

'We would like to see leaks in the vascular system more or less eradicated. It would be nice to think we could present a commercial argument showing that prophylactic application of the sealant will improve patient care and reduce overall healthcare costs by

reducing the risk of leaks and the need to go back to the operating room to fix them', he concluded.

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Pioneers in cardiology

Klaus Peter Rentrop, MD, FACC, FACP, known for his pioneering streptokinase reperfusion therapy in acute myocardial infarction



Born in Cologne, Germany, Rentrop graduated from the University of Heidelberg in 1966, where he wrote his MD thesis on the 'Pathophysiology of Haemodilution Shock' at the Institute for Experimental Surgery, supported by the 'Studienstiftung des deutschen Volkes'. In 1968, he was the first intern in the newly opened Coronary Care Unit at the University of Giessen, where Prof. Lasch investigated the 12h infusion regimen of intravenous streptokinase for acute myocardial infarction (AMI) patients, popular in Europe at that time. The rationale for this treatment had shifted from the resolution of an occluding coronary thrombus in the late 1950s to the 'modern' concept of improving the micro-circulation and reducing afterload.

Rentrop completed his training in the USA at Detroit General Hospital and the Cleveland Clinic from July 1968 through June 1973. American physicians then believed that AMI was caused by a mismatch between myocardial oxygen demand and supply, due to a severe fixed coronary stenosis and that the infarct size could be limited by reducing myocardial oxygen demand. Coronary thrombosis was not viewed as the cause of AMI but as an irrelevant consequence. Thrombolytic therapy was rejected as a risky method to reduce afterload. At the Cleveland Clinic, Rentrop learned coronary angiography from its inventor Dr Mason Sones and witnessed the beginnings of reperfusion by acute coronary artery bypass surgery pioneered by Dr Renee Favaloro. However, reperfusion remained controversial throughout the 1970s due to fear of fatal arrhythmias and myocardial haemorrhage causing infarct extension.

In the years 1977–80 at the University of Göttingen, Germany, Rentrop's research group performed coronary angiography in a total of 145 patients within the first hours of AMI. Their findings and those obtained at the same time by cardiologists in Spokane, WA, USA, provided knowledge of the coronary anatomy in AMI for the first time.

Prof. W. Schaper in 1977, working in the same research consortium as Rentrop and Dr Reimer in the USA, showed in dogs that reperfusion within 3–6 h after coronary occlusion salvages myocardium; collateral flow extends this time window. From July 1978 to June 1979, encouraged by these studies, Rentrop performed the world's first primary percutaneous coronary interventions (PCIs) in 16 AMI patients. Initially, he used 0.032 or 0.038 in. guidewires. In later studies, a recanalization catheter with an external diameter tapering from 1.7 to 0.7mm at the tip was advanced over a 0.018 in. guidewire to widen the lumen. Antegrade flow was restored in 10 patients. These interventions demonstrated for the first time that reperfusion does not increase infarct size or cause uncontrollable arrhythmias and that it may improve myocardial function.

Only after his first primary PCIs did Rentrop learn that in the previous year, Dr Andreas Grüntzig in Zürich had dilated chronic coronary plaques with balloon catheters he had developed. In the winter of 1978/79 Grüntzig made his balloon catheters available to Rentrop and encouraged him to use them in AMI patients. However, Rentrop felt that these prototype balloon catheters, which had a short stiff wire mounted at the tip, were not malleable enough to be steered safely in ruptured plaques complicated by thrombus. Primary balloon angioplasty became widely accepted only in the mid-1980s, after Dr Hartzler in Kansas City used steerable guidewires and over-the-wire balloons.

Although the concept that AMI is caused by plaque rupture complicated by an occlusive coronary thrombus was not generally accepted in the late 1970s, Rentrop became convinced of its validity when he correlated his *in vivo* angiograms with the autopsy findings of Prof. Sinapius, Head of Cardiac Pathology at the University of Göttingen. However, Oliva in 1977 and Maseri in 1978 demonstrated reperfusion in infarct patients following intracoronary or sublingual administration of nitroglycerin and postulated a central pathogenetic role for spasm.

The first-ever study to clarify the pathogenetic role of coronary thrombosis and spasm was conducted by Rentrop from 1979 to 1980. An intracoronary bolus of nitroglycerin was followed by selective intracoronary infusion of streptokinase in 62 patients with AMI and 10 with pre-infarction angina. Fibrinolysis turned out to be the decisive factor in achieving re-flow. Improvement

of infarction symptoms and decrease in ST elevations immediately after successful thrombolysis conclusively proved for the first time the pathogenetic role of coronary thrombosis in AMI. When these results and conclusions were presented at the Annual Meeting of the American Heart Association in Anaheim, CA, USA, in 1979, a worldwide paradigm shift in the treatment of AMI ensued: from reduction of myocardial oxygen demand to reperfusion.

In 1981, Rentrop and his team moved to Mount Sinai Hospital, New York City, where they conducted randomized trials to further assess the risks and benefits of acute cardiac catheterization and reperfusion therapy. Under the auspices of the European Society of Cardiology, Rentrop organized an International Registry which in 1982 became the basis for FDA approval for intracoronary lysis. The validity of the reperfusion concept was established for intravenous streptokinase by the Gissi and ISIS II Trials in the late 1980s and for primary PCI in the late 1990s.

In 1991, Rentrop became Founder and President of Gramercy Cardiac Diagnostic Services in New York. He sees an exciting

future in cardiac positron emission tomography (PET). 'With PET we are now moving from assessment of relative coronary flow to measuring absolute coronary flow and coronary flow reserve', he states. 'This will finally complete the work begun by Grüntzig in 1977: patients with stable angina to whom PCI confers a survival benefit will be identified based on the reduction of their coronary flow reserve'.

Rentrop currently has clinical privileges at Lenox Hill Hospital and NYU Medical Center in Manhattan, where he is a Clinical Professor. He describes himself as an avid reader, a lover of music and spends his spare time with his family in his beach house on Long Island.

I am most grateful to Dr Rentrop for all the information he has made available to me for the writing of this article, which inevitably, limited by length, can only provide a mere snapshot of all his achievements and academic honours.

Diana Berry, MA

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