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# Performance and metabolic and endocrine changes with emphasis on glucose metabolism in high-yielding dairy cows with high and low fat content in liver after calving[1]

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## ABSTRACT

Elevated liver fat content occurs in high-yielding dairy cows during the transition from pregnancy to lactation after fat mobilization and may affect hepatic glucose metabolism, but the degree of liver fat storage is highly variable. Therefore, we studied metabolic and endocrine changes and hepatic glucose metabolism in cows that markedly differ in liver fat content. Multiparous cows from the same herd with high (HFL; n = 10) and low (LFL; n = 10) liver fat contents (mean of d 1, 10, and 21 after calving for each cow, respectively) were studied from 60 d before expected calving to 56 d in milk. Cows were fed ad libitum and all cows received the same diets. Liver samples were taken on d 1, 10, and 21 after calving; mean fat content (±SEM) in liver of HFL cows was 174 ± 9.6 mg/g, whereas mean liver fat content in LFL cows was 77 ± 3.3 mg/g. Blood samples were taken 20 and 7 d before expected calving and 0, 7, 14, 28, and 56 d after calving to measure plasma concentrations of nonesterified fatty acids, β-hydroxybutyrate, glucose, insulin, glucagon, insulin-like growth factor-I, and leptin. In liver, glycogen content as well as mRNA levels of phosphoenolpyruvate carboxykinase, pyruvate carboxylase, glucose-6-phosphatase, and glucose transporter were measured by quantitative real-time PCR. Back fat thickness decreased and dry matter intake increased with onset of lactation, and back fat thickness was higher but dry matter intake was lower in HFL than in LFL. Energy-corrected milk yield did not differ between groups, but milk fat content was higher and lactose content was lower in HFL than LFL at the beginning of lactation. Energy balance was more negative in HFL than in LFL. Plasma nonesterified fatty acids and β-hydroxybutyrate concentrations increased and plasma glucose concentration tended to decrease more in HFL than LFL with onset of lactation. Glucagon to insulin ratios increased more in HFL than LFL with onset of lactation. Hepatic glycogen content was higher in LFL than HFL, whereas mRNA levels of glucose-6-phosphatase and pyruvate carboxylase were higher in HFL than in LFL, and cytosolic phosphoenolpyruvate carboxykinase mRNA level increased similarly after parturition in both groups. In conclusion, an elevated liver fat content was related to greater fat mobilization and reduced feed intake and was associated with effects on hepatic glucose metabolism. As environment and feeding management were the same, individual cow factors were responsible for differences in energy metabolism during the transition period.
**Key words:** liver fat content, dry matter intake, glucose metabolism, dairy cow

## INTRODUCTION

Because of insufficient feed intake to meet energy requirements resulting from high milk production, high-yielding dairy cows often develop severe negative energy balance (**NEB**) during early lactation (Block et al., 2001; Drackley et al., 2001; Grummer et al., 2004). Cows mobilize fat depots to provide NEFA as an energy fuel (Block et al., 2001; Drackley et al., 2001; Kokkonen et al., 2005). Hepatic fat content increases in the postpartum period as a consequence of fat mobilization (Grummer, 1993; Herdt, 2000; Vernon, 2005). Excessive NEFA concentrations and extremely high liver fat content can result in metabolic imbalances that are related to clinical diseases such as ketosis and fatty liver syndrome (Bobe et al., 2004; Ingvartsen, 2006). However, liver fat content shows large variations between cows in practice, and a high liver fat content as well as a high level of body fat may not always lead to disorders related to hepatic metabolism (McNamara, 2000; Jorritsma et al., 2001; Vernon, 2005), but may

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change hepatic energy metabolism (i.e., endogenous glucose production; Rukkwamsuk et al., 1999; Drackley et al., 2001; Ingvartsen, 2006).

Providing adequate amounts of glucose to the mammary gland is essential to enable high milk production in dairy cows (Drackley et al., 2001; Brockman, 2005). As glucose supply in dairy cows depends predominantly on endogenous production in the liver (Nafikov and Beitz, 2007), elevated fat content in liver may interfere with the capacity for hepatic glucose production during early lactation (Rukkwamsuk et al., 1999; Murondoti et al., 2004). However, measurements of impaired hepatic gluconeogenic capacity were mainly taken from cows with induced fatty liver by manipulating feeding regimens. Hepatic glucose production is clearly impaired in cows with fatty liver syndrome (Rukkwamsuk et al., 1999; Bobe et al., 2004) but, in principle, oxidation of NEFA in the liver is needed to provide ATP for gluconeogenesis (Bell, 1995; Drackley et al., 2001; Lam et al., 2003). Therefore, the range between physiological and pathological effects of fatty acids on glucose metabolism in liver is blurred and may vary among cows. In addition, long-chain fatty acids can affect systemic and hepatic glucose metabolism and decrease glucose postliver supply probably independently from the degree of fat storage in liver (Benson et al., 2002; Hammon et al., 2008).

Hepatic fat content and its effects on liver metabolism seem to be highly variable among cows. This indicates that individual cow factors beyond management and feeding conditions affect hepatic and body fat storage and consequently performance of high-yielding dairy cows during the transition period (McNamara, 2000; Ingvartsen, 2006). Such individual cow factors may be best studied in one herd under identical feeding, housing, and management conditions. We, therefore, have investigated high-yielding dairy cows with low and high liver fat contents after calving. The objective was to study effects on performance and metabolic changes with emphasis on glucose metabolism in dairy cows fed ad libitum and that markedly differed in liver fat content during the transition from pregnancy to lactation. Furthermore, we hypothesized that hepatic gene expression with regard to glucose metabolism may be impaired when high amounts of fat are stored in liver.

## MATERIALS AND METHODS

### *Animals, Husbandry, Feeding, and Measurement of Zootechnical Data*

The experimental procedures were supervised by the cattle and swine clinic, Department of Veterinary Medicine, Freie Universität Berlin, Germany, and liver biopsies were performed for diagnostic purposes. Dairy cows originated from the herd of the State Institute for Agriculture, Forestry and Horticulture of Saxony-Anhalt (Iden, Germany). In total, 48 multiparous (from second to seventh lactation) high-yielding dairy cows (>11,000 kg of milk/305 d × cow) were routinely monitored for liver fat content by liver biopsies on d 1, 10, and 21 after calving. All cows were clinically healthy. Based on mean fat content in liver on d 1, 10, and 21, the 10 cows with the highest fat content in liver after calving (**HFL**) were compared with the 10 cows with the lowest fat content in liver (**LFL**) in the herd. Mean fat content (± pooled SEM) in liver of HFL cows was 113, 213, and 197 ± 9.2 mg/g of liver wet weight on d 1, 10, and 21, respectively, whereas mean liver fat content in LFL cows was 70, 82, and 79 ± 5.4 mg/g on d 1, 10, and 21, respectively.

Cows were kept in a free-stall barn, and housing and feeding management was the same for all cows. The dry-off period started 8 wk before expected calving. Feed intake was ad libitum and was measured on an individual basis. Separate rations (TMR) were fed during the dry-off period (wk 8 to 4 before calving), close-up period (wk 3 to 1 before calving), and lactation (wk 1 to 8 after calving). Ingredients and chemical composition of the different diets are shown in Table 1. Cows had free access to water. One week before calving and from wk 2 to 8 of lactation, TMR was placed in troughs on scales, which were connected to a computer, and individual feed intake was calculated for each day. Measurement of individual feed intake around calving was unfortunately not available because the calving area in the barn was not equipped with such troughs. Dry matter content was determined daily for grass and corn silages and weekly for other ingredients. Feed samples for measurement of chemical composition of the diets were collected weekly. Dry matter, CP, crude fiber, starch, and sugar were determined according to the Weender standard procedure (Naumann and Bassler, 1993). The $NE_L$ and utilizable protein in the diets were calculated according to the German Society of Nutrition Physiology (2001).

Body weight was measured on d 60 and 20 before calving, immediately after calving, and on 7, 14, 28, and 56 DIM after morning milking. Cows were milked 3 times daily at 0400, 1200, and 2000 h, and milk yield was recorded daily. Milk samples were taken once weekly for determination of milk protein, milk fat, and lactose by an infrared spectrophotometric method (Milkoscan, Foss Germany, Rellingen, Germany) at the State Institute for Agriculture, Forestry and Horticulture (Iden, Germany). Energy-corrected milk was calculated as follows: ECM (kg) = (0.038 × g of crude fat + 0.024 × g of CP + 0.017 × g of lactose) × kg of milk/3.17.