Veterinary Bioscience: Metabolism

WEEK 3 – THE LIVER IN DISEASE

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INTENDED LEARNING OUTCOMES

At the end of this lecture, you should be able to:

- describe the various patterns of necrosis that are seen in livers and understand their diagnostic significance
- recognise the considerable regenerative capacity of the liver and explain the means by which the organ can regenerate after a necrotising event
- understand the source and potential significance of fibrosis of the hepatic parenchyma
- define cirrhosis and recognise a cirrhotic liver from its gross appearance
- understand the potential consequences of cirrhosis.

KEYWORDS

focal necrosis, multifocal necrosis, zonal pattern, zonal necrosis, hypoxia, hepatic congestion, hepatotoxins, massive necrosis, reactive oxygen species, antioxidants, hepatic regeneration, oval cells, ductal precursor cells, biliary hyperplasia, fibrosis, stellate cell, post-necrotic scarring, diffuse fibrosis, bridging fibrosis, cirrhosis, portal hypertension, acquired portosystemic shunting

LECTURE 9 – NECROSIS, REGENERATION AND REPAIR OF THE LIVER

The high metabolic rate of hepatocytes and their receipt of potentially noxious agents in the portal venous blood that drains the gastrointestinal tract render them susceptible to lethal injury. Toxins, hypoxia, a variety of infectious agents (viruses, bacteria, fungi) and parasites, immune-mediated inflammation and reactive oxygen species (free radicals) are important causes of **hepatic necrosis**. The gross and microscopic distribution pattern of necrosis provides important clues to the likely causes. We will review the various patterns of necrosis (**focal**, **multifocal**, **zonal** and **massive**) and explain their diagnostic significance, building on your foundational knowledge of hepatic anatomy and physiology.

A necrotising insult to the liver will usually induce some degree of fibrosis and parenchymal regeneration in animals that survive the event. The liver has considerable regenerative capacity. The means by which necrotic hepatocytes can be replaced will be discussed.

Severe, persistent or repetitive injury to the hepatic parenchyma provokes progressive **fibrosis** (collagen deposition or scar tissue formation). **Stellate cells** (located in the perisinusoidal spaces of the parenchyma) are the major source of new collagen synthesis within injured livers. Fibrosis can lead to irreversible compromise of the vascular perfusion of hepatocytes and encourage the development of abnormal vascular connections within the liver. Fibrosis that dissects through or bridges across the hepatic parenchyma is particularly likely to lead to progressive damage to the hepatocytes and ultimately cirrhosis.

Cirrhosis refers to an end-stage liver. Cirrhosis is always a generalised process that involves the entire organ and is characterised by the presence of bridging or diffuse fibrosis, the formation of numerous, hyperplastic, regenerative nodules of surviving hepatocytes, and permanent distortion of the hepatic architecture. Common causes of cirrhosis in domestic animals include persistent or repetitive exposure to plant or fungal hepatotoxins, chronic inflammation centred on the biliary tree, chronic immune-mediated inflammation of the hepatic parenchyma, chronic hepatocellular copper accumulation, and long-term therapeutic administration of certain drugs such as anti-epileptics.

Cirrhosis can lead to increased resistance to the flow of afferent portal venous blood into the hepatic sinusoids and a rise in pressure within the portal vein and its tributaries (**portal hypertension**). This in turn leads to congestion of the splanchnic viscera, ascites and, over time, **acquired portosystemic shunting**.

FURTHER READING

DL Brown, AJ Van Wettere and JM Cullen. Hepatobiliary system and exocrine pancreas. In: JF Zachary (ed.), *Pathologic Basis of Veterinary Disease*. 6th ed., Elsevier, St Louis, Missouri, USA (2017)

JM Cullen and MJ Stalker. Liver and biliary system. In: MG Maxie (ed), *Jubb, Kennedy and Palmer's Pathology of Domestic Animals*. 6th ed., Vol 2. Elsevier, St Louis, Missouri, USA (2016)