

theoretical curves demonstrate why anagen follicles are less "sensitive," why larger follicles are less "sensitive," and why with larger follicles there is less difference between follicles treated in anagen or telogen. The assumption of Lubnow that the individual granule sites or lipochochondrial precursors are "hit" by the radiation would appear untenable. Even the small zigzag hair follicles of mice have in the pigmented matrix cone no less than 30 cells with no less than 100 pigment granules (C-57 Black strain of mice) in each. The dose-response distributions and the fact that most hairs of the smallest type are fully pigmented or all-white suggest that the entities to be "hit" must be relatively few and extrinsic to the matrix cells.

Mosaic (partially pigmented) hairs do occur with a somewhat greater frequency in larger follicle types, as might be predicted on the basis of the above analysis. In later hair generations the percentage of mosaics decreases as the percentage of all-whites increases. Lubnow (4) makes the same observation in his work on the rabbit. We have seen in active zigzag follicles in the mouse cases of mosaic hair shafts being produced. Only one, or at most 2, pigmentary dendritic cells are present. Some matrix cells apparently receive no granules, some receive a few, and some receive full complements (10, 11, 14). It is suggested here that such pigmentary cells have lost the capacity to divide but not entirely the capacity to produce pigment granules and to "inoculate" matrix cells.

The analysis presented in this paper, involving the number and presence of extrinsic entities, is in the nature of a tentative hypothesis and suggests further investigation. Two other lines of work should be mentioned briefly, the first somewhat contradictory, the second, confirmatory. The first is the classic investigation of Packard (15) on the effect of comparable moderate x-ray doses on the hatchability of fertilized *Drosophila* eggs. Sigmoid exponential distributions, very similar to ours, were obtained. The explanation offered was not in terms of number of entities but in terms of variations in egg sensitivity. The other line of work is that of Taylor (16) on the effect of freezing on the "melanophores" in the rat. He obtained all-white and mosaic hairs, the dendritic cells being relatively easily destroyed by freezing.

Certain conclusions are suggested from the evidence reviewed, from the analysis presented, and from the discussion in this paper. All-white hairs are the result of a complete inactivation (apparently destruction) of the dendritic cells. Mosaics are the result of a complete inactivation of some and a partial inactivation of those remaining—that is, no cell division but the retention of some melanogenic function. The basic pigment sites in the matrix cells are of extrinsic origin, specifically from a small "reservoir" of potentially pigmented dendritic cells.

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## Quantum Yields, Ionic Yields, and Molecular Weights of Proteins

A. D. McLaren

*Institute of Polymer Research,  
Polytechnic Institute of Brooklyn, New York*

Recently, on the basis of inactivation quantum yield ( $\Phi$ ) data, it has been suggested (1) that the larger the molecule (enzyme, or virus) the smaller is the fraction of the absorbed light absorbed by the sensitive volume (the active center?), and hence the lower the quantum yield for inactivation (Fig. 1). If

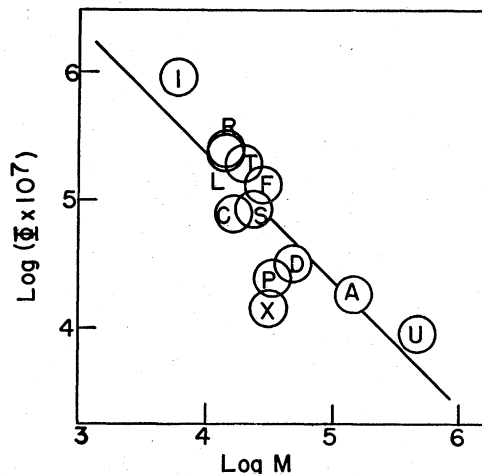


FIG. 1. Plot of  $\log (\Phi \times 10^7)$  vs  $\log M$  for a number of enzymes and related proteins. The equation  $\Phi = Q/M$ , where  $Q$  is a constant, is approximately obeyed (1, 3, 4). (Aldolase, A; carboxypeptidase, X; chymotrypsin, C; triosephosphate dehydrogenase, D; ficin, F; insulin, I; lysozyme, L; pepsin, P; ribonuclease, R; soybean trypsin inhibitor, S; trypsin, T; urease, U.)

this be true, the ionic yields for the indirect effect in aqueous solutions by x- and  $\gamma$ -rays could expectedly show a similar trend; i.e., the larger the molecule the smaller the fraction of reacting ions reacting with the sensitive volume.

A search of the literature reveals two examples (1, 2) for which both quantum yields (2,537 A) and

indirect ionic yields are available (Table 1). The two substances, ribonuclease and tobacco mosaic virus, are of widely different molecular weights (*M*), however. The striking similarity of the yields for each substance should encourage further comparative studies.

TABLE 1

Substance	Quantum yield	Ionic yield	Molecular wt
Ribonuclease (1, 2)	0.026	0.03	15,000
Tobacco mosaic virus (1, 2)	0.000043	~ 0.0001	42,000,000

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## Successful Treatment of Ulcer Disease in Brook Trout (*Salvelinus fontinalis*) with Terramycin

S. F. Snieszko, S. B. Friddle, and P. J. Griffin

Microbiological Laboratory, U. S. Fish and Wildlife Service, Kearneysville, West Virginia

Prior to this report, all chemotherapeutic agents employed in the treatment of ulcer disease of trout proved unsatisfactory (1-4). Investigations on the treatment of this disease were hindered by the lack of adequate information concerning the etiological agent involved. Recently Snieszko *et al.* (5) proved *Hemophilus piscium* to be the causative agent of ulcer disease in the Eastern United States, and Flakas (6) isolated an unidentified gram-positive bacillus from a similar disease in Wisconsin. Snieszko *et al.* confirmed the assumption that ulcer disease frequently occurs as a mixed infection in conjunction with *Bacterium salmonicida*, the cause of fish furunculosis.

Investigations carried out by Gutsell (7) and Snieszko *et al.* (8) had shown that fish furunculosis could be treated effectively with certain sulfonamides. Further observations indicated, however, that ulcer disease was apparently refractory to treatment with these drugs. It therefore seemed likely that the few instances in which ulcer disease had been successfully treated with sulfonamides occurred only in cases of mixed infections.

Some of the newer antibiotics, such as aureomycin (9) and terramycin (10) were employed in an attempt to treat infections of ulcer disease. These drugs can be administered orally with food without significant loss of their therapeutic properties. This is an important factor, since parental administration of drugs to fishes is impractical.

During the summer of 1950, three pilot experiments were run with separate lots of fingerling brook

trout having ulcer disease. Aureomycin hydrochloride was used in form of "Spersoids" (Lederle) at the rate of 50 mg/kg trout/day. Terramycin hydrochloride (Pfizer) was given at a rate of 75 mg/kg fish/day. The dosages were calculated as the pure substance without filler. The drugs were mixed with the food, and the fish were fed twice each day; the temperature of the water was 13° C; the weight of the trout in various lots ranged from 6 to 12 g per fish, and the fish used in each experiment were of fairly uniform size. Examination had shown that in all outbreaks *H. piscium* was present in the lesions and tissues of infected trout. In all outbreaks of the disease, some trout were also infected with *Bact. salmonicida*.

Ulcer disease usually has an incubation period of 2-3 weeks, and trout with advanced pathological changes can live for a number of days and sometimes even recover. Infected fish usually have oral ulcerations that hinder feeding (2). Therefore, the success of any oral treatment depends to a large degree on the number of fish in the treated lots which still can take the medicated food at the start of the treatment.

Of the two antibiotics used, aureomycin had no therapeutic value. Terramycin was effective, the proportion of surviving trout depending on the rate of mortality at the onset of treatment. In the first experiment, with 6.5% mortality per day at the start, the losses were 80% in the treated fish, and 90-95% in controls after 2 weeks of treatment. In the second experiment, with an initial mortality rate of 1%/day, after 40 days of treatment 25% of the trout died in the treated lot and 97% in controls. In the third experiment, with approximately 3% mortality per

TABLE 1  
MORTALITIES IN FINGERLING BROOK TROUT AFTER  
TREATMENT WITH TERRAMYCIN

Periods	Terramycin-treated				Controls		
	Replicates		Av (A and B) % mortality per day*		Replicates		Av (A and B) % mortality per day*
	A	B			A	B	
August	4-8	7	6	2.3	13	6	3.2
"	9-13	9	12	4.4	8	6	3.1
"	14-18	2	5	1.8	14	8	6.0
"	19-23	2	1	0.8	3	9	4.0
"	24-28	2	2	1.2	6	6	5.8
"	29-						
September	2	1	0	0.3	1	11	6.4
September	3-7	0	0	0	2	1	3.1
Total number dead	23	26			47	47	
Initial number of trout	55	55			55	55	
Average wt/trout	12.7 g	12.7 g			13.0 g	12.4 g	
Total dead (percentage)	42	47			85	85	

\* Calculated from total mortalities during 5-day periods.