hrs), and packaging it in a section of the sphere which is to be imploded.

Occasionally, Group CM-14 is called upon to prepare smaller sources (10 mc to 20 c) which usually are composed of the Ba-La equilibrium mixture.

Essentially, two types of hazards are encountered in these separations:

a. External gamma radiation

b. Radio-active poisons (beta-gamma) ← ?

Since the sources used are, as mentioned above, of extremely high intensity and since the material handled is in an open system, these hazards can obviously assume extremely large proportions.

A. Methods of Monitoring Radiation:

Monitoring of radiation in the Bayo Canyon chemistry building is carried out in two ways:

a. Direct monitoring of personnel

b. Monitoring of locations

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All personnel in Group CM-14 working with active material wear both Victoreen and Henson pocket chambers in order to measure external gamma dosage. These meters are measured at frequent intervals while working and the total dose is recorded daily. A factor of 1.5 is applied to all readings in order to account for low reading caused by the rarified atmosphere at this altitude. This factor was determined by actual calibration of the meters at Los Alamos by exposing the meters to a standard (N. B. S. calibrated) radium source for various lengths of time. Film badges, as supplied by T/5 Carl Hornberger of Group A-6, are also worn and are used to supplement and check dosage determinations as made by the Victoreen and Henson chambers.

At frequent intervals during the day, various significant locations within the chemistry building are monitored with the Victoreen survey meter to determine the external gamma radiation level at these points. Blackboards at these points are then used to post the "safe working time" (time required to receive 0.1 r).

Several air counts have been made in the past in order to determine the degree of air-born contamination. None of these counts has ever exceeded the tolerance limit of 160 c/m per liter.

As a means of warning all personnel within the building and in the vicinity of the building when the radiation level exceeds the usual safe working level, an air ionization chamber is located within two meters of the operations location. This meter is connected to a circuit which automatically activates an alarm and warning lights when the radiation level exceeds a predetermined level (usually 2 r/hr. at one meter from the operations location.) Furthermore, this circuit is connected to a recording milliammeter which is used to follow the various changes which occur in the radiation level. Although it has been shown (see appendix A) that no correlation can be drawn between the meter readings and the radiation level in any part of the building except in the vicinity of the chamber, the recording milliammeter has proved invaluable in the following respects:

a. At least a qualitative record of the radiation level is maintained at all times.

b. By observing trends on the recording, dangerous levels can be predicted before they occur.

c. Mechanical and chemical difficulties can sometimes be traced by ananalysis of the recording.

B. Methods of Personnel Protection:

The various methods of personnel protection are logically divided into two basic procedures:

a. Direct personnel protection

b. Personnel protection by equipment and procedure revision.

Direct personal protection from external gamma radiation is accomplished by a so-called "dose rationing system." Since the total group dose often averages as high as 3-4 r/day, it has been found necessary to distribute this dose as equitably as possible between all the members of the group. This is accomplished by pre-assigning jobs down to the minutest detail. In this scheduling of operations the following factors are taken into consideration:

a. Probable dose which will be received

b. Previous exposure of person involved

c. Experience of person with particular job

d. Blood count history of person involved

During operations, one person is given the job of making certain that the schedule is adhered to. In the event that emergency operations are necessary, he and the A-6 representative determine any revisions which are to be made in the schedule. Jobs are assigned by number and the numbers are rotated between the various members of the group so that a more even distribution is possible.

Protection of personnel from radio-active poisons is accomplished by a system of contamination control which is designed to prevent spread of contamination from one part of the building to another and to prevent personal contamination. The building itself is divided into three sections:

a. Highly contaminated (working area)

b. Lightly contaminated (hall, workshop, contaminateddressing rooms, and contaminated office.

c. Uncontaminated (washrooms, uncontaminated dressing rooms, clothing storage rooms, and lunchroom)

Spread of contamination from one portion of the building to another is prevented by isolation of the working area from the hallway by a glass door which is kept closed during operations and by separation of the entire uncontaminated portion of the building by means of an air-lock system. Protective clothing is always worn in the contaminated section of the building and is completely changed to uncontaminated clothing when going through the air-locks to the uncontaminated section. This clothing is changed frequently to prevent the individual from becoming contaminated and all contaminated clothing is stored in a special isolated room within the contaminated section. Contaminated clothing is allowed to decay for about a month before being laundered. A Geiger-Muller circuit has been installed in the washrooms in order to check personal and clothing contamination.

Indirect protection of personnel by revision of procedures and equipment has proved to be extremely effective. Re-design of filter gadgets, in order to eliminate many difficulties which were formerly encountered during source preparation and during decontamination, has resulted in a substantial decrease in dosage. A large number of these filter gadgets have been procured in order that they may be allowed to decay and thus eliminate the decontamination of highly radio-active apparatus.

The decontamination procedure itself has also been revised. A special decontamination pit, complete with water outlet and hand crane, has been put into use within the last month. Through the use of this pit, doses received during decontamination procedures have been considerably reduced.

A high- power telescope, first put into use on May 22, 1945, has almost completely eliminated the necessity for observers close to the point of operation. It has previously been necessary to have an observer within four feet of the point of operation during certain parts of the separation procedure. Frequently, large doses were accumulated by the necessity for this close observation.

Determination of the liquid level formerly was made by personal visual observation by several members of the group at frequent intervals during the separation procedure. However, a remote control liquid level indicator, placed into use during the week of May 14th has made it possible to determine the liquid level from a position about twenty feet from the point of operation. The accuracy of determination has also been very greatly increased.

The control panel and material handling method has been considerably revised and simplified, primarily by adopting a single-pressure-vacuum tube to replace the three-tube system in operation up to the beginning of May. This has resulted in increased efficiency and ease in handling material. Fewer emergency operations have become necessary and, thus, dosage has been decreased.

The chemical separation process has also been considerably revised. Originally, a single step phosphate separation was used. However, the unduly long filtration times (12-36 hrs.) resulted in large doses. During the month of March, 1945, considerable research was carried out to eliminate the difficulties which were inherent in the phosphate process. The result was a two-step hydroxide-oxalate process which reduced filtration times down to 4 - 6 hours. Although the adoption of the hydroxide-oxalate process did not directly result in dose reduction, it was felt that this was due primarily to the increase in the activity of the sources handled. On May 22nd, a two-step hydroxide-fluo-oxalate process was put into use with a view toward eliminating several difficulties which were inherent in the hydroxide-oxalate process.

C. Active Problems:

During the period a Geiger-Muller recording meter was in operation in the vicinity of the control panel. It was the purpose of this meter to provide a continuous record of the gamma level at this location. However, four difficulties have been noted regarding the use of this meter:

a. Large zero drift

b. Frequent spurious readings

c. High inertia

d. Extremely narrow range

It is expected that a more adequate method for continuously recording the radiation level in the vicinity of the control panel will soon be in operation

Hand counters which were supplied to us by Dick Watts' section proved to be inadequate for the following reasons:

a. High inertia

b. Difficulty of measuring beta-gamma hand contamination in the presence of a high external radiation density.

A lead-shielded aluminum-wall-chamber has been procured and has been placed in operation. The chamber and its housing is protected from contamination by means of a replaceable cellophane membrane. Difficulty is being encountered due to the instability of the instrument. However, it is felt that frequent recalibration will make this negligible.

The need for a continuous recording differential air counter has become increasingly great as the size of the sources handled has increased. A counter of this type has been designed and will be placed in operation as soon as it is received.

It is obvious that a power failure during operations would result in extremely dangerous conditions for the following reasons:

a. If the failure occurred during filtration, resulting in the interruption of operation of the vacuum pump, radiation induced decomposition of the oxalate would undoubtedly result in a high degree of contamination of the entire building.

b. If the failure occurred during transfer of the source from one lead shield to another, the cart upon which the lead shields are mounted could not be moved, and consequently, the radiation level in any part of the building or in the vicinity of the building would be extremely hazardous.

The installation of a stand-by generator is in the process of completion and it is expected that it will be in operation by June 18, 1945.

VI. Contamination of Inhabited Areas:

Air counts taken on Los Alamos Mesa during and after shots have never given any results other than negative. (See Rala file, Memoranda by Sgt. P. N. Levine.)

Air counts taken at the firing site by W. Miller reveal that the highest air contamination ever recorded at that point was 24 c/m per liter.

(The Los Alamos weather station has been requested to submit data on wind direction and velocities on the days when shots have been fired. As yet this information has not been received.)