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The CHARISMA Trial and the REACH Registry Outcomes

An Addendum to the Current Consensus on Antiplatelet Therapy in Individuals at Risk for Atherothrombotic Events

Dear Editor,

Since our original communication, "Antiplatelet Therapy in Populations at High Risk of Atherothrombosis,"¹ was accepted for publication, results of two important studies referenced therein have been disclosed.^{2,3} In view of the established efficacy of clopidogrel/aspirin combination therapy in patients with unstable angina/non-ST-segment elevation acute coronary syndromes, the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) trial investigated the efficacy and safety of dual antiplatelet therapy with clopidogrel and aspirin in 15,603 patients with a history of symptomatic coronary artery disease, cerebrovascular disease or peripheral arterial disease, or who were asymptomatic but had multiple risk factors (e.g., those with diabetic nephropathy).² CHARISMA was a worldwide trial involving 768 active sites in 32 countries on six continents in which all patients received low-dose aspirin (75–162 mg/day) in addition to randomized treatment with either clopidogrel (75 mg once daily) or placebo. Results indicate that there was no overall benefit of dual antiplatelet therapy, with the primary efficacy endpoint (a composite of vascular death, myocardial infarction or stroke) occurring in 6.8% of clopidogrel recipients and 7.3% of

placebo recipients [relative risk (RR): 0.93; $p=0.22$]. A nonsignificant increase in the primary safety endpoint of GUSTO-defined severe bleeding was observed with clopidogrel versus placebo (1.7% vs. 1.3%; RR: 1.25; $p=0.09$). Patients with multiple risk factors did not benefit from dual antiplatelet therapy, with a primary efficacy endpoint rate of 6.6% for clopidogrel, compared with 5.5% for placebo (RR: 1.2; $p=0.2$) and a nonsignificant increase in the rate of severe bleeding (2.0% vs. 1.2%; $p=0.07$). However, the CHARISMA study does support the dual antiplatelet therapy approach to secondary prevention in patients with established cardiovascular disease, with the primary efficacy endpoint occurring in 6.9% of clopidogrel recipients versus 7.9% of placebo-treated patients in this subgroup (RR: 0.88; $p=0.046$). In this subgroup, there was no significant difference between clopidogrel and placebo in the risk of severe bleeding (1.6% vs. 1.4%; $p=0.39$). These findings warrant additional studies to confirm the benefit of dual antiplatelet therapy in patients with established atherothrombotic disease.

The second major study, the Reduction of Atherothrombosis for Continued Health (REACH) registry was a worldwide survey of 67,888 patients at high risk of atherothrombotic events across all vascular beds.³ Data from the REACH registry showed that risk

factor profiles were similar among atherothrombotic patients across the geographic regions studied, with a high proportion having hypertension (81.8%), hypercholesterolemia (72.4%) and diabetes (44.3%). Furthermore, patients were generally undertreated with evidence-based pharmacological therapy, in particular statins (69.4% overall) and antiplatelets (78.6% overall). The REACH registry demonstrated that classic cardiovascular risk factors are consistent and common but are largely undertreated and undercontrolled in many parts of the world.

The results of the CHARISMA and REACH studies further elucidate the current importance of antiplatelet agents for patients with a wide range of atherothrombotic diseases as part of a dual modification of risk factors via lifestyle changes and pharmacological therapy.

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Respectfully,

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Obesity Prevention in Pediatrics

*Free at Last! Free at Last!
Thank God Almighty, I am
Free at Last!*

—Reverend Dr. King¹

We know that things are getting better when we learn that our “Cookie Monster”^{2,3} is now eating healthily—no longer limited to actually just eating cookies.⁴

“Our Healthy People 2010 Report, while naming ‘reducing obesity’ in children and adolescents as one of its main objectives, distinctly acknowledged that prevention is ideally best effected through combined family and patient education efforts within both the community and the healthcare setting.”⁵

In a previous issue of *Journal of the National Medical Association*, our outstanding Texas Agriculture and Manufacturing [Texas A&M] Temple Texas Pediatric Residency Team of the Scott and White Clinic⁶ well documented their method—that needs to become our method—of approaching our obesity epidemic by and with the education of our healthcare provider professionals.

The Reverend Dr. Martin Luther King, Jr. endorsed, “The essential tragedy of violence is that violence begets violence, producing an ever downward spiral into a night already devoid of stars.”⁷

- We believe that the Reverend Dr. King, in his wisdom, knew and knew well that our ethnic children and adolescents suffer with obesity.
- We believe that King would enthusiastically allow us to substitute obesity for violence in his words.
- We believe that King would approve of the leadership, wisdom and foresight of our [Texas A&M] Temple Texas Pediatric Residency Team of the outstanding Scott and White Clinic.



- We believe that King would truly want our ethnic children and adolescents to be free of their obesity at last!

Disclosure: The author wishes to disclose that he himself is ethnic—specifically, he is “Eastern European American Caucasian”—and that he was previously obese, that then he manifested diabetes, that he took insulin for a time, and that he is now down to the weight at which

he himself left active military service in the Far East. He is reasonably physically fit and has achieved tight control of his diabetes disorder. Nevertheless, he fully anticipates his eventual return to insulin.

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REFERENCES

1. Inscribed on the Memorial Marker-Gravestone of the Reverend Doctor Martin Luther King Jr.
2. A Muppet—actually created by Mr. Jim Henson (1936–1990) by combining the words “marionette” and “puppet”. The Cookie Monster may well be viewed on Public Television: the children’s show “Sesame Street.”
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