An unresolved and still open issue in the recent AHA scientific statement on Fontan circulation

Short title: a neglected issue

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We really appreciated the masterful, comprehensive review released by the AHA for the 50th anniversary of the surgical intervention introduced by Fontan **[1].** Though dealing with nearly all elements related with this so particular setting, at least an important point seems not to be enough highlighted, namely the potential risk of infective endocarditis (IE) and the indication for antibiotic prophylaxis (AP).

Since 2007, the AHA Guidelines on IE suggested that AP is reasonable for the subset of "high risk" population **[2]** such as patients with complex congenital heart disease, namely:

> *-unrepaired cyanotic defects, including palliative shunts and conduits*
> *-completely repaired defects with prosthetic material or device, whether placed by surgery or catheter intervention (during the first 6 months after the procedure)*
> *- repaired defects with residual shunts at the site or adjacent to the site of a prosthetic patch or prosthetic device*

In this respect, the majority of Fontan patients seem to belong to the "high risk" category, as they have a cyanotic complex congenital heart disease and because of the presence of homograft valved conduit in some "classic" Fontan procedures (nowadays abandoned for early calcification and pathways obstruction), use of prosthetic material for the intra-atrial tunnel or extracardiac conduit, presence of residual shunt in case of fenestrated total cavo-pulmonary connection and use of devices to close the fenestrated Fontan counduits, coils to embolize veno-venous collaterals, stents for stenotic pulmonary branches. Finally, we should consider -in a philosophical way- that this procedure is palliative and not a definitive repair for anatomical or functional univentricular heart.

Furthermore, the 2015 AHA Update on IE in childhood outlined that "the disproportionately large focus on AP" should be replaced by "oral hygiene and prevention of oral disease", thus implicitly accepting the paradigm introduced in 2007 for adults. No specific mention of Fontan patients was made at all **[3].**

Such an important and comprehensive review should answer a still open question:
Is Fontan population likely to develop IE? Is AP needed to prevent IE in this setting?

There is no doubt that IE occurrence in Fontan patients is extremely rare, with very few anecdotal literature reports, thus confirming our personal experience. It implies two things markedly contrasting each other: 1) AP is always efficient in the Fontan setting,

which to put it bluntly is unlikely *or* 2) Fontan patients are not at “high risk” for IE. Regarding the latter, in the so called “IE triangle”, a new approach capable of explaining the complex interplay leading from an uncomplicated bacteremia to IE, the apex of the triangle (favourable anatomical substrate) should include also a turbulent blood flow to make bacterial adhesion easier **[4].** Conversely, in the Fontan circuit the hematic flow is very slow, owing to the lack of a “pumping” sub-pulmonary ventricle. The post-capillary energy of systemic circulation drives the flow through pulmonary capillaries without any turbulence. It may explain why Fontan individuals are so resistant to IE.

Overall, we are still wondering whether Fontan patients should undergo AP to prevent IE during dental procedures.

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Response to letter from Bassareo, Calcaterra and Gargiuolo: "An unresolved and still open issue in the recent AHA scientific statement on Fontan circulation.

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Letter Response:

Although intended to be as comprehensive as possible, we acknowledge the gap in our recent AHA scientific statement on Fontan circulation (1), as regards infective endocarditis (IE) prophylaxis, as raised by Bassareo et al. There is little published information on the risk of IE in patients living with a Fontan circulation. Two recently published series are potentially informative. Among adults with congenital heart disease (CHD) who have developed sub-acute bacterial endocarditis (79 cases in 85,000 patient years), no cases were reported in Fontan patients (2) and in adults with Fontan circulation followed for over 30,000 patient years, no cases of IE were reported (3).

IE in the patient with a Fontan circulation appears to be a very unusual and rare event. Nevertheless, the current AHA recommendations concerning SBE prophylaxis identify individuals at high-risk with concepts that may apply (4,5). The following patient groups with CHD are associated with the highest risk of adverse outcome from endocarditis and thus prophylaxis is reasonable: 1) unrepaired cyanotic CHD including palliative shunts and conduits, 2) completely repaired CHD with prosthetic material or device, placed by surgery or catheter, during first 6 months after procedure, or 3) repaired CHD with residual defects at the site of a prosthetic patch or prosthetic device (which inhibits endothelialization).

One could readily see how an individual with a Fontan circulation might fall into one or more of these categories, yet we acknowledge the challenge of a perfect fit into this construct. A number of valid questions can be raised. For example, are those with a Fontan circulation and mild cyanosis “repaired” or “un-repaired”? The extra-cardiac conduit and lateral tunnel-type Fontan surgeries include prosthetic material, but these exist within a venous, low flow state. Is there increased risk of bacterial adhesion in such conditions? Is a fenestration a “residual defect” and does it increase risk?

For the moment decisions on IE prophylaxis may need to be left to the judgment of healthcare providers as applied to individual patients within the context of the current AHA guidelines. As with many aspects of care and management for the patient with Fontan circulation, gaps in knowledge exist and and the ideal strategies to optimize long-term health and wellness are still emerging. The role of IE prohphylaxis will require

further investigation before definitive evidence based recommendations specific to this population can be made.

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