

The Origin of Tear Lysozyme¹ (35788)

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(Introduced by F. H. Epstein)

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The lysozyme activity of human tears is greater than that of any other body fluid (1), nevertheless the source of the enzyme in tears is uncertain. An obvious question is whether or not it represents an ultrafiltrate of the serum or is synthesized *de novo* in lacrimal cells.

Human serum lysozyme activity varies widely in a variety of hematologic disorders (2-5), mostly in relationship to the turnover of body granulocytes and monocytes (6, 7). In this study, simultaneous tear and serum lysozyme activity measurements were made in patients with wide variations in serum lysozyme activity to determine whether or not the lysozyme activities of these fluids are related.

Materials and Methods. Serum lysozyme activity was determined on venous blood samples from 39 patients with a variety of hematologic, renal, and other clinical disorders. Enzyme assay was by the lysoplate technique of Osserman and Lawlor (3) using a human lysozyme standard. Tear samples from the right eye were collected on Shirmer strips and assayed according to the technique of Bonavida and Sapse (8). Each determination was read to 0.5 mm on the lysoplate which represented such wide variations in concentration in the high activity range that activities above 6200 $\mu\text{g/ml}$ were not specifically determined.

Results. Serum lysozyme values varied from a low of 0.7 $\mu\text{g/ml}$ in a patient with

		TEAR LYSOZYME ($\mu\text{g/ml}$)	
		< 1400	> 1400
SERUM LYSOZYME ($\mu\text{g/ml}$)	< 6	9	11
	> 6	8	11

FIG. 1. Relationship between serum and tear lysozyme in the 39 patients included in this study.

acute lymphocytic leukemia to a high of 82 $\mu\text{g/ml}$ in a patient with acute myelomonocytic leukemia (Table I). The median value was 6.2 $\mu\text{g/ml}$. Tear lysozyme varied from a low of 380 $\mu\text{g/ml}$ in a patient with Sjögren's syndrome to a high of >6200 $\mu\text{g/ml}$ in a patient with metastatic cancer (Table I). The median value was 1500 $\mu\text{g/ml}$. There was no evidence of a relationship between serum and tear lysozyme activity (Table I and Fig. 1). A striking individual example of this disparity was a patient with diabetes who had a serum lysozyme of 0.95 $\mu\text{g/ml}$ and tear activity of 6200 $\mu\text{g/ml}$. Another patient with serum activity of 82 $\mu\text{g/ml}$ had 1100 $\mu\text{g/ml}$ of tear activity.

Discussion. The objective of this study was to determine whether the lacrimal apparatus simply collects, concentrates, and excretes lysozyme from the blood, or synthesizes and excretes it *de novo*. The assumption was made that if the lacrimal gland only pro-

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TABLE I. Summary of Tear and Serum Lysozyme Data According to Type of Disease.

Clinical condition	No. of patients	Serum lysozyme ($\mu\text{g/ml}$)		Tear lysozyme ($\mu\text{g/ml}$)	
		Median	Range	Median	Range
Acute leukemia	9	14.4	0.7–82.0	1100	1100–3000
Myeloproliferative disorders	5	11.8	7.4–42.0	1100	700–1500
Lymphoproliferative disorders	4	3.8	1.2–6.2	1500	1100–6200
Azotemia	7	7.7	6.3–15.6	2200	700–>6200
Miscellaneous	14	2.4	0.95–11.8	1500	380–>6200

cessed serum lysozyme, the enzyme activities of tears and serum would bear a relationship. The discordance of enzyme activity data in the same patients, however, strongly favors the hypothesis that lacrimal cells synthesize rather than collect lysozyme.

Human tear lysozyme probably is identical in structure to serum lysozyme and that of all other human secretions (9). Its activity in ocular tissues is greatest in the lacrimal apparatus (10). Presumably the very high lysozyme activity of tears plays some role in bacterial growth inhibition in areas bathed in lacrimal gland secretions. Clinical studies have shown decreased human tear lysozyme activity in Sjögren's syndrome (11–13), smog eye irritation (14), industrial exposure (15), tear hypersecretion (9), and conjunctivitis (10, 16, 17). Although these observations may have certain clinical implications they contribute little to knowledge concerning the origin of the enzyme within the lacrimal system. They are, however, quite consistent with the concept of an autonomous lysozyme synthesizing system within lacrimal cells.

Summary. Simultaneous serum and tear lysozyme studies were performed on 39 adults with a wide range of serum lysozyme activities. Failure to establish a relationship between the enzyme activities of serum and tears is in accord with the concept that lysozyme is synthesized *de novo* by lacrimal cells.

1. Fleming, A., and Allison, V. D., *Brit. J. Exp. Pathol.* **3**, 252 (1922).
2. Perillie, P., Kaplan, S. S., Lefkowitz, E., and Finch, S. C., *Blood* **28**, 1000 (1966).
3. Osserman, E. F., and Lawlor, D. P., *J. Exp. Med.* **124**, 921 (1966).
4. Perillie, P. E., Kaplan, S. S., Lefkowitz, E., Rogaway, W., and Finch, S. C., *J. Amer. Med. Ass.* **203**, 317 (1968).
5. Wiernik, P. H., and Serpick, A. A., *Amer. J. Med.* **46**, 330 (1969).
6. Fink, M. E., and Finch, S. C., *Proc. Soc. Exp. Biol. Med.* **127**, 365 (1968).
7. Perillie, P. E., Kaplan, S. S., and Finch, S. C., *N. Engl. J. Med.* **227**, 10 (1967).
8. Bonavida, B., and Sapse, A. T., *Amer. J. Ophthalmol.* **66**, 70 (1968).
9. Jollès, J., and Jollès, P., *Biochemistry* **6**, 411 (1967).
10. Thompson, R., and Gallardo, E., *Amer. J. Ophthalmol.* **19**, 684 (1936).
11. Erickson, O., *Stanford Med. Bull.* **13**, 292 (1955).
12. McEwen, W. K., and Kimura, S. J., *Amer. J. Ophthalmol.* **39**, 200 (1955).
13. Regan, E., *Amer. J. Ophthalmol.* **33**, 600 (1950).
14. Sapse, A. T., Bonavida, B., and Stone, W., Jr., *Amer. J. Ophthalmol.* **66**, 76 (1968).
15. Erickson, O. F., Hatlen, R., and Berg, M., *Amer. J. Ophthalmol.* **47**, 499 (1959).
16. Thompson, R., and Gallardo, E., *Amer. J. Ophthalmol.* **19**, 684 (1936).
17. McEwen, W. K., and Kimura, S. J., *Amer. J. Ophthalmol.* **39**, 200 (1955).

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