

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

INVESTIGATION OF HYALURONIDASE ACTIVITY AS A METHOD OF EVALUATION OF ACTIVITY OF RHEUMATIC FEVER

E. I. Tanyukhina

Clinical Department (Head, Professor M. I. Khvilivitskaya) and Department
of Functional Methods of Investigation (Head, Docent I. I. Likhmitskaya),
Leningrad Research Institute of Assessment of Working Capacity and Resettlement
of the Disabled

(Presented by Active Member AMN SSSR V. M. Karasik)

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The use of investigation of the hyaluronidase activity of the urine to assess the state of the hyaluronidase-hyaluronic acid system was first suggested in 1954 [1].

Since hyaluronidase is one of the antigens of the β -hemolytic streptococcus, which plays an important part in the etiology of rheumatic fever, and because of the activation of the tissue hyaluronidase in the course of development of rheumatic fever [2], several writers [3, 4] have suggested that investigation of the hyaluronidase activity of the urine may be used to determine the stage of rheumatic fever.

However, during the study of patients with rheumatic fever no consideration was paid to the relationship, established by A. G. Ginetsinskii and co-workers, between the hyaluronidase activity of the urine and the diuresis.

We have attempted to assess the significance of this relationship in various stages of rheumatic fever.

EXPERIMENTAL METHOD

The hyaluronidase activity of the urine was determined by a viscosimetric method. Hyaluronic acid was obtained from umbilical cords by the method of McClean and Hale [5].

The hyaluronidase activity of the urine was expressed in conventional units, the unit being taken as the amount of hyaluronidase activity lowering the viscosity of a 0.2% solution of hyaluronic acid by 1%. The difference between the viscosity of a mixture consisting of hyaluronate in a buffer solution at pH 4.9 and urine at the beginning of the experiment and the viscosity of distilled water was taken as 100%. Bearing in mind that substances other than enzymes, capable of causing depolymerization of hyaluronic acid, are present in the urine each experiment was accompanied by a control investigation, for which the test urine was heated in a water bath for 30 min to inactivate the enzyme. Bearing in mind, too, that in healthy persons the hyaluronidase activity of the urine is strictly dependent on the value of the diuresis and falls after water loading along the course of a characteristic curve, the volume of the diuresis was expressed in milliliters per square meter body surface (deduced from the weight and height).

EXPERIMENTAL RESULTS

Determination of the hyaluronidase activity of the urine of healthy persons gave a curve showing the relationship between this activity and the diuresis. This largely coincided with the curve obtained by A. G. Ginetsinskii and co-workers (Fig. 1, a). Investigations were carried out on 10 healthy persons and 75 patients with a cardiac form of rheumatic fever (see table).

The curve in Fig. 1, b shows that the hyaluronidase activity of the urine in patients with rheumatic fever is much higher at high levels of diuresis than in healthy persons under the same conditions. Activity was found even at levels of diuresis at which none was present in the healthy subjects (see Fig. 1, a).

Study of the results obtained in the healthy persons and patients with rheumatic fever shows that the latter lose the power to modify the hyaluronidase activity of their urine in accordance with the diuresis. This feature is especially

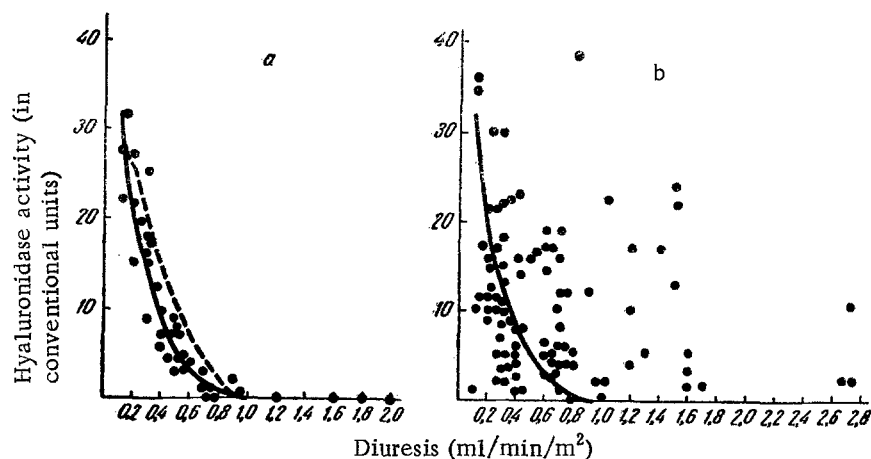


Fig. 1. Relationship between hyaluronidase activity of the urine and diuresis in (a) healthy persons and (b) patients with rheumatic fever. Curves plotted from mean data. The curve drawn in a broken line is that obtained by A. G. Ginetsinskii and co-workers, the continuous line is the curve plotted from our own results.

Distribution of Patients According to Age, Sex, and Clinical Diagnosis

Diagnosis	Males		Females		Total
	under 30 years	from 30 to 60 years	under 30 years	from 30 to 60 years	
Healthy	1	2	3	4	10
Active stage of rheumatic fever	9	3	7	9	28
Stage of quiescence	2	2	4	6	14
Stage of remission	3	7	3	20	33
Total	15	14	17	39	85

noticeable during examination of Fig. 1, b, in which the values of the hyaluronidase activity corresponding to various levels of diuresis in all the patients investigated are shown by points. It can be seen that the relationship between the hyaluronidase activity and the degree of diuresis is disturbed. This disturbance is small at low levels of diuresis but increases at the high levels. This is confirmed by plotting the individual curves for each patient. Two examples are given below.

T., aged 35 years, healthy. Diuresis 0.2 ml/min/m² - hyaluronidase activity of the urine 2.1 units; diuresis 2.4 ml/min/m² - hyaluronidase activity of the urine 2.1 units; diuresis 2.4 ml/min/m² - hyaluronidase activity of the urine 12.5 units.

The individual curves shown in Fig. 2 are straight lines joining two points characterizing the hyaluronidase activity of the urine at high and low levels of diuresis. In patients with rheumatic fever in the active stage there was no characteristic relationship between the hyaluronidase activity and the diuresis, but another relationship was found: at low levels of diuresis the hyaluronidase activity of the urine was low and it increased with an increase in the diuresis. In the patients with rheumatic fever in the stage of quiescence the values of the hyaluronidase activity of the urine were close to those found in the healthy persons. The results obtained in the patients with rheumatic fever in the stage of remission showed a remarkable variation: in 6 of the 12 curves a regular relationship was found between the hyaluronidase activity of the urine and the volume of the diuresis, while in the other 6 curves this relationship was absent. However, the curves obtained in the stage of remission showed some flattening out and they were at a lower level than the corresponding indices in the active stage. This demonstrates that the hyaluronidase activity of the urine is low in the stage of remission.

These findings demonstrate that when the hyaluronidase activity of the urine is used as an index of the stage of rheumatic fever, the investigation of the relationship between the hyaluronidase activity of the urine and the diuresis is of considerable interest. The abnormal character of this relationship characterizes the stage of rheumatic fever with the greatest accuracy.

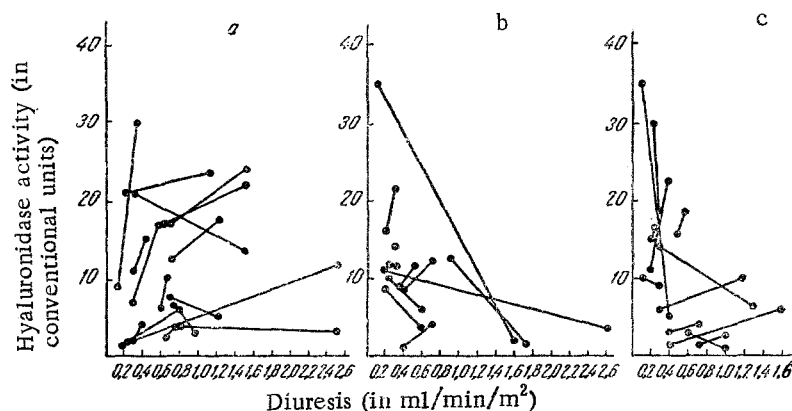


Fig. 2. Relationship between the hyaluronidase activity of the urine and the volume of the diuresis in patients with rheumatic fever (a) in an active stage, (b) in a stage of quiescence, and (c) in a stage of remission.

At the same time it is important to note that a relationship of the same character is present in persons with no clinical manifestations of renal pathology. This centers attention on the mechanism of this change in the relationship between the hyaluronidase activity of the urine and the diuresis in rheumatic fever and points to the need for further study of this problem in other human diseases.

SUMMARY

This work deals with a method of determining the hyaluronidase activity of the urine, suggested by A. G. Ginetsinskii and associates, for determination of the stage of rheumatic fever.

Ten healthy individuals and 75 rheumatic fever patients were examined (28 — in the active stage, 14 — in the stage of decline and 33 during remission). In the healthy individuals a curve was obtained which coincided with that presented by A. G. Ginetsinskii. In the patients with rheumatism hyaluronidase activity of the urine in considerable diuresis was greater than in the same conditions in the healthy persons. In the patients a active stage of rheumatism and to a lesser degree in the stage of decline an abnormal relationship of the hyaluronidase activity of the urine to diuresis was noted.

LITERATURE CITED

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.
