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EDITORIAL POINT OF VIEW

How Can We Cheat Arterial Atherosclerosis?

Mircea CINTEZA[a,b]

[a] Department of Cardiology, Emergency University Hospital, Bucharest, Romania
[b] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

In our days, arterial atherosclerosis which leads to atherothrombosis is the principal cause of death in many, if not in most countries. To fight against we have two categories of interventions: prevention and direct therapies. The direct therapies of today include some drugs, from which statins are the most important, interventional cardiology with stents and bypass surgery.

To analyse other therapies we have first to put some appropriate questions:

- Why internal mammary artery is atherosclerosis free?
- Why don't we have success in angiogenesis?
- Why are we not capable to construct functional artificial arteries of medium and small size?

Let us begin with the first question. To continue, we have to put new "sub-questions": Why medium size arteries are differently affected by atherosclerosis (ATS)? And some observations have to be added:

- Leg arteries make ATS often
  - Because of gravity ! – it is said
- And forearm do not
  - Because of the lack of gravity – it is said again
- But what about head arteries who are so atherosclerotic despite lack of gravity ?
- And why radial artery or mesenteric arteries are not as good as grafts like the mammary on al long term?

Let us try to find some answers from the internal mammary artery structure (1,2). Histologically, compared with other arteries, the mammary artery has:

- Fewer fenestrations of the endothelium
- Lower intercellular permeability
- Greater antithrombotic molecules
- Greater NO production

Is this relevant for the clinician? Maybe. But most of all: it may have therapeutic consequences. For the moment everything is played at basic science: "Arterial territory-specific phosphorylated retinoblastoma protein species and CDK2 promote differences in the vascular smooth muscle cell response to mitogens" say Lange and coll (3). And Hiesinger and coll add: ... (these are) ... "factors and mechanisms that

Address for correspondence:
Mircea Cinteza, Department of Cardiology, Emergency University Hospital, 169th Independentei Avenue, 5th District, Bucharest, Romania.
E-mail: mirceacinteza@gmail.com

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convert SMCs to a phenotype that promotes plaque stabilization versus plaque destabilization" and are "...new targets to potentially manipulate the phenotypic state of arterial SMCs for therapeutic purposes" (4). We shall live and see such examples of molecular manipulation coming to a therapeutic level.

Let us continue with the second question: Why did we not succeed yet to use neovascularisation in severe cases of ischemia – be it coronary or not – where neither angioplasty nor bypass surgery cannot intervene beacause of the precariousness of the native vessels? And not only: neo-vessels could add flow in earlier stages of ischemia, not waiting for no-solution cases (but transplant, when appliable).

There can be three main types of neo-vessel development:

- ANGIOGENESIS – formation of new capillaries
- ARTERIOGENESIS – development of the existing but nonfunctional collateral vessels
- VASCULOGENESIS - new vessel growth derived from progenitor/stem cells

The first two could be developed from the natural existing, but nonfunctional vessels in a person without earlier chronic ischemia (5). The third could be promoted through bio-engineering methods, which seem to develop towards a clinical level (6). Use of inflammation as a tool to promote vasculogenesis is promising (6,7). However, we have not to forget that vasculogenesis could also be dangerous, leading to neoformation tissues.

The third question – why are we not capable to construct artificial vessels of medium or small size (like artificial coronaries) is also in hard work for biological engineers. For the moment, simple Dacron or other current material used successfully for aorta and large arteries produces clots when having smaller diameters. The closest hope today seems to be from the stent grafts (8). Stent grafts do no permit new tissue development and restenosis inside. But at their proximity the restenosis is aggressive. They have other advantages and disadvantages (8). But the most promising perspective with stent grafts is that, before other artificial vessels, they will be „seeded" with endothelial cells to make a very friendly surface of an artificial vessel.

In one sentence – the three answers to the questions put before are already today in the hands of engineers and basic science researchers. We wait with impatience that these therapeutic tools will be transferred in the hands of clinicians.

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