

# Early Agonist-Induced Intracellular Acidification Is Increased in Platelets From Patients With Essential Hypertension

1. Clara Lechi<sup>1</sup>,
2. Patrizia Guzzo<sup>1</sup>,
3. Enrico Arosio<sup>1</sup>,
4. Francesca Paluani<sup>1</sup>,
5. Pietro Delva<sup>1</sup>,
6. Paolo Bellavite<sup>1</sup> and
7. Alessandro Lechi<sup>1,2</sup>

[±](#) Author Affiliations

1. <sup>1</sup>Istituti di Clinica Medica e di Chimica Clinica, University of Verona, Verona, Italy.

1. Address correspondence and reprint requests to Prof. Alessandro Lechi, Clinica Medica, Università di Verona, Policlinico di Borgo Roma, 37100 Verona, Italy.

## Abstract

Enhanced  $\text{Na}^+/\text{H}^+$  exchange has been reported to be increased in patients with essential hypertension. However, early variations of intracellular pH, although influenced by the antiport, are only partially dependent on the exchange. In this study, we measured the initial platelet pH response to agonists in a group of untreated subjects with essential hypertension (EH,  $n = 24$ ) and in a group of age- and sex-matched normotensive control subjects (CS,  $n = 24$ ). Intracellular pH was measured with the specific fluorescence indicator 2'7'-bis(carboxyethyl)-5,6-carboxyfluorescein. Measurements were performed on platelets in the presence or absence of extracellular calcium, in a carbonate-free medium. Intracellular calcium was measured by the Fura 2 method.

Mean pH values were slightly higher in the platelets of EH ( $7.469 \pm 0.017$  U) compared with CS ( $7.423 \pm 0.012$  U,  $P < .05$ ), although there was a substantial overlap. When stimulated with physiologic agonists ADP and thrombin and with the calcium ionophore ionomycin, a biphasic response consisting of early acidification followed by alkalinization was observed, the second phase not being detectable with ADP. The initial acidification was greater in EH, particularly with ADP (EH,  $-0.046 \pm 0.002$  U; CS,  $-0.036 \pm 0.002$  U,  $P < .001$ ) and with ionomycin (EH,  $-0.074 \pm 0.007$  U; CS,  $-0.051 \pm 0.005$  U,  $P < .05$ ). This acidification proved in some way calcium dependent, as it was reduced in the absence of extracellular calcium (EGTA) in both EH and CS. After incubation with amiloride a further decrease in intracellular pH, more marked in EH, was observed. Alkalinization induced by thrombin was increased in EH ( $P < .05$ ). These results demonstrate that early pH variations induced by agonists are significantly altered in platelets of EH, in which acidification was more marked. Because acidification seems to be partly calcium related, it may be associated with altered calcium handling; alternatively, it could depend on an as yet unidentified metabolic abnormality affecting the first phase of activation.