directly allow for quantitative evaluation in the more exact sense that model measurements do in the evaluation of steric factors. The evaluation of polarizing forces as illustrated above may fulfill to some extent this gap in the theoretical tools of the "structure-activity" pharmacologist.

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Hypothesis of the Biological Action of Radiation

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Numerous investigations on the effect of radiation on living organisms have brought us to a stage where the mechanism of action of radiation on cells may be clarified by mathematical interpretation. The studies of the late D. E. Lea (*1*) initiated such an approach.

Lethal effects of radiation have been studied by a number of authors with a wide variety of experimental materials, partly because of the ease with which experiments can be done in which the criterion of the effect of radiation is the death of the organism or cell, and partly because of the practical importance of the lethal action of radiation on cells in the treatment of cancer.

The manner in which radiation effects the killing of bacteria, or the inactivation of viruses, is becoming clearer. With viruses, the biological effect is believed to be due to a single ionization in the virus; with these materials exponential curves are typical in plots of inactivation vs. dosage. With bacteria, in some cases, such plots give sigmoid curves. Lea attributes sigmoid response curves to the tendency of some bacteria to clump. However, most of the survival curves for cells of higher organisms are also of a sigmoid nature. The formula of Blau and Altenburger (*2*), which is known as the multihit theory, is considered as explaining the facts of the case reasonably well. There are some discrepancies in it, in the experimental results from some studies, which cannot be fitted even by modifications of their formula.

Comparisons have been made between experimental data and the formula arising from the following hypothesis.

Rather than consider that there is only one radiation-sensitive region in a cell, which is the viewpoint of the multihit theory, assume that there are in a cell n molecules essential to the continued existence of the cell. Assume that the cell can survive if no more than r molecules out of the n are damaged by ionization from radiation—that is, the cell dies if more than a certain percentage of the n molecules are damaged, and that each molecule is damaged by one ionization. Then the following considerations arise:

a) Just as in the disintegration of radioactive elements, the probability that a molecule escapes damage is $e^{-\sigma t}$ where σ = action coefficient and t = duration of radiation; accordingly, $1 - e^{-\sigma t}$ represents the probability that a molecule is damaged.

b) If we take a large number of cells, each of which contains n molecules, the first term in the expansion of the formula

$$[e^{-\sigma t} + (1 - e^{-\sigma t})]^n$$

gives the probability that a cell suffers no damage to any of the n molecules after time t, the second term that one in n is damaged, and the $(r+1)$st term gives the probability that r of the n molecules suffer damage.

If we suppose that the cell can survive if no more than r molecules are damaged, then the survival curve is given by the following formula:

$$y = e^{(-\sigma t)n} + ne^{(-\sigma t)(n-1)} \cdot (1 - e^{-\sigma t}) + \dots + {}_nC_r e^{(-\sigma t)(n-r)} \cdot (1 - e^{-\sigma t})^r$$
$$= \sum_{i=0}^{i=r} {}_nC_i e^{(-\sigma t)(n-i)} \cdot (1 - e^{-\sigma t})^i. \tag{1}$$

For simplicity, we may substitute x for $e^{-\sigma t}$ and we may then write Eq. (1) as follows:

$$y = \sum_{i=0}^{i=r} {}_nC_i x^{n-i}(1-x)^i,$$
$$\frac{dy}{dx} = (n-r)\,{}_nC_r x^{n-r-1}(1-x)^r.$$

The integral of this last expression is

$$y = (n-r)\,{}_nC_r \int_0^x x^{n-r-1}(1-x)^r dx. \tag{2}$$

The incomplete β-function is defined by

$$\beta_x(p, q) = \int_0^x x^{p-1}(1-x)^{q-1}dx,$$

so the indefinite integral in Eq. (2) can be expressed as

$$\beta_x(n-r, r+1).$$

The complete β-function is

$$\beta(p, q) = \int_0^1 x^{p-1}(1-x)^{q-1}dx = \frac{(p-1)!(q-1)!}{(p+q-1)!},$$

so that

$$\beta(n-r, r+1) = \frac{(n-r-1)!r!}{n!}.$$

The coefficient in (2) is

$$(n-r)\,{}_nC_r = \frac{n!}{(n-r-1)!r!}.$$

Thus the survival curve (2) can be expressed in the form

$$y = \frac{\beta_x(n-r, r+1)}{\beta(n-r, r+1)},\ x = e^{-\sigma t}. \tag{3}$$

The values of this expression can be found in Pearson's Tables of the incomplete β-function. The survival curves obtained from this formula are similar to those of Blau and Altenburger, although it is difficult to decide upon the values of n and of r from the experimental curve. Such an attempt has been made, for example, by determining the ratio of the doses required for 10% kill and for 90% kill.

If we put $n = 1$ and $r = 0$ in (1) or in (3), the survival curve is an exponential. For $n > 1$ and $r = 0$, an exponential curve is also obtained. This case is known as multitarget, not multihit. Finally, the case $r = n - 1$, $n \geqq 2$ corresponds to clumping, and a sigmoid curve is obtained.

If we consider delayed division of the cell rather than lethal action, then r or r/n will vary with the stage of the cell (for example, prophase) and will therefore be a function of the time of irradiation: $r/n = F(t)$. Thus the hypothesis that has been advanced in this paper makes it easy to understand the concept of the cumulative dose as formulated by D. E. Lea.

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Comments and Communications

A Citizen's Duty

EVERYONE should vote in our national and local elections. The votes of the readers of this journal, who represent a group of the highest intelligence, are especially desirable. Yet those who are responsible for arranging national meetings of scientific, technical, and trade associations apparently have no regard whatever for election day. Last election day the country was flooded with technical meetings ranging from the National Academy of Sciences and American Petroleum Institute to countless trade organizations. In very few states is it possible to vote *in absentia* or by letter. Many technical people, therefore must choose between their duty at the polls and their presence at a society meeting. Why not recognize our obligations as citizens and, throughout the country, arrange all association meetings on dates that will not conflict with voting?

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Flash in Photomicrography[1]

A MAJOR problem in photomicrography is the elimination of vibration in the apparatus or in the building housing the apparatus. This problem becomes acute whenever long exposures or high magnifications are required. Photomicrography in this laboratory has been relatively difficult because the framework structure contains vacuum pumps and compressors, which may be in operation throughout the working day. Although several methods were used to eliminate vibration in the photomicrographic equipment, none was completely successful. The introduction of flash lighting eliminated the effects of vibration and yielded excellent photomicrographs (*1*).

A microscope lamp (Spencer #735A) with a 100-w coil filament, bayonet base projection bulb was aligned and adjusted to provide "Köhler illumination" (*2*). After the desired field had been selected and brought into critical focus, the projection bulb was replaced by either a Westinghouse speed midget (SM) or G-E #5 flash bulb. The SM flash bulb was ideal for photomicrography because of its speed and safety. It should be noted that the flash bulb must be fired with a d-c voltage of not more than 6 v. Illumination may be controlled by neutral density filters, crossed polaroid disks, or a ground-glass filter. Should the illumination prove insufficient, as could be the case with oil immersion objectives and long bellows extension, a faster film may be used.

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[2] The opinions and assertions contained in this report are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or naval service at large (Art. 1252, *U. S. Navy Regulations* [1948]).

Reservist Reaction

THE comments by Charles G. Wilber, entitled "Mobilization of the Reserve," which appeared in SCIENCE, December 7, 1951, merit reply. . . . No mature reservist expects to avoid performance of duty very long merely on the basis of personal preference. Similarly, the scientist-reservist does not expect blanket deferment, hoping merely that when he is called to duty the position to be occupied will permit him to perform optimally in a professional capacity. Surely, and rightly so, the medical profession would