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COMMENT ON NOLAN ET AL.

Insulin Resistance as a Physiological Defense Against Metabolic Stress: Implications for the Management of Subsets of Type 2 Diabetes. Diabetes 2015;64:673–686

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We read with much interest the article by Nolan et al. (1) on insulin resistance (IR) as a defense against metabolic stress. This is the third in a cluster of reviews beginning with the hypothesis that IR protects the heart from fuel overload in dysregulated metabolic states (2) and coincides with a review by Connor et al. (3). In our article (2), we stressed the deleterious effects of dysregulated glucose and fat metabolism on the function of the heart and proposed physiologic and biochemical mechanisms by which IR protects the heart from fuel overload. Nolan et al. (1) focused on insulin-induced metabolic stress and expanded on the view that overriding IR with intensive insulin treatment could be harmful (4). Lastly, Connor et al. (3) stressed that many of the adaptations occurring in metabolic diseases characterized by nutritional excess can be viewed as protective in nature rather than pathogenic per se. The observations that excessive insulin signaling exacerbates systolic dysfunction when the heart is subjected to pressure overload (5) and the demonstration that IR improves metabolic and contractile efficiency in the inotropically challenged heart (6) complement each other. Lowering blood glucose levels at all costs may be harmful. We have proposed that in the management of diabetes of patients with heart failure the target should be the source rather than the destination of excess fuel (7). The three reviews and other published work (8) argue in support of the concept that IR is a physiological defense mechanism against metabolic stress. One can only hope that the concept will gain further traction.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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