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Water Intake of Guinea Pigs as Parameter in Oral Drug Therapy of Experimental Irradiation.*† (22203)

FRIEDRICH ELLINGER.
Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.

In the study of the effects of drugs on X-ray-induced mortality of experimental animals, the use of peroral route is preferable in many instances to injection because of increased bleeding tendency exhibited by some laboratory animals. This is particularly true with respect to guinea pigs. In this species the pronounced bleeding tendency may cause fatal bleeding at the site of injection. Oral drug administration is usually performed by tube feeding, to control amount of medication as well as possible. This procedure is, however, not suitable for irradiated animals since these are particularly sensitive to infections. The small lacerations caused by such forced feeding experiments may open ports of entry for bacteria and thus superimpose a death rate caused by infection, which would becloud true results of such studies.

Administration of water-soluble drugs with the drinking water appeared, therefore, as a method of choice. Since, obviously, the amount of drug given in this manner would depend on water consumption of experimental animals, it was necessary to obtain information about their drinking habits.

Methods. Fifty-one male guinea pigs of the Institute stock with an average weight of 450 g (range 250-660 g), were kept in individual cages in air-conditioned quarters. Preliminary investigations had indicated that guinea pigs kept on our standard diet B, consisting of guinea pig pellets, lettuce, and a half orange daily, were drinking quite irregularly. To force experimental animals to drink, lettuce and oranges were withdrawn from the diet. Instead they were offered 235 cc of water to which was added 50 mg vit. C. The water was

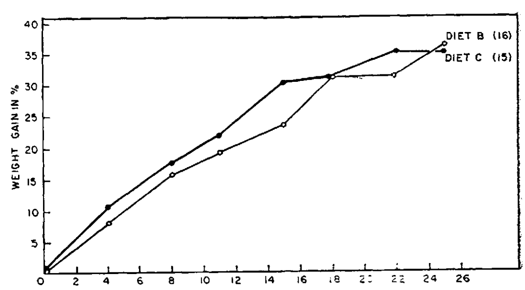

FIG. 1. Comparison between wt gains of guinea pigs kept on standard diet B and experimental diet C (dry food and drinking water plus 50 mg vit. C/235 cc). Figures in parentheses in this and subsequent curves designate No. of animals.

* The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

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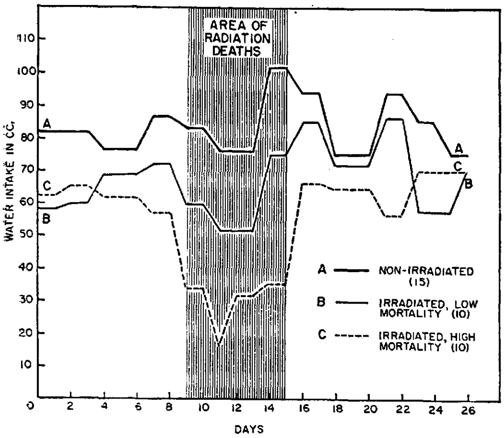

FIG. 2. Analysis of influence of X-ray-induced mortality on daily water intake of guinea pigs. Note decreased water intake in irradiated animals between 9th and 15th postirradiation day is proportional to percentage mortality caused by respective X-ray doses.

given in bottles which were coated with aluminum paint to preclude deterioration of the vitamin in daylight. The amount of water consumed was measured every other or third day.

Results. The first step was to ascertain whether this diet was satisfactory. The weight gain of 16 guinea pigs kept on the usual laboratory diet B was compared with that of 15 animals kept on the new diet C. The result is shown in Fig. 1 which indicates that there was no important difference in weight gain between these 2 groups.

The 15 guinea pigs kept on diet C for 26 days drank an average of 83.6 cc (stand. dev. ± 14 cc). A similar study was then performed on 20 irradiated animals, 10 of which had been exposed to the LD 30/26 days of 2000 KV X-rays and 10 animals which had received LD 80/26 days of 200 KV X-rays. The water consumption in this group averaged 61.7 cc (stand. dev. ± 14.8 cc). Fig. 2 shows in detail the variation in water intake during 26 days' observation. Curve A represents water consumption of non-irradiated animals, curve B that of animals exposed to X-ray dose causing a low mortality, and curve C that of animals exposed to the dose causing a high mortality rate. The time during which death occurred in irradiated animals is marked. There was no important difference in water consumption between groups B and C until the 9th postirradiation day. At this time some of animals showed symptoms of radiation illness and deaths began to occur in both groups. However, with occurrence of the first fatalities, a notable reduction in water intake in both groups took place, more pronounced in the group exposed to the X-ray dose causing the higher mortality. This observation induced us to consider water intake of survivors separately. In Fig. 3, curve A represents water consumption of non-irradiated animals, curve B shows that of the total group of irradiated animals, and curve C that of all survivors. As this graph indicates, those animals which were to survive, continued to consume water at a fairly constant rate. It is thus clearly recognized that reduction in water consumption was due to the fact that the animals which died reduced water intake shortly before expiration. Some stopped drinking 24 hours before death occurred.

Discussion. Water consumption of irradiated animals during the first week after irradiation was reasonably uniform irrespective of radiation dose. This seems to permit administration of a standard drug dose by mouth with a satisfactory amount of accuracy during this period which is most important for postirradiation protection. The standard procedure of this laboratory, for the evaluation of drugs on lethal effect of total-body

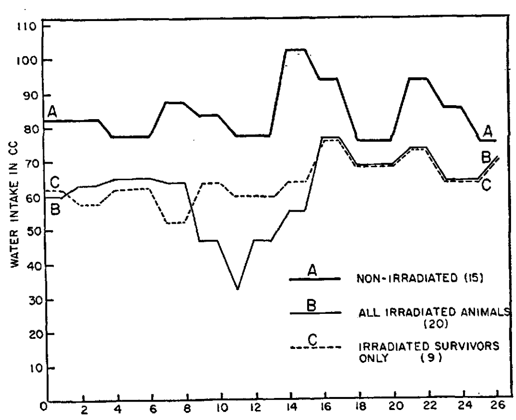

FIG. 3. Comparison of water intake of irradiated animals surviving X-ray irradiation (Curve C) with that of all irradiated animals (Curve B). Note that Curve B does not show the drop in water intake.

radiation, is to administer one fixed drug dose for 5 days after irradiation without adjusting medication to changes in weight of individual animals. The procedure of oral drug administration as outlined appears just as accurate as the injection method.

The oral route offers the advantage of administering larger total drug doses to animals by extending time of medication and of accomplishing this without additional stress to the animals. Extension of injections over equally long periods of time raises the obstacle of burdening the irradiated animal with larger amounts of vehicle substances which may in themselves adversely affect survival rate, as shown by us(1) and others(2) with respect to saline. The saving in time otherwise needed for injections is a further advantage of oral drug administration.

Summary. 1. Drinking habits of guinea pigs kept on a diet of dry food and drinking water have been studied to ascertain the amount of daily water consumption which may serve as a parameter for oral drug administration. 2. There is a difference between water intake of non-irradiated and irradiated animals. 3. This difference is chiefly accounted for by reduced water intake of animals succumbing to irradiation, which stopped drinking prior to death. 4. Water consumption of irradiated animals is not materially altered during the critical first 8 days after irradiation, irrespective of death rate produced later on. 5. Use of oral administration of water-soluble drugs with drinking water appears therefore possible with a sufficient degree of accuracy.

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A Urinofecal Separator for Laboratory Rat. (22204)

H. H. DRAPER AND A. F. ROBBINS. (Introduced by B. C. Johnson.)
Division of Animal Nutrition, University of Illinois.

The problem of obtaining urinary and fecal samples free from intercontamination is a major obstacle to some studies of absorption and metabolism utilizing laboratory animals. In the course of a study of the efficiency of absorption of dietary thiamin by the rat, using a conventional apparatus, serious errors attributable to contamination of fecal samples with urine were encountered. Subsequently a glass separator of new design was constructed which has been shown to effect this separation with a high order of efficiency. The design and operation of this apparatus are described herewith.

The construction of the separator is outlined in Fig. 1. An essential feature is the flared funnel stem which serves to draw the urine away from the pathway of the feces, which fall directly into the feces tube. Glass-to-glass contact must be maintained between tip of funnel stem and the inside surface of the separator, so that urine may flow readily around the interior of the bulb and be drained off by the urine tube. Urine is prevented from falling directly into the feces tube by the glass cone which rests on three legs ½ in. long. The feces tube is flared to 35 mm O.D. at the top, thereby being extended beneath the shoulder of separator bulb. The wire cage was constructed according to a design obtained from the Nutrition Division, Food and Container Institute, Quartermaster Corps, Chicago, Ill.

The whole apparatus may be attached to a ring stand by means of a 6 in. iron ring to support weight of the funnel and cage, and by 2 clamps fastened to neck of separator and to the feces tube, respectively.

The efficiency of the separator was tested according to the following scheme. Two nor-