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Mini Review

Cause of the Obesity, Type 2 Diabetes and Metabolic Syndrome Epidemics, Vaccine Induced Immune Overload versus Nutrition Overload

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Abstract

There is an epidemic of obesity, type 2 diabetes, metabolic syndrome and associated conditions. Patients with these conditions often have markers of increased inflammation. Many researchers have published that nutrition overload caused the epidemic of obesity and the associated inflammation which leads to type 2 diabetes and metabolic syndrome. A contrasting view has provided extensive evidence that vaccine induced immune overload has caused an epidemic of inflammation and this inflammation caused epidemics of obesity, type 2 diabetes and metabolic syndrome. The data reviewed in these manuscripts provides proof that immune overload, not nutrition overload has been the major contributing factor for the epidemics and inflammation associated with the epidemics. Several lines of evidence are reviewed including evidence that inflammation precedes obesity in many patients, the lack of inflammation in many obese patients, an epidemic of inflammation in thin patients, and an epidemic of obesity in children under 6 months of age. The failure to control the obesity epidemic is blamed on the focus on nutrition and ignoring the root cause, vaccine induced immune overload. Once a patient has developed metabolic syndrome with type 2 diabetes providers are too frequently subjecting their patients to further immune overload by administering yearly influenza vaccines and many other vaccines. This action makes metabolic syndrome more difficult to reverse. The plan to reduce obesity must be focused on preventing immune overload and not blaming patients for their diet. The epidemic of obesity can be reversed through discontinuation of vaccine practices that result in immune overload.

INTRODUCTION

There is little doubt that there is an epidemic of obesity and related type 2 diabetes and metabolic syndrome in Western Nations. There is also little controversy that in many patients obesity, type 2 diabetes, and metabolic syndrome are closely associated with inflammation. There is however two very different explanations for the epidemics of obesity and diabetes/metabolic syndrome and many have published that the epidemics are caused by nutrition overload and this leads to an increase inflammation. A contrasting view states there is an epidemic of immune overload caused by vaccination that this immune overload is causing the epidemics of obesity and metabolic syndrome.

While both those was proposing the nutrition overload theory and those supporting immune overload agree that inflammation is important for development of diabetes and other components of metabolic syndrome, there is disagreement as to the extent that obesity is causing inflammation. The different opinions on the origins of the epidemics are based on two different lines of study. The nutrition overload theory was based primarily by studying humans and animals with obesity. The data indicating immune overload is the cause of the epidemics was derived from broad population studies of initially healthy babies and studying their responses to vaccines. For example nutrition overload does not explain the obesity epidemic in children 6 month of age who don't drink many sodas, don't eat a lot of fried foods and have never been very active. Recent data from a Massachusetts HMO showed a 73% increase in overweight infants under 6 months of age from 1980 to 2001 [1]. By contrast immune overload caused by the large increase in childhood immunizations can explain this observation. This paper reviews some of the key weaknesses to the theory that nutrition overload caused the epidemics of obesity and metabolic syndrome. This paper also reviews the evidence that immune overload is causing the epidemics.

THEORY THAT NUTRITION OVERLOAD AND OBESITY CAUSE INFLAMMATION

Numerous review papers have been published describing the theory of nutrition overload as the cause of obesity and the associated inflammation [2-4]. According to its proponents, over eating causes a chain of events that leads to inflammation and then metabolic syndrome. There are several prevailing explanations on how obesity induces inflammation [2,5]. According to one theory free fatty acids can activate the immune cells *in vitro* [6] and it has been suggested fat cells in obese patients may produce more free fatty acids [7]. However it is noted that in weight loss, free fatty acids are released but weight loss does not increase the risk of metabolic syndrome. The mechanism by which obesity causes increases in free fatty acids is unclear. Another theory to

explain the association between inflammation and obesity is that fat cells produce TNF [8] but the evidence that obesity causes more TNF production and this leads to inflammation is not well established.

Another proposed mechanism of obesity inducing inflammation involves adiposities attracting macrophages and the macrophages releasing inflammatory mediators. The presence of activated macrophages in the adipose tissue of some obese patients is clearly documented, but the triggers are less clear. One theory [9,10] states that enlarging fat cells need more blood vessels and this leads to hypoxia. Hypoxia causes fat cells to release factors that stimulate macrophages. The theory is intriguing, but lacks solid evidence, and is not unique to fat cells. Exercise induces hypoxia as well and leads to increased blood vessels in hypertrophied muscles. However exercise is not associated with increased risk of developing inflammatory diseases including diabetes, in fact the opposite. Furthermore, as discussed below, many obese individuals don't have inflammation so the theory does not consistently hold true.

Another theory [10] states that fat cell derived adipokine production causes inflammation. An example is leptin, a known immune stimulant. There are multiple other hormones that are secreted by adipocytes and many are known to modulate the immune system. These include IL-6 [11,12], resistin [13], retinol-binding protein4 (RBP-4) [14], omentin [15], chemerin [16-18], pro- granulin [19], and monocyte chemoattractant protein-1 (MCP-1) [20-22]. However there is no clear data this theory is true, in particular there is no clear data that obesity causes increases in adipokine activity.

INFLAMMATION PRECEDES DEVELOPMENT OF OBESITY AND METABOLIC SYNDROME

In contrast to the belief that obesity is causing inflammation there is data that inflammation precedes the development of obesity and causes obesity. Ding [23] showed that inflammation preceded the development of obesity in mice. Frazier [24] also found evidence that inflammation preceded obesity in animal models. Research suggests CRP levels in children are predictive of adult obesity [25]. Furthermore it has been shown that CRP levels predict future weight changes [26]. Data has been published showing a genetic link between a genetic variant of CRP and fat mass [27]. A review article [28] published evidence that gut inflammation preceded and caused obesity. A study on Finnish middle age men [29] found men with elevated CRP concentrations had higher age-adjusted risk of developing metabolic syndrome. A study of men and women in Mexico [30] found women with elevated CRP in the highest tertile had an increased relative risk of developing metabolic syndrome.

OBESITY DOES NOT CONSISTENTLY CAUSE INFLAMMATION

Additional evidence against obesity as the cause of epidemic of inflammation is the fact that obesity routinely occurs in the absence of inflammation. Patients with a primary Cushingoid condition are obese and immune suppressed but don't have an inflammatory condition. There are multiple papers written about metabolic "healthy" obese populations versus metabolic "unhealthy" obese populations [31]. Metabolic healthy obese patients have satisfactory insulin sensitivity, and glucose control. Published estimates vary between 20-30% of the obese population are metabolically healthy depending on the study. The difference between studies is based in part on the criteria for defining metabolic healthy versus unhealthy [32-36]. One study found that difference between healthy and unhealthy obese women is that the healthy population had low CRP levels indicating low levels of inflammation [37]. In a second study [38] logistic regression analysis was used to show metabolically healthy obese patients had lower levels of several inflammatory markers than those with obesity that were not metabolically healthy: complement component 3 (odds ratios [ORs], 2–3.5), IL-6 (ORs, 1.7–2.9), plasminogen activatorinhibitor-1 (ORs, 1.7–2.9), and white blood cells (ORs, 2.1–2.5).

INFLAMMATION EPIDEMIC IN THE THIN

Another line of support that inflammation precedes obesity is the finding that inflammation also occurs in thin individuals. There is a well documented epidemic of inflammation and inflammatory conditions in thin individuals in Western countries. This epidemic of inflammation indicates that obesity is not the cause of inflammation in a large group of individuals that are not obese. This observation is important because it is unlikely that there is one cause for an epidemic of inflammation in thin individuals and a second and different cause of an epidemic of inflammation in obese individuals.

NAHME III data from the US children 8-16 year old from 1988-1994 [39], shows elevated CRP was present in children of all BMI quintiles. While there are a higher percentage of obese patients with elevated CRP, the Odds Ratios compared to normal weight children was not great. Elevated CRP was 3.74 times more prevalent in overweight males and 3.17 times in overweight women. Researchers have found substantial overlap in inflammation in nonhealthy obese, healthy obese, and nonhealthy non-obese [38,40]. There is a clear epidemic of type 1 diabetes in children, an autoimmune/inflammatory condition [41]. Type 1 diabetes is associated with thinner populations [42]. These facts do not support the theory that the epidemic of obesity is causing the epidemic of inflammation associated with it but is consistent with an epidemic of inflammation that can cause obesity in certain genotypes.

IMPORTANCE OF GLUCOCORTICOIDS IN DETERMINING WEIGHT

Glucocorticoid production is one of the most important, if not most important factors in determining a person's weight, yet this parameter is rarely measured in obesity studies. Untreated patients with Cushing's disease are almost always obese, while untreated patients with Addison's disease are almost always thin. If one takes an obese patient with Cushing's disease and starves the patient, the patient will lose weight. However it is cortisol excess, not nutrition overload that causes patients with Cushing's disease to be obese. One can titrate the weight of a patient with Addison's disease by titrating the amount of glucocorticoids a patient is given. Prolonged administration of high doses of glucocorticoid steroids will cause patients to develop obesity, hypertension, and dyslipidemia and insulin resistance.

Alterations in the activity of genes responsible for

glucocorticoid metabolism can also affect the risk of metabolic syndrome. Published data has shown evidence that activation of cortisol as a result of increased enzymatic activity of 11-beta hydroxysteroid dehydrogenase type 1 may increase the risk of components of metabolic syndrome [43,44]. It has been suggested that children from Sardinia, who have a high prevalence of conditions that cause decreased cortisol activity [45], glucose-6 phosphate dehydrogenase deficiency and thalassemia, had the lowest levels of childhood obesity in Italy but the highest rates of type 1 diabetes [46].

INFLAMMATION IS A MAJOR DRIVER IN GLUCOCORTICOID PRODUCTION AND CAN CAUSE OBESITY

Because of the strong ability of glucocorticoid steroids to cause obesity, agents that increase glucocorticoid activity can cause obesity. Inflammation is a strong activator of glucocorticoid activity and thus has the potential to cause obesity. Both IL-1 [47,48] and IL-6 [49-51] enhance cortisol release and thus have the potential to cause obesity and metabolic syndrome. IL-6 has been associated with the development of metabolic syndrome [52,53]. In addition IL-6 has been directly associated with the development of diabetes [54], insulin resistance [55] and altered lipid levels [56-58].

Hyperactive glucocorticoid activity induces fat gain especially in the omentum and visceral region as opposed to the periphery. This phenomenon has been explained by the ability of visceral adipocyte to convert inactive corticosone to cortisol [59]. This explains why abdominal obesity is more strongly associated with inflammatory markers than BMI or total body fat [61-63].

VACCINES INDUCED IMMUNE OVERLOAD AS THE CAUSE OF THE OBESITY EPIDEMIC

There is strong evidence that vaccine induced immune overload is causing the epidemic of obesity. The central thesis is that vaccine induced immune overload causes many different manifestations. Obesity and metabolic syndrome are just a few of the manifestations. Other manifestations linked to vaccine induced immune overload include type 1 diabetes [64], multiple different autoimmune diseases, allergies, asthma [65] and autism [66]. The identification of a single cause of inflammation with multiple different manifestation including type 1 diabetes and obesity is a more traditional and logical explanation than hypothesizing separate causes for each inflammatory condition.

Previous publications have shown that an increase vaccine induced immune overload has caused an epidemic of both type 1 [64,67-69] and type 2 diabetes/metabolic syndrome [46,70-72]. Data indicates vaccine recipients who produce low levels of cortisol tend to develop type 1 diabetes while vaccine recipients who produce higher levels of cortisol tend to develop type 2 diabetes and metabolic syndrome [65].

Immunization causes both short term and long term immune stimulation. Multiple papers have studied short term cytokine release following immunization. The acellular diphtheria tetanus pertussis vaccine causes the release of IL-6 [73] while the DT-Polio-Typhim vaccine stimulates IL-6 production [74]. Immunization with the DTwP vaccine but not the DTaP vaccine increases IL-6 levels at 2 days post immunization [75]. Research have also found that the influenza vaccine stimulated release of IL-6 and IL-10 [76] and the influenza and pneumococcal vaccine caused rises in CRP [77] over the short term. Long term vaccine induced inflammation has been demonstrated by researchers in France. These scientists have linked aluminum adjuvants in vaccines to prolonged activation of macrophages (lasting possibly decades) and shown the adjuvants cause an inflammatory condition called myofascititis [78,79].

It is well established that immunization of children can increase cortisol levels at least in the short term [80-87]. Furthermore there is a clear racial difference in cortisol production that mirrors the propensity to develop type 1 versus type 2 diabetes. Caucasian children [6] produce much less cortisol following immunization than Japanese children [88]. The finding explains why the discontinuation of school age BCG immunization was followed by a decreases of type 1 diabetes occurred in a population of Caucasian children [68] but a decreases in type 2 diabetes occurred in Japanese children [72].

CONCLUSION

Both nutrition overload and immune overload have been blamed for the epidemics in obesity, inflammation, type 2 diabetes, and metabolic syndrome. The data reviewed in these manuscripts provides proof that immune overload, not nutrition overload has been the major contributing factor for the epidemics. The plan to reduce obesity must be focused on preventing immune overload and not blaming patients for their diet. The medical industry must take ownership for causing of the epidemics through the inappropriate recommendations and gross over utilization of vaccines. Once a patient has developed metabolic syndrome with type 2 diabetes providers are too frequently subjecting their patients to further immune overload by administering yearly influenza vaccines and many other vaccines. This action makes metabolic syndrome more difficult to reverse. The epidemics of obesity and metabolic syndrome can be reversed through discontinuation of medical vaccine practices that result in immune overload.

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