The difference between ballistocardiography and stem cells

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The next five years we will be swamped with stem cell papers, presentations, working groups and task forces. Maybe there is already a society for stem cells and cardiovascular therapy. If there is something potentially interesting on the horizon, we all start running instead of thinking.¹ There are numerous stem cell variants, sources and ways to apply them. There are also many diseases that need a better and more aetiological treatment than just pharmacology. Clearly, the stem cell field and the expectations provide all the ingredients for a hype. So let us focus on the horizon, forget the obstacles and enjoy the hype for as long as it lasts.²⁻⁸

One of the key issues with respect to the stem cell confusion is the terminology. Therefore, the work by Qian et al. is important as they try to provide some insight into the various kinds of endothelial progenitor cells (EPCs).^{9,10} Although the classification as presented is useful, it seems almost impossible to comprehend that one cell type, the EPC, has so variable and counterbalancing functions. They distinguish EPCs from bone marrow, early circulating EPCs and late circulating EPCs. Other groups proposed a classification into type 1 and type 2 based on behaviour in cell culture. The unifying concept is that the early EPC has an important role in growth factor production and the late EPC contributes to vessel repair and outgrowth.^{2,11} Especially the protein expression pattern of bone marrow EPCs is completely different from both circulating cell types. The authors seek the explanation in the niche story. The cells surrounding the EPC determine the phenotype and function of the EPC. It is a popular concept based more on lack of knowledge than on actual proof of the function of the niche. Again there are important

differences between a niche in the heart compared with a niche in the bone marrow. Our work on cardiomyocyte progenitor cells proved the opposite, showing there are different progenitor cells in the heart compared with bone marrow.^{7,8} Whether the niche is crucial to keep the cells undifferentiated or decide fate in pathological circumstances is still unclear.

In part 2 the authors provide more insight into the role of various cytokines and chemokines on stem cell behaviour and vessel formation.¹⁰ The key factors are briefly discussed and in addition various drugs and proteins are presented that could be of benefit for EPC integration and neovascularisation, including statins, epo, ACE inhibitors and angiotensin II type receptor blockers. An interesting small peptide is the Ang-(1-7), a cleavage product of angiotensin II, with counterbalancing effects to angiotensin II. Ang-(1-7) is proposed to stimulate proliferation and differentiation of bone marrow EPC. In addition, oestrogens are considered beneficial for EPC function. Oestrogens have various beneficial effects on heart and vessels, including direct NO release and blocking hypertrophy.^{12,13} Striking is the lack of information with respect to EPC behaviour and the role of ischaemia in heart failure in both articles, in sharp contrast to the title. This does not make the articles less interesting. The general information provided is potentially of more interest to the readership.

Ballistocardiography was a hype 40 years ago.¹⁴ The therapeutic potential was considered relevant for heart failure. By moving the bed at the right moment, the cardiac output of a patient could be increased. Moving the bed, however, is nauseating for the patient. Therefore, the concept of a cardiac rhythm related shaking bed had to be abandoned. Isolating, culturing and reinjecting cells into a patient who is continuously circulating stem and progenitor cells seems to be irrational. Yet we are all doing it, or thinking about it.¹⁵ If growth factors are crucial, we need to find the correct growth factor concoction for injection. The main difference between stem cell injections and ballistocardiography is that the position of the bed is fixed. The chances of resolving cardiac failure with

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EPC therapy are small. Therefore, the attention by Qian et al. to pharmacological activation and priming of EPCs is the way to go. At the end of the day, we will have to find a way to improve the endogenous regenerative capacity of the cardiovascular system. Ballistocardiography is still alive for diagnostic applications, so the subject of stem cells is probably here to stay as well, maybe for diagnostic purposes. ■

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