Circulation

CARDIOLOGY NEWS

From the Literature

Tracy Hampton, PhD

Inhalation Therapy May Help Treat Heart Failure

Researchers have created biocompatible and biodegradable calcium phosphate nanoparticles (CaPs) composed of a material that closely resembles bone and teeth to be used as a potential delivery approach for the treatment of heart failure.

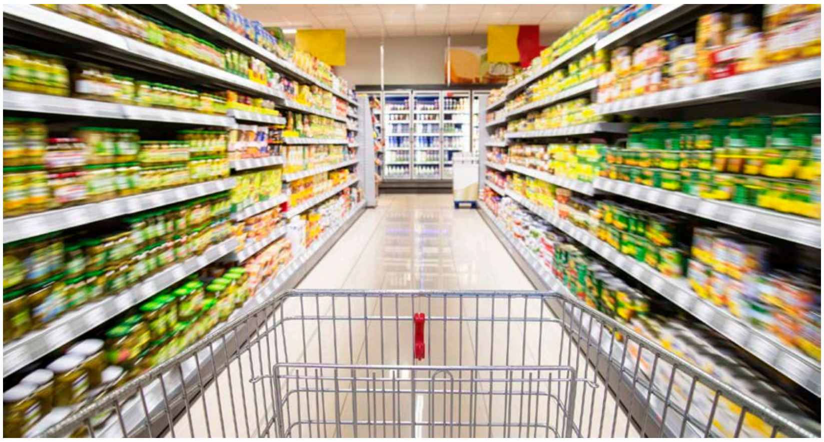
Inhalation has long been studied for the treatment of pulmonary diseases, but its use for targeting of the heart and management of cardiac failing conditions has not been explored. In a recent *Science Translational Medicine* study, inhalation of CaPs loaded with a therapeutic mimetic peptide previously demonstrated to improve myocardial contraction successfully restored cardiac function in rodent models of diabetic heart failure without any major adverse effects.

Investigators also showed that CaPs rapidly accumulated in the heart after inhalation in healthy pigs, demonstrating the efficiency of the CaP inhalation approach for intramyocardial delivery of compounds in a large animal.

"Results from our in vivo studies show that the CaP-based inhalation approach provides faster and more efficient heart targeting compared with traditional drug administration such as intravenous or oral. This might lead to the possibility for a drastic reduction of drug dose per administration," said senior author Daniele Catalucci, PhD, of the Humanitas Clinical and Research Center, and the National Research Council, in Italy. "An additional advantage in comparison with current systems is that the therapeutic drug, which is entrapped in CaPs, is protected from adverse systemic and gastric degradation. Side effects due to targeting of other organs might also be reduced."

Additional studies are needed to evaluate the long-term safety of nanoparticles and to determine how the CaPs used in these experiments cross the pulmonary barrier. Twelve academic and industrial partners (including Dr Catalucci's institution) are currently working together within the European Union–funded Cupido project to optimize biocompatible and biodegradable inhalable nanoparticles that can self-assemble and encapsulate novel and established drugs for the treatment of cardiovascular disease.

Miragoli M et al. Inhalation of peptide-loaded nanoparticles improves heart failure. *Sci Transl Med*. 2018;10:eaan6205.



Research in animals suggests that a high-salt diet causes changes in the immune system that can lead to deficits in cognitive function.

Research Provides Clues to How High-Salt Diet Affects the Brain

A high-salt diet in mice can cause changes in the immune system in the gut that then lead to deficits in cognitive function, according to a recent *Nature Neuroscience* study.

Within a few weeks, the high-salt diet led to dysfunction of the endothelial cells that line blood vessels, a reduction in cerebral blood flow, and cognitive impairments in several behavioral tests, but no changes in blood pressure. Investigators also noted increased numbers of TH17 white blood cells in the gut and increased levels of interleukin-17 (IL-17), the proinflammatory molecule these cells release.

Experiments revealed that this increase in IL-17 in the bloodstream caused the diet's negative effects on cerebrovascular function and behavior. Specifically, IL-17 suppressed brain endothelial cells' production of nitric oxide, a compound that is critical for vasodilation to allow sufficient blood to reach the brain and maintain neuronal health. Such loss of nitric oxide reduced the blood supply to the brain and caused neuronal dysfunction that led to impaired cognition.

In humans, IL-17 similarly affects cerebral endothelial cells, suggesting that a high-salt diet might also negatively impact brain health in humans, regardless of its effect on blood pressure.

The effects of the salty diet were reversible after the mice were returned to a normal diet or were treated with pharmacological interventions. "The good news is that, if the salt consumption is brought back to normal, the damaging effects on cognition subside, and cognitive function becomes normal again. Therefore, curbing salt intake may be effective in reversing the deleterious effects of dietary high salt," said senior author Costantino Iadecola, MD, of Weill Cornell Medicine.

Dr Iadecola noted that the findings may also be applicable to human diseases characterized by an increase in TH17 cells and IL-17. These include multiple sclerosis, psoriasis, rheumatoid arthritis, and other conditions. "These patients have increased risk of cardiovascular and cerebrovascular diseases, and our study suggests that the harmful effects of IL-17 on the brain's blood vessels could be the cause."

Faraco G et al. Dietary salt promotes neurovascular and cognitive dysfunction through a gut-initiated TH17 response. *Nat Neurosci*. 2018;21:240–249.

Implanted Devices Can Help Measure Heart Function

Researchers have devised a method to help clinicians accurately measure heart function in patients with cardiogenic shock supported by mechanical circulatory support devices, by tracking interactions between the failing heart and the support device to glean metrics of cardiac function.

Although there is increasing interest in the use of mechanical circulatory support in patients with cardiogenic shock, it is difficult for a clinician to determine how to optimally titrate and when to withdraw mechanical support.

In a *Science Translational Medicine* study, researchers investigated the potential correlation between the performance of implanted devices that improve circulation, such as the Impella CP from Abiomed, and heart function. The team evaluated changes in the current required to power the device and the aortic pressure measurement obtained from the device itself to estimate left ventricular end-diastolic pressure, an important metric of ventricular performance, without the need for any additional external measurements or calibration.

In benchtop circulatory loops and in porcine models, the team determined that the algorithm-derived left ventricular end-diastolic pressure estimate correlated well with directly measured values and was superior to estimates based on pulmonary capillary wedge pressure measurements, the current clinical method for estimating left ventricular end-diastolic pressure. The algorithm was then evaluated in a patient undergoing mechanical support with an Impella device, yielding similar results in comparison with pulmonary capillary wedge pressure.

"We believe that this work has been a significant step in demonstrating how support devices can also be leveraged to provide critical diagnostic information," said coauthor Steven Keller, MD, PhD, of the Massachusetts Institute of Technology, Brigham and Women's Hospital, and Harvard Medical School. "Our hope is that this and future methods can be integrated into mechanical circulatory support devices to enable clinicians to use this information as a means to guide decisions of mechanical support titration and weaning without additional interventional devices."

Chang BY et al. Mechanical circulatory support device-heart hysteretic interaction can predict left ventricular end diastolic pressure. *Sci Transl Med*. 2018;10:eaao2980.

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