Gateways, gangways, getaways and the one-trick dog misjudged

Karl T. Weber

Tuesday, September 18, 1990, and the streets of Chile's capital were filled with proud acclamations that proclaimed their day of independence from Spain in 1810. Santiago was known for its ethnic diversity as reflected in today's celebrants that included Araucanian Indians, mestizos and those of European descent, and its shops and factories which bore such names as Haddad, Berovich, Kupfer, Luchetti and Mackenzie. The city's major thoroughfare, Alameda Bernardo O'Higgins, paid tribute to the country's first Director Supreme. Chile was likewise justifiably proud of its economic vitality, a claim other Latin American countries would have difficulty rivaling.

A well-earned vacation was awaiting Dr. Nicole Hernandez-Chamorro, third year resident in internal medicine at the distinguished University Hospital in Santiago. At her apartment that night, fellow residents gathered to toast her imminent departure with pisco sours and chicha, machas and chores, and a sharing in triumphs and sorrows associated with patient care. They wondered whether Nicole's getaway to leisure would take her west to Vina del Mar or north to La Serena. Early next morning, she would climb the gangway to her getaway. By early afternoon, the Pacific's alluring waves provided needed solitude. She now could reflect on several challenging patients. Mr. S., a 57-year-old restaurateur with documented, uneventful myocardial infarction (MI) 8 months earlier, had now been hospitalized with advanced cardiac failure. Nicole had learned that 40% loss of myocardium could account for his low output state. But when did Mr. S. lose all these cardiac myocytes? Not with his known MI. Were there repeated, albeit silent infarcts? If not, what other factors could account for the progressive nature of his failure? Was it true that we are born with a fixed number of terminally differentiated cardiac myocytes — parenchyma so specialized as to be a one-trick dog? In the fetal heart, myocytes divide. The fetal phenotype was needed here. Could this puzzle be unlocked or would this prove deleterious? This reminded her of Mr. R., a 33-year-old newspaper reporter who presented to her clinic with exertional dyspnea and near-syncope. On examination, no evidence of structural heart disease or pulmonary hypertension was found. ECG showed left bundle branch block; chest X-ray, enlargement of the cardiac silhouette and mediastinum. A localized thickening of the interventricular septum of uncertain etiology, with disordered wall motion and pericardial effusion, was seen on echocardiography. Because of his widened mediastinum and effusion, a malignancy was suspected. Mr. R. died suddenly days later. At autopsy, rhabdomyosarcoma with metastatic spread to thoracic lymph nodes was found. Nicole noted that this implicated both striated muscle and embryonic connective tissue cells. Had myocytes stimulated sarcomatous growth or vice versa? Relative to other organs, malignancy was rare in the heart. Did this relate to the inability of adult myocytes to divide? She longed to discuss these issues with her Professor. In the meantime, she would ponder them while basking in the sun. Perhaps the respite and a good novel would clear her thoughts.

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The scar of MI accounts for 30% of total fibrous tissue while 70% is related to replacement and interstitial fibrosis that appear remote to the MI and involve the right and left ventricles.

Short-term biochemical studies previously suggested that myocytes were unable to proliferate (or divide) and the 20 million or so myocytes present at birth were all that was available. Recent morphologic evidence, obtained in hearts with long-standing hypertrophy of diverse cause, indicates that myocyte proliferation does occur. Experimental studies would suggest that gene therapy may unlock the puzzle and promote myocyte division. Whether such an approach would pose the potential for malignant growth is presently unknown.