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Commentary: Round and round the mesenchymal stromal cells go; where they stop, we hope to know

Gregory S. Matte, CCP, LP, FPP,[a] and
James A. DiNardo, MD, FAAP[b,c]

Gregory S. Matte, CCP, LP, FPP

CENTRAL MESSAGE

Successful administration of mesenchymal stromal cells (MSCs) into pediatric cardiopulmonary bypass circuits requires careful analysis of the circuit components' effects on MSC adhesion and function.

It is well documented that mesenchymal stromal cells (MSCs) possess immunomodulatory properties that create a microenvironment that may enable damaged tissues, including neurons, to regenerate in the face of significant inflammation.[1] When MSCs are exposed to an inflammatory environment, they coordinate local and systemic innate and adaptive immune responses through the release of immunosuppressive molecules, growth factors, exosomes, chemokines, complement components, and various metabolites.[1] It is entirely reasonable to conclude that MSCs could mitigate the organ damage induced by the inflammatory response associated with cardiopulmonary bypass (CPB). This hypothesis would be of particular interest in neonates and infants, in whom the prime and surface area of the CPB circuit is necessarily large as compared with the patient's own blood volume.

In this issue of *JTCVS Open*, Maeda and colleagues[2] take the first thoughtful step in determining whether the introduction of MSCs into a CPB circuit is technically feasible by using an ex vivo mock pediatric CPB circuit. The consequences of injection of MSCs into an isolated arterial line filter were evaluated as well. The intent of the investigation was to ascertain whether the cells impact oxygenator performance and whether their viability is preserved. These are exceedingly important questions to answer, and the proof-of-concept here is exciting.

At this point, however, the more difficult work begins. Hollow fiber membrane oxygenators and CPB circuits typically are thought to have similar construction and performance characteristics across manufacturers and even patient sizes. This simply is not true. The term "oxygenator" is often used to refer to the microporous membrane as well as the cardiotomy venous reservoir inclusive of its venous and cardiotomy filters, the heat exchanger, and even the integrated arterial line filter.[3] In addition, the vast majority of the CPB circuit components used in the United States are coated with the manufacturers' unique proprietary surface-modifying agent, ostensibly to limit blood activation and platelet adhesion within the hollow fiber membrane and in some cases the heat exchanger.[3-5] The adhesion of MSCs to these various components will likely vary, and adhesion to certain surfaces could impede MSC function. Nowhere is this more apparent than in the report of injection of MSCs into an ex vivo extracorporeal membrane oxygenation circuit, leading to alarming decrease in oxygenator performance.[6] This was likely due to the presence of the surface-modifying agent polymethylpentene.

In addition, custom tubing packs for CPB are not standardized. Each manufacturer uses proprietary CPB circuit coating or uses no coating at all. Consequently, CPB circuit components must be considered both individually and collectively for a particular case.[3,4]

From the [a]Department of Cardiac Surgery and [b]Division of Cardiac Anesthesia, Department of Anesthesiology, Boston Children's Hospital; and [c]Harvard Medical School, Boston, Mass.

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Address for reprints: James A. DiNardo, MD, FAAP, Department of Anesthesiology, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115 (E-mail: james.dinardo@childrens.harvard.edu).

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The current report serves as proof of concept for the safe, effective delivery of MSCs through a CPB circuit consisting specifically of a roller pump, a pediatric membrane oxygenator with integral arterial filter with a pore size of 32 μm (CAPIOX FX05; Terumo Corp, Ann Arbor, Mich), and X-coated tubing (Terumo Corp). We applaud the authors' efforts and look forward to the authors' next step in reporting on the possible neuroprotective effects of MSC delivery in pediatric cardiac surgery patients.

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