1. **DIABETES MELLITUS IS ASSOCIATED WITH HYPERREACTIVITY OF SMOOTH MUSCLE CELLS DUE TO ALTERED SUBCELLULAR Ca²⁺ DISTRIBUTION IN THE HUMAN UTERINE ARTERY**

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Alterations of vascular smooth muscle function have been implicated in the development of vascular complications and circulatory dysfunction in diabetes mellitus. However, little is known on changes in smooth muscle contractility and the intracellular mechanisms contributing to such altered responsiveness in blood vessels from diabetic patients. Thus, smooth muscle reactivity to increased K⁺, norepinephrine (NE) and phenylephrine (PE) and acetylcholine-induced endothelium-dependent relaxation were assessed in uterine arteries from control individuals (CI) and diabetic patients (DM). Smooth muscle sensitivity to K⁺, NE and PE was enhanced by 1.4-, 2.3- and 9.7-fold and relaxation was reduced by 64% in vessels from DM. In addition, in freshly isolated smooth muscle cells from DM an increased perinuclear Ca²⁺ signaling to K⁺ (30 mmol/l: +73%; 30 mmol/l: +68%) and NE (300 nmol/l +86%; 10 μmol/l +67%) was found, which promotes smooth muscle contraction. In contrast, subplasmalemmal Ca²⁺ response, which favors smooth muscle relaxation due to activation of Ca²⁺-activated K⁺ channels, was reduced by 38% in DM, indicating a significant change in the subcellular Ca²⁺ distribution in vascular smooth muscle cells during diabetes. In contrast to the altered Ca²⁺ signaling found in freshly isolated cells from DM, in cultured smooth muscle cells isolated from CI and DM no further difference in the Ca²⁺ signaling to stimulation with either K⁺ or NE was found. Hence, production of superoxide anions (iO₂⁻) in intact and endothelium-denuded arteries from DM was increased by 150 and 136%, respectively. Incubation of freshly isolated smooth muscle cells from CI with the iO₂⁻ generating system xanthine oxidase/hypoxanthine mimicked the effect of DM on subcellular Ca²⁺ distribution in a SOD-sensitive manner. From these findings, we conclude that during diabetes mellitus, smooth muscle reactivity is increased due to changes in subcellular Ca²⁺ distribution upon cell activation. Increased iO₂⁻ production seems to play a crucial role in the alteration of smooth muscle function.

2. **THE PROBLEMS IN THE USE OF HERBAL AND NATURAL SUBSTANCES, WITH SPECIFIC EXAMPLE CONCERNING THE CARDIOVASCULAR SYSTEM**

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Cardiovascular medicine is a fast moving field. During the last few decades, advances in our understanding of the physiology, pathology and pharmacology of the cardiac and vascular systems have been both stunning and overwhelming. In the meanwhile, the use of drugs in the treatment of cardiovascular diseases has experienced exponential growth. The awareness of side effects of synthetic drugs has led to the exploration of the use of natural or traditional medicine. What is needed is to bring together modern medicine and natural or traditional medicine. This presentation attempts to provide an example of how natural medicine can play a role in a new development in cardiovascular science. PHF, parathyroid hypercytocalcic factor, is a newly discovered hormone closely related to low-renin salt-sensitive hypertension. Our recent studies discovered a natural substance preparation which acts as a natural PHF antagonist. However, the use of natural medicine is currently experiencing a creditability problem. This presentation will also describe solutions to the problematic issues in natural medicine.
This abstract summarizes a 40 year evolution of heart valve replacement surgery. In the late 1950s, the only surgery performed on a valve was a closed mitral valvotomy. The first successful valve replacements with the Starr-Edwards caged ball valve in 1960 were a milestone in the advancement of heart surgery. Operative mortality for the first mitral series decreased steadily from 50% in 1960 to near 0 within 5 years. Regression analysis showed that long-term survival was related to intrinsic patient preoperative characteristics. Other milestones in the advancement of heart surgery were the development of the aortic homograft, the Bjork-Shiley valve, the Hancock porcine valve, the St. Jude valve, pericardial and stentless valves. Porcine valves show a wide variation in structural failure among series, ranging from 55% to 90% and 50% to 80% at 10 years in the aortic and mitral positions, respectively. Increased patient age has an important effect on failure rates. Thromboembolism rates among series with a particular valve type vary greatly due to non valve-related factors. Valvular thrombosis is a relatively rare complication, and the majority of biological valve series have none, especially in the aortic position. Infection rates for most series are below 1% per year, for both positions and classes of valves. There has been significant progress in diminishing operative mortality and enhancing long-term survival over the past 4 decades. Late complication rates are approximately similar with all valve types. The future will require more durable tissue valves and safer anticoagulation for mechanical valves, and perhaps less invasive surgery.