Obesity: Ecology to Evolution Learnings from the International Congress of Obesity

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Introduction

Recently I had a chance to present at the prestigious International Congress of Obesity (ICO) in Sao Paulo, Brazil; organized by the World Obesity Federation (WOF); which has a long history of being a key platform; for the exchange of ideas, knowledge and promoting research, education and collaboration in the field of obesity. With several new molecules in the pipeline and an enhanced understanding of pathways that lead to obesity, I take this opportunity to share with you some of the pearls of wisdom I gained during this well organized and executed scientific meeting.

Background

Almost 20% of Brazil's population[1] is having obesity and by 2030 over 7.6 million children will be affected making Brazil one of the five nations with the largest number of minors with this condition in the world. Obesity was probably rare before 1800[2], but by the year 2000, the global population crossed an historic watershed where for the first time the number of adults carrying excess body weight exceeded the number of those who were underweight[3]. What is driving this pandemic and how can we address it and better treat it?

The Ecology of Obesity

Raubenheimer et al[4] proposed the "protein leverage model" that shows how human beings favor protein as the primary macronutrient and as protein constitutes a smaller proportion of the total intake, paradoxically, it may drive human ingestive behavior. Simply explained, till such a time as we reach the target of 15-20% protein we keep on eating. This is how protein has leverage on human behavior. Hence eating protein first may help in several ways.

Similarly, the role of ultra-processed food (UPF)[5,6] which are high in sugar, fat, and sodium content while being low in protein, and fiber lead to an increased calorie intake and hence weight gain; while eliminating UPF leads to weight loss. Applying the NOVA classification[7] in order to identify UPF was recommended as a global initiative to curb the ever-increasing production and consumption of UPF as part of the work of the UN Sustainable Development Goals and its Decade of Nutrition.[5]

Hence needless to say, lifestyle interventions ranging from caloric restriction[8], macronutrient manipulation, intermittent fasting strategies[9], methods for browning of adipose tissue[10], and exercise interventions such as resistance training[11] remain the cornerstone of any weight loss intervention; in order to lose fat and preserve lean body mass. The gut microbiota[12] and their impact on obesity was a huge area of discussion and how this affects development of metabolic diseases such as diabetes, cardiovascular disease, and even metabolic dysfunction-associated steatotic liver disease (MASLD).

Treatment through lifestyle interventions, fecal transplantation and bio-engineered precision nutrition can be aimed at a diverse gut microbiota, using the Firmicutes/Bacteroidetes (F/B) ratio as a marker[12].

Newer Vistas

The gut hormones and their role[13] as an endocrine mediator of obesity was certainly the hallmark of the congress due to the increasing number of molecules in the pipeline for the same. Tirzepatide which is a dual agonist for both glucose-dependent insulinotropic polypeptide (GIP) (GIP) and glucagon-like peptide-1 (GLP-1) receptors is a perfect example of how GIP has

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also emerged as an important target in the treatment of obesity. GIP/GLP-1 receptor co-agonism causes superior weight loss to GLP-1 receptor agonism (semaglutide) alone.

The pleiotropic effects of these molecules for the benefits on the kidney (semaglutide)[14], heart failure (semaglutide)[15] and MASLD (tirzepatide)[16] highlight the importance of treating not just obesity; but focusing on health outcomes such as cardio-renal-metabolic. Newer molecules such as triple agonist retatrutide (GLP-1, GIP, and glucagon)[17]; cagrilintide with semaglutide[18] (amylin and GLP-1), survodutide[19] (GLP-1/glucagon); orforglipron[20] (GLP-1 small molecule); and mazdutide[21] (GLP-1/glucagon) are promising new candidates for obesity treatment. Additionally, what I found most interesting were three molecules as proposed by Henriksen et al to watch out for in the future both as biomarkers as well as potential treatment targets: endotrophin[22], leptin, and adiponectin; not just for obesity but also for cardiovascular disease, cancer, and as predictors of treatment response[23].

How do we Address this Growing Pandemic?

We must constantly strive to take away the stigma related to obesity and instead address it as an adiposopathy based chronic disease[24]. Second of all it is important when we start treating or addressing obesity, in addition to weight loss; we must constantly focus on quality of life and health outcome measures[25], and in the future more trials designed to evaluate the same will be needed; as behavior modification is complex[26].

Obesity management must be made country, culture and ethnicity-specific; and guidelines must be formulated.

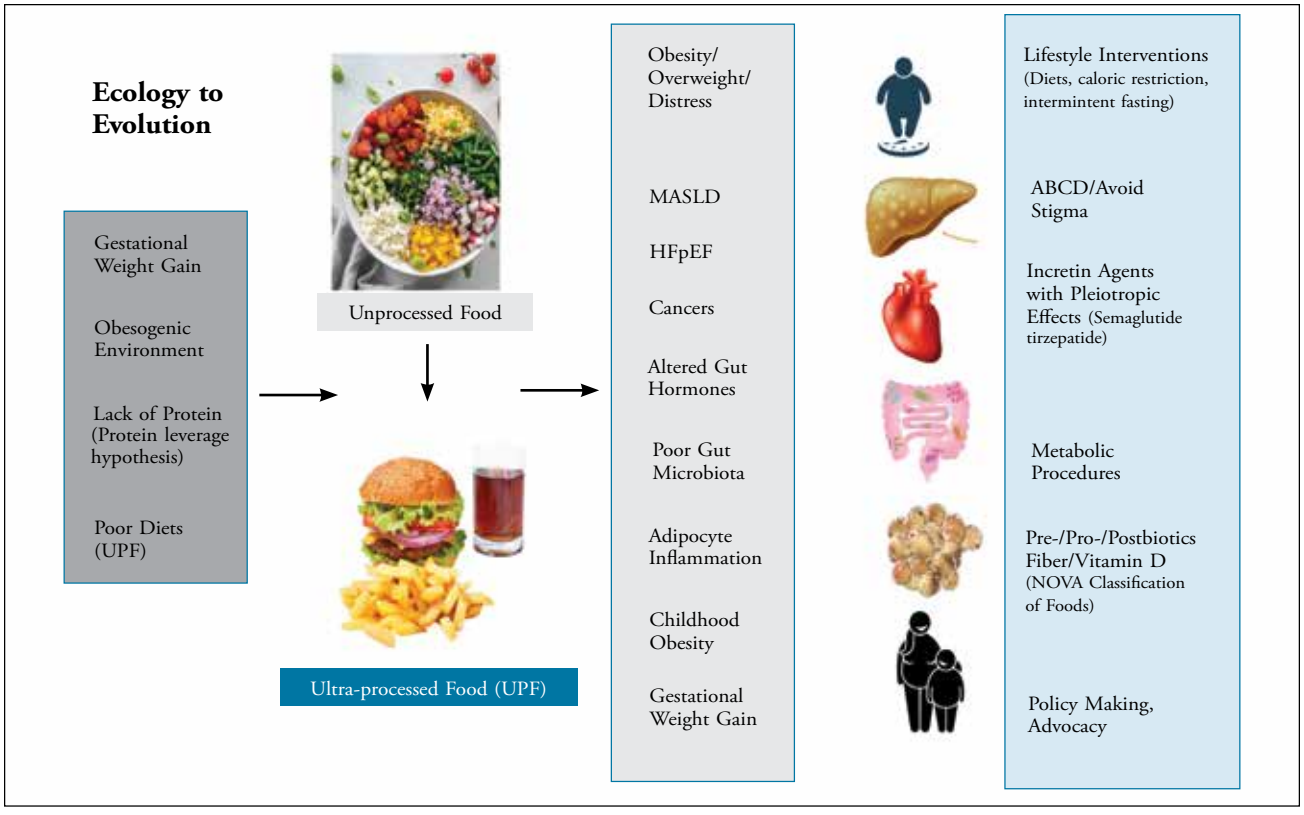
If we are to prevent this pandemic of obesity, two key groups that must be addressed are children and pregestational women[27,28,] through advocacy, education and awareness, and policy making.

Preconception intervention strategies not only improve pregnancy outcomes but may also influence epigenetic programming leading to healthier babies who will grow up to be healthier adults.

A digital revolution will be needed for us to stand united in this fight against obesity. We need more clinicians being trained as metabolic physicians.

The WOF offers an online Specialist Certification of Obesity Professionals in Education (SCOPE) learning platform which I highly recommend should you desire to become one.

Graphical Abstract



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