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Thimerosal induced changes of intracellular calcium in human endothelial cells

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Abstract — We have measured the effects of the -SH oxidizing agent thimerosal on the intracellular calcium concentration in single endothelial cells from human umbilical cord vein.

Application of 1 μM thimerosal after a 10 s prepulse of 10 μM evoked oscillations of intracellular calcium. Concentrations higher than 10 μM induced a few oscillations which were followed by a long lasting increase in intracellular calcium between 120 and 980 nM at 10 μM thimerosal, between 250 and 1290 nM at 100 μM.

The plateau level of the thimerosal induced increase in intracellular calcium depended on the extracellular calcium concentration, and was clearly decreased in calcium free solution. It was also reduced if the extracellular potassium concentration was increased to 140 mM. Nickel (5 mM) did not block the elevation of intracellular calcium. Thimerosal induced quenching of the Fura-2 fluorescence in Ca^{2+} free solutions containing 1 mM Mn^{2+}. These effects indicate that thimerosal opens a pathway for Ca^{2+} entry from the extracellular side.

The amount of calcium which could be released by histamine was drastically reduced after initiation of the thimerosal response. If refilling of Ca^{2+} stores was prevented by incubation of the cells in Ca^{2+} free solution, histamine still induced a transient, but not maintained, increase in $[Ca^{2+}]_i$. After application of thimerosal in Ca^{2+} free solutions to prevent refilling of the stores, a transient increase in $[Ca^{2+}]_i$ could still be recorded but the histamine response on $[Ca^{2+}]_i$ almost disappeared indicating a discharge of Ca^{2+} stores by thimerosal.

It is concluded that thimerosal induces long lasting elevations of the intracellular calcium concentration by emptying intracellular agonist sensitive Ca^{2+} pools and activating a transmembrane Ca^{2+} entry from the extracellular space.

Many physiological functions in non-excitable cells are modulated by changes in intracellular calcium ($[Ca^{2+}]_i$). Compounds which disturb intracellular Ca^{2+} homeostasis are often connected to oxidation of groups. It is well known that the oxidizing compound thimerosal induces long-lasting vasodilation. It inhibits the enzyme acyl-coenzyme A : lysolecithin-acyltransferase [1]. As a consequence,