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Hepato-pancreato-biliary fat: the good, the bad and the ugly

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Abstract
Obesity has become epidemic in the United States, in Europe, and in many urban areas in the developing world. The globalization of certain 'fast foods' and 'soft drinks' may, in part, be contributing to this epidemic. Diets high in saturated fatty acids and trans fats as well as drinks that have high fructose corn syrup levels may be particularly harmful. Recent research suggests that fat is a dynamic endocrine organ and that visceral fat is associated with the metabolic syndrome. Central obesity leads to organ steatosis and altered serum adipokines including reduced adiponectin and markedly elevated leptin. This abnormal adipokine milieu results in increased tissue infiltration of monocytes and macrophages which produce proinflammatory cytokines that alter organ function. Over many years, the combination of steatosis and local inflammation leads to fibrosis and eventually to cancer. Nonalcoholic fatty liver disease (NAFLD) is a precursor for nonalcoholic steatohepatitis (NASH). NAFLD and NASH (1) lead to cirrhosis and hepatocellular carcinoma, (2) increase the risk of liver resection, and (3) compromise the outcome of liver transplantation. Similarly, in the pancreas nonalcoholic fatty pancreas disease (NAFPD) may lead to nonalcoholic steatopancreatitis (NASP). NAFPD and NASP may (1) promote the development of chronic pancreatitis and pancreatic cancer, (2) exacerbate the severity of acute pancreatitis, and (3) increase the risk of pancreatic surgery. In the gallbladder nonalcoholic fatty gallbladder disease (NAFGBD, cholecystosteatosis) may lead to steatocholecystitis. Cholecystosteatosis may be an explanation for (1) the increased incidence of chronic acalculous cholecystitis and (2) the increased number of cholecystectomies.

Key Words: *adipokines, cholecystosteatosis, obesity, steatohepatitis, steatopancreatitis*

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motion picture which provides the subtitle for this Presidential Address.

The obesity epidemic

In the USA obesity has become epidemic over the past 15 years. Obesity is currently defined as a body mass index (BMI) of >30. In 1990 only 10–12% of the US population had a BMI >30. However, by 1995, 14–16% of Americans met this definition of obesity. In 2000, 18–20% of the US population were obese, and in 2005 nearly 25% of Americans had a BMI >30. The obesity problem is not confined to the USA but is truly a global epidemic. In the Americas outside of the USA obesity is increasing in developing countries. In Europe, the percentage of people who are obese varies among the many countries from 10% to 40%. In Africa and Asia the problem of obesity is greater in urban than in rural areas because of the relative increased availability of food and decreased level of activity. As in the USA and in Europe, the problem of obesity is growing rapidly in several countries in south-east Asia.

Diet and obesity

A key factor in the obesity epidemic is diet. Both dietary fats and carbohydrates are likely to be playing a role. For some time, the importance of dietary cholesterol has been appreciated in the pathogenesis of cardiovascular disease. As a result, the concept of 'good' and 'bad' cholesterol has emerged. Consequently, high density lipoprotein (HDL) cholesterol has been termed 'good' whereas low density lipoprotein (LDL) cholesterol has been termed 'bad'. However, very low density lipoproteins (VLDL) also are not good. Therefore, to fit the terminology of this talk, cholesterol carriers can be termed 'good' (HDL), 'bad' (VLDL), and 'ugly' (LDL).

Similarly, fatty acids may be grouped into three categories based on their relative value for health (Table I). In general, polyunsaturated fatty acids (PUFA) and omega-3 fatty acids are 'good'. In comparison, monounsaturated and saturated as well as omega-6 fatty acids are 'bad'. Even worse, trans fatty acids, sphingolipids, and ceramides are the most 'ugly'. Among the various oils and fats that we eat, the relative proportion of PUFA, monounsaturated fatty acids (MUFA), and saturated fatty acids are represented in Figure 1. At one end of the spectrum, fish oils, which are entirely PUFA and omega-3 fatty acids, fall in the 'good' category. At the other end of the spectrum, butter fat and animal fats have the highest percentage of saturated fatty acids and other toxic fats which make them the most 'ugly'.

Table I. Good, bad, and ugly fatty acids.

Good	Bad	Ugly
Polyunsaturated	Monounsaturated Saturated	Trans fatty acids
Omega-3	Omega-6	Sphingolipids Ceramides
Fish oil	Peanut oil	Animal fat
Corn oil	Olive Oil	Butter fat

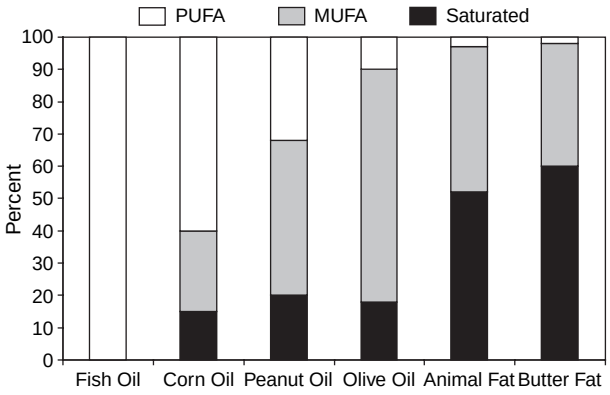

Figure 1. Fatty acids in various dietary oils and fats. PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids.

Coincident with the obesity epidemic in the United States and around the world has been the proliferation of 'fast food' restaurants. These establishments have been serving diets high in saturated and trans fatty acids, 'ugly' fats. At the same time the per capita consumption of 'soft drinks' has more than doubled in many parts of the world. These drinks are rich in high fructose corn syrup. Interestingly, the rise in consumption of high fructose corn syrup has paralleled the obesity epidemic (Figure 2). Unfortunately, an unproven theory suggests that drinks with high fructose corn syrup as the primary carbohydrate may be another factor leading to the increased incidence of obesity. Unfortunately, the typical fast food diet has more than double the number of calories (3800 versus 1800) of a 'balanced' diet. Moreover, a fast food diet has twice as many carbohydrate (1900 vs 850) and fat (1500 vs 750) calories with a dramatic increase in saturated fats. Thus, the globalization of certain fast foods and soft drinks may, in part, be contributing to the obesity epidemic.

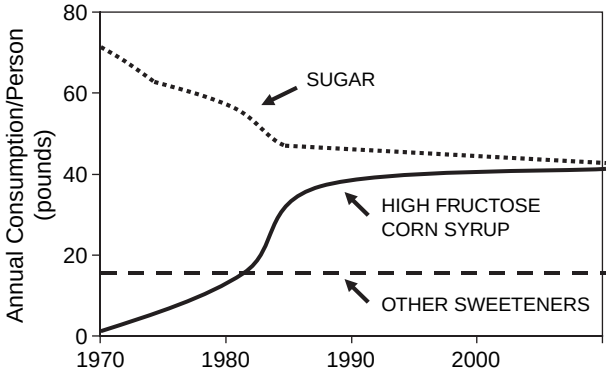

Figure 2. Annual consumption of sugar, high fructose corn syrup, and other sweeteners in the United States.