

LEPROSY AND HISTAMINE

By

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Histamine is considered to play an important role in the development of allergic reactions.

Sir Henry Dale was the first to become acquainted with the interesting effects that histamine can produce and the first who envisioned its role in various biological reactions.

Histamine is very widely distributed. The problem of relationship between histamine and the allergic conditions has been comprehensively dealt by Ccde C. F. (1944).

The role played by histamine as related to skin changes of various types e. g. urticaria, eczema, burns and other traumatic injuries has been the subject of study of many investigators; some based on direct determination of histamine content of the skin extracts or electrodyalytic fluids etc., while others are based on indirect study of histamine content in blood or examinations of gastric juice.

Immunology of leprosy is still an area of confusion. Until recently the immunology of leprosy was mainly concerned with use of lepromin and interpretation of its reactions. In the classical cases of tuberculoid leprosy the lepromin test is strongly positive while in the lepromatous type it is negative. A tneory was propounded that the positivity of the test indicates "allergy", and the negativity "anergy" (Rotberg, A. 1939; Davy, T. F. 1946).

Pathogenesis of acute and subacute exacerbated phases (familiarily designated as "reactions") of leprosy are still a chellange. The current opinion favours an immunological phenomenon as the basic mechanism of production of these reactive phases. Whether the reactive phases are a hypersensitivity phenomenon or whether they are basically an autoimmune phenomenon is not yet clear.

Histaminase activity becomes apparent in the serum at the end of the second month of pregnancy reaching its maximum between about 22nd and 26th week of gestation. During pre-eclamptic toxemia of pregnancy, the histaminase activity is considerably reduced.

Free histamine is present in the blood and urine. Variations in the histamine content of blood are known to occur in certain allergic states. There is some evidence that the amount of free histamine in urine is increased in certain allergic conditions (Adam H. M., Hunter R. B., and Kinnear T. W. G. 1950).

Histaminase controls the activity of histamine in the same sort of way that cholinesterase controls the action of acetylcholine. The histamine content of tissues represents a balance between production and destruction. A deficiency of histaminase and excess of histamine in the tissues might be expected to diminish the rate of disappearance of histamine in the body (Gaddum, J. H. 1951).

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*Received for publication on 20-11-1970.

Therefore, it was thought, it would be good to study simultaneously histaminase activity of the blood along with free histamine in the blood and in the urine.

Procedure of Estimations :— Methods used for estimation of histamine in blood and urine were as follows :

The method adopted here for estimation of histamine in the blood is more or less a combination of methods of McIntyre, F. Cr Roth, L. W. and Shaw J. L. (1947) and R. Lubscher (1950)

It consists of the following steps .

1) Extraction of histamine from the sample into n-butanol 2) Adsorption of histamine from n-butanol on cotton acid succinate. 3) Elution and colorimetric estimation of histamine in its purified form,

Method of estimation of free histamine in urine

A modification of Rosenthal and Tabor (1948) colorimetric method for estimation of histamine was studied and standardized. This method is similar to the above method of determination of blood histamine with only two variations.

- 1) Before extracting histamine into n-butanol, the urine is aerated in order to expel all the ammonia from it.
- 2) Conjugated histamine present in the urine is adsorbed together with free histamine on the cotton acid succinate column. The conjugated histamine is quantitatively removed from the column by washing it with 0.014M phosphate buffer. Procedure after these steps is the same as in the case of blood.

The H substance extracted from the blood by the method described was identified as histamine chemically.

It was then tested for its pharmacological action in the experimental animal (dog). Pharmacologically also it behaved like histamine. Its effects were counteracted by an antihistaminic drug (Anthisan).

Quantitative estimations by pharmacological and chemical methods tallied well.

Method of histaminase estimation: Volumetric method of Kapeller-Adler- (1951).

Results : The following table of range of variations of the histaminase activity and histamine content of blood and urine is based on the sample studied during the course of the work.

	Micrograms Histamine base per 100 cc of blood.	Histaminase activity in P. U. units.	Micrograms Histamine base in 24 hours. urine.
Normal	0.4-13.60	0.3-6.00	4.84-69.00
Pregnancy	0.9-11.55	1.8-10.50	3.80-89.60
Leprosy	0.5-17.50	0.5-10.00	6.80-78.20

In order to examine whether in leprosy cases any of the characteristics differ from that in the normal cases the means in the leprosy cases are tested with those in the normal cases.

No. of cases	Normal 61	Leprosy 52	Value of t	Degrees of freedom
Histamine base (Micro-gramme) per 100 cc of blood	4.8395	9.2887	4.499	111
Histaminase activity expressed in terms of potassiumpermanganate units.	2.0648	2.7754	2.072	111
Histamine base (Micro-grammes per 50 c. c. samples of freshly collected urine.)	0.6251	1.2787	2.439	111

The differences between histamine content of blood of normals and of the leprosy cases are highly significant at even one percent level of significance; so that on the basis of the data on hand it may be said that the quantity of histamine in blood in leprosy is higher than in normals. B. B. Gokhale (1958) has reported significant higher histamine levels in the bloods of cases of tuberculoid type of cases. This finding is interesting in view of the fact that lepromin test is strongly positive in cases of tuberculoid type of leprosy.

As for histaminase activity and the quantity of free histamine in fresh 50 c.c. samples of urine it may be stated that though the differences are significant at 5% level they are not so at 1% level and hence though there are indications that the histaminase activity of the blood and the histamine content of the urinary sample are higher in leprosy than in normals the evidence is not conclusive (More observations are necessary)

It would be interesting to study at this juncture the results of our study in pregnancy.

	Normal 61	Pregnancy 19	Value of t	Degree of freedom
Histamine (Micro-grammes) per 100 c. c. of blood.	4.8395	4.8967	0.078	83
Histaminase activity expressed in terms of potassiumpermanganate units.	2.0648	4.2250	4.139	83
Histamine base (Micro-grammes) per 50 c. c. samples of freshly collected urine.	0.6251	1.1133	3.477	83

The data shows that there are no significant differences between the normals and the pregnancy cases as far as the histamine levels in the blood are

concerned. But the histaminase activity in the normal pregnancies is higher and that the levels of free histamine in the given samples of urine are higher than in normals

Concluding remarks : A correlation between the symptoms and the blood histamine has been observed by Ake Nilzen (1947). The histamine content of blood, sinks when the symptoms increase and rises during the periods of improvement. Adam et. al (1950) has reported increased free histamine in urine in certain allergic conditions. Kirchev et. al. (1966) examined 50 cases of urticaria, and have reported increased histaminase activity in acute cases of urticaria, and in chronic forms during the phases of aggravation. In view of these findings and the results of the preliminary study reported, of a group of leprosy cases, suggest further study of larger number of cases along with a linear study of individual cases of leprosy of various types and in different clinical phases of the disease (such as exacerbations and quiescence) since a great variation was found in the individual cases.

ACKNOWLEDGEMENTS

The author is very thankful to the Indian Council of Medical Research who sponsored this study; the staff of the National Chemical Laboratory, Poona; the Department of Pharmacology, G. S. Medical College, Bombay; Colleagues at the Sassoon General Hospital, Poona and B. J. Medical College, Poona and M/s. S. K.-Gokhale, Dr. N. K. Bhide, Dr. V. M. Dandekar of Gokhale Institute of Politics and Economics Poona and R. Shivaraman of the National Chemical Laboratory, Poona.

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