Chronic constrictive pericarditis, a consequence myriad causes, is an inflammatory process that involves both the fibrous and serous pericardial layers. Postpericardiotomy syndrome occurs in 10% to 40% of patients and clinically behaves very similarly. The resultant fibrosis and calcification in both processes can influence diastolic filling and may reduce cardiac function. Although neoplasm is always on the differential diagnosis in pericardial disease, patients with constrictive pericarditis have a low likelihood of harboring an undiagnosed neoplasm. Is there or should there be a physiologic relationship between constrictive pericarditis and malignancy? Admittedly, our understanding of cell signaling in constrictive pericarditis is primitive. Taking our ignorance a bit further, some patients with subclinical constrictive pericarditis who have fibrosis, calcification, and remodeling do not require surgical management and are only treated medically. Others present with a more “malignant” phenotype and benefit from pericardiectiony. And yet another subset has post-pericardiotomy syndrome that is self-limited without any observable long-term effect. We wonder whether anyone could posit why that is.

In this issue of *The Journal of Thoracic and Cardiovascular Surgery*, Han and colleagues elegantly attempt to answer some of these questions. Relative to normal control cells, in cells from patients with pericarditis Han and colleagues discovered shortened telomere length, upregulation of inflammatory cytokine programs (greater chemotaxis, more adhesion, and increased proliferation), higher extracellular matrix collagen deposition, large flattened cell architecture, and positive immunostaining, along with a lower predilection for apoptosis. Han and colleagues hypothesized that senescent pericardial interstitial cells promote pericardial structural remodeling, exhibiting phenotypic and functional alterations and affecting their cellular milieu through paracrine effects. This is the first time that anyone has proclaimed even a thimble of understanding about cellular senescence, apoptosis, and autophagy as potential mechanisms in constrictive pericarditis. Although the question of who cares virtually asks itself, it is clinically important that a lower rate of neoplastic transformation could be due to apoptotic regulation and could be the attributable cause of homeostasis rendered by senescent pericardial cells.

What about any gain of function or gain of altered function by these cells? As mentioned before, only some patients with chronic constrictive pericardial disease need medical or surgical therapy, whereas others improve and are weaned from medical therapies completely. So why is this happening, and how may this observation become more clinically relevant? The increase in cellular proliferation and greater extracellular matrix deposition may be reparative. Cardiovascular tissues express G-protein–coupled relaxin receptors that are activated by circulating relaxin or regionally generated relaxin and mediate pleiotropic effects that are cardioprotective through diverse signaling pathways. These characteristics in senescence could be clinically beneficial, because pluripotent cells could be induced to differentiate into nascent pericardial cells and reverse fibrosis through regenerative (antifibrotic, antiapoptotic) mechanisms. This area of work could enlighten and inform the clinical problem of constrictive pericarditis.

A criticism of this study is that whole pericardial tissue was used in experiments. Although it would be easy to...
be dismissive, it would also be naive. The inability to differentiate the cellular contributions of fibrous from visceral pericardia and pericardial from lymphatic fluid is an area of future study. The study presented here by Han and colleagues\(^3\) is an important initial step in understanding the signaling of pericardial cells. Learning more about their contributions to remodeling and expression of immunogenic properties on local environments will broaden the scope of this early work and lay the foundation for us to understand the true value of senescent cells. We challenge the readership to read this article enthusiastically as we learn more about the mechanistic pathways of constrictive pericarditis and to ride this carousel from apoptosis to remodeling, and from malignancy to regeneration.

References