MILK HOMOGENIZATION AND HEART DISEASE

By Mary G. Enig, PhD

One widely held popular theory singles out homogenization as a cause of the current epidemic of heart disease. The hypothesis was developed by Kurt A. Oster, MD and studied from the early 1960s until the mid 1980s. In studying and comparing the structure and biochemistry of healthy and diseased arterial tissue, Oster investigated *plasmalogen*, an essential fatty component of many cell membranes in widely scattered tissues throughout the human body. *Plasmalogen* makes up a substantial part of the membranes surrounding heart muscle cells and the cells that make up the walls of arteries. It is also present in the myelin sheath surrounding nerve fibers and in a few other tissues. But it is not found in other parts of the human anatomy.

Oster discovered that heart and artery tissue that should contain *plasmalogen* often contained none. It is well known that atherosclerosis begins with a small wound or lesion in the wall of the artery. Oster reasoned that the initial lesion was caused by the loss of *plasmalogen* from the cells lining the artery, leading to the development of plaque.

The big question was what caused the lack of *plasmalogen* in the heart muscle and the tissue lining the arteries. Oster believed that the enzyme xanthine *oxidase* (XO) has the capacity to oxidize, or change, *plasmalogen* into a different substance, making it appear that the *plasmalogen* had disappeared. The body makes XO, but XO and *plasmalogen* are not normally found in the same tissue; the heart, therefore, normally contains *plasmalogen* but not XO. In a paper published in 1974, Oster argued that the presence of XO in the liver and in the mucous membrane of the small intestine was directly responsible for the natural absence of *plasmalogen* from the cell membranes at these sites.[1] If XO somehow made its way to the heart and its arteries, that might explain the absence of *plasmalogen* in the surgical specimens and autopsy tissues from pathological hearts.

What was the source of the XO found in the autopsy tissues? Normal human serum (the fluid part of the blood) does not contain XO. Oster and his partner Ross considered two possible sources. One was liver cells; patients with acute liver disease showed increased serum levels of *xanthine oxidase*, and those with chronic liver disease occasionally showed moderate elevations. Another potential source was cow's milk, "…presently under investigation in this laboratory since it has been shown that milk antibodies are significantly elevated in the blood of male patients with heart disease."[2]

Cow's milk is the most widely consumed food containing high levels of XO. Thorough cooking destroys XO, but pasteurization destroys only about half of the XO in milk.

Knowing this, Oster now looked for a link between XO in milk and the loss of *plasmalogen* in arteries and heart muscle tissue.

He knew that people have drunk milk for upwards of 10,000 years, and that milk and milk products were central in the dietaries of many cultures. But the epidemic of atherosclerosis was recent. These facts argue against traditional milk and milk products being the culprit. But the homogenization of milk became widespread in America in the 1930s and nearly universal in the 1940s—the same decades during which the incidence of atherosclerotic heart disease began to climb. Oster theorized that the homogenization of milk somehow increased the biological availability of *xanthine oxidase*.

According to Oster, XO that remains in pasteurized, unhomogenized milk is found on the exterior of the membrane of the milk fat globules, where it is broken down during digestion. XO in raw milk is similarly digested. Oster postulated that because homogenization reduces the fat globules to a fraction of their original size, the XO is encapsulated by the new outer membranes of the smaller fat globules which form during the homogenization process. He believed that this new membrane protected the XO from digestive enzymes, allowing some XO to pass intact within the fat globules from the gut into the circulatory system when homogenized milk is consumed.[3] He referred to these fat globules as liposomes and argued that the liposomes carrying XO were absorbed intact. After entering the circulation, they travel to the capillaries, where the lipoprotein membranes appear to be digested by the enzyme lipoprotein lipase, thus freeing the XO for absorption into the body, including the heart and artery tissues, where it may interact with and destroy *plasmalogen*.

In essence, Oster's theory replaces cholesterol as the cause of heart disease with another mechanism, summarized as follows:

Homogenization causes a supposedly "noxious" enzyme called *xanthine oxidase* to be encapsulated in a liposome that can be absorbed intact.

XO is released by enzymatic action and ends up in heart and arterial tissue where it causes the destruction of a specialized protective membrane lipid called *plasmalogen*, causing lesions in the arteries and resulting in the development of plaque.

Neither the opponents nor the proponents of the *xanthine oxidase/plasmalogen* hypothesis have presented convincing evidence in all of their writings. However, the more scientific reviews questioned the validity of Oster's hypothesis, and pointed to some of the inconsistent findings.

A fundamental flaw in Oster's theory involves the difference between a fat globule and a liposome. Fat globules basically contain triglycerides and cholesterol encapsulated in a

lipid bilayer membrane composed of proteins, cholesterol, phospholipids and fatty acids. They occur naturally in milk in a wide range of sizes. The fat globules in unhomogenized bovine milk are both very small and very large, ranging in size from 1,000 nanometers to 10,000 nanometers. After homogenization, the average globule size is about 500 nanometers with a range from 200 nanometers to 2000 nanometers.

Oster considered homogenization of cow's milk to be a "procedure which foists unnaturally small particles on our digestive tracts."[4] Yet sheep's milk fat globules are reported to be "very small. . . [and consequently]. . . easier to digest" and in fact globules from this milk are described as "naturally homogenized."[5] The milk fat globule membrane from sheep's milk does not separate and butter cannot be made from such milk even though there is twice as much fat in sheep's milk as in cow's milk. The fat globules from goat's milk are similarly small. Once again, goat's milk is considered easier to digest than cow's milk for this reason. So there is nothing unnatural about small milk fat globules.

Fat globules of all sizes are broken down during digestion, releasing the hundreds of thousands of triglycerides as well as any enzymes they contain. (Milk fat globules actually contain more than seven enzymes, of which XO is one. The other major ones are NADH2, iodonitrotetrazolium, 5-nucleotidase, alkaline phosphatase, phosphodiesterase and gamma-glutamyltranspeptidase.) These enzymes are broken down into individual amino acids (enzymes are specialized proteins) and the triglycerides are broken down into individual fatty acids and monoglycerides.

Although Oster described these small milk fat globules in homogenized milk as liposomes, several researchers have pointed out that liposomes are very different in basic composition. Liposomes are typically 200 nanometers or less in size and do not contain complex protein components. Liposomes do not occur in nature but were developed by scientists as a way of delivering components such as drugs to the cells in the body. They are composed of a phospholipid layer in which the phosphorus moiety is on the outside and the lipid moiety is on the inside. The layer encapsulates a watery liquid, not fatty acids. A liposome is not broken down during digestion. For this reason, scientists have looked at liposomes as a way of delivering compounds taken orally to the cells. In fact, a 1980 study led by Oster's colleague D. J. Ross reported that liposome-entrapped insulin effected blood sugar-lowering in diabetic rats.6 Ross claimed that this proved that large molecules could be absorbed.

A team led by A. J. Clifford looked carefully at Oster's theories. In a study published in 1983,[7] they noted that "neither liposome formation during homogenization of milk nor absorption of intact liposomes from the gastrointestinal tract has been demonstrated." In reviewing the major published findings, Clifford reported that "absorption of dietary *xanthine oxidase* has not been demonstrated." Clifford's team cites studies showing lack

of activity of serum *xanthine oxidase* from pigs and humans fed diets that included milk or were without milk[8,9] Further, Clifford's team noted that "a relationship between intake of homogenized ‘dairy foods' and levels of *xanthine oxidase* activity in the blood has not been established."

There was even one study which showed an increase in serum *xanthine oxidase* when corn oil was fed, whereas milk and cream showed no such increase.[10] Oster had argued that homogenization came into widespread use during the 1930s and 1940s, the same years during which heart disease incidence went up dramatically. But these were the same years in which vegetable oils came into widespread use. (And if Oster's theories are correct, then only those who drink modern milk would get heart disease, a conclusion that is obviously untrue.)

As for Ross's study on insulin, Clifford argued that recent evaluation by others showed the insulin phenomenon to be an artifact of the methods used and not due to the delivery of insulin to the cells. Thus one of Oster's published proofs turned out to be erroneous. (In fact, scientists have subsequently tried to use liposomes in humans as a way of delivering insulin taken orally to the cells but without success. However, liposomes have been used successfully to deliver an enzyme needed for the treatment of Gaucher disease.) When the Clifford team examined the electron micrograph presented in Ross's 1980 paper, he reported that it did not match the typical liposome stucture as reported by a noted authority in liposomes.[11]

In the second part of his theory, Oster maintains that XO causes the destruction of *plasmalogen*. However, Clifford's team reported that "a direct role for *xanthine oxidase* in *plasmalogen* depletion under physiological conditions has not been established." They cite animal studies where bovine *xanthine oxidase* was given intravenously in large doses.[12] This treatment failed to deplete *plasmalogen* in the arteries or in the coronary tissue, nor did it introduce formation of plaque.

The fact that Oster's theory has been disproven does not mean that the homogenization process is benign. During homogenization there is a tremendous increase in surface area on the fat globules. The original fat globule membrane is lost and a new one is formed that incorporates a much greater portion of casein and whey proteins.[13] This may account for the increased allergenicity of modern processed milk.

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