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An evidence-based review of pharmaceutical interventions to limit the systemic inflammatory response in cardiac surgery

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Introduction
We report here the first evidence-based review of pharmaceutical strategies to limit the systemic inflammatory response in adult coronary artery bypass grafting surgery.

Methods
The review was confined to randomized drug trials published in the peer-reviewed medical literature between 1970-2008. To be included, at least one inflammatory marker had to be measured. Pediatric, off-pump, valve, and other CT procedures were excluded. For studies satisfying these minimal inclusion criteria, organ function to the following index organs was recorded: heart, lung, kidney, brain, and gut. Evidence was gathered, synthesized and graded by two reviewers in accordance with the recommendations put forth by the American College of Cardiology and American Heart Association. Discrepancies in this evaluation process were resolved by an independent reviewer.

Results
Of 645 articles initially identified from a systematic search of the literature using a combination of search terms, 61 met the minimal inclusion criteria of measuring a single inflammatory marker and, of these, only 17 went on to describe drug effect(s) on organs (mostly heart and lung). No meta-analyses satisfied the minimal inclusion criteria. The only drug category to achieve a provisional Class IIa recommendation was steroids: Methylprednisolone was assigned a Class IIa recommendation with Level of Evidence A; Dexamethasone, Class IIa Level B; Hydrocortisone, Class IIa Level B. Antifibrinolytics were assigned either category IIb or III recommendations: High dose Aprotinin, Class IIb Level A; Low Dose Aprotinin, Class III Level A; Tranexamic Acid, Class IIb Level B; ε-Aminocaproic Acid, Class III Level B. Finally, Atorvostatin was assigned Class III Level B.

Conclusions
These are the first guidelines aimed at producing ACC/AHA clinical recommendations on pharmaceutical strategies to combat the systemic inflammatory response in the setting of cardiac surgery. We highlight the paucity of evidence in the literature, with very few studies identified that could demonstrate any linkage between drug effects on the systemic inflammatory response and organ function. The majority of studies failed to measure any inflammatory markers, while many others studied soft end-points, such as length of hospital stay, and merely assumed this was somehow linked to the systemic inflammatory response. The only drug intervention meriting a provisional Class IIa recommendation based on multiple randomized trials was Methylprednisolone.