

## **Gender-differences in the relative contribution of NO and EDHF on the regulation of vasomotor tone of rabbit mesenteric arteries**

**Paola Del Basso Orsini**<sup>1</sup> Simona Calciano<sup>1</sup> Tiziana Coletta<sup>1</sup> Maria Zurlo<sup>1</sup>  
Fulvia Fabi<sup>1</sup>

<sup>1</sup> Istituto Superiore di Sanita, Department of Drug Research and Evaluation, Roma, Italy

The endothelium controls the vascular tone through synthesis and release of relaxing factors, namely nitric oxide (NO) and endothelium hyperpolarizing factor (EDHF). Since gender differences in the endothelium-dependent regulation of vascular smooth muscle tone have been observed, we hypothesized that a different contribution of NO and EDHF may account for the phenomenon. Therefore, endothelium-dependent relaxations induced by carbachol (CC) or vasoconstrictor sympathetic responses induced by transmural adrenergic nerve stimulation (TNS) were studied in ring segments of rabbit mesenteric arteries (RbMa) of both sex. In presence of the NOS inhibitor, L-NNA, the concentration-response curves to CC were significantly rightwardshifted in both sex in comparison to their own controls, but the relaxations of female were significantly reduced more than those of males. Accordingly, L-NNA shifted to the left frequency-contractile curves induced by TNS in both sex, but the vasoconstrictor responses of female vessels were higher than those of males. By contrast, the presence of the putative EDHF inhibitors, apamin plus charybdotoxin, significantly reduced the vasodilator responses to CC and potentiated the sympathetic contraction of male vessels, whereas it did not affect the vasoconstriction induced by TNS in female arteries. These data demonstrate that the relative contribution of NO and EDHF in the agonist stimulated vasodilatation and in the modulation of sympathetic vasoconstriction differs between males and females. Although NO appears to exhibit a primary role to modulate the vascular tone in both sex, it is functionally more important in females, whereas EDHF is a necessary contributor in males.