高度腎機能障害患者における
GLP-1受容体作動薬による夜間無自覚遷延性低血糖

3つの課題

1. 成因と病態生理

2. 早期診断と治療のツールとワークフロー

3. 夜間無自覚遷延性低血糖と認知機能

MCTの投与による低血糖の改善に関する報告

Effects of medium-chain triglyceride feeding on glucose homeostasis in the newborn rat

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PEGORIER, JEAN PAUL, ARMELLE LETURQUE, PASCAL FERRE, PATRICE TURLAN, AND JEAN GIRARD. *Effects of medium-chain triglyceride feeding on glucose homeostasis in the newborn rat.* Am. J. Physiol. 244 (Endocrinol. Metab. 7): E329–E334, 1983.—The mechanism of the profound hypoglycemia that develops in newborn rats during a fast of 16-h beginning at birth has been investigated. This fasting hypoglycemia was completely reversed by giving oral medium-chain fatty acids (MCT). The rise in blood glucose induced by MCT feeding was not secondary to a decreased uptake of glucose by peripheral tissues because [6-^{3}H]glucose turnover rate was increased in MCT-fed neonates. Several lines of evidence strongly suggest that MCT feeding was associated with a stimulation of hepatic gluconeogenesis. *1*) The rate of [6-^{3}H]glucose turnover was enhanced after MCT feeding. *2*) A fivefold increase in the conversion of labeled lactate into glucose was observed in vivo after MCT feeding. *3*) The rise in blood glucose induced by MCT feeding was totally suppressed by an inhibitor of gluconeogenesis (3-mercaptopicolinate). Despite their utilization for glucose synthesis, blood levels of lactate, alanine, and pyruvate were increased two- to threefold after MCT feeding. When MCT feeding was given in association with dichloroacetate, an activator of pyruvate dehydrogenase (PDH), no increase in blood lactate, alanine, and pyruvate was observed and the rise in glycemia was prevented. This suggested that hyperketonemia due to MCT feeding could decrease the oxidation of 3-carbon glucose precursors in peripheral tissues, secondary to an inhibition of PDH, and thus enhanced their release in blood. These data indicate that MCT feeding stimulates glucose production in the newborn rat, both by increasing the availability of gluconeogenic precursors and by a direct effect on hepatic gluconeogenesis.

induced by fasting (6, 8). Similarly, an increased rate of glucose production was observed when long-chain fatty acids were added to isolated hepatocytes from 1-day-old fasting rats (11). The rat milk, a high-fat low-carbohydrate diet (16), contains 30% of the ingested calories in the form of medium-chain triglycerides (5, 25). Medium-chain fatty acids have a different metabolic fate than long-chain fatty acids. First, medium-chain fatty acids are absorbed rapidly from the gut directly into the portal vein and therefore go directly to the liver (21). In contrast, long-chain fatty acids are reesterified in the gut, packaged, and transported to the circulatory system via the lymphatics (20). Second, medium-chain fatty acids can enter freely into the mitochondria and bypass the acylcarnitine transferase step (18). In isolated hepatocytes from newborn rats, medium-chain fatty acid oxidation yields more ketone bodies than long-chain fatty acids (11, 13) and can sustain an active gluconeogenesis from lactate (11). This situation would be particularly relevant during the neonatal period because high concentrations of ketone bodies could decrease the oxidation of glucose by peripheral tissues (24) concomitantly with an increase in lactate, pyruvate, and alanine release, thus, sparing glucose and providing gluconeogenic precursors. The present study was performed to examine whether the ingestion of medium-chain fatty acids could reverse the fasting hypoglycemia of newborn rats.

MATERIALS AND METHODS

Animals

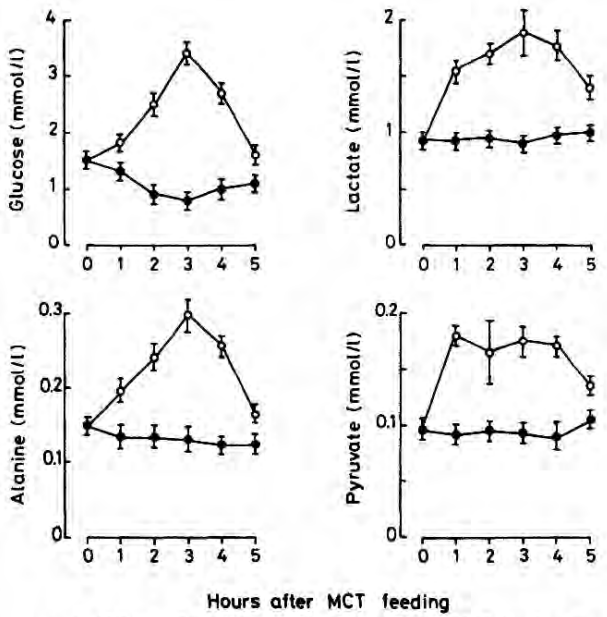

FIG. 1. Effects of medium-chain triglycerides (MCT) feeding on circulating substrates in newborn rats. Newborn rats (18-h-old) were starved from birth and fed at 13 h with a solution of NaCl (●—●) or of MCT (○—○). Each point is mean ± SE of 8–10 different animals.

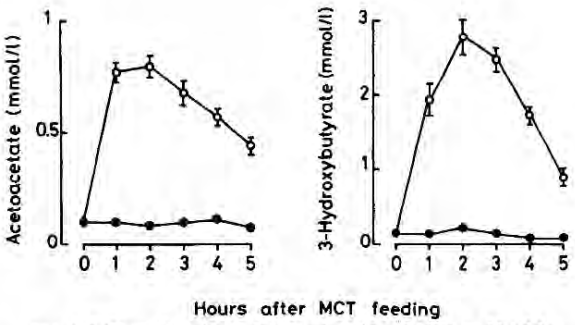

FIG. 2. Effects of medium-chain triglycerides (MCT) on blood ketone bodies in newborn rats. Newborn rats (18-h-old) were starved from birth and fed at 13 h with a solution of NaCl (●—●) or of MCT (○—○). Each point is mean ± SE of 8–10 different animals.

Pegorier JP, J.Am J Physiol. 1983 Apr;244(4):E329-34.

MCT投与の糖尿病患者の糖代謝の改善に関する報告

Dietary Substitution of Medium-Chain Triglycerides Improves Insulin-Mediated Glucose Metabolism in NIDDM Subjects

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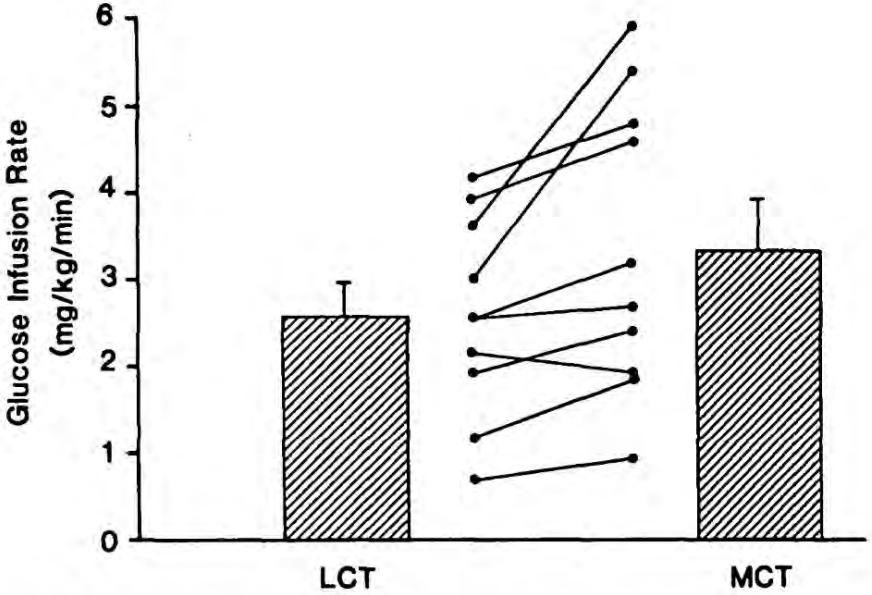


FIG. 1. Glucose infusion rates for maintenance of euglycemia during sustained hyperinsulinemia in 10 diabetic patients on medium-chain triglyceride (MCT)- versus long-chain triglyceride (LCT)-containing diets. Individualized data and means ± SE for the 2 diets are shown. The difference between the diets was statistically significant ($P = 0.01$ by Wilcoxon's paired-sample test).

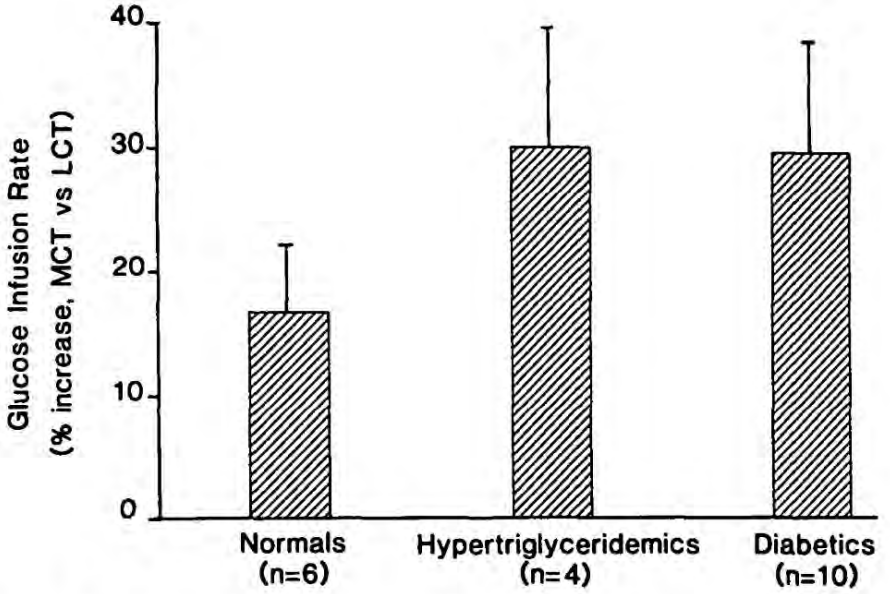
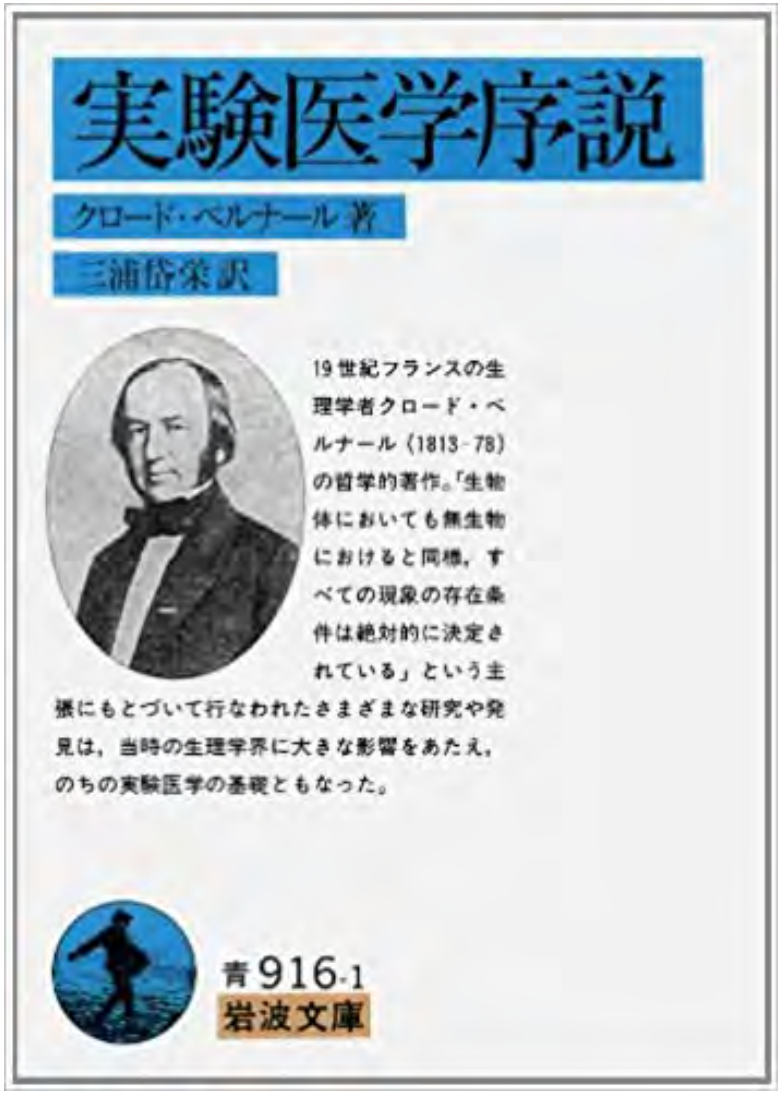


FIG. 2. Percentage increase in glucose infusion rates ($mg \cdot kg^{-1} \cdot min^{-1}$) for maintenance of euglycemia during sustained hyperinsulinemia on medium-chain triglyceride (MCT)-containing diets (100% of control) is shown for 3 groups: normotriglyceridemic control ($n = 6$), hypertriglyceridemic ($n = 4$), and diabetic ($n = 10$) subjects. Difference between affected groups and normals was not significant by Wilcoxon's unpaired analysis and analysis of variance.

Eckel RH, Diabetes. 1992 May;41(5):641-7.

現代医学は、19世紀のパリを中心とした 純粋に経験主義に基づく「病院の医学」と実験科学としての医学を目指す「研究室の医学」の統合の過程によって第一歩を踏み出した。

このような医学の一大転換期の中心人物が「生理学そのもの」と言われた実験医学の祖、生理学者クロード・ベルナール（1813～1878）である。



『自分の観念をあまりに信頼している人々は、
発見をするのにはあまり適していない。』

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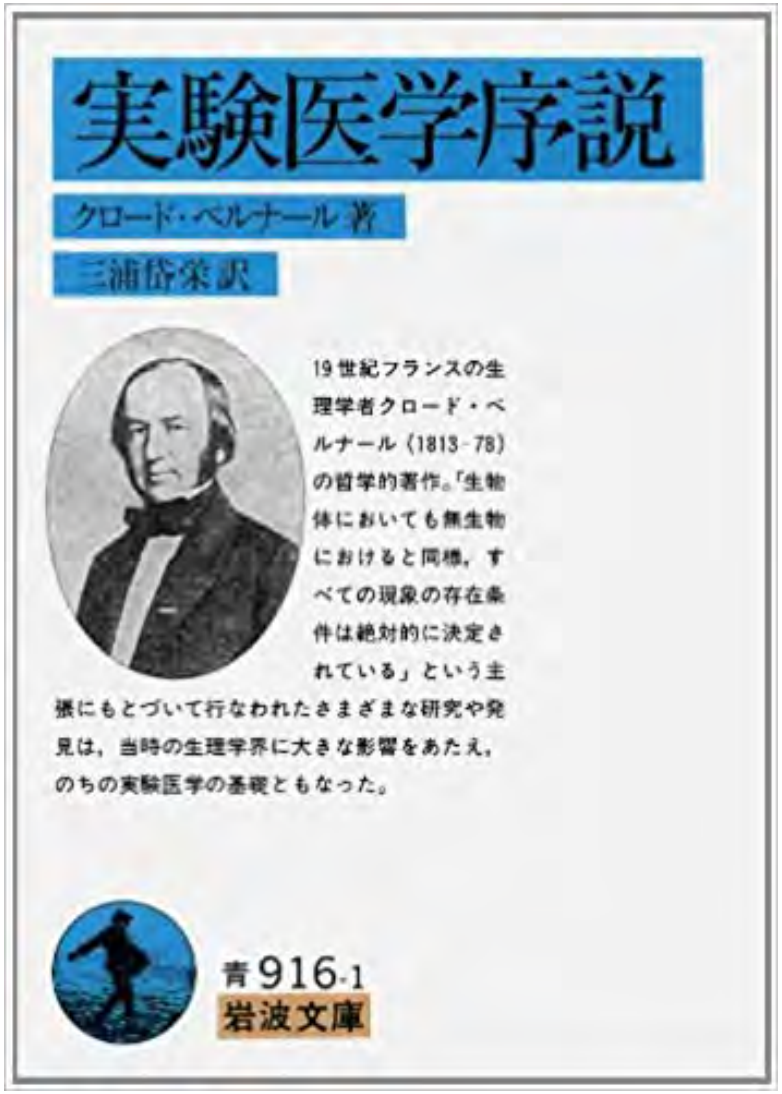

『すでに知っていることが、
私たちの学びをしばしば妨げるのだ。』