

Serum Histaminase in Leprosy¹S. C. Lahiri, K. Saha, A. Basu and M. M. Mittal²

It has been previously reported that 80% of a total of 20 leprosy patients, irrespective of type of illness, had failed to exhibit positive Prausnitz-Kustner (P-K) reactions when tested with homologous reaginic sera, which had given highly positive (++ to +++) P-K reactions in normal individuals (11). It was further observed that reactions to histamine were significantly depressed in leprosy patients as compared with healthy controls. It is interesting to recall that in the patients with tuberculoid leprosy with reaction, histamine content of the affected tissue, measured pharmacologically, was less than that of normal or tuberculoid tissue (3). Mast cells were found degenerated and without granules and their number was less than in quiescent tuberculoid leprosy. Thus, a possibility of altered histamine catabolism is indicated in patients with leprosy; this has stimulated the authors to study the histaminase levels in these patients.

MATERIALS AND METHODS

The study involved 65 individuals, of which 36 suffered from leprosy and the remaining were normal. The former group was comprised of 27 cases of lepromatous leprosy including 14 patients with *erythema nodosum leprosum* and 9 cases of tuberculoid leprosy. The lepromatous group included cases of borderline lepromatous leprosy while the tuberculoid group included patients of borderline tuberculoid variety. Classification of leprosy type was based on clinical history, physical examination, lepromin (Mitsuda type) test and skin biopsy (12).

Ten milliliters of blood were collected by venipuncture and the serum thus obtained was stored at -20°C. The blood samples

were not collected from pregnant or menstruating women. Serum histaminase was estimated according to the microspectrophotometric method of Arsen and Kemp (1). The results were expressed in provisional units (Pr U), one provisional unit being equal to the amount which produced an increase of 0.01 in optical density at 470 m μ after incubation for four hours.

Fig.-1

SERUM HISTAMINASE VALUES IN CONTROLS & LEPROSY PATIENTS

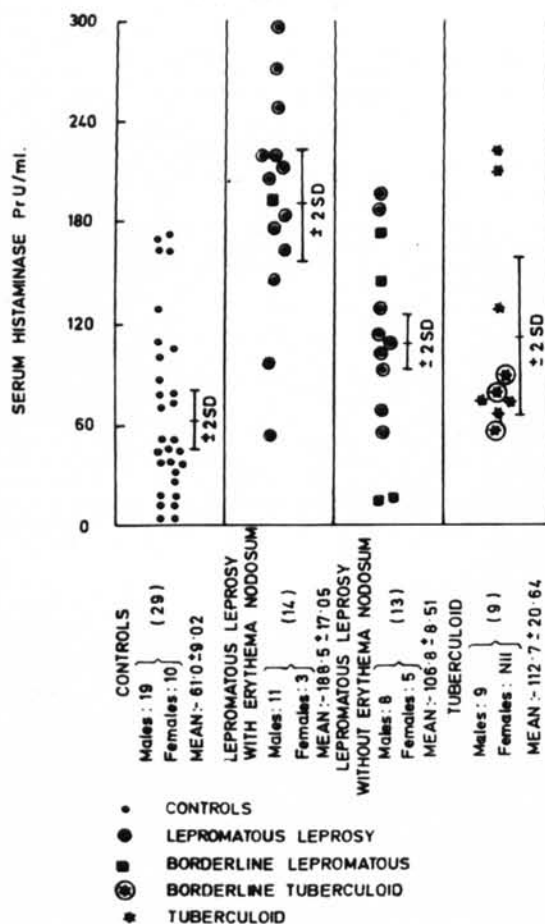


FIG. 1. Shows the variations in the level of serum histaminase in normals and different types of leprosy patients.

¹Received for publication 6 June 1973.

²S. C. Lahiri, M.D., Ph.D. (Edin.), Professor of Pharmacology, School of Tropical Medicine, Calcutta; K. Saha, M.Sc., M.B.B.S., Ph.D., Associate Professor of Microbiology, G.B. Pant Hospital and Maulana Azad Medical College, New Delhi; A. Basu, M.Sc., D.Phil. (Cal.), Research Fellow, School of Tropical Medicine, Calcutta; M. M. Mittal, M.D., Hon. Physician, Sir Ganga Ram Hospital, New Rajendra, Nagar, New Delhi, India.

RESULTS

Figure 1 and Table 1 show the serum histaminase values in leprosy patients and normal individuals. The histaminase values ranged between 0 to 173 Pr U/ml (mean 66.04 ± 9.02) in the control group, and between 14 to 292 Pr U/ml (mean 139.75 ± 11.89) in the leprosy group. The values are significantly higher in patients with leprosy. Serum histaminase varied between 14 to 292 Pr U/ml (mean 149.45 ± 14.05) and between 60 to 215 Pr U/ml (mean 111.56 ± 20.64) in lepromatous and tuberculoid patients respectively. The values in both these groups are significantly higher than the controls but there was no significant difference between the histaminase values of lepromatous and tuberculoid cases. Patients having lepromatous leprosy with *erythema nodosum* showed significantly higher histaminase levels in comparison to both tuberculoid and lepromatous leprosy without *erythema nodosum*. Again no difference was observed between the values for tuberculoid patients and lepromatous leprosy patients without *erythema nodosum*.

DISCUSSION

Oxidative deamination by histaminase is an important pathway of histamine catabolism. Histaminase occurs widely in different

organs of many species (2). Although plasma histaminase levels have been known to be enhanced in pregnancy for some time, its interrelationship with tissue injury has been realized only very recently. Raised histaminase has been reported in plasma and/or tissue in experimental thermal injury (6,7), anoxia and anaphylaxis (9,10), hepatic damage (4), myocardial infarction (8) and status asthmaticus (5). It has been speculated that enhanced histaminase levels are a part of the general response of tissue to injury (6).

In an earlier study it was observed that 80% of leprosy patients had exhibited negative P-K reaction, when tested with homologous reaginic sera, irrespective of type of leprosy (11). Similarly the present findings have shown a significantly raised serum histaminase level in leprosy patients irrespective of type of disease, as compared to healthy persons. There was no significant difference between the values in patients of lepromatous leprosy without *erythema nodosum* and tuberculoid cases. On the contrary, serum histaminase levels were significantly higher in patients with lepromatous leprosy with *erythema nodosum* than in those without *erythema nodosum* or in those suffering from tuberculoid leprosy. Histaminase levels are known to be enhanced during immediate type of hypersensitivity reactions

TABLE 1. Comparison of serum histaminase values in different leprosy groups.

Groups	No. individuals	Serum histaminase (Pr U/ml) mean \pm S.D.	Significance of difference between various means
A Normal	29	66.04 ± 9.02	Vs B; $P < 0.001$ (S)
B Leprosy	36	139.75 ± 11.89	Vs A; $P < 0.001$ (S)
C Lepromatous leprosy	27	149.45 ± 14.05	Vs A; $P < 0.001$ (S) Vs F; $0.2 > P > 0.1$ (NS)
D Lepromatous leprosy with <i>erythema nodosum</i>	14	188.50 ± 17.05	Vs E; $P < 0.001$ (S) Vs F; $P < 0.02$ (S)
E Lepromatous leprosy without <i>erythema nodosum</i>	13	106.77 ± 8.51	Vs D; $P < 0.001$ (S) Vs F; $P < 0.5$ (NS)
F Tuberculoid leprosy	9	111.56 ± 20.64	Vs A; $0.02 > P > 0.01$ (S) Vs C; $0.2 > P > 0.1$ (NS)

Vs = versus; S = significant; NS = not significant.

(9). The finding that histaminase levels were significantly raised in patients with lepromatous leprosy with *erythema nodosum* as compared to those without *erythema nodosum* supports the view that development of *erythema nodosum* is an immediate type of hypersensitivity (Arthus type) reaction (13).

Histaminase levels may have some diagnostic or prognostic significance in leprosy, which is difficult to comment on at present, but the matter is being studied.

SUMMARY

Serum histaminase was estimated in 29 healthy adults and in 36 leprosy patients including 27 lepromatous leprosy and 9 tuberculoid leprosy cases. Of the 27 lepromatous leprosy individuals 14 suffered from *erythema nodosum leprosum*. The serum histaminase levels were significantly raised in leprosy patients as compared with normal controls. But there was no significant difference in the enzyme values between patients having lepromatous leprosy without ENL and those with tuberculoid leprosy. However, the value of serum histaminase was found to be further elevated when the lepromatous leprosy patients developed ENL.

RESUMEN

Se determinó histaminasa sérica en 28 adultos sanos y en 36 pacientes con lepra, incluyendo 27 casos con lepra lepromatosa y 9 con lepra tuberculoide. De los 27 casos con lepra lepromatosa, 14 individuos tenían *erythema nodosum leprosum*. Los niveles de histaminasa sérica estaban significativamente aumentados en los pacientes con lepra en comparación con los controles normales. Pero no hubo diferencia significativa de los valores enzimáticos entre los pacientes que tenían lepra lepromatosa sin ENL y los que tenían lepra tuberculoide. Sin embargo, el valor de la histaminasa sérica estaba aún más aumentado cuando los pacientes con lepra lepromatosa desarrollaban ENL.

RÉSUMÉ

Chez 29 adultes normaux en bonne santé, et chez 36 malades atteints de lèpre, dont 27 lépromateux et 9 tuberculoïdes, on a procédé à l'estimation de l'histaminase du sérum. Sur les 27 malades souffrant de lèpre lépromateuse, 14 présentaient un érythème noueux lépreux. Les taux d'histaminase sérique étaient significativement augmentés chez les malades atteints de lèpre, comparés aux témoins normaux. Il n'a cependant pas été noté de différence significative dans les valeurs de cette enzyme entre les patients souffrant de lèpre lépromateuse sans érythème noueux lépreux, et ceux qui présentaient une lèpre tuberculoïde. Toutefois, on a observé une élévation encore plus accrue de l'histaminase sérique lorsque les malades lépromateux développaient un érythème noueux lépreux.

frant de lèpre lépromateuse sans érythème noueux lépreux, et ceux qui présentaient une lèpre tuberculoïde. Toutefois, on a observé une élévation encore plus accrue de l'histaminase sérique lorsque les malades lépromateux développaient un érythème noueux lépreux.

Acknowledgment. We extend our thanks to Dr. B. Sharma, Officer-In-Charge, Leprosy Home, Shahdara, Delhi, and Prof. A.B. Chaudhury, Director, School of Tropical Medicine, Calcutta, for their cooperation during the period of study; to Mr. B.S. Negi and S. Banerjee for their technical assistance; and Dr. P.V. Kurian, S.L.R. Sanatorium, Karigiri, India for supplying lepromin.

REFERENCES

1. ARSEN, P.N. and KEMP, A. Rapid spectrophotometric micromethod for determination of histaminase activity. *Nature* **204** (1964) 1195.
2. BUFFONI, F. Histaminase and related amine oxidases. *Pharmacol. Rev.* **18** (1966) 1163-1199.
3. CHATTERJEE, M.L. and DE, M.S. Histamine content of skin in tuberculoid (reaction) cases of leprosy; *Bull. Calcutta Sch. Trop. Med.* **15** (1967) 107-108.
4. GUHA, T.K., CHAKRAVARTI, H.S., BANERJEE, S., DAS, M.M. and LAHIRI, S.C. Histaminase level changes in liver damage. *Res. Commun. Chem. Pathol. Pharmacol.* (1972). In press.
5. GUHA, T.K., CHAKRAVARTI, H.S., BASU, A. and LAHIRI, S.C. Plasma histaminase levels in status asthmaticus. *Bull. Calcutta Sch. Trop. Med.* **18** (1970) 37-39.
6. LAHIRI, S.C., BASU, A. and BANERJEE, S. Changes in histaminase content following experimental thermal injury. *Biochem. Pharmacol.* **20** (1971) 3225-3230.
7. LAHIRI, S.C., BASU, A. and DAS, M.M. Tissue histaminase levels in experimental animals following thermal injury. *Aspects Allerg. Appl. Immunol. (India)* **3** (1970) 27-32.
8. LAHIRI, S.C., DE, T.K. and BANERJEE, J.C. Enhancement of plasma histaminase levels in myocardial infarction. *J. Indian Med. Assoc.* **50** (1968) 95-98.
9. LOGAN, G.B. Release of histamine destroying factor during anaphylactic shock in guinea pigs. *Proc. Soc. Exp. Biol. Med.* **107** (1961) 466-469.
10. LOGAN, G.B. Source and time of release of histamine destroying (histaminase) during anaphylactic shock in rats. *Proc. Soc. Exp. Biol. Med.* **111** (1962) 171-174.

11. MITTAL, M.M., SAHA, K., SHALI, P.L. and SHIVPURI, D.N. A study of Prausnitz-Küstner reaction in leprosy. *Clin. Exp. Immunol.* **8** (1971) 657-661.
12. RIDLEY, D.S. and JOPLING, W.H. Classification of leprosy according to immunity. *Internat. J. Leprosy* **34** (1966) 255-273.
13. TURK, J.L. and WATERS, M.F.R. Immunological basis for depression of cellular immunity and the delayed allergic responses in patients with lepromatous leprosy. *Lancet* **2** (1968) 436-438.