CLINICAL IMPLICATIONS

Hypertension in Former Extremely Low Birth Weight Children (p 443)

Low birth weight and prematurity are fore-runners of hypertension in adulthood. Few studies reported on plasma renin activity in preterm or full-term born children. In prematurely born children with birth weight <1000 g (extremely low birth weight) and healthy controls, we tested the hypothesis whether renin might modulate the pathogenesis of hypertension associated with preterm birth. In cases compared with controls, systolic blood pressure was found to be 7.5 mm Hg higher, but plasma renin activity was found to be 0.54 ng/mL per hour lower. Plasma renin activity decreased with systolic blood pressure but was unrelated to sodium excretion. Extremely low birth weight predisposes young children to a low-renin volume-expanded sodium-sensitive type of hypertension. Extremely low birth weight children might therefore benefit from a life course reduction in salt intake and, if hypertensive, are probably more responsive to diuretics than to inhibitors of the renin–angiotensin system. The currently recommended first-line treatment in children with high blood pressure. Above all, our study highlights the importance of screening for hypertension in all prematurely born infants to avoid the complications associated with high blood pressure later in life. Finally, information on birth weight and on the perinatal history of patients might provide clinically relevant cues to physicians managing hypertension in adults.

Interferon Regulatory Factor 3 Modulates Atherosclerosis (p 510)

Atherosclerosis is a chronic inflammatory disease in which endothelial dysfunction plays an important role. A major feature of endothelial dysfunction is enhanced adhesion molecule expression, leading to adherence and transmigration of inflammatory cells, including monocytes and macrophages. In this study, we demonstrate that IRF3 (interferon regulatory factor 3) plays an important role in this inflammatory response. IRF3 was found to promote endothelial secretion of vascular cell adhesion molecule-1 and expression of intercellular adhesion molecule-1 by directly binding to its gene promoter. IRF3 was found to promote endothelial secretion of sFlt-1 and soluble endoglin. They decrease endothelial dysfunction. Furthermore, they found that the proinflammatory cytokine IL-1β increases the stability of atherosclerotic plaques. Because plaque stability is more significant than plaque size in predicting acute clinical events, IRF3 represents a promising target for the treatment of atherogenesis and for prevention of its untoward clinical outcomes.

Proton Pump Inhibitors to Treat Preeclampsia (p 457)

Preeclampsia is a major complication of pregnancy, responsible for 70,000 maternal deaths annually and far greater fetal losses. A treatment that can quench the disease process could be a major advance, saving the lives of many mothers and babies. Sadly, no treatment exists, except delivery. The preeclamptic placenta releases elevated levels of the antiangiogenic factors sFlt-1 (soluble fms-like tyrosine kinase-1) and soluble endoglin. They disseminate throughout the maternal circulation and cause widespread endothelial dysfunction and hypertension, which then leads to injury to multiple maternal organs. In this issue of Hypertension, Onda et al report preclinical studies showing proton pump inhibitors may have diverse biological effects that make them an unlikely candidate treatment for preeclampsia. Using many functional assays performed on primary human tissues, they show that proton pump inhibitors decrease placental release of sFlt-1 and soluble endoglin, and they decrease endothelial dysfunction. Furthermore, they found that the proton pump inhibitor omeprazole vasodilates blood vessels isolated from pregnant women and potently decreases blood pressure in a transgenic animal model of preeclampsia where sFlt-1 is overexpressed in the placenta. Proton pump inhibitors are widely prescribed to pregnant women to relieve gastric acid reflux. Large epidemiological studies suggest that proton pump inhibitors are safe to give to pregnant women. Therefore, the exciting clinical implication is that proton pump inhibitors may have the potential to treat or prevent preeclampsia. The team has translated these findings into a phase II placebo-controlled clinical trial to see whether omeprazole can be used to treat preterm preeclampsia.
Clinical Implications

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