



EAT your heart out!

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I have always thought that the phrase, “eat your heart out,” was an odd expression as it is used most commonly to taunt a competitor. The origins of this phrase are contentious and there are at least three different etymologies. To these three, this issue of our journal adds a dysmorphic fourth.

The focus of this issue is the effect of diet on the cardiovascular system. This effect can either be direct, through food constituents entering our bloodstream, or indirect. Indirect effects are quite hard to envisage until you delve into the article by **Max Nieuwdorp**. This article highlights the massive fauna of bacteria that live in our gastrointestinal tract and how they can profoundly influence the efficiency with which we extract calories from our diet. The fauna, or microbiota, also synthesize molecules that trigger very specific signaling pathways that regulate metabolism. The article is not for the faint-hearted since it will change your view of coprophagia and fecal transplantation! The description of the underlying biology, and of the clinical findings, is compelling. Furthermore, this topic affects the interpretation of the other articles in this issue that predominantly focus their explanations on the direct effects of diet. I, therefore, suggest it is worth reading **Max Nieuwdorp's** review first, since it offers holistic insight to the complex issue of dietary manipulation.

We are fortunate to have the article by **Ramon Estruch**, the lead author and coordinator of the PREDIMED study (PREvención con Dieta MEDiterránea).¹ This landmark dietary intervention study showed that a Mediterranean diet supplemented with fat, in the form of extra virgin olive oil or tree nuts, significantly reduced events as measured by a composite of hard cardiovascular end points (MI, stroke, or CV death). This was a primary prevention study in an easily identifiable at risk group (men >55 years or women >60 years, with either type 2 diabetes mellitus or at least three of the following: smoking,

hypertension, LDL >160 mg/dL, HDL <40 mg/dL, BMI >25 kg/m², or a family history of premature coronary heart disease). The article contains a table of the diet instructions to wet your appetites. **Ramon Estruch** and **Gemma Chiva-Blanch** highlight that the exact component of the diet responsible for the salutary effect is not known. However, this knowledge is not necessary since it should be used as part of a lifestyle package in combination with reductions in dietary salt and regular exercise. This advice sounds like “motherhood and apple pie,” but as you will see from their table, commercial bakery products were discouraged.

The likely contents of commercial bakery products and other industrialized aspects of our diet are highlighted by **Thomas Sanders**. The refresher corner article looks at our diet from a public health viewpoint and emphasizes the impact of government policy on its constituents. These have been particularly effective at driving reductions in the consumption of salt and saturated and/or trans fatty acids, at least in the UK. It is clear from this article that public policy can curb dietary components thought to be harmful and supplement those thought to be beneficial, but it is much more difficult to mandate the form of food, such as fruit and the PREDIMED diet.

While “motherhood and apple pie”-style advice is directly applicable to individuals and can be enshrined in a policy to influence a population, it does not reveal the mechanism responsible for the benefit. Ultimately, this needs to be known in order to identify a therapeutic target amenable to direct and specific manipulation. The article by **Manlio Vinciguerra** discusses how such targets (eg, Insulin-like growth factor-1, Fibroblast growth factor-21, Sirtuins, and PPAR α) were revealed after caloric restriction or from the study of metabolic changes at birth. The switch from the hypoxic environment of the uterus to the oxygen and fat (maternal milk)-rich environment of the neonate is of particular interest. The premise being

that the diseased heart is reverting to a more primitive/fetal phenotype, more dependent on glucose and less dependent on fat. We are reminded that this scenario is also impacted by profound alterations in gut microbiota at birth, which is, in part, contributed to by the ingestion of meconium, as discussed by **Max Nieuwdorp**. Time will tell if these fundamental signaling processes can be harnessed to slow the aging process and its detrimental effects on heart muscle.

In the morbidly obese, dietary restriction is challenging. In such patients, bariatric surgery can bring the benefits of caloric restriction, which is highlighted by **Manlio Vinciguerra** despite patient's satiety. The case report by **Rahul Mukherjee** emphasizes the systemic benefit of profound weight loss on whole-body metabolism and markers of cardiovascular risk, essentially completely reversing the metabolic syndrome. In contrast, the hot topics article by **Oliver Rider** discusses the changes that occur within the heart following bariatric surgery. **Oliver Rider** also highlights the dilemma posed by the obesity paradox, where overweight patients with heart failure tend to do better than their thinner counterparts. These are complex issues with multiple confounders.

The focus on trimetazidine article has been written by **Roberto Ferrari** and provides a succinct overview of cardiac metabolism and how dietary substrates are turned into high energy phosphate. On this backdrop, actions of trimetazidine are explained in terms of improved efficiency and reduced oxygen requirement.

Finally, **Ronak Rajani** provides a fascinating article that discusses the detection of fat at various locations within the heart. One that seems to have a particular prognostic relevance is the epicardium. Epicardial adipose tissue (EAT) shows wide inter-individual variation and even within an individual, it is dynamically regulated, and regresses markedly with weight loss following bariatric surgery. Given its prognostic importance, and the overwhelming evidence of diet's influence, it is definitely time to "EAT out your heart!" ■

REFERENCES

1. Estruch R, Ros E, Salas-Salvadó J, et al; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013;368(14):1279-1290.