enzyme levels increase rapidly after the onset of shock. It is possible that corticosteroid application would be most effective when used prior to insult as, indeed, Weissman and others(8) have demonstrated in other shock-producing traumas.

Summary. Hydrocortisone administered to tourniquet traumatized rats, in infusion fluids, was effective in lowering the levels of beta-glucuronidase in the serum. However, survival in hydrocortisone-infused animals was less than in saline-infused animals. Moreover, an effective infusate containing Cohn Fraction II of lyophilized, reconstituted, human plasma did not significantly alter the level of beta-glucuronidase in the blood. Hydrocortisone, as given in these experiments, proved an ineffective agent for resuscitation from tourniquet shock. Serum levels of beta-glucuronidase, presumed to reflect lysosomal enzyme release, did not correlate with survival.

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Rate of Initial Entry of Ca^{47} and Sr^{85} from the Intestine into the Vascular Space.[*] (32447)

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Extensive studies have been previously performed in this Research Unit on the absorption and excretion of both radioactive calcium and radioactive strontium in man (1-4). The net absorption as well as the true absorption, taking into consideration the endogenous fecal excretion, has been determined from plasma levels, from cummulative fecal and urinary excretions, and from a comparison of the plasma levels following a single oral and a single intravenous dose of the radioisotope in the same person(5). However, the dynamics of the rate of entry of the radioisotopes from the intestinal tract into the blood stream have not been completely clarified. In this study the rate of the initial entry of both radiocalcium and radiostrontium has been determined. The initial entry rate must be differentiated from the integrated steady state rate of absorption along the entire gastrointestinal tract. The initial entry rate denotes entry of the radioisotope from one compartment into another compartment without consideration of recirculation or feedback and reflects the gradual passage of the remaining unabsorbed dose through different portions of the intestinal tract exhibiting different transport activity. It is calculated by adapting an integral equation approach for use with a digital computer. A short review of the history of this approach has been published recently (6).

Material and methods. Three male patients with mild osteoporosis ranging in age from 42-

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46 years and one male patient, 31 years of age, were studied under strictly controlled dietary conditions on the Metabolic Research Ward. The patients received a low calcium diet, containing an average of 209 mg calcium and 750 mg phosphorus per day. The diet was analyzed for calcium, phosphorus, nitrogen, sodium and potassium.

Four studies each were performed in Patients 1, 2 and 3. These patients received tracer doses of both Sr^{85} and Ca^{47} by the oral and by the intravenous route in separate studies. Two studies were performed in Patient 4 who received tracer doses of Ca^{47} orally and intravenously.

A single tracer dose of Sr^{85} and of Ca^{47} as the chloride was given in separate studies by the oral route with breakfast as previously described(1). Plasma levels and urinary and fecal excretions of Ca^{47} were determined from the start of the study. On the first day, plasma was obtained for Ca^{47} and Sr^{85} assay at ½, 1, 2, 3, 4, 6, 8 and 24 hours. Subsequently, the Sr^{85} and Ca^{47} plasma levels were determined at less frequent intervals. Urine collections of the first day were obtained in fractions from 0-1, 1-2, 2-3, 3-4, 4-6, 6-8 and 8-24 hours. Each stool specimen was analyzed for Sr^{85} and Ca^{47}. Following the completion of these studies (approximately 1 month later), these patients received a single tracer dose of Sr^{85} and Ca^{47} intravenously and the plasma levels, and urinary excretions of the two radioisotopes were determined at the same time intervals as following the oral administration of Sr^{85} and Ca^{47}. Fecal excretions of the two radioisotopes were also determined throughout these studies.

Plasma levels of Sr^{85} and Ca^{47} were expressed as percent of dose per liter plasma, urinary Sr^{85} and Ca^{47} excretions as percent of dose for each urine collection and fecal excretions of the radioisotopes as percent of dose for each stool specimen. The radioassays of plasma, urine and stool were performed in a well-type NaI crystal γ-scintillation counter equipped with a single channel pulse height analyzer which permitted counting of both Sr^{85} and Ca^{47}.

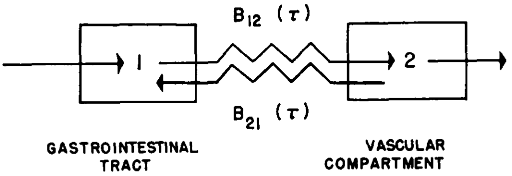

FIG. 1. Rate of initial entry of Ca^{42} and Sr^{85} from the intestine into the vascular space.

A simple non-contiguous two-compartment model was applicable to this study. In Fig. 1, compartment 1 represents the gastrointestinal tract while compartment 2 represents the vascular system. Homogeneous mixing and consequently valid sampling of Sr^{85} and Ca^{47} was assumed to occur in the vascular compartment. No measurements of the actual radioactivity of the gastrointestinal tract were necessary and homogeneity of compartment 1 is nowhere assumed in the analysis.

Let F(t) be the plasma activity curve after intravenous tracer injection of a steady state system at time $t_0 = 0$. It follows from the basic assumption of tracer analysis (*i.e.*, tracers *per se* do not disturb system response) that the plasma activity curve G(t) following an *oral* tracer dose at time $t_0 = 0$ must necessarily be a linear superposition of the plasma activity curves of all the individual differential initial entries $B(\tau)d\tau$, from the gastrointestinal tract into the vascular system. $B(\tau)$ is the rate of initial entry and $d\tau$ is of course the differential time interval in which it occurs. In effect, introducing a tracer *via* the oral route is, from the vascular compartment point of view, equivalent to labelling the vascular system with a continuous intravenous infusion rather than a single intravenous injection. $B(\tau)$ is simply that variable rate of intravenous infusion which would give rise to the same blood curve as was observed following the oral dose.

The three functions F(t), G(t) and B(t) satisfy a Volterra integral equation(7,8,9):

$$G(t) = \int_0^t B(\tau)\ F(t-\tau)\ d\tau. \qquad 1.$$

Since G(t) and F(t) are experimentally determined, the initial entry function $B(\tau)$ can be evaluated analytically by the standard device of using Laplace transforms:

$$B(s) = \frac{G(s)}{F(s)} \qquad 2.$$

In the present work, however, it was numerically more convenient to deal directly with discrete experimental data. Noting that in the present study no pertubations are involved, equation "7" of reference(9) reduces to equation "1" of the text. Similarly, equations "8" of reference(9) reduces to the set of simultaneous equations listed below† which are the discrete equivalent of equation 1:

$$\begin{aligned} G(1) &= B(1)\ F(1) \\ G(2) &= B(1)\ F(2) + B(2)\ (F(1) \\ &\cdot \\ &\cdot \qquad\qquad\qquad\qquad 3. \\ G(N) &= B(1)\ F(N) + B(2)\ F(N - 1) + \cdots B(N)\ F(1) \end{aligned}$$

Equations 3 are readily adapted to the computer calculation of $B(\tau)$ and the program employed is given in Appendix I. The experimental points obtained at 0, ½, 1, 2, 3, 4, 6, 8, 12 and 24 hours were plotted and a smooth curve was drawn. In order to minimize the error associated with replacing the continuous integral equation 2, by the discrete system of simultaneous equations 3, it was necessary to insert intermediate values at 15-minute time intervals. These intermediate values were read off the smooth curves. Repeated tests indicated that after the first hour small variations ($\sim 5\%$) in isolated intermediate values caused insignificant changes ($<2\%$) in the calculated initial entry rates.

Results. The plasma curves following intravenous and oral doses of Ca^{47} and Sr^{85} upon which all calculations are based are shown in Fig. 2 and 3. The concentration of both Ca^{47} and Sr^{85} increased gradually, reaching a maximum at 4 hours, and decreased with

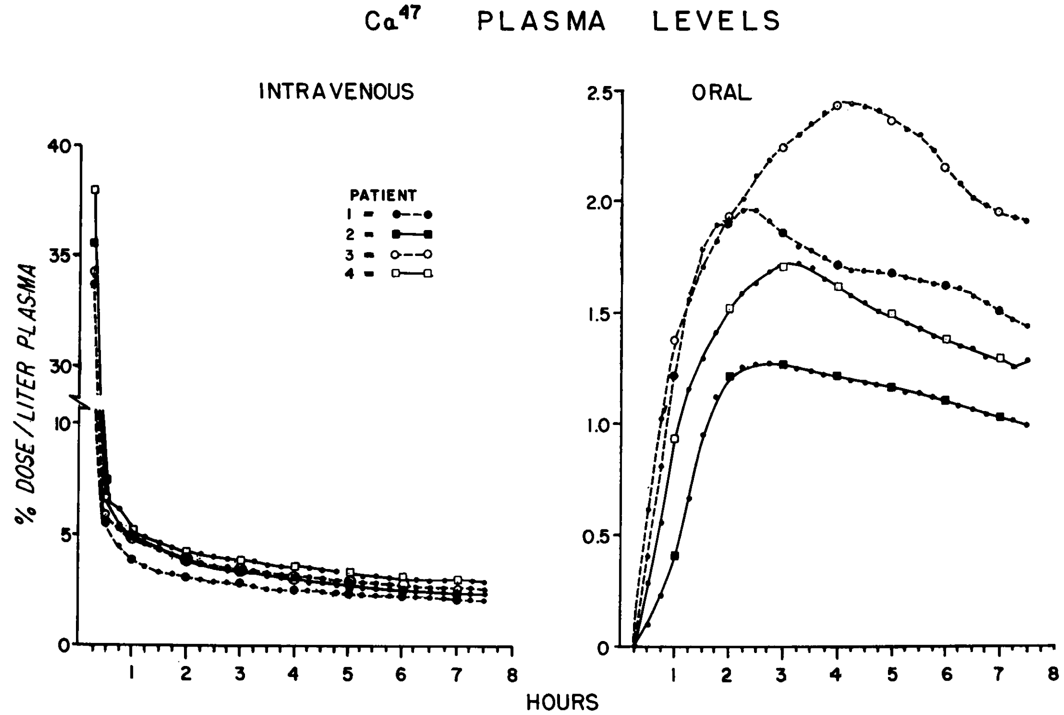

FIG. 2. A single dose of Ca^{47} was given both by oral and intravenous route in separate studies. Plasma levels of Ca^{47} at ½, 1, 2, 3, 4 and 6 hours are experimental points. Plasma levels at the 15 minute time intervals are interpolated points.

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† For convenience in computer calculation, all indices start at 1 in equation 3 rather than 0 as in equation 8 of reference (9).

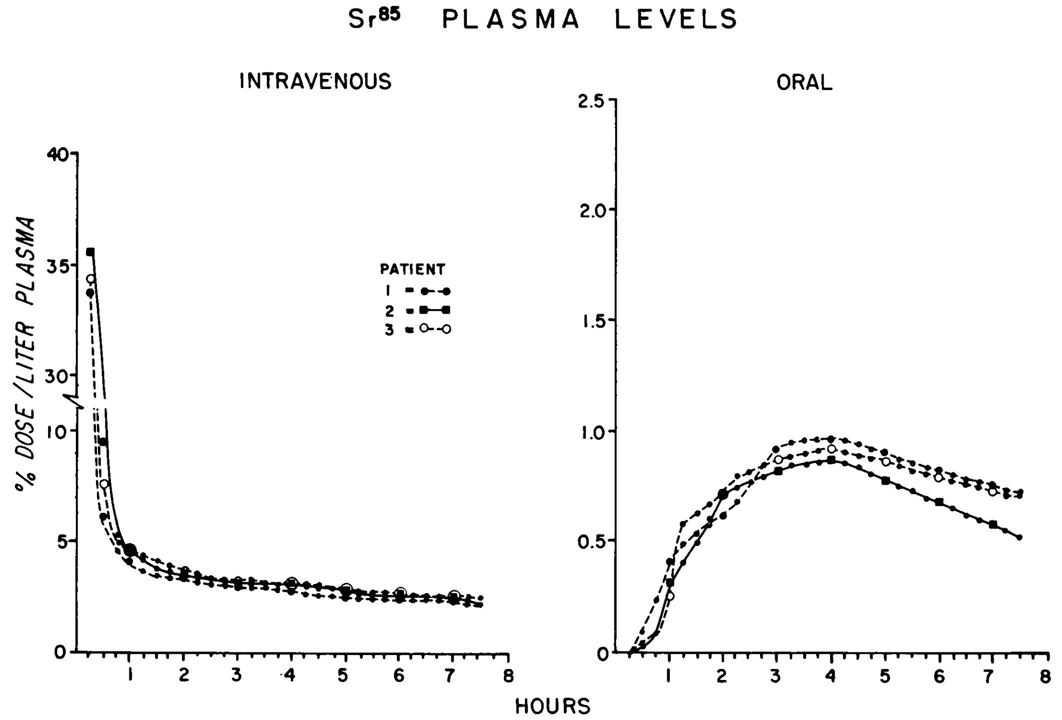
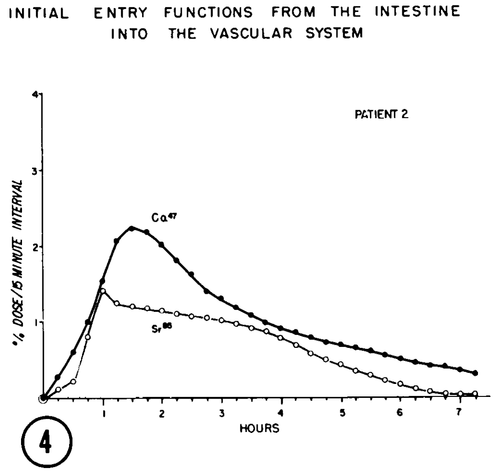


FIG. 3. A single dose of Sr^{85} was given both by oral and intravenous route in separate studies. Plasma levels of Sr^{85} at ½, 1, 2, 3, 4 and 6 hours are experimental points. Plasma levels at the 15 minute time intervals are interpolated points.



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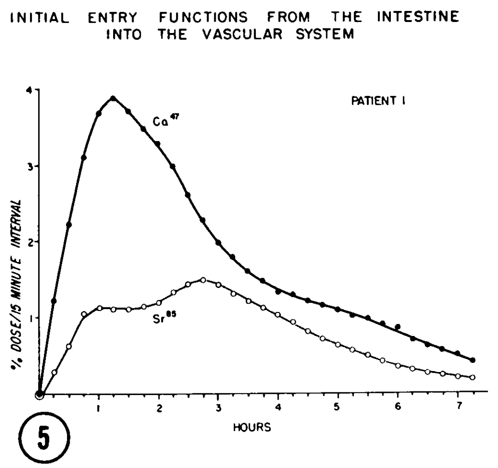

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FIG. 4. Rate of initial entry calculated from plasma levels following a single oral and intravenous dose of Ca^{47} and of Sr^{85}.

FIG. 5. Rate of initial entry calculated from plasma levels following a single oral and intravenous dose of Ca^{47} and of Sr^{85}.

time thereafter. The plasma Sr^{85} levels were consistently lower than those of Ca^{47}. Fig. 4, 5 and 6 show the comparative initial entry of radiocalcium and radiostrontium from the intestinal tract into the blood stream for 3 patients. The scale of the ordinate is graphed in percent of dose per 15 minutes corresponding to the discrete time intervals employed in the calculations. For example, a rate of initial entry of 1.0% per 15-minutes for B(τ) indicates that approximately 1% of the ingested dose will be initially absorbed within the 15-minutes interval straddling the time τ. The maximal rate of initial Ca^{47} absorption, ranging in the 3 patients from 2.2% (Fig. 4) of the administered dose per 15-minutes to 3.8% per 15 minutes (Fig. 5) was reached within 1½ hours following oral administration of a tracer dose of Ca^{47}. This maximal rate of entry was sustained for approximately one hour. Thereafter, the rate of initial absorption for Ca^{47} decreased progressively between the 2nd and 7th hour. This rate decreased much more steeply for Patients 1 and 2 (Fig. 4 and 5) than for Patient 3 (Fig. 6). However, by the 7th hour the rate of initial entry was approximately 0.4% per 15-minutes for all 3 patients.

The curves for Sr^{85} show that the rate of initial absorption is less than that for Ca^{47} never exceeding 1.5% per 15 minutes (Fig. 4, 5 and 6). Also, the initial rate of absorption for Sr^{85} is relatively more sustained between the first and fourth hour. Thereafter, the rates of intial entry of Sr^{85} and Ca^{47} are almost proportional.

In a fourth patient, the 31-year-old male, the rate of initial absorption was determined for Ca^{47} only. The results obtained for this patient (Fig. 7) are similar to those obtained for the other 3 patients.

TABLE I. Comparison of Absorption of Ca^{47} and Sr^{85} Determined by Integral Equations and from Fecal Excretions.

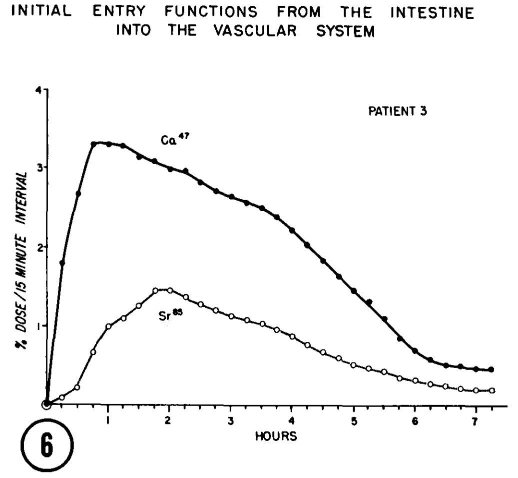
	Absorption, % dose			
	Sr^{85}		Ca^{47}	
Patient	At 7½ hr*	Total†	At 7½ hr*	Total†
1	24	28	51	59
2	18	26	30	44
3	21	25	56	72
4	—	—	35	50

* Cumulative absorption calculated from initial entry data for the first 7½ hr.

† Total absorption calculated from fecal excretions collected for many days.

By integrating the area under the initial entry curves one obtains the cumulative absorption for Sr^{85} and for Ca^{47}. Numerical integration of the time period 0-7½ hours gave in fact results in reasonable agreement with the total absorption calculated from fecal excretions of the radioisotopes. These results are given in Table I.

Discussion. The calculated initial entry values, appropriately normalized, represent a sum or integral of the products of the concentration of unabsorbed dose and absorption rates for each differential area of the intestine. The initial entry rate at a given time is a reflection of two factors: the then existing



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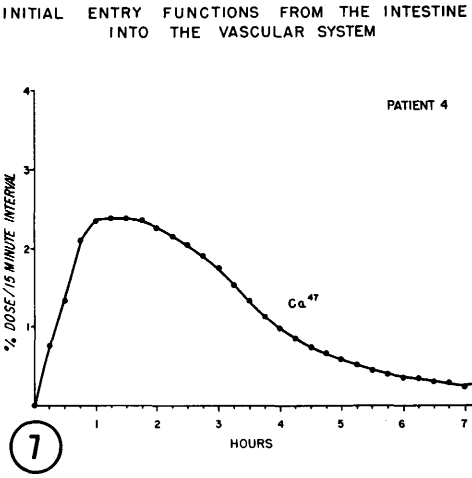

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FIG. 6. Rate of initial entry calculated from plasma levels following a single oral and intravenous dose of Ca^{47} and of Sr^{85}.

FIG. 7. Rate of initial entry calculated from plasma levels following a single oral and intravenous dose of Ca^{47}.

geographical distribution of the unabsorbed dose and the variable absorption activity along the gastrointestinal tract.‡ The present study therefore provides information on the rate at which calcium and strontium (under controlled dietary loading conditions) are initially absorbed from the gastrointestinal tract following ingestion of the radioisotopes without really specifying a detailed profile of absorption activity along the tract.

For example, while the peaks in Fig. 4 at 1 hour and 1½ hours represent the maximal rates of initial absorption for strontium and calcium respectively, the most active sites of intestinal activity need not be at the means of the 1 hour or 1½ hour distributions of the unabsorbed dose. Nonetheless, the 1 hour-1½ hour peaks do indicate that the upper small intestine must include major sites of calcium and strontium absorption. The early 1-1½ hour peaks in initial absorption should be contrasted with the 4 hour maximal plasma values observed for both isotopes. The maximum plasma concentration at 4 hours of course reflects the effect of the composite contributions of plasma retention and recycling as well as initial entry While detailed and quantitative knowledge of all these processes would be necessary to explain the observed plasma concentrations, it should be emphasized that the initial entry functions here evaluated are essentially exact.

The reduced rate of initial entry of both Ca^{47} and Sr^{85} by the 7th hour indicates that the absorption of the radioisotopes was largely completed by that time, Table I indicating that the order of 70% of the total absorption has occurred. The lower rate of initial entry of Sr^{85} compared to that of Ca^{47} is not unexpected in view of the known intestinal discrimination in absorption of the two ions (1,2,10-12).

Multiple tracer studies performed after varying time intervals in the same person have yielded reproducible results(13). It can therefore be assumed that the rate of initial entry of the radioisotopes from the intestine into the vascular compartment also remains in similar range in the same person as long as the metabolic status of the patients does not change. Calcium absorption rates determined by intubation and perfusion of the intestine in man varied in different subjects but were rather constant in serial studies performed in the same persons(14).

The use of this approach in quantitating the capacity of the intestine to absorb minerals at different rates may be expected to elucidate certain physiologic aspects of the rate of entry of minerals from the gastrointestinal tract into the vascular space. The use of this technique may also clarify differences in intestinal function in regard to the absorption of minerals in different pathophysiological states.

The integral equation technique employed here is not restricted to calculations based on plasma levels. It can be applied to measurements of any readily accessible compartment for which the vascular system provides a necessary intermediary between the gastrointestinal tract and the compartment to be measured. In principle, the initial entry rates from the gastrointestinal tract into the vascular system here determined need not have been based on plasma levels of the radioisotopes which require serial blood sampling. The calculation of the initial entry rates may be based on several types of radioactivity measurement, for instance, on the observed urinary excretions of Ca^{47} following oral and intravenous doses or better still on values obtained by external counting of any accessible region such as the counting of a finger or any other area excluding the gastrointestinal tract itself. G(t) in equation "1" might then be the observed radioactive time dependence of a finger held in a well counter following an oral dose of Ca^{47}; F(t) would be the corresponding time dependence following intravenous administration of Ca^{47}.

Summary. The rate of initial entry of both radioactive calcium and strontium from the

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‡ Analytically $B(\tau) = K\int_{0}^{L} D(x, \tau)\, A(x)\, dx$ where K is a proportionality constant, L is the length of the intestinal tract, $D(x, \tau)$ is the distribution of unabsorbed dose as a function of time and position, and $A(x)$ is the variable absorption activity along the tract. It can be shown formally that if $B(\tau)$ and $D(x, \tau)$ are know, then $A(x)$ can be uniquely determined for some but not all functions D(x,

gastrointestinal tract into the vascular system has been determined in man by adapting an integral equation approach for use with a digital computer. A single tracer dose of Ca^{47} and of Sr^{85} was given both by the oral and intravenous route in separate studies and serial samples of plasma were obtained for radioassay. The maximal rate of initial entry of Ca^{47} per 15-minute interval ranged from 2.2% to 3.8% of the dose and was reached within 1½ hours. This rate was sustained for about one hour and decreased thereafter with time. The rate of initial entry for Sr^{85} was less than that for Ca^{47}, not exceeding 1.5% of the dose in any 15-minute interval, but was relatively more sustained from the first to the fourth hour After the fourth hour, the rates of initial entry of Sr^{85} and Ca^{47} were almost proportional.

APPENDIX I

```
0    $IBFTC  FHGJ
1    Dimension B(30), F(30), G(30)
2    Read 100, (F(J), G(J), J = 1,30)
7    B(1) = 0.0
10   Print 120, B(1), F(1), G(1)
11   Do 80 J = 2,30
12   K = J - 1
13   S = 0.0
14   Do 70 L - 1,K
15   M = J + 1 - L
16   70 S = B(L) * F(M) + S
20   B(J) = (G(J)-S)/F(1)
21   80 Print 120, B(J), F(J), G(J)
23   100 Format (2F8.4)
24   120Format (1H, F8.4,3X,F8.4,2X,F8.4)
25   Stop
26   End
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Effect of X-irradiation on Host Resistance to the Dwarf Tapeworm.*

(32448)

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It is known that the course of certain infectious processes is aggravated in animals following sublethal doses of ionizing radiation. To date most studies have been concerned with the role of bacteria. There is some information on host susceptibility to parasitic infections following radiation exposure, but there is no information on cestodes and interest has centered primarily on a single nematode, *Trichinella spiralis*(1).

Although man and rodents are susceptible to infection with the dwarf tapeworm, *Hymenolepis nana,* host resistance to egg infection is relatively pronounced in that only a small percentage of ova consumed develop into adult forms. Furthermore, acquired host resistance to reinfection is striking following

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