finity, the equilibrium voltages must be obtained upon integration of the right-hand sides. Integration between these limits yields the following relationship for the rate constants:

$$\frac{k}{k'} = \frac{aC'_o + b}{aC_o + b} = \frac{(a/b)\ C'_o + 1}{(a/b)\ C_o + 1} \tag{7}$$

If a value of 0.1 is selected for the constant (a/b), the rate constant for a depolarization as a consequence of changing the potassium concentration from 2.5 to 100 mM will be about 10 times greater than for the subsequent repolarization.

If the integrations of Eqs. 5 and 6 are performed between the limits of time = 0 and time = t, the following time dependence of the voltage is predicted for change 1 to 2 (Eq. 8) and for change 2 to 1 (Eq. 9).

$$V_t = V_1 + \frac{\Delta n(aC'_o + b)}{Qk}(1 - e^{-kt}) \tag{8}$$

$$V_t = V_2 - \frac{\Delta n(aC_o + b)}{Qk'}(1 - e^{-k't}) \tag{9}$$

With $(a/b) = 0.1$ in Eq. 7, a depolarization-repolarization sequence is plotted from Eqs. 8 and 9 when C_o = 2.5 mM and C'_o = 100 mM, k being chosen as 2 sec^{-1} consistent with the half-time of the Hodgkin and Horowicz "on effect." The voltage behavior is similar to that presented by Hodgkin and Horowicz (*1*) for muscle under similar conditions. The value selected for (a/b) is not an unreasonable one since it is of the same order as the value required by Sjodin (*3*) to fit transmembrane flux data (Fig. 1).

It is to be emphasized that the assumption of simple exponential time processes may be regarded as an approximation only. Some quantitative deviations may be expected as a consequence. It has been assumed, for example, that only the external solution is effective in site loading and unloading. The model probably provides a good approximation for the change 1 to 2 in the direction of depolarization. When the outer concentration is changed from a high to a very low value (state 2 to state 1), the approximation may not be as good since the now higher efflux from the cell will become a source of ions for site loading from the inside of the cell. This effect will tend to keep the membrane in the depolarized state and will become less and less a factor as the membrane potential returns to the initial high value. In reality, the driving force for the "off site" movement may vary some while the membrane potential varies, so that the change 2 to 1 cannot be truly exponential as assumed. As this refinement leads to nonintegrable equations, it is not included in the derivation. It is noteworthy, however, that this effect would increase the asymmetry by leading to an even slower "off site" process than calculated. In any event, the source of the time asymmetry is the fact that the processes of site loading and site unloading are different. Site loading is a bimolecular process whereas site unloading is a monomolecular process.

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References

1. A. L. Hodgkin and P. Horowicz, *J. Physiol. (London)* **153**, 370 (1960).
2. E. J. Harris and R. A. Sjodin, *ibid.* **146**, 56P (1959).
3. R. A. Sjodin, *J. Gen. Physiol.* **44**, 929 (1961).

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Radioprotective Activity of a Phenanthrene Derivative in Mice

Abstract. 2-Acetyl-7-oxo-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydrophenanthrene possessed radioprotective activity when injected subcutaneously (in sesame oil) into 20-day-old male Swiss mice once daily for the 10 days prior to irradiation by cobalt-60 at 30 days of age. Female mice similarly treated were not protected.

Rugh and Wolff (*1*) demonstrated that castration enabled mature male mice to survive whole-body x-irradiation better than intact males. Randall and Selitto (*2*) reported that 2-acetyl-7-oxo-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydrophenanthrene (Ro 2-7239) has antiandrogenic and antimyotrophic activity when administered to testosterone-treated, immature, castrated male rats, while having neither estrogenic nor antiestrogenic activity in female rats. At high doses, Ro 2-7239 also has androgenic activity (*3*). This report considers the radioprotective activity of this phenanthrene derivative in male mice.

The methods used in this study have been previously described (*4*). The mice received 710 r of whole-body Co^{60} irradiation at the rate of 17 to 18 r/min (adjusted to decay of source).

Table 1 gives a summary of five separate experiments, in each of which approximately 12 mice were used at each dose level. Compound Ro 2-7239 both delayed the onset of radiation death and reduced the total mortality, the significance of the protection afforded by the 1000-μg dose at 35 days being $P < 0.01$.

Table 1. Protective action of Ro 2-7239 against Co^{60} irradiation when given in daily injections for 10 days before irradiation.

Total dose (μg)	Mice (No.)	Deaths (No.) at specified days after irradiation				
		9	14	21	28	35
0	57	15	39	50	51	51
250	59	7*	29*	38†	41†	42‡
500	57	7	28*	38†	42*	42*
1000	60	9	24†	37†	39†	39†

* $P < 0.05$. † $P < 0.01$. ‡ $P < 0.02$.

Not only did the 1000-μg dose level give optimum protection against radiation death, but it also provided some protection against weight loss due to irradiation. At the observation made 14 days after irradiation, the mean weight of the surviving mice which received 1000 μg of Ro 2-7239 was approximately 2 g (10 percent) greater than the mean weight of the irradiated control mice. An analysis of the variance showed the difference between the means to be statistically insignificant, however. The tendency noted, though, is in contrast to that of the radioprotection elicited by estradiol-17β, in which the mean body weight of the survivors at 15 days after irradiation was essentially the same as that of the irradiated, nontreated survivors (*4*).

Compound Ro 2-7239 elicited no radioprotection whatever when given at the same dose levels to female mice of the same age as the male mice and when given the same dose of irradiation. Approximately 24 mice were used in each of the three treatment groups as well as in the control group. A mortality of 92 to 100 percent was observed for each of the four groups.

These data do not elucidate the mechanism of the radioprotection afforded by Ro 2-7239 (*5*).

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References and Notes

1. R. Rugh and J. Wolff, *Proc. Soc. Exptl. Biol. Med.* **92**, 408 (1956).
2. L. O. Randall and J. J. Selitto, *Endocrinology* **62**, 693 (1958).
3. R. I. Dorfman, *Science* **131**, 1096 (1960); R. I. Dorfman and D. Stevens, *Endocrinology* **67**, 394 (1960).
4. W. Rooks II and R. I. Dorfman, *ibid.*, in press.
5. Whether this activity is related to its antiandrogenicity is under investigation. . The technical assistance of Robert J. Duclos is gratefully acknowledged. This work was supported in part by contract No. AT(30-1)-918 with the U.S. Atomic Energy Commission, and by a grant-in-aid from Hoffmann-La Roche, Inc.

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