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Type of Fatty Acids, Lipoprotein Secretion from Liver and Fatty Liver Syndrome in Laying Hens

Rahim Aydin

Department of Animal Science, Kahramanmaras Sutcu Imam University, 46060 Kahramanmaras, Turkey

Abstract: Unlike other vertebrates, liver is the main site of lipid biosynthesis and is particularly very active in egg laying adult females. Yolk lipids and proteins are secreted as lipoproteins under the influence of estrogen in the liver. When hepatic lipogenesis exceeds the capacity of fat transport as lipoproteins, triacylglycerols commence to accumulate in the liver, leading to fatty liver syndrome. Fatty liver syndrome is an important metabolic disorder in laying flocks after they reach peak in egg production. The liver is generally enlarged, pale and shows extreme infiltration of fat and hemorrhages. It is a problem associated with the transport of triacylglycerols from liver to the developing oocyte. The effect of type and level of certain fatty acids may play an important role in the occurrence of the disorder. There is a correlation between delta-9 desaturase enzyme activity and secretion of very low-density lipoproteins from the liver. Certain fatty acids (i.e. sterculic acid, conjugated linoleic acids) inhibit the activity of this enzyme in the liver and cause lower levels of oleic acid which has a significant role in the secretion of triacylglycerols from chicken hepatocytes compared to other fatty acids such as linoleic or palmitic acids.

Key words: Fatty acids, lipoprotein secretion, fatty liver syndrome and laying hens

Introduction
Fatty liver syndrome (FLS) is one of the most important metabolic disorders seen in laying hens in the period of high production. The first sign of the disease is often an increase in mortality in the flocks. The dead chickens have generally enlarged and pale livers. Liver cells distended with fat vacuoles and different size of hemorrhages (Riddell, 1997).

Fatty liver in chickens results from the excessive accumulation of fats in hepatocytes when lipoprotein transport is disrupted. The fat content of liver in the chicken ranges from 40% to 70% dry weight (Riddell, 1997). The actual cause for the disease is not known. To understand the disease condition in chickens, one has to understand the normal fat transport or secretion from liver to the circulation or other tissues.

Lipid Biosynthesis in Avian Species: Unlike mammals whose adipose tissue has an important role in *de novo* fatty acid synthesis, liver is the main site of synthesis and incorporation of lipids such as triacylglycerols and cholesteryl esters into lipoproteins in avian species (Brady *et al.*, 1976). It is particularly very active in adult females producing eggs (Klasing, 1998). Two thirds of the total lipid biosynthesis in domestic fowl occurs in the liver (Saadoun and Leclercq, 1983). The production of a clutch of eggs requires large amounts of lipids, which is mostly synthesized during the several days prior to ovulation (Klasing, 1998). Although a laying hen may receive 3 g of fat per day from a commercial laying diet, the average egg yolk contains 6 g lipid (Griminger, 1986). Therefore, *de novo* hepatic fatty acid synthesis in a female hen is essential to meet the lipid requirement of producing an egg.

Avian Lipoproteins and Fat Transport from Liver to Developing Oocyte: As *de novo* fatty acid synthesis is limited in extra hepatic tissues, the liver is particularly active in the synthesis of fatty acids in laying birds. At the onset of ovulation, yolk lipids and proteins are synthesized as lipoproteins under the influence of estrogen (Speake *et al.*, 1998) and sent from the liver to the oviduct via circulation. Very low density lipoprotein (VLDL) is the major lipoprotein responsible for the transport of lipids from hen's liver to oocyte and accounts for 60% of the dry yolk mass (Speake *et al.*, 1998). This lipoprotein has unique structural and biochemical properties for targeting into the ovary. VLDL has apoprotein VLDL-II (apo-II) on its surface, making it a poor substrate for lipoprotein lipase (LPL). Consequently, the triacylglycerols within VLDL are not well used by skeletal muscle or adipose tissue. Its small size permits it to pass through the granulosa basal lamina of the ovarian follicle and bind to the apolipoprotein B (apo-B) receptor on the oolemma (Klasing, 1998). Vitellogenin is another lipoprotein synthesized in the liver and functions in the transport of lipids from liver to the oocyte and accounts for about 24% of the dry mass of egg yolk (Speake *et al.*, 1998). A 95 kDa protein receptor was found in the oocyte membrane by using ligand blotting and filter-binding assays (Nimpf *et al.*, 1989). The binding is mediated by the apo-B moiety of VLDL. These lipoproteins are released into the oocyte and the receptors are recycled

back on to the plasmalemma. After the receptor-mediated endocytosis, the apo-B of the VLDL particle undergoes specific proteolysis (Nimpf et al., 1989).

Type of Fatty Acids and Triacylglycerol Accumulation in Liver: Specific fatty acids are metabolized differently and have different regulatory roles in cellular metabolism and signaling. Number and chain length of carbon, position of double bonds and conformation are important factors influencing the metabolism of fatty acids. Overproduction of lipoproteins by the liver was reported to be responsible for hyperlipidemia (Teng et al., 1986). There are certain fatty acids that contribute hepatic lipidosis. It was reported that dietary menhaden oil rich in n-3 fatty acids contributed to hepatic lipidosis in laying hens (Elswyk et al., 1994). In humans, it was shown that n-3 fatty acids decreased serum triacylglycerols (Harris, 1989). The actual mechanism how n-3 fatty acids decrease the level of triacylglycerols in the blood stream is unknown. It is also not known if n-3 fatty acids cause declines in the level of serum triacylglycerols by increasing the oxidation of fats in the liver. Triacylglycerol secretion in the form of VLDL from liver cells is highly dependent on the activity of stearoyl-CoA desaturase, an enzyme converting saturated fatty acids into monounsaturated fatty acids (Cook, 1991). It was shown a correlation between plasma VLDL and stearoyl-CoA desaturase enzyme activity (Legrand & Hermier, 1992). Hepatic packaging and secretion of VLDL require synthesis of apoB-100 as well as sufficient amount of oleic acid (C18:1, n-9), originating from the diet or synthesized by stearoyl-CoA desaturase (Ntambi et al., 1999). A previous in vitro study showed that C18:1 (n-9) enhanced the secretion of triacylglycerol from hepatocytes (Legrand et al., 1997). In the studies conducted, C18:1 (n-9) was shown to be the most effective fatty acid facilitating the secretion of triacylglycerols in a form of lipoproteins (Davis and Boogaerts, 1982; Kohout et al., 1971). Conjugated linoleic acid (CLA) mixture was shown to decrease plasma triacylglycerol as well as VLDL and LDL in rabbits (Lee et al., 1994). CLA also was shown to decrease apoB-100 synthesis and triacylglycerol secretion in HepG2 cells (Lee et al., 1998). In recent studies, researchers showed that C18:1 (n-9) stimulated the synthesis and secretion of VLDL and apoB-100 in cultured hepatocytes (Moberly et al., 1990). These studies suggested that CLA might have decreased VLDL and apoB-100 secretion due to its inhibitory effects on the activity of stearoyl-CoA desaturase enzyme (Ntambi et al., 1999). The mechanism by which C18:1 (n-9) activates triacylglycerol secretion remains unclear. A study demonstrated that C18:1 (n-9) protected newly synthesized apo-B, which is an important apoprotein in the secretion of triacylglycerols in VLDL, against intracellular degradation
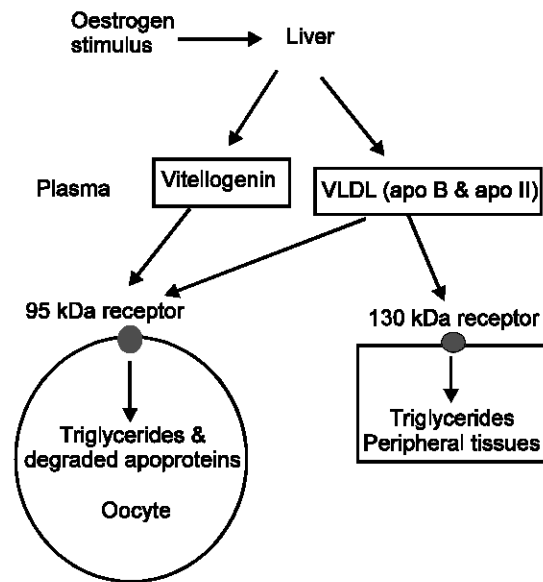

Fig. 1: Receptor-mediated uptake of lipoproteins by developing oocyte and by somatic cell (Nimpf & Schneider, 1991).

(Dixon et al., 1991). It was hypothesized that the presence of double bonds modifies the physical state of the fatty acids by lowering its melting point and might facilitate fatty acid incorporation into VLDL (Jeffcoat, 1979). Recently, CLA was reported to decrease the level of hepatic C18:1 (n-9) in a dose dependent manner in Japanese quail (Aydin and Cook, 2004). CLA was also resulted in decrease in egg size and components and an increase in the liver size. Decreased hepatic export of lipid could also explain CLA-induced increase in the liver size (Aydin and Cook, 2004).

Conclusion: Certain fatty acids may result in fatty liver by inhibition of secretion of triacylglycerols and by affecting apo-B production. The author believes that any problem disrupting lipoprotein transport will cause fatty acids to be accumulated in the liver instead of being secreted. If the level of triacylglycerols in the bloodstream decreases, this does not mean that the fatty acids will be oxidized and not accumulated.

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