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MASTER

ACCIDENTAL NUCLEAR EXCURSION

RECUPLEX OPERATION

234-5 FACILITY

APRIL 7, 1962

FINAL MEDICAL REPORT

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FROM

THE HEALTH OPERATION

GENERAL ELECTRIC

HANFORD ATOMIC PRODUCTS OPERATION

RICHLAND, WASHINGTON

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FINAL MEDICAL REPORT
ACCIDENTAL NUCLEAR EXCURSION
RECUPLEX OPERATION
234-5 FACILITY
ON 4-7-62

FROM THE HEALTH OPERATION
HANFORD ATOMIC PRODUCTS OPERATION
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A. INTRODUCTION

The April 7, 1962 criticality accident involving human exposures was the first to have occurred in any production facility at Hanford. The accidental nuclear excursion did not result in any mechanical damage or spread of contamination. Three employees of the General Electric Company received over-exposure to gamma and neutron radiation. None were fatally exposed and in each case the over-exposure was recognized promptly.

Following an initial period of medical observation and testing, the men were released to work. They continued to be followed clinically. Clinical studies performed were hematological procedures including leukocyte chromosome aberrations, morphologically aberrant blood cells, bone marrow evaluations, blood chemistry determinations, amino acid excretion studies, seminal fluid, urinary gonadotropins and estrogen excretion studies, testicular biopsies and crystalline lens examinations.

These studies, along with a brief description of the accident and of the dosimetry, are summarized in this report by those participating in the studies. In view of the dose ranges received in these cases, both the negative and positive findings are considered to be of unusual interest due to the lack of knowledge of effects following human exposures at these levels. The three cases were (H. A.) referred to in this report as employee #1, (F. L.) as employee #17, and (J. W.) as employee #23.

The individual contribution of the great majority of persons participating in the care and study of these cases is not acknowledged here because of their large number. However, their cooperation and contributions in conjunction with those of the authors

and consultants were essential to the complete investigation of these cases. Special acknowledgement must be given to our consultants, G. A. Andrews, M.D. of the Oak Ridge Institute of Nuclear Studies, M. L. Ingram, M.D. of the University of Rochester, C. C. Lushbaugh, M.D. of the Los Alamos Scientific Laboratory and C. A. Paulsen, M.D. of the University of Washington who saw these cases soon after the exposures. Special acknowledgement must also be given to the exposed individuals who contributed so greatly by their splendid cooperation and understanding.

P. A. Fuqua, M.D.
Occupational Health Operation
Hanford Atomic Products Operation
Richland, Washington

DOSIMETRY INVESTIGATIONS OF THE
RECUPLEX CRITICALITY ACCIDENT

Hanford Laboratories*

INTRODUCTION

At 10:59 AM (PST), Saturday, April 7, 1962, a criticality accident occurred in a plutonium waste chemical recovery facility at the Hanford Atomic Products Operation, operated for the Atomic Energy Commission by the General Electric Company. Four men were hospitalized but were released after medical observation and after estimates of the radiation doses received were available. This report describes the dosimetry investigation that was made following the accident. This investigation was facilitated by the fact that all employees affected had personnel dosimeters in their possession when the incident occurred. The interpretation of the data supplied by these dosimeters was supplemented by information gathered by techniques that were developed in connection with other accidents. Below, the available information is first presented and then applied in a discussion of the dosimetry of the people involved in the accident.

DESCRIPTION OF THE ACCIDENT

The accident occurred in a facility known as Recuplex within a building known as the 234-5 Building. When the accident occurred, there were twenty-two persons in the 234-5 Building. The criticality alarm siren started almost at once (several people reported that air-proportional alpha contamination monitors broke down slightly before the siren sounded). All persons

* This report was prepared by a committee consisting of C. C. Gamertsfelder, H. V. Larson, J. M. Nielsen, W. C. Roesch (Chairman), and E. C. Watson. It reports the work of a number of people at Hanford.

in the 234-5 Building evacuated to a gate house (2701-Z) about a hundred yards from 234-5 and then took shelter behind another building (2704-Z) when the former area was found to have an exposure rate of about 200 mr/hour. Within five to ten minutes they had evacuated these areas in the evacuation bus or by private car. Two patrolmen, stationed in the gate house at the time of the excursion, increased the total number of evacuees to twenty-four.

The evacuees went to the first aid building for the area (except for one who went to the area badge house and was directed to first aid). By this time the employees who had been in the Recuplex area and had seen the Cerenkov radiation flash were known; however, all employees were given a "Quick Sort" examination to determine who had been exposed to significant fast neutron doses¹⁾. The counting rate of a Geiger counter held at their abdomen was observed while the person bent over around the counter. Only those employees who had been in the Recuplex area gave significant readings.

Contamination surveys of the evacuees were also made while they were at the first aid building. No contamination was found. Their personnel dosimeters were collected for examination. Personal effects were examined for radioactivity and then sent in for laboratory study. The first blood and hair samples and excreta collections were made.

After examination and treatment at Kadlec Hospital, four persons, including the three most highly exposed, were sent to the Hanford Whole Body Counter for examination. The next day all but one of the remaining evacuees were also examined at the Counter; the last man was examined the following day. Whole body counts and blood and excreta collection were repeated on the most highly exposed persons until no radioactivity of interest was detectable.

Information was obtained immediately from each employee to establish where he had been when the criticality alarm sounded and how he left the building. Detailed personal interviews were made during the following week. All but five people in the 234-5 Building evacuated immediately upon hearing the siren; all but one had left within about two minutes; the last man was out within four minutes. The routes each one followed in leaving the building are shown in Figures 1 and 2.

Information for the three most highly exposed persons was made as detailed as their recollections would allow. Figure 3 shows where these people were standing at the time they saw the Cerenkov radiation flash. Employee #1 was standing immediately below the critical vessel, the K-9 Tank, manipulating a valve at the face of the hood containing the tank. His body was very close to the hood wall. His eyes were about 5 feet from the center of the K-9 Tank; the parts of the trunk of his body were between 6 and 8 feet away. Employee #17 was standing about 2 feet to the side and about 5 feet behind Employee #1. There was a movable lead shield behind #1, but #17 was in full view of #1 and of the K-9 Tank. #17's eyes were about 10 feet from the center of K-9 and the trunk of his body was 10 to 11 feet away. The K-9 Tank is cylindrical with a capacity of 69 liters; it contained about 45 liters when the excursion occurred. The tank has a Pyrex wall about $3/8$ inch thick and a steel bottom plate about one inch thick. #1 and #17 were exposed to radiations coming through both the wall and the bottom. The only other materials between them and the tank were the half inch thick lucite hood walls and some plumbing inside the hood. Employee #23 was standing in front of another hood about 26 feet from the center of K-9. Most of the radiation reaching him probably came through the sides of the tank. The only materials between him and K-9 were the lucite walls of

FIGURE 1

Routes followed by employees evacuating the 234-5 building (first floor).

FIGURE 2

Routes followed by employees evacuating the 234-5 building (second floor).

FIGURE 3

Positions of employees in the Recuplex area at the time of the accident. The position of the threshold dosimeter is also shown.

the hood containing K-9 and the hood he was facing and the thin metal back of the latter.

Of the next two most highly exposed people, Employee #6 was about 30 feet from K-9 with one concrete wall about 4 inches thick and one metal partition wall in between. This employee delayed to lock up some classified documents but was outside the building in about 25 seconds. Employee #21 was about 40 feet away and was shielded by an 8 inch thick concrete wall.

Before considering the measurements made for each individual, information of general interest can be obtained from instruments that were near the scene of the accident. Two recording BF_3 counters (one for high levels, one for low) were operating at the time of the accident in an incinerator room in the 234-5 Building. The data from the chart recorders are plotted in Figure 4. They indicate an initial excursion the exact magnitude of which cannot be determined because the flux level is recorded only every 30 seconds and it may be expected to vary by orders of magnitude within such a time period. Following this initial pulse which presumably activated the criticality alarm there was a continuing nuclear reaction of a magnitude sufficient to keep the recorder off-scale for a period of about 30 minutes. After the recorder returned to on-scale readings the fissioning continued at a generally reduced rate till 36 hours after the incident began. It appears that those in a position to be most seriously exposed to the critical vessel evacuated in time to limit their exposure to only a part of the initial excursion.

A threshold detector²⁾ was located about 26 feet from the critical vessel. Its position is shown in Figure 3. At least one of the steel beams of the stairway shown in the figure was on the line-of-sight between the

FIGURE 4

Data from a recording BF_3 counter operating in the 234-5 building at the time of the accident.

vessel and the dosimeter. The metal grid floor of the mezzanine level, the stairway, and another hood at the head of the stairs provided masses of material in which radiation from K-9 could scatter and then reach the detector. These certainly influenced the relative spectra of the neutrons reaching the detector as compared to those reaching the men. For lack of other information, however, the spectrum received by the detector was used in analyzing other pertinent data. The detector was removed about 96 minutes after the accidental excursions started so it was present during the large excursion shown in Figure 4 as well as during the time the people were present.

The results obtained from analysis of the threshold detector are given in Table I. The results relative to the neutrons/cm² measured with the plutonium foil are also given. The latter is assumed to include all the neutrons above 1 Kev.

TABLE I

Threshold Detector Results

<u>Neutron Energy Band</u>	<u>n/cm²</u>	<u>Relative* n/cm²</u>	<u>Relative* Dose</u>
Thermal	1.17 x 10 ¹⁰	0.39	0.005
1--750 Kev	1.26 x 10 ¹⁰	0.42	0.25
0.75--1.5 Mev	1.05 x 10 ¹⁰	0.35	0.40
1.5--2.5 Mev	0.34 x 10 ¹⁰	0.11	0.15
>2.5 Mev	0.35 x 10 ¹⁰	0.12	0.20

*Relative to n/cm² or to dose for neutrons above 1 Kev.

The number spectrum is presented in Figure 5. For comparison several other spectra obtained with threshold detectors³⁾⁴⁾⁵⁾ and normalized in the same way are shown in Figure 6. Figure 7 shows histograms prepared from calculated spectra⁶⁾; since information is lost in going from the calculated spectra to

FIGURE 5

Spectrum measured with threshold detector during recuplex accident.

FIGURE 6

Experimental spectra measured with threshold detectors.

FIGURE 7

Theoretical spectra (histograms) calculated for threshold detectors.

the histograms, the original normalized spectra are given in Figure 8. There is not close agreement between the present spectrum and any of the others, but the general features are the same and the differences are of the sort to be expected if the present results include the effects of a significant number of scattered, and hence lower energy, neutrons. Table I also contains the dose spectrum normalized to unit dose for the neutrons above 1 Kev.

The threshold detector was calibrated and interpreted in a slightly different manner⁷⁾ from that described in the original reference²⁾. The calibration constant provided for the sulfur disk in reference 7 was increased by a factor $1.5 = 0.34/0.23$. The 0.34 is the cross section in barns of the S(n,p) reaction at 4.2 Mev, the energy used in the calibration. The 0.23 is the effective cross section in barns for neutrons above 2.5 Mev for spectra similar in shape to fission spectra above this energy. The intermediate neutron energy spectrum was estimated from the activation in the gold and cadmium-covered gold foils in the detector. If ϕ_{th} was the thermal neutrons/cm² and if σ_{2200} is the activation cross section of gold for neutrons whose velocity is 2200 m/sec, then the difference in activity of the two foils is proportional to $\frac{1}{2}\sqrt{\pi}\sigma_{2200}\phi_{th}$. If the intermediate neutron flux is assumed to be given by $k\phi_{Pu}/E$, where E is the neutron energy, k is a constant, and ϕ_{Pu} the flux measured by the shielded plutonium foil, then the activation of the cadmium covered foil is proportional to

$$k \phi_{Pu} \int \sigma_{act} (dE/E)$$

where the integral is over the activation cross section of gold. Measured foil activities of 1.6 and 1.0×10^6 disintegrations/min, Hughes⁸⁾ values of the cross sections, and flux ratios from Table I give $k = 0.042$. This is shown as a dashed line in Figure 5 and is in good agreement with the spectrum determined with the threshold foils.

FIGURE 8

Theoretical spectra from which the histograms of Fig. 7 were prepared.

PERSONNEL DOSIMETERS

Each of the persons near the critical vessel* at the time of the accident was wearing his Hanford Film Badge Dosimeter⁹⁾. The dosimeters had last been exchanged 15 days before the accident; therefore, particularly for the smaller doses, a significant part of the darkening of the film may have been produced during employment prior to the accident.

The exposures of Employees #1, #17, and #23 were so great that the developed sensitive (508) film from their dosimeters was too dark to permit optical density measurements. The insensitive (1290) film from their dosimeters was used to obtain their doses. Because of slow neutron activation of the aluminum and silver absorbers in the dosimeters, there was additional darkening of the areas of the dosimeter covered by them so the usual interpretation methods could not be used. The doses were determined from the densities of the unshielded portion of the dosimeter (the open window). There is an uncertainty in doing this¹⁰⁾ because during both exposure and calibration the film is affected by secondary electrons produced by the photons in the environment of the dosimeter as well as in the material of the dosimeter itself. In the present case the dose determined from the open window could have been as much as 15 percent too low because of this effect. The dosimeter contains a lead strip in which the payroll number and other information is punched. For the films in question there was enough unused area under the lead tape to take a densitometer reading. These readings were compared with similar readings on the calibration films; they gave dose estimates that confirmed those from the open window readings. In making this comparison it is assumed that there is no appreciable slow neutron

*Two patrolmen stationed in the gate house received negligible doses and are not considered further in this report.

activation of the lead tapes and no effect due to different photon spectra.

Some of the darkening of these films must have been due to neutron activation of the materials in the emulsion. It has been reported¹¹⁾ that 0.13 rad of thermal neutrons or about 40 rads of fast neutrons (first collision dose) would produce the same darkening of 1290 film as 1 r of Co-60 gamma rays. For example, if the exposure of Employee #1 was 25 rads of fast neutrons plus 0.5 rad of thermal neutrons, the darkening predicted would be equivalent to 4.5 r of gamma radiation. This is 7 per cent of the dose measured as described above.

The dosimeters of the other people in the 234-5 Building were, where necessary, read by these same methods but with the 508 film. The results of all the film badge dosimeter measurements are given in Table II. No corrections have been made for the neutron darkening just mentioned.

TABLE II

Personnel Dosimeter Results (All Exposures in Roentgens)				
<u>Employee</u>	<u>508</u>	<u>1290</u>	<u>Neutron</u>	<u>Finger</u>
#	<u>Film</u>	<u>Film</u>	<u>Film</u>	<u>Ring</u>
1		63		80
2	0.03			
3	0.12			
4	0.15			
5	0.02			
6	0.98			
7	0.04			
8	0.10			
9	0.05			
10	0.06			
11	0.07			
12	0.20			
13	0.13			
14	0.70			
15	0.20			
16	0.1			
17		23		
18	0.40			
21	1.0			
22	0.05			
23		13	10	5.7
24	0.02			

Employees #21 and #23 were wearing neutron film badge dosimeters¹²⁾.

In each case the nuclear track plate was so darkened by the photon exposure that recoil tracks could not be identified. In the case of #23, approximate readings of the 508 film in the dosimeter could be made. They indicate a gamma ray dose of about 10 r, in agreement with his regular dosimeter, and about 3.5×10^9 neutrons/cm² of thermal neutrons.

Employees #1 and #23 were wearing film ring dosimeters. These indicated doses of 80 and 5.7 r, respectively.

Two additional studies were made with the personnel dosimeters of Employees #1, #17, and #23. The very dark 508 films were exposed to slow neutrons and measurements of the activation of the developed silver used as a measurement of the gamma ray dose received¹³⁾¹⁴⁾. The activation of the films was done in the large moderator used for producing slow neutron fluxes with the Van de Graaff accelerator¹⁵⁾. The radioactivity was easily measurable¹⁶⁾, but it was found that the three films were at or very near the first maximum of the curve of activity versus dose for the calibration film¹⁷⁾. It was not possible to get accurate dose estimates. The same slow neutron facility was used to estimate the neutron flux that had produced the excess darkening on the 1290 film behind the silver shields. Fresh films were exposed to gamma ray doses in the range of those to which the people were exposed and then exposed to slow neutrons until the total flux producing the same density pattern as on the personnel film was found. The neutron fluxes found in this way were decreased by a factor 0.79 to allow for the fact that part of the activation during the accident was due to intermediate energy neutrons. The factor was calculated from the gold foil activities in the threshold detector and the thermal neutron cross sections

and resonance integrals of gold and silver⁸⁾. The thermal neutron fields estimated by this method are given in Table III.

TABLE III
Thermal Neutron Estimates
From Film Badges

<u>Employee</u>	<u>Thermal Neutrons/cm²</u>	<u>Estimated Uncertainty</u>
# 1	2.3×10^{10}	10%
#17	6.5×10^9	50%
#23	3.1×10^9	200%

WHOLE BODY COUNTING

The occupants of the 234-5 Building at the time of the accident were counted in the Hanford Whole Body Counter¹⁸⁾. The measured values of Na-24 activity, corrected for decay since the time of the accident, and the individual's weights are given in Table IV. No correction was made for Na-24 that might have been eliminated before the counting took place; it is estimated that only a few percent was missed in this way for those counted immediately. The quotient of the number of microcuries by the body weight in kilograms was multiplied by 215 rad-kg/ μ c to obtain the first collision dose to the person.

The factor 215 rad-kg/ μ c was obtained by averaging the following two experimental values. Measurements¹⁹⁾ with a burro at the mock-up of the Oak Ridge criticality accident gave 204 rad-kg/ μ c. An experiment with solutions of sodium salts in bottles at the Godiva II reactor gave 226 rad-kg/ μ c²⁰⁾.

Recently the dosimetry investigation of the Vinca critical accident was reported⁵⁾ for which an average factor of 81 rad-k_g/μc was used (neglecting corrections for the weights of the individual persons). The difference between this figure and those above is due to the presence of a very large proportion of thermal neutrons near the Vinca reactor. If the threshold detector measurements reported for that reactor and those reported above for the present criticality accident are used to estimate the neutron first collision dose per unit Na-24 activation²¹⁾, the rad-k_g/μc factor for the Hanford accident is about 2.3 times that for the Vinca, i.e., about 190 rad-k_g/μc. This is satisfactorily close to the value used above. Although, as remarked above, the threshold detector measurements for the Hanford accident probably represent a different spectrum than that to which the employees were exposed because of attenuation and scattering, the comparison of the Vinca and Hanford spectra to estimate the above factor is not much affected by the difference.

It is estimated that the Na-24 burdens were determined to an accuracy of about 5 percent where counting data were not limited by statistics. Counting statistics became important for burdens of about 0.001 μc (before correction for decay). Those employees in whom less than 0.001 μc was detected were assigned a dose of less than 0.01 rad.

TABLE IV

Whole Body Counting Results

<u>Employee</u>	<u>μc Na-24</u>	<u>Weight kg</u>	<u>Neutron First Collision Dose--rads</u>
# 1	7.55	70.4	23
2	0.001	85.3	< 0.01
3	0.014	71.8	0.04
4	0.022	95.4	0.05
5	0.001	93.4	< 0.01
6	0.088	55.3	0.34
7	0.002	68.5	< 0.01
8	0.004	71.2	0.01
9	0.001	61.2	< 0.01
10	0.006	71.7	0.02
11	0.001	73.5	< 0.01
12	0.008	75.9	0.02
13	0.001	70.8	< 0.01
14	0.034	70.3	0.10
15	0.003	67.1	< 0.01
16	0.010	84.8	0.02
17	4.20	98.1	9.2
18	0.019	85	0.05
21	0.055	72.7	0.16
22	0.001	56.7	< 0.01
23	1.12	82.4	2.9
24	0.001	78.9	< 0.01

The presence of K-42 was noticed in those people who had large Na-24 burdens. The amounts present were consistent with estimates from abundance and cross-section data which indicate that there should be about one seventh as many microcuries of K-42 as of Na-24. Employees #1, #17, and #23 were counted several more times at the whole body counter. The Na-24 was observed to disappear with the expected 15 hour half-life. Each of these three men was found to have had some Au-198 produced in fillings in his teeth. In the case of #17 the gold was in bridge-work that could be removed. This made it possible to count him with the P-32 counter²²⁾. After the original report on the counter, the detector was moved to a counting position over the head rather than over the chest in order to reduce interference by other isotopes;

the presence of radioactive gold fillings would have prevented such measurements. The first count for P-32 was made on #17 ten days after the accident. The P-32 was easily detected. The counting rate due to the P-32 decreased exponentially with a 14.5 day half-life (i.e., the radioactive decay half-life) rather than the 8 to 10 day half-life observed for subjects who receive P-32 intravenously. This indicated that most of the P-32 being observed was formed in the relatively tightly bound phosphorous, probably that in the skull, rather than that more mobile portion in which the intravenously injected P-32 appears. Thus the calibration of the counter, which was done with intravenously injected subjects, was not applicable; if applied anyway, the calibration would have indicated two to three times as much P-32 as predicted from the activity of the Na-24 present.

Na-24 IN BLOOD

Two 2 cm³ blood samples each for Employees #1, #17, and #23 were counted for Na-24. The first samples were counted on a three inch well crystal scintillation counter. They had coagulated before they could be counted. The second set of samples was treated with heparin to prevent coagulation. They were counted for 30 minutes on a total absorption gamma-ray spectrometer²³⁾. The results of the two counts, corrected for decay from the time of the accident, are given in Table V. The agreement is considered reasonably good.

The activity density of the Na-24 in the whole blood was converted to neutron first collision dose by multiplying by the factor 1.65×10^5 rad-cm³/μc. This is the ratio of first collision dose to blood activity found in the Oak Ridge burro experiment¹⁹⁾.

If the sodium in the whole body and in the blood are equally irradiated by slow neutrons or if there is rapid equilibration of the sodium throughout all compartments in the body, then this factor should be related to the factor used above with the whole body counter data. The ratio of uc/kg of Na-24 in the body to uc/cm³ in the blood should equal the ratio of the density of sodium in the body (105 g/70 kg for the standard man²⁴) to that in the blood (1.91 x 10⁻³ g/cm³ ²⁵): (1.91 x 10⁻³ x 70)/105 = 1.27 x 10⁻³. 1.65 x 10⁵ x 1.27 x 10⁻³ = 210 rad-kg/uc, in good agreement with the figure chosen above for the whole body counting. This comparison is significant because the blood and whole body activities of the burro were determined in different ways. A similar comparison can be made using the data obtained after the critical accident at Los Alamos. The fatally exposed employee was found to have 0.00531 uc/cm³ of Na-24 in whole blood and 293 uc in his whole body, which weighed 71.5 kg²⁶). (0.00531 x 71.5)/293 = 1.30 x 10⁻³ in good agreement with the above value. This latter value is particularly significant because the neutron dose distribution in the man's body was very non-uniform. The agreement between the two results indicates that the sodium had been able to effectively equilibrate throughout the body.

TABLE V
Na-24 in Blood
(Two Samples From Each Employee)

<u>Employee</u>	<u>Na-24</u> <u>uc/cm³ blood</u>	<u>Neutron First</u> <u>Collision Dose</u> <u>rads</u>
# 1	1.5 x 10 ⁻⁴	25 $\nless$ 2.5
	1.8 x 10 ⁻⁴	30 $\nless$ 3.0
# 17	8.8 x 10 ⁻⁵	15 $\nless$ 2.2
	7.3 x 10 ⁻⁵	12 $\nless$ 1.2
# 23	2.0 x 10 ⁻⁵	4.0 $\nless$ 1.2
	2.1 x 10 ⁻⁵	3.4 $\nless$ 0.8

Na-24 IN EXCRETA

The first urine samples from Employees #1, #17, and #23 were counted on a three inch well crystal scintillation counter. These measurements were repeated and all later samples were measured on a five inch well crystal scintillation counter²⁷⁾. Sample size varied from 2 to 500 cm³ and counting time from 5 to 30 minutes depending on the activity of the sample. The results, corrected for decay from the time of the accident, are given in Table VI. The na-24 activity found in feces was negligible.

TABLE VI

Na-24 in Urine

<u>Employee</u>	<u>Date</u>	<u>Average Dis./min-ml</u>	<u>Total ml</u>	<u>Total Dis./min</u>
#1	4/7/62	174.1	1685	2.93 x 10 ⁵
	4/8/62	210.9	3800	8.01 x 10 ⁵
	4/9/62	229.7	4340	9.97 x 10 ⁵
	4/10/62	142.0	2500	3.55 x 10 ⁵
	4/11-12/62	77.8	4900	3.81 x 10 ⁵
	4/12-13/62	135.0	4280	5.78 x 10 ⁵
#17	4/7/62	339.5	580	1.97 x 10 ⁵
	4/8/62	310.7	3020	9.38 x 10 ⁵
	4/9/62	185.5	3200	5.94 x 10 ⁵
	4/10/62	120.0	3300	3.96 x 10 ⁵
	4/11-12/62	136.8	3225	4.41 x 10 ⁵
	4/12-13/62	135.0	1950	2.63 x 10 ⁵
#23	4/7/62	66.7	1415	0.94 x 10 ⁵
	4/8/62	44.3	3935	1.74 x 10 ⁵
	4/9/62	27.8	3850	1.07 x 10 ⁵
	4/12-13/62	40.5	3050	1.24 x 10 ⁵

P-32 IN HAIR

Samples of hair were taken from Employees #1, #17, and #23 from several locations on their bodies. The P-32 was separated from the hair²⁸⁾ and counted in a low background proportional counter. The sulfur content was determined for several samples by a spectrometric method and found to agree

with the results of Peterson, et. al.²⁹⁾ so their value, 47.7 mg sulfur per gram of hair, was then assumed for all calculations. The results are listed in Table VII. The time integral of the flux density of neutrons having energies greater than 2.5 Mev and the first collision dose due to these neutrons were calculated using the formula given by Peterson, et. al. Their formula gives factors of 6.44×10^6 neutrons/cm² per dis./min-g sulfur and 0.0246 rads per dis./min-g sulfur.

TABLE VII

P-32 in Hair

<u>Employee</u>	<u>Hair Sample</u>		<u>dis/min-g</u>	<u>Neutrons Above 2.5 Mev</u>	
	<u>Type</u>	<u>cm from Top of Head</u>		<u>Neutrons/cm²</u>	<u>First Collision Dose</u>
#1	Head,	0		2.4×10^9	9.3
	Posterior				
	Chest	33-77		2.9×10^9	11
	Pubic	87		1.8×10^9	6.9
	Leg	135-161		1.5×10^9	5.6
	(Fingernail				
	Left		24		
	Right)		37		
	(Toenails)		11		
#17	Chest	43-73		1.4×10^9	5.2
	Pubic	94		7.7×10^8	2.9
	Back	34		9.1×10^8	3.5
#23	Head	0		4.3×10^8	1.6
	Pubic	93		3.8×10^8	1.4

RADIOACTIVITY OF OTHER OBJECTS

A variety of other objects was collected from the three principals and measured for radioactivity in a five inch well crystal scintillation counter²⁷⁾. Later these same objects were activated with slow neutrons in the large moderator in the same way as in the study of the film badges described above¹⁶⁾. The neutron fluxes in the large moderator that produced the same activity as in the accident were corrected to allow for the intermediate energy neutron activation during the accident. The effective resonance integral for the gold in the eye frames of Employee #17's glasses was found to be 581 barns (compared to 1300 for thin foils⁸⁾) by the cadmium ratio. Otherwise, the thin foil values were used. The thermal neutron fluxes estimated in this way are listed in Table VIII.

RBE DOSE

RBE dose (in rem) is the product of the absorbed dose in rads by an agreed RBE multiplier. Its function is to provide a common, additive measurement of all radiations that expresses the radiation protection hazard involved in exposures to the radiations. NBS Handbook 59³⁰⁾ recommends RBE values which are dependent upon the linear energy transfer to tissue by the charged particles generated by the radiation. These values of RBE are to be used in assessing hazards due to long continued low level irradiation. The value usually accepted for neutron irradiation is 10, but this is not applicable for the acute exposures described in this report. Indeed, one of the reasons for the careful analysis of the data provided by such accidents is to provide RBE's that might be suitable. For this reason none of the doses given in this report has been converted to an RBE dose. For purposes of administrative recording of whole body radiation exposures

TABLE VIII

Radioactivity of Other Objects

<u>Employee</u>	<u>Item</u>	<u>Location cm from Top of Head</u>	<u>Radioisotope Measured</u>	<u>Large Moderator Neutrons/cm²</u>	<u>Thermal Neutrons/cm²</u>
# 1	Silver shield from	~ 40	Cu-64	1.49×10^{10}	1.34×10^{10}
	film badge				
	Ball point pen, minus	45	Cu-64	1.37×10^{10}	1.23×10^{10}
	tip				
	Tip of ball point pen	45	Cu-64	0.99×10^{10}	0.89×10^{10}
# 17	Silver shield from	~ 40	Cu-64	0.73×10^{10}	0.66×10^{10}
	film badge				
	Nickel	100	Mn-56	0.48×10^{10}	0.42×10^{10}
	Belt buckle	73	Cu-64	0.42×10^{10}	0.38×10^{10}
	Lens of eye glasses	12	Na-24	0.63×10^{10}	0.59×10^{10}
	Frame of eye glasses	12	Au-198	1.07×10^{10}	
# 23	Silver shield from	~ 47	Cu-64	0.22×10^{10}	0.22×10^{10}
	film badge				
	Pencil clip	47	Mn-56	0.18×10^{10}	0.16×10^{10}
	Button	34	Cu-64	0.19×10^{10}	0.17×10^{10}
	Watch band	(86)	Mn-56	0.16×10^{10}	0.14×10^{10}

of the employees involved an RBE factor of 2 for acute neutron exposure was assumed. This is largely based on extrapolation from experimental animal exposures and data from previous accidental exposures of humans¹⁹⁾. The doses to the eyes were recorded with an assumed RBE of 10^{31} .

CONCLUSIONS AND SUMMARY

Our primary sources of information concerning the exposure of individuals during the accident are their personnel dosimeters for the gamma rays and the whole body counts and blood activation for the neutrons. The dosimeters constitute practically point detectors. The backscattering for gamma rays is small so the dosimeters indicate the first collision photon dose where they were worn. The activation of Na-23 takes place throughout the body. The experiments performed to relate Na-23 activation to neutron dose, however, have related the activation to the first collision dose. Consequently, these primary sources give us information on the first collision dose. It has been customary to report first collision doses in accidents such as the present one in the belief that greater complexity would hinder rather than help correlation of observed biological effects with physical dose measurements.

Employees #1 and #17 were close enough to the critical vessel that the actual absorbed dose must have been fairly non-uniform within their bodies. The relation of Na-23 activation to first collision dose may not, therefore, be quite the same as in the calibration experiments. The relationship is even more complicated by the fact that we do not know the exact course of events following the first critical excursion. During this period the men were moving rapidly and their position and orientation relative to the critical vessel were constantly changing. We do not know if there were

any other critical excursions during this period or whether they received practically all their dose during the first one. The only indication we have that these subsequent motions were not very important is the value of the ratio of the gamma ray to the neutron dose. This ratio was between 2 and 3 for the two men close to the critical vessel. This is in good agreement with values observed in similar circumstances⁶⁾. Their motions and the possible later excursions would affect their personnel dosimeter readings even more than the Na-23 activation because of the changing shielding of the dosimeters by the body. The fact that they do not appear to have had a substantial effect on the ratio suggests that most of the dose came during one critical excursion while they were nearly stationary.

The doses determined from sulfur activation in hair were about one half those obtained from Na-23 activation. They should, of course, be lower because they are the doses for only those neutrons above 2.5 Mev. The threshold detector, Table I, would indicate that only 20 percent of the dose should come from such neutrons. The application of the latter data are suspect because, as already discussed, the detector may not have been exposed to exactly the same spectrum as the people. On the other hand, some of the difference may be due to a difference in the relation between first collision dose and Na-23 activation in the calibration experiments and in the present accident because of greater non-uniformity of the dose distribution during the accident. The neutrons/cm² detected by sulfur activation can also be compared with the number of thermal neutrons. There are several measurements of the two on exposed people that are for nearly the same parts of the body. A ratio of neutrons/cm² above the sulfur threshold to thermal neutrons/cm² of about 0.2 was obtained where such

measurements were made. The threshold detector gave 0.3. Probably this is as close agreement as we can expect. The scattering and absorbing materials in a human body are enough different from those near the detector to produce this much difference in the thermal flux density. (It will be noted that these ratios differ by just the factor of 1.5 by which the calibration of the threshold detector was changed to allow for the energy at which the calibration was made. Some of the difference may be due to error in this factor. The calibration was performed at 4.2 Mev. The $S(n,p)$ cross section has a sharp maximum at this energy. A small error in energy would have resulted in decreasing the factor.)

It appears that there may be some uncertainty in the doses determined from Na-23 activation, but that it is probably not very great. Employee #1 received the highest exposure. The first collision doses were 23-30 rads from fast neutrons and 63 roentgens in the central region of his body. The dose due to thermal neutrons was negligible in comparison. The P-32 measurements in hair suggest a variation by a factor of at least two for the doses in different parts of the body. This is compatible with variation as the inverse square of the distance from the center of the critical vessel. The neutron dose to the eyes is considered to be of importance in an exposure such as this because of the possibility of cataract formation. Inverse square variation suggests a dose of 42-54 rads of neutrons for his eyes.

Employee #17 received the next highest exposure. They were 9-12 rads from neutrons and 23 roentgens in the central region of the body. These doses are related to those received by #1 by the inverse square of the distance from the center of the critical vessel. By the inverse square law the neutron dose to his eyes must have been 11-14 rads.

Employee #23 received about 3 rads from neutrons and 13 roentgens and these must have been pretty uniform over his body. Employees #6 and #21 each received about 1 roentgen and 0.34 and 0.16 rads from neutrons, respectively. The rest of the people in the 234-5 Building at the time of the accident received considerably less exposure. The doses they did receive can be taken to be those given by their personnel dosimeters, Table II, and their whole body counts, Table IV.

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CLINICAL NOTES

P. A. Fuqua, M. D.
Occupational Health Operation
Hanford Atomic Products Operation
Richland, Washington

4-7-62 On release of the patients by radiation monitors, the patients were taken to separate rooms in the emergency out-patient department of the hospital and examined. On completion of these examinations and further monitoring and sample collecting, they were all admitted to the hospital as bed patients in separate private rooms before 2:00 P.M. Estimated dosages in rem, Employee #1 - 110, Employee #17 - 43, Employee #23 - 19, were received at approximately 4:00 P.M. and each patient was immediately so advised by the physician assigned to his care. The clinical course of all patients thus far had confirmed the estimated dosages by the absence of any clinically significant events. The patients all ate good evening meals. They were sedated with nembutal at about 9:00 P.M. They all rested well and there were no significant developments during the night.

4-8-62 General examinations were repeated. Employee #1 had developed a temperature in the vicinity of 100°F. His fluid intake was high. He had had a nasal allergy and a low grade chronic eczema on dorsum of fingers of the right hand. Examinations of Employee #17 and Employee #23 were essentially negative. A bone marrow aspiration biopsy from each patient's sternum was taken in the early afternoon. Dr. Bender of the Oak Ridge National Laboratory was contacted and it was agreed that he would come to Richland to obtain blood samples for tissue culture and chromosome aberration studies. During the course of the evening patients were sent individually to the whole body counter for Na²⁴ evaluation, and then to the office of Dr. Davis, ophthalmologist, for slit-lamp examination for free floating red cells in the anterior chamber of the eye. None were seen. Additional hair samples for P³² evaluation were taken. The clinical course continued to be excellent.

4-9-62 Dr. Bender obtained tissue cultures for chromosome studies between 7:00 and 8:00 A.M. and returned to Oak Ridge. General examinations were repeated. Employee #1 requested nose drops and his fluid intake remained high. His temperature had returned to normal. Telephone consultation was carried out by Dr. Fuqua with Dr. Joe Howland of the University of Rochester Medical School and Dr. Norwood in Chicago. Dr. Howland requested concurrence in sending out Dr. Ingram, a University of Rochester Medical School hematologist, for the purpose of definitive blood and bone marrow examination. Concurrence was given. Urine and blood chemistry studies were planned. The clinical course and daily blood counts continued to confirm estimated dosages.

4-10-62 General examinations were repeated. Employee #1's chronic eczema on dorsum of fingers of right hand was activated and there was a palpable tender epitrochlear node. Hot soaks and cortisone ointment was ordered. Employee #1 was sent to the whole body counter to better evaluate dosage being received from induced activity of a fixed gold inlaid dental bridge of upper central incisors. At Mr. Schier's request to procure two consultants to look over the overall case management, Dr. Fuqua had telephone consultations with Dr. Andrews of the Oak Ridge National Institute of Nuclear Studies, with Dr. Lushbaugh of Los Alamos, and with Dr. Norwood in Chicago. Dr. Andrews and Dr. Lushbaugh were asked to see patients in consultation and accepted. Details of laboratory studies were arranged. Dr. Fuqua also made arrangements with Dr. Paulsen, a University of Washington School of Medicine endocrinologist, to carry out endocrinological studies.

7-2-62 Employee #1 has complained of fatigue mild and intermittent described by employee as "no gas" or "no get up and go". May or may not be directly related to exposure. Sperm count has dropped from 199 million to 45 million.

Employee #17 has some mild complaints referable to fatigue. The relationship to exposure is questionable.

Employee #23. Testicular biopsy site did not primarily heal as in the other cases. Surgical excision of indurated area resulted in post-operative hemorrhage into scrotal tissues requiring hospitalization. As of 6-30-62 secondary healing of biopsy site was almost complete and there was little interference with his usual activities.

11-1-63 Since last notation blood, urine and seminal fluid specimens have been collected at appropriate intervals. Another testicular biopsy was taken from Employee #1 and Employee #23. There have been no clinical complaints considered to be of any significance. A work restriction placed on Employee #17 was as follows. "Remove for a period of 6 months from any radiation activity where there can reasonably be expected exposure in excess of one-tenth the normal occupational limit. Insofar as possible the work situation during this period should be such as not to involve the possibility of emergency exposure."

The work restriction placed on Employee #1 was as follows. "Should work where he can reasonably be expected to not receive exposure in excess of one-tenth the normal occupational limit. Insofar as possible the work situation should be such as not to involve the possibility of emergency exposure."

Individual Case Summaries

Employee #1 was admitted to Kadlec Methodist Hospital 4-7-62. He was a married white male, with three children, age 40, who stated that he had always been well. His wife was pregnant. He was obviously apprehensive when first seen. He believed that he had received a fatal exposure. His apprehensiveness, however, was very well controlled. After seeing the flash, he has described feeling an instant sensation of heat over his upper body and a dry sensation of his mouth which persisted for several hours. One high blood pressure reading was recorded prior to receiving dosage information. His fluid intake was above normal for several days. He described a heavy or tense feeling in his stomach for several hours. He was, however, able to eat his evening meal well, at about 6:00 P.M., or seven hours after the accident. He had a temperature in the vicinity of 100°F developing the next morning after the accident and persisting for about 24 hours. He experienced great relief following notification of dosage estimate about 5 hours after the accident. There was no nausea or erythema at any time. He vomited once after breakfast on the 7th day.

On the third day he experienced an activation of a chronic eczema on the dorsum of his fingers on the right hand. There was a palpable tender epitrochlear node. This subsided in about 36 hours with local treatment. He had some nasal allergy prior to the accident. He had been receiving a vaccine.

Daily blood counts were done. Blood and urine samples were collected for detailed chemical studies. On the 1st and 7th day bone marrow aspiration biopsies were made. On the 5th day a testicular biopsy was performed. The clinical and laboratory findings to date have been grossly compatible with the estimated dose and essentially within normal ranges. The fluctuations in the absolute lymphocyte counts have not been below or above the usual normal range but could be interpreted as minor variations resulting from the exposure.

A slit-lamp examination of both eyes was done and will be repeated at appropriate intervals. Follow-up sperm studies are planned at three week intervals into July and at appropriate intervals thereafter as indicated.

This employee was an extremely cooperative patient and has participated most willingly in studies being carried out.

On the 4th, 7th and 8th days, this employee was released from the hospital to his home between the hours of 1:00 and 9:00 P.M. He was discharged from the hospital on the 9th day, 4-16-62.

Employee #17 was admitted to Kadlec Methodist Hospital 4-7-62. He was a married white male, with four children, age 50, who stated that he had always been well. He saw the flash but because of the promptness of the warning signal, admitted to no apprehension, nor did he show any when first seen. There was no nausea or vomiting at any time. There was a streak of redness on his abdomen on the second day but this appeared to be due to the abrasion of his clothing.

On the second day just before lunch he experienced a very mild shock-like reaction which he described as a sudden feeling of weakness. There was no pain and he recovered rather quickly.

Daily blood counts were done. Blood and urine samples for detailed studies were collected. On the 1st and 7th day, bone marrow aspirations were made. On the 5th day, due to a hypotensive reaction, a testicular biopsy procedure had to be discontinued. No biopsy was obtained. The clinical and laboratory findings to date have compatible with the estimated dose and essentially within normal ranges.

This employee has been a very cooperative patient and has participated most willingly in studies being carried out, although he admits to some concern and some apprehensiveness about hospital procedures.

On the 4th, 7th and 8th day, he was released from the hospital to his home between the hours of 1:00 and 9:00 P.M. He was discharged from the hospital on the 9th day, 4-16-62.

Employee #23 was admitted to Kadlec Methodist Hospital 4-7-62. He was a single white male, dark complexioned, age 27, who stated that he had always been well. He experienced no nausea or vomiting. On the evening of the 4th day he developed an erythema on his face believed to have resulted from being in the sun and wind for about 45 minutes during the preceding afternoon.

Daily blood counts were done. Blood and urine samples were collected for detailed chemistry studies. On the 1st and 7th day, bone marrow aspirations were made. On the 5th day, a testicular biopsy was performed. There has been no physical or laboratory findings to date which might be attributable to radiation exposure.

This employee was a very cooperative patient and participated willingly in all studies being carried out.

On the 4th, 7th and 8th day, patient was released from the hospital to his home between the hours of 1:00 and 9:00 P.M. He was discharged from the hospital on the 9th day, 4-16-62.

Ophthalmological Examination Summary -- L. L. Davis, M. D., Ophthalmologist
Richland, Washington

4-8-62 A slit lamp examination was done to determine if there were free floating red cells in the anterior chamber.

Employee #1. Eyes were not red and there was no evidence externally of injury. The cornea was normal. No aqueous flare or red cells or leukocytes could be seen in the anterior chambers. The iris was normal in both eyes. No opacities were seen in any of the layers of the lens fibers.

Employee #17. There was no evidence externally of injury. The corneal epithelium was normal. No aqueous flare was present. No blood cells in anterior chamber. No injury to iris. No opacities were seen in any of the layers of lens fibers.

Employee #23. Eyes were not red. Cornea normal. No blood cells could be seen in the anterior chamber. The aqueous flare was questionable due to the narrow palpebral fissure. No opacities were seen in any of the lens fibers.

4-20-63

Employee #1. Vision in both eyes was 20/20. No abnormality seen on visual inspection. No opacities could be seen in the lens with the ophthalmoscope and the fundi were normal. No abnormalities which could be called pathological were seen with the slit lamp. Special attention was directed for posterior lens opacities.

Employee #17. Vision in both eyes 20/20 with correction. No abnormality seen on visual inspection. No opacities could be seen in the lens with the ophthalmoscope and the fundi were normal. No abnormalities which could be called pathological were seen with the slit lamp. Special attention was directed for posterior lens opacities.

Employee #23. Vision in both eyes was 20/30 - 1 correctable to 20/20. No abnormality seen on visual inspection. No opacities could be seen in the lens with the ophthalmoscope and the fundi were normal.

9-26-62 Employee #1 was referred for definition of complaint of loss of sharpness or blurring for vision. There was no external abnormality and fundi appeared normal. No opacities were seen on slit lamp examination. The posterior parts of the lenses were especially observed and no opacities were seen. A refraction showed one-half diopter myopia in both eyes.

10-1-63 Employee #1. Vision was right eye 20/40 and left eye 20/25. Ophthalmoscopic examination was normal. No opacities were seen in either lens, except there appeared to be one very minute one on the posterior cortex of left lens, which is not considered of significance. Visual acuity is worse in the right eye than a year ago. Patient is near-sighted but does not wear a correction.

BLOOD COUNTS AND BLOOD CHEMISTRY

Sidney Marks, M. D.
Benira C. Ritter, M. T.
Kadlec Methodist Hospital
Richland, Washington

The following hematologic procedures were employed: microhematocrit, hemoglobin, manual erythrocyte count, manual leukocyte count, differential count and platelet count (phase). Absolute neutrophil and lymphocyte counts were calculated. Blood counts were taken daily through day 4 after the event, then 3 times a week through day 27, twice a week through day 55, weekly through day 97, every other week through day 181 and every fourth week subsequently through day 365. Results of the blood counts are presented in Tables 1, 2 and 3 and in Figures 1, 2 and 3.

The only significant change in the level of a blood count was a depression in the absolute lymphocyte count of Employee #1. Values obtained in annual examinations for five years prior to the event and subsequent to 5 months after the event were predominantly in the range of 3000 to 4000. For the first several weeks after the event, his absolute lymphocyte values were predominantly between 1500 and 3000. The return to his normal range was gradual. A temporary reduction in hemoglobin, PCV and erythrocyte count values occurred in the case of Employee #23 immediately after the episode of hemorrhage at the testicular biopsy site. Irregular elevations in the neutrophil and platelet counts in the first few days after the event were considered nonspecific.

Blood chemistry results are listed in Table 4. No abnormal results were obtained.

TABLE 1

BLOOD COUNT DATA - EMPLOYEE #1								
Date	Hgb.	PCV	RBC (x 10 ⁶)	WBC (x 10 ³)	Platelets (x 10 ⁵)	Abs. Lymph. (x 10 ³)	Abs. Neut. (x 10 ³)	Reticulo- cytes (per cent)
5-1-57	13.4		5.1	10.2		3.7	7.0	
6-4-58	13.4		4.9	10.7		4.1	7.4	
7-22-59	13.1	43		8.6		3.3	5.1	
6-24-60	14.0	43		11.1		2.9	7.3	
6-30-61	14.0	39		12.1		4.0	7.6	
4-7-62 (3pm)	14.1	42	4.5	16.1		1.8	14.2	
4-7-62 (9pm)				13.2		2.9	9.6	
4-8-62	13.7	41	3.7	8.6	3.3	1.5	6.7	0.7
4-9-62	13.6	41	4.2	9.5	2.8	2.6	6.5	1.1
4-10-62	14.2	43	5.4	17.7	2.1	2.8	14.1	1.1
4-11-62	13.5	43	4.6	8.1	2.2	2.3	5.5	0.4
4-13-62	13.0	41	4.4	8.5	2.1	1.9	6.1	0.5
4-15-62	13.7	44	4.4	8.9	2.2	2.4	6.1	0.8
4-17-62	13.4	41	4.4	12.8	2.1	4.6	7.8	
4-20-62	13.5	41	4.1	9.8	2.5	1.9	7.3	1.1
4-23-62	13.8	43	4.5	9.4	2.2	2.6	6.5	1.0
4-25-62	14.1	45	4.5	11.5	2.1	3.1	8.0	1.4
4-27-62	13.9	43	4.4	9.0	2.0	3.5	4.8	0.8
4-30-62	14.2	44	4.4	7.8	2.0	2.1	5.0	0.8
5-2-62	13.4	44	4.2	9.5	1.9	3.1	6.0	0.8
5-4-62	14.0	44	4.5	9.2	1.9	3.1	5.6	0.9
5-8-62	13.9	43	4.2	8.4	2.1	2.9	5.1	0.8
5-11-62	13.5	46	4.2	8.1	2.0	2.5	5.2	0.8
5-15-62	13.7	44	4.2	10.5	2.2	4.1	6.0	0.8
5-18-62	13.8	44	4.3	10.1	2.3	3.2	6.5	
5-22-62	14.2	46	4.5	10.3	2.1	3.0	7.0	0.8
5-25-62	13.8	44	4.1	8.6	2.2	3.2	5.1	0.7
5-29-62	14.7	44	4.3	11.4	2.1	4.1	7.1	
6-1-62	14.1	44	4.1	7.6	2.0	2.4	4.9	0.7
6-8-62	13.6	39	4.1	8.9	2.0	3.4	5.1	0.7
6-15-62	13.7	41	4.5	8.2	2.0	3.1	4.7	0.8
6-22-62	13.1	41	4.1	8.3	2.0	3.6	4.3	0.8
6-29-62	12.9	41	4.1	9.6	2.0	2.8	6.2	0.9
7-6-62	14.7	46	4.3	10.0	1.9	3.0	6.7	0.7
7-13-62	12.4	41	3.8	7.5	1.9	2.7	4.5	0.7
7-27-62	13.0	44	4.1	8.6	2.0	3.3	4.7	0.7
8-10-62	14.4	43	4.2	8.3	2.0	2.7	5.3	1.0
8-27-62	15.0	45	4.5	11.2	2.0	3.0	7.5	1.0
9-7-62	13.6	43	4.0	9.6	2.0	3.7	5.4	0.7
9-21-62	13.5	43	4.0	9.8	1.8	3.4	5.9	0.8
10-5-62	14.0	42	4.3	12.1	1.9	3.5	7.9	1.0
11-2-62	14.0	43	4.2	11.2	2.0	3.8	6.9	1.1
11-30-62	13.4	43	4.1	7.5	2.2	3.5	3.7	0.9
12-28-62	13.2	44	4.4	8.8	2.0	3.0	5.2	1.0
1-25-63	14.2	45	4.4	9.4	2.0	3.5	5.3	0.4
2-21-63	14.4	44	4.5	11.8	2.0	3.7	7.4	0.5
3-22-63	14.3	44	4.4	9.7	1.9	4.4	4.8	1.1
6-26-63	13.5	39	3.8	10.5	2.0	2.9	6.7	1.0
9-30-63	13.6	41	4.1	12.4	2.1	4.2	7.2	0.8
12-27-63	12.7	40	4.4	13.6	1.7	4.6	8.0	1.1

TABLE 2

BLOOD COUNT DATA - EMPLOYEE #17

<u>Date</u>	<u>Hgb.</u>	<u>PCV</u>	<u>RBC</u> ($\times 10^6$)	<u>WBC</u> ($\times 10^3$)	<u>Platelets</u> ($\times 10^5$)	<u>Abs.</u> <u>Lymph.</u> ($\times 10^3$)	<u>Abs.</u> <u>Neut.</u> ($\times 10^3$)	<u>Reticulo-</u> <u>cytes</u> (per cent)
3-11-57	14.0		5.6	6.0		1.6	4.0	
3-5-58	14.8		5.4	5.2		1.6	3.5	
2-23-59	15.4	46		5.6		1.8	3.4	
2-15-60	14.9	47		7.1		2.3	4.6	
1-16-61	15.7	46		5.7		2.3	3.2	
2-13-62	17.0	54		8.7		2.8	5.5	
4-7-62 (3pm)	14.3	43	5.0	10.3		2.8	7.1	
4-7-62 (9pm)				6.8		1.7	4.4	
4-8-62	14.7	49	4.5	6.8		2.2	4.0	0.8
4-9-62	15.9	48	5.7	5.6	1.9	1.6	3.7	1.4
4-10-62	16.4	50	7.0	5.9	2.0	1.7	4.0	0.9
4-11-62	16.0	49	5.6	7.6	2.2	1.9	5.0	1.0
4-13-62	15.9	50	5.1	8.7	2.0	2.7	5.2	0.9
4-15-62	15.5	49	5.3	10.3	2.2	2.5	7.1	0.8
4-17-62	15.0	48	5.2	8.8	2.0	2.2	6.0	
4-20-62	15.7	47	5.1	8.5	2.0	1.7	5.9	1.0
4-23-62	15.3	47	5.0	6.6	2.0	1.6	4.3	0.9
4-25-62	15.2	46	5.2	7.2	2.0	1.4	5.3	1.2
4-27-62	15.8	49	5.4	6.8	1.9	1.8	4.5	0.8
4-30-62	15.4	46	5.3	6.0	1.9	1.4	4.1	0.9
5-2-62	15.0	48	5.2	7.7	1.8	2.0	5.3	0.8
5-4-62	15.4	46	5.0	7.0	1.9	2.6	3.9	1.1
5-8-62	15.4	48	5.5	6.9	1.9	2.2	4.4	0.9
5-11-62	15.4	48	5.3	6.5	1.9	1.8	4.2	1.0
5-15-62	15.7	48	5.1	6.7	1.8	2.0	4.2	0.8
5-18-62	15.8	50	5.0	8.6	2.1	1.5	6.4	
5-22-62	15.8	50	5.2	7.6	2.1	1.7	5.7	0.5
5-25-62	15.6	48	4.9	6.7	1.9	2.5	3.9	0.5
5-29-62	15.7	47	5.0	7.2	2.0	2.8	3.7	
6-1-62	15.5	48	5.0	7.2	2.0	2.1	4.5	0.7
6-8-62	14.1	44	4.8	7.0	2.0	2.3	4.4	0.7
6-15-62	14.9	45	4.9	6.3	1.9	2.3	3.5	0.8
6-22-62	15.6	46	4.7	6.2	2.4	2.1	3.7	0.8
6-29-62	15.2	50	5.2	5.8	1.9	1.5	3.8	0.7
7-6-62	15.7	49	5.0	5.6	1.9	1.5	3.6	0.8
7-13-62	16.1	50	5.3	8.0	2.0	2.0	5.6	0.9
7-27-62	15.9	49	5.1	6.5	2.0	2.3	3.8	1.0
8-10-62	14.7	43	4.4	6.2	1.8	2.0	3.7	0.9
8-27-62	No count							
9-7-62	14.7	46	4.6	6.8	2.0	1.6	4.6	0.8
9-21-62	15.1	46	4.5	5.3	1.8	2.1	2.9	0.9
10-5-62	16.2	51	5.5	6.4	2.0	2.5	3.3	1.2
11-2-62	15.8	47	4.8	5.2	2.2	1.2	3.5	1.0
11-30-62	15.1	47	4.8	6.8	2.2	2.1	4.4	0.9
12-28-62	15.1	47	5.1	6.8	2.3	2.1	4.1	0.9
1-25-63	16.0	49	5.1	7.5	1.8	3.1	3.7	0.5
2-21-63	14.8	45	5.0	7.1	2.1	2.4	3.9	0.8
3-22-63	15.5	49	4.6	5.7	1.8	1.3	4.1	0.8
6-26-63	14.0	45	5.0	6.4	1.9	2.1	3.5	1.0
9-30-63	15.0	46	5.2	7.0	2.0	2.2	4.0	0.7
12-27-63	14.8	46	5.5	7.7	2.1	2.9	4.2	0.8

TABLE 3

BLOOD COUNT DATA - EMPLOYEE #23

Date	Hgb.	PCV	RBC (x 10 ⁶)	WBC (x 10 ³)	Platelets (x 10 ⁵)	Abs. Lymph. (x 10 ³)	Abs. Neut. (x 10 ³)	Reticulo- cytes (per cent)
11-15-60	16.8	57		9.2		3.6	5.2	
2-14-62	15.9	48		9.7		2.4	6.8	
4-7-62 (3pm)	15.4	47	5.0	10.8		1.6	8.3	
4-7-62 (9pm)				12.0		2.7	8.5	
4-8-62	15.3	49	5.1	8.0	2.2	3.3	3.3	0.8
4-9-62	16.0	50	4.7	7.7	2.5	2.5	5.0	0.8
4-10-62	17.5	50	7.2	13.0	1.9	4.4	7.9	1.3
4-11-62	16.0	49	5.0	10.3	2.0	2.0	8.1	1.4
4-13-62	15.9	50	5.1	9.2	2.1	2.3	6.4	1.0
4-15-62	15.7	50	5.5	7.8	2.2	2.7	4.7	0.9
4-17-62	15.4	49	5.0	9.8	1.9	3.6	5.5	
4-20-62	16.6	53	5.6	9.9	2.0	2.8	6.3	1.0
4-23-62	16.7	51	5.2	9.1	2.2	3.2	5.5	1.1
4-25-62	16.8	52	5.5	9.1	2.1	2.8	5.8	1.2
4-27-62	16.8	55	5.5	9.7	2.0	3.4	5.6	0.9
4-30-62	16.9	52	5.5	8.0	1.9	3.0	4.5	1.1
5-2-62	16.4	52	5.2	10.5	2.0	4.5	5.2	0.9
5-4-62	16.9	51	5.3	8.3	2.0	3.9	4.0	1.0
5-8-62	16.2	52	5.5	9.0	2.0	3.7	4.8	1.0
5-11-62	16.0	48		16.6		4.3	12.1	
5-14-62	12.4	38	4.1	8.5	1.9	2.0	6.2	1.9
5-18-62	12.0	43	4.0	9.0	2.2	1.7	7.1	
5-22-62	13.4	44	4.2	8.6	2.9	3.7	4.6	1.3
5-25-62	13.1	40	4.0	8.9	2.1	3.5	5.3	1.1
5-29-62	14.6	45	4.5	7.2	2.4	2.9	4.0	
6-1-62	14.7	46	4.7	8.7	2.1	3.7	4.7	0.8
6-8-62	14.3	46	4.7	7.9	1.9	2.9	4.4	0.8
6-15-62	16.1	51	5.8	7.6	1.9	2.4	4.7	1.0
6-22-62	15.5	48	5.0	8.9	2.0	3.2	5.3	0.8
6-29-62	14.9	48	4.9	10.8	2.1	2.7	7.9	0.8
7-6-62	15.9	49	5.0	8.6	1.8	3.0	5.1	0.8
7-13-62	16.3	51	5.3	8.6	1.8	2.8	5.3	0.8
7-27-62	15.3	49	5.0	9.1	2.0	3.3	5.0	0.9
8-10-62	16.8	54	5.5	10.0	1.9	3.7	5.6	1.0
8-27-62	No count							
9-7-62	16.0	51	5.2	9.4	1.9	3.8	5.1	0.8
9-21-62	16.2	51	5.4	8.9	2.1	3.1	5.2	0.7
10-5-62	16.4	53	5.2	11.9	2.1	3.9	7.4	1.0
11-2-62	16.7	51	5.4	8.7	2.0	3.2	4.9	1.0
11-30-62	16.8	51	5.1	9.1	2.0	3.0	5.4	1.0
12-28-62	17.2	55	5.4	9.5	1.9	4.0	4.8	0.7
1-25-63	17.5	54	5.5	9.8	1.9	3.3	5.7	0.6
2-21-63	17.0	54	5.3	10.8	2.0	3.5	6.6	0.7
3-22-63	16.9	55	5.5	11.5	2.1	3.1	7.8	0.6
6-26-63	15.9	51	5.4	10.2	2.1	3.8	5.9	0.8
9-30-63	17.0	51	5.7	10.4	1.9	4.3	5.3	1.0
12-27-63	16.2	53	6.2	10.3	1.8	3.4	6.3	1.5

TABLE 4

BLOOD CHEMISTRY EXAMINATIONS

<u>Procedure</u>	<u>Date</u>	<u>Normal Range</u>	<u>#1</u>	<u>#17</u>	<u>#23</u>
Alkaline phosphatase	4-11	1.5-4.0 Bodansky units per 100 ml	4.0	1.6	2.4
Amylase	4-10	60-160 amylase units per 100 ml	56	61	56
Bilirubin, total	4-10	0.25-1.0 mg/100 ml	0.4	0.4	0.4
Bilirubin, direct	4-10	0-0.4 mg/100 ml	0.2	0.1	0.2
Calcium*	4-23	4.5-5.7 meq/liter	4.9	5.0	5.2
Cephalin flocculation, 24 hr	4-11	0-2+	trace	trace	2+
Cephalin flocculation, 48 hr	4-11	0-2+	trace	trace	3+
Chloride	4-12	98-106 meq/liter	102	101	105
Cholesterol*	4-17	135-315 mg/100 ml	250	298	279
Creatinine	4-10	0.3-1.0 mg/100 ml	0.6	0.9	0.9
Glucose	4-10	65-90 mg/100 ml	88	94	110
	4-11		89	100	89
	4-16		74	84	68
Phosphorus	4-11	3.0-4.5 mg/100 ml	3.8	4.0	3.3
Potassium	4-12	3.5-5.0 meq/liter	4.5	4.2	4.6
Protein**					
Albumin	4-16	3.5-5.3 g/100 ml	4.5	4.7	
	4-23		4.6	5.0	5.3
Alpha 1	4-16	0.17-0.38 g/100 ml	0.34	0.29	
	4-23		0.30	0.24	0.18
Alpha 2	4-16	0.3-0.8 g/100 ml	0.7	0.6	
	4-23		0.5	0.5	0.6
Beta	4-16	0.5-1.0 g/100 ml	0.7	0.8	
	4-23		0.5	0.8	0.5
Gamma	4-16	0.6-1.8 g/100 ml	1.2	0.9	
	4-23		1.0	0.8	0.9
Total protein	4-16	6.5-8.1 g/100 ml	7.3	7.3	
	4-23		7.0	7.3	7.5
Prothrombin time	4-10		~100%	~100%	~100%
Sedimentation rate	4-8	0-10 mm/hr	10	11	9
Serum glutamic oxalic transaminase (SGOT)	4-11	8-40 units	20	20	18
Serum glutamic pyruvic transaminase (SGPT)	4-11	5-35 units	21	18	12
Sodium	4-12	136-145 meq/liter	138	140	140
Thymol Turbidity	4-10	0-4 units	1.8	3.0	3.2
Urea nitrogen	4-12	10-20 mg/100 ml	14	17	10
Uric acid	4-10	3.0-6.0 mg/100 ml	3.8	4.6	4.5

* Performed by Bio-Science Laboratories, 12330 Santa Monica Blvd.,
Los Angeles 25, California.

** Fractionation by paper electrophoresis performed by J. Salvatore,
University of Rochester School of Medicine and Dentistry.

FIGURE 1

Total Leukocyte, Absolute Neutrophil, and Absolute Lymphocyte Counts on Employee 1

FIGURE 2

Total Leukocyte, Absolute Neutrophil, and Absolute Lymphocyte Counts on Employee 17

FIGURE 3

Total Leukocyte, Absolute Neutrophil, and Absolute Lymphocyte Counts on Employee 23

BONE MARROW

Gould A. Andrews, M. D., R. M. Kniseley, M. D.
Oak Ridge Institute of Nuclear Studies,
Oak Ridge, Tennessee

I have looked at the smears and made a qualitative interpretation and Dr. Ralph Kniseley independently looked at the sections. There is some discrepancy in the findings, particularly in connection with the fat content in Employee #1. In the smears it appeared that he had an excess amount of fat in all specimens, but this was not confirmed by the sections.

In general, neither the sections nor the smears show any profound damage. In Employee #23 the specimens were all close to normal except for the smears of the specimen of April 14th which contained a rather large number of lymphocytes and naked nuclei. I believe that these changes represented an incidental finding and not radiation effect. Employee #17's marrow appears to show mild radiation effects, and I am quite sure that Employee #1 shows very definite, but not severe, radiation effects, although the apparent excess of fat noted in the smears, even on the first day, is probably somewhat a normal characteristic of his marrow and only in part a radiation effect.

Perhaps the reason that we are so vague about these marrow effects is that we are looking for rather small changes and none of the marrows are really far outside normal limits according to the usual criteria for bone marrow studies. None of them show as much damage as was seen in all of the five high-dose Y-12 accident patients. It is possible that a more detailed cytologic analysis would help to confirm radiation effects and even give some index of dose. There has not been a great deal done on interpreting the bone marrow changes from total body radiation in normal persons and we are really not as familiar with the changes as we are with those that appear in the peripheral blood.

Employee #1

4-8-62: Good marrow preparation, perhaps somewhat hypocellular, with many fat spaces. Megakaryocytes normal in number. E-G ratio is normal. Erythrocyte precursors include some slight increase in early forms and a few with karyomeres. Granulopoiesis shows predominantly mature forms; there are some rather large myelocytes and metamyelocytes. Eosinophils present in normal numbers. Very few plasma cells.

4-14-62: Good preparation. Fairly cellular but with large number of fat spaces and much stromal material. Megakaryocytes normal in number. E-G ratio normal. Granulopoiesis mostly late forms. A few large hyper-segmented mature neutrophils noted; also a few large myelocytes and metamyelocytes. Red cell precursors seem a little more mature than in the previous specimen. A few normoblasts with karyomeres seen. Eosinophils in normal numbers. Plasma cells normal in number, perhaps more than in previous specimen.

4-23-62: Very much fat and stroma - moderate number of cells - hypocellular perhaps. Megakaryocytes normal in number. E-G ratio in normal range but red cell precursors are relatively more plentiful than in previous specimen. A binucleate early normoblast noted but no cytoplasmic granules observed. Granulopoiesis not remarkable. Plasma cells infrequent.

5-7-62: A very fatty marrow, perhaps somewhat hypocellular. Stromal elements prominent. E-G ratio normal. Lymphocytes fairly plentiful, as are naked nuclei of lymphocytic type. Red cell maturation normal without prominent cytoplasmic bodies. Granulocyte development normal. Eosinophils in normal numbers. Plasma cells present, not increased. Occasional mast cells.

Employee #17

4-8-62: Cellular marrow. Well stained. Normal amount of fat. Megakaryocytes, normal number. E-G ratio normal. Normal appearing precursors and stages of development in both series as judged without differential count. Eosinophils and plasma cells present in normal numbers.

4-14-62: Relatively more fat and more amorphous fibrils and stromal elements than in previous marrow. Megakaryocytes plentiful; in fact they seem somewhat increased in relation to cellular elements in some zones on the films where fat and stromal elements predominate. Some megakaryocytes are immature. Plentiful precursors of red and white cells without remarkable abnormalities noted on survey.

4-23-62: Like preceding but clumps of amorphous fibrils, stromal elements, and packed cells, seem less well spread out and seem larger in relation to fat cells. There is a pinkish background precipitate. Cellular clumps on edges of these areas of fat and stroma show a larger proportion of unidentifiable naked cell nuclei -- most of these resemble rather smooth lymphocyte nuclei but some are rather large to be of lymphocyte origin. Otherwise cell types and stages of development are not remarkable on survey.

5-7-62: Like the preceding but a larger portion of the film is taken up by dilute marrow. Pink background persists. Fat and stromal elements prominent in one clump seen. Still many unidentified cell nuclei. Megakaryocytes fairly plentiful.

Employee #23

4-8-62: Cellular marrow with moderate amount of fat. Megakaryocytes present in normal numbers. E-G ratio normal. Erythropoiesis normal. No cytoplasmic bodies noted. Granulopoiesis shows normal stages of maturation. Lymphocytes and eosinophils in normal numbers. Plasma cells rare.

4-14-62: Somewhat less cellular than the previous marrow with considerable amounts of fat and stromal elements. Megakaryocytes fairly plentiful. Lymphocytes and unidentified mononuclear cells and nuclei are present in more than usual numbers -- in some areas of the film they are the predominant cells present. Elsewhere a more normal cell pattern exists. Here the E-G ratio is normal and stages of maturation in both series are normal. No morphologic features of radiation effect are noted in individual cells. Eosinophils present in normal numbers. Plasma cells not increased. This picture may well represent a chance penetration of a lymphoid nodule in an essentially normal marrow, although certain features do resemble a radiation effect.

4-23-62: Normally cellular marrow with a moderate amount of fat. Megakaryocytes present in normal numbers. Normal E-G ratio. Granulopoiesis normal with plentiful myelocytes and metamyelocytes. Erythropoiesis shows normal stages of development. A moderate number of lymphocytes is seen -- many fewer than in the previous specimen. Plasma cells infrequent. Eosinophils present in normal numbers.

5-7-62: Fewer and smaller clumps than in the previous marrow, but cellularity and the amount of fat are within normal limits. E-G ratio normal; maturation in erythroid and granulocyte series normal. Lymphocytes and nuclei without cytoplasm quite plentiful, especially in the thicker parts of the clumps. Eosinophils and plasma cells in normal numbers; occasional mast cells.

5-7-62: Fewer and smaller clumps than in the previous marrow, but cellularity and the amount of fat are within normal limits. E-G ratio normal; maturation in erythroid and granulocyte series normal. Lymphocytes and nuclei without cytoplasm quite plentiful, especially in the thicker parts of the clumps. Eosinophils and plasma cells in normal numbers; occasional mast cells.

TABLE 1

HISTOLOGIC PREPARATIONS OF BONE MARROW

<u>Patient</u>	<u>Date</u>	<u>Slide No.</u>	<u>Cellularity</u>	<u>Pattern</u>	<u>Fat</u>	<u>Megakaryocytes</u>	<u>Comments</u>
Employee #1	4-8-62	S-528-62 (a)	N	N	N	N, -1	
" "	4-8-62	S-528-62 (b)	N	N	N	N, -1	
" "	4-14-62	S-583-62	N, +1	N	-1	N	
" "	4-23-62	S-643-62	N, +1	N	N	N	
" "	5-7-62	S-694-62	N, -1, -2	N	N, +1	-1, -2	Cells not ideally stained
Employee #23	4-14-62	S-582-62	N, +1	N	-1	N	
" "	4-23-62	S-645-62 (a)	N, +1	N	N	N	Thick sections
" "	4-23-62	S-645-62 (b)	+1, +2	N	-1	N	Particles small
Employee #17	4-8-62	S-527-62	N, -1	N	N	N, -1	
" "	4-14-62	S-584-62	N, -1	N	N	-1	
" "	4-23-62	S-644-62	(N, -1 (Small Particle	N	N	-1	Scant particles
" "	5-7-62	S-695-62	N	N	N	N	

R. M. Kniseley, M. D.
ORINS Med. Div.

REPORTS ON BONE MARROW ASPIRATIONS

R. J. Kramer, M. D.

Employee #1

Sternal bone marrow aspiration -- performed on 4/8/62: The M-E ratio of the marrow is normal. The erythrocytes and granulocytes are developing normally. There is, in general, a larger amount of fat in the peripheral smears than would be expected. In other words, a slightly hypocellular marrow as based on smear. Smears, by themselves, are inadequate to detect a complete marrow cellularity.

Sternal bone marrow aspiration -- performed 4/14/62: Smears were prepared and a clot of the bone marrow material was also formalin-fixed and submitted to Dr. Marks for section. Good bone marrow slides were obtained. There were many developing red and white cells in all stages of development. No abnormalities can be found.

Sternal bone marrow aspiration -- performed on 4/23/62: This is relatively a hypocellular marrow on smears. Plasma cells are frequent. Red blood cells are developing and morphologically are normal. There is a greater proportion of naked nuclei, that is cells without cytoplasm present. These appear to be of the lymphocytic series. There is slight increase in the relative proportion of the lymphocytes.

Sternal bone marrow aspiration -- performed on 5/7/62, at a site distant from the previous sternal marrow aspirations. The best bone marrow on all three men was obtained this date from this patient. This is entirely normocellular on smear with slight increase in plasma cells and eosinophiles. Red blood cells show good maturation and adequate numbers as do granulocytes. The bone marrow clot was fixed in formalin and forwarded to Dr. Marks for histological section.

Employee #17

Sternal bone marrow aspiration -- performed on 4/8/62: In general, reviewing eight or ten cover glass slide preparations, adequate marrow was obtained for diagnostic purposes. However, the marrow, in general, appears to be somewhat hypocellular with increased amounts of fat. There are small areas where the bone marrow cells are devoid of cytoplasm and large collections of nuclei are present; these have some vacuoles in the nucleus, perhaps representing early degenerative changes. In general, the M-E ratio is normal in the marrow. There are adequate numbers of immature blast cells in both the myeloblastic and erythroblastic series. Megakaryocytes are present.

Sternal bone marrow aspiration -- performed on 4/14/62: Fairly decent marrow sample was obtained. Red blood cells and granulocytes are seen in all stages of development and appear to be maturing normally. There does not seem to be an increase in reticulum cells. Lymphocytes are normal in number.

Sternal bone marrow aspiration obtained 4/23/62: The smears generally show hypocellularity. A formalin-fixed marrow clot was sent to Dr. Marks for histological section. The smears show normal developing red cells and granulocytes. There appear many naked nuclei, that is cells without cytoplasm, which again appear to be of the lymphocytic variety. This essentially is a negative marrow.

Sternal bone marrow aspiration -- performed on 5/7/62, at a site different from previous sternal marrow aspirations. Thirty-two smears were prepared. A very large amount of marrow fat was obtained. The smears therefore appear hypocellular because of increase in marrow fat on the smears. The M:E ratio is slightly increased. There is a moderate increase in what appear to be naked lymphocytes or lymphocytes devoid of cytoplasm. It is also noted at this time that there is a slight increase in plasma cells and eosinophiles. The bone marrow clot was fixed in formalin and forwarded to Dr. Marks for histological section.

Employee #23

Sternal bone marrow aspiration -- performed on 4/8/62: Shows essentially normal marrow except for some hypocellularity. The M.E. ratio is normal. The red cells and white cells are developing normally. Megakaryocytes are present in the marrow in approximately normal numbers.

Sternal bone marrow aspiration -- performed on 4/14/62: Excellent slides were obtained. There appears to be normal maturation of both red cells, granulocytes; no definite increase in lymphocytes were seen; no increase in reticulum cells; megakaryocytes are normal. The clot of the bone marrow was forwarded to Dr. Marks, in formalin, for histological section.

Sternal bone marrow aspiration -- performed on 4/23/62, shows essentially a normal marrow. No changes can be detected between this marrow and the previous two marrows.

Sternal bone marrow aspiration -- performed on 5/7/62, at a site in the sternum, distant from the previous marrow aspiration sites. A large amount of marrow fat was obtained in relation to marrow cells. The M-E ratio is slightly increased. Plasma cells are increased, as are marrow lymphocytes. Some of the smears show scant red blood cell precursors and in others, these are normal in appearance. There are a larger number of cells which are devoid of cytoplasm and appear to be in the lymphocytic series in the marrow. Megakaryocytes are adequate. The bone marrow clot was fixed in formalin and forwarded to Dr. Marks for histological section.

MORPHOLOGICALLY ABERRANT BLOOD CELLS
IN HANFORD ACCIDENT CASUALTIES

M. L. Ingram, M. D.
(with the technical assistance of Rita McDaniels,
Bernice Morehouse and Gladys Yettewich)
University of Rochester, Rochester, N. Y.

Radiation exposures sustained by the Hanford accident casualties, while not great enough to cause serious depression of blood cell production, were nevertheless in the range in which one would expect injury of some cells of the sensitive hematopoietic tissue. Maintenance of blood cell production and normal levels of circulating blood cells can probably be attributed in part to marked inhomogeneity of dose throughout the body.

Following exposure to a small radiation dose or to a larger dose delivered to a relatively small proportion of the hematopoietic tissues, morphological changes in blood cells may be the most striking hematological change. This is true of the Hanford casualties. Morphological changes observed in peripheral blood and bone marrow cells of these men are of the same types as those observed in a group of men receiving accidental x-ray exposure in 1960,^(1,2) and it is interesting to compare the two accidents with respect to the types and magnitude of changes observed following various radiation doses. Doses received and peripheral blood leukocyte and platelet count responses are summarized in table 1.

Numbers of peripheral blood cells as determined by routine counting procedures showed negligible changes in two of the three Hanford casualties. The leukocyte count of the man receiving the highest dose was unstable during the first post-exposure week, showing leukocytosis on the first and third post-exposure days, a change compatible with mobilization of leukocytes from tissue (especially marrow) stores. Instability of the leukocyte counts during the first post-exposure week was also observed in the higher dose Lockport and in the Y12 casualties.^(1,3) The increase was primarily limited to the granulocytic and monocytic series of cells. Lymphocytes, while they remained within "normal" limits, were somewhat lower than the characteristic values for this man (a good illustration of the importance of accumulating periodic normal values in order to define the characteristic blood picture for each radiation worker).

METHODS:

Morphologically aberrant cells were studied using conventional Wright's stained films of peripheral blood and bone marrow and Wright's and peroxidase stained films of leukocyte concentrates prepared according to a method used in this laboratory for many years.⁽⁴⁾ Some studies, including micrometry and studies of cellular characteristics on preparations stained with stains other than Wright's and peroxidase are still in progress as part of a continuing study of readily identifiable morphological characteristics likely to be useful in identifying both common and uncommon types of blood cells by means of automatic pattern recognition techniques. The major types of aberrant cells found in the radiation accident casualties are as follows:

1. binucleate lymphocytes (bnl): These cells fulfill the morphological criteria for mature lymphocytes except that they are somewhat larger and have two distinct nuclei, each comparable in size to the nucleus of a normal small lymphocyte. The rate of occurrence in peripheral blood of normal unirradiated men is approximately 1/10,000 lymphocytes or one in 30,000 leukocytes. MPE range doses are adequate to produce transient increases in this type of cell.⁽⁵⁾

2. lymphocytes with nuclear fragments: These cells, almost never seen in the blood of normal healthy persons who have not been exposed to agents noxious to hematopoiesis, probably reflect chromosome breaks that result in micronuclei. In the high dose Lockport casualties, they have persisted (for more than two years at last examination) but the number found decreased after the first post-exposure month.
3. monocytosis: An increase in the number of normal monocytes/mm³ of peripheral blood.
4. immature monocytes: These cells are of approximately the same size as the largest normal monocytes. The nucleus has the characteristic finely reticular monocyte structure and there is commonly little or no nuclear indentation or lobulation. Cytoplasm is considerably more basophilic than that of the usual mature monocyte and contains fewer peroxidase positive granules on peroxidase stained smears. Some of the cells have no peroxidase positive granules.
5. giant hypersegmented granulocytes: neutrophil granulocytes that are nearly double the size of normal granulocytes and have, usually, five, six or more nuclear lobes. As a rule, these cells are found most frequently only during the first two weeks following relatively high level (as contrasted to MPE or low level) exposures. Giant eosinophils, basophils and monocytes may also be found occasionally.
6. granulocytes with shaggy chromatin structure: typical granulocytes except for the presence of several filamentous chromatin appendages. Some of the appendages very closely resemble the sex chromatin appendage. Cells showing this anomaly usually have several chromatin appendages so that the nucleus tends to appear "shaggy". The nuclear anomaly in these cells is probably the same as that referred to as "karyoschizes" by Bessis,⁽⁶⁾ and as "nuclear extrusions" by Duplan⁽⁷⁾ who studied the phenomenon in irradiated guinea pigs. Our criterion for "shaggy chromatin" is the presence of more than two appendages on the nucleus.
7. plasma cells: normal plasma cells with deeply basophilic cytoplasm and nuclear chromatin pattern characteristic of this series of cells.
8. plasmacytoid early mononuclear cells (pem): cells ranging from plasmacytoid lymphocytes to very large cells with coarse, clumpy nuclear chromatin pattern and deeply basophilic, opaque cytoplasm. Some of the cells have a clear or light staining area adjacent to the nucleus. Many of these cells, although they may have no nucleoli apparent with ordinary Romanowsky stains, would probably be classed as "blasts" when encountered during routine differential wbc counting.
9. binucleate monocytes and monocytes with nuclear fragments: monocytes with two nuclei are usually the size of normal monocytes and the "nuclei" are probably two fragments of a single nucleus. For this reason, these two classes are considered together as probably representing nuclear fragmentation in both instances. Rarely an abnormally large cell that appears to be polyploid may be found.
10. blasts, mitotic cells and other cells that occur rarely but are not readily classified into any of the groups above.
11. nucleated red cells
12. giant platelets: platelets larger than red cells; many as large as leukocytes, or larger. They are usually found in blood in which platelet size in general shows increased heterogeneity.

Examples of the types of unusual cells are shown in Figure 1.

When cells occur extremely rarely, it may be necessary to examine many thousands of their normal counterparts in order to be certain that the rate of occurrence is indeed increased. Otherwise, one may be led astray by a disproportionately high index of suspicion about unusual cells seen in the exposed individuals. In considering the incidence of the most rarely occurring cell types in the blood specimens from the Hanford casualties, only leukocyte concentrations provided adequate numbers of cells. The incidence of some types of unusual cells occurring more frequently could be evaluated on regular unconcentrated blood films.

RESULTS:

In general, the Hanford casualties show relatively low levels of the cytological stigmata of radiation injury. During the first two post-exposure weeks, the most prominent readily apparent changes are those representing changes in chromatin structure of peripheral blood granulocytes. These are prominent in cells on the regular blood smears. Chromatin damage was also apparent as abnormal mitotic figures with lagging chromosomes, chromosome bridges in anaphase and telophase cells, chromosome fragments and "smudged" chromatin of chromosomes in mitotic bone marrow cells one day after the exposure. Many of the later stages of nucleated red cells contained nuclear fragments even at that early period. Among 100 consecutive nucleated red cells on the marrow smear of the man receiving the highest dose, for example, 13% contained nuclear fragments. All of these were either polychromatophilic or orthochromic erythroblasts.

Granulocytes:

Even on the day of exposure, a third or more of the peripheral blood granulocytes had shaggy chromatin as judged by the presence of more than two thread-like or heavier strands of chromatin extending out from the nucleus proper. In some instances small fragments appeared to have broken free. Shaggy chromatin was not more common in "older" cells, many of the cells with shaggy chromatin structure being two and three-lobed cells. Even smears showed the phenomenon. The numbers of cells showing such nuclear structure decreased after the first two weeks post exposure. In bone marrow specimens available from the first post-exposure day, similar changes are apparent in some early metamyelocytes, and in many late metamyelocytes and smears, but not in earlier cells of the myelocytic series. Giant granulocytes were most readily found in peripheral blood during the first two post-exposure weeks and probably most frequently during the first week although additional samples must be examined in order to obtain statistically meaningful estimates of incidence during the period when concentrate preparations were not made. In contrast, Fliedner, et al report a maximum incidence in Oak Ridge Y12 casualties on the 8th-10th post-exposure days. (8) Anisocytosis of granulocytes without typical giant forms as well as moderate hypersegmentation of the normally sized cells were also most prominent during this period. Occasional abnormally large metamyelocytes were apparent in the bone marrow specimen from the first post-exposure day.

Granulocytes with pyknotic nuclei were not conspicuous in this material.

Lymphocytes:

The two most readily identified aberrant lymphocyte forms are the binucleate lymphocytes and lymphocytes with nuclear fragments. Binucleate cells, which appear in increased numbers after low-level exposures, were only

modestly increased in number in the Hanford material except in the man receiving the lowest dose. Of the Hanford casualties, only the man receiving the highest dose had lymphocytes with nuclear fragments. These cells are virtually never seen in "control" material from men without history of exposure to hematotoxic agents and are seen extremely rarely (approximately 1 per 10,000 lymphocytes) in uranium miners and other radiation workers receiving low-level exposures. As in the case of the Lockport casualties, the incidence of lymphocytes with nuclear fragments decreased with time. The rates of occurrence of these cells on the days when leukocyte concentrations were studied are presented in table 2 where the Hanford data may be compared with findings in high, medium and low dose Lockport casualties at comparable times post exposure. Incidence of the aberrant lymphocytes after exposure are presented graphically in Figures 2 and 3.

Monocytes:

Monocytosis of mild degree was observed in all of the casualties during the first post-exposure week and was accompanied by increased numbers of immature monocytes in peripheral blood, an increase that was quite striking in employee #1 who received the highest dose. These data are presented in Table 3. Increased numbers of immature monocytes is probably analogous to the "shift to the left" often seen in the granulocytic series during granulocytosis.

Marked monocytosis was observed in the Lockport casualties⁽¹⁾ and it is perhaps relevant that the number of monocytes per cubic millimeter of blood in U.S. uranium miners shows a strong correlation with radiation level of the mines in which the miners work, i.e. in long term low-level exposures. An impression of increased numbers of immature monocytes is also recorded in the description of the Y12 casualties receiving doses in the range of 300 r.⁽³⁾

Plasmacytoid Early Mononuclear Cells:

These cells probably make up a large proportion of the group of peripheral blood cells that label with tritiated thymidine (i.e. synthesize DNA) and are presumably capable of undergoing mitosis. Bond, Flidner, Cronkite and Andrews⁽⁹⁾ describe the morphology of the tritiated thymidine labeled cells as follows: "Some labeled cells resemble monocytes, others, immature lymphocytes, atypical lymphocytes and plasma cells (none are typical plasma cells)."⁽⁹⁾ Our studies would place most of the labeled cells in a group of plasmacytoid mononuclear cells, ranging from plasmacytoid lymphocytes to very large plasmacytoid cells such as those pictured in Figure 1. Almost all of the cells have markedly basophilic (and pyroninophilic) cytoplasm.

While the total number of leukocytes examined on the various post-exposure dates permits only a general comparison of the Hanford and Lockport casualties, the Hanford men have levels of pem's that correspond to the lowest dose Lockport casualties. This is not readily apparent in the tabulated data (table 2) but is readily apparent in Figure 5. The high dose Lockport casualties, on the other hand, had increases in pem's that correspond surprisingly closely in both time and magnitude of response with the fluctuations in tritiated thymidine labeled cells in the Y12 casualties, as shown in Figure 4.

Nucleated red cells:

One or more nucleated rbc, always orthochromatic normoblasts, were found in peripheral blood on the 23rd post-exposure day in the two higher dose casualties. The numbers of cells examined was relatively small except on days when concentrate preparations were available so that it is not possible to

identify the duration of the period during which these cells were released into the peripheral circulation, but they were not found on concentrates prepared on the fifth post-exposure day or on concentrates prepared on July 1, 1962, approximately three months after exposure. There was no antecedent anemia and the reticulocyte counts give no indication that erythropoiesis was particularly brisk during the fourth post-exposure week when nucleated rbc were found. One might speculate that the phenomenon may represent not so much a spurt of erythropoietic activity as an alteration in the mysterious physiological mechanism that normally excludes nucleated red cells from the peripheral circulation in man with astonishing efficiency.

Conclusion and Summary:

The incidence of certain rarely occurring blood cells and more common types of cells showing relatively subtle morphological aberrations has been studied in peripheral blood specimens from three men exposed to mixed gamma and neutron radiation in a critical excursion accident at the Hanford Atomic Products Operation, Richland, Washington on April 7, 1962. Bone marrow specimens aspirated one day after exposure have also been studied. Damage to hematopoietic tissues was not severe enough to produce leukopenia or lymphopenia.

The types of morphological aberrations observed include (1) changes in the nuclear structure of granulocytic series, in peripheral blood and bone marrow; (2) increased immaturity of monocyte series as well as mild, transient monocytosis; (3) binucleate lymphocytes and lymphocytes with nuclear fragments; (4) increased numbers of plasmacytoid early mononuclear cells; (5) the occurrence of nucleated red cells in peripheral blood and (6) chromatin and chromosome abnormalities in the marrow nucleated red cells. The magnitude of the changes observed when compared with changes observed in Y12 and Lockport casualties is seen to correspond most closely to the low dose Lockport casualties.

Most of the changes represent direct radiation damage to either mature or stem cells. Aberrant forms were most numerous during the first two weeks after exposure. The occurrence of an occasional nucleated red cell in peripheral blood is not readily explained, but may represent some alteration in the mechanism that normally excludes these cells from peripheral blood. Conceivably, very early stages of the erythroid series may have been damaged at the time of exposure, ultimately producing normoblasts that are altered in some way that interferes with the ability of the marrow's physiological "gate keeper" to recognize the cell as one not yet qualified for release into the circulation.

Studies of the material representing the accidentally irradiated Hanford Operation personnel continue.

Acknowledgements

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TABLE 1

DOSE AND LEUKOCYTE COUNT IN HANFORD AND LOCKPORT CASUALTIES

HANFORD CASUALTIES

Casualty (Employee No.)	Estimated Dose			<u>Leukopenia</u>	<u>Lymphopenia</u>
	<u>Gamma (r)</u>	<u>Neutron (rads)</u>	<u>Total* (rems)</u>		
1	63	23 - 30	109 - 123	No	No
17	23	9 - 12	41 - 47	No	No
23	13	3	19	No	No

LOCKPORT CASUALTIES

	Estimated Exposure Dose			<u>Leukopenia</u>	<u>Lymphopenia</u>
	<u>Head and shoulders</u>	<u>Total body</u>			
KS	at least 1500 r	~ 300 r	} high dose	Yes (m.c. **1379)	Yes (m.c. 136)
EL	at least 1000 r	~ 300 r		Yes (m.c. 2247)	Yes (m.c. 305)
JP	< 1000 500 r	< 300 r		Yes (m.c. 3203)	Yes (m.c. 588)
GL	< 1000, 500 r, J. P.	< 200 r		Yes (m.c. 4425)	Yes (m.c. 789)
WR	> 200 r	Not more than ~ 50 r	} medium dose	No	No
DM	> 200 r	"		No	No
WL	> 200 r	"	} low dose	No	No
JK		< 50 r		No	No
WK		< 50 r		No	No

* assuming RBE for neutrons = 2

** minimal count in cells per cubic millimeter

TABLE 2

INCIDENCE OF RARELY OCCURRING MONONUCLEAR CELLS
IN CONCENTRATED LEUKOCYTE PREPARATIONS

<u>Time</u> <u>post-exp.</u>	<u>Employee</u> <u>No.</u>	<u>Lymphs</u> <u>Examined</u>	<u>WBC</u> <u>Examined</u>	<u>Cells per thousand lymphocytes#</u>			
				<u>bnl</u>	<u>lymph-frag</u>	<u>pem</u>	<u>plas.</u>
1st week	1	13,807	39,947	0.2 (1)*	0.1 (1)	1 (14)	0.1 (1)
	17	13,250	45,294	0.2 (2)	0 (0)	0.2 (2)	0. (0)
	23	10,769	32,325	0.5 (5)	0 (0)	0.8 (8)	0.3 (3)
	High L.	4,642	48,300	0.5 (2)	1.08 (5)	1.08 (5)	0 (0)
	Med. L.	32,983	101,795	(7)	0.15 (5)	2.1 (69)	0.3 (9)
	Low L.	11,756	37,213	0.4 (5)	(1)	2.5 (30)	0.2 (2)
4th week	1	12,748	36,532	0.5 (5)	0.3 (3)	0.5 (6)	0.2 (2)
	17	11,911	39,796	0.1 (1)	0 (0)	0.7 (7)	0.1 (1)
	23	10,799	32,769	0.5 (5)	0 (0)	1.4 (15)	0.3 (3)
	High L.	10,747	45,081	0.2 (2)	4.09 (44)	1.7 (18)	0.1 (1)
	Med. L.	9,899	25,297	0 (0)	0 (0)	3.2 (32)	0.2 (2)
	Low L. (1-2 mo.)	20,195	52,674	0.4 (8)	0.05 (1)	0.7 (14)	0 (0)
3 months	1	12,404	35,471	0.1 (1)	0.2 (2)	0.5 (5)	0.2 (2)
	17	10,040	32,433	0 (0)	0 (0)	0.7 (7)	0 (0)
	23	11,019	31,269	0.1 (1)	0 (0)	0.3 (3)	0 (0)
	High L.	6,254	18,572	0 (0)	0.95 (6)	0.5 (3)	0 (0)
	Med. L. (2 mo.)	2,051	7,267	0 (0)	0 (0)	1. (2)	0.5 (1)
	Low L.	3,587	13,062	0 (0)	0 (0)	2.8 (10)	0.3 (1)

binucleate lymphocytes, lymphocytes with nuclear fragments, plasmacytoids with early mononuclear and plasmacytes respectively.

* Number in parenthesis is the total number of cells found in the sample examined.

1 Highest dose Lockport casualty (See Table 1)

2 Medium dose " " " " "

3 Low dose " " " " "

TABLE 3

NUMBER AND IMMATURITY OF MONOCYTES

<u>Time post-exposure</u>	<u>Casualty (Employee No.)</u>	<u>monocytes/mm³ (regular smears)</u>	<u>% monocytes that are "immature"</u>	<u>WBC examined</u>	<u>monocytes examined*</u>
1 week	1	840	8%	4,000	250
	17	538	2.2%	6,000	540
	23	580	2.1%	5,000	380
2 week	1	880	1.9%	2,000	160
	17	343	1.8%	3,000	110
	23	360	0.8%	3,000	120
3 week	1	520	2.7%	2,000	110
	17	398	0	1,000	60
	23	483	0	1,000	50

* Total monocytes examined each day was determined (total wbc examined on a given day x % monocytes from differential blood counts on that day). The sum of the daily monocyte totals is the weekly total shown.

A. Granulocytes with shaggy chromatin

B. Giant hypersegmented granulocyte (Note chromatin shreds)

C. Giant monocyte

D. Lymphocyte with two nuclear fragments

E. Plasma cell

F. Plasmacytoid early mononuclear cell (pem)

G. Plasmacytoid early mononuclear cell. This cell has extremely basophilic cytoplasm, almost as dark as the nucleus. (Red cells are approx. 7μ dia.)

FIGURE 1

Morphologically aberrant blood cells in Recuplex cases.

FIGURE 2

Incidence of Bi-Nucleated Lymphocytes in Radiation Casualties

FIGURE 3

Incidence of Lymphocytes with Fragments in Radiation Casualties

FIGURE 4

Incidence of Plasmacytoid Early Mononuclears in Radiation Casualties

PRELIMINARY REPORT

ANALYSIS OF LEUKOCYTE CHROMOSOME ABERRATIONS

M. A. Bender, Ph.D. and P. C. Gooch
Biology Division, Oak Ridge National Laboratory
Oak Ridge, Tennessee

Data for the first 18 post-irradiation months

Analyses have been made of chromosome aberrations induced in the peripheral leukocytes of the men irradiated in the Recuplex nuclear excursion of April 7, 1962. These studies were undertaken for several reasons. Our knowledge of the radiosensitivity of human somatic chromosomes has derived entirely from measurements made in vitro with various cell culture systems. The present cases provided our first opportunity to check the in vitro observations against material irradiated in vivo. The future usefulness of somatic chromosome aberration analysis as a "biological dosimeter" depends on our having "calibration checks" in the form of actual measurements on irradiated subjects whose physical dose is reasonably well known, and also, to a lesser extent, on our understanding of the kinetics of loss and replacement of the cells used for analysis.

The standard leukocyte method was used for the preparation of mitotic figures suitable for analysis. Leukocytes were separated from 10-ml peripheral blood samples and put into short-term tissue culture in a standard medium containing the substance Phytohemagglutinin, which stimulates mitosis of some of the leukocytes. On the third day after the cultures were initiated, metaphases were collected with colchicine and the cells were fixed and mounted for subsequent staining. The first set of samples was drawn roughly four hours after the accident and refrigerated until after the second set was obtained. This second set was drawn at about 44 hours. Both lots of samples were put into culture at Hanford and maintained at 37°C in a portable incubator during their transportation to Oak Ridge. A third set of samples was drawn at about one week and was shipped to Oak Ridge under refrigeration, but the cultures made from these samples failed to yield satisfactory mitoses. A fourth set was therefore drawn at about two weeks and put in culture at Hanford. Fifth, sixth, seventh, eighth, ninth, and tenth sets of samples were obtained at about 4 weeks, 6 weeks, 14 weeks, 25 weeks, 1 year, and 18 months, respectively. These samples were successfully shipped to Oak Ridge and cultured there. In addition, several other sets of samples were shipped but not successfully cultured due to delays en route. The first set of samples included one from a man later estimated to have received about 1 rad. Subsequent samples were obtained only from the three men receiving larger doses.

The leukocyte technique is extremely suitable for human chromosome aberration analysis. Peripheral blood samples are readily obtained. Since it is known that the cells which later divide and are scored in leukocyte cultures are in the pre-DNA-synthesis (G_1) stage while they are in the circulation, the problem of cell stage sensitivity differences is avoided. Because the cells do not start dividing until the second culture day, and do not undergo any second divisions until at least the fourth day under our culture conditions, one can be sure of obtaining a sample of cells from the culture which are in their first post-irradiation division. This is particularly important because some aberrations are lost at the first division, and a sample of cells containing second or later post-irradiation divisions would yield an inaccurate measure of chromosome breakage in vivo. Previous work with this system has shown that spontaneous chromosome type aberrations occur rarely, if at all, either in culture or in the circulation,

although spontaneous chromatid type aberrations are relatively frequent. It is thus possible to be sure that virtually all of the chromosome type aberrations in the leukocytes of irradiated subjects were induced in vivo by the irradiation.

Two scoring methods are being used: visual inspection for aberrations, and karyotype analysis. Visual scoring includes counting the chromosomes, noting breaks, dicentrics, etc., and checking the form of the more readily identified chromosomes of the human set. This procedure will not detect certain more subtle alterations. Karyotype analysis, in which the chromosomes from an enlarged photomicrograph of the cell are paired and identified, is necessary to correct this deficiency.

Results to Date

We have so far completed the visual scoring of all of the successful samples through the 18-month set from the three "high dose" cases. In addition, the single sample from the man receiving about 1 rad has been partially scored. The results are shown in Table 1. The dose estimates were made from the physical description of the Recuplex accident prepared by W. C. Roesch, et al. The chromatid aberration frequencies are, as expected, not different from those seen in samples from unirradiated individuals. Neither does the frequency of cells with chromosome numbers other than the normal human diploid number of $2n = 46$ seem to be significantly elevated above that found in control material. Only one ring chromosome was observed in any of the samples. The column "Other" contains mainly cases of symmetrical translocation, which result in changes in the length of readily identified chromosomes. This category was excluded in calculating the total breakage values, as has been done in previous work, on account of the subjective nature of their determination. In the breakage totals each dicentric was counted twice, because it takes two breaks to produce this aberration. In all samples from the first four weeks, the fragments produced along with a dicentric were invariably present in the cell. In the 6-week and 14-week samples, however, dicentric chromosomes began to appear without the expected fragments. Thus, at 6 weeks only one (from individual #1) of the four dicentrics seen had accompanying fragments. In this sample there was also a tricentric chromosome, which was also without fragments. In the 14-week samples, two of the three dicentrics observed lacked fragments. These findings suggest that the peripheral leukocytes scored by our technique had not yet divided in vivo at four weeks, but had begun to do so by six weeks after irradiation.

As mentioned previously, the samples obtained at one week were unsatisfactory. The 44-hour sample was not scored because the preparations were poor, and, as the results from the 2- and 4-week samples were consistent with there being no change in the observed aberration frequency over this period, the extra labor of scoring these samples was judged to be unprofitable.

Karyotype analyses have been completed for all of the successful samples. The results are shown in Table 2. Unfortunately, several of the samples are quite small. Spreading of the mitoses in these samples, while adequate for visual scoring, did not permit more karyotypes to be constructed. All of the karyotypes from #23 who was estimated to have received the lowest dose and who showed the fewest aberrations in visual scoring, were normal. In the 4-hour samples, both #17 and #1 had a symmetrical translocation. Deletions without fragments were found in the 2-week sample from #17 and in the 4-week sample from #1. This finding suggests that there is some peripheral leukocyte replacement by cell division during the first 4 weeks after irradiation.

Translocations found in the 4-week sample from #1, in the 6-week sample from #23 and in the 3 1/2-month sample from #17 appeared to be examples of the same aberration in different cells. This, of course, implies cloning of cells with aberrations. This phenomenon has been noted in peripheral leukocytes from men exposed in the Y-12 criticality accident. In none of the present cases did aberrations which could have been the same appear in cells from samples obtained at different post-irradiation times.

Interpretation

The results shown in Table 1 suggest that no change occurs in the aberration frequency in the leukocytes from irradiated individuals over the first 4 weeks. There is no way of telling, however, whether the cells drawn in the later samples were in the peripheral circulation at the time of the accident. They could equally well represent cells that were part of a solid tissue which had later, perhaps, differentiated and been released into the circulation. If this is true, however, they must have had the same radiosensitivity as the circulating cells. Also, it is certain (from the presence of fragments in the visually scored samples) that most differentiation that takes place does so without cell division. The karyotype analyses, on the other hand, show that at least a few cells are replaced by cell division. Further investigation of the accident cases will doubtless elucidate the kinetics of this process.

Because we have previously obtained information from the X irradiation of freshly drawn human blood, it is possible to make some rough dose estimates from the observed aberration rates. Such estimates may be made either from the deletion yield or from the dicentric yield. We have made both estimates, using the pooled data from the first three samples for each man. Since the yield of deletions is related to dose in the following manner: $\underline{Y} = \underline{a} + \underline{bD}$, where $\underline{Y}$ = yield, $\underline{a}$ = the spontaneous deletion rate, $\underline{b}$ = the coefficient of deletion production per rad, and $\underline{D}$ = the dose; and, since we have measured $\underline{a}$ to be 0.0025 and $\underline{b}$ (for X rays with a hvl of 2 mm Cu) to be 0.0011 per cell per rad, the dose is given by:

$$\underline{D} = \frac{\underline{Y} - 0.0025}{0.0011}$$

Dicentrics follow the expression $\underline{Y} = \underline{cD}^2$, where $\underline{c}$ is the coefficient of dicentric production per rad² (the measured spontaneous rate is zero), whence:

$$\underline{D} = \sqrt{\frac{\underline{Y}}{0.52 \times 10^{-5}}}$$

The results of our calculations are given in Table 3. It will be seen that, if the physical dose estimates are correct, and if the neutron RBE is of the order of 5, as is suggested by other evidence, the dicentrics seem to provide the better of the two types of estimate. Unfortunately, the dicentric rate is low enough to have a large standard error. This method would be more accurate, theoretically, if the doses were larger. Case #1 appears to have received a relatively inhomogeneous dose, which would be expected to yield abnormally high dose estimates from dicentric frequency. This is borne out, in a general way, by the comparison between the deletion and the dicentric estimates for the three men.

The data available for two-hit aberrations induced by fast-neutron irradiation of both *Tradescantia* microspores and human leukocytes suggest that a better dose calculation for cases of mixed gamma and neutron irradiation might be made from the expression:

$$\underline{Y} = \underline{aD_n} + (0.45 \times 10^{-5}) \underline{D_\gamma}^2$$

where a is the coefficient of dicentric production by neutrons. Dicentrics are a linear function of neutron dose in Tradescantia and in human leukocytes, at least up to 2.5 Mev. The calculations of the value of a are given in Table 4. It must be remembered that inhomogeneity of gamma dose will lead to an overestimate of the dicentric yield from the neutron component of the irradiation. Since individual #1 is supposed to have received an inhomogeneous dose, it is apparent that the values of a calculated for the three individuals are in excellent agreement.

It is obvious that further work on these and other cases will be necessary in order to properly evaluate the use of chromosome aberrations in peripheral leukocytes as a useful "biological dosimeter." The present data, however, are extremely valuable already, as they provide one first direct quantitative measurement of the sensitivity of human chromosomes to ionizing radiation.

TABLE 1

Chromosomal aberrations in the blood of men irradiated in the "Recuplex" criticality accident of April 7, 1962 at Hanford, Washington.

One hundred cells scored for each of the samples
unless otherwise indicated.

Case	Estimated Dose (rads)	Time of Sampling	Chromatid Aberrations	Chromosome-type Aberrations				Breaks ^b (%)
				2 $\neq$ 46	Deletions	Dicentrics	Other ^a	
#23	12.0*	4 hours	4	3	9	0	0	9
		2 weeks	1	3	5	1	0	7
		4 weeks	0	6	4	0	0	4
		6 weeks	1	6	1	0	5	1
		3 1/2 months	1	6	1	0	2	1
		6 months	--	--	--	--	--	--
		1 year	--	--	--	--	--	--
		1 1/2 years	0	1	0	0	2	0
#17	22.5*	4 hours	6	4	15	1	0	17
		2 weeks	0	6	4	2	1	8
		4 weeks	0	5	9	1	2	11
		6 weeks ^c	1	4	0	1	2	4.6
		3 1/2 months	1	10	0	1	1	2
		6 months ^d	1	5	5	1	0	6.8
		1 year	2	15	9	1	3	11
		1 1/2 years	1	9	3	0	0	3
#1	47.0*	4 hours	4	5	6	3	1	12
		2 weeks	1	6	8	4	0	16
		4 weeks	3	5	10	3	0	16
		6 weeks	1	6	2	4 ^e	6	12
		3 1/2 months	1	10	8	2	3	12
		6 months ^f	0	1	0	0	0	0
		1 year	3	8	5	3	2	13 ^g
		1 1/2 year	2	10	2	0 + 1 ring	0	4

^aPericentric inversions, symmetrical translocations, etc.

^bDeletions + twice the dicentrics; inversions, etc., are excluded because of the subjective nature of their determination.

^c43 cells scored. ^eone tricentric. ^g1 ring included.

^d103 cells scored. ^f61 cells scored.

* Refer to Table 4, Editor's note.

TABLE 2

Karyotype analyses of apparently normal cells from the blood of men irradiated in the "Recuplex" criticality accident of April 7, 1962 at Hanford, Washington.

Case	Sample	Cells Examined	Normal	Inversion	Deletion	Translocation	Abnormal Cells (%)
#23	4 hours	4	4	0	0	0	0
	2 weeks	6	6	0	0	0	0
	4 weeks	10	10	0	0	0	0
	6 weeks	11	7	0	0	4 ^a	44
	3 1/2 months	7	6	0	1	0	14
	6 months	--	---	--	--	--	--
	1 year	--	--	--	--	--	--
	1 1/2 years	10	9	0	0	1	10
#17	4 hours	7	6	0	0	1	14
	2 weeks	10	8	0	1	1	20
	4 weeks	9	9	0	0	0	0
	6 weeks	6	5	0	1	0	16
	3 1/2 months	13	10	0	0	3 ^b	23
	6 months	13	12	0	1	0	8
	1 year	6	5	0	0	1	16
	1 1/2 years	11	11	0	0	0	0
#1	4 hours	2	1	0	0	1	50
	2 weeks	4	4	0	0	0	0
	4 weeks	11	8	0	1	2 ^c	27
	6 weeks	8	8	0	0	0	0
	3 1/2 months	3	3	0	0	0	0
	6 months	8	8	0	0	0	0
	1 year	1	1	0	0	0	0
	1 1/2 years	8	8	0	0	0	0

^aAll four appeared to be the same.

^bTwo appeared to be the same.

^cBoth appeared to be the same.

TABLE 3

Dose estimates for the men involved in the "Recuplex" criticality accident
of April 7, 1962 at Hanford, Washington.

Biological estimates based on pooled data for the first four weeks.

Individual	Physical Estimate (rad)	Deletion Frequency	Dose (rad) Estimate from Deletions ¹	Dicentric Frequency	Dose (rad) Estimate from Dicentrics ²
#23	12.0*	0.006	52.3	0.003	25.2
#17	22.5*	0.093	82.3	0.010	43.8
#1	47.0*	0.080	70.4	0.033	80.9

$$^1\text{From } \underline{Y} = 0.0025 + 0.0011\underline{D}; \underline{D} = \frac{\underline{Y} - 0.0025}{0.0011}$$

$$^2\text{From } \underline{Y} = 0.52 \times 10^{-5} \underline{D}^2; \underline{D} = \sqrt{\frac{\underline{Y}}{0.52 \times 10^{-5}}}$$

* Refer to Table 4, Editor's note.

TABLE 4

Average dicentric frequencies and neutron component estimates for men
irradiated in the "Recuplex" criticality accident.

	Individual		
	#23	#17	#1
Gamma exposure (r)	13	23	63
Conversion factor to average gamma dose	0.67	0.50	0.35
Average gamma dose $\bar{D}_\gamma$ (rads)	8.7	11.5	22.0
Neutron dose estimate $\bar{D}_n$ (rads)	3.3	11.0	25.0
Average dicentric yield ($\bar{Y}$)	0.003	0.01	0.033
Neutron coefficient of dicentric production ($\bar{a}$)	0.81×10^{-3}	0.86×10^{-3}	1.31×10^{-3}

* Editor's note: The conversion factors used here take into account attenuation of the dose by tissue absorption and the variation of the dose due to the inverse square law, considering the source as a point source. The dose estimates for gamma radiation used elsewhere in the document are at the body surface, facing the source near the center of that surface.

AMINO ACID EXCRETION

J. W. Howland, M. D., Frank Ganis, Ph. D., M. W. Hendrickson
University of Rochester School of Medicine and Dentistry
Rochester, N. Y.

Method of Examination

Proportional aliquots (5×10^{-3} times the total 24-hour volume) of the urine specimens were taken and diluted to a common volume. This allowed for a comparative analysis of the daily patterns. Twenty-five microliters of each urine were applied to Whatman #1 filter paper strips with each day in sequence.

Quantitative analysis was accomplished by using a two phase descending solvent system, butanol: acetic acid: water (4:1:5), employing a staggering of time intervals of development. After development, the chromatograms were stained using a ninhydrin reagent mixture which provides a polychromatic differential between the amino acids. The urinary amino acid patterns of the Hanford patients were visually compared to the patterns of a large group of normal individuals and also to graded concentrations of amino acid standards.

Results

The urinary amino acid patterns of the Hanford casualties fell within the range of those in normal urine. The excretion patterns of the patients were studied with particular interest in the following amino acids: cystine, histidine, proline, tryptophan, glycine, serine and betaaminoisobutyric. These amino acids have been noted in abnormal concentration in studies of other human radiation injuries. No significant change in the excretion of these amino acids by the Hanford casualties was observed.

STUDIES ON GONADAL FUNCTION FOLLOWING THE
RECUPLEX CRITICALITY ACCIDENT

C. Alvin Paulsen, M.D., Associate Professor of Medicine
Adelina deSouza, M.D., Senior Fellow in Medicine
University of Washington School of Medicine,
Seattle, Washington

In order to assess gonadal function consequences of their exposure to irradiation the following studies were carried out in three of the men involved:

- (1) Testicular histology
- (2) Seminal fluid examination
- (3) Urinary gonadotrophin excretion
(general gonadotrophin and LH assays)
- (4) Urinary estrogen excretion
- (5) Chromosomal studies of testicular tissue cultures

Testicular Histology

Four days after the accident the senior author interviewed and examined Employees #1, #17 and #23 to determine the status of their gonadal function "prior" to the accident. Employee #17 had undergone a bilateral vasectomy several years previously, so that seminal fluid analyses were not possible. Otherwise, his testicular function was considered to be normal. Employee #1 was also considered to be normal and his wife was in the last trimester of gestation. Employee #23 was single and also exhibited normal testicular function.

Examination of the testicular biopsy specimens obtained from Employee #1 (Figure 1) and Employee #23 on April 12, 1962 revealed a normal histologic pattern. All germinal elements were present and Leydig-cell morphology was normal. A testicular biopsy was attempted in Employee #17 but cancelled when he experienced a mild vagal reaction. Past history revealed previous episodes of this nature during minor surgical procedures.

Approximately eight months later, on December 4, 1962, a repeat testicular biopsy specimen was obtained from Employee #1 (Figures 2 & 3). Microscopic examination revealed a varied pattern of damage. Some of the seminiferous tubules were devoid of germinal epithelium and were populated by sertoli-cells only. Others showed a minimal to moderate reduction in germinal cells, whereas other tubules demonstrated essentially normal spermatogenesis. The tubular membranes showed very little in the way of sclerosis and hyalinization, even those containing no germinal epithelium. Leydig-cells were considered to be normal in all respects.

At this same time, a testicular biopsy specimen was obtained from Employee #17 (Figure 4). Microscopic examination revealed minor deviations from normal. These consisted of reduced germinal elements, particularly in the more mature stages of spermatogenesis, and a greater degree of tubular sclerosis. In view of the fact that we did not have a "control" biopsy specimen for comparison, it is not possible to relate these changes to his exposure to irradiation.

Since Employee #23 did not show any significant changes in seminal fluid analyses (except those associated with a temporary episode of bilateral epididymitis, following his first biopsy) a second biopsy was not performed.

Seminal Fluid Examinations

Serial seminal fluid specimens were obtained from Employees #1 and #23 for evaluation (Table 1). As mentioned previously, there was a temporary reduction in Employee #23's sperm count but this was considered due to his post-biopsy epididymitis. When this cleared, the seminal fluid returned to normal and remained so.

On the other hand there was a significant reduction in Employee #1's sperm count nine weeks after the accident and by the twenty-seventh week, reached a low of 0-2 sperm per high power field. Thereafter, the sperm counts increased and were virtually normal by the 46 - 49th weeks after the accident. It was not possible to accurately assess motility due to transportation of the seminal fluid.

Urinary Gonadotrophin Excretion

Serial determinations of urinary gonadotrophin excretion were made in each man. (Table 2)

A general or total gonadotrophin assay which measures both Follicle-Stimulating-Hormone (FSH) and Luteinizing-Hormone (LH) was carried out in each instance. At various intervals LH assays were performed. The latter assay is considered to be a more specific barometer of Leydig-cell function in a reciprocal sense. The normal values for adult males varies from 0.15 to 0.9 mg-eq. pergonal-25 for both assay methods.

The general urinary gonadotrophin titers for Employee #17 and Employee #1 were normal initially, but increased to pathologic levels by the seventh week (Employee #17) and the eighteenth week (Employee #1). Employee #1's gonadotrophin titers returned to normal levels by the 35th week and Employee #17's titers were normal at the 68th week. These changes reflect impaired gonadal function which developed after exposure to irradiation with a return towards normal later in the follow-up. Aside from an isolated elevated LH titer for Employee #1 at the fourteenth week, LH excretion titers were normal for both Employee #1 and Employee #17. It is felt that this elevated value may have been an assay error.

Both the general gonadotrophin and LH titers remained normal for Employee #23. This finding corroborates our previous conclusion, based on clinical and seminal fluid observations, that his testicular function was not altered as a consequence of the criticality accident.

Urinary Estrogen Excretion

Urinary estrogen excretion titers are considered by us as a somewhat better index of Leydig-cell function than urinary 17-ketosteroid excretion levels. Mainly, this is based on the fact that the major portion of the urinary estrogen pool is derived from testicular rather than adrenal cortical metabolism. This is in direct contrast to the urinary 17-ketosteroid pool where approximately 75% is derived from adrenal cortical metabolism. Using our assay method which measures the total biologically active estrogens, the normal range for adult males is from 0.4 to 3.0 µg. equivalents estradiol benzoate per twenty-four hours.

For each of the men, urinary estrogen excretion was normal and remained so with the exception of one observation for Employee #1 at the twenty-seventh week when no urinary estrogens were detected. It is tempting to correlate this with his clinical complaint of transient impotence, but further evidence would be required to conclude that his Leydig-cell function had been temporarily impaired. In view of the vast animal data that shows the Leydig-cells are resistant to the effects of ionizing irradiation, this is considered unlikely.

Chromosomal Studies

Tissue culture of testicular material obtained from the December 4, 1962 biopsies on Employees #1 and #17 was carried out for chromosomal studies. Analyses of the metaphase plates were scanned for abnormalities. Chromatid deletion was observed in Employee #17's preparation and a chromatid gap was noted in Employee #1's preparation. Although these types of abnormalities are seen following irradiation and/or as an artifactual consequence of in vitro culture, control studies were not made and thus proper evaluation of these findings was not possible.

Summary

Our studies indicate that Employee #1 who was exposed to a gonadal dose of 28 r (gamma) and 19 - 24 rads (neutron) sustained damage to his spermatogenesis. This was of a "transient" nature in that his seminal fluid and urinary gonadotrophin excretion titers returned to normal within twelve months after the accident. Some residual damage was present with respect to his testicular morphology as noted in the biopsy specimen obtained eight months following exposure. Employee #17 who was exposed to a gonadal dose of 17 r (gamma) and 8 - 10 rads (neutron), sustained lesser damage which also returned to normal limits within fifteen months after exposure. Due to our inability to study the seminal fluid in Employee #17, our evaluation was less precise. Finally, Employee #23, who was exposed to a gonadal dose of 13 r (gamma) and 3 rads (neutron) did not sustain any significant abnormality in his gonadal function as a consequence of the criticality accident.

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TABLE 1
SEMINAL FLUID EXAMINATION

DATE	WEEKS AFTER EXPOSURE	EMPLOYEE #1		EMPLOYEE #23	
		VOLUME (Ml.)	Million/ml.*	VOLUME (Ml.)	Million/ml.
4/11/62	4 (days)	4.4	182	3.0	391
5/2/62	4	4.8	199	0.5	97
5/23/62	7	5.0	65	--	--
6/4/62	9	2.8	45	--	--
7/10/62	14	4.0	14.1	4.5	2.9
8/8/62	18	--	1.2	--	155
9/12/62	23	--	2.5	--	150
10/10/62	27	--	0-2/hpf	--	126
11/14/62	32	--	--	7.0	119
1/10/63	40	4.0	20	3.2	107
2/14/63	45	--	--	2.5	190
2/21/63	46	4.0	51	--	--
3/14/63	49	4.8	58	3.2	107
4/11/63	53	4.0	171	3.0	212
5/9/63	57	4.2	57	4.5	196
7/25/63	68	4.2	77	3.4	277
10/10/63	84	2.5	103	3.0	127
12/7/63	94	5.5	78	3.0	201

* Normal range is 50 to approximately 400 million per ml.

TABLE 2

URINARY GONADOTROPHIN EXCRETION

DATE	WEEKS AFTER EXPOSURE	EMPLOYEE #1		EMPLOYEE #17		EMPLOYEE #23	
		GENERAL ^{*1}	LH ⁺²	GENERAL [*]	LH ⁺	GENERAL [*]	LH ⁺
4/14-6/62	1	0.30	0.43	0.74	0.58	0.30	0.40
4/30-5/1/62	4	0.43	0.46	0.60	0.44	0.54	0.44
5/21-2/62	7	0.94		1.62	0.74	0.44	
7/9-10/62	14	0.80	2.0	1.23		.56	0.53
8/7-8/62	18	1.1		0.95		0.7	
9/11-2/62	23	1.57	0.50	1.00	0.44	0.60	0.54
10/8-10/62	27	0.96	0.47	0.84	0.44	0.61	0.44
12/3-6/62	35	0.60		1.29		--	
1/8-9/63	40	0.60	0.44	N.G.	0.16	0.51	
2/12-16/63	45	0.8		1.03		0.30	
3/12-3/63	49	N.G.		--		--	
4/9-11/63	53	N.G.		--		0.30	
5/7-9/63	57	0.6		0.95		0.57	
7/23-5/63	68	N.G.		0.60		0.30	
10/8-9/63	84	0.3		0.6		0.3	
12/5-6/63	92	0.3				0.5	

*General gonadotrophin titers, which include measurement of FSH and LH, were determined by bioassay and expressed as mg.-eq. Pergonal-25/24 hours. The immature female rat (Sprague-Dawley strain) was used and the paired ovarian weight served as the assay end-point.

+LH or Luteinizing Hormone titers were determined by bioassay in immature hypophysectomized male rats. The ventral prostate weight served as the assay end-point and the values expressed as mg.-equivalents Pergonal-25/24 hours.

¹Normal range is 0.15 to 0.9 mg.-eq. Pergonal-25/24 hours.

²Normal range is 0.15 to 0.9 mg.-eq. Pergonal-25/24 hours.

TABLE 3

URINARY ESTROGEN EXCRETION*1

(ug-eq. estradiol benzoate/24 hr.)

DATE	WEEKS AFTER EXPOSURE	EMPLOYEE #1	EMPLOYEE #17	EMPLOYEE #23
4/14-5/62	1	0.9	0.8	1.5
4/30-5/1/62	4	0.8	0.5	1.6
5/21-2/62	7	0.9	0.7	--
7/9-10/62	14	0.6	0.5	1.5
8/7-8/62	18	0.9	0.6	1.8
9/11-2/62	23	--	0.3	1.5
10/8-10/62	27	<0.2	--	2.0
11/6-8/62	31	0.6	0.4	1.4
12/3-6/62	35	1.2	0.3	--
1/8-9/63	40	0.6	0.4	2.2
2/12-4/63	45	1.2	0.7	2.0
4/9-10/63	53	1.1	--	2.3
5/7-9/63	57	1.0	0.4	0.9
10/8-9/63	84	1.1	0.9	1.0
12/5-6/63	92	0.9		Not completed as yet.

*Urinary estrogens were determined by bioassay using the uterine weight of the immature female rat as the assay end-point. The values expressed as ug-equivalents of the standard estradiol benzoate represent total estrogenic activity of the urine extracts.

1 - Normal range is 0.4 to 3.0 ug-eq. estradiol benzoate/24 hr.

FIGURE 1

Photomicrograph of the testicular biopsy specimen obtained from patient #1 six days following radiation exposure (160X). Note that all germinal elements are present, indicating essentially normal spermatogenesis.

Fig. 2

Fig. 3

Photomicrograph of testicular biopsy specimen obtained from patient 1 eight months following radiation exposure. Note the varying degree of damage. Some tubules contain all germinal elements whereas the most severely damaged lack germinal cells. These are populated by Sertoli cells. Tubular membrane fibrosis is minimal in some areas and nonexistent in others. Although not shown here, Leydig cells appeared normal.

FIGURE 4

Photomicrograph of testicular biopsy specimen obtained from patient 17 eight months after radiation exposure. Note that the germinal elements are less in number in most tubules than normally seen; however, all stages of maturation can be seen in many tubules such as the upper tubule in this figure. Leydig cells appeared to be normal. Earlier biopsy specimens for comparison were not obtained.

DISCUSSION AND SUMMARY

W. D. Norwood, M. D.
Occupational Health Operation
Hanford Atomic Products Operation
Richland, Washington

A criticality accident in a plutonium waste chemical facility at Hanford resulted in the exposure of three employees to doses of neutrons and gamma radiation estimated to be as follows:

Employee #1

	<u>Gamma (r)</u>	<u>Neutrons (rads)</u>	<u>Assumed R.B.E. (Quality Factor) for Neutrons</u>	<u>Total (rems)</u>
Whole Body	63	23 - 30	2	109 - 123
Eyes	90	42 - 54	7	384 - 468
Gonads	28	19 - 24	10	218 - 268

Employee #17

	<u>Gamma (r)</u>	<u>Neutrons (rads)</u>	<u>Assumed R.B.E. (Quality Factor) for Neutrons</u>	<u>Total (rems)</u>
Whole Body	23	9 - 12	2	41 - 47
Eyes	28	11 - 14	7	105 - 126
Gonads	17	8 - 10	10	97 - 127

Employee #23

	<u>Gamma (r)</u>	<u>Neutrons (rads)</u>	<u>Assumed R.B.E. (Quality Factor) for Neutrons</u>	<u>Total (rems)</u>
Whole Body	13	3	2	19
Eyes	13	3	7	34
Gonads	13	3	10	43

The primary sources of information concerning the exposure of these employees were their personnel dosimeters for the gamma rays and the whole body counts and blood activation analyses for the neutrons. Secondary methods were used to help in estimating the probable range of accuracy of the primary results. The estimated degree of accuracy was considered to be satisfactory and offered a good opportunity to study the effects of such doses on normal humans.

Initial Clinical and Laboratory Observations

Study in the hospital of the three employees for a period of 8 days revealed no signs or symptoms of injury attributable to radiation except fear. Early fears were allayed in about five hours when the employees could be assured that the doses were such that serious consequences were not to be expected.

Blood counts were within normal ranges and deviations in morphology were observable only by using research techniques. Some 27 different blood chemistry examinations failed to reveal any significant abnormality.

LONG TERM AND SPECIAL STUDIES

Blood Counts

Study of values of blood counts over a period of many months and comparison with those observed at annual examinations prior to the accident failed to reveal any abnormality except for a slight drop in the absolute lymphocyte count immediately following the accident for employee #1. The absolute lymphocyte count for several years before and 8 to 12 months after the accident averaged 3600 while the average during the first week following the accident was 2290. The drop of 36% is considered to be statistically significant, though both values are within normal limits. The leukocyte count of employee #1 was unstable during the first post exposure week, a change compatible with mobilization of leukocytes from tissue stores, especially from bone marrow.

Morphologically Aberrant Blood Cells

By use of special research techniques it was demonstrated that the employees showed relatively low levels of the cytological stigmata of radiation injury. Changes observed in varying degree in the three employees were (1) changes in the nuclear structure of the granulocytic series in blood and bone marrow; (2) increased immaturity of monocyte series as well as mild transient monocytosis; (3) binucleate lymphocytes and lymphocytes with nuclear fragments; (4) increased numbers of plasmacytoid early mononuclear cells; (5) the occurrence of nucleated red cells in peripheral blood and (6) chromatin and chromosome abnormalities in the marrow nucleated red cells.

Bone Marrow

Histological sections and smears of bone marrow were taken 1, 7, 16 and 30 days after the exposures. These revealed minor changes in employee #1, very minor changes in employee #17 and no changes in employee #23.

Leukocyte Chromosome Aberrations

This was the first time that a study of the effects of measured doses of radiation on human leukocytes circulating within the body had been made, and it facilitated progress in the use of somatic chromosome aberrations as a biological dosimeter. Blood was collected at 4 hours, 2, 4 and 6 weeks, 3-1/2 and 6 months, and 1 and 1-1/2 years. Leukocytes were separated, cultured, and treated to stimulate mitosis. They were fixed on the third day after inoculation of the cultures and mounted for study. The samples of cells from cultures during the initial period were all in their first post-irradiation division, so no aberrations were lost. Scoring was by visual inspection under low magnification for more obvious aberrations. Less obvious abnormalities were detected by close study of suitable cells, using enlargements of photographs which were used to construct "paste up" karyotypes. There was no increase in aberration frequency in the leukocytes from irradiated individuals during the first four weeks. The findings suggest that peripheral leukocytes scored by the above technique had begun to divide in vivo by six weeks after irradiation.

The estimate of rad dose based on frequency of dicentrics correlated fairly well with the physical estimate of rad dose for employees #1 and #17 and less well for employee #23. Further work on these and other cases will be required in order to properly evaluate the usefulness of chromosome aberrations in peripheral leukocytes as a biological dosimeter. The present data are valuable in providing a first direct quantitative measurement of the sensitivity of human chromosomes to ionizing radiation.

Amino Acid Excretion

Twenty-four hour samples of urine were collected after the exposures and quantitatively analyzed for excretion of the following amino acids: cystine, histidine, proline, tryptophan, glycine, serine and betaaminoisobutyric acid. These amino acids have been found to be elevated in previous accidents in which the radiation doses were higher than those sustained by our employees. There was no significant change in the excretion of these amino acids.

Gonad Effects

To evaluate the effects of the estimated doses of radiation on gonad function, the following studies were performed on the three employees:

- (1) Testicular histology.
- (2) Seminal fluid examination.
- (3) Urinary gonadotropin excretion.
- (4) Urinary estrogen excretion.
- (5) Chromosomal studies of testicular tissue cultures.

These studies indicated that employee #1 sustained gonad damage which resulted in impaired spermatogenesis, histologic damage and increased gonadotropin excretion. That the damage was transitory was indicated by a return to normal of seminal fluid and gonadotropin excretion titres within twelve months following the exposure. Employee #17 sustained lesser damage to gonads and gonadotropin titers returned to normal within fifteen months. Employee #23 sustained no demonstrable abnormality.

Eye Effects

To date there have been no changes in the lenses of any of these employees. The dose to the lens of employee #1 is below the threshold value for damage by X-rays set by the National Academy of Sciences (600 to 1000r). The lenses will be carefully examined on a routine basis as long as this employee is available for examination, though the possibility of cataract resulting from an exposure of this magnitude appears to be small.

SUMMARY

Extensive clinical and laboratory studies covering a period of twenty-one months have failed to reveal harmful effects to three employees exposed to whole body doses of mixed neutron and gamma radiation ranging from 19 to 123 rems. Harmful effects refer to "any body injury, disease, or impairment, except where such condition is transitory, infrequent, or of short duration and does not endanger persons so affected", as defined by the National Committee on Radiation Protection and Measurements. Special research techniques and laboratory studies have revealed various changes which are not considered to be harmful in the present state of our knowledge. Observations of these employees will be continued.

Blood counts were within normal ranges and deviations in morphology were observable only by using research techniques. Some 27 different blood chemistry examinations failed to reveal any significant abnormality.

LONG TERM AND SPECIAL STUDIES

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