

# The Effect of Insulin on the Liver

## A Symposium

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DR. LEVINE: For the past forty years, almost since the discovery of insulin, the mode of action of insulin on the liver has attracted attention of investigators. It is known from physiological studies that the liver is a very important source of heat for the human body. It has been a source of much heat in the diabetic field—heat, light, smoke, and some blood. I had hopes that we would see more heat, more light, more smoke and more blood today, but I am sorry to say that I will prob-

ably be disappointed. It is beginning to look as if sweetness and light are invading the area. However, I am still hoping for a little clash, because it would make for greater interest. The distinguished members of the panel have each worked extensively in the field of insulin action, and have concentrated their attention, in some of their work, on the effects exerted upon the liver. I call first on Dr. Sidney Weinhouse, whose previous studies concerning insulin action on glucose handling by liver and the extrahepatic tissues are well known to all of us. He will present his views on the action of insulin on the inhibition of sugar output and uptake by the liver.

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## Effects of Insulin on Hepatic Glucose Production and Utilization

*Sidney Weinhouse, Ph.D., Bernice Friedmann, M.A., and  
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In discussing the role of the liver in diabetes, we are embroiled in an ancient controversy, which began over seventy years ago and is evidently not yet resolved. Claude Bernard, who discovered the role of the liver as a source of blood glucose, pointed out<sup>1</sup> that diabetic hyperglycemia may be due to overproduction of glucose by the liver. When Minkowski<sup>2</sup> later demonstrated the role of the pancreas in diabetes, he considered the disease a manifestation of faulty glucose utilization. The focus of this issue was sharpened when Banting and Best isolated insulin in 1921,<sup>3</sup> and the controversy has continued unabated to the present. This

is a sad reflection on our progress in the physiology of this hormone, in contrast with the spectacular development of our knowledge of its chemical structure.

If insulin lowers the blood glucose through some effect on the liver it must do so either by decreasing the hepatic glucose output or by stimulating hepatic glucose uptake, or by doing both.

### *Hepatic glucose output*

Listed in table 1 are four types of experimental observation pointing to a suppressive or restraining action of insulin on hepatic glucose output.

1. Evidence based on decreases in glucose gradients across the liver or the splanchnic tissues may be summarized by stating that despite some contradictory evidence<sup>4-6</sup> there is strong experimental support for the assumption that insulin suppresses net hepatic glucose outflow.<sup>7-11</sup>

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