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CH-1742
(A-2454) 39-A

Metallurgical Project

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REPORT FOR MONTH ENDING MAY 31, 1944

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Report Received: June 8, 1944 - Figures received: June 20, 1944
Issued: JUN 27 1944

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A. ABSTRACTS

Radiation Measurement

The percentage of off-scale readings of pocket chambers has increased from 3.68 to 4.75 in the last two months. A comparison of pocket chamber and film meter readings show differences due for the most part probably to non-simultaneous wearing. 14 sources have been calibrated for W. 10 others, mixed sources, have been partially calibrated. Contamination of laundry as observed to date is removed in the laundering process. A Lindemann electrometer has been assembled in a vacuum tight box. The new 2 r pocket chamber shows readings which are about 30% high in X-ray region. The electrometer for the new chamber makes ordinary pocket chambers good to 0.4 r. Measurements indicate that pocket chambers monitor slow neutrons.

Biological Research

Rats with ligated esophagi and exposed to Sr^{89} mist through a tracheal cannula gave a distribution essentially the same as for normal animals. Active material was removed in a few hours from lungs and bronchi; intestinal excretion was considerable. Normal and operated rats were similarly exposed to Zr^{93} mist; activity in the lung did not drop significantly during 2 days, and intestinal excretion was negligible.

Mice injected with Sr^{89} in doses from 0.016 to 2×10^{-6} C/gm are being maintained for chronic effects. At seven weeks no retardation in growth is apparent.

Mature female goldfish concentrate fission mixture in the ovaries 10 - 15 times, which is similar to concentration by skeletal tissues. Strontium is not so concentrated by the ovaries.

Mid-lethal dose of Sr^{89} for rats is 6.5×10^{-6} C/gm by injection and 8.5×10^{-6} C/gm by stomach tube. Mid-lethal dose of fission mixture for rats is 15×10^{-6} C/gm by stomach tube.

Depression of white cell count was found in rats receiving 27.5×10^{-6} C/gm of fission mixture by stomach tube, or 10^{-6} C/gm of $Ba^{140} - La^{140}$ by injection; or 10^{-6} C/gm of P^{32} by injection.

The microscopic damage in rabbits after 100 r has been summarized and suggests that some effects may be apparent after 25 r, but probably not after a smaller dose.

A sample of water from the extraction stack sump at Clinton indicates that it can be used for a source of carrier-free I^{131}. More than half of the activity remained after I^{131} extraction, and this was found to be due to a mixture of fission products which may have been carried as spray.

Clinical Medicine and Medical Research

Rats radiated with a single dose of x-rays (800 r) showed no change in the serum protein concentration up to the appearance of gastro-intestinal symptoms, when the serum protein and the N.P.N. values rose considerably. The QO_2 values of liver slices from rats treated with x-rays (single dose from 800 to 200 r) showed some diminution when measured in the presence of succinate

and pyruvate. This inhibition was observed when a single dose of 800 r and 400 r were applied to the rats. With 200 r the effect was insignificant. Myosin (adenosinetriphosphatase) in borate buffer was largely inhibited by application of 5000 r at 0°; in veronal buffer it was completely inhibited. Partially inhibited myosin was reactivated by addition of glutathione.

All necessary pre-employment examinations were done during the month. Color photography of hands was begun. Fingerprint impression studies have continued. Product excretion studies were started. Product laboratories in New Chemistry continue to show high pluto readings. Film badges have been supplied to the Cyclotron crew at St. Louis.

A resume of the clinical laboratory examinations during the period from April 15, 1944 to May 15, 1944 is given. A total of 5074 laboratory procedures were done. A total of 890 abnormalities were found. Three individuals were thought to have blood abnormalities as a result of overexposure to irradiation.

A graphically exposed summary of the biochemical studies on project personnel is presented. Porphyrin metabolism is definitely affected in individuals exposed to heavy metals. Oxyfluoride exposure produces an elevated urine coproporphyrin value. Serum sulfur is elevated in individuals exposed to tuballoy. The fluorescence technique permits the estimation of considerably less than 1/10 gamma of tuballoy in urine.

N. C. I.

There are no essential changes in the blood picture of all experimental mice since last month's report. Only the mice of the 8 r per 8 hour level have a constantly lower than normal white count, not counting, of course, those animals that developed malignant lymphoma. All animals on the lower levels show an essentially normal blood picture. The dose of the 8 r per 8 hour level has reached 3500 r to date. Of the original 48 animals of this level, 33 are still alive at an age of approximately 17 months. There is also no essential change in the blood picture of the experimental guinea pigs since last month's report. On the 8 r per 8 hour level, two of the first series are still alive (total dose 3500 r); one of the second series (total dose 1500 r); none of the male inbred guinea pigs (family 2). All female guinea pigs of the family 2 are still alive (total dose 1050 r). Four male and four female inbred guinea pigs of family 13 are exposed on this level since the beginning of the month. Those guinea pigs that came to autopsy during the month due to moribund condition or died, showed all severe anemia, with the exception of one, a low total white count, low platelet count, and a relative lymphocytosis. The lethal dose of the inbred male guinea pigs ranged from 1200 to 1600 r, and that of the hybrid guinea pigs of the second series (one still living) from 625 to 1300 r. The guinea pigs of the 4 r per 8 hour level show persistant low values of all counts. One guinea pig of this level was killed during the month on account of anemia (total dose 1700 r). So far, 6 out of the 18 guinea pigs of this level were killed and autopsied with lethal doses ranging from 900 to 1700 r. The guinea pigs on the lower levels show an essentially normal blood picture. The blood picture of the rabbits is normal with the exception of that of the three animals on the 8 r per 8 hour level which show a lowered total white count with lymphopenia (total dose 2700 r).

The lungs of male mice used in the breeding experiment show suggestive evidence of a slight increase in lung tumor incidence with doses above 1000 r.

A new experiment was set up on the 8 r per 8 hour level for the study of lung tumor incidence following doses of 2000 r or more. For this experiment, Strain A mice were used as their susceptibility to lung tumors is higher than that of LAF_1 mice.

In mice approximately 50 r, when given as an acute exposure early in life, results in disappearance of all follicles from the ovaries at old age, whereas this result is not found when a comparable total dose is given chronically at the rate of 0.1 r per day.

Testes will recover completely from an acute exposure of 50 r.

Another malignant lymphoma has been observed in a male mouse that had been exposed on the 8 r per 8 hour level for a total of 3000 r.

Guinea pigs of the 8 r or 4 r per 8 hour level that came to autopsy continue to have patchy ecchymoses of the small intestine. Testicular atrophy is extreme while ovaries contain numerous small and large follicles. Bone marrow atrophy is slight to moderate in amount.

Two male guinea pigs of the 8 r per 8 hour level examined after a total dose of 250 r failed to show any testicular atrophy. It has previously been reported that animals receiving a total of 500 r at this level showed marked tubular atrophy.

U. of C. Radiation Laboratory

Radio-autographic and decontamination studies are being continued. Tracer studies with γ 4 tellurium up to 32 days indicate that no striking degree of localization takes place in any of the organs with the exception of the kidney. Following intrapulmonary administration the lung retention was found to be relatively small. At the end of this interval approximately 90% of the tellurium in the body was eliminated. Other work being done by the Berkeley group appears elsewhere.

RADIATION MEASUREMENT SECTION

L. A. Pardue, Acting Section Chief
E. O. Wollan, Consulting Section Chief

A. Pocket Chambers and Film Meters

These activities have been carried on as usual. It may be pointed out that the blackening in new developer is about 10% low. After a few days it comes back to the value of old developer and retains it indefinitely.

A summary of the readings for the past two months is included:

Pocket Chambers

Total number of readings (daily)	9342
Number of off-scale readings	433
" " readings 150 mr - 200 mr	82
" " " 100 mr - 150 mr	185
" " " 75 mr - 100 mr	190
" " " 50 mr - 75 mr	490

Film Meters (weekly)

Total number of readings	3030
Number of readings above 500 mr	18
" " " 400 mr - 500 mr	13
" " " 300 mr - 400 mr	28
" " " 200 mr - 300 mr	53

The total exposures for the two month period for those individuals (approximately 275) having both meters have been tabulated. The results for 25 people chosen at random from the list are given below:

POCKET CHAMBER READINGS	FILM METER READINGS
970 mr	730 mr
820	140
1730	910
700	140
730	100
910	2130
50	180
310	300
1090	390
50	280
1000	220
880	180
180	570
1300	[illegible]
760	2000
930	170

POCKET CHAMBER READINGS	FILM METER READINGS
550	520
750	830
390	250
2030	1370
840	560
900	680
530	920
60	170
340	220

Besides the errors inherent in the instruments and those committed in reading there are other reasons why the totals differ. Perhaps the most important of these is that the meters are not always worn simultaneously. However making the assumption that workers wear one or the other or both when their jobs are "hot" - this is borne out fairly well by observation - it is clear that the exposure of workers does not reach hazardous levels. The fact that the percentage of off-scale readings has increased from 3.68 to 4.75 since the last tabulation two months ago may be due to higher humidity. It should be pointed out that readings are taken at 24 hour intervals.

B. N Source Calibration

Brown, Wesenberg and Lester have continued the calibration of sources for N. Also adequate and convenient shields have been provided for them. When the job is finished 32 sources will have been measured - 16 RaBe sources and 16 unmixed sources. The Ra content of all and the neutron emission of the mixed sources are to be determined. During the month the following measurements were made:

Source No.	Nominal Ra Content	Measured Ra Content	Neutron/sec.
68	500 mg	513 mg	6.68×10^6
69	500 mg	515	6.56×10^6
74	10	10.95	Not yet measured
75	10	10.94	"
76	10	10.82	"
77	10	10.84	"
78	10	10.76	"
79	10	10.74	"
80	10	10.70	"
81	10	10.52	"
82	10	10.71	"
83	10	10.33	"
88	1	.889	
89	1	.965	
90	1	.930	
91	1	.888	
92	1	.974	
93	1	.934	

Source No.	Nominal Ra Content	Measured Ra Content	Neutron/sec ?
94	1	.952	
95	1	.929	
96	1	.949	
97	1	.953	
98	1	.971	
99	1	.899	

A new electrometer designed for source calibration has been constructed by Landsverk. It has rather good proportionality between intensity and rate of movement of fibre.

In addition to the source measurements, the facilities of the calibration room were used further by the calibration of survey instruments. Some of this work was a service to other sections. Requests for repairs to Lauritsens and the projection minometer have been larger than usual.

C. Laundry

A rather encouraging result came out of an experiment to determine to what extent ordinary laundering decontaminates garments. 69 contaminated items and 37 non contaminated were sent to the laundry. 1000 counts/min. was chosen as the line separating the two. Of the 93 pieces returned at the time the second count was made, 91 were not contaminated and 2 pieces had counts of 1100/min. and 1300/min. It is very doubtful if these counts indicate a hazard.

D. New Equipment

The Instrument Section is about ready to supply meters for the hand counter and shoe counter assembled in our group for Test Stands. It is hoped they will be ready for use in the near future.

After some delay due to shop concentration on other work the vacuum box for a Lindemann electrometer has been completed. Goldstein and Crane have completed the electrometer system and are testing it. It has been determined already that 3 μg or less of Uranium in the chamber can be detected. The system can be used to measure the activity of dust samples collected in the precipitron. It has been designed for double chamber work and parts have been constructed. The vacuum box should eliminate insulator troubles in the electrometer. Such troubles in the chamber insulator are not removed. If they should predominate, the system may not be as big an improvement over the Dershem electrometer as was hoped. However, the new system is adaptable to several types of measurements. For example all the missing parts for an extrapolation chamber have been constructed and it should be easy to put one in operation.

The new 2 r pocket chamber has been put through more tests. The insulator has now a leakage less than .05 r in 40 hours and is improving. There is no reason for it to regress as it is protected from outside air. It has been investigated for wave length independence. Readings are about 30% high in the X-ray region (50KV to 100KV) by comparison with a Victoreen

thimble chamber. The results could be better or worse - one would expect the former - since the readings were taken on a 25 r Victoreen instrument and only the first two divisions of the scale were used. In connection with these tests we compared the readings with some 0.2 r chambers, some having the graphite removed from the central electrode. In the X-ray region the chambers without the graphite ran about 10% higher.

The new projection electrometer containing a Lansverk type electroscope has been tested with some 0.2 r chambers. With it the chambers are found to be good up to 0.4 r as the following data will indicate

Exposure (r)	Electrometer reading (volts)
0	178
.1	165.6
.2	149.2
.3	135.2
.4	122.0

After the .4 r exposure the chamber still has a potential difference of approximately 40 volts which should be enough for saturation. The probability that this instrument will hold its characteristics recommend it strongly.

E. Slow Neutrons

Wilson (CH84) has shown from theoretical considerations that the capture radiation due to slow neutrons incident in the body have a fairly constant intensity for the first 4 cms in the body and then falls off. A pocket chamber worn in the usual way should therefore give adequate monitoring of slow neutrons. To test this a paraffin block was constructed to simulate a section of the body. Ionization chambers were placed at different depths in the block. Some time ago this system was exposed to slow neutrons at the Chicago Cyclotron and more recently at the Argonne. At the Cyclotron three sets of readings were taken; one without any shield around the paraffin, one with a Cd. shield and one with a Boron shield. The Cd shield was omitted at the Argonne. Figures I and II show the results graphically. While the curves depart somewhat from the theoretical curve and differ at the two machines the difference curves between the Boron and no shield give strong evidence that an ordinary pocket chamber does monitor slow neutrons. It might be pointed out that while the Boron absorbed all the slow neutrons some gamma radiation is given off by it.

F. Surveys

Goldstein and Crane have made frequent surveys at Site B, the Cyclotron and West Stands. The proceedings of the Liaison Committee contain many of the details. New Chemistry is now being serviced in this regard by their own group. It is anticipated that West Stands will come into their orbit shortly as it is expected that this laboratory will soon do chemistry almost exclusively. It is believed that the best way to inculcate protection of scientific personnel is to get the workers interested in achieving it for themselves. This can be brought about best if it is encouraged by the administrative superiors of the workers. Without such stimulation the results will fall short of hopes.

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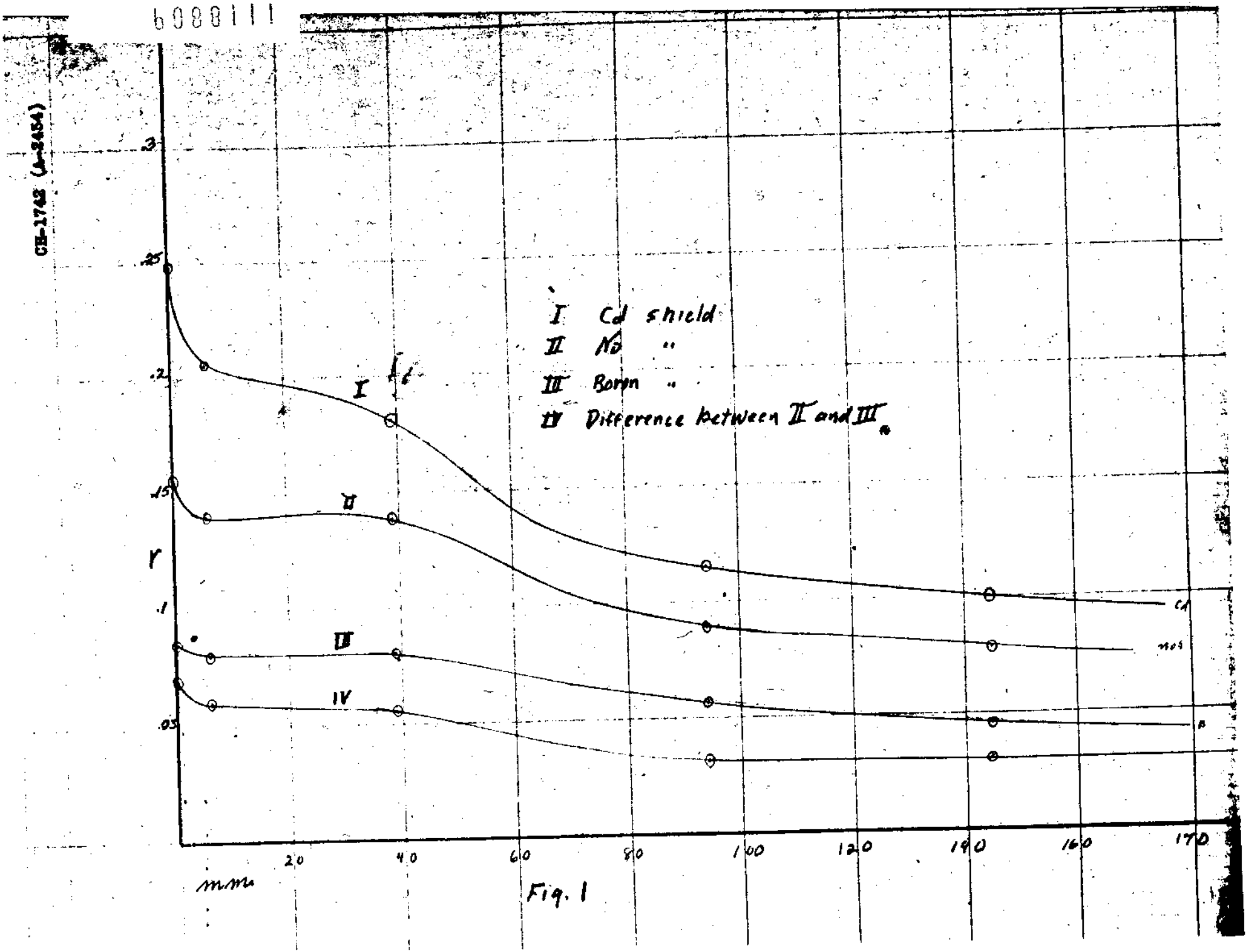
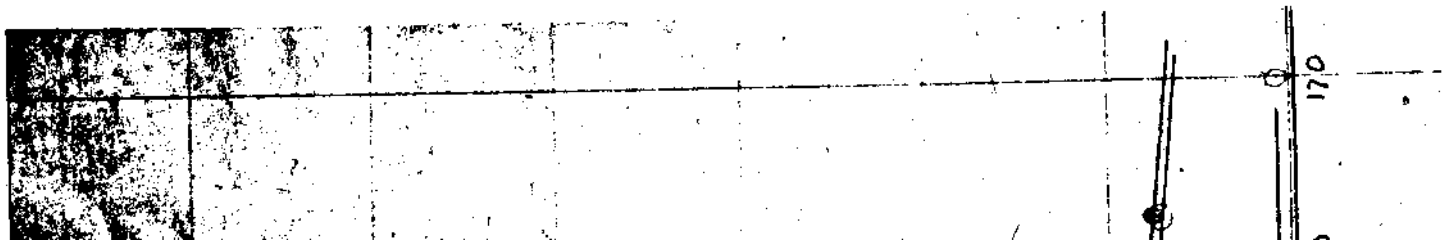


Fig. 1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BIOLOGICAL RESEARCH SECTION

K. S. Cole, Section Chief

A. RADIOACTIVE MATERIALS - MAMMALS

1. Xenon - Preparation

A number of compounds have been investigated in the quest for a substance that will release gaseous fission products. These include $U(OH)_4$, $U(OH)_4$ coprecipitated with $Al(OH)_3$ and $Fe(OH)_3$, ammonium uranate coprecipitated with $Al(OH)_3$ and $Th(OH)_4$, and finely divided UO_4 hydrates. In all cases tested, aging at 100°C slowly destroys the emanating power. The $Th(OH)_4$ coprecipitate and the UO_4 hydrates seem the most promising.

2. Iodine - Preparation

The sump water from the base of the extraction plant at Site X has been investigated as a source of I^{131}. The solution is concentrated in the presence of CrO_3 to keep the iodine present as IO_3. After addition of oxalate to the solution, the I_2 is distilled out. The iodine content of two batches was 0.08 mC/li and 0.03 mC/li at the time they were sent to Chicago. Their past history is unknown here. It is possible to obtain 90% yields of carrier-free iodine.

3. Ruthenium Tetroxide - Preparation

A number of oxidizing agents have been tested to be used in generating RuO_4. Persulfate seems to be the most satisfactory. A preliminary test indicates that it will be possible to keep RuO_4 passing through a glass chamber without losing more than 50% on the walls.

To check on the possibility of RuO_4 distilling off during the dissolving of the slugs, we tried to distill Ru from concentrated HNO_3. When 98 γ were added, 32 γ distilled out.

In looking for sources of radioactive Ru, carrier was added to sump water from the extraction plant stack and Ru distilled out. Yield was low: 1.33×10^{-4} mC per li.

4. Aerosols - Sr^{89} Exposure

The tracer exposures reported last month were repeated using anesthetized animals breathing through a tracheal cannula and having either severed or ligated esophagi. The results were essentially the same as those reported for normal animals. Within two hours the Sr in the lung dropped from 50.6% of total body activity down to 5.6%, while bone rose from 14.4% to 36%. Excretion into the gut is significant, amounting to almost 10% immediately after exposure and remaining essentially constant for the 15-hour duration of the experiment. An interesting observation was that Sr was eliminated from the trachea and large bronchi at about the same rate as from the alveoli. Yet no liquid was observed to leave the open end of the cannula.

Thus Sr is probably absorbed from these large passages, either by direct absorption through the epithelium or by phagocytosis.

5. Aerosol - Zr^{93} -Exposure

Since Zr^{93} was available in tracer quantities, a group of rats were exposed exactly as had been done with Sr^{89}. Fifteen normal animals were used while four had ligated esophagi and breathed through tracheal cannulas. This experiment is still in progress and only partial data are available. Unlike Sr, after 48 hours, the activity in the lung has not dropped significantly. Activity of the kidney, liver, and skeleton is slowly increasing over the 48-hour period. There is practically no excretion into the gut. More complete results will be presented next month.

6. Sr^{89}

a. Carrier-Free Preparation

A method has been perfected for the recovery of large amounts of Sr^{89} from fission mixtures without added carrier. The main step involves the removal of lead as plumbate. The method involves only one piece of apparatus (thus minimizing loss contamination and hazard) and is expected to yield a high recovery and a purer product.

b. Acute Radiotoxicity - Rats

The mid-lethal dose of Sr^{89} appears to be 6.5×10^{-6}C/gm at 15 days when administered intraperitoneally. At 55 days, the mid-lethal dose is about 4.5×10^{-6}C/gm. This value approximates the value obtained in mice very closely. When given by stomach tube, the lethal dose is about 8.5×10^{-6} C/gm. in rats.

c. Chronic Radiotoxicity - Mice

Mice in a chronic series (1.6×10^{-8} to 2×10^{-6}C/gm) are gaining weight normally at seven weeks. Female mice appear to retain more injected activity than do males; this is more striking among the Carworth than Bar Harbor brown strain.

7. Zr^{93} Tracer Injections Into Blood Stream

Radio active zirconium tracers were injected into a few rats, intracardially and intravenously (tail vein). The tails of the intravenously injected animals retained 18% of the material. However, the hearts of the intracardially injected animals showed only 1.5% of the activity as retained. The activity in the blood is low by the second hour, and is slowly further lost from the blood. The plasma appears to transport about six times as much Zr as do the cells.

8. Fission Mixture

a. Radiotoxicity - Rats

The mid-lethal dose was found to be 15 x 10^{-6}C/gm. when administered to rats by stomach tube. This is in agreement with the values previously determined. The difference between the lethal doses for Sr^{89} and mixed fission products indicates that the mixture acted largely upon the gastro-intestinal tract; while the strontium also was absorbed, and the absorbed function contributed to the damage. The findings upon gross examination of the dead animals are consistent with this point of view. Those which received the mixture show much greater gross gastro-intestinal damage than was seen in strontium animals.

b. Hematology

Rats were given fission mixture by stomach tube at 1.7, 7.0 and 27.5 x 10^{-6}C/gm. No unequivocal effect was observed except at the highest dose. Both the total white cells and the absolute lymphocytes were depressed at the highest dose.

c. Chemical Toxicity of Slug Impurities

Unactivated slugs were dissolved and extracted with ether to simulate the preparations of mixed Fission Products. This inactive preparation contained 10^{-5} of the original uranium content plus many of the metals (copper, nickel, manganese, etc.) present as impurities in the slug. The preparation was administered to white rats of both sexes.

One tenth of a slug was given to the animals by stomach tube and appears to be non-toxic. Therefore, 25 mC (beta) of mixed fission products could be administered by this route without danger of chemical toxicity.

One-fiftieth of a slug was fatal within seven days, intraperitoneally. 4/1000th part of a slug also appears to be toxic, particularly to the kidneys by this route. If mixed fission products are to be injected, the preparations must be purer than are now available, or studies will have to be made at low levels only.

9. Ba^{140} -La^{140} -Hematology - Rats

Rats were injected intraperitoneally with Ba^{140} -La^{140} at 10^{-6}C/gm. A control series received 0.048 mg inactive lanthanum and 0.48 mgms inactive barium. No alteration in the white blood cell picture occurred in the controls, but after 10^{-6}C/gm. a reduction in lymphocytes was detected at 48 hours; lymphocytes reached a minimum at 14 days and returned to normal by 35 days.

10. P^{32} Hematology - Mice

P^{32} in doses of 8.35, 4.15, 2.08, 1.04 and 0.52 x 10^{-6}C/gm was injected into mice. Except with the smallest dose, a depression in the total white cells per mm^3 occurs. The degree of this reduction is largely a factor of dose. After 8.35 and 4.15 x 10^{-6}C/gm death occurs before any apparent attempt in recovery. With the other doses, 2.08 and 1.04 x 10^{-6} C/gm, a tendency toward a recovery is apparent after 408 hours. The absolute heterophiles per mm^3 have been completed in only the controls and the 3 highest doses. With these doses, a mild depression occurs. Return to the normal range is seen by 720 hours after a dose of 2.08 x 10^{-6}C/gm. The absolute lymphocytes show a precipitious fall between 24 and 27 hours with the three highest doses and behave essentially as the heterophiles.

B. RADIOACTIVE MATERIALS - GOLDFISH

1. Fission Mixture and Sr^{89} -Uptake by Mature Fish

Tests with large ripe female goldfish show that ovaries concentrate fission mixture 10 to 15 times. This is about the same as the skeleton and skin and scales, less than gills and intestine but more than muscle. Ovaries do not concentrate strontium appreciably. Testes appear not to concentrate either type of activity.

C. X-RAY EFFECTS

1. Daily doses on Rats - Survival

Rats receiving 25r have accumulated 3,675r. Those receiving 12.5r have accumulated 1825r. No deaths have occurred.

2. Tests of Therapeutic Agents

Rebbits: The effects of injections of pentnucleotide, ascorbic acid, yellow bone marrow extract, and certain phenol derivatives on recovery of leucocyte levels have been investigated. Preliminary data indicate that pentnuclectide, ascorbic acid, and phenol derivatives stimulate recovery of leucocyte counts when administered after exposure to x-rays. The phenol derivatives have caused transitory spastic paralysis at the site of injection (intramuscular in thigh).

Mice: Initial experiments designed to test the effects of pentnucleotide on mouse survival indicate that injections given after exposure have no protective effect. Injections administered for several days prior to exposure may have protective action.

3. Hematology

Analysis of the distribution of normal white blood cell counts in rabbits has yielded some suggestions as to leucocyte dynamics. The study is being extended to determine the relation between radiation effects and normal leucocyte dynamics.

4. Histopathology

a. Summary of Effects of 100r on Rabbits

Small lymphocytes, whether in the spleen, lymph nodes, thymus, lung or gastrointestinal tract are sensitive to 100r irradiation to the extent that many of them, but certainly not a majority, are destroyed. The debris is cleaned up by the reticular macrophages usually by 24 hours. Death of small lymphocytes may be noted as early as 50' (spleen and thymus), may be maximum anywhere from 3 to 14 hours after irradiation (3 in the spleen, 14 in the thymus). Mitosis is always depressed at 1 and 3 hours, and may still be depressed at 8 hours (lymph node). There may be an increase of mitoses above normal (spleen at 8, 14 hours) resulting (in most locations) in a rapid repopulation with small lymphocytes. This homoplastic type of lymphopoiesis is in contrast to the prominent heteroplastic formation of new lymphocytes observed in the higher dose animals. Reticular cells increase in prominence and show slight nuclear changes ("guinea pig" type) in the early stages. Similar changes are seen in a few of the large and medium lymphocytes.

The bone marrow shows a few dead cells, mostly erythroblasts, occasional "guinea pig" nuclei and rare megamyelocytes. The pancreas shows slight changes in the nuclei of the islet cells as well as the usual depression of mitotic activity. The same depression occurs in the gastro intestinal epithelium. Otherwise suggestive nuclear changes and occasional dead epithelial cells are the only evidence of effect here. Great variation in the age and maturity of the rabbits used obviates conclusions which might be drawn from the sections of male or female reproductive tracts.

Lung, kidney, adrenal, heart and nervous tissue show no changes except those in the lymphatic tissue present.

When the dose given to a rabbit is as low as 100r, definite qualitative differences appear, which are not evident when we compare 400r and 800r. After 100r enough normal free cells remain in all locations to repopulate the organs plastically. Furthermore, there is very little evidence of a secondary wave of degeneration following the early recovery phase. The unusually high incidence of involution in the thymus of the long interval experimentals (100r) might be regarded as evidence of a secondary degeneration, but on the other hand the lymph nodes, spleen, bone marrow and gut are indistinguishable from the controls after the first rapid recovery. The amount of damage seen at this level suggests that some change is to be expected at lower levels, possibly as low as 25r, but probably not much lower.

b. Summary of Effects of 800r on 3wk and 11wk Old Chickens

Chickens have been used extensively in our preliminary work. Their uniformity of development, ease of handling, availability and relatively low cost make them a useful additional biological object in any case, but their histological structure is peculiarly advantageous for study of the blood forming organs. The sites of red cell and granulocyte formation in the marrow are spatially separated. In addition the marrow cavity contains true lymphatic nodules for direct comparison of effects in identical circumstance. Also the 3wk chick permits observation of effects on still developing organs (e. g. the metanephrogenic tubules).

The llwk chicken reacts to 800r radiation in a manner very similar to that of the rabbit. The lymphatic tissue of the spleen, bone marrow, thymus, lung and gastrointestinal tract shows severe damage to small lymphocytes, less damage to medium and large lymphocytes and a resistent, though definitely affected reticular cell network. This affect on the reticular cells is evidenced by "guinea pig" nuclei and bizzare maturation and eventual degeneration of the cells arising from this irradiated reticulum. The degenerative and repair processes are extremely rapid in the chicken compared to the mammal. A 3-5 hour stage in the former corresponds to a 24 hour stage (or later) in the latter.

Bone marrow - The process here is again very rapid. There is striking degeneration of erythroblasts within 14 hours, complete depletion at 8 hours, more delayed but also complete depletion of myelopoiesis. It is in the chicken bone marrow that the secondary wave (or waves) of degeneration in both red cell and granulocyte series is most clearly demonstrated.

Gut epithelium - The damage here is much greater than in the rabbit, probably comparable to that seen in the rat. Again the cells rapidly dividing are the hardest hit.

Other organs were relative resistant to irradiation at this dose, showing in this respect a further resemblence to mammalian organs. The testis may prove to be an exception. It was not affected in the llwk chicken. The data on mature mammals is not yet available for comparison. The only changes seen in mature chickens after 800r that were not found in rabbits were death of Schwann cells in the nerve ganglia and increased phagocytosis by the liver macrophages at the height of cell destruction throughout the body.

The 3wk chickens differ from the above description as follows: The metanephrogenic areas in the kidney are severely damaged, as well as the epithelium of the ureter and renal pelvis. Adrenal "cortical" and "medullary" cells show scatte ed degeneration and possibly the bronchial epithelium of the lung as well. Spermatogenesis is wiped out in the developing testis. Severe hemorrhages seen in the gut of the 3wk chicks are not seen in the llwk chickens.

5. Physiology

a. Weight Changes - Rat

Analysis of rat weight data indicates that after 100r the rate of growth is depressed relative to both the preirradiation rate and the rate of growth of controls of comparable age.

b. Peripheral Circulation - Rabbits

Total body radiation (800r) causes a fall in blood pressure of 50 per cent at 1½ hours; irradiations of hind legs only causes a fall in blood pressure of 35 - 40 per cent. Histaminase (2 units) prevented the fall in pressure in two rabbits which received 800r on the hind legs. Methods are

being developed for measurement of toxic products which may be liberated into the blood stream.

D. MISCELLANEOUS

1. The Effects of Single Doses of Fast Neutrons on Rabbits

Current data indicate 50% survival of rabbits after approximately 145 n. Since the median lethal dose of X-rays is approximately 900r, the X/n ratio is near 5.5.

2. Extraction Stack Sump Activity

Both I_2 and Ru were removed from the sump water from the base of the extraction stack at Clinton, and it was found that the major part of the activity remained behind. An absorption curve indicated several components. A partial analysis by Mr. Winsberg indicated 17% of the activity was Ce and that other rare earths constituted 11%. We have found that Sr is 10% of the activity. Thus it becomes evident that a spray from the dissolver is reaching the stack. In the samples we have had, the beta activity has been as high as 50 μC/li. There is also alpha activity in the solution, most of which seems to be uranium. The possible hazard from this source requires further investigation.

3. Quantitative Histopathology

It has become almost imperative to express much of the histological observations in quantitative form. The group has spent a considerable part of the past month in working out practical approximate methods and has applied them particularly to the 800r chicken bone marrow.

CLINICAL MEDICINE AND MEDICAL RESEARCH

C. J. Watson, M.D., Associate Director

L. O. Jacobson, M.D., Section Chief

1. Effect of radiation on proteins, enzyme systems and cellular metabolism - E. S. Guzman Barron, M.D.

A. Changes of the Serum Protein Content of Rats Treated with X-Rays. -- In order to see if radiation has any effect on the protein forming function, rats were exposed to 900 r. The serum protein and blood non-protein nitrogen were determined at different intervals of time after radiation. Both values remained unaltered 4 and 24 hours after radiation. In the samples taken 48 hours after, there was slight diminution of the serum protein and slight increase of the blood N.P.N. 72 hours later, the serum proteins rose by 46%, and the blood N.P.N. by 300% above the normal values. The increase in serum protein content must be due to loss of water by the diarrhea which starts 48 hours later; the high N.P.N. value must be due to kidney and liver alterati ns produced by radiation (Table I).

B. Effect of Radiation on Tissue Metabolism. --It has been shown in previous reports that massive single radiations--from 800 r to 200 r--produced inhibition of respiration of the small intestines, the thymus gland and the spleen. The inhibition was most pronounced in the O_2 uptake in the presence of pyruvate (Pyruvate oxidase is an -SH enzyme). We present in Table II data on the effect of radiation on the O_2 uptake of liver slices of rats treated with x-rays. With 800 r, the O_2 uptake of the liver was slightly inhibited 4 hours after radiation. The inhibition increased to 25% in the successive days after irradiation. The results obtained in the presence of succinate (an -SH enzyme) were variable. In the first series of experiments the QO_2 succinate values remained within normal values up to 48 hours after irradiation after which they diminished by 23%. In the second series of experiments there was a more constant inhibition of the QO_2 succinate values. The QO_2 pyruvate and the Q pyruvate values showed also some decrease. The same results were obtained with 400 r. When rats were treated with 200 r, although the total QO_2 value of the liver was slightly below normal, the QO_2 succinate and the QO_2 pyruvate values were within the normal limits. From these experiments it can be concluded that single radiations--from 800 to 400 r--applied to rats produced an alteration in the metabolism of the liver manifested by a diminished QO_2 value as well as a diminution in the ability to oxidize succinate and pyruvate, both -SH enzymes.

C. Effect of X-Rays on the Activity of Adenosinetriphosphatase (Myosin). -- Myosin (three times precipitated) seems to possess enzyme activity. It acts in the dephosphorylation of adenosine triphosphate to adenosine diphosphate, as shown by Engelhardt and Ljumubova.(1) The enzyme is an -SH enzyme as shown by Barron and Singer.(2) The enzyme activity is proportional to myosin concentration within large limits (Fig. 1). This property, as well as the purity of the protein, make myosin an excellent system for testing our theory of -SH enzyme damage by radiation.

Myosin was prepared from the hind legs and back muscle of rabbit according to the method of Bailey. (3) It was stored at 3° in 0.5 M KCl, the concentration of the protein being 22 mgs. per cc. as determined by the micro-Kjeldahl method. The Ba salt of adenosine triphosphate was converted to the Na salt (ATP) and made up to contain about 0.12 mgs. of "7 minutes P" per 0.5 cc. of solution. The actual available P was determined by hydrolyzing 0.5 cc. of this solution in N HCl at 100° for 7 minutes and determining the liberated P by Gomori's method (4) 0.5 cc. of ATP solution was equivalent to 96.9 micrograms P (7 min. P); one-half of this, 48.4 micrograms was available for enzyme activity: ATP $\rightleftarrows$ ADP + PO_4H_3. The concentrated myosin solution was diluted with borate and veronal buffers to 1:100; 1:150; 1:200; and 1:250. The buffer solutions contained 0.5 M KCl, the pH value being 7.4.

The activity was measured by putting into each of a series of test tubes, 0.5 cc. of the ATP solution and 0.05 cc. of 0.18 M $CaCl_2$ and equilibrating at 38°. To each tube 1 cc. of enzyme was added at 30 second intervals and the tubes were incubated for 10 minutes at 38°. The reaction was stopped by addition of 1.5 cc. of 10% CCl_3COOH. After addition of 1 cc. of water the tubes were centrifuged and the inorganic P was determined. The blanks contained ATP, enzyme, and all other additions except that CCl_3COOH was added first. The low activity of the enzyme in veronal must be due to withdrawal of ionic calcium through formation of the Ca barbiturate salt.

The enzyme solutions were irradiated with 5000 r (Table IV). The enzyme in veronal was completely inhibited at all dilutions. In borate buffer it was inhibited by 85% in dilute solutions; by 44% in more concentrated solutions (Table III).

To the irradiated and control samples, 0.2 cc. of 0.01 M glutathione was added (pH 7.4) in order to determine the degree of reactivation. Table IV shows that when the enzyme was half inhibited by radiation it could be reactivated completely on addition of glutathione. When the enzyme was inhibited more than half, the reactivation was only partial. When the enzyme was completely inhibited (in veronal buffer) the reactivation was nil. It may be concluded from these experiments that radiation produced in this enzyme two effects: oxidation of the -SH groups--a reversible phenomenon--and denaturation of the protein molecule possibly through rupture of the H bonds of the molecule--an irreversible phenomenon.

(1) Engelhardt, W. A., and Ljumubova, M.N., Nature, 144, 668(1939).
(2) Barron, E. S. G., and Singer, T. P. Science, 97, 356(1943).
(3) Bailey, K., Biochem. J., 36, 121(1942).
(4) Gomori, G., Journ. Lab. Clin. Med., 27, 955(1942).

TABLE I

Effect of X-Rays on the Serum Protein Content of Rats Treated with 900 r.

Time animal was sacrificed	Non-protein Nitrogen	Serum Protein	
hours	mgs. %	g. %	
4	33	6.78	
4	42	6.72	
24	30	6.72	
24	41	6.74	
48	63	5.20	(Diarrhea)
48	57	6.40	"
72	110	10.16	"
72	167	9.58	
Normal Values	36	6.80	
	42	5.60	
	41	5.62	

TABLE II

Effect of X-Rays on the Metabolism of Rat Liver (Slices).

Amount of Radiation	Time after radiation (hours)	QO_2 GLUCOSE	QO_2 SUCCINATE	QO_2 PYRUVATE	Q PYRUVATE
800 r	4	9.76	13.9	9.9	9.0
	4	8.34	7.5	9.4	7.3
	24	7.96	6.4	-	9.1
	24	7.72	12.75	9.8	10.0
	48	7.91	10.6	8.4	6.6
	48	8.89	11.1	9.2	5.95
	72	9.81	9.95	10.45	9.87 (Diarrhea)
	72	5.6	4.8	6.11	- "
	96	3.4	7.9	5.1	6.04 Pregnant Diarrhea
	96	8.2	6.6	9.7	6.2 Diarrhea
	120	8.4	10.3	9.0	5.55
	120	8.27	10.9	8.7	6.74
400 r	4	10.33	13.0	11.9	7.38
	24	8.26	11.3	8.81	5.56
	48	9.49	8.24	10.6	7.81
	72	9.32	11.45	10.07	6.22
	96	8.66	13.1	10.25	10.5
	120	8.44	12.6	8.25	8.81
200 r	4	10.36	13.6	10.8	8.1
	22	8.2	14.0	9.44	10.84
	47	9.6	10.75	11.2	8.49
	70	8.8	14.5	9.97	7.65
NORMAL VALUES		10-12	12-14	10-12	7-9

TABLE III

Effect of X-rays on the Activity of Adenosin Triphosphatase (Myosin).

The protein was treated at 0° with 5000 r.

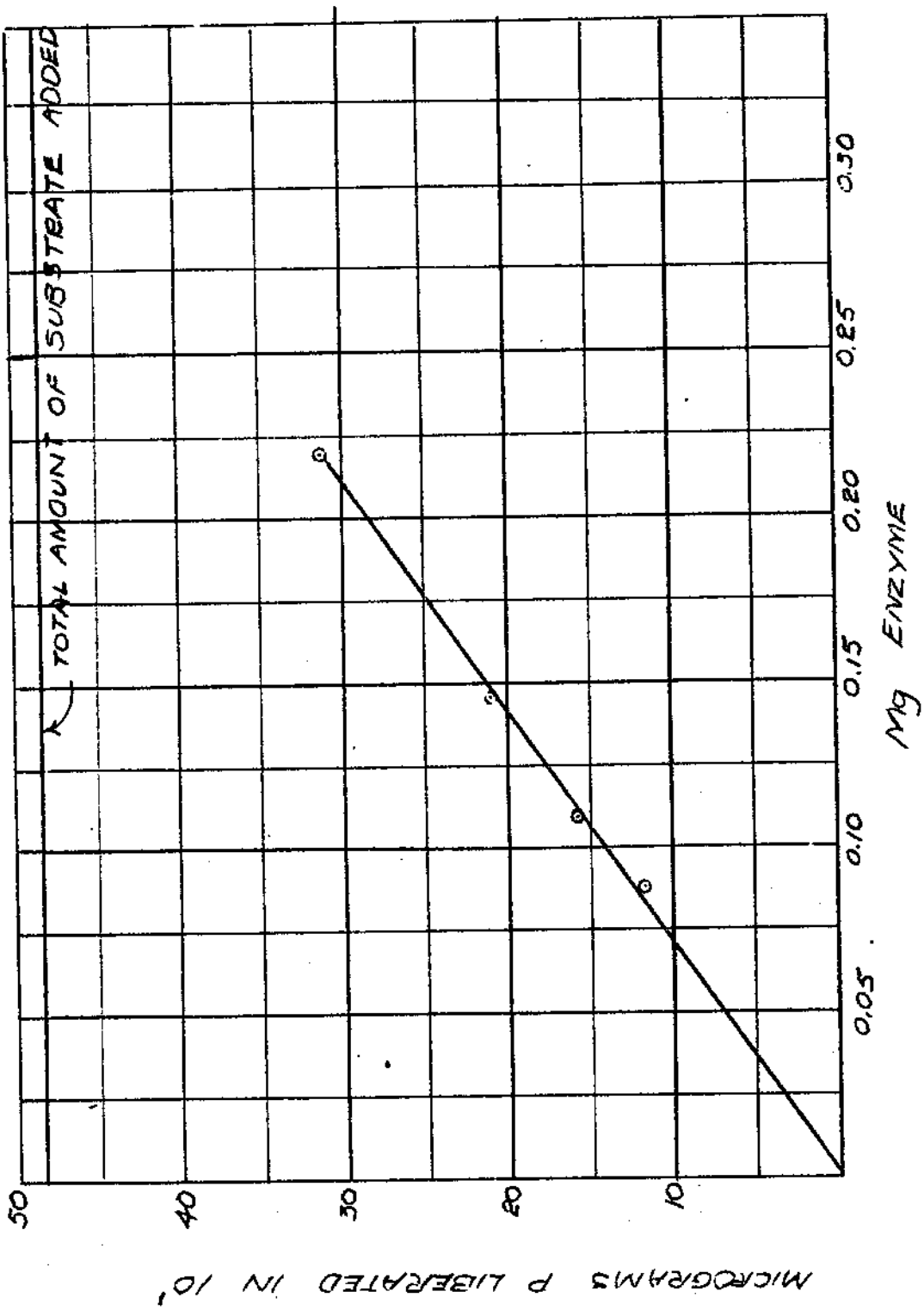
Amount of protein mgs. per cc.	Buffer	P liberated in 10 minutes Control (micrograms)	Irradiated	Inhibition %
0.220	Veronal	26.1	0	complete
0.220	Borate	31.2	17.4	44.2
0.147	Veronal	14.5	0	complete
0.147	Borate	21.0	7.50	64.4
0.110	Veronal	7.50	0	complete
0.110	Borate	15.8	2.20	86.1
0.088	Veronal	5.96	0	complete
0.088	Borate	11.2	2.75	75.4

TABLE IV

Reactivation by glutathione (GSH) (0.01 M) of Adenosintriphosphatase (Myosin) inhibited by X-rays (5000 r).

Amount of protein mgs. per cc.	Buffer	Micrograms P Liberated in 10 min. at 38°				Reactivation per cent
		Control	Control + GSH	Irradiated	Irradiated + GSH	
0.220	Borate	31.2	33.6	17.4	32.5	97
0.220	Veronal	26.1	-	0	0.71	?
0.147	Borate	21.0	30.4	7.5	15.2	48.7
0.147	Veronal	14.5	-	0	0.3	?
0.110	Borate	15.8	23.1	2.2	7.21	31.2
0.110	Veronal	7.5	-	0	0.3	?
0.088	Borate	11.2	19.9	2.7	5.87	29.7
0.088	Veronal	5.9	-	0	-	-

OH-1742



2. Metallurgical Laboratory Health Service - E. Clay, M.D. and J. J. Nickson, M.D.

During the month ending May 14, 1944, 207 pre-employment examinations were done. 159 were on non-academic personnel, 48 on academic personnel. 6 persons were rejected on the basis of the pre-employment examination.

3. Medical Industrial Hazards - J. J. Nickson, M.D., Section Chief

A. Color Photographs of the hands were taken on 3 individuals with various skin conditions. Mr. MacIntosh is working with Dr. Margaret Nickson in carrying out this program and setting up equipment for routine photographs of selected personnel.

B. Finger Impression Studies have continued. Approximately 400 sets of impressions were sent in during the past month. Dr. Harvey's readings on the previous impressions have not shown anyone on the project with unequivocal evidence of damage due to radiation. It is planned to continue these studies in the future by obtaining prints at intervals on exposed project personnel.

C. Sputum and Urine Studies for product were begun during the past month. The work has not progressed sufficiently to report the results in detail. Mr. Russell of Mr. Ashcraft's Section has been very helpful in developing the techniques used.

D. Metallurgical Laboratory Surveys — New Chemistry: An 0.8 curie slug was dissolved in New Chemistry during the past month. The shielding during the dissolving was satisfactory. Shielding for storage and workup of portions of the solution was initially unsatisfactory. Many individuals received greater than tolerance amounts of radiation for a period of about 1 week. Adequate shielding was eventually installed. No evidence of blood count abnormality has been found.

A 1.6 curie slug (approximate) was dissolved in Room 28, New Chemistry, during the week of 5-22-44. The shielding for most of the operation was adequate. The alpha ionization surveys in New Chemistry indicate that the situation is still unsatisfactory. The majority of the rooms surveyed gave off-scale readings. This indicates greater than 1.2 μg product per 120 sq. centimeters of surface measured. A major difficulty is the lack of dieners. It has proved to be extraordinarily difficult to obtain men for this position.

Site B Annex - Weekly surveys have been done in the Site B Annex. The general level of radiation has been below 100 milliroentgens, except for the hot lab. Here, levels of activity considerably greater than tolerance have been found consistently.

Beta hand counts have continued to be done on a weekly basis in New Chemistry. The incidence of hands with counts greater than 300 per minute has been low. In all but a few instances, ordinary washing of the hands has been sufficient to reduce the counts to below 300.

8 surveys on individuals with low blood counts were done during the month. No instance of over exposure was found.

104 surveys were done on persons whose pocket meters read 100 milliroentgens or more. 37 readings were felt by the surveyor to be due to exposure to active materials.

West Stands - The conditions in the semi-works, West Stands, producing high shoe counts have ameliorated somewhat during the past month. Dr. Pardue has set the upper limit for shoe counts at 5000 c/m with the present counter.

E. Industrial Surveys: On May 9, 1944, a plant fabricating tuballoy rods was inspected at the request of the Du Pont Company. Results and recommendations will be found in MUC-HG-479. On May 25, 1944, the Ames projects were visited. The details of the report are in MUC-HG-503. On May 27, 1944, a plant concerned with the canning of slugs was visited at the request of the Du Pont Company.

F. Washington University, St. Louis

The blood counts for the month of April showed the following abnormalities: Out of a total of 14 counts there were 4 white blood cell counts less than 5000, 8 lymphocyte counts less than 1,500, 1 polymorphonuclear less than 2500 and 4 monocyte counts greater than 6%. The exposure records taken with pocket meters ranged from 0.1 to 4.0 r for the month. Inquiry has revealed that the values measured represent less than the individual has received for two reasons. First, the meters are not always worn when exposure is taking place, and second, the range of the meter is too limited to measure the higher exposures. To correct the latter fault, film badges have been issued to the men. The film will be developed at weekly intervals in Chicago.

4. Clinical Laboratory Examinations - L. O. Jacobson, M.D.

A resume of the clinical laboratory examinations made from April 15, 1944 to May 15, 1944 is given below:

	Number Done	Number Abnormal
Hemoglobins	822	108
Red counts	607	75
White counts	1064	115
Differentials	1064	250
Platelets	271	22
Urines	790	145
Retics	97	3
Blood for Wassermann	219	
Miscellaneous	47	
Sedimentation rates	47	
Hematocrits	43	

New patients with abnormalities	138 out of 211 or 65%
Controls with abnormalities	54 out of 100 or 54%
Work hazard group with abnormalities	244 out of 896 or 27.2%
Total persons with abnormalities	436 out of 1207 or 36%

In the March report CH-1562 (A-2232) a resume of the routine criteria for classifying laboratory abnormalities was given. The aspects of the peripheral blood which we follow most closely are the total leukocyte count, lymphocyte-polymorphonuclear ratio, the absolute numbers of these latter constituents per mm^3, monocytosis and eosinophilia. Normal individuals with

no known or detectable exposure to chemical or physical agents or with various diseases will show abnormalities in these constituents. Each individual that presents such abnormalities are followed closely in an attempt to evaluate the relationship of such abnormalities to the work hazard.

During the past month three individuals were found to have blood abnormalities consistent with over exposure to radiation. Two of these abnormalities were low leukocyte counts per mm^3, the third had a lymphocyte-neutrophil ratio reversal. Surveys of the work areas did not show radiation levels exceeding 100 mr/8 hr. day in the first two instances. The third person has exposure above accepted tolerance standards on frequent occasions.

5. <u>Biochemical Group</u> - S. Schwartz, M.D.

A. Blood and/or urine studies on over 300 project members and medical students have been completed to date. The results are summarized in figures 1 through 8 below. (See Feb. report for basis of test scores. 0 = normal range; 1 = borderline; 2-4+ = increasingly positive reactions.)

Where repeated studies have been done on the same individual, only the first study is included here in order not to unduly weight the data.

Each individual is classified according to his predominant exposure, though it is clearly realized that other exposures may possibly play a determinate role in the test score. It is believed that chemical exposure may be of major importance in the workers in the radiation groups exhibiting increased scores. For example in the scores for the erythrocyte protoporphyrin (Fig. 3) it is seen that the individuals in the group believed to have received relatively heavy radiation exposure were all entirely normal, while several of those in the group believed to have received less radiation, nevertheless had increased values. The significance of this is not clear, but the explanation may be in an associated chemical exposure in the latter. It is believed that the tuballoy workers, except for the oxyfluroide group (Fig. 2) are less subject to mixed chemical exposure. It may be noted that the control group in these studies is open to criticism on the grounds that about half of the individuals may have had chemical or metal exposures incident to previous occupations.

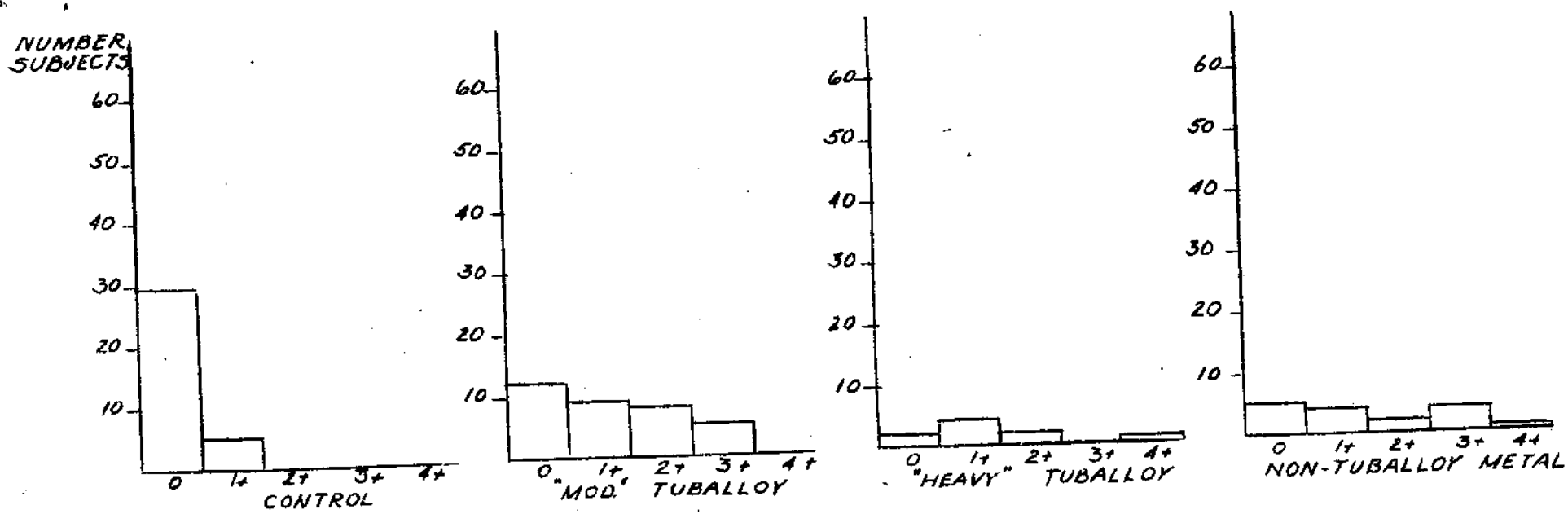
Plans are under way to control our data by studying other industrial workers with chemical and non-tuballoy metal exposures similar to ours. From the studies shown in Figs. 1-8, the following conclusions may be drawn:

(1) In general the total score is the most commonly positive index of exposure.
(2) Porphyrin metabolism is definitely affected in the metal exposure group.
(3) Serum sulfur appears to be elevated more in the tuballoy exposure group than in the non-tuballoy metal group, i.e. lead, mercury, brass, and tin. However, we have no adequate control series for the higher aged members of the former group as compared to other groups which we have studied.

Recent studies (mostly not included in the graphs) indicate that oxyfluoride exposure especially produces an elevated urine coproporphyrin value. Thus 25 determinations done on 13 individuals with varying amount of oxyfluoride exposure at Site B showed an average excretion of over 15 gamma percent (3 plus). 7 of the 13 individuals had a 4 plus coproporphyrin excretion on at least one test.

B. Preliminary studies of urine tuballoy indicate that the fluorescence technique suggested by Dr. Bloor of Rochester, New York, will permit the estimation of considerably less than 1/10 gamma. This method is based on the fluorescence of tuballoy in fused sodium fluoride. Detectable amounts of tuballoy have been found in 2 cc. aliquots of urine from highly exposed Ames personnel.

C. A study of radiation effect on five patients with polycythemia is under way in cooperation with Dr. Jacobson. Two have been treated with total body radiation and three with radioactive phosphorus.



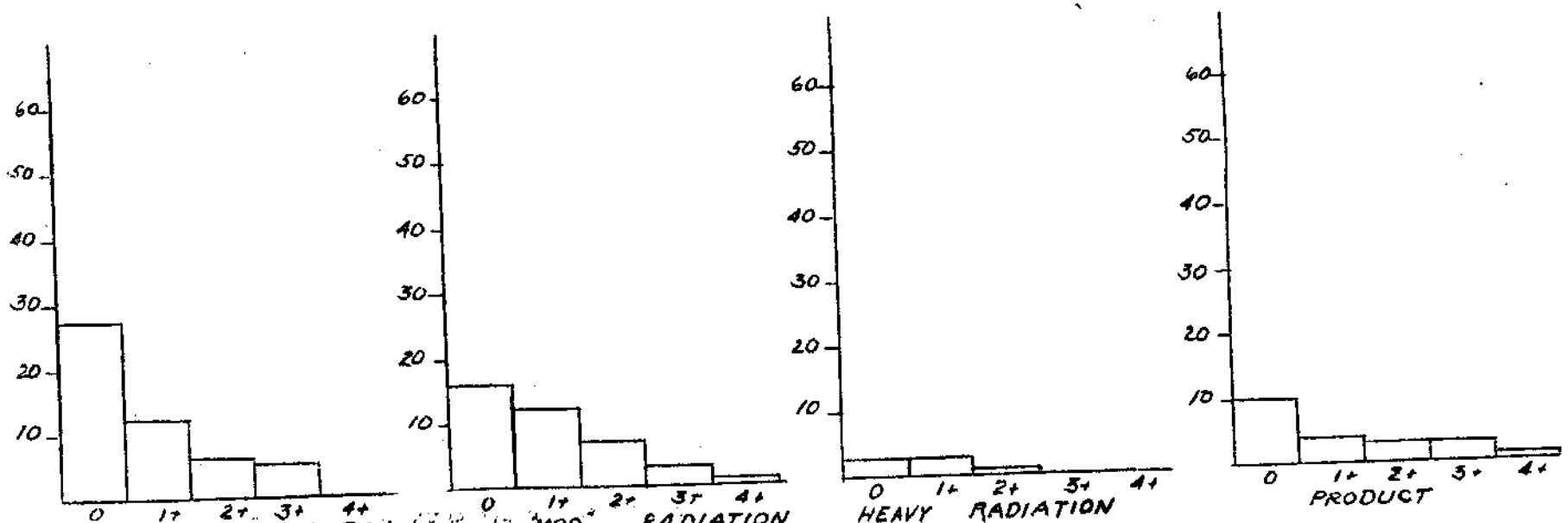


FIG. 1 AVERAGE SCORE

TOTAL SCORE DIVIDED BY NUMBER OF PROCEDURES USED IN GIVEN INSTANCE, AS FOLLOWS:

0.0 - 0.5 = 0
0.51 - 0.8 = 1+
0.8 - 1.1 = 2+
1.11 - 1.4 = 3+
> 1.4 = 4+

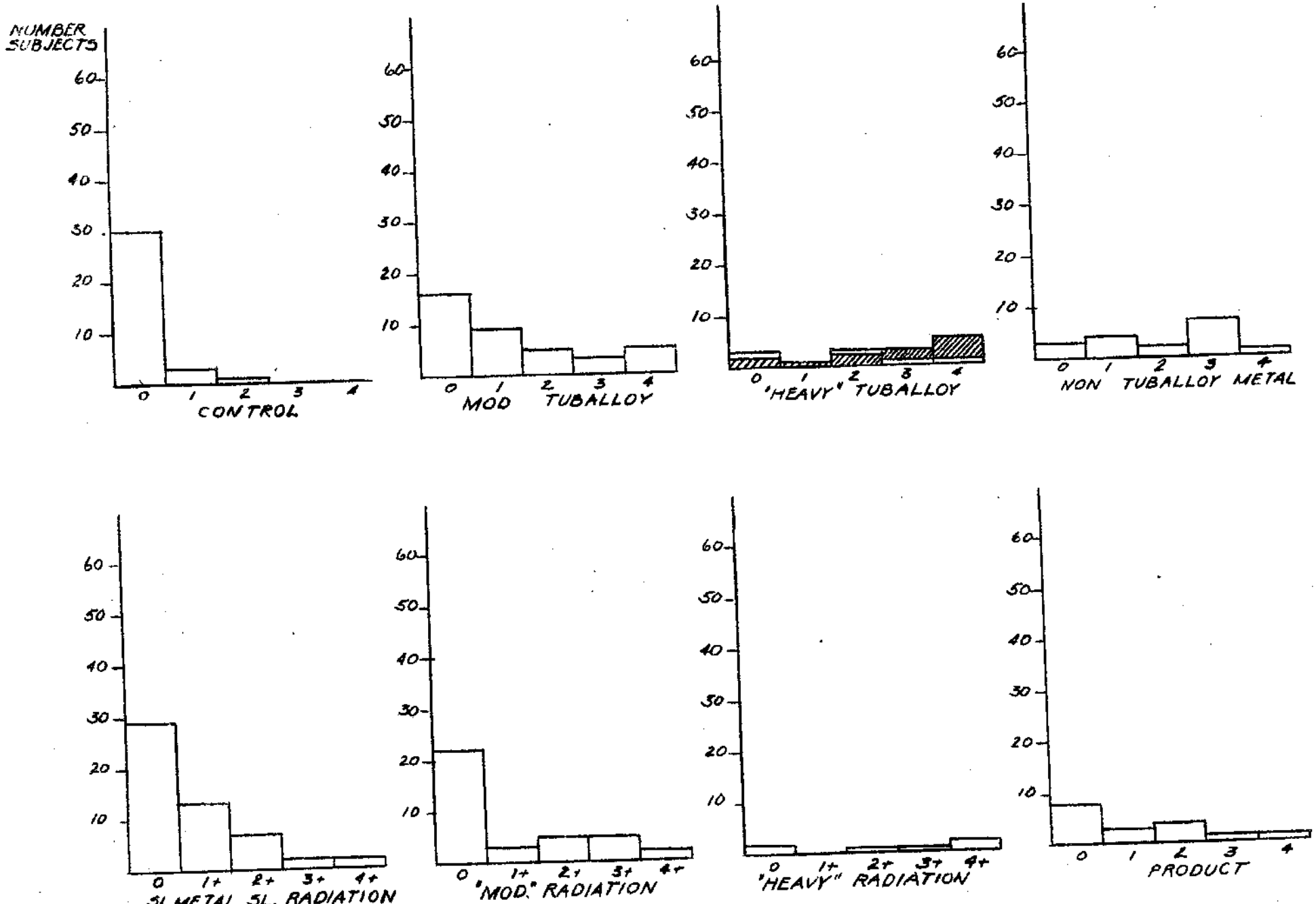


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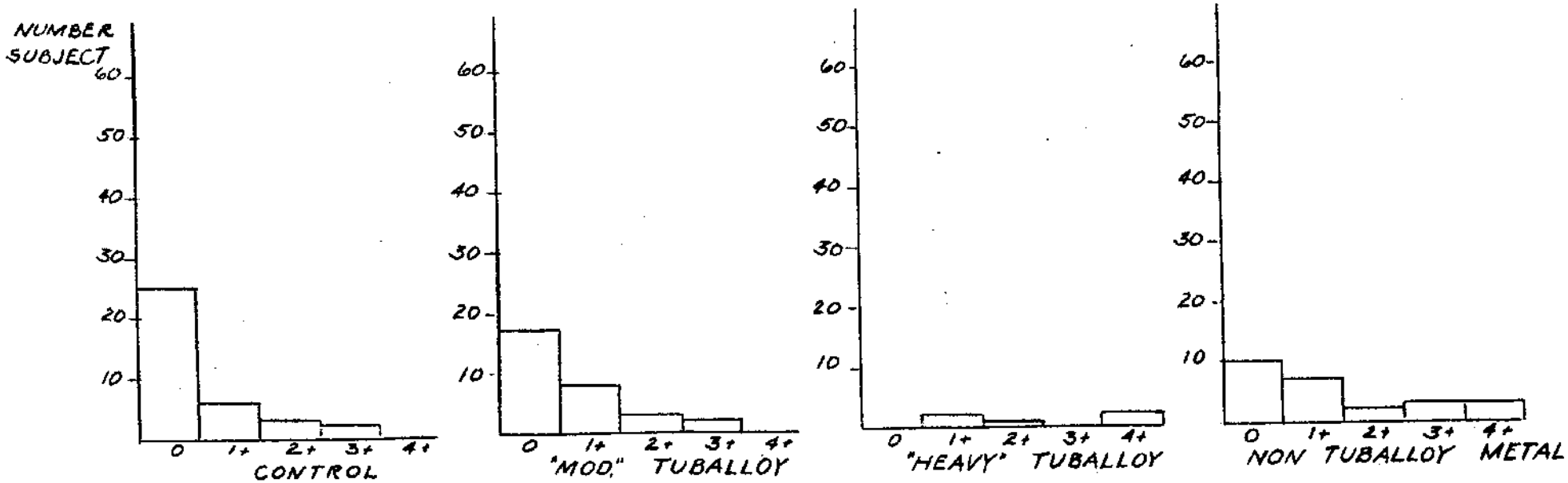
FIG. 2 COPROPORPHYRIN



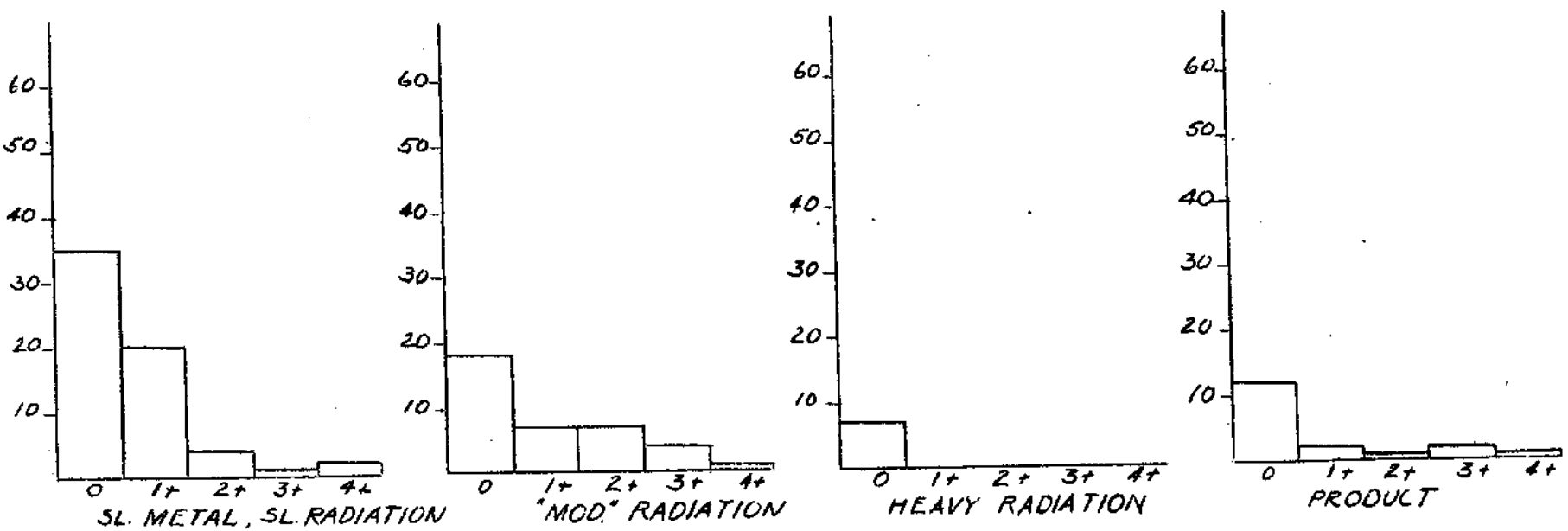


FIG. 3 RBC PROTOPORPHYRIN

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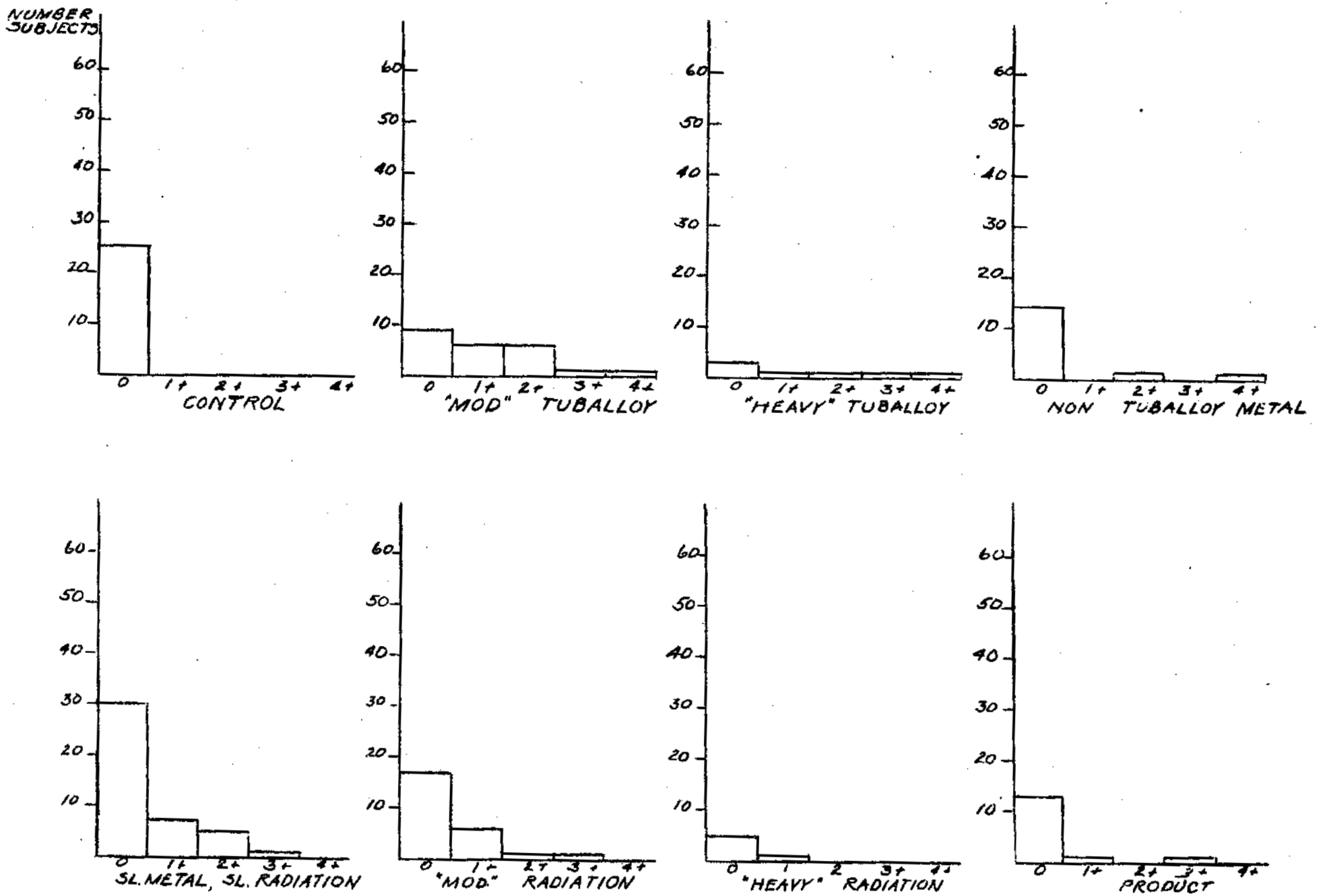
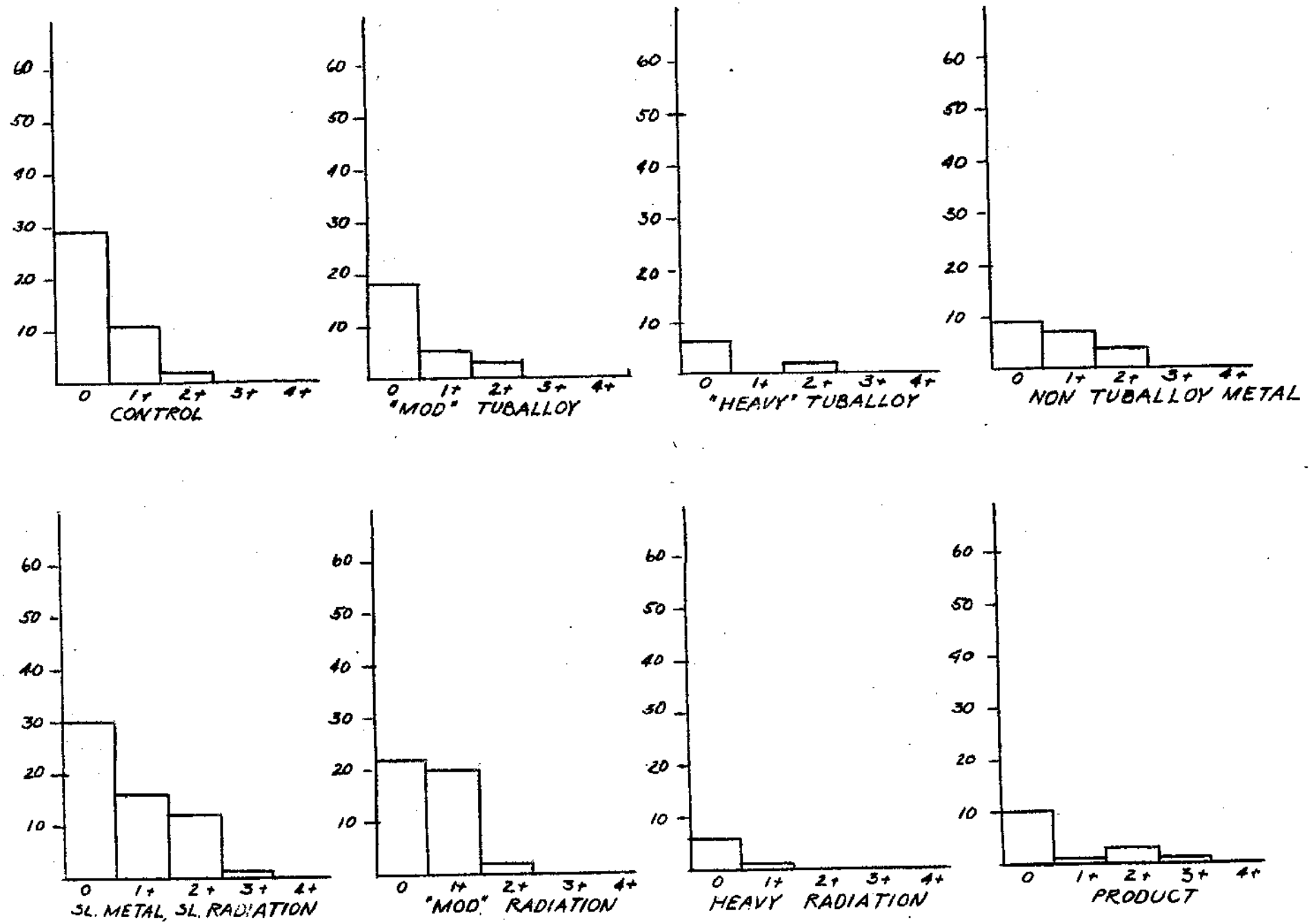
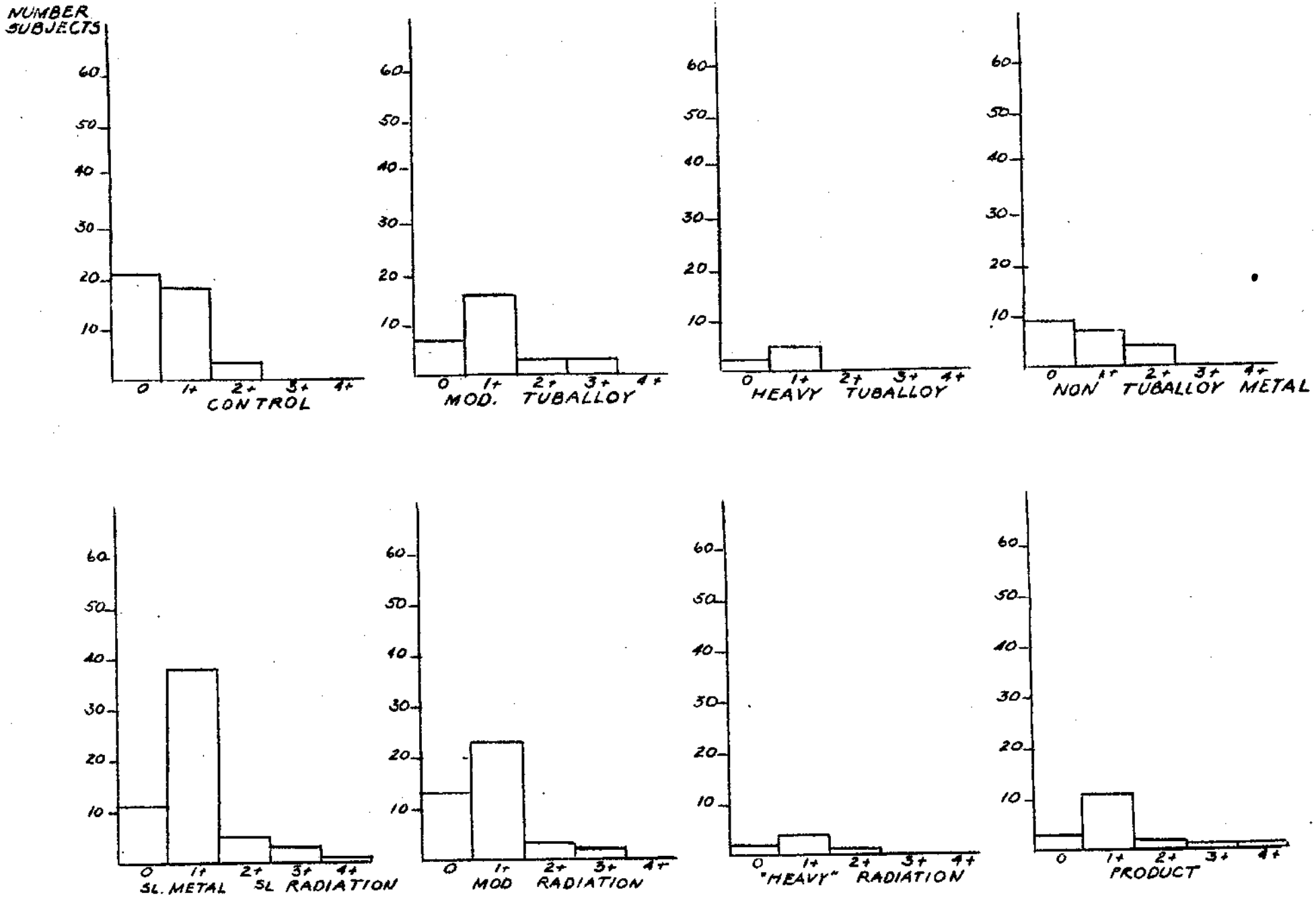


1118632 FIG. 4 BL. SERUM SULPHATE



1118833 FIG. 5



1118834 FIG. 6 COLLOIDAL GOLD

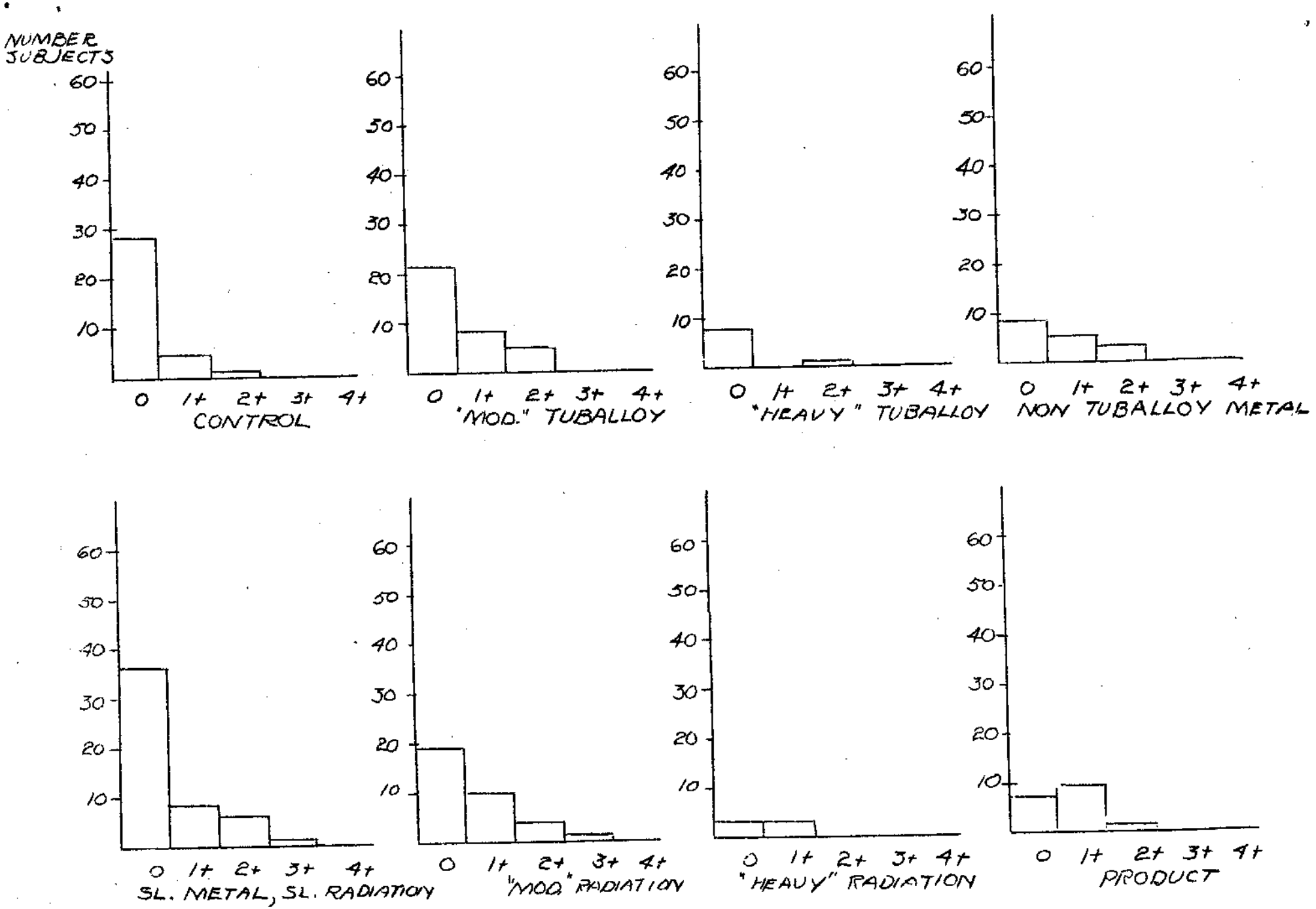


FIGURE 7 ABSORPTION AT 400 MM

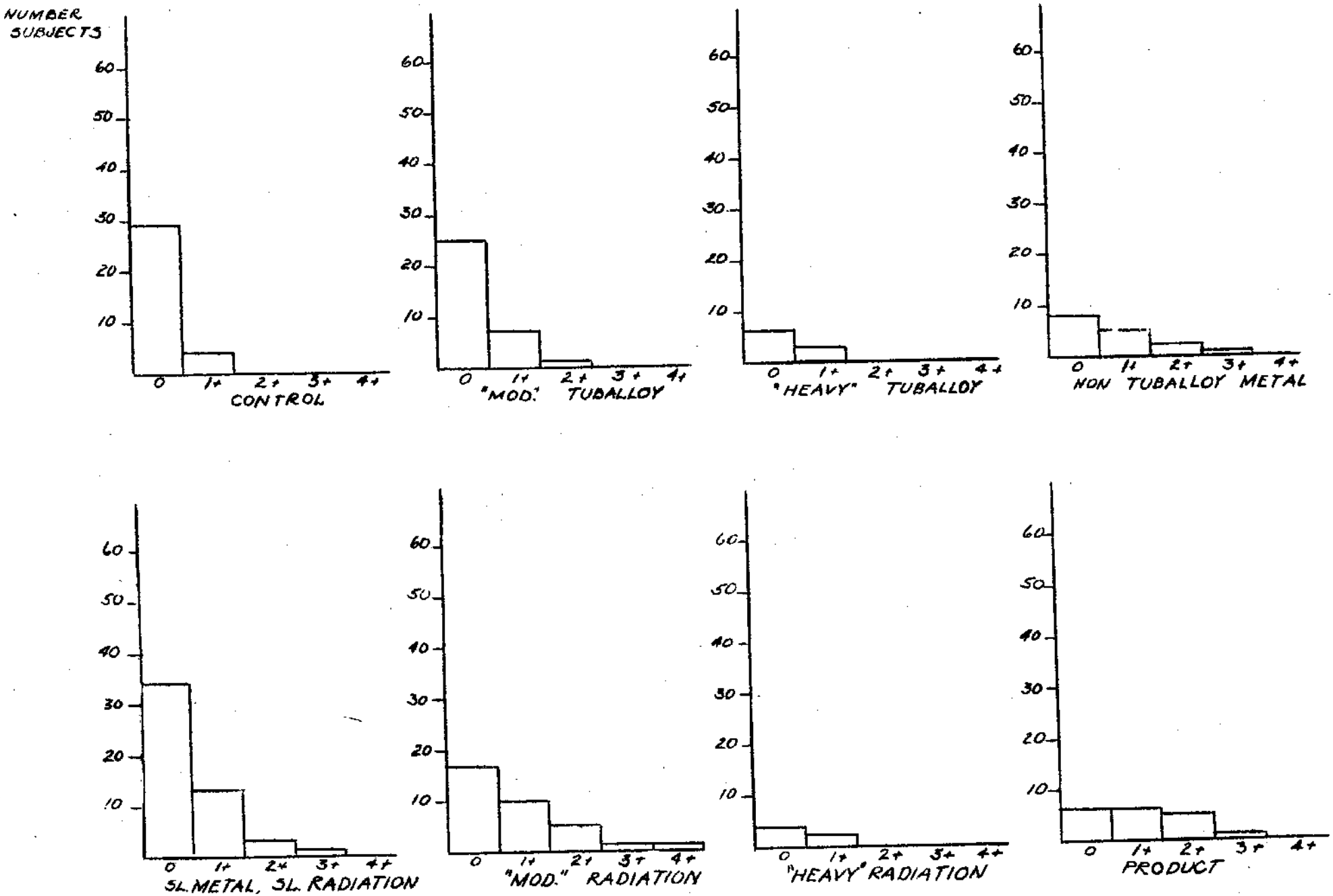


FIG. 8 ABSORPTION AT 520 MU

ASSOCIATED PROJECTS

I. N.C.I. - R. R. Spencer, Chief

BIOLOGICAL ACTION OF GAMMA AND X RADIATION

A. B. Eschenbrenner, M. B. Shimkin, W. E. Heston, M. K. Deringer and E. Lorenz

I. Continuous exposure for 8 hours daily.

Approximate doses up to date (mice and guinea pigs 1st series) 3500 r, 1750 r, 875 r, 440 r, and 49 r (acute exposures of 12.5 r or 50 r not added). Approximate dose up to date (rabbits) 2700 r, 1350 r, 675 r, 340 r, and 32 r (acute exposures of 12.5 r or 50 r. not added). Approximate dose of male inbred guinea pigs (family 2) up to death of last pig exposed on 8 r per 8 hour level 1600 r and of female inbred guinea pigs (family 2) 1050 r. Approximate dose up to date of hybrid guinea pigs (2nd series) exposed on the 8 r per 8 hour level 1500 r. Approximate dose up to date of male and female inbred guinea pigs (family 13) 250 r.

A number of mice about equally divided among the different levels were killed and autopsied due to intercurrent disease (tumor formation, pneumonia or infections). Two female control mice, one female mouse had received an acute exposure of 125 r and one female mouse had received an acute exposure of 50 r; and 3 female mice of the 0.1 r / 8 hr level, 2 of which had received in addition 12.5 r or 50 r respectively, were killed and autopsied. This was done to verify the finding (see April report, page 6) that an acute dose of 50 r in 5 hours given at the approximate age of 5 months showed at the age of approximately 16 months, ovaries devoid of follicles with extensive invagination of the germinal epithelium. This finding was confirmed (see IV) and it indicates that an acute dose of 50 r in 5 hours in early life will show in late life extensive damage to the ovaries while approximately the same dose given at the rate of 0.1 r per 8 hours will produce no damage in comparison to controls. One more mouse (female) of the 8 r per 8 hour level developed malignant lymphoma (gross observation) bringing the total of animals with malignant lymphoma on this level to 9. One mouse exposed to an acute dose of 50 r in 5 hours also showed malignant lymphoma at autopsy. This is considered of spontaneous origin. So far, 3 cases of malignant lymphoma, considered to be spontaneous, have been found in mice of the lower levels, none in the controls. This is not surprising, however, as the number of control mice is much smaller than the number of experimental animals.

Two guinea pigs of the first series of the 8 r per 8 hour level are still alive, after a total dose of 3500 r. All guinea pigs of the second series died or were killed in moribund condition (lethal dose ranging from 625 r to 1300 r) with the exception of one female having received so far a total dose of 1500 r. All male inbred guinea pigs (family 2) either died or were killed in moribund condition, the lethal dose ranging from 1200 r to 1600 r. As only 4 male guinea pigs of this series have come to autopsy, (the females have not reached this dose level as yet) it is difficult to say whether these inbred guinea pigs are somewhat more radioresistant than the hybrid guinea pigs and whether this radiosensitivity is more uniform as evidenced by the comparatively narrow range of the lethal dose.

One female guinea pig of the 4 r per 8 hour level was killed during the month in moribund condition (dose 1700 r). So far, 6 out of 18 guinea pigs

of this level were killed in moribund condition, the lethal doses ranging from 900 to 1700 r. On the 8 r per 8 hour level, 13 guinea pigs out of 18 died or were killed and autopsied in moribund condition for a lethal dose ranging from 600 to 1700 r. This seems to indicate that the amount of recovery due to the greater dilution of the dose of the animals on the 4 r per 8 hour level is comparatively slight in comparison to those of the 8 r per 8 hour level.

The guinea pigs on the other levels are still comparable to the controls (weight and blood picture).

All rabbits are alive.

Breeding Experiments

Aside from some data on lung tumors which are presented in this report, there is nothing to add to the last report.

All mice of the breeding experiments have been observed for the presence of lung tumors at autopsy. The nodules that were found have later been sectioned for histologic verification. The results of these findings are tabulated as follows:

Lung Tumors in Irradiated and Control Mice of Breeding Experiment

	Irradiated			Control		
Dosage	Age at autopsy months	Num. of mice	Num. with lung tumor	Age at autopsy months	Num. of mice	Num. with lung tumor
Males						
600 r - 4r/day	5 to 8	15	1			
800 r - 4r/day	6½ to 8	15	0 1/			
1000 r - 4r/day	9 to 12	15	7			
600 r - 2r/8 hrs.	11	8	2	11	8	1
600 r - 4r/8 hrs.	6 to 9	12	1	6	8	0
800 r - 4r/8 hrs.	7 to 9	12	1	7½	8	0
1000 r - 4r/8 hrs.	9 to 10½	12	3	9	7	0
600 r - 8r/8 hrs.	4½ to 6	12	1	3½	8	0
800 r - 8r/8 hrs.	6 to 9	12	1	3 to 4½	8	0
800 r - 8r/8 hrs.	4½	8	0 2/			
1000 r - 8r/8 hrs.	6 to 9	12	3	5	8	0
1600 r - 8r/8 hrs.	7½ to 12	13	3			
1000 r - 8r/8 hrs.	5	8	1			
Females						
800 r - 8r/day	7 to 8	5	2			
600 r - 8r/day	6 to 7	14	1			
500 r - 8r/day	6 to 7	15	1			
400 r - 8r/day	5 to 6	15	0			
300 r - 8r/day	4½ to 6	15	0	4½ to 6½	15	
500 r - 4r/day	7 to 8	14	0			
400 r - 4r/day	6 to 8	14	0			

Continuation of table

Dosage	Age at autopsy months	Num. of mice	Num. with lung 6 tumor	Age at autopsy months	Num. of mice	Num. with lung tumor
300 r - 4r/day	6 to 6½	15	2	6 to 7	15	1
200 r - 4r/day	5 to 6½	15	1	5 to 7	15	0
100 r - 4r/day	4 to 5	15	0	4 to 5	14	0
500 r - 2r/day	10 to 12	9	1			
400 r - 2r/day	9½ to 11	13	2			
300 r - 2r/day	8½ to 10	15	1	8½ to 9	14	1
200 r - 2r/day	7 to 8½	15	3/			
100 r - 2r/day	5 to 6½	14	0			
300 r - 1r/day	12½ to 17	10	1	11½ to 16½	13	3
200 r - 1r/day	10 to 11	14	0	9 to 11	14	0
100 r - 1r/day	6 to 8	15	1	6½ to 8	15	2/
100 r - 0.5r/day	11 to 12	13	0			
300 r - 4r/8 hrs.	6 to 6½	14	1			
400 r - 4r/8 hrs.	7 to 8	7	1			
500 r - 4r/8 hrs.	8 to 13	10	3			
500 r - 8r/8 hrs.	6 to 7	6	1			
400 r - 4r/day	9 to 10	6	1/			
400 r-- 4r/day	8 to 11	8	0			
400 r - 4r/day	10 to 11	6	1			

1/ Two have not been sectioned for histologic verification.
2/ One has not been sectioned for histologic verification.
3/ One " " " " " " "
4/ One " " " " " " "
5/ Has not been sectioned for histologic verification.

The lung tumor incidence of the irradiated females is not considered significantly different from that of the control females. The males which on the whole received larger total doses than the females gave results which suggest that there may be an increase in lung tumor incidence in the irradiated males over that of the controls.

The evidence is far from conclusive, but it does suggest the advisability of a more complete test. Accordingly, an additional experiment has been started, using the highly susceptible lung tumor strain A. Twenty-five male and 25 female strain A mice between one and two months of age have been placed on the 8 r/8 hr. level, and 25 male and 25 female littermates have been set aside for controls. It is planned to run this experiment for 8 to 10 months, depending upon how well this strain tolerates the irradiation, and after the irradiation, the lung tumor incidence of the experimental mice will be compared to that of the control. This strain has an incidence of around 50% at 12 months of age.

As no blood counts are to be taken on these animals, 20 strain A male mice are also being irradiated on the 8 r/8 hr. level and their blood counts are being followed. These will serve as safeguards against deaths due to irradiation in the lung tumor experiment.

Only rarely lung nodules were found in animals of the 8 r per 8 hour level not used in the breeding experiment which were killed and autopsied since January 1. These animals ranged in age from 12 to 16 months and had received doses from 2500 to 3400 r. This finding is, however, not in contradiction to the above statement as the number of animals is small, the animals were sick prior to autopsy, and no controls of comparable age were available.

II. Continuous exposure for 24 hours daily.

Nothing new to report.

III. Single acute exposure (300 r in 7½ minutes)

The animals of this experiment (female LAF_1) are still alive and have remained sterile since the birth of one litter approximately 5 months ago.

IV. Pathology.

Mice

One male mouse that had received approximately 360 r on the 1 r per 8 hour level was autopsied because of poor general condition. There was hemorrhagic necrosis of one lobe of the liver, apparently due to torsion and occlusion of the venous return of that lobe; a condition occasionally seen in untreated mice. Testes appeared normal, as did other organs.

One male mouse that had been exposed on the 8 r per 8 hour level daily for a total of 3000 r had enlargement of all lymph nodes, enlargement of the spleen and infiltration of all organs including the bone marrow. This has been designated a malignant lymphoma, type unclassified. There was extreme atrophy of the testes. No spermatogenic elements could be identified. Another male mouse exposed on the same level for a total of 3100 r had similar atrophy of the testes. Lymph nodes were very small and composed of a single giant follicle. The spleen was slightly larger than normal and composed of conglomerate Malpighian corpuscles. There was no bone marrow atrophy.

A group of female mice that had received a small total chronic or acute exposure was autopsied. The condition of the ovaries is shown in the table below. The downgrowths of germinal epithelium was similar to that previously reported for animals receiving larger amounts of radiation. The difference between the effects of acute and chronically administered radiation over a long period of time of approximately the same total amount is apparent. It has previously been reported that male mice that received 50 r as an acute dose under the same conditions had normal testes.

Age in months	Chronic level in r	Chronic total in r	Acute total in r	Total chronic & acute in r	Follicles	Downgrowths germinal epithel.
16	0	0	0	0	plus	minus
16	0	0	0	0	plus	minus
16	0	0	12.5	12.5	plus	minus
16	0	0	50	50	minus	plus
16	0.1/8h	45	0	45	plus	minus
16	0.1/8h	45	12.5	57.5	plus	minus
14	0.1/8h	35	50	85	minus	plus
16	0.1/8h	45	50	95	minus	plus

Acute doses given at approximate age of 5 months.

Guinea Pigs

One female guinea pig on the 4 r per 8 hour level was autopsied because of poor general condition (R. B. C. 1.06 million) after receiving a total dose of 1500 r. Ovaries contained numerous small and large follicles. There was moderate bone marrow atrophy, no fibrosis. Lymph nodes contained numerous very small and several giant follicles. The spleen was small, containing very small Malpighian bodies.

One male and one female guinea pig (2nd series) of the 8 r per 8 hour level which had received a total dose of 900 r were autopsied because of poor condition and marked anemia. There was moderate bone marrow atrophy. Lymph nodes contained small and giant follicles. Malpighian bodies in the spleen were small and few in number. There were patchy extravansations of blood in the submucosa of the proximal half of the small intestines. Ovaries contained numerous large and small follicles. There was extreme testicular atrophy, no spermatogenic elements being identified.

Two male hybrid guinea pigs that had been exposed to 8 r per 8 hour daily for a total of 250 r had apparently normal testes. There was active spermatogenesis and the tubular-interstitial proportions appeared normal. These guinea pigs were killed to establish a dose which does not produce damage to the testes. As previously reported, 500 r. produced marked tubular damage.

Two male inbred guinea pigs that had been exposed on the 8 r per 8 hour level for a total of 1200 r were autopsied because of poor general condition and anemia. There were patchy submucosal extravasations of blood in the proximal portion of the small intestines. Spleens were small and contained few and small Malpighian bodies. Lymph nodes were small and contained numerous small and a few giant follicles. There was moderate bone marrow atrophy. Testes were extremely atrophic, no spermatogenic elements being identified in the tubules.

V. Hematology.

No significant changes have occurred in the blood picture of the animals since the report of last month. A few experimental mice that showed sudden high total white counts with a relative lymphopenia showed at autopsy signs of intestinal infection (gross observation). Only one more mouse developed anemia (dose 3200 r on the 8 r per 8 hour level). In all other mice of this level the red and platelet count is still within normal limits.

The guinea pigs, which came to autopsy, showed the previously described low red, platelet and white cell count with a relative lymphocytosis, with the exception of one inbred male guinea pig, which had a red count of 4 million but a total white count of 500 with no polys. In this guinea pig the ecchymosis of the small intestine, stomach and heart were absent.

The blood count of all rabbits is within normal limits, with the exception of the white cell count, of the animals on the 8 r per 8 hour level (total dose 2100 r) which is lowered. These animals also show lymphopenia.

II. U. of C. Radiation Laboratory

J. G. Hamilton and Associates

TECHNICAL PROGRESS REPORT ON THE METABOLIC STUDIES OF FISSION PRODUCTS

1. Radio-Autographic Studies

The lung radio-autographic studies with long life fission products are now essentially complete and a detailed report containing both the results and full descriptions of methods is being prepared by Miss Axelrod. Suitable celloidin imbedded bone preparations are now available and will be cut as soon as we receive our sliding microtome for which the promised delivery date is August 1, 1944.

2. Decontamination Studies

The animals for the long term decontamination studies with cerium, yttrium and strontium have been sacrificed and the tissues are now being assayed. Results of these experiments will be available shortly.

3. Tellurium

The intramuscular and oral studies with $f4$ carrier free tellurium have been almost completed by Professor Chaikoff and his associates for the 1, 4, 16, and 32 day intervals. Approximately 25% of the administered dose is absorbed by way of the digestive tract. The rate of elimination following both routes of administration is quite rapid. Approximately 25% is excreted during the first day, 40% at the end of 4 days, 70% at 16 days, and 90% at 32 days. These values indicate the half-time of retention of the absorbed portion in the body to be of the order of 10 days. The highest uptake per gram of wet weight was in the kidney while the greatest uptake per organ was found to be in the blood for all four time intervals. Otherwise no striking selective localization took place in any of the tissues assayed including the skeleton. Lung experiments were done but the interpretations of the results were somewhat confused by the relatively high absorption in the digestive tract. From the qualitative point of view the pulmonary retention of $f4$ tellurium is apparently relatively small and can be considered to be of slight importance as a health hazard when compared to the more abundant long life fission products which show a high degree of lung retention. It is of interest to note in passing that the high recovery of administered tellurium in the tissues and excreta which ranged from 90% to 93%, indicated that no large fraction of the administered dose was excreted by way of the lungs following either intramuscular or oral administration. It will be recalled that it has been stated frequently that following tellurium poisoning in humans some excretion does take place by way of the lungs through the exhalation of volatile tellurium compounds.

4. Projected Studies for the Next Two Months

Tracer studies and decontamination studies are to be concluded.