## Intestinal Damage by Radiation and its Chemical Modification

The deoxyribonucleic acid content of the whole small intestine of mice and rats has been used as a measure of cell population in order to follow intestinal damage after X-irradiation, and has been found to be more reliable than simply measuring the intestinal weight. The method of Schmidt and Thannhauser[1] was used for separating the deoxyribonucleic acid and its concentration measured by Allen's method[2] of phosphorus determination and by ultra-violet spectrophotometry. At least three animals from different litters were used for each time interval after each radiation dose, and a control animal from each litter. The mean total deoxyribonucleic acid per small intestine from 43 control mice was found to be 0·72 mgm. The individual values were dependent on body-weight.

Consistent dose-response curves were obtained. The initial decrease in total deoxyribonucleic acid which became detectable 12 hr. after a dose of 200 r. was only slightly dependent on dose, and at 24 hr. after irradiation represented a reduction of approximately 30 per cent compared with controls. The time at which recovery began and the rate of recovery were markedly dependent on dose over the range 200–5,000 r.

Intraperitoneal injection into mice of β-mercaptoethylamine ('Becaptan') in doses of 150 mgm./kgm. 2–5 min. before X-irradiation significantly reduced the effect of 1,000 r. on intestinal deoxyribonucleic acid content 2, 3 and 4 days later to the same order as that of 750 r. (Table 1). Similar results, using 100 mgm. 'Becaptan'/kgm., were obtained in rats. The reduction of deoxyribonucleic acid content throughout the time 1–5 days after irradiation was greater than in mice, in agreement with the greater radiosensitivity of the rat intestine as judged by the clinical picture.

Mechanisms suggested for the action of 'Becaptan' are the promotion of regeneration without a concomitant reduction in the initial damage, or the reduction of initial damage without an effect on recovery[3]. When the time at which recovery begins and the rate of recovery are dependent upon dose, as in the intestine, bone marrow and lymph-nodes, the distinction may be easily confused, for a reduction in the degree of initial damage will show itself in an accelerated recovery, as illustrated in Table 1. A comparison on day 4 of the effects of 1,000 r. and 1,000 r. preceded by 'Becaptan' might suggest a marked enhancement of recovery by the drug. However, when account is taken of the time course of events after different doses it is clear that 'Becaptan' reduced the damaging effect of radiation by 25 per cent or a little more without intrinsically altering the course of recovery. This degree of effect is in quite good agreement with that given by Salerno[4] for the protective effect of 'Becaptan' on mortality in mice.

Table 1. Total Deoxyribonucleic Acid in Mouse Small Intestine

Mean values (mgm.) ± S.E. Figures in parentheses are numbers of animals used.

| Days after X-ray | 750 r. | 'Becaptan' before 1,000 r. | 1,000 r. | 1,000 r. followed by 'Becaptan' |
|---|---|---|---|---|
| 2 | 0·48 ± 0·02 (6) | 0·48 ± 0·01 (4) | 0·43 ± 0·02 (7) | 0·40 ± 0·01 (4) |
| 3 | 0·42 ± 0·02 (5) | 0·47 ± 0·03 (3) | 0·30 ± 0·01 (8) | 0·27 ± 0·01 (3) |
| 4 | 0·67 ± 0·02 (8) | 0·76 ± 0·04 (4) | 0·45 ± 0·05 (3) | |
| 5 | 0·61 ± 0·06 (3) | | 0·56 ± 0·06 (3) | |
| 6 | | | 0·61 ± 0·01 (4) | |

After the recent report by Nerurkar and co-workers[5] the effect on deoxyribonucleic acid content of 1,000 r. with and without previous injections of methionine was determined, but neither in intestine, spleen, bone marrow nor liver could any protective effect be detected. The determination of total deoxyribonucleic acid in an organ or tissue provides a possible screening test for substances which might modify the effects of radiation. It has the advantages over the test commonly used with acute killing as the end-point of giving a result in less than a week, and of providing, with very few animals, a quantitative measure of any modification produced.

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## Isotopic Tracer Method for measurement of Iron lost into and re-absorbed from Gastro-intestinal Bleeding Lesions

It has been shown[1,2], with the help of rabbit and sheep erythrocytes labelled with iron-59, that appreciable amounts of iron from hæmoglobin were absorbed when these cells were administered orally to human beings. So far as we know, no information is available on the re-absorption of hæm-attached iron from intestinal bleeding lesions. A method for measuring such a re-absorption is here proposed.

Approximately 10 microcuries of iron-59 in the form of ferric ammonium citrate (from Abbott Laboratories, Oak Ridge) are injected intravenously. Blood radioactivity is determined on the subsequent days until a plateau is reached. A 20 c.c. aliquot of blood is then marked with 60 microcuries of chromium-51 and reintroduced in the patient's circulation[3]. Fæces are collected quantitatively in three 4-day periods, and blood obtained at the start of each period. Fæces are homogenized and prepared as previously described[4], and radioactivity from chromium-51 and iron-59 determined separately, with appropriate corrections[5], in a well-type scintillation counter (Nuclear-Chicago model 3037-*B*) with a pulse-height analyser (Radiation analyser, Chicago-Nuclear). Blood taken at the beginning of each fæcal collection period serves as a standard for that period. The amount of blood $B_i$ (in ml./day) which is lost into the intestine can be readily calculated for each 4-day period:

$$B_i = \frac{R_f \times Q}{R_b \times 4} \qquad (1)$$