



The MACARENHA connection: a holistic approach to understand and fight the cardiometabolic epidemics that ravage Mexico

La conexión MACARENHA: un enfoque holístico para entender y combatir las epidemias cardiometabólicas que asolan México

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In 1827, the British physician and scholar Richard Bright (1789-1858) described the association among edema, albuminuria, cardiac enlargement, «hard pulse» (later related to high blood pressure, HBP), uremia and neurological catastrophes like seizures, blindness, and coma.¹ Bright's disease, as it was named for many years, acute and chronic nephritis, was an early attempt to intertwine the clinical manifestations of pathologies affecting organs and systems anatomically distant from each other. Although several physicians had related HBP to cardiac hypertrophy, the

British of Indian and Irish origin physician Frederick Henry Horatio Akbar Mahomed (1849-1874), measuring blood pressure with a primitive quantitative sphygmogram of his own (improved from Marey's invention), described HBP in the absence of kidney disease, but linked it with cardiac hypertrophy, aortic aneurysms, stroke, arteriolar fibrosis, and other cardiovascular (CV) outcomes.² In 2004, the term «cardiorenal syndrome» (CRS) was introduced by the National Heart, Lung, and Blood Institute Working Group, focused on describing the close interplay

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between the kidney and heart physiologies.³ The concept has evolved, highlighting the hemodynamic, neurohumoral, biochemical, immunoinflammatory, and hematologic links between both organs.⁴ As it is known, the four categories of CRS⁴ describe the conditions in which the failure of one of these two organs adversely affects the other and vice versa.⁴

In 2023, the American Heart Association coined the term «cardiovascular-kidney-metabolic (CKM) syndrome», incorporating cardiovascular, renal, and metabolic conditions, foremostly diabetes and obesity (diabesity) in a single nosological entity.⁵ This conceptual consolidation not only refers to the pathophysiological links between the different elements of the CMK syndrome but also applies principally to a more comprehensive diagnostic, preventive, and therapeutic management.⁶

From this evolutionary, modern, and holistic comprehension of HBP, which infrequently emerges as a solitary risk factor, the GRETHA Group, one of the sister medical associations of ANCAM, held a meeting at the end of the past year in Mexico City and launched the concept of MACARENHA connection. The acronym was composed with the following initials: MA, stands for **M**etabolic and **A**diposity; CA, for **C**ardiac and **A**rterial; R, for **R**enal, and EN for **E**ntero-**H**epatic, and HA, for **N**eurological-**B**ehavioral, in **H**ypertension (HA in Spanish).

This concept underlines the physiopathology entanglement among the heart, the kidney, the arterial vessels, the metabolism (mainly carbohydrates and lipids), obesity or overweight, the intestine, and the nervous system. Furthermore, the connection (using a nice feminine name, also the title of a popular danceable song) will easily remind caregivers that diagnosis and treatment must encompass all the elements of the acronym. If HBP is found in a patient, it is mandatory to correct the weight problem; determine the serum concentration of glucose and the complete lipid profile (total cholesterol, high and low-density lipoproteins cholesterol, triglycerides, and all atherogenic indices); evaluate the heart, nervous system, and kidney statuses; and achieve, through an appropriate diet, healthy intestine function and microbiota. All risk factors must be diagnosed, treated, and

controlled or reduced as soon as possible. The neurological-behavior component includes not only acute and chronic brain conditions (stroke, dementia, and lacunar infarcts) but also mood alterations such as anxiety and depression.

In the Mexican pathological and epidemiological scenario, the foundation stone on which rests the enormous load of type 2 diabetes and ischemic heart disease, the two leading causes of general mortality, in adults of both genders,⁷ is the obesity/overweight (O/O) syndrome affecting almost 80% of the population over 20 years of age.⁸ In most cases, O/O, through varied pathogenic mechanisms, detonates in the same patient the rise of blood pressure, dysglycemia (prediabetes and diabetes), and a lipid disturbance called lipid triad or atherogenic dyslipidemia.⁹ More recently, the set of liver pathologies enclosed in the term «metabolic dysfunction-associated steatotic liver disease (MASLD)»¹⁰ has surpassed the interest of gastroenterology and hepatology and is gaining general interest. Firstly, liver fat infiltration is a manifestation/cause of the binomial insulin resistance/hyperinsulinism syndrome, so the hepatic pathology is linked to dysglycemia, dyslipidemia, inflammation, and cardiovascular and cerebrovascular diseases. And secondly, rapidly, MASLD is converting into the leading cause of cirrhosis and hepatoma worldwide. Again, gastroenterologists, hepatologists, and internists who usually diagnose and treat this liver pathology must remember the ties with other dreadful extra gastrointestinal conditions. Finally, the intestine interplay in the MACARENHA connection via two players, the enterogastric hormones of the liver-gut-pancreas-hypothalamus axis influencing the cycle of hunger-satiety¹¹ and the energetic expenditure, and the intestinal microbiota and mucosa. Human intestinal microbiota, through diverse, complex mechanisms, plays essential roles in the genesis of obesity, insulin resistance, type 2 diabetes, MASLD, and HBP, among many other pathologic conditions.¹²

GRETHA will present an extensive document describing the MACARENHA connection in more detail, with the explicit purpose of putting in the minds of general practitioners, family physicians, specialists, decision makers, nurses,

nutritionists, and all those whose activity is related to health, this essential holistic approach to diagnose, prevent, and treat all the constitutive elements of this kaleidoscopic framework of cardiovascular, renal, cerebrovascular and hepatic-enteral diseases.

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