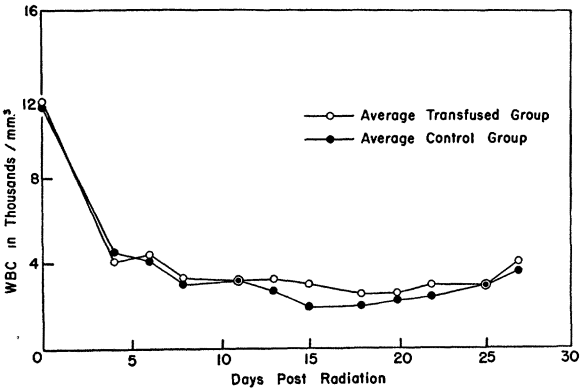

FIG. 3. Average leucocyte counts.

equivalent as determined by other dose-mortality data from each laboratory. In both instances the total body dose given appeared to be the greatest that could be administered in each laboratory without producing death (except in the rare highly susceptible dog).

Although the present experiment offers no direct evidence, it seems possible that the transfusion reactions encountered by Allen *et al.* may be responsible for the mortality of the otherwise nonfatally irradiated dogs. Incompatible transfusion, not fatal to the normal dog, may constitute an injury that is lethal to some of the irradiated animals. This point is under investigation in our laboratory at present.

Typing for the presence of the canine A factor in the erythrocytes of both donors and recipients and crossmatching were carried out on all transfusions of dog blood administered during the course of these experiments. We would take strong exception to the statement of Allen *et al.* that the blood groups of dogs are much less well defined than those of man. In the laboratories of the Department of Medicine of the University of Rochester up to the present time, 8 distinct dog blood-grouping factors have been demonstrated, and the respective isoantibodies characterized. The *in vivo* and *in vitro* characteristics of the first 5 of these have been described in detail in previous publications (*2–12*). These isoantibodies are produced by immunization of dogs with erythrocytes containing agglutinogens which they do not possess in their own red cells. The first of these antibodies described, canine anti-A, is a potent hemolysin capable of producing severe hemolytic transfusion reactions when either anti-A-containing plasma is given to an A+ dog, or A+ cells are given to a recipient immunized for this factor. The A factor is a very potent antigen, thus giving rise to potential hemolytic transfusion reactions in dogs subjected to repeated transfusions. Since approximately 65% of dogs carry this factor, the possibility of isosensitization is high with randomly chosen donors and recipients. Canine anti-A may be very difficult to detect in saline-containing systems, and crossmatches done by this method may not detect this incompatibility. Thus, proper choice of donor and recipient with regard to this factor is important if major hemolytic reactions are to be avoided in experiments involving transfusions of dogs with donor blood.

Anti-B, -C and -D behave as simple agglutinins and the corresponding factors are less antigenic than the A factor. Anti-E occupies a position intermediate between these two groups of antibodies in that under some circumstances it is capable of causing rapid destruction of donated cells. The detailed characteristics of these and the more recently encountered isoantibodies will be published elsewhere (*13*).

Using these precautions, we have administered over 400 therapeutic transfusions to irradiated dogs during the past year, many of which were given to previously transfused dogs, during the course of this and other experiments. We have seen no clinical hemolytic transfusion reactions in this experience, neither have we encountered anaphylactoid reactions with aggravation of the hemorrhagic diathesis of the irradiated dog. An occasional animal vomited or defecated following too rapid infusion of blood. However, we have been unable to detect evidences of hemolysis following such reactions. We do not feel that the irradiated dog is more susceptible than normal to transfusion reactions when compatible blood is administered. In experiments where therapeutic effects of transfusion are being measured it is very important that these precautions to minimize transfusion reactions be observed.

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Effect of Posture on the Elimination of Radon in the Breath[1]

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In persons retaining a substantial radium burden 1 year after contamination, over 95% of the radium is fixed in the skeletal tissues (*1*). A large portion of the radon which emanates from the radium is carried away by the blood stream as a dissolved gas. Much

[1] This work was supported by a grant from Atomic Energy of Canada, Ltd., Chalk River, Ontario.

of the dissolved radon diffuses into the air in the lungs and is exhaled. The rate of elimination of radon in expired air should be proportional to the radium content of the body. Therefore the amount of radon in exhaled air has been used to estimate the amount of radium present in the body, using empirical constants (*2*). The radon output in breath must, however, be subject to physiological variables. To study these variables we have used healthy subjects with a well stabilized burden of radium.

The subjects were males between 33 and 63 years of age, who were carrying appreciable amounts of radium but had not been working in any radium industry for more than 1 year. Special tests were devised to exclude the possibility of superficial contamination of the respiratory tract by particles of radium.

In preliminary experiments the subjects were seated comfortably in an armchair and were made to breathe through a BMR mouthpiece fitted with appropriate valves. A period of at least 10 min was allowed to flush the lungs with radon-free air.

Samples of approximately 6 l of expired air were collected in a gasometer at intervals of 10–12 min. Measurements were made of the volume of each sample and of the time required for its collection. From the gasometer the gas was transferred into 2-l Pyrex bottles by water displacement, and from there to the ionization chambers for alpha pulse counting (*3*).

After analyzing 125 samples from 4 subjects it became evident that in any 1 subject fluctuations in the elimination of radon, whether expressed as radon/l of breath or as radon eliminated/min, were significantly greater than the experimental error. In 3 of the subjects the maximum values exceeded the minimum values by a factor greater than 2. Sometimes great variations occurred in successive samples without any obvious change in the physiological conditions of the subject.

TABLE 1

RADON EXHALED IN SUPINE AND ERECT POSTURES

Subject		10^{-12} c/l of expired air			10^{-12} c/min of breathing		
		Supine 12th–45th min	Supine after 60 min	Erect	Supine 12th–45th min	Supine after 60 min	Erect
A	m	6.0	5.3	2.6	54.0	40.6	24.8
	S.D.	0.8	0.8	0.4	15.3	4.8	5.0
	n	6	9	5	6	9	5
B	m	3.8	3 8	1.9	22.8	20.8	12.7
	S.D.	0.3	0.3	0.2	1.6	2.7	1.0
	n	6	3	12	6	3	12
C	m	5.0	3.9	2.0	36.8	23.6	18.4
	S.D.	0.7*	0.3	0.2	10.3*	1.0	2.9
	n	2	6	4	2	6	4
D	m	0.54	0.53	0.25	5.3	3.7	2.3
	S.D.	0.09	0.02*	0.00*	0.1	0.0*	0.1*
	n	3	2	2	3	2	2
E	m	0.99	0.95	0.46	7.1	6.8	4.7
	S.D.	0.11*	0.00*	0.06*	1.3*	1.6*	0.7*
	n	2	2	2	2	2	2

m = mean, S.D. = standard deviation, S.D. with * = range, n = number of samples.

TABLE 2

RELATIVE RADON OUTPUTS*

Radon	Supine	Seated	Erect
Concentration in exhaled air	1	0.79	0.50
Exhaled/unit time	1	0.87	0.64

* Weighted averages, based on 90 measurements on 5 subjects. Supine figures refer to the 2nd and subsequent hours.

The effects of acid and alkaline diets, and of fasting and feeding, were studied and found to be neither large nor consistent. However, when the posture of the subjects was varied, large effects were observed consistently.

Experiments in the erect posture, i.e., with the subject standing or supported with the legs dependent, were conducted for as long as tolerated by the subject, which was usually about half an hour. Experiments in the supine posture were generally of 90-min duration but were extended in two cases to 3 and 6 hr.

In the supine posture both the radon content of expired air and the output of radon/unit time were consistently much greater than in the erect posture (Table 1).

In the supine posture the radon output and the range of fluctuation were greatest between the 12th and 45th min after lying down, but afterward the radon output dropped to a somewhat lower and fairly constant level with a smaller range of fluctuation. With the subject sitting in an armchair the radon output was lower (Table 2) and the fluctuations greater than in the stable phase of the supine posture.

Important physiological responses on assuming the erect posture include: (a) decreased cardiac output, (b) decreased circulating blood volume, (c) increased pulse rate, (d) pooling of blood in the legs, (e) increased interstitial fluid volume in the legs, (f) increased pulmonary ventilation, (g) increased volume of functional residual air in the lungs, and (h) peripheral vasoconstriction (*4–6*). The first 7 changes (a–g) should cause only transitory changes in radon output. We have, however, observed no tendency for the radon output to return towards the recumbent values either in the erect posture or in the much longer observations with the subjects seated. Thus our observations suggest that in the erect and seated positions a decrease occurs in the clearance of radon from the site of its production. We suggest that this is due to vasoconstriction in the bones.

To explain the irregular variations in radon output in prolonged experiments in the seated posture, we postulate irregular modification of the vasoconstriction in bones because of inevitable small changes in position assumed by the subject.

The greater radon output between the 12th and 45th min after lying down may be due to clearance

of dissolved radon from tissues where it has accumulated previously when conditions for clearance were less favorable. The practical implications of the present findings are that exhaled air for radon determination should be collected with the subject supine and the sampling should be done after he has been lying down for about 45 min.

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Ion Exchange Effect on Alkaline Phosphatase of Serum with Reference to Cancer[1]

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The utilization of ion exchange resins has been rather limited in clinical biochemistry (*1–4*). As far as we know, no detailed investigation of the effect of ion removal upon the alkaline phosphatase in human sera has been published. We report here the results of our studies on the effect of ion exchange upon the alkaline phosphatase of the serum of normal, of noncancerous, and of cancerous individuals.

The sodium form of analytical grade Amberlite IR-120 (H),[2] was prepared and dried in an oven at 37° C. The dry resin is suspended in distilled water immediately preceding use, and 1.5 ml of the resin is transferred to a 3-ml micro filter funnel with fritted disk of coarse porosity (Pyrex 36290). The excess water is aspirated by suction applied to the stem of the funnel. The serum is introduced into the funnel. The rate of flow should not exceed 1 ml/min, and not more than 8 ml is allowed to pass through the resin; the first 0.5 ml is discarded. The following determinations were made on the serum before and after passing it through the ion exchange resin: total protein (*5*), calcium (*6*), magnesium (*7*), sodium and potassium,[3] pH with the glass electrode using the Beckman model G pH meter, alkaline phosphatase using adenylic acid as the substrate (*8*), lipase (*9*), and diastase (*10*).

A comparison of the analyses of the resin treated serum and the untreated serum showed no changes in the total protein; more than 95% of the calcium and all the magnesium and potassium were removed. There was also a slight lowering of the pH of the serum. There were slight increases in the sodium. There were no demonstrable changes in the lipolytic or diastatic activity. There was a loss of alkaline phosphatase activity in the resin treated serum as a result of ion exchange.

The results of our experiments indicate that concomitant with the removal of divalent ions from the serum by a cation exchange resin there is a diminution of alkaline phosphatase activity, designated as Kase-Mg, both in the serum of noncancerous persons, and in those with a malignant tumor (Table 1). Since elevated serum alkaline phosphatase values are generally accepted as indicating either bone disease or liver damage, such cases were excluded from our series. The nonmalignant group was composed of 16 normal males and females, 5 cases of pregnancy, and 32 others known to be free from neoplastic disease.

The cancer group consisted of 46 individuals with some form of neoplastic malignant disease, in whom the diagnosis was confirmed by biopsy or post-mortem examination. The phosphatase was determined before surgical intervention or other treatment was instituted. These cases classified according to the site of the tumor are as follows: liver and pancreas 4, genitourinary system 18, gastrointestinal tract 20, breast 3, lung 3, and miscellaneous 3.

There is greater diminution of alkaline phosphatase activity of the serum of patients with neoplastic malignant disease, which cannot be entirely attributed to the fact that the initial alkaline phosphatase of the serum is usually increased in cancer, as shown in a previous communication (*8*); a comparison of the means of the Kase-Mg of the cancer and nonmalig-

TABLE 1

STATISTICAL ANALYSIS OF ALKALINE PHOSPHATASE ACTIVITY OF HUMAN SERUM AS A RESULT OF ION EXCHANGE

	No. of patients	All phosphatase values in mg%			
		Control phosphatase	Resin-treated phosphatase	Loss in phosphatase Kase-Mg	% change in Kase-Mg
Normal and nonmalignant	53				
Mean		2.3	1.45	0.85	37
Stand. Dev.		0.7	0.55	0.37	11
Range		1.0–4.5	0.5–3.1	0.1–2.2	7–52
Cancer	46				
Mean		5.0	2.9	2.1	44
Stand. Dev.		3.4	2.15	1.69	12
Range		1.9–18.7	0.8–10.8	0.6–5.8	28–80
Cancer with low alkaline phosphatase	13				
Mean		2.5	1.4	1.1	44
Stand. Dev.		0.3	0.27	0.31	11
Range		1.9–2.9	0.9–1.9	0.6–1.8	29–67

[1] Under a grant from the Lewis Memorial Fund.

[2] Rohm and Haas, Philadelphia.

[3] Flame photometer, Process Instruments Photometer, Brooklyn, N. Y.