Breezy Summer Reads

Upates from the Journals

Bile Acids Rising

"Racey" Horse Tips

If liver disease were a story, you might expect it to have too many characters for a summer read but bear with me. It gets interesting.

Histologically liver disease is classified as either circulatory, biliary, parenchymal or neoplastic disease. Circulatory is broken down again into congenital vascular anomalies, hepatic congestion or portal hypertension. Biliary disease is split up into cholestasis, biliary cystic disease or atresia, cholangitis and diseases of the gall bladder itself. Parenchymal disease is a bigger family of diseases including reversible hepatocytic injury (steatosis, steroid induced or cloudy swelling), hepatic amyloidosis, hepatocellular death, inflammatory hepatopathies, hepatic abscesses and granulomas, hepatic metabolic storage diseases and the long lost cousin: miscellaneous. Nodular hyperplasia is upset at landing in the neoplastic group for fear of being given a bad reputation. The neoplastic group includes all benign and malignant liver neoplasms as well as metastatic neoplasia.

Ok – so yes it is a bit "War and Peace" with all of these disease processes. However it provides several important reminders! This list demonstrates the big limitation a basic biochemistry panel has with respect to a specific diagnosis.

Liver disease as a diagnosis is an all encompassing umbrella term.

The list reminds us of the differentials to consider if pre and post prandial bile acids come back abnormal.

Bile acids are abnormal when there is:

- Abnormal portal blood flow.
- Significant parenchymal disease resulting in an inability of the hepatocyte to produce or extract bile acids from the portal circulation.
- Impaired bile excretion (cholestasis).

Most importantly this list reminds us that liver disease is definitively diagnosed with histopathology along with adjunctive imaging. One needs biopsies from not just one lobe but multiple lobes. A definitive diagnosis has implications for treatment and prognosis!

Would it not be helpful, even dreamy, if the aforementioned bile acids could actually help differentiate the various causes of liver disease ?

Researchers in the UK attempted to do just that via a retrospective case study of 341 dogs with histology and bile acids within 7 days of the biopsy. The majority of cases had resting serum bile acids while just under half had corresponding post prandial bile acids.

Were they successful?

No, not surprisingly there was major overlap between the various liver diseases and bile acid results.

Circulatory anomalies had the highest values.

What you might find surprising is that 4/45 cases of dogs with circulatory anomalies had normal post prandial bile acids, while another two dogs had minimal elevations.

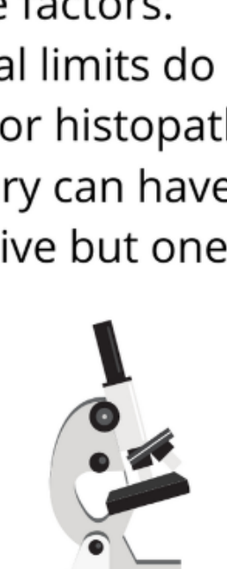
It is presumed that gall bladder responsiveness, altered peak timing, intestinal transit times as well as diurnal variations could be reasons why we might see "false negative" bile acids. On those rare occasions when you are surprised by your bile acid results compared to your clinical concern and previous diagnostics, keep this in mind.

For similar reasons it was noted that in ≈ 25% of the cases the pre-prandial bile acids were higher than the post prandial. This matches previous reports and our clinical experience.

The study was also useful in confirming that reversible hepatic injury like we see with steroid use can cause elevated bile acids. In this study 5/10 dogs with reversible hepatic injury had significantly elevated bile acids presumed due to significant hepatocyte swelling and cholestasis. These results overlapped with patients diagnosed with cholangitis, chronic hepatitis and circulatory diseases.

Take home points of this summer read ?

- Bile acids still cannot provide a linear means of categorizing liver disease. Circulatory diseases tend to have the highest values.
- A pre and post prandial bile acid test is a dynamic test dependent on multiple factors.
- Bile acids within normal limits do not rule out the need for additional diagnostics or histopathology.
- Reversible hepatic injury can have abnormal bile acids.
- Bile acids are informative but one also needs tissue!

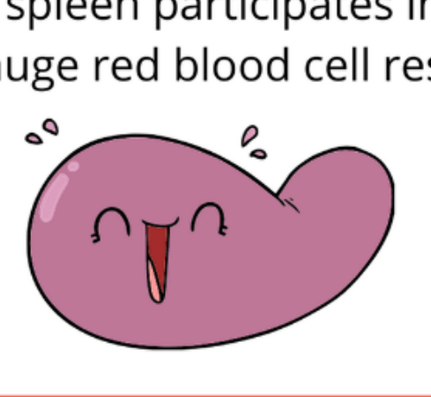


Reference: (open access)
Pena-Ramos J, Barker L, Saiz R, Walker DJ, Tappin S, Hare CHZ, Roberts ML, Williams TL, Bexfield N. Resting and postprandial serum bile acid concentrations in dogs with liver disease. J Vet Intern Med. 2021 May;35(3):1333-1341. doi: 10.1111/jvim.16134. Epub 2021 May 6. PMID: 33955592; PMCID: PMC8163115.

WHAT HAPPENS ON THE TRACK?

Racing Equine Clinical Pathology Tips and Timing!

The equine athlete is awe-inspiring to watch whether it is endurance riding, show jumping or racing. The training and exercise schedule can impact several different facets of equine clinical pathology. Red cell mass increases in response to training and age and is correlated with racing performance. A fit thoroughbred racehorse can deliver **greater than 80 liters** of oxygen per minute to the tissues thanks to these physiologic changes! The equine spleen participates in this exercise physiology as it is a huge red blood cell reservoir.



Even a walk from the stable to the track can cause a mild degree of splenic contraction however significant excitement or nervousness associated catecholamine contraction of the spleen can increase the Hct by 25%.

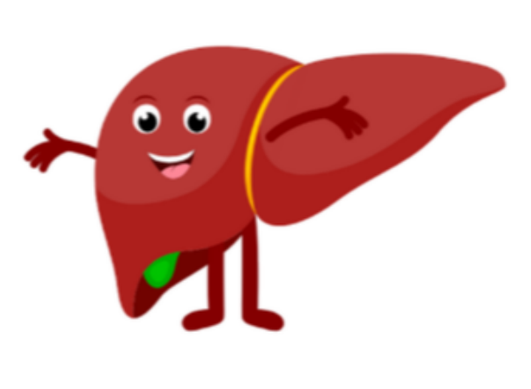
From a blood collection timing consideration it is important to know that this effect can last for at least two hours before returning to baseline.

Racing causes extravascular fluid shifts. Environment associated fluid losses include moisture lost in the breath and sweating. All of these factors will also contribute to the increased Hct post exercise.

Because training can influence the Hct one may need to pay attention to relative decreases in an individual.

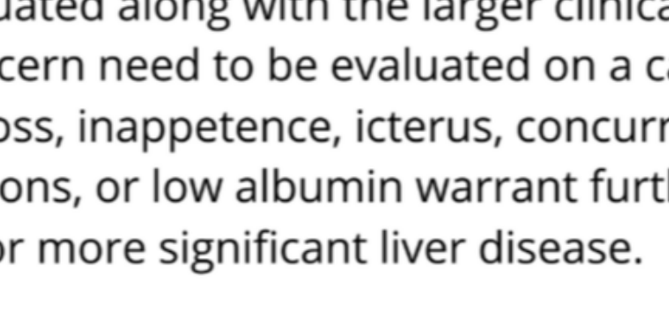
Stress or intense exercise can potentially cause a mild lymphocytosis or stress leukogram.

Mild increases in GGT and unconjugated bilirubin have been seen in outwardly healthy horses during training of which the mechanisms are unknown. GGT elevation has also been associated with poor performance.



GGT is believed to be a marker of training intensity until further research elucidates the mechanism or cause.

Viral causes of GGT elevations have been investigated to date but there is no statistical association. Liver enzymes should always be evaluated along with the larger clinical picture. Causes for concern need to be evaluated on a case by case basis. Weight loss, inappetence, icterus, concurrent liver enzyme elevations, or low albumin warrant further investigation for more significant liver disease.



Creatinine kinase (CK) and aspartate aminotransferase (AST) increase in response to muscle injury whether it be traumatic, inflammatory or necrosis related. CK climbs quickly and peak levels are within 4-6 hours. After an acute insult the CK falls very quickly given the extremely short half life of 2 hours. In response to muscle or liver injury AST peaks within 12-24 hours. Because AST is not specific to the muscle, it needs to be assessed together with the rest of the biochemical or liver panel. AST has a much longer half life of 7-8 days and takes several days to weeks for it to return to baseline after a single insult.

Submaximal exercise is not expected to cause CK or AST enzyme elevations.

Over-training should be ruled out as a cause of CK and AST elevations. If ongoing mild CK or AST elevations are noted (at rest or in response to conscientious training) this would raise concern for an underlying muscle disorder (myopathy).

A provocative test is to evaluate a CK at baseline, complete a short 12-15 minute trotting exercise and check a resting 4 hour CK. If there is a 2-4 fold rise this can also be suggestive of a myopathy.

In racing timing is everything.

The majority of a baseline database (CBC & Chemistry) is expected to return to pre-race day by 2-3 days post race however GGT, CK and AST may take longer.

Reference:
Hurcombe SDA. Clinical Pathology of the Racehorse. Vet Clin North Am Equine Pract. 2020 Apr;36(1):135-145. doi: 10.1016/j.cveq.2019.12.004. Epub 2020 Jan 25. PMID: 31992502.

Reference Range Study Complete

Thank you to everyone that participated in our reference range study. Your help was essential. We have received sufficient samples, and the study is now closed.

Monday August 2 Stat Holiday

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