BIOLOGICAL EFFECTS OF IONIZING RADIATION

A. GENERAL CONSIDERATIONS

EXPOSURE TO ANY IONIZING RADIATION PRODUCES HARMFUL EFFECTS IN BIOLOGICAL MATERIALS. THE MECHANISM OF DAMAGE CONCERNS THE DELIVERY OF SUFFICIENT RADIANT ENERGY TO DISLODGE ORBITAL ELECTRONS IN THE TISSUE CONCERNED. THIS PRODUCES IONS AND DISRUPTS THE MOLECULAR BONDS. WHEN THE MOLECULAR AND SUBCELLULAR PROCESSES ARE DISTURBED, NORMAL FUNCTIONING OF THE LIVING CELL IS IMPAIRED. ALTHOUGH THE DISRUPTIVE PROCESSES ARE NUMEROUS AND COMPLEX, THE ULTIMATE EFFECT OF IONIZATION IS ALMOST CERTAIN DAMAGE OR DEATH OF THE CELL. SINCE A SINGLE IONIZING EVENT CAN PRODUCE MOLECULAR CHANGE, IT IS ASSUMED THAT THERE IS NO THRESHOLD TO THE RISK OF RADIATION INJURY AT THE CELLULAR LEVEL.

QUALITATIVELY, THE DESTRUCTIVE EFFECTS OF ALL RADIATION WHICH PRODUCES IONIZATION ARE SIMILAR. QUANTITATIVELY, HOWEVER, THE EXTENT OF DAMAGE IS RELATED TO (1) THE TOTAL ENERGY ABSORBED OVER A PERIOD OF TIME (2) THE INTENSITY OF THE ENERGY (3) THE FREQUENCY OF EXPOSURE AND (4) THE DURATION OF THE EXPOSURE. WITH LOW INTENSITY EXPOSURES, REPEATED AT INTERVALS, THE REPAIR PROCESS IN THE TISSUES MAY BE ABLE TO COMPENSATE IN PART FOR THE DAMAGE PRODUCED. THEREFORE, GREATER TOTAL DOSES CAN BE TOLERATED IF THEY ARE FRACTIONATED THAN IF ADMINISTERED AT ONE EXPOSURE. HOWEVER, MANY OF THE EFFECTS OF REPEATED SMALL DOSES OF IONIZING RADIATION ARE CUMULATIVE. THE TYPE AND SEVERITY OF DAMAGE PRODUCED ALSO DEPENDS ON THE (1) AMOUNT OF THE TISSUE EXPOSED (2) THE SENSITIVITY OF THE TISSUE WHICH ABSORBS THE ENERGY, AND (3) WHETHER THE RESPONSE IS EARLY OR DELAYED. THE DIFFERENT CELL TYPES OF THE BODY VARY GREATLY IN THEIR SUSCEPTIBILITY TO RADIATION DAMAGE.

THE ACCUMULATED KNOWLEDGE OF RADIATION DAMAGE AT THE CELLULAR LEVEL PROVIDES A BASIC UNDERSTANDING OF HOW RADIATION DAMAGE IS PRODUCED, BUT THIS KNOWLEDGE IS NOT SUFFICIENT AT THE PRESENT TIME TO PROVIDE THE CRITERIA ON WHICH TO PREDICT THE RESPONSE IN A COMPLEX, MULTICELLULAR ORGANISM SUCH AS MAN. IT IS NECESSARY FOR US TO RELY TO A LARGE EXTENT ON THE DATA OBTAINED FROM OBSERVATIONS OF MAN EXPOSED TO IONIZING RADIATION FOR MEDICAL PURPOSES, FROM VARIOUS ACCIDENTS, OR FROM NUCLEAR BOMB EXPLOSIONS. THESE DATA HAVE BEEN SUPPLEMENTED BY CONSIDERABLE INFORMATION ON ANIMAL RESPONSE TO RADIATION. VERY LITTLE OF THE AVAILABLE DATA FOR MAN IS BASED UPON THE RADIATIONS OF MAIN CONCERN TO MANNED SPACEFLIGHT. THEREFORE, NOT ONLY IS IT OFTEN NECESSARY TO EXTRAPOLATE DATA FROM ANIMAL TO MAN, BUT ALSO TO EXTRAPOLATE FROM EFFECTS DUE TO CONVENTIONAL TYPES OF RADIATION SUCH AS X-RAY TO THOSE TYPES OF RADIATION FOUND IN SPACE (PRIMARILY PARTICULATES). THUS, IT MAY BE SUMMARIZED THAT HUMAN RESPONSE TO SPACE RADIATION IS NOT KNOWN WITH GREAT PRECISION.

OTHER FACTORS KNOWN TO INFLUENCE RADIATION RESPONSE SHOULD BE CONSIDERED. AMONG THEM ARE AGE, SEX, AND THE GENERAL PHYSIOLOGICAL CONDITION OF THE SUBJECT. IN GENERAL, THESE FACTORS ARE CONTROLLED IN THE SELECTION OF CREW MEMBERS. OTHER FACTORS, SUCH AS THOSE IMPOSED BY THE SPACE OR CABIN ENVIRONMENT MAY REQUIRE MORE CONSIDERATION. THE DEGREE OF OXYGENATION OF TISSUES IS KNOWN TO INFLUENCE RADIATION SENSITIVITY, GENERALLY MAKING IT MORE SENSITIVE. LITTLE IS KNOWN ABOUT THE INFLUENCE OF RADIATION COMBINED WITH OTHER STRESSES, SUCH AS WEIGHTLESSNESS, INHERENT IN THE SPACE ENVIRONMENT.

B. RADIATION EFFECTS IN MAN

THE BASIC DAMAGE TO THE HUMAN BODY PRODUCED BY IONIZING RADIATION OCCURS AT THE TIME OF EXPOSURE. THE EFFECTS OF THIS EXPOSURE CAN BE RECOGNIZED BY THE APPEARANCE OF VARIOUS CLINICAL SIGNS AND SYMPTOMS.

THE EFFECTS OF RADIATION EXPOSURE MAY BE DIVIDED INTO TWO GENERAL CATEGORIES: SOMATIC EFFECTS, (OR THOSE EFFECTS WHICH ARE MANIFESTED DIRECTLY BY THE IRRADIATED INDIVIDUAL) AND GENETIC EFFECTS (OR THOSE EFFECTS WHICH SHOW UP IN THE INDIVIDUAL'S PROGENY OR OFFSPRING). SOMATIC EFFECTS MAY BE DIVIDED FURTHER INTO (1) EARLY AND (2) LATE, OR DELAYED, EFFECTS.

(1) EARLY EFFECTS ARE THOSE WHICH PRODUCE SIGNS AND SYMPTOMS OF EXPOSURE FROM WITHIN MINUTES TO THE FIRST 30 TO 60 DAYS. THESE EFFECTS APPEAR TO BE THRESHOLD PHENOMENA, THEY ARE HIGHLY DOSE-RATE DEPENDENT AND THEIR INCIDENCE AND SEVERITY INCREASE NONLINEARLY WITH INCREASING DOSE.

THE MOST PERTINENT EARLY RADIATION RESPONSES MAY OCCUR IN LESS THAN 2 HOURS AFTER EXPOSURE AND ARE SUMMARIZED IN CHART I, TAKEN FROM A 1967 REPORT OF THE SPACE RADIATION STUDY PANEL, NATIONAL ACADEMY OF SCIENCES. THE BEST ESTIMATES OF THE ABSORBED DOSES CORRESPONDING TO THE 10, 50, AND 90 PERCENT RESPONSE LEVELS OF THE POPULATION ARE TABULATED. ALL DOSE ESTIMATES ARE PROVISIONAL, AND ESTIMATES AT THE 10 AND 90 PERCENT RESPONSE LEVELS MAY BE IN ERROR BY $\pm$ 50 PERCENT OR MORE. THE ERRORS AT THE 50 PERCENT LEVEL MAY BE SOMEWHAT LESS. IT IS NOTED THAT THE DATA CHARTED HERE ARE FROM HUMAN CANCER PATIENTS IN A NORMAL EARTH ENVIRONMENT. SPACE RADIATION RESPONSE PREDICTIONS MAY BE ADDITIONALLY UNCERTAIN DUE TO THE LACK OF KNOWLEDGE OF OTHER PHYSICAL STRESSES ASSOCIATED WITH SPACEFLIGHT.

ESTIMATED ABOSRBED DOSES OF HIGH-INTENSITY RADIATION FOR PRODUCTION OF EARLY CLINICAL RESPONSE

CHART 1

PROBABILITY OF RESPONSE

CLINICAL SIGN	10 PERCENT	50 PERCENT	90 PERCENT
	RAD *	RAD *	RAD *
LOSS OF APPETITE	40	100	240
NAUSEA	50	170	320
VOMITING	60	215	380
DIARRHEA	90	240	390

* ANATOMICAL REGION OF INTEREST FOR DOSE ESTIMATION, A 26-CM DIAMETER SPHERE IN THE MID-TORSO REGION.

ANOTHER SOMATIC RESPONSE IS DEPRESSION OF CIRCULATING BLOOD CELLS. THE BONE MARROW IS THE SITE OF BLOOD CELL PRODUCTION AND THE EXPOSURE OF THE BONE MARROW TO PENETRATING RADIATION RESULTS IN A REDUCTION OF THESE CIRCULATING ELEMENTS IN THE BLOOD. MANIFESTATIONS OF THIS DAMAGE BEGIN TO APPEAR WITHIN 1 TO 10 DAYS DEPENDING ON THE DOSE OF RADIATION. SIGNS AND SYMPTOMS MAY APPEAR EVEN WHEN THE DOSE IS PROTRACTED OVER SEVERAL WEEKS.

CHART 2

ESTIMATED ABSORBED DOSES OF HIGH-INTENSITY RADIATION FOR PRODUCTION OF BLOOD CELL DEPRESSION

	REDUCTION FROM NORMAL		
CIRCULATING ELEMENT	25 PERCENT	50 PERCENT	75 PERCENT
	RAD *	RAD *	RAD *
PLATELETS	50	120	250
LYMPHOCYTES	60	150	300
NEUTROPHILS	80	190	390

* ANATOMICAL REGION OF INTEREST FOR DOSE ESTIMATION, AVERAGE DEPTH OF 5 CM, TOTAL-BODY EXPOSURE.

ONE OF THE MOST IMPORTANT CONSIDERATIONS CONCERNS THE EFFECTS OF RADIATION ON THE SKIN.

EARLY SIGNS OF RADIATION DAMAGE MAY OCCUR WITH SUBLETHAL DOSES WHEN EXPOSURE IS LOCALIZED OR IS FROM RADIATION OF LOW PENETRABILITY. THE SKIN, BEING THE OUTERMOST ORGAN OF THE BODY, ABSORBS ALL OF THE SOFT COMPONENTS OF RADIATION. UNDER CONDITIONS OF LIGHT SHIELDING SUCH AS IN THE APOLLO SPACECRAFT, HIGH INTENSITY RADIATION WILL BE DEGRADED MATERIALLY, AND EXPOSURE OF THE SKIN WILL OCCUR WITH A SMALLER AMOUNT OF RADIATION TO THE DEEP TISSUES.

THE FIRST SIGN OF RADIATION INJURY IN THE SKIN IS THE DEVELOPMENT OF A SEVERE REDDENING, RESEMBLING SUNBURN. DEPENDING ON THE TYPE OF RADIATION, THE DOSE, AND DOSE RATE, THIS REDDENING MAY APPEAR WITHIN A FEW HOURS TO A FEW DAYS. WITH LARGER DOSES, THE REDDENING PROGRESSES TO LOSS OF HAIR, THE FORMATION OF BLISTERS, AND DENUDING OR SLOUGHING OF THE SKIN LAYERS WITH RESULTANT ULCERS. THESE ULCERS ARE SLOW TO HEAL AND CONSIDERABLE SCARRING COULD BE EXPECTED. CHART 3 DESCRIBES THE PROBABILITIES OF THESE TWO CLINICAL SIGNS OCCURRING WITH CERTAIN DOSES OF RADIATION.

CHART 3

ESTIMATED ABSORBED DOSES OF HIGH-INTENSITY RADIATION FOR PRODUCTION OF SKIN INJURY

	PROBABILITY OF RESPONSE		
CLINICAL SIGN	10 PERCENT	50 PERCENT	90 PERCENT
	RAD *	RAD *	RAD *
SEVERE REDDENING	400	575	750
DENUDATION-ULCERATION	1,400	2,000	2,600

* SITE OF INTEREST FOR DOSE ESTIMATION, 0.1-mm DEPTH; AREA EXPOSED, 35 TO 100 cm^2

DEATH FROM EXPOSURE TO RADIATION IN THE DOSE RANGES SHOWN IN CHART 4 IS A DISTINCT POSSIBILITY AND WOULD BE THE RESULT OF BONE MARROW DAMAGE WITH CONSEQUENT BLEEDING TENDENCIES AND INFECTION. EARLY CLINICAL SIGNS AND SYMPTOMS WOULD BEGIN WITHIN A FEW HOURS AFTER ACCUMULATING THE DOSE, FOLLOWED BY PROGRESSIVE BLOOD CELL DEPRESSION TERMINATING IN DEATH IN ABOUT 2 TO 8 WEEKS DEPENDING ON THE DOSE.

CHART 4

ESTIMATED ABSORBED DOSES OF HIGH-INTENSITY RADIATION TO PRODUCE EARLY DEATH

DEATH PROBABILITY LEVEL (PERCENT)	ABSORBED DOSE* (RADS)
10	220
50	285
90	350

* ANATOMICAL SITE OF INTEREST FOR DOSE ESTIMATION, 11-cm DEPTH, TOTAL- BODY EXPOSURE.

NEXT WE SHALL DISCUSS LATE OR DELAYED EFFECTS.

THIS TYPE OF RADIATION DAMAGE APPEARS AFTER A PERIOD OF MONTHS OR YEARS. THE EFFECTS ARE NON-SPECIFIC IN THAT THEY CANNOT BE CORRELATED TO ANY PARTICULAR RADIATION EXPOSURE, BUT MUST BE EVALUATED IN STATISTICAL TERMS IN RELATION TO TOTAL ACCUMULATED DOSE. THEY ARE ASSUMED TO BE NON-THRESHOLD PHENOMENA; THAT IS, THEY ARE LESS DOSE-RATE DEPENDENT THAN EARLY EFFECTS, AND THEIR OCCURRENCE AND SEVERITY GENERALLY APPEAR TO BE LINEAR FUNCTIONS OF TOTAL ACCUMULATED DOSE. DOSE-RESPONSE STATEMENTS FOR THE MOST SIGNIFICANT LATE RESPONSES ARE SUMMARIZED IN THE FOLLOWING CHARTS:

CHART 5, DAMAGE TO THE LENS OF THE EYE.

ALTHOUGH NO DEFINITE RESPONSE-PROBABILITY VALUES FOR PRODUCTION OF LENS OPACITIES OR CATARACTS CAN BE ASSIGNED TO SPECIFIC RADIATION DOSES, IT HAS BEEN SUGGESTED THAT THE DOSE RESPONSE RELATIONSHIPS SHOWN IN CHART 5 BE USED FOR SPACE APPLICATIONS. THE GREATER THE LEVEL OF EXPOSURE, THE GREATER WILL BE THE PROBABILITY THAT ANY CATARACTS PRODUCED WILL BE PROGRESSIVE AND THE SHORTER WILL BE THE LATENT PERIOD BEFORE DEVELOPMENT.

CHART 5

ABSORBED DOSES* OF RADIATION FOR PRODUCTION OF LATE CHANGES IN THE LENS OF THE EYE.

PROBABILITY OF CATARACT OR LENS OPACITY	HIGH-INTENSITY SINGLE (1-DAY) DOSE	PROTRACTED DOSE (7 WEEKS OR LONGER)
	RAD *	RAD *
MINIMAL ($p \geq 0$)	150	300
MEDIAN ($p \simeq 0.5$)	300	600
MAXIMAL ($p \leq 1$)	650	1,300

* POINT OF INTEREST FOR DOSE ESTIMATION, 3-mm DEPTH.

CHART 6

AS WITH THE LATE RESPONSE OF THE LENS OF THE EYE, THERE MAY BE A LATE RADIATION RESPONSE OF THE SKIN (PRIMARILY DEATH OF SKIN CELLS AND SCARRING) WHICH MAY NOT OCCUR UNTIL MANY MONTHS OR YEARS AFTER EXPOSURE. THE FREQUENCY AND SEVERITY OF THE LSEIONS ARE PROPORTIONAL TO THE ACCUMULATED DOSE TO THE EXPOSED AREA. IT SHOULD BE NOTED THAT FROM 5 TO 25 PERCENT OF CASES MAY PROGRESS TO THE FINAL STAGE OF SKIN CANCER.

CHART 6

SUGGESTED ABSORBED DOSES* OF REFERENCE RADIATION FOR PRODUCTION OF SKIN CELL DEATH AND SCARRING

PROBABILITY OF SKIN CELL DEATH AND SCARRING	HIGH-INTENSITY SINGLE (1-DAY) DOSE	FRACTIONATED OR PROTRACTED DOSE (7 WEEKS OR LONGER)
PERCENT	RADS	RADS
10	2,000	4,600
50	2,800	6,400
90	3,600	8,200

* POINT OF INTEREST FOR DOSE ESTIMATION, 0.1-mm DEPTH; AREA EXPOSED < 150 cm^2

THERE IS A CONVINCING BODY OF DATA WHICH INDICATES THAT RADIATION WILL STATISTICALLY SHORTEN THE LIFE OF IRRADIATED ANIMALS IN PROPORTION TO THE ACCUMULATED DOSE RECEIVED. WHILE SURVIVAL ANIMALS APPEAR COMPLETELY NORMAL IN EVERY WAY FOLLOWING SUBLETHAL RADIATION DOSES, THEY DIE SOONER THAN UNIRRADIATED ANIMALS. IN MANY CASES THE CAUSE OF DEATH IS NOT STRIKINGLY EVIDENT AND IT IS GENERALLY STATED THAT AGING HAS INCREASED IN THESE ANIMALS.

DUE TO THE LONG LIFE SPAN OF MAN WE HAVE LITTLE MEASURABLE HUMAN EVIDENCE TO SUPPORT THE ANIMAL OBSERVATIONS. IT IS THOUGHT HOWEVER, THAT THERE WILL BE INCREASED "AGING" AND EARLIER DEATH FOR THOSE EXPERIENCING DAMAGING RADIATION.

CHART 7 SUGGESTS A NUMERICAL VALUE FOR GENERAL LIFE SHORTENING AND SPECIFICALLY FOR THE INCIDENCE OF LEUKEMIA RESULTING FROM RADIATION.

CHART 7

SUGGESTED RADIATION DOSE-RESPONSE RELATIONSHIPS FOR GENERAL LIFE-SHORTENING AND INCREASED INCIDENCE OF LEUKEMIA

RESPONSE	HIGH-INTENSITY EXPOSURE * (50 RADS/DAY & GREATER)	LOW-INTENSITY EXPOSURE * (1 RAD/DAY AND LESS)
LIFE SHORTENING	$\sim$ 10 DAYS/RAD	$\sim$ 3 DAYS/RAD
LEUKEMIA INCIDENCE	2-4 PER 10^6 MAN-YR/RAD	1-2 PER 10^6 MAN-YR/RAD

* SITE OF INTEREST FOR DOSE ESTIMATION, 5-cm DEPTH; WHOLE-BODY EXPOSURE

GENETIC EFFECTS

GENETIC EFFECTS OR RISKS FROM FORSEEABLE SPACE FLIGHT CREW EXPOSURE TO RADIATION ARE INSIGNIFICANTLY SMALL TO THE TOTAL POPULATION BUT MAY BE OF SOME CONCERN TO ANY PARTICULAR CREW MEMBER AND HIS OFFSPRING. IT HAS BEEN ESTIMATED THAT FOR A 100 RAD DOSE TO THE GONADS, THE PROBABILITY OF A NEW MUTATION IN THE IMMEDIATE OFFSPRING WOULD BE 2.5×10^{-3} . WHILE SUCH A PROBABILITY STATEMENT MUST BE ACCEPTED WITH CONSIDERABLE RESERVE, IT DOES SERVE TO INDICATE THAT THE GENETIC RISK TO AN INDIVIDUAL CREW MEMBER IS NOT UNACCEPTABLY HIGH.

RADIATION DOSE CRITERIA FOR MANNED SPACEFLIGHT

A QUESTION OF INTEREST TO THOSE CONDUCTING MANNED SPACEFLIGHT OPERATIONS IS, WHAT OPERATIONAL RADIATION EXPOSURE CRITERIA SHOULD BE USED THAT WILL, AT THE SAME TIME, PROVIDE ADEQUATE PROTECTION TO THE CREW BUT NOT BE OVERLY RESTRICTIVE TO FLIGHT OPERATIONS. IN THIS APPARENT CONFUSION OF CONFLICTING AIMS, ONE POINT IS CERTAIN: THERE IS NO SINGLE DOSE CRITERIA WHICH CAN BE USED TO ASSESS THE RADIATION HAZARD FOR ALL PROPOSED MISSIONS. EACH PROPOSED MISSION, OR TYPE OF MISSION, MUST FIRST BE EVALUATED WITH RESPECT TO ITS IMPORTANCE AND UNIQUENESS AND ONLY THEN MAY A PARTICULAR RADIATION CRITERION FOR THAT MISSION BE ESTABLISHED. THIS PARTICULAR CRITERION SHOULD ADHERE TO THE FOLLOWING GENERAL CONCEPTS IN VARYING DEGREES (REF.):

1. ANY RADIATION EXPOSURE WILL BE CONSIDERED POTENTIALLY DETRIMENTAL AND THEREFORE, WILL BE KEPT TO A MINIMUM APPROPRIATE WITH THE RISK VS GAIN CONCEPT.
2. RADIATION EXPOSURE SHOULD BE KEPT BELOW THE LEVEL WHICH MIGHT RESULT IN AN UNACCEPTABLE PROBABILITY OF INFLIGHT RESPONSE CAPABLE OF JEOPARDIZING CREW SAFETY OR MISSION SUCCESS.

3. THE REUSE OF PREVIOUSLY EXPOSED, EXPERIENCED CREWMEN SHOULD BE GOVERNED BY THE NATURE AND EXTENT OF PREVIOUS EXPOSURE AND THE PREDICTED EXPOSURE RISK OF THE PROPOSED MISSION. COGNIZANCE SHOULD BE TAKEN OF THE IMPORTANCE THAT IS PLACED ON HAVING ANY PREVIOUSLY EXPOSED CREWMAN ENGAGE IN A PARTICULAR FLIGHT.

4. ANY RADIATION EXPOSURE THAT MIGHT EXCEED THE DOSE LIMITS PRESCRIBED FOR THE MISSION WILL BE PERMITTED IF THE CONCOMITANT HAZARD INCURRED BY ACTIONS TO AVOID THE RADIATION FIELDS OR TO PROTECT ONESELF AGAINST THE POTENTIAL INJURY IS DETERMINED TO BE GREATER THAN THE HAZARD ASSOCIATED WITH THE EXCESS RADIATION DOSE.

5. WITH REGARD TO LATE EFFECTS, THE SELECTION OF DOSE LIMITS FOR THE SHORTER TERM RESPONSES WILL AUTOMATICALLY ESTABLISH CERTAIN PROBABILITIES FOR THE OCCURRENCE OF GENERALIZED LIFE SHORTENING, LEUKEMIA, AND OTHER LATE MANIFESTATIONS. THERE IS NO IMMEDIATELY OBVIOUS WAY OF APPROACHING THE PROBLEM OF SETTING LIMITS FOR THE LONG TERM EFFECTS THAT DOES NOT ALSO IMPLY CERTAIN CAREER-DOSE LIMITS, AND THE LACK OF OPERATING EXPERIENCE PRECLUDES ESTABLISHING A FIRM COMMITMENT HERE.

I WISH TO EMPHASIZE THAT THE MEDICAL RESEARCH AND OPERATIONS DIRECTORATE IS A MEMBER OF THE RADIATION CONSTRAINTS PANEL AND HAS CONSTANT INPUT INTO ITS DISCUSSIONS AND RECOMMENDATIONS. WE ENDORSE THE OBJECTIVES AND MISSION RULES RESULTING FROM ITS DELIBERATIONS.