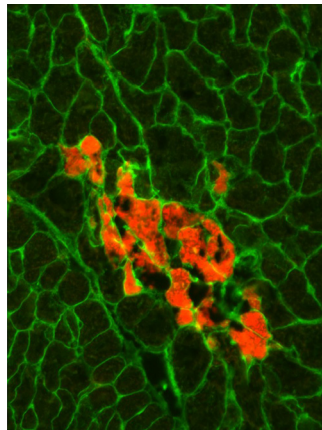


Macrophage Expansion in Chronic Heart Failure (p 853)

Macrophages accumulating in the heart after an infarction come from local and peripheral sources, report Sager et al.

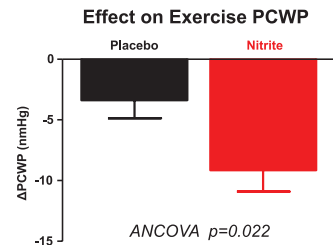
After a heart attack, myocardial remodeling results in altered structure and reduced function. These muscular changes are accompanied by inflammation, with the numbers of monocytes and macrophages in the heart increasing significantly. While these immune cells are necessary for wound healing, they can cause tissue damage if the inflammation is not resolved quickly. To learn more about the origins of the expanded monocyte and macrophage population in mouse hearts after infarction, Sager and colleagues performed fate mapping experiments. They found evidence for both proliferation of resident heart macrophages and recruitment of circulating monocytes—with the latter accounting for approximately one third of the expanded monocyte and macrophage population. To investigate whether reducing the numbers of recruited monocytes might lessen tissue damage, the team used nanoparticle delivery of silencing RNAs to suppress the expression of adhesion molecules (required for monocyte exit from the circulation) in the cardiac endothelium of the mice. They found that this procedure diminished remodeling and prevented the decline in left ventricle function. Together, the results indicate that minimizing monocyte infiltration after infarction could improve functional recovery.



Isoproterenol-Induced Myocyte Injury (p 865)

A recently described cardiac regeneration model may not be what it seems, suggest Wallner et al.

In recent years, cardiac stem cells (CSCs) have received considerable attention for their potential to promote the recovery of injured hearts. But while some reports indicate that CSC form myocytes, others suggest that there is minimal transdifferentiation of CSCs into adult cardiac myocytes. Georgina Ellison of Kings College London and colleagues have reported that, following a high-dose injection of isoproterenol, which kills ≈10% of cardiac myocytes in mice, CSCs can rapidly—within a couple of months—replace the dead cells. Given the utility of such a model for studying CSC-driven cardiac myocyte regeneration, Wallner and colleagues decided to validate these findings. They found that while injection of isoproterenol (at an equivalent dose to that used by Ellison) certainly damaged myocytes, it tended not to kill the cells. Moreover, by fate mapping experiments, Wallner and coworkers showed that the proportion of CSC-derived cells did not increase in the hearts of isoproterenol-treated animals, suggesting that the myocytes simply recovered from injury rather than being replaced. Based on these findings, the authors concluded that isoproterenol injection is not a reliable model for CSC-driven cardiac regeneration.



Inhaled Nitrite Improves Hemodynamics in HFpEF (p 880)

Patients suffering from heart failure with preserved ejection fraction may benefit from a new treatment strategy, say Borlaug et al.

Approximately half the patients suffering from heart failure (HF) do not show a reduction in the ejection fraction (EF) of the heart. Known as heart failure with preserved ejection fraction (HFpEF), the condition is characterized by shortness of breath, elevated cardiac filling pressure, and pulmonary hypertension. Because of its vasodilatory effects, injection of nitrite—which converts to NO in the body—has been investigated as a potential treatment for HFpEF. Encouragingly, the treatment has been shown to temporarily improve symptoms: reducing cardiac filling pressure and hypertension. However, frequent injections are undesirable as a long-term treatment regimen. Borlaug and colleagues, therefore, investigated whether administering nitrite via inhalation might offer a less invasive alternative. In a randomized, double-blind, placebo-controlled trial, 26 HFpEF patients were treated with either nebulized sodium nitrite or saline (placebo). The effects of nebulized sodium nitrite were similar to those observed with nitrite injection and led to a temporary reduction in ventricular filling pressures and pulmonary artery pressures, both at rest and during exercise. These promising preliminary results now set the stage for longer-term studies using regular sodium nitrite inhalation for amelioration of HFpEF symptoms.

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