

Mr. H. R. [unclear]

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CRITICALITY ACCIDENT AT THE Y-12 PLANT *

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On 16 June, 1958, a criticality accident occurred at the Y-12 plant in Oak Ridge.² The name "Y-12" is simply to identify one of the facilities at Oak Ridge and has no particular meaning. This plant is federally owned and operated by the Union Carbide Corporation under contract with the government as represented by the United States Atomic Energy Commission. The accident occurred in an area designated for the salvage of enriched uranium. Criticality developed when some enriched uranium was allowed to drain into a 55-gallon drum, which was intended to contain only water.

This took place about 2.00 p.m. At the time of the initial nuclear burst one of the operators had just noticed yellow-brown fumes arising from the liquid in the 55-gallon drum. He stepped back and within a few seconds noted an odd bluish flash, which he did not understand. Almost immediately thereafter the radiation evacuation siren was heard. The five employees who were nearest the drum and three others at a slightly greater distance all left the room very promptly. The man closest to the drum fortunately chose the exit that would most rapidly remove him from the nuclear reaction. It was estimated that it took from 3 to 5 seconds for the warning sirens to reach a sufficient sound level to be easily heard. The high level of neutron and gamma radiation persisted for from five to fifteen minutes, but personnel were quickly evacuated from the area of high exposure.

Five men who had received the highest dose were admitted to the Medical Division hospital at 1.00 a.m. on the following day. Between the time of

* The information presented in this report represents the work of a large number of staff members of the Medical Division of the Oak Ridge Institute of Nuclear Studies with additional support and help from several organizations outside the Medical Division.
¹ Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee, under contract with the United States Atomic Energy Commission.
² Detailed accounts of this accident will be found in the final report published by the Union Carbide Nuclear Company (1958) and in the medical report issued by the United States Atomic Energy Commission (Brucer, 1959).

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the accident and their admission to the hospital they had been studied in a whole-body counter and blood samples had been drawn for radioactive sodium determinations.

Dosimetry

The initial estimates of radiation dose were exceedingly high, within the lethal range, but during the three days following the accident, refinements were developed and rather accurate dose estimates were made available.

By means of a mock-up experiment it was possible to reproduce the accident and to establish the radiation doses quite accurately. A donkey was exposed to radiation and the sodium activation in its blood used as a basis for comparison with the measurements of sodium activation in the blood of the exposed patients.

Table 1 gives the ^{24}Na levels and radiation doses determined by this method in the 5 men admitted to hospital. It will be seen that the exposures varied from 236 to 365 rad. Three other men had exposures of 23-69 rad.

TABLE 1
SODIUM-24 LEVELS AND RADIATION DOSES IN THE FIVE EXPOSED PERSONS

Occupation	Age (years)	^{24}Na (microcuries per ml whole blood) ^a	Radiation dose	
			rad	rem ^b
Chemical operator	40	5.8×10^{-1}	365	461
Electrician	32	4.3×10^{-1}	270	341
Maintenance mechanic	39	5.4×10^{-1}	339	428
Electrician	51	5.2×10^{-1}	327	413
Maintenance mechanic	35	3.7×10^{-1}	236	298

^a Corrected for the time of the accident.

^b Assuming a relative biological efficiency of 2 for neutrons.

In addition to measurements made in the whole-body counter at the Oak Ridge National Laboratory, the patients were studied with a linear scanner at the Medical Division. Fig. 1 shows the linear scanner. Fig. 2 is an example of scans obtained from one of the patients. There was no surface contamination; all the activity shown is believed to be due to induced radioisotopes resulting from the neutron bombardment. Calculations indicate that the amount of radiation absorbed from these short-lived radioisotopes would not contribute significantly to the total radiation dose in the patient. However, the level of activity may of course be a very important index of the total neutron dose absorbed by the patient.

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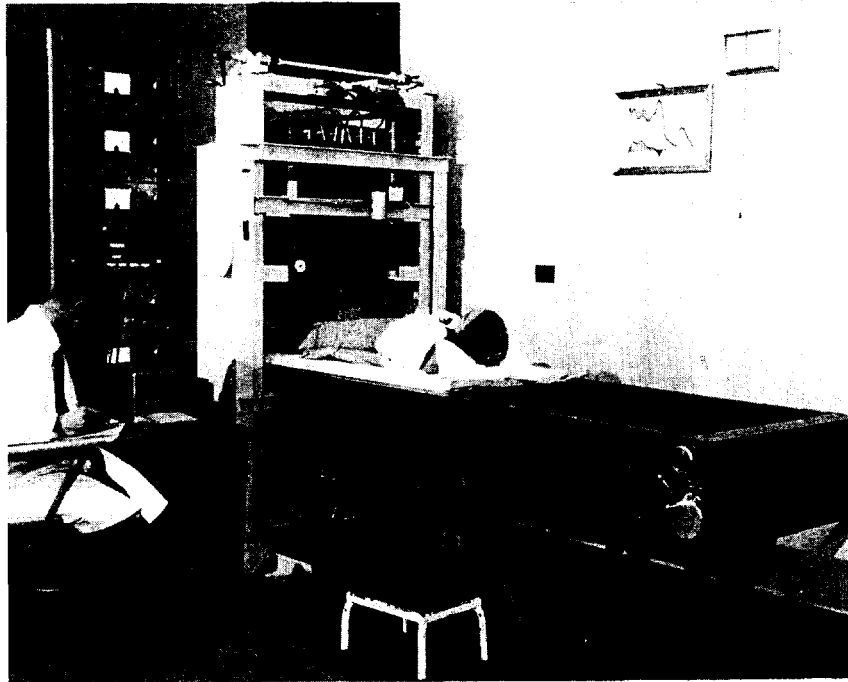


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FIG. 1

LINEAR SCANNER USED AT THE ORINS MEDICAL DIVISION HOSPITAL



Clinical Observation and Treatment

Of the 5 patients receiving the highest dose, 3 had nausea and vomiting within 2-4 hours after the accident. One became nauseated after about 5 hours but did not vomit until the second day after exposure. Another patient had neither nausea nor vomiting. On the day following the accident all patients were free from symptoms, but on the second morning, 18 June, 3 patients had nausea and vomiting, including one who had not vomited before. At this time, slight nausea was noted in the patient who initially had not had either nausea or vomiting.

Plans were made for attempting bone marrow graft therapy in these patients. Techniques for obtaining and administering aspirated marrow had previously been developed here for use in patients with leukaemia given large doses of therapeutic radiation. Potential donors were selected from the families of the accident victims and arrangements were made for them to stay in Oak Ridge until a decision on the use of marrow could be made. Some of these potential donors travelled to Oak Ridge from distant places. On the fourth day after the accident it was decided that there were good chances

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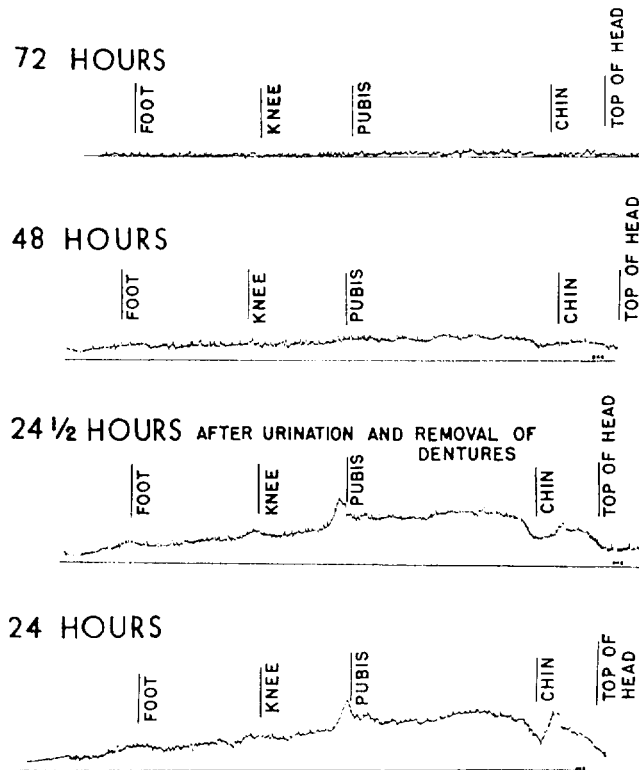
DOSED PERSONS

Radiation dose	
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270	341
339	428
327	413
236	298

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FIG. 2

LINEAR SCANS OBTAINED ON ONE OF THE FIVE PATIENTS AT DIFFERENT INTERVALS AFTER THE ACCIDENT



The two lower scans were obtained one day after the accident, the other two scans at subsequent 24-hour intervals.

for recovery of the patients without marrow therapy and plans for using marrow were abandoned. (At that time it was believed that the marrow would probably be effective only if given within a week or so after exposure.)

The patients were observed carefully but given very little medication. Two of them received courses of tetracycline for specific infections. The others had nothing more than an occasional dose of aspirin or sedative.

From the third day after the accident onward the patients were in generally good condition. Certain specific symptoms and signs developed, but none of these was very alarming. The greatest apprehension experienced by the medical staff was during the period 4-6 weeks after the accident and was based more upon laboratory findings than upon any symptoms or physical findings. Fig. 3 shows the average haematological values in the 5 patients and also gives some information about signs and symptoms.

FIG. 3
AVERAGE HAEMATOLOGICAL VALUES FOR THE 5 PATIENTS, TOGETHER WITH CERTAIN CLINICAL SIGNS AND SYMPTOMS

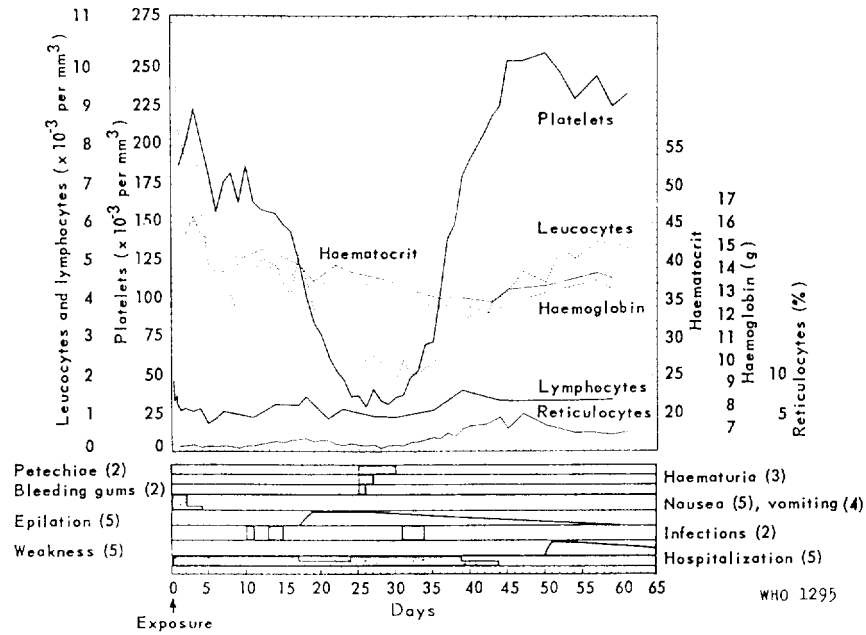


FIG. 4
PHOTOGRAPH OF THE BACK OF THE HEAD OF ONE PATIENT BEFORE AND AFTER THE DEVELOPMENT OF SIGNIFICANT ALOPECIA



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Loss of hair

On the 17th day after exposure all 5 men noticed loss of hair from the scalp. In 3 of the patients soreness of the scalp preceded the loss of hair by 2 or 3 days and lasted for several days. In 2 of the patients the loss of hair from the scalp became so extensive that a bald area was easily observable even from a distance. In both cases, the area of greatest loss was on the occiput (Fig. 4). We did not have any reason to believe that the exposures of these two men had been greater in this area and we thought that perhaps the hair loss was most severe there because the patients were lying in bed. All 5 patients had some loss or thinning of the hair all over the head and also on the body, although this was less obvious. By 44 days after the exposure the hair loss had almost stopped, but there was no evidence of regrowth. Later, regrowth occurred and it was complete by 6 months.

Fever

Temperature records are not available for the first 11 hours after the accident. Fever was not present after this except in 2 patients who had specific infections.

Diuresis

No excessive fluid output was recorded at any time. The amount of urine passed during the 11 hours immediately following exposure is not known.

Gastrointestinal symptoms

In addition to the nausea and vomiting already alluded to, one patient had vague gastrointestinal symptoms, including discomfort in the epigastrium and subscapular region, during the first 4 days after the accident. The same patient had an episode of lower abdominal pain on the 24th day after the accident. No diarrhoea was noted at any time in any of the patients. Three of the patients lost about 2 lb in weight during the first few days after the accident, but by the time they were discharged from the hospital, 44 days after exposure, all 5 showed a weight gain ranging from 3 to 13 lb.

Infections

Two patients had furuncles while they were in the hospital but these did not occur at the time of greatest marrow depression. In addition, 2 patients developed pharyngitis associated with alpha and beta haemolytic streptococci, one on the 13th day and the other on the 31st day. This last infection was the only one that developed during the period of greatest marrow depression. Both patients were treated with tetracycline and both responded promptly.

Haemorrhagic

Slight evidence of petechiae, with a minimal amount of platelets. The number of platelets had evidence of a decrease in the findings indicated.

Weakness

Two patients while they were in the hospital, however, until they were discharged from the hospital.

Haematology

The impact of the exposure to the blood count. Nuclear Studies chart, based on the same code is considered as follows:

Leucocytes

About 2 hours after the exposure the total white count rose to 22,000 per cubic millimetre, definitely within the total white count range.

Haemorrhagic tendency

Slight evidence of a bleeding tendency was noted on the 25th to 28th days. Three patients developed slight bleeding from the gums and 2 patients had petechiae, which in one case were quite plentiful. Three patients showed a minimal amount of microscopic haematuria, which would not have caused any particular comment except for the fact that it did occur at the time the platelets were most depressed. However, the patient with the largest number of petechiae did not have any red cells in the urine. Two patients had evidence of occult blood in the stools, but they were not on meat-free diets and the finding was not made during the same period as the other findings indicating a haemorrhagic tendency.

Weakness

Two patients who became somewhat anaemic complained of weakness while they were in the hospital during the 4th and 5th weeks after the accident. The symptom of weakness did not really become prominent, however, until the men began to resume their normal activities after discharge from the hospital.

Haematological Changes during the first two Months after Radiation

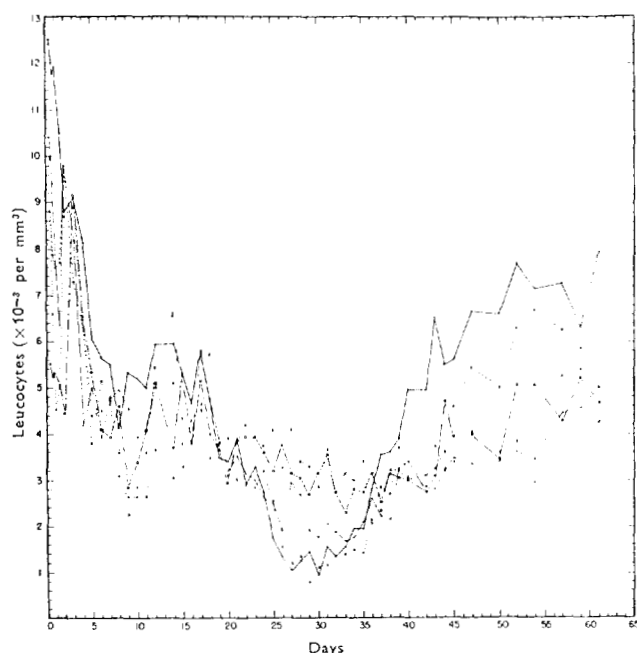
The important post-irradiation haematological values for the 5 men exposed to high doses are given in Fig. 5-9. The values charted do not include the pre-exposure base-line levels. The charts start with the first blood count done at the Medical Division of the Oak Ridge Institute of Nuclear Studies about 12 hours after the accident, except that the lymphocyte value obtained about 1½-2 hours after exposure is included. A composite chart, based upon average haematological values for all 5 men, is shown in Fig. 3. In the other figures, each patient is represented separately. The same code is used throughout. The day of the radiation exposure is considered as zero day, and the following day as No. 1.

Leucocytes

About 2 hours after exposure all the men had higher white blood counts than their normal pre-exposure averages. One had a leucocytosis of 17 350. This patient's highest pre-exposure white count had been 12 500. The total white count stayed at high normal values for 2 days and then decreased until about the 9th day. Between the 9th and 16th days the total white count rose slightly. Abnormal large and hypersegmented neutrophils contributed significantly to this cell population. From the 16th to the 22nd days, the total white cell count fell gradually from low normal to definitely subnormal levels. On about the 22nd day a more rapid fall in the total white count began, particularly in the 2 patients, who had

FIG. 5

INDIVIDUAL WHITE CELL COUNTS IN THE 5 PATIENTS AFTER THE ACCIDENT

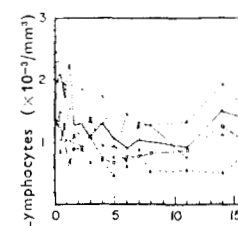


received the highest radiation dose. In these 2 men the lowest value was reached at the 29th and 30th days, and they subsequently showed a rather rapid recovery. In the 3 men exposed to slightly lower radiation doses, the lowest white cell values were reached at a slightly later time, from the 33rd to the 36th day, after which the men began to recover. During the period of lowest total white blood count, the differences among the patients were confined chiefly to differences in neutrophil levels; there was very little difference in the absolute lymphocyte count. For example, 31 days after exposure patient A had a white blood count of 1150 with 80% lymphocytes, while patient E had a count of 3150 with 31% lymphocytes. It is interesting that the 2 men who had received the highest radiation dose and whose white counts reached the lowest levels showed the most pronounced rise during recovery, and around the 50th day they had the highest white counts of the group.

Lymphocytes

During the first 48 hours the decrease in lymphocytes contributed significantly to the changes in the total white count. After that time the chief factor was the variation in the number of neutrophils.

INDIVIDUAL LYMPHOC



Most of the decrease in lymphocytes occurred within the first 48 hours, and by about the 5th day the lymphocyte levels tended to stay between 0.5 and 1.5 $\times 10^3$ per mm³. After about 30 days the lymphocyte levels tended to stay between 0.5 and 1.5 $\times 10^3$ per mm³. One patient who had received the highest radiation dose had a lymphocyte count of about 500 on one occasion during the first month. In the other patients there was no definite correlation between lymphocyte count and the severity of the late effects.

Platelets

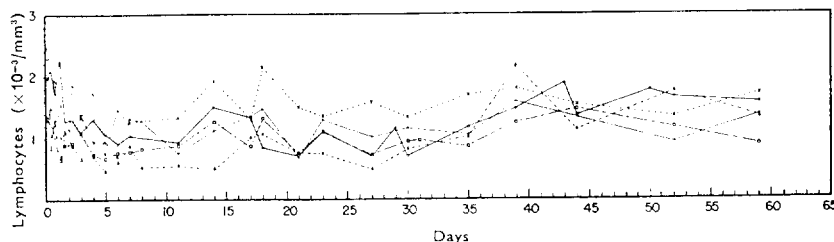
Platelets were measured by the method of Cronkite (1953). The result of the radiation was that platelet values tended to remain between 100 and 200 $\times 10^3$ per mm³. They fell progressively, reaching a minimum of about 50 $\times 10^3$ per mm³ by the 50th day. A rebound effect was noted in the two men who had received the highest radiation dose, and their platelet counts had been exposed to a rebound effect reaching 500 $\times 10^3$ per mm³ by the 50th day.

Red cell values

The haemoglobin concentration and the haemoglobin content of the red cells in these red cell values showed a correlation with the hydration of the patient. The radiation showed

FIG. 6

INDIVIDUAL LYMPHOCYTE COUNTS IN THE 5 PATIENTS AFTER THE ACCIDENT



Most of the decrease in lymphocytes occurred during the first 48 hours, to an average of about 1000, but slightly lower values were reached on about the 5th day. After the initial decrease in numbers, the lymphocyte levels tended to stay quite stationary, with a slight increase toward normal after about 30 days. The lowest lymphocyte values were reached in the patient who had received the highest radiation dose. His values fell to about 500 on one occasion and remained below 800 during most of the first month. In the other 4 patients, however, there did not appear to be a definite correlation between the degree of early lymphocyte depression and the severity of the later granulocyte depression.

Platelets

Platelets were by the counted method of Brecher, Schneiderman & Cronkite (1953). There may have been an initial increase in platelets as a result of the radiation, but there is no direct evidence on this point. The values tended to remain rather stationary until about the 15th day and then fell progressively, reaching low levels between the 25th and 35th days. The thrombocytopenia correlated with the clinical symptoms of haemorrhagic tendency noted in these patients. The lowest values were reached in the two men who had received the highest radiation dose, and the patient who had been exposed to the highest radiation dose of all showed a pronounced rebound effect reaching abnormally high platelet levels between the 40th and 50th days.

Red cell values

The haemoglobin and haematocrit determinations showed a close correlation and there was no significant change in mean corpuscular haemoglobin concentration during the period of study. Initial fluctuations in these red cell values may have been related to variations in the state of hydration of the patients. The 2 patients who received the highest dose of radiation showed definitely lower red cell values after the 20th day and

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FIG. 7
INDIVIDUAL PLATELET COUNTS IN THE 5 PATIENTS AFTER THE ACCIDENT

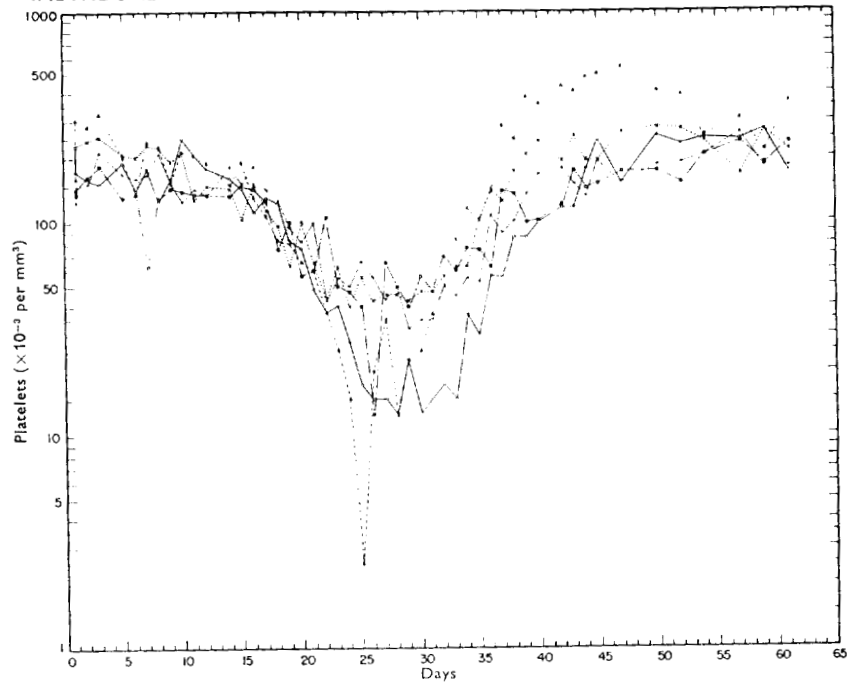


FIG. 8
INDIVIDUAL HAEMOGLOBIN VALUES IN THE 5 PATIENTS AFTER THE ACCIDENT

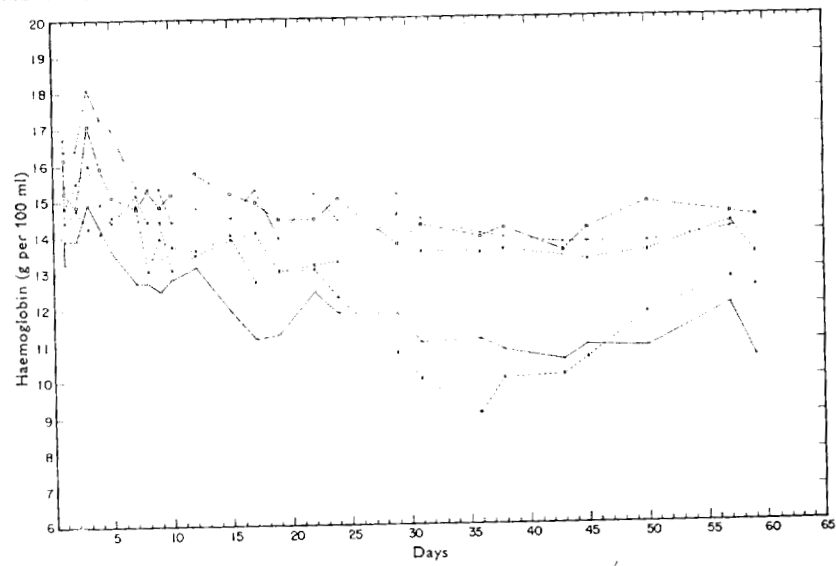
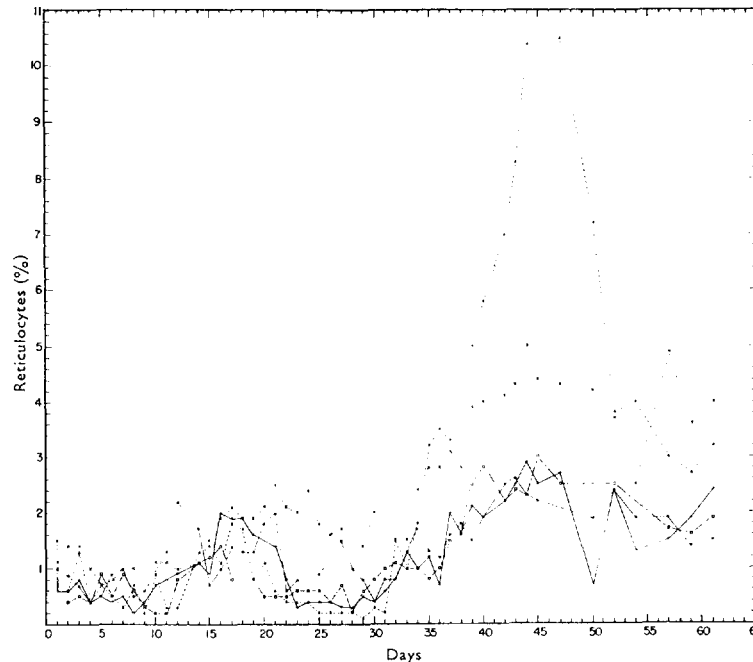


FIG. 9

INDIVIDUAL RETICULOCYTE LEVELS IN THE 5 PATIENTS AFTER THE ACCIDENT



both became significantly anaemic; the other 3 developed only a very mild anaemia. The lowest values for the red cells were reached between the 35th and 45th days. Some contribution may have been made to the anaemia by the withdrawal of significant amounts of blood for various studies.

The values for the reticulocytes were of considerable interest. There was some fall in reticulocyte levels during the first 8 days, but they never reached zero. There was an abortive rise in reticulocytes between the 13th and 25th days, and then a distinct rise after the 30th day, reaching a peak around the 45th day. The highest reticulocyte value occurred in the patient who had received the highest radiation dose.

Morphological changes in blood cells

Significant changes were seen in the blood films in the 5 patients exposed to high doses. Within the first few hours there were degenerating white cells of various types, many of them apparently granulocytes. Atypical cells made their appearance and many of these were difficult or impossible to identify. These cells never made up more than a small percentage of the total white cells, however.

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Within the first few days, young and "toxic" monocytes appeared. These abnormal monocytes persisted for many weeks. Some of them had irregular or lobulated nuclei.

Young lymphocytes and lymphocytes with dark blue cytoplasm—"irritation forms"—were present within a few days and persisted for a considerable period of time. Some lymphocytes with fissured nuclei were seen, but binucleate forms were not found among the numbers of cells counted. Occasional lymphocytes were seen with peculiar large solitary cytoplasmic bodies. There were also lymphoid and monocytic cells with endothelioid characteristics.

One of the most interesting cell types was the giant granulocyte. In addition to being very large, some of these granulocytes had hypersegmented nuclei, and some showed small nuclear projections. These cells began to appear within 3 or 4 days and were seen in all the patients about the end of the first week. Within a few days, they became less plentiful and they were rare after the first 5 weeks. During the recovery phase, toxic granulation of the neutrophils was prominent and an occasional nucleated red cell was seen.

Bone marrow

Serial studies of aspirated bone marrow were performed. The marrow was aspirated from different sites, usually from the iliac crest or posterior iliac spine. The possibility was considered of aspirating simultaneously from several different sites in the same patient to determine whether there was uniform damage to the bone marrow in various areas. However, it was believed that the radiation dose was fairly uniform and that there would probably not be any important differences in the dose to the marrow at various sites that could be shown to depend on the position of the person in relation to the source of radiation. The sites of aspiration were recorded; no important effects related to the site of aspiration were noted.

The first marrow was aspirated about twelve hours after the accident. There were no clear-cut abnormalities seen at this time. Some of the specimens seemed somewhat more cellular than normal with prominent clumps of fibrils and stromal elements. The average erythrocyte/granulocyte (E/G) ratio for all 5 specimens was about 0.4. The second bone marrow obtained two days after the exposure was quite similar; however, by this time the E/G ratio had decreased somewhat. The bone marrow samples on the 3rd and 4th days showed some mild decrease in cellularity. The E/G ratio was in the neighbourhood of 0.2 on the 3rd and 5th days; thus there was some further relative decrease in red cell precursors. Subsequently, the greatest decrease was in granulocyte forms and the ratios increased. On the 9th day total cellularity was distinctly diminished; megakaryocytes were decreased in number, and morphological abnormalities of the megakaryocytes were very striking. On the 24th day the marrows

reached a severe degree of hypocellularity and megakaryocytes were at their lowest ebb. Degenerating forms were again present. By this time, the granulocyte forms were much diminished and the E/G ratio was above 2.0. On the 39th day, the marrows were still exceedingly hypocellular. Between the 39th and 54th days, no samples were obtained, so that the marrow recovery phase is not well documented. On the 54th day cellularity appeared to be greater than normal.

Giant neutrophil forms were most prominent in the marrows towards the end of the first week and persisted beyond the second week.

At no time were the bone marrows characterized by the presence of numerous degenerating cells. There were, however, some degenerating cells in the early marrow specimens. They later became less plentiful and then more numerous again around the period of hypocellularity at the 29th day. Plasma cells were sometimes relatively plentiful but the count was never strikingly high. Eosinophils were persistently present; the absolute variation in their numbers is difficult to estimate.

In summary, the bone marrows showed an initial drop in cellularity during the first 3 days, and then a gradual further diminution with some fluctuation, hypocellularity being at a maximum between the 24th and 39th days. After this there was rapid regeneration to normal or increased cellularity by the 54th day. During the first 3 days after radiation there was a slight relative diminution in red cell precursors, which reached their lowest level at about the 3rd to 5th day. This was followed by a pronounced depression of the granulocytes, so that on the 24th day the number of granulocytes was exceedingly small. During the 2nd to 16th days, giant abnormal neutrophil precursors were present. Degenerating megakaryocytes were prominent during the 5th to 29th days, and the total number of megakaryocytes reached the lowest level at about the 24th day.

Clinical and Laboratory Findings after Discharge from Hospital

The patients left the hospital 44 days after the accident. When seen 9 days later, they complained of very pronounced fatigue. It is possible that this might have been noticed earlier in an environment that would have permitted more nearly normal activities. They noticed a dull aching in the thighs and legs, and found it very difficult to stand up or walk for any length of time. Most of them also complained of tenseness and insomnia. In addition to these complaints, one man said that he had noticed considerable difficulty in keeping his balance while walking, and also that his memory was impaired. A careful neurological examination failed to show any objective abnormalities associated with these symptoms. During the 18 months following the accident, the symptoms of nervousness and fatigue showed a general tendency to improve. All the men are now

working regularly and at the time of the last examination there were no objective findings on general physical examination indicating radiation injury. However, in one case slit-lamp examination of the eye showed definite but slight abnormalities, particularly peripheral punctate densities in the lens, chiefly in the posterior subcapsular and cortical regions. These findings do not constitute clear-cut evidence of a radiation effect. There was doubtful evidence of similar abnormalities in another man, but even in the man in whom they were definitely present, they were not pronounced enough to affect vision.

Sperm studies were done on a voluntary basis. Incomplete data suggest that 3 weeks after the accident sperm cells were still present but that they were either non-motile or showed greatly reduced motility. Four months after the accident, sperm studies were done in 4 of the 5 patients. In 3 of them, no spermatozoa were found, while in the 4th there were a small number with a low percentage of motility. Nine months after the accident 3 patients were studied. Only one of them had any spermatozoa and he had only a small number of non-motile forms. Twenty-two months after the accident there was evidence of a return toward normal but the number of living spermatozoa was still relatively small.

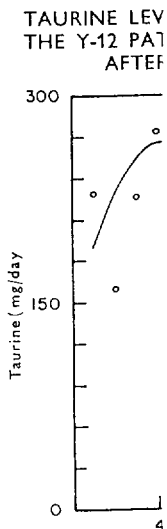
Biochemical Changes

Biochemical studies on blood

The serum uric acid did not show any abnormal values at any time although the initial level obtained 24 hours after exposure was somewhat higher than later levels. Plasma α -amino nitrogen determinations were also within normal limits. Studies of serum proteins by Dr Granvil Kyker and Miss Lois Gerst showed rather high levels of serum albumin during the first 10 days after exposure, and another elevation in serum albumin at about 50 days after exposure. Changes in the globulin content of the serum were only slight and not distinctly abnormal (Fig. 10).

Urinary studies

Levels of creatine and creatinine were not abnormal. Total urinary nitrogen was slightly elevated during the period from the 4th to the 12th day after exposure, and the urine volume was also slightly increased. Studies of specific amino-acids yielded data of interest. Taurine was increased during the first week after exposure in the patients with the highest doses. The peak was apparently reached during the latter part of the first week (Fig. 11). β -Aminoisobutyric acid was also increased, but the peak level seemed to be reached during the first day or two after exposure (Fig. 12). An interesting observation (Kretchmar, 1959) was the absence of free serine from the urine in the patients with the highest levels of exposure (Fig. 13).



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FIG. 10

TYPICAL SERUM PROTEIN LEVELS IN ONE OF THE Y-12 PATIENTS

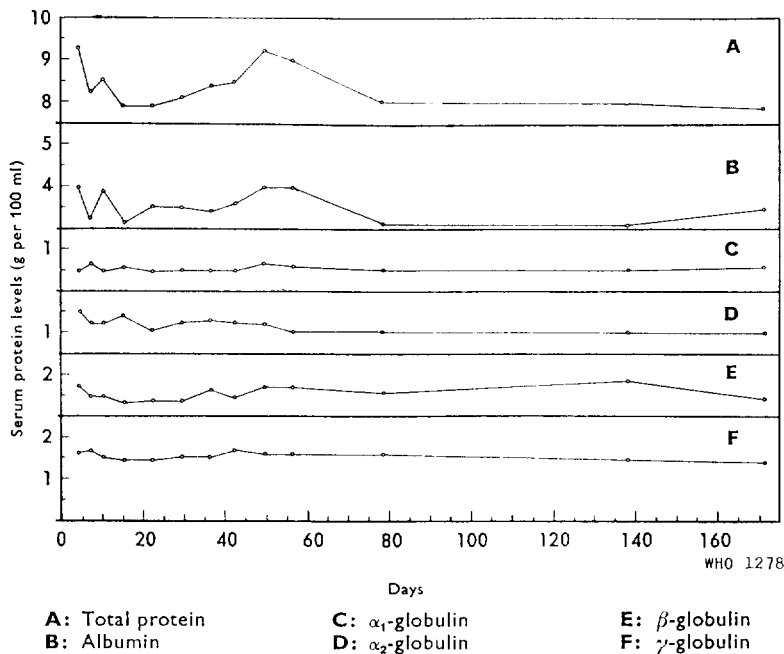


FIG. 11

TAURINE LEVELS IN THE URINE OF ONE OF THE Y-12 PATIENTS AT VARIOUS INTERVALS AFTER EXPOSURE TO 365 rad

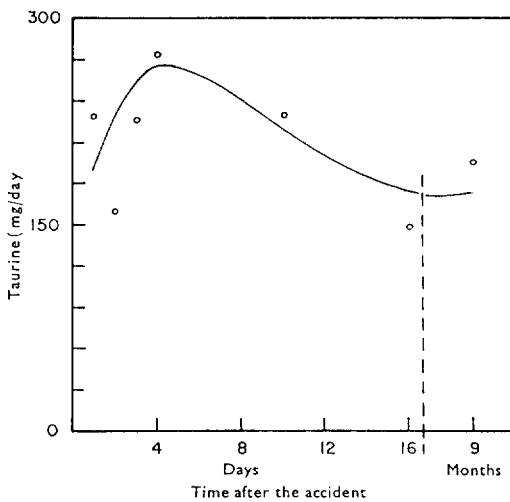


FIG. 12

β -AMINOISOBUTYRIC ACID LEVELS IN THE URINE OF ONE OF THE Y-12 PATIENTS AT VARIOUS INTERVALS AFTER EXPOSURE TO 365 rad

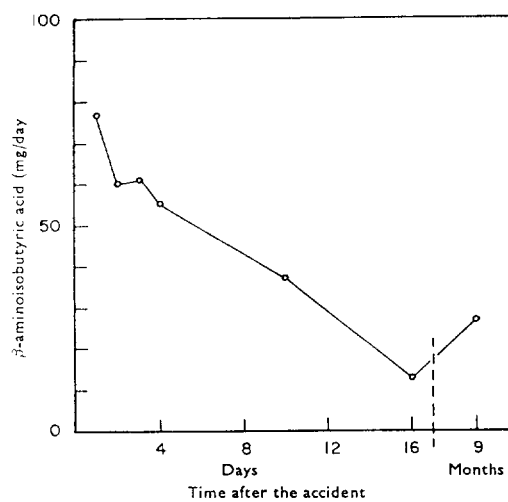
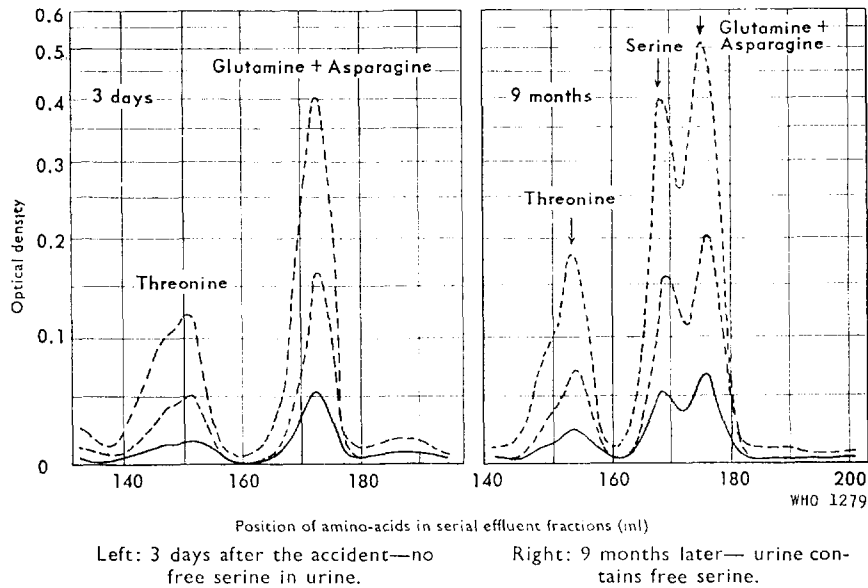


FIG. 13

TRACINGS FROM THE SPACKMAN-MOORE-STEIN AMINO-ACID ANALYSER
ON THE URINE OF ONE OF THE Y-12 PATIENTS



Studies on Blood Coagulation Mechanism

Studies of clotting factors were performed by Gauthier and others of the Tufts Medical Service of the Boston City Hospital. Most of the tests performed gave values that were not distinctly abnormal; these included clotting time, prothrombin time, partial thromboplastin time, and tests for thromboplastin generation and for the presence of fibrinolysin. However, there were somewhat elevated levels of Ac-globulin and distinctly high levels of antihæmophilic globulin at the time when thrombocytopenia was most pronounced (Table 2).

Comparison of the Yugoslav Accident Victims with the Y-12 Patients

It is obviously worth while to compare the clinical and hæmatological data on the Y-12 and Yugoslav accident victims, since the nature of the exposure was quite similar and since there has been a difference of opinion about the absolute radiation dosages received by the two groups.¹

¹ Reports on the Yugoslav accident have been published by Jammet et al. (1959) and by Mathé et al. (1959) and a comparison between the two accidents has been made by Fljedner (1960); see also the papers by Pendic (p. 67), Jammet (p. 83), Radojičić et al. (p. 105) and Auxier (p. 141) in these Proceedings.

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TABLE 2
BLOOD COAGULATION STUDIES:
AVERAGE VALUES FOR THE FIVE EXPOSED PERSONS

Days after accident	Platelets per mm ³	Ac-globulin ^a (%)	Anti-haemophilic globulin ^a (%)	Fibrinogen (mg)
11	190 000	—	—	549
29	30 000	155	239	389
94	235 000	122	103	333

^a Expressed in terms of normal = 100%.

If a dosage comparison is made on the basis of haematological effects, some qualitative differences between the two groups of patients are clearly revealed. The Yugoslav group showed much greater granulocyte and lymphocyte depression, but, except in the patient who died, the platelet depression was no more severe than in the Y-12 group. Biological and clinical information indicates that the one Yugoslav victim who died almost certainly received a much higher dose than any of the victims in the Y-12 group. At the other extreme, the one Yugoslav who recovered without bone marrow treatment probably received a dose lower than the average received by the 5 in the Y-12 group. The most critical comparison is between the 4 Yugoslavs who were given bone marrow and recovered and the 5 in the Y-12 group. For this purpose, the blood data were averaged for each group and comparisons made of the averages. Analysis of the charts thus obtained indicates the following:

Reticulocytes (Fig. 14)

Neither group showed complete suppression of reticulocytes. The Yugoslavs had somewhat lower levels on the 5th day than the Y-12 group. Subsequently, an increase occurred and the levels in the two groups remained almost identical, with a secondary depression between the 25th and 31st days. After that a striking reticulocytosis was seen, considerably more profound in the Yugoslav than in the Y-12 group, the peak level being reached in both groups about 47 days after exposure.

Lymphocytes (Fig. 15)

The early lymphopenia was much more profound in the Yugoslav group and lymphocyte levels remained distinctly lower throughout the first two months. Both groups showed some increase in lymphocytes at the 40th day, and then another slight fall during the subsequent three weeks.

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FIG. 14

COMPARISON OF THE AVERAGE RETICULOCYTE LEVELS IN THE Y-12 PATIENTS AND IN 4 VICTIMS OF THE VINČA ACCIDENT

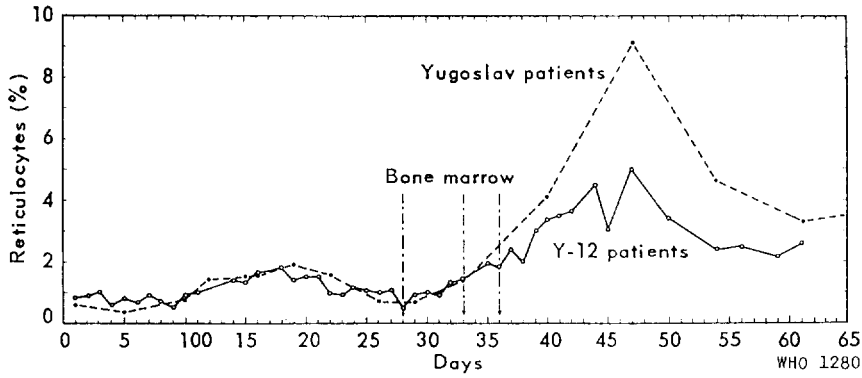
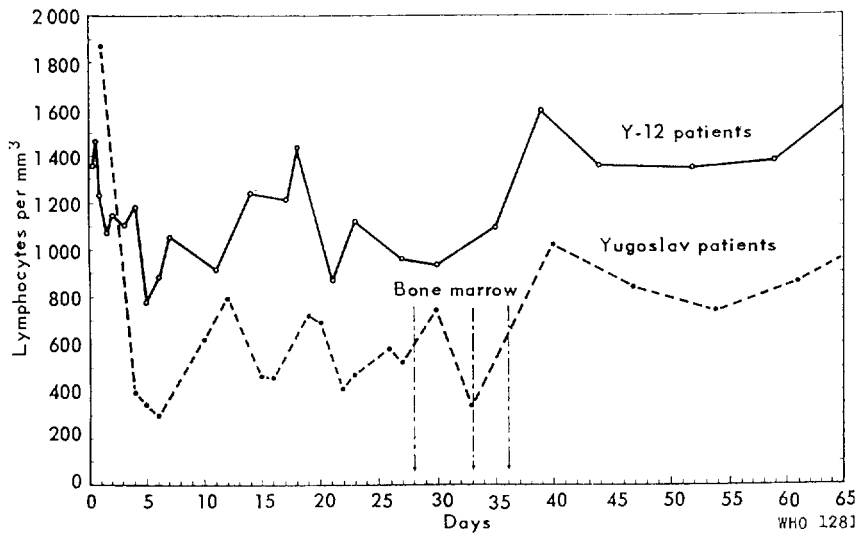
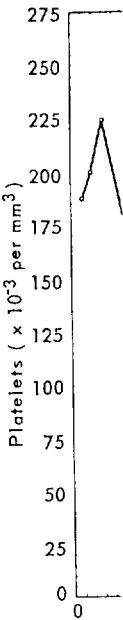


FIG. 15

COMPARISON OF LYMPHOCYTE COUNTS IN THE Y-12 PATIENTS AND IN 4 VICTIMS OF THE VINČA ACCIDENT



COMPARIS



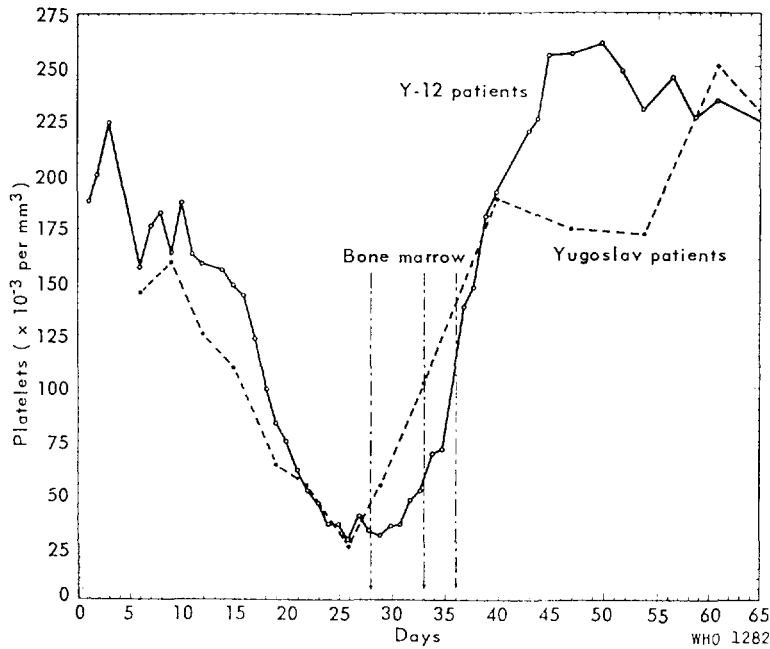
Platelets (Fig.

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of Feissly and
initial platelet
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however, reco
in the Y-12 gr
the 40th and
Yugoslav gro

Granulocytes (

Granulocy
group and rea
26th and 35tl
in the two gr

FIG. 16

COMPARISON OF PLATELET COUNTS IN THE Y-12 PATIENTS AND
IN 4 VICTIMS OF THE VINČA ACCIDENT*Platelets* (Fig. 16)

Differences in methods may influence comparison of the platelet counts. For the Y-12 accident group the method of Brecher, Schneiderman & Cronkite (1953) was used, while for the Yugoslav accident, the method of Feissly and the Piette modification of the Feissly method were used. The initial platelet levels were somewhat lower in the Yugoslav group, but at about the 22nd day the curves became coincident. After the 27th day, however, recovery in the Yugoslavs took place a little more rapidly than in the Y-12 group. On the other hand, later in the recovery phase, between the 40th and 50th days, the Y-12 levels were higher than those in the Yugoslav group.

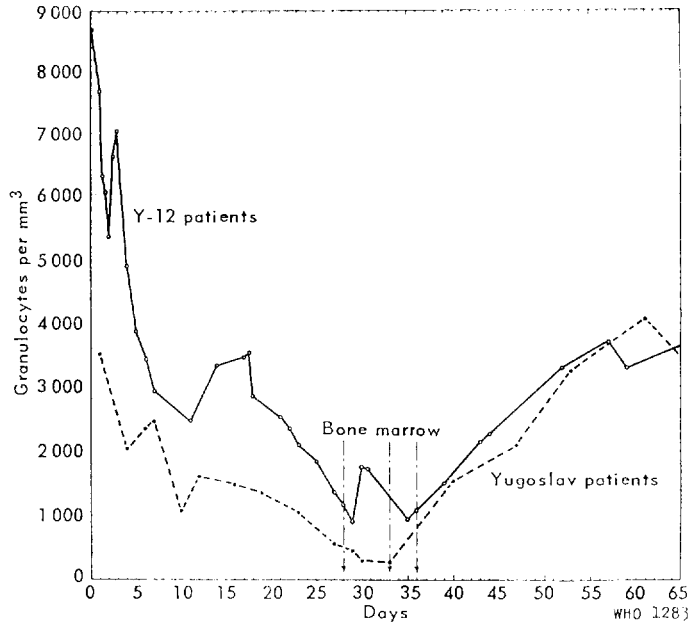
Granulocytes (Fig. 17)

Granulocytes were much more profoundly depressed in the Yugoslav group and reached much lower levels than in the Y-12 group between the 26th and 35th days. Recovery seemed to occur at about the same time in the two groups.

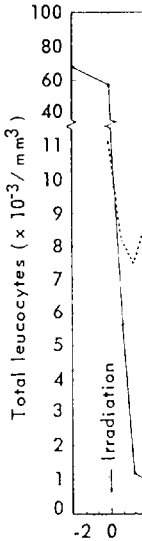
1005330

FIG. 17

COMPARISON OF GRANULOCYTE COUNTS IN THE Y-12 PATIENTS AND IN 4 VICTIMS OF THE VINČA ACCIDENT



COMPARISON OF TOTAL LEUCOCYTES IN 3 SELECTED PATIENTS



In attempting to assess this information in terms of evidence relating to the success or failure of the marrow graft in the Yugoslav patients, several serious problems are encountered:

1. The dose of radiation was not established with certainty for either group.
2. Comparison of clinical and laboratory data is handicapped by the differences in methods used and by the fact that the Yugoslavs were given more supportive medication and treatment.
3. The bone marrow was given to the Yugoslavs rather late, shortly before spontaneous recovery might have been expected, if it is assumed that the Yugoslavs would have followed the same pattern as the Y-12 group.

In spite of all these difficulties, we should like to present the following tentative conclusions:

1. The 4 Yugoslav victims subject to an intermediate exposure probably received a significantly higher radiation dose than the 5 Y-12 victims subject to the highest exposure. This opinion is based upon clinical data as well as upon haematological comparisons.

COMPARISON OF PLATELET COUNTS IN 3 SELECTED PATIENTS

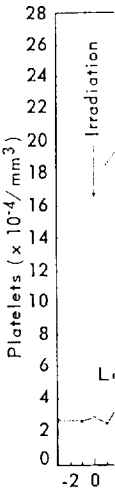


FIG. 18

COMPARISON OF WHITE CELL COUNTS IN THE Y-12 PATIENTS AND IN 3 SELECTED PATIENTS WITH ACUTE LEUKAEMIA WHO HAD REMISSIONS AFTER WHOLE-BODY IRRADIATION WITH 200-350 r.

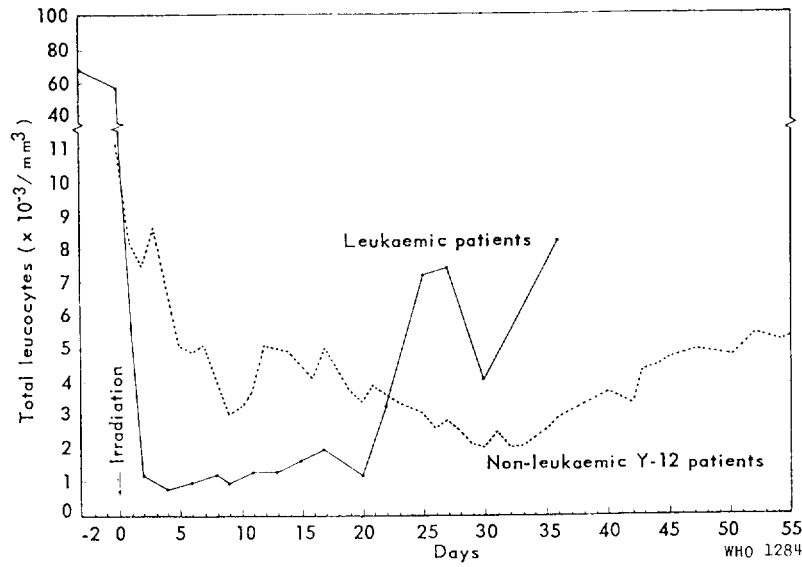
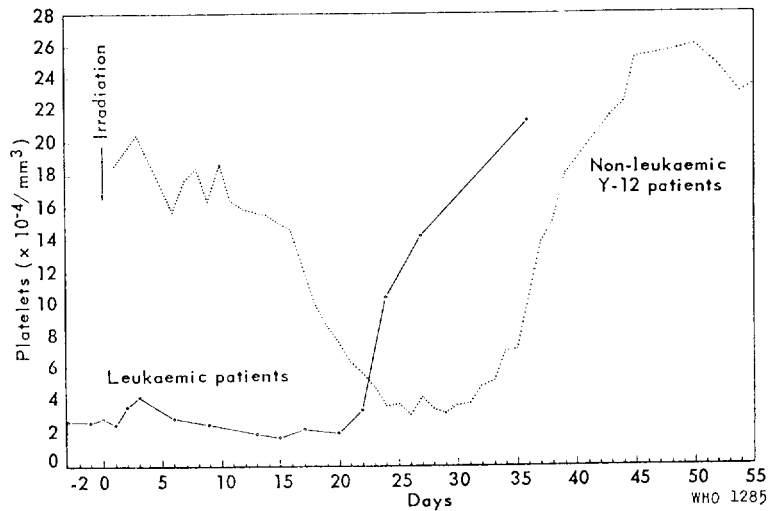


FIG. 19

COMPARISON OF PLATELET LEVELS IN THE Y-12 PATIENTS AND IN 3 SELECTED PATIENTS WITH ACUTE LEUKAEMIA WHO HAD REMISSIONS AFTER WHOLE-BODY IRRADIATION WITH 200-350 r.



2. Recovery in the Yugoslav group took about the same length of time as in the Y-12 group. If it can be agreed that the radiation dose was higher for the Yugoslavs and that recovery normally takes longer after exposure to higher doses, then it appears that the marrow treatment may have hastened recovery somewhat.

3. The standard haematological data give no strong evidence for the proliferation of the graft; the main evidence rests upon the red cell identification studies.

Comparison of Y-12 Patients with Patients with Acute Leukaemia Treated by Whole-body Irradiation

Preceding the experience with the Y-12 patients, we had been attempting to treat patients with acute leukaemia by means of whole-body irradiation and bone-marrow grafts. A detailed report of the results would not be pertinent to this discussion. One item of interest, however, is the fact that in 3 children with acute leukaemia remissions have apparently been produced by the irradiation alone. One of these patients received no bone marrow and the other two received marrow but showed no definite evidence of a temporary or permanent graft. A comparison between these 3 patients and the Y-12 group shows an interesting difference in haematological values. The children with acute leukaemia started out with very low platelet counts. White counts varied from very high to very low. In all of them a profound leucopenia developed within 3 or 4 days after irradiation. A remarkable difference between the two groups was that in the leukaemic children a rise in normal white cells and platelets occurred much earlier than in the Y-12 group, beginning at around 21 days (Fig. 18 and 19). Various explanations of this difference in haematological response to radiation have been considered.

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