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From: Prof.Dr.Dr.Werner Mohl

To: 'Prof. Stans Murad'

Sent: Sunday, March 13, 2011 7:16 AM

Subject: WG: Mechanical control of tissue morphogenesis, regeneration and wound healing

Dear Professor!

I really liked your interesting review on retrograde delivery of stem cells and the historic edition on coronary sinus interventions. If I may I would like to include your email into the news section of our Homepage. I wonder however why another important parameter is overlooked. There is strong evidence that epigenetics and not only molecules or cells are heavily involved in regeneration of degenerative structural disease. For instance we work on a special form to treat myocardial ischemia and setting regenerative impulses using mechanotransduction of venous endothelium. PICSO is a clinically feasible form activating coronary venous endothelium and has a lot in common with the present state of the art of stem cell research. Our focus is more the mechanical force of flowing blood on venous endothelium as well as pulsatile pressure on veins. There is evidence that PICSO by upregulating hemoxygenase has also anti-atherosclerotic potential and we found to the first time also significant long term effects on statistically significant reduction of re-infarction and major adverse cardiac events. Cardiac resident stem cells might also be activated and seem to potentiate positive effects observed.

There seems to be a conservation of regenerative mechanisms normally seen during development. Although our knowledge on the whole perspective is still quite limited, there is a easy available salvage therapy on the horizon. Stem cell effects without stem cell transplantation can be achieved by a simple interventional catheter method without severe ethical restrictions or biohazard normally seen in reprogramming to achieve pluripotency. We think that this opens up a new horizon on potential methods based on our hypothesis "embryonic recall"

I am located in the University of Vienna as cardiac surgeon and if you need more information please let me know. I would be also very interested to hear comments on our hypothesis "embryonic recall".

I enclose some of the recent literature on this topic published by our group. Since you are one of the early pioneers in the field I am very pleased to discuss this important issue with you, since it will be possible that it may set an impulse for a paradigm change in cardiac regeneration. If there would be a chance to visit you or give a presentation in your postgraduate school I would consider to come to your institution as visiting professor!

Best regards from Vienna

ao. Univ. Prof. DDr. Werner Mohl

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Von: Prof. Stans Murad [mailto:profstans@uol.com.br]

Gesendet: Sonntag, 13. März 2011 02:05

An: Prof.Dr.Dr.Werner Mohl

Betreff: Fw: your work on retrograde coronary sinus therapies;

Dear colleague,

I would like to thank you for the kindly words of your e-mail.

I am sending the video of Prof.Dr.Jan J. Piek with the excellent demonstration of the PICSO procedure to experts in hemodynamic of Rio de Janeiro and I will show it in the 1st day of the postgraduate course of cardiology.

.I start the coronary arteriography in Brasil using both vena cava occlusion with an special double balloon catheter and simultaneous injection of contrast material in the aorta (Murad-Netto et al Arch Inst Nac Card Mexico 1963;33(6):753-757). Actually, I am 80 years old and I change the cath Lab work to be director of a Posgraduate Medical School that have about 70 doctors in the cardiology course from all over Brasil, Latin America Countries and Angola

Since 1961-62 in the Gensini Service (USA) we have been performing catheterization of the coronary sinus for diagnostic and therapeutic purposes.:

On April 28,1962 we presented before the 22nd Chapter of the ACCP "The Motion picture studies of the coronary venous circulation," a film in which we showed clearly that with the experimental occlusion of the LAD and injection of cardiogreen or contrast medium into the coronary sinus in dogs, particularly with the coronary sinus occluded with a catheter balloon after the emerging posterior descending vein, that the predominant distribution of the flow was directed to the ischemic area of the myocardium (Rev Bras Cardiol 2010;23(5):286-291).

In 1963 The hemodynamics studies of this investigation was published as Coronary Venous Occluded Pressure Arch of Surgery 1963;86:72-80.

In 1972, I presented my doctorate dissertation in cardiology with the theme "Hipoxia miocardica com cinecoronariografia normal" measuring the lactic acid in the aorta and in the coronary sinus before and after increasing the heart rate with a pacemaker catheter at the right atrium in 15 patients. One of them, a young athlete, had anaerobiosis at rest which was increased after increasing the heart rate to 150 b/min with a pacemaker resulting in ventricular fibrillation immediately cardioverted. This man had an EKG with anterior ischemia from V1-V6 and ST supra and a normal cinecoronary arteriogram. The ventricular fibrillation occurred during the period of increased heart rate and not after the injection of drugs.

In 1973 at the "II Simposio Nacional sobre Aterosclerose Coronaria" in S.Paulo, we presented the paper "Importancia do cateterismo do seio coronario no diagnostico da insuficiencia coronária."(II Simposio Nacional sobre atherosclerose coronária.São Paulo 1973. Editor J.Eduardo Sousa Pg 73-7) At that time we had studied 20 patients with necrosis and/or myocardial ischemia who underwent cinecoronary arteriography and retrograde coronary venography if the retrograde coronary injection could show ischemic areas of the myocardium. The coronary sinus catheterization was well tolerated by the patients despite the amount of contrast medium injected into the venous circulation. In this small number of patients we did not clearly find a greater distribution of contrast material to the ischemic area of the myocardium, probably because of the poor definition of the hemodynamic equipment at that time, the diameter of the catheter, and/or the predominance of fibrosis over the ischemia.

In 2004 at the Roberto Viña Service in Argentina,,the largest experience in stem cell of Latin America, the retrograde coronary perfusion technique was used to introduce stem cell in a case of acute myocardial infarction (Arq Bras Cardiol 2004;83(4):352-354)

In 2005 we present a new technique to evaluate the relation of endothelial lesion and infection in atherosclerosis (Rev Socerj 2005;18(3):241-243) collecting blood from the coronary sinus in two cases of acute coronary insufficiency during angioplasty in order to screen for bacteria, viruses and viral DNA fragments.We did not find infection..

I woul like to use hemodiluted blood (low viscosity) for retroperfusion that probably will need less perfusion pressure with consequently less capillary injury and easier flow of blood and debris of PTCA in the coronary venous circulation. This is the investigation work that I would like to send you for your website.

Thank you for the time you spent with this historical report.

Best regards and congratulations for your important work

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