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Key Words: myocardial ischemia-reperfusion injury, pulsed ultrasound, cholinergic anti-inflammatory pathway

Discussion

Dr Friedhelm Beyersdorf *(Freiburg, Germany)*. You have clearly shown that HG increases infarct size 3-fold, which poses a major problem. Your hypothesis is that insulin doesn't work? So that means you believe that HG will damage the tissue, but if you treat HG, it still doesn't work. Why is this so?

Dr Eric J. Charles *(Charlottesville, Va)*. We think HG affects the splenic leukocytes and primes them for their inflammatory response. Once that priming has happened, even if you correct HG with insulin, those cells are already on a trajectory to release a lot more cytokines and produce a greater inflammatory response than otherwise would have happened.

Dr Beyersdorf. Do you think that pUS might also work, first of all, after ischemia without reperfusion, and thereafter if you think it might also work after reperfusion has already occurred?

Dr Charles. Those are both great questions, which we are currently working on answering in the lab. I doubt there will be much effect in the scenario of ischemia without reperfusion, because the detrimental inflammatory response that we are modulating in our model occurs with the onset of reperfusion. However, applying pUS after ischemia but before reperfusion will likely be beneficial. Additionally, applying it after reperfusion has already occurred may show a benefit in reducing further injury, but the overall response may be less. To translate this clinically, it would be valuable if we can demonstrate a beneficial effect with application of pUS at these other time points.