CALL FOR PAPERS | Metabolic Syndrome

From clinical insights to new therapies

Pontus B. Persson
Institute of Physiology, Humboldt University, Charité, Berlin, Germany

THERE WAS A VERY POSITIVE RESPONSE to the special call, Metabolic Syndrome, appearing in this issue of the American Journal of Physiology—Regulatory, Integrative and Comparative Physiology. This is an opportunity to look back at the important studies related to this topic that have appeared in this journal over the recent years.

The metabolic syndrome was referred to as syndrome X by Reaven in 1988 (15), who noted that several risk factors commonly cluster together. The most common among these risk factors are abdominal obesity, atherogenic dyslipidemia, hypertension, insulin resistance, inflammation, and prothrombotic states. Development of the metabolic syndrome is related to a complex interaction of multiple factors involving not only lifestyle and genetic contributions, but also hepatic, vascular, and immunologic factors. Besides cardiovascular diseases and type 2 diabetes, individuals with metabolic syndrome more often develop fatty liver, polycystic ovary syndrome, asthma, sleep disturbances, cholesterol gallstones, and some forms of cancer (18).

Many of the studies aiming at clarifying the pathogenesis on the metabolic syndrome have appeared in this journal. In particular, there has been a strong focus on insulin sensitivity and insulin resistance (1, 3, 11, 13). Several measures are effective in improving insulin resistance, such as exercise (16), PPARγ agonism (2), fish oil (17), and perhaps, even high-protein diet (10).

Insulin resistance is known to impair ACh responsiveness of various vascular beds. The blunted ACh-response in coronary arteries is mediated via calcium-dependent K-channels (12). Conversely, impaired cerebral artery dilatation in response to ACh seems to involveoxidant stress (14). However, several vasoconstrictor mechanisms of the cerebral circulation are not affected in insulin resistance (5). Not only is the vascular responsiveness of various vessels affected in the metabolic syndrome, microvessel rarefaction is also a common observation. Microvessel rarefaction of the skeletal muscle appears to come about by reduced nitric oxide availability caused, in part, by oxidative free radicals (7).

Various approaches have been undertaken to elucidate fetal programming, genetic (8), and developmental aspects of risk factors found in the metabolic syndrome. The diet during pregnancy and the suckling age appears to be decisive. Khan et al. (9) demonstrated that adult offspring of fat-fed rats can acquire features of the metabolic syndrome both antenatally and during suckling. Interestingly, this study also showed that exposure during pregnancy confers adaptive protection against endothelial dysfunction induced by maternal fat feeding during suckling.

Perturbed glucose homeostasis in these offspring of rats receiving fat-enriched diet during pregnancy can be linked to altered insulin secretory granule morphology of pancreatic beta cells (19). Moreover, mitochondrial genes appear to be down-regulated in these offspring (19). In addition to a fat-rich diet during pregnancy, maternal protein deficiency (6) and prenatal ethanol exposure (4) perturb glucose homeostasis. The latter appears to be related to a dysregulation of enzymes controlling gluconeogenesis, in particular, phosphoenol-pyruvate carboxykinase, and the transcription factor peroxisome proliferator-activated receptor coactivator, which promotes gluconeogenesis (4).

The articles appearing in response to the special call on Metabolic Syndrome provide new insights into altered vascular reactivity, in particular, with regard to endothelin, carbon monoxide, and calcium sensitivity. Moreover, features of chronic systemic inflammation in obese animals are investigated, as are the mechanisms behind insulin resistance.

REFERENCES


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Address for reprint requests and other correspondence: P. Persson, Institute of Physiology, Humboldt Univ., Charité, Tucholskystr. 2, 10117 Berlin, Germany (e-mail: pontus.persson@charite.de).


