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THE INFLUENCE OF INFECTION ON THE HEMATOLOGICAL EFFECTS AND MORTALITY FOLLOWING MID-LETHAL X-RADIATION

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Abstract

Frequent blood cultures were made on 54 dogs receiving mid-lethal whole body x-radiation. A relatively high incidence of positive blood cultures (17%) was found. Infection appeared to be definitely related to mortality in animals surviving the first two weeks of irradiation, and to a lesser extent in animals dying at an earlier time. No direct correlation between the leukocyte level and the bacteremia exists. A possible correlation between the definite anemia of dying animals and infection can be made. The presence of E. Coli and gram negative organisms within the circulating blood appears to be definitely related to subsequent death of these animals.

THE INFLUENCE OF INFECTION ON THE HEMATOLOGICAL EFFECTS AND MORTALITY FOLLOWING MID-LETHAL X-RADIATION

In almost all studies on the nature of the mortality following exposure to lethal amounts of ionizing radiation the role of bacterial infection has been included as a dominant feature. An extended series of studies directed toward evaluating the effects of radiation on the immunological process have been carried out and are reviewed by Craddock and Lawrence (1). However, very little data exist on the incidence or nature of bacterial infections and the effects on radiation morbidity and mortality. Warren and Whipple (2) studied by culture methods the blood and tissue of dogs sacrificed 2, 3, and 4 days following large dosages of x-radiation to the abdomen. The dosage used was consistently lethal in 3-6 days and caused extensive destruction of the intestinal epithelium. In these animals the incidence of positive blood cultures was higher than the control animals, but no evidence of overwhelming sepsis was shown. This evidence is extended by Chron (3), Lawrence and Tennant (4) who noted a high incidence of positive cultures of enteric organisms in the blood and tissues of mice during the second week after large doses of x-ray or neutrons.

In the following study the blood cultures of 54 dogs receiving mid-lethal doses of 350 to 450 r of whole body radiation were studied. Positive blood cultures of varying types of organisms were found during the period of survival. Gram negative organisms appeared to be more clearly related to the terminal state. A correlation exists between the leukocyte counts and the mortality. In dying animals a consistent relationship between infection and anemia may be noted.

METHODS

Dogs used in this experiment were healthy, mongrels 6 months to two years of age. All were being used in the various studies of Vitamin P compounds given three times daily in the pre- and post-radiation state (5). Radiation dosages were between 350 and 450 r, the mid-lethal level previously determined for this laboratory. Complete hematological studies were performed pre-radiation and continued three times weekly following irradiation. Bacteriological studies were carried out at the same time, the cultures being taken from the jugular vein following surgical preparation by shaving, soap and water scrubbing and application of zephyrn. Four cc. samples of blood were obtained, half of which was placed in Douglas broth and half in deep meat broth. Aerobic cultures were kept five days and anaerobic cultures seven days. All organisms noted were identified by standard bacteriological techniques. Four plates for the estimation of the total bacteriological count (number of organisms per mm. of blood) were not performed routinely and results from these studies are not included in this report.

RESULTS

Because of the difficulty in evaluation of much of the data the results of the entire study are comprehensively given in Table I. Of the 54 animals studied, 53 control cultures were carried out prior to radiation. Only 1 of these was positive and that for gamma streptococcus. In the total series 430 cultures were made during the first 30 days following irradiation. Of these 74 were positive, an over-all value of 17%. The organisms found are listed in Table II. Of the 34 cultures taken after the 30th day none were positive and are not shown. From examination of the blood cultures during the last 24 hours of life, it appears significant that E. coli appears to be highest in its incidence. Cl. welchi was, on the other hand, the most predominant but did not appear to be definitely associated with mortality or morbidity.

Table I

DOG	PRE RADIATION				DAYS POST RADIATION																												
NO.	5	3	Z	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	4.8 21,750	5.9 21,550	neg 5.3 19,400	6.2 6,450	neg	5.3 5,000	neg		neg 4.8 1,650		neg 4.5 1,450		neg 4.8 0,088			POS-1 2.8 0,088	†																POS-1 Staph Aureus
2	7.3 12,350	8.0 9,200	neg 6.5 8,800	8.6 3,850	neg	5.5 3,300	neg		POS-1 5.5 0,466		neg 4.6 0,688		neg 5.2 0,111			POS-2 4.9 0,155		neg 3.6 0,244	†														POS-1 Staph Albus POS-2 Diptheroids
3	6.8 10,900	5.6 20,250	6.0 14,500	4.1 6,950	neg	4.6 4,500	neg		neg 4.8 1,500		neg 5.5 1,500		neg 5.5 0,662			neg 5.7 0,311		POS-1 3.0 0,133	†														POS-1 Diptheroids and Hemophilus
4	6.0 14,850	5.6 15,550	neg 6.6 12,550	7.0 2,400	POS-1	7.3 3,500	neg		neg 6.8 1,550		neg 5.2 2,350		POS-2 6.8 1,550			neg 4.2 0,733		neg 5.0 0,288		neg 5.0 0,155			neg 5.0 0,800		POS-3 4.0 1,250		neg 4.7 2,350			neg	4.3 4,900	neg	POS-1 Welchi POS-2 Gram + rod POS-3 Alpha Strep
5	5.6 13,700	6.8 14,500	neg 6.6 9,500	POS-1 6.7 6,700		neg 8.4 2,250			neg 5.8 0,377		neg 6.6 0,066		neg 6.8 0,066			neg 5.8 0,044	†																POS-1 Gram + cocci
6	6.2 9,700	5.3 10,700	neg 5.5 21,800	neg 6.4 9,100		neg 6.7 2,400			6.1 0,488		neg 5.3 0,222		neg 6.3 0,066			POS-1 3.7 0,022	†																POS-1 E coli
7	7.7 9,050	6.1 8,050	6.0 6,100	6.8 3,250	neg	neg 5.5 1,700			neg 6.1 1,050		7.4 1,250	neg	5.8 1,750	neg		neg 6.1 0,600		neg 4.9 0,466		POS-1 6.3 0,733		neg	6.0 1,000		POS-1 3.9 0,822		neg 5.5 0,950		POS-2	5.4 1,000	neg		POS-1 Welchi POS-2 Aerogenes
8	5.5 11,000	5.8 13.400	neg 5.9 12,450	neg 5.6 5,300		POS-1 6.2 1,950			neg 5.4 0,488		neg 5.2 0,444		neg 5.3 0,022			POS-2 2.6 † 0,022																	POS-1 Gram + rod POS-2 Alpha Strep
9	8.0 11,700	neg 7.0 10,600	neg 6.3 9,800	POS-1 8.0 8,250		POS-2 6.8 2,350			POS-3 5.8 0,422		neg 4.9 0,400		neg 4.6 0,288		neg	neg 4.3 0,111	POS-4 †																POS-1 (Hem. Strep and C. Welchi POS-2 Gram neg rod POS-3 Hem. Staph Alb. POS-4 E. Coli
10	7.2 10,350	neg 6.8 13,300	neg 6.4 16,900	neg 7.0 10,150		neg 7.2 2,400			neg 5.3 0,822		neg 4.3 0,444		neg 4.2 0,222			†																	
11	7.0 16,300	neg 7.6 15,300	neg 6.6 16,300	neg 7.0 9,150		neg 6.8 3,100			neg 7.0 1,050		neg 6.5 1,600		neg 5.7 1,950	†		neg 5.2 0,755		neg 4.4 0,833		neg 5.3 1,250			neg 4.7 1,750		neg 4.3 2,100		neg 4.9 3,000				neg 4.4 4,250		
12	8.7 20,350	neg 8.0 13,000	neg 6.4 7,250	neg 7.7 4,000		POS-1 6.6 1,350			neg 4.9 0,177		neg 5.1 0,111		POS-2 3.1 0,066																				POS-1 Welchi, Hem. Staph. Aureus, Diptheroids POS-2 Hem. Staph Alb.
13	7.5 8,600	neg 7.8 10,650	neg 7.8 5,600	neg 7.7 5,251		neg 7.3 2,900			neg 6.1 0,355		neg 6.3 0,133		neg 5.0 0,111		†																		
14	5.1 14,400	6.3 12,300	5.4 10,100	5.2 9,900		neg 5.2 2,850		5.4 1,150	neg		3.9 0,488	neg 4.4 0,800	4.3 0,650	3.7 0,555	neg	3.8 0,400	4.8 † 0,133																
15			6.3 13,300	6.4 8,050		6.0 2,600		5.2 1,600		neg 5.6 0,899			neg 5.9 2,000		POS-1 6.0 0,555	neg	neg 5.7 0,355	POS-2		neg 5.3 0,266		neg 4.1 0,088		neg 3.3 0,111			neg 1.8 0,044		neg 1.2 0,044	neg	POS-3 †		POS-1 C. Fallax POS-2 Staph Albus POS-3 Diptheroids and Hemophilus
16	9.0 10,350	neg 8.3 8,400	neg 8.8 7,250	POS-1 9.2 10,800		neg 8.5 3,400			neg 6.6 1,350		POS-2 7.2 1,600		neg 5.8 1,540			neg 6.2 0,555		neg 6.2 0,333		POS-2 6.2 0,377			neg 4.8 0,466		neg 5.6 0,622		neg 4.7 0,733			neg	4.9 2,050	neg	POS-1 Alpha Strep POS-2 Staph Albus
17	8.9 9,200	neg 7.9 6,900	neg 6.9 5,800	neg 8.0 2,900		neg 8.0 1,700			neg 6.2 1,450		neg 7.0 0,844		neg 6.2 1,500			neg 6.1 0,224		neg 3.8 0,333		neg 5.0 0,177			neg 4.0 0,330		POS-1 4.6 0,566		†						POS-1 Hem. Staph
18	7.7 8,950	neg 7.5 8,000	neg 6.1 8,050	neg 7.0 5,000		neg 5.0 1,800			neg 5.1 0,888		neg 4.8 0,777		neg 5.1 1,250			neg 5.2 0,755		neg 4.4 1,051		neg 3.8 0,933			neg 5.0 0,844		neg 4.1 0,800		neg 3.7 1,100			neg	3.4 1,600	neg	

Animals 1 through 15 received 450 r and animals 16 through 54 received 350 r.

Table I (Con't)

DOG PRE RADIATION DAYS POST RADIATION

NO.	5	3	Z	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
19	neg	neg 8.6 12,700	neg	5.6 4,550		6.4 3,700			POS-1 6.3 1,400		neg		neg 6.4 1,450			neg 5.1 0,244		neg		neg 5.6 1,000			neg 5.2 1,550		neg		neg 5.1 2,350			neg	4.9 2,900	neg	POS-1 C. Fallax
20	neg	neg 5.7 14,700	neg	6.7 8,850		4.6 5,950			neg 5.0 1,000		neg		neg 4.8 0,200	neg neg	†																		
21	neg	neg 5.0 9,650	neg	5.8 7,500		5.7 5,950			neg 5.6 1,000		neg		neg 5.5 2,250			neg 4.9 0,266		neg		neg 4.4 0,355			neg 4.8 1,300		neg		neg 4.7 2,350			neg	4.4 4,300	POS-1	POS-1 C. Welchi
22	neg	neg 5.2 14,850	neg	5.5 9,150		4.9 7,150			neg 5.9 1,700		neg		neg 6.5 3,400			neg 6.2 1,100		neg	neg	neg 5.4 0,778			neg 4.5 1,200		neg		neg 3.1 0,977			neg	4.2 2,850	neg	
23	neg	neg 5.4 8,250	neg	4.9 5,200		5.6 5,350			neg 6.0 4,950		neg		neg 5.9 5,000			neg 5.2 2,200		neg		neg 4.8 1,400			neg 4.7 2,550		neg		neg 4.7 2,100			POS-1	4.8 1,600	neg	POS-1 Pseudotetanicus
24	neg	neg 5.0 9,100	neg	5.7 13,250		5.7 6,900			neg 5.1 0,600		neg	†																					
25		6.2 10,300		4.2 8,450		5.5 6,150			6.2 1,555	neg			neg 4.6 0,688			neg 4.0 0,622		neg		neg 4.4 3,250			neg 3.8 7,550		neg		POS-1 2.2 12,750				3.4 8,200		POS-1 C. Welchi
26		6.2 11,000		7.3 7,555		7.9 6,600			6.6 2,450	neg			neg 6.5 2,050			neg 7.0 1,200		neg		neg 6.6 0,711			neg 5.2 0,266		neg		neg 5.2 1,150				5.7 1,600		
27		5.9 13,450		5.9 7,200		6.5 5,500			5.0 1,500	neg			neg 4.6 1,300			neg 5.8 0,222		neg		POS-1 3.3 † 0,111													POS-1 B. Subtilis
28		6.5 15,000		6.1 7,700		5.7 5,850			6.3 1,200	neg			neg 4.8 0,088	POS-1	†																		POS-1 Hemophilus
29		6.0 9,550		7.1 10,800		6.8 3,350			5.8 1,250	neg			neg 6.8 0,622			neg 4.9 0,100		POS-1		neg 2.3 0,111	POS-2	†											POS-1 C. Welchi POS-2 E. Coli
30		5.8 12,000		6.5 8,100		6.6 5,800			5.0 2,150	neg			neg 5.8 0,150			neg 4.8 1,200				neg 4.6 1,951			neg 4.8 2,100		POS-1		neg 4.5 3,400				4.7 5,100		POS-1 Staph Albus Hem.
31		5.5 11,200	neg	neg 6.8 6,450		POS-1 5.7 5,150			neg 5.8 1,650		neg		neg 6.0 1,300			neg 4.3 0,022		neg	†														POS-1 Staph Albus Hem.
32		6.0 17,350	neg	neg 6.1 14,300		neg 5.5 5,800			neg 4.9 0,933		neg		neg 4.9 0,333			POS-1 4.4 0,022	†																POS-1 E. Coli & C. Welchi
33		4.8 16,850	neg	neg 6.4 5,300		neg 5.4 6,100			neg 5.3 1,450		POS-1		POS-1 5.2 1,350			POS-1 4.6 0,488		neg		POS-2 3.5 0,133		†											POS-1 C. Welchi POS-2 Salmonella
34		5.7 11,800	neg	neg 5.8 7,650		POS-1 3.7 4,900			neg 3.9 1,200		neg		neg 3.4 0,733		†																		POS-1 Alpha Strep.
35		6.0 3,250	neg	neg 5.7 8,050		neg 5.8 4,700			POS-1 5.0 5,100	neg	POS-2		neg 4.7 5,700			neg 4.8 4,750		neg		neg 5.5 3,050			POS-3 5.4 2,450		POS-4		4.5 3,950			neg 5.1 6,150		neg	POS-1 Salmonella POS-2 Staph Albus POS-3 C. Welchi POS-4 Diptheroid
36	5.8 12,650	7.5 18,050	5.9 12,750	5.6 6,250		5.9 4,150			5.2 2,500		5.9 1,000		5.8 1,100			6.5 0,422		4.0 0,422		POS-1 POS-2 4.3 † 0,066													POS-1 < Strep. AM POS-2 < Strep & gram - rod PM

Table I (Con't)

DOG	PRE RADIATION			DAYS POST RADIATION																													
NO.	5	3	Z	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
37		5.0 10,800		4.9 5,200		4.7 5,050			neg 4.9 0,488		POS-1		neg 5.2 2,150			neg 5.4 1,250		neg		neg 4.2 1,850			neg 4.3 1,350		neg		neg 4.3 1,300			neg	3.4 1,150		POS-1 Gram + rod
38		5.1 18,750		4.5 12,100		4.8 5,250			neg 4.0 0,555		neg	†																					
39		4.6 21,900		4.7 10,850		4.8 9,150			POS-1 5.1 1,750		neg		neg 5.2 1,000			neg 4.2 0,222		POS-2	†														POS-1 Strep and Diptheroids POS-2 E Coli
40		5.8 16,800		6.1 7,000		6.2 6,000			neg 5.1 6,250				neg 4.8 4,150			neg 4.7 3,750		POS-1		neg 5.4 3,750			neg	5.4 2,750	POS-2		POS-2	5.1 5,350		neg		4.8 5,100	POS-1 Staph Hem. POS-2 C. Welchi
41		4.2 16,200		4.0 12,800		3.8 8,600			neg 4.1 2,650		neg		neg 4.2 0,688		†																		
42		5.1 12,800		4.8 5,250		5.7 6,700			neg 5.3 2,400		neg		neg 4.6 1,300			neg 4.4 0,533		neg		POS-1 3.2 0,066 †													POS-1 Beta Strep
43			neg 6.6 5,100	neg 6.2 3,050		neg 7.2 2,200			neg 7.0 1,100		POS-1 5.8 0,822		neg 5.6 1,200			neg 4.8 0,244		neg 3.4 0,133		POS-2 2.6 0,133	†												POS-1 An Gram - rod POS-2 An Strep
44			neg 6.6 5,350	neg 6.1 6,300		neg 7.0 3,300			neg 6.4 1,850		neg 5.7 1,450		neg 6.0 3,150			neg 7.2 1,200		neg 5.8 1,350		neg 5.6 1,250			neg 6.2 1,550	POS-1	5.4 2,750		neg 5.0 2,050		POS-2		4.2 2,600	neg	POS-1 Staph Aureus POS-2 An Gram + rod
45			neg 6.7 13,000	neg 6.4 4,200		neg 6.7 3,500	neg		neg 6.7 1,100		neg 6.1 2,050		neg 6.7 1,550			POS-1 6.6 0,666		neg 5.7 1,100		neg 5.5 0,666			neg 4.0 0,688		POS-2 4.9 0,488		neg 4.8 0,666			neg	4.3 1,200		POS-1 Staph Albus POS-2 Welchi
46			neg 5.6 7,850	neg 4.7 9,750		neg 7.4 3,800			neg 4.7 0,900		neg 5.8 2,600		neg 5.2 2,500			neg 3.7 0,577		neg 4.4 0,622		neg 4.3 0,622			neg 3.7 2,400		neg 2.4 2,300		POS-1 1.8 3,250	POS-1		POS-2 †			POS-1 Alpha Strep POS-2 Beta Strep
47	7.1 13,200	6.6 14,600	neg 6.7 14,950	neg 6.7 9,100		POS-1 5.4 5,100			neg 5.2 1,000		neg 5.8 1,300		neg 5.2 0,688			POS-2 4.4 1,000		neg 5.6 0,311		POS-3 4.4 0,311			neg 4.4 1,540		POS-4 3.9 1,150		neg 4.7 3,600			neg	3.3 10,250	neg	POS-1 Diptheroids POS-2 Welchi POS-3 Staph Albus POS-4 Gram - rod
48	7.0 17,850	POS-1 7.7 13,600	neg 7.0 9,500	neg 7.3 6,150		neg 7.2 2,700			neg 6.8 1,250		neg 5.8 1,950		neg 6.2 1,300			neg 5.4 0,622		neg 6.1 0,366		POS-2 4.9 0,800			neg 4.6 1,400	neg	neg 5.4 1,150		POS-3 5.0 2,150			neg	4.8 2,950	neg	POS-1 Gamma Strep POS-2 Gram + rod POS-3 Welchi, Diptheria
49	7.6 10,850	6.0 8,450	6.8 11,900	6.2 5,500		5.4 4,150			5.8 0,866		neg 5.0 1,000		neg 6.1 1,600			neg 5.2 1,000		neg 6.4 0,822		neg 3.9 0,577			neg 4.8 0,777		neg 4.7 1,400		neg 4.2 2,400			neg	5.2 2,850		
50	6.1 7,050	6.6 7,200	5.8 6,850	6.3 5,750		6.8 2,540			6.3 1,000		neg 5.4 1,400		neg 5.2 1,550			neg 5.8 1,050		neg 4.8 0,400		neg 4.3 0,444			neg 5.1 0,600		neg 4.7 0,711		neg 4.8 2,100			neg	4.9 2,000		
51	5.7 12,650	5.2 12,100	5.0 10,800	4.5 11,500		4.8 8,900			4.1 1,100		neg 4.8 1,850		neg 4.4 2,400			neg 4.8 3,550		neg 4.0 3,950		neg 4.5 3,700			neg 4.6 3,750		4.0 5,050		POS-1 4.2 5,500			neg	5.2 6,150		POS-1 Subtilis
52	6.3 7,800	6.3 7,100	6.1 14,100	7.2 3,350		6.6 3,850			5.9 1,088		neg 5.7 1,300		neg 6.2 1,350			neg 5.1 0,444		neg 6.0 0,511		neg 4.6 0,066			POS-1 4.5 0,111 †										POS-1 Gram - rod
53	5.3 21,100	5.9 24,000	5.0 20,800	4.4 12,750		4.9 8,600			3.5 0,666		neg 4.4 0,711		neg 3.8 0,666	neg	†																		
54	6.8 12,500	6.1 15,950	6.6 13,900	5.4 5,000		5.7 5,100			5.3 1,050		neg 6.0 0,622		neg 5.4 0,466			neg 5.3 0,266		POS-1 4.9 0,111 †															POS-1 E. Coli AM & PM

Table II

	Number of Positive Cultures	Number of Positive Terminal Cultures
Staph Aureus	2	1
Staph Albus	6	
Staph Aureus Hem	1	
Staph Albus Hem	5	1
Staph Hem	2	1
Gram - Cocci	1	
Strep	2	1
Strep	9	3
Strep	2	1
C. Welchi	18	
Gram - rod	5	
C. Fallax	2	
Pseudotetanicus	1	
B Subtilis	2	1
Aerogenes	1	
E. Coli	7	7
Salmonella	2	1
Gram - rod	5	1
Hemophilis	3	3
Diptheroids	8	2

MORTALITY

In the entire series of the 54 dogs studied, 32 of these animals died, an over-all mortality of 59%. Of the 32 animals dying, 22 were studied within the 24 hour period prior to death, and 17 of these or 77% were found to show positive blood cultures. It must be noted that the 5 animals without positive cultures died 10 to 18 days post-radiation, a time at which a severe metabolic disturbance from radiation could be expected without complicating infection. (For example dog #20 showed 2 negative cultures in the last 24 hours). All animals dying after the 18th day showed positive cultures. It might be postulated that some evidence exists that in the first two week period following x-radiation, death may occur due to radiation only and to a greater extent to a combination of radiation and infection. After that period infection plays a much more dominant role in radiation mortality.

RELATIONSHIP OF POSITIVE CULTURES TO LEUKOCYTE COUNT

Table III shows the frequency of positive cultures noted in this study compared directly with the leukocyte count at the time in which the culture was taken. It must be noted that as high a percentage of positive cultures were noted in radiated animals with leukocyte counts in excess of 5,000 as in those with counts below 500. It must be commented upon, however, that although positive blood cultures were frequent in animals with leukocyte counts in excess of 3,000 cells per cu. mm., none apparently died as the direct result of such infection, inasmuch as repeated negative cultures were always found in those animals prior to death. It is significant, however, that the type of bacteria noted in animals showing counts in excess of 3,000, gram positive rods and cocci predominated, while in the severe leukopenia of less than 500, E. Coli and gram negative rods predominated. In the latter animals terminally hemophillus,

Table III.

<u>Relation of WBC to Cultures</u>

WBC	Negative	Positive	Positive in Last 24 Hrs. of Life	Negative in Last 24 Hrs. of Life
over 5000	25	7		
3000 to 5000	28	7		
2000 to 3000	33	4		
1000 to 2000	81	11		
500 to 1000	55	7	1	2
0 to 500	58	8	19	7

salmonella, beta and alpha strep were also frequent.

It is common knowledge that a direct correlation between leukocyte counts and mortality exists. This series lends concrete support to this idea, inasmuch as all animals succumbing showed leukocyte counts below 500 during the 24 hours prior to death. Careful examination of our data does not suggest that bacterial invasion or sepsis may be related to the severe leukopenia, inasmuch as close inspection of Table I indicates that a severe depression of white cell count often exists 2-5 days before positive terminal blood cultures are obtained. Similar depressed counts are also noted in animals dying without positive cultures, although it is possible that such animals might often have shown infection had cultures been repeated with greater frequency.

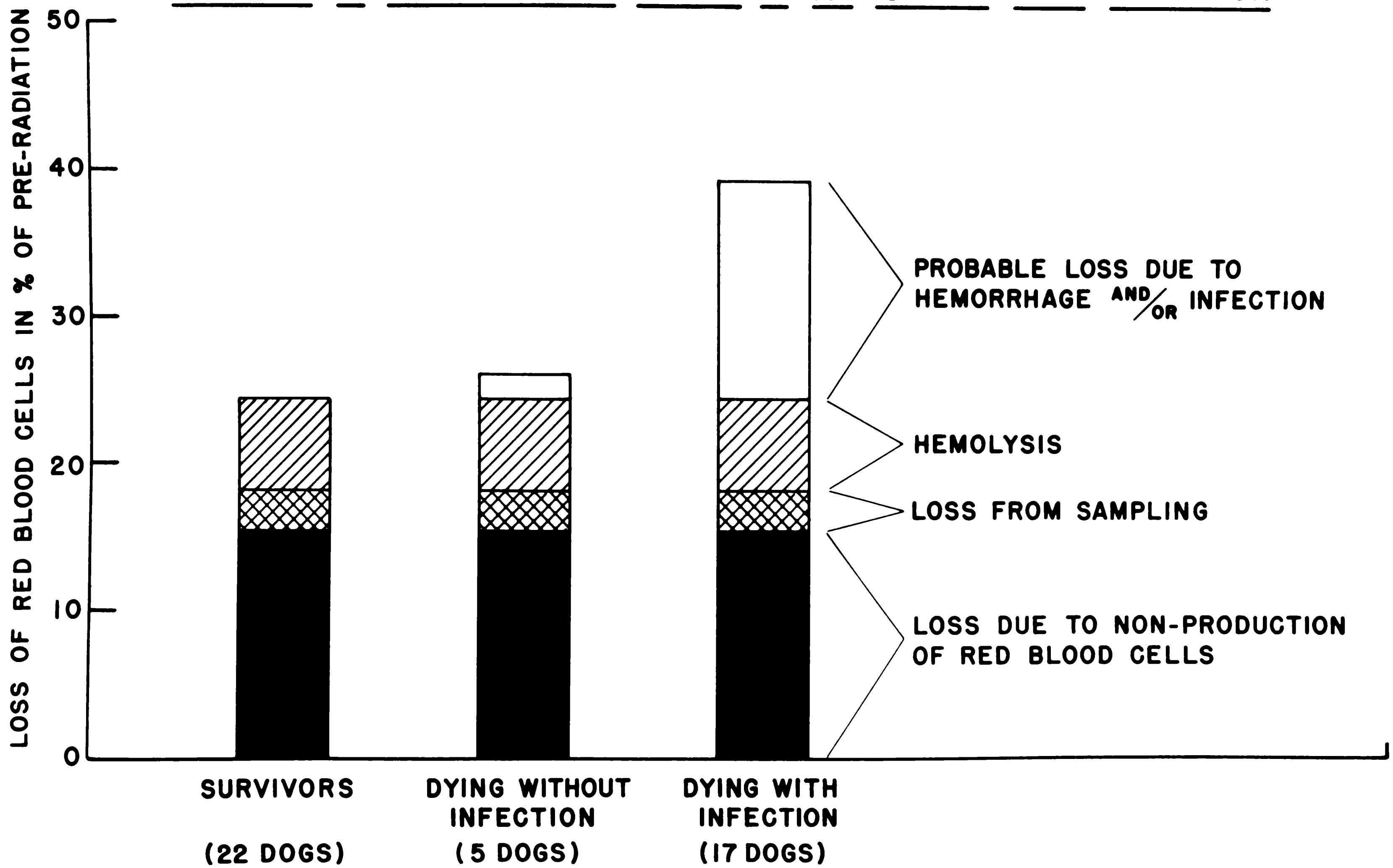
RELATIONSHIP OF INFECTION TO ERYTHROCYTE COUNT

The high percentage of positive cultures of hemolytic organisms suggests that radiation effects on the circulating red cell mass might be modified by the presence of added hemolysis, primarily related to infection. In a study of the possible effect one notes the following observations. Red blood cell production is almost invariably stopped following irradiation, as evidenced by the reticulocyte count being depressed in almost all animals. Only 1 animal of this series did not show this finding. Surviving animals showed a marked fall in red cell mass between the 3rd and 4th week post-radiation. When one correlates this finding of absent erythropoiesis with the observations of Prosser and associates (7) that following radiation the mean blood volume shows no change and with the information that the dog red cell life is approximately 120 days, one can calculate a decrease in the circulating red cell mass of approximately 1% per day. That radiation causes a hemolytic effect is well shown by the rise in urobilinogen commensurate with 1-2% blood destruction in animals not receiving lethal dosage (6). The other factor which may complicate analysis is the possibility of hemorrhage either of massive or diffuse nature. Accordingly, the question of hemolysis by bacterial infection becomes difficult to evaluate.

However, when animals showing evidence of bacterial infection are compared with those showing no infection, a definite difference is shown. This is best observed within the first 18 days post-radiation and, as will be shown, exceeds that normal loss of red cells calculated from normal red cell aging in the absence of erythrocyte production. The possible hemolytic effects are best studied at this time correcting as far as possible the error for the changes due to the above known causes. In animals dying without demonstrable infection a fall to 74% is found, comparing favorably to the fall of those surviving animals to 76% of the pre-radiation red cell counts. In animals dying following infection a mean value of 61% is noted, 13% less than that of the non-infected and surviving animals. The loss of red cells in the surviving and non-infected animals may be accounted for in the following fashion. Blocked production of new cells and death of old cells in the first 18 days, 16%; hemolysis as measured by urobilinogen excretion, 7%; and blood sampling, 3%, giving a total loss of 76% of the pre-radiation value. This is well shown in Graph I. Of the infected group 5 animals showing profound anemia with loss of red blood count to 30-40% of pre-radiation values, all except 1 had bacteremia (E. Coli) with hemolytic organisms. It becomes impossible to account for this marked loss in circulating red cell mass without addition of another factor. It would appear reasonable to assume that infection with hemolytic organisms could play a large part in the added red cell destruction, or hemorrhage occurring as a secondary mechanism following the known vascular effects of bacterial invasion.

GRAPH I

CHANGES IN ERYTHROCYTE COUNT IN 1ST 18 DAYS POST RADIATION



SUMMARY

The careful analysis of blood cultures taken on 54 dogs following whole body x-radiation demonstrated the relative frequency of blood cultures of all types of organisms. Infection appears to be definitely related to mortality in animals surviving the first two weeks of irradiation, and to a lesser extent in animals dying at an earlier time. No direct correlation between the definite anemia of dying animals and infection can be made. The presence of E. Coli and gram negative organisms within the circulating blood appears to be definitely related to subsequent death of these animals.

As a result of such observations preliminary experimentation has been carried out to determine the effect of varying anti-bacterial agents on rats surviving at the present time, streptomycin and aureomycin having already been used.

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