

PLASMA KININS AND THE JARISCH-HERXHEIMER REACTION

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Abstract. Plasma kinin formation by Hageman factor activation was studied in 12 patients with early syphilis before and after or during the Jarisch-Herxheimer reaction. No changes in amounts of kinins could be demonstrated. This does not exclude the possibility that small amounts of kinins may participate in the reaction. However, it seems unlikely that these mediators play a major role in the pathogenesis of the reaction.

The Jarisch-Herxheimer reaction (J-H reaction) has long been known to be a common occurrence in the treatment of syphilis. The reaction has generally been attributed to release of endotoxins or spirochaetae breakdown products following the initial administration of spirochaetocidal drugs. Although destruction of spirochaetae seems to be an essential factor, the basic mechanism of the reaction is not well understood. Immune mechanisms have been proposed to take place (3, 6, 8), but definite proof is lacking. The failure of antihistaminic agents to inhibit the J-H reaction suggests that release of histamine is not an essential factor in the production of the reaction (6).

The present study was undertaken to elucidate whether or not plasma kinins participate in the J-H reaction. Plasma kinins are vasoactive peptides which have been implicated in inflammatory processes (1, 2, 10). Large amounts of kinin-forming enzymes exist in inactive form in blood plasma (2). Theoretically the breakdown of large amounts of spirochaetae could activate the Hageman factor, which in turn could lead to activation of kinin-forming enzymes and produce kinins. Kinin formation by Hageman factor activation was studied in blood from patients with early syphilis. Samples were taken prior to, during, and after a J-H reaction.

MATERIAL AND METHODS

Ten patients with early syphilis who had a rise in temperature to 38°C or more following an initial injection of 600 000 units

of procain penicillin PAM were studied before and 24 hours after the injection. Two patients had blood samples drawn before and every third hour following their first injection of penicillin, five samples in all.

Blood was collected by siliconized needles in polypropylene tubes containing heparin in the proportion of 10 ml blood to 0.1 ml heparin, 1 000 units/ml. Plasma was separated in the same tubes removed with siliconized pipettes and frozen at -20°C until immediately before incubation. The plasma was incubated for 120 minutes at 20°C with Celite, EDTA and phosphate buffer, pH 6. Celite is a diatomaceous silica product which activates Hageman factor. The method of incubation has been described in detail elsewhere (5). The biological determination of plasma kinins formed was made by assay on the rat uterus against a standard sample of synthetic bradykinin.

RESULTS

The data summarized in Table I show that the J-H reaction did not reduce the amounts of kinins formed by Celite activation of Hageman factor 24 hours after penicillin administration. Table II demon-

Table I. *Formation of kinins by Hageman factor activation in blood from 10 patients with a Jarisch-Herxheimer reaction before and 24 hours after initial penicillin administration*

Pat. no.	Sex	Age	mug Kinins per ml Plasm	
			Before	After
1	♂	42	380	390
2	♂	27	375	375
3	♂	37	400	400
4	♂	21	370	375
5	♀	18	450	230
6	♀	21	575	555
7	♂	27	625	625
8	♂	22	340	240
9	♂	35	640	640
10	♀	22	370	370
Mean ± S.E.			453 ± 37	420 ± 39

Table II. Formation of kinins by Hageman factor activation in blood from 2 patients with a Jarisch-Herxheimer reaction before and every third hour during the first 12 hours after initial penicillin administration

Pat. no.	Sex	Age	Before	m μ g Kinins per ml plasma			
				3 h	6 h	9 h	12 h
11	♂	30	535	535	565	535	535
12	♂	28	470	485	485	480	510

strates that no alterations in kinin formation were to be found in the blood of the patients studied every third hour during the first 12 hours after initial administration of penicillin.

DISCUSSION

No changes in the amount of substrate for kinin formation could be demonstrated in our study. This does not exclude the possibility that small amounts of kinins may participate in the J-H reaction. However, we find it most unlikely that these mediators play a major part in the pathogenesis of the reaction. In hereditary angioneurotic edema where kinins are supposed to play an important role, there can be found a significant reduction in amounts of kinins which can be formed when studied after an attack (9).

During recent years various methods have been tried to diminish the J-H reaction (3, 4, 7, 8). The results, however, have been conflicting and difficult to evaluate. A better understanding of the pathogenesis of the reaction and the mediators involved

would certainly be beneficial. The present investigation was performed as an attempt to contribute to this understanding.

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Received March 22, 1974

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