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TO : Files
THRU C. L. Dunham, M.D., Director
Division of Biology and Medicine

DATE: January 26, 1959

FROM : H. D. Bruner, M.D., Chief
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Division of Biology and Medicine
JHB for HDB

720239

SUBJECT: MEDICAL EFFECTS OF HIGH DOSES OF RADIATION - CONFERENCE HELD AT WALTER REED ARMY INSTITUTE OF RESEARCH, JANUARY 20-21, 1959

SYMBOL: BMM:HDB

After a welcome by Colonel Mason and General Cooney, Colonel Maupin stated the problem: What numbers of high dose (relative to duration) can a man take and still be functional? It is hoped that this conference will produce better numbers and guide a research program. One of the reasons for this, the Davy Crockett system, was then described.

Payne Harris, LASL, referred to LA 1910, March, 1956, Effects of High Doses on Monkeys, (Classified), and then showed a movie. At high altitudes the radiation range may be greater than the blast range. The 9000 curies of Ba^{140}-La^{140} source at Los Alamos was used to study rats and then monkeys. The report is on physiological and pathological effects from high dose rates and high total doses. At rates up to 10,000 r, there is an immediate failure of performance and the animal has no motivation. There is then a recovery period whose length is inversely proportional to the total dose. This is about $3\frac{1}{2}$ days for 5000 r. Monkeys with their higher CNS integration may be able to take only half the high dose of rats for CNS deaths. Hence, 5000 rad total dose would cause immediate incapacitation - 2 to 3 minutes after exposure. Nausea, vomiting, and diarrhea are prominent.

Some monkeys exposed to the Godiva for same dose in 50 m sec gave a latency for the immediate CNS depression of 2-3 minutes. Size of monkeys, up to 40 lbs., made no difference. The monkey accumulates about 2500 r before he shows the first gross reaction which is scratching and a sort of slumping.

Colonel McDonnel described the Plumbbob experiment on 1200 landrace pigs. On priscilla the pigs got up to 20,000 rep and died. At 2000 rep they survived the radiation but died of burns and blast. At about 500 to 1000 rep deaths were in 5 to 15 days and they were not incapacitated. At 39,400 to 230,000 rep air dose animals lived up to 85 hours. In tanks, the doses were up to 20,000 rep and lived for up to 6 hours but the interior of the tank was up to 130° F. (He talked too fast and I could not get doses, times, etc. together, but it was clear that the dosimetry was very terrible and unreliable).

Colonel Moncrief talked about the Humbolt shots where the interest was in the immediate lethality in pigs. The animals were in foxholes and tanks. The pigs showed severe radiation effects on the gut and CNS almost at once. This was followed by a recovery period, but they did not eat. Death at 2.5 to 60 hours was accompanied by convulsive movements. The dose may have been up to 26,000 rad of neutrons and 15,000 to 36,000 rads of gammas. Dosimetry here, too, was inconclusive. The foxholes helped but did not prevent death. There were no thermal effects of any consequence, but blast effects tend to complicate the picture somewhat.

Howard Andrews reported that mice seem to feel the presence of radiation at 100 r/min or greater and mice tend to move out of the way.

The guinea pig was exposed while EEGs were taken to the 3.5 Mev generator at rates of about 2000 to 3000 r/minute. With hamsters the survival time is proportional to log of the dose after the intestinal dose level is passed. Rats behave similarly, but the value for the regression line is different from that of the hamster. Mice have different line constants. Exposure of the head versus the body only gives different lines, but head and total body are essentially the same.

Pentobarbital helped protect against the lethality of CNS death in guinea pigs.

EEG traces of guinea pigs after 25,000 r are not too abnormal. The EKGs also are not too bad - some brachycardia, but no change in conduction time, etc. The wave durations in the EEG were skewed toward the longer, slower waves but not very spectacularly. The same thing occurred with the body shielded. With the body only exposed, the slow waves were much more prominent than when the head was exposed. (Very curious!)

He also used the Hardy-Wolff "pain threshold" system to test the guinea pigs and saw no changes of the afferent-reflex center (s) efferent responses up to the time of death. He reported fractionation of dosage where the two dosages were equal. The longer the interval between the two doses the longer was the total survival time. He tends to give excessive significance to this, but has not published these data. At 15,000 r (450 r/min) the survival time averaged 72 hours; at 21,000 r some lived 72 hours and some lived less than 30 hours or so with an average of 50.5 hours; at 24,000 r mean survival was 13.9 hours.

There seems to be a feeling that a total of about 1500 r causes the animal to respond in a way that suggests nervous system effects.

After lunch Colonel Pickering showed the movies of the monkeys which had received high doses of mixed gamma and neutrons. They had severe immediate depression which regressed in some before death. There was circulatory depression which developed acutely and may have contributed.

Tom Shipman reported on the Kelley accident; the dosage is not yet at all certain. Dr. Shipman's description added little to what we have but he showed some pictures. He showed CNS depression, nausea, vomiting and diarrhea; erythema; HR = 150 and BP 60/40 at a guess. By 8 hours post exposure he was in better shape mentally, but still fuzzy. He vomited once more after midnight. He was anuric from 10 hours onward. The rest of the time he was more or less quiet, nauseated and dozing.

The initial Hb and RBC were high but were reduced by 8 liters of fluid. The polys rose from 4,000 to 24,000 and the lymphocytes went to zero and stayed there. The NPN and uric acid rose steadily as the renal function ceased.

The patient with about 140 rad (rem) has had no symptoms. His lymphocytes have dropped to about 1/5 of the normal level and the polys from 7,000 to 3,000/mm^3 or so.

Dr. P. Harris suggested that the patient was standing against the tank. There was about 3 kg of plutonium and 10^{17} fissions. It did not oscillate. Enough heat to raise the temperature about 800° F occurred in about 50 m sec, so that there must have been the formation of vacuolation. He thinks they can get neutron data from the solution and gamma ray data from fresh film badges in a rack 135 feet away. A part of the difficulty in the dose for gammas is Kelley's position relative to the tank. They propose to use Na^{24} activation for the neutron dose using a $Na^{23}Cl$ filled polyethylene bag. Present estimates indicate about 400 to 500 rad. Activation of S^{32} in the tissues is also being studied. The γ/n ratios may be as much as 10/1 but they do not know. They cannot pick an exact dose but Harris thinks about 5,000 rads.

Dr. Shipman assembled the attached table.

Harris thinks the skin nerve ends are being stimulated by the thermal neutrons. This may explain the excessive scratching of the monkeys during exposure to mixed radiation.

Dr. Haymaker: Described the histopathology of monkeys dying spontaneously after 1,000 - 30,000 r. Another group of monkeys was sacrificed after comparable doses. (Dose rate at 1,000 r/min.).

5,000 r produces an internal reaction of the endothelium of the vessels of the choroid plexus and meningeal vessels may see focal meningitis which may be related to the blood vessels. Thus, vasculitis was an outstanding important feature: Swelling of the collagen is also prominent.

There are also clearly pyknoses of the granular cells of the cerebellum at doses of 5,000 or above and becomes more consistent as the dose increases. Same is true of the basophil cells of the pituitary.

In monkeys receiving 10,000 r, there are meningitis (peak at 8 hours), vasculitis (peak at 12 hours), choroid plexitis (peak at 8 hours), and pyknosis of the granular layers of the cerebellum (peak at 24 hours). The white matter changes are maximal at 4-5 days which gives spotty, patchy areas of poorly staining myelin.

The brain weighed 200-300 grams more than it should; it was apparently edematous with low protein fluid. There was little or no meningitis but some evidence of macrophages having engulfed blood pigment. There were vessels in the brain with areas of mononuclear cells - a low grade vasculitis in the brain. The picture is not that seen in shock. Dr. Haymaker is willing to be quoted on this. The picture is not that seen following burns or uremia of such short duration. Damaged leukocytes were circulating in the blood stream.

He showed slides of guinea pigs which had been at 100,000 feet purporting to show histological evidence of the passage of a neon nucleus-cosmic ray. The histological picture was that of a cylinder of cellular damage.

The histological picture in the brain after head-shielded deaths (from high doses) is not the same as that seen after the head-exposure. He quoted Vogel's conclusion that the histological picture from head only and head + body exposure to high doses were identical.

Colonel Glass (psychiatry) discussed the effects of a nuclear weapon on behavior both before and after exposure to weapons. We worry about the "no hope of survival - no chance of getting out of it." In this situation we come apart - hopeless apathy. "There are no superlatives when one is contemplating death."

If there is a chance, a man carries on often with bravado, especially if it is his first experience. A near miss gives caution - a far miss gives confidence.

The recovery phase or secondary phase is a problem. To return a man to duty who then dies or comes apart causes general deterioration of morale. But it is practically impossible to distinguish between functional and psychiatric incapacity.

Payne Harris thinks men with 200 to 1000 r will look perfectly O.K. for a few days but then will come apart. How can we be sure he has been radiated?

We have a dilemma: If they are knowledgeable about the weapon so that they can act independently and effectively, then they will also have the information upon which to develop neuropsychiatric symptoms and become psychiatric casualties or at the least reluctant combatants.

The discussions of the second day were taken up entirely by the Committee attempting to come to agreement on the dosage needed to produce a given level of clinical effect. See Dr. Van Cleave's report for their findings.

Attached is Dr. Shipman's tabulation of the signs and symptoms of the recent cases and the membership of the Committee.

Attachments:
(1) Tabulation as stated.
(2) Membership of Committee.

Compendium of O.R. Cases

EARLY SIGNS AND SYMPTOMS OF DIAGNOSTIC AND PROGNOSTIC IMPORTANCE IN SEVERE RADIATION INJURY

Dalcin Shoton Kelly

	Case I > 300 rem	Case II 800 rem	Case III 1900 rem	Case IV 12,000 rem
Ataxia and Disorientation	No	No	No	Prompt
Shock	No	? Mild	No	Severe
Nausea and Vomiting	Mild, 2 hrs.	Troublesome, 1-1/2 hrs.	Mild, 1 hr.	Severe, 15 min.
Diarrhoea	No	No	Once, 4 hrs.	Severe, 45 min. Explosive Propulsive
Erythema, Onset	No	3 days	24 hrs.	Immediate
Fever	?	Slight and Irregular Late	Moderate and Irregular Late	at once 103.5°, falling to normal in 12 hrs.
Hemoconcentration	No	Moderate and Gradual	Moderate and Gradual	Prompt and Severe
WBC, Total Count	Initial Rise, followed by drop, Mild	Rise to 16,000 in 24 hrs.	Rise to 18,000 in 24 hrs.	Rise to 28,000 in 12 hrs.
Lymphocytes	Drop to > 1000	Drop to a few hundred, 48 hrs.	Drop to near 0, in 24 hrs.	Complete Disappearance, in 10 hrs.
Renal Impairment	No	3 days	24 hrs.	Immediate complete at 24 hrs
Death	No	24 days	9 days	35 hrs.

Dr. Shipman says he would rely on the total lymphocyte count over a period of 0-48 hours

COMMITTEE FOR EVALUATING HIGH DOSE EFFECTS OF RADIATION
FROM NUCLEAR WEAPONS

Conference at Walter Reed Army Institute of Research

20 - 21 January 1959

CLINTON S. MAUPIN, Colonel, M.C., USA	Chairman, OTSG, DA
HOWARD L. ANDREWS, Captain, USPHS	National Institutes of Health
SVEN A. BACH, Lt. Colonel, M.C., USA	Armed Forces Special Weapons Project
MARSHALL BRUCER, M.D.	Oak Ridge Institute of Nuclear Studies
SAVINO W. CAVENDER, Colonel, M.C., USA	A.E.C. Division of Biology&Medicine
PAUL F. DICKENS, Captain, USN (MC)	Bureau of Medicine & Surgery Dept of the Navy
ALBERT J. GLASS, Colonel, M.C., USA	OTSG, DA
PAYNE S. HARRIS, M.D.	Los Alamos Scientific Laboratory
JAMES B. HARTGERING, Lt. Colonel, M.C.USA	Walter Reed Army Institute of Research
WRIGHT H. LANGHAM, PhD	Los Alamos Scientific Laboratory
RALPH M. LECHAUSSE, Colonel, USAF (MC)	OTSG, U. S. Air Force
GERALD M. McDONNEL, Lt. Colonel, MC, USA	OTSG, DA
WILLIAM H. MONCRIEF, Lt. Colonel, MC, USA	Walter Reed Army Institute of Research
JOHN H. PICKERING, Colonel, USAF	School of Aviation Medicine Randolph Air Force Base
THOMAS L. SHIPMAN, M.D.	Los Alamos Scientific Laboratory
FREDERICK W. TIMMERMAN, Colonel, M.C., USA	OTSG, DA

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