

3) DNA polymerase- γ is suggested for the most recently described DNA polymerase that copies A_n-dT₁₅ with high efficiency, but does not copy DNA well (8). This enzyme has been called R-DNA polymerase to suggest its propensity for copying synthetic polyribonucleotides, but no evidence exists at present as to its ability to copy natural RNA. Polymerase- γ is acidic, has a molecular weight >100,000, and requires sulphydryl-containing compounds for maximal activity.

4) Mitochondrial DNA polymerase (DNA polymerase-mt) is an enzyme separable from the others (9, 10); it is named for its subcellular localization, which is so characteristic of the enzyme.

Table 1 shows how α , β , and γ have been named in some previous publications by some workers.

The nomenclature of DNA polymerases - α , - β , - γ , and -mt is being and will be utilized by us in the future (11). As new or different eukaryotic DNA polymerases are identified, the system could be expanded by the use of additional Greek letters or other symbols. It is our hope that others will utilize this system in order to avoid ambiguity.

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11. The descriptors α , β , and γ should be attached to "polymerase" as above, but never to DNA, as in "the α -DNA polymerase," which gives an erroneous impression. Use of "the α -polymerase" in proper context is acceptable.
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Histamine and Radiation-Induced Taste Aversion Conditioning

Levy, Carroll, Smith, and Hofer (1) reported that rats treated with an antihistamine do not subsequently develop radiation-induced taste aversions, and suggested that radiation-induced histamine production is the critical event responsible for the formation of radiation-induced taste aversions. In an attempt to evaluate the generality of this conclusion, I have found that if the Levy *et al.* experiment is repeated with a slight alteration of design, the administration of antihistamine potentiates, rather than blocks, radiation-induced taste aversions.

The design employed by Levy *et al.* was exceptional in that the initial exposure to the taste stimulus, a 0.1 percent saccharin solution, occurred after drug treatment and irradiation. The typical taste aversion design would have called for the initial saccharin ingestion before any drug or radiation treatment. This would have precluded the possibility that the administration of the drug prior to drinking might have interfered with conditioning by making the animals ill before they tasted the saccharin. I have conducted an experiment similar to that of Levy *et al.*, but following a design in which the antihistamine was administered after the ingestion of the saccharin solution and before exposure to radiation.

The procedures described by Levy *et al.* were followed as closely as possible, with the exception that the four groups of seven water-deprived rats were allowed 20-minute access to the saccharin solution *before* they were injected (intraperitoneally) with saline or the antihistamine chlorpheniramine maleate (20 mg/kg). Irradiation with 105 roentgens of x-rays or sham irradiation followed the injections. Twenty-four hours later, the rats were again allowed to drink saccharin solution. The saline-injected, sham-irradiated group drank 16.7 ml (mean) during this test. The saline-injected, irradiated group drank 5.2 ml, demonstrating their conditioned aversion for the solution. The drug-treated, sham-irradiated group also showed a significant aversion, drinking only 7.5 ml. The drug-

treated, irradiated group drank 1.8 ml, significantly less than either group that received drug or radiation alone (2).

There are two points of disagreement between these results and those of Levy *et al.* First, their chlorpheniramine-treated, sham-irradiated animals did not develop aversions, while the corresponding animals in my study did. Also, their drug-treated, irradiated animals did not develop aversions, while the corresponding group in my study showed the most severe aversions of all, contrary to what the Levy *et al.* histamine hypothesis would have predicted.

The timing of the chlorpheniramine injections appears to be the crucial difference between the two studies. It is clear from the present results that chlorpheniramine maleate itself produces taste aversions when injected after saccharin consumption. In addition, many of the rats injected with the drug showed abdominal muscular spasms and assumed abnormal postures within 10 minutes after their injections, indicating toxic effects of the drug. It may be suggested then, that both chlorpheniramine-treated groups in the Levy *et al.* experiment did not learn aversions because they were already ill when they first tasted the saccharin solution. Thus, the effect of chlorpheniramine illness and not attenuation of radiation-induced histamine release provides the best explanation of the results of both studies.

Levy *et al.* clearly recognized this issue, for in another experiment they effectively showed that prior treatment with chlorpheniramine did not interfere with taste aversion conditioning resulting from lithium chloride poisoning. However, this does not rule out the possibility that the prior treatment with chlorpheniramine in the original experiment could have resulted in toxic interference with conditioning when x-rays were used.

Taken together, the present work and the Levy *et al.* experiment provide examples of an inherent methodological problem involved in attempting to demonstrate radioprotective properties of drugs, with the use of taste aversion as the dependent

measure. If a drug is administered before exposure to the taste stimulus, as in the Levy *et al.* design, any aversive effects of the drug administration could inhibit conditioning to the subsequent radiation treatment. On the other hand, if a drug is administered after exposure to the taste stimulus, as in my experiment, the same aversive consequences could themselves be expected to induce taste aversions. In this case, any protective effects that the drug might produce against the radiation might be obscured. This methodological dilemma remains to be resolved before an adequate test of the Levy *et al.* hypothesis can be conducted. While the hypothesis that histamine release is responsible for radiation-induced taste aversion conditioning is clearly tenable, the supporting evidence presented by Levy *et al.* must be considered inconclusive.

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3. I thank D. Dommers of Denison University for assistance in the data collection.

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It is known that conditioned taste aversions produced by ionizing radiation are strongest when test animals are irradiated before the ingestion of the taste stimulus. In contrast, drugs typically produce conditioned taste aversions only if administered after ingestion of the taste stimulus (1). We deliberately designed our experiment to

maximize radiation-induced taste aversion and to avoid any aversion that would be conditioned if the chlorpheniramine maleate injection followed saccharin consumption. Therefore, we cannot agree with Sessions' statement that our experimental design was "exceptional."

Sessions says that rats which have been "made ill" by injection of chlorpheniramine prior to tasting saccharin cannot learn taste aversions. Although we showed that LiCl-induced aversions were not blocked by prior treatment with chlorpheniramine, Sessions suggests "that the prior treatment with chlorpheniramine in the original experiment could have resulted in toxic interference with conditioning when x-rays were used." We know of no evidence which supports this notion. In fact, injections of physostigmine (a drug which can produce conditioned taste aversions) prior to saccharin ingestion and irradiation significantly augments the resultant saccharin aversion (2).

We are not surprised that injection of chlorpheniramine maleate after saccharin consumption produced a saccharin aversion. Conditioned taste aversions have been produced by a wide variety of agents from tranquilizers to isotonic saline at doses that are not toxic and do not cause observable sickness (3).

However, Sessions' finding that chlorpheniramine potentiated the radiation-induced saccharin aversion is difficult to understand. We agree with Sessions that the timing of the chlorpheniramine injection is crucial. In our laboratory the 100-roentgen exposure (at 10 roentgens per minute) is maximally aversive 90 minutes after onset of irradiation (4). Under these conditions injection of the antihista-

mine immediately prior to radiation exposure seems to produce optimum blocking of the subsequent aversion. Unfortunately, Sessions does not give the parameters of his radiation exposure, so there is no way to predict the best time to administer the antihistamine.

In short, we still feel that our data constitute a strong argument in favor of the hypothesis that histamine is responsible for radiation-induced taste aversions. The final test of this hypothesis will have to await pharmacological and physiological measurements on radiation- and drug-treated animals. Further studies that manipulate the order of radiation and drug treatments in relation to saccharin ingestion are unlikely to confirm or disprove the histamine hypothesis.

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