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Cyclosporine in Acute Myocardial Infarction

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To the Editor

In the article by Piot et al. (July 31 issue),¹ cyclosporine, an inhibitor of the mitochondrial permeability transition, decreased infarct size after percutaneous coronary intervention (PCI) when administered just before the procedure. Although promising, cyclosporine has drawbacks, including immunosuppression, nephrotoxicity, and variable bioavailability. Cyclosporine is effective at lower concentrations (0.5 to 2 μ M), but protection is lost at higher concentrations ($> 5 \mu$ M); thus the drug has a narrow therapeutic window.² Nonimmunosuppressive analogues of cyclosporine, such as NIM811, seem not to lose efficacy at high doses and might be more suitable for PCI.³ Other drugs block the mitochondrial permeability transition, prevent reperfusion injury, and are promising drug candidates. One such drug is minocycline, a tetracycline derivative that blocks the calcium-dependent mitochondrial permeability transition by inhibiting mitochondrial calcium uptake.⁴

The mitochondrial permeability transition is also emerging as a pathogenic mechanism in many chronic diseases (e.g., neurodegeneration and heart failure).⁵ For such diseases, long-term immunosuppression is undesirable, and non-immunosuppressive mitochondrial permeability-transition inhibitors therefore show better promise as therapeutic agents.

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