



Ancient Origins of the Remarkable Ability of the Human Liver to Regenerate Itself: Three References from the Babylonian Talmud and Two References from Greek Mythology

Letter to the Editor:

We congratulate Jindal *et al.*¹ on their recent timely publication (March–April 2022) in this Journal in which they comprehensively review remarkable advances during the past two decades in the proliferation, differentiation, and storage mechanisms of hepatic progenitor cells. This research aims to provide a scientific basis to enhance hepatic regeneration to replace poorly functional liver after massive hepatic pharmacologic injury (e.g., acetaminophen ingestion), catastrophic hepatic infarction (e.g., hepatic vascular thromboembolism), subtotal hepatic resection (e.g., large focal hepatoma resection), or even potentially chronic liver injury (e.g., cirrhosis) to successfully regenerate a new, “young” liver to restore vital metabolic and homeostatic hepatic functions.

This concept counters traditional beliefs that a minimum of 25% of a human liver is needed to regenerate itself into a completely functional liver.² However, the concept that a tiny percentage of liver is needed to regenerate itself is, indeed, ancient. The Babylonian Talmud in Tractate Chullin, composed from 200 to 500 in the Common Era, states “if the liver be torn away (i.e., destroyed) but there remains (viable liver tissue) the size of an olive” the liver can successfully regenerate itself in humans.³ Notably, this claim is asserted in three different places in Tractate Chullin.^{4–6} Notably, this source also quantifies the residual amount of viable liver needed for successful regeneration as “about the size of an olive” which weighs on average about 5 gm compared with an average adult healthy human liver that weighs about 1.5 Kg.

The remarkable ability of the human liver to regenerate itself was also alluded to in an even earlier Greek myth that Zeus punished Prometheus to punish Prometheus (for stealing fire and giving it to mankind) by an eagle swooping down daily to consume part of his liver, only to completely regenerate his liver nightly for eternity.^{7,8} The ubiquity of this concept in ancient Greece is evidenced by Tityus also completely regenerating his liver nightly after receiving the identical punishment by Zeus.⁹ This report is also consistent with numerous clinical reports of the human liver regenerating itself following massive hepatic destruction. For example, Khoury *et al.*¹⁰ reported in 1990 a patient recov-

ered completely, with restoration of relatively normal hepatic function, after suffering massive hepatic infarction from a hypercoagulopathy (lupus coagulant or anticardiolipin syndrome) associated with systemic lupus erythematosus. The findings of Jindal *et al.*¹ are also consistent with the known ability of the liver in rats to successfully regenerate themselves completely if rats are provided with free access to drink water containing glucose.¹¹

The work by Jindal *et al.* reviews exceptional progress during the past twenty years in use of hepatocyte progenitor cells, stem cells, and other progenitor cells to enhance hepatocyte regeneration in combination with optimizing intracellular matrix composition, paracrine effects, cytokines, and growth factors that lay the groundwork for anticipated future clinical advances in liver regeneration. Remarkably, ancient Talmudic ritual and ancient Greek mythology adds some perspective to this modern notion of liver regeneration by apparently recognizing the exceptional capacity of the liver to regenerate itself in comparison with most other mammalian body organs (e.g., brain).

The views reported herein represent the opinions of the authors and do not reflect the position of the U. S. Veterans Administration or the United States Government.

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