probiotic Lactobacillus species. The microarray data were highly variable across individuals: transcriptional responses were more similar for different treatments on the same individual than for the same treatments on different individuals. Nevertheless, network analysis of the transcriptomes identified a number of networks that responded to the different Lactobacillus species, and certain networks that responded to more than one of the probiotic bacteria. Although the actual transcriptional levels varied among individuals across the study, the network responses appeared to be conserved, allowing interrogation of what otherwise seemed to be a near-uninterpretable dataset.

Although the regulatory networks described in Van Baarlen were not created from transcriptomic data (instead, networks were created by combing the literature for experimental data), they demonstrate the power of gene network discovery for analysis of large transcriptomic datasets in symbiotic systems. Network creation from transcriptomic data has recently been used to study mammalian gastrointestinal symbiotic systems, and has also been used successfully, sometimes with experimental verification, with transcriptomic data in a variety of organisms.

Conclusions. Omics approaches are taking our understanding of symbioses to a new level of molecular sophistication. Indeed, the monumental efforts to define and characterize human-associated microbial communities by initiatives such as the Human Microbiome Project are attainable only by implementation of omics methods. Some types of interactions, such as regulation of the nutritional status and cell proliferation patterns of the host, make intuitive sense, but interpreting other results of omics experiments will require further research on the function of certain gene classes. For example, one-third of the proteins that differ in abundance between pea aphids bearing and experimentally deprived of their Buchnera bacteria are cuticular proteins, a result that cannot be related to any currently known aphid-Buchnera interaction. As this result illustrates, omics experiments have great potential to spur efforts to understand molecular function in symbiosis.

From a symbiotic perspective, gene classes of particular potential interest are those that respond specifically to perturbation of the symbiosis and have no known function. Conserved genes of this class may represent the deep history that defines the predisposition of animals for symbioses with microorganisms, while recently evolved, lineage-specific genes may underpin the unique functions of individual associations. Elucidation of these patterns will contribute not only to our understanding of symbiosis, but also to the resolution of central problems posed by conserved and lineage-specific genes of no known function.

BIOCHEMICAL INDICATORS IN ADRENAL DISORDERS IN THE BACKGROUND OF LIVER CIRRHOSIS

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Introduction. Hypoproteinaemia states represent a challenge when assessing hypothalamus-pituitary-adrenal (HPA) axis functionality. This scenario is common in cirrhosis and further complicated by significant overlap between clinical manifestations of adrenal insufficiency (AI) and decompensated liver disease. Additionally, AI exists along a spectrum in patients with cirrhosis and

thus it is incumbent on the evaluating physician to determine whether adrenal function is sufficient, relatively insufficient (RAI), or absolutely insufficient (absolute AI).

Relative adrenal insufficiency was originally described in the critically ill population and is currently termed critical illness-related corticosteroid insufficiency (CIRCI). Marik et al. first reported the condition in patients with cirrhosis in 2005, naming it the “hepato-adrenal syndrome”. At baseline, patients have adequate adrenal reserve to meet homeostatic demands but are unable to either produce excess cortisol or respond at the tissue receptor level to increased cortisol production.

The aim. Study of literary and meta data on the mechanism of influence of liver pathology on adrenal function.

Materials and methods. Resources of scientific articles, monographs, and analytical data from practical medicine.

Research results. The liver is the principal site of apolipoprotein synthesis. One of the key apolipoproteins, ApoA1, comprises a large fraction of high-density lipoprotein (HDL) particles.

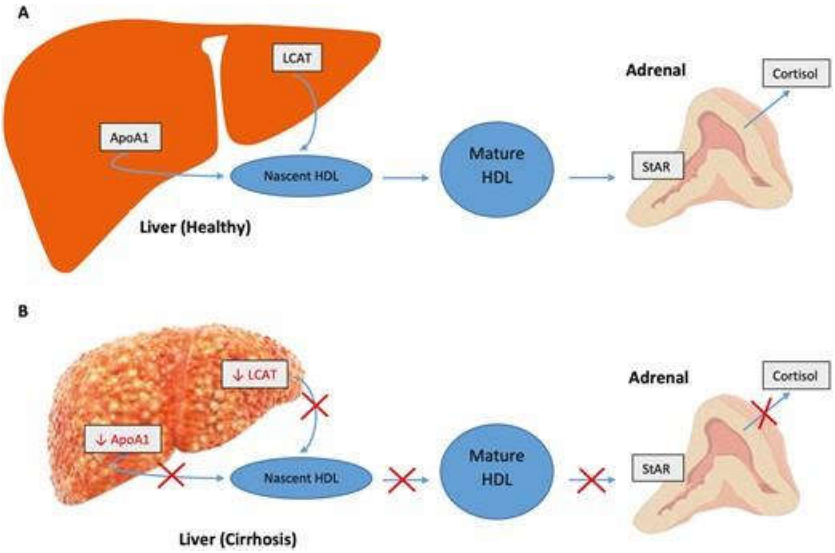

Figure 1. Lipid metabolism and the adrenal gland.

The hepatically derived lecithin-cholesterol acyltransferase enzyme (LCAT) binds to ApoA1 on HDL and esterifies free cholesterol. Once this process is complete, the HDL particle is mature and can be trafficked to peripheral tissues **(Fig. 1)**. Within the adrenal gland, cholesterol is offloaded, and uptake occurs through the mitochondrial steroidogenic acute regulatory protein (StAR), which is the rate-limiting step in the production of steroid hormones (A). In cirrhosis, this process is disrupted by decreased hepatic synthesis of both ApoA1 and LCAT, leading to impaired formation of adequate mature HDL molecules to provide adequate substrate for normal adrenal steroidogenesis. However, whether this leads to a clinically significant decrease in cortisol production is unknown (B).

Besides dyslipidaemia, several other mechanisms **(Fig. 2)** are conceptually valid for implication in the development of AI in cirrhosis but require further study:

- ❖ deficient intrinsic adrenal enzymatic activity leading to either excess precursor steroids (in relation to cortisol) or pathway shunting.
- ❖ altered vascular tone in the setting of splanchnic vasodilation and low effective circulating volume leading to chronic adrenal hypoperfusion.
- ❖ suppressive effects of pro-inflammatory cytokines on HPA axis hormonal secretion.

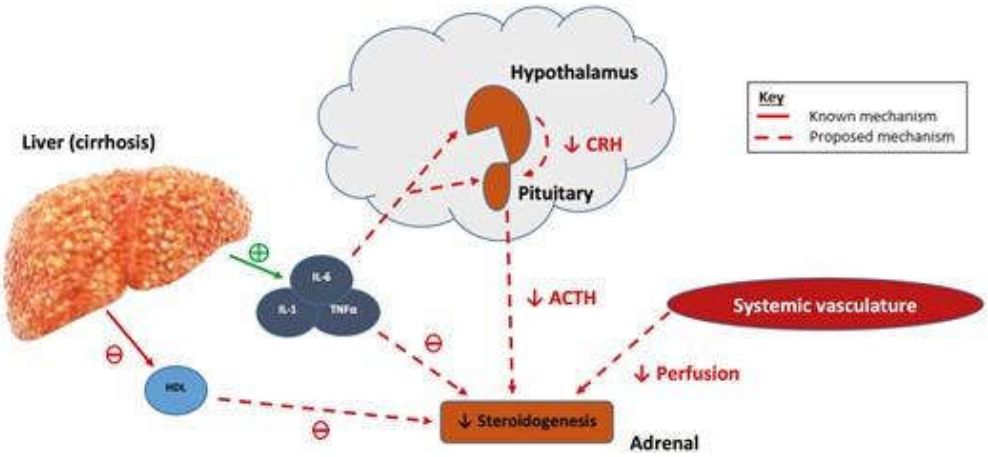

Figure 2. Pathogenesis of adrenal insufficiency in cirrhosis.

Conclusions. Assessment of AI in cirrhosis is difficult and requires careful attention to many patient-related variables. Traditional endocrinology approaches to the diagnosis and management of AI do not account for the physiology in the cirrhotic state. Importantly, the majority of AI in cirrhosis is "relative" but represents an independent predictor of short- to medium-term mortality. More research is needed to fully understand the mechanisms underlying AI in cirrhosis. Given the lack of clear benefit of glucocorticoid replacement in many common clinical scenarios, low TC levels in the absence of consistent signs and symptoms of AI do not warrant empiric treatment. Additionally, clinicians should consider the risks of exogenous glucocorticoids, including exacerbating baseline immunodeficiency and/or induction of an iatrogenic Cushing syndrome.

INFLUENCE OF PHOSPHOLIPASE A2 ENZYME ACTIVITY ON THE DEVELOPMENT OF ATHEROSCLEROSIS

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Introduction. Circulating levels and enzymatic activity of two families of phospholipase A2 enzymes, secretory phospholipase A2 (sPLA2) and lipoprotein-associated phospholipase A2 (Lp-PLA2), have been evaluated as biomarkers of cardiovascular risk in population-based studies inclusive of apparently healthy individuals, and patients with established coronary heart disease (CHD). In the EPIC (European Prospective Investigation of Cancer) Norfolk study, the increased CHD risk associated with the oxidation specific biomarker, oxidized phospholipids on apolipoprotein B (apoB) or lipoprotein(a), was enhanced further among individuals with high sPLA2 concentration and activity than Lp-PLA2 activity. This study and other observational studies have shown that both enzyme concentration and activity predict incident cardiovascular events. The evidence that these phospholipase A2 enzymes retain their importance as biomarkers of risk in statin-treated patients is less certain; however, in one trial, LpPLA2 concentration was associated with future CVD events in models that adjusted for baseline covariants and apolipoprotein concentrations. The importance of this phospholipase A2 enzyme biomarker data should not be overemphasized, as circulating levels of these two groups of PLA2 enzymes and their various members may not encompass their multifarious downstream pro-atherosclerotic effects