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'The Quality Clinical Pathology Service'

Trace Elements in Ruminants

This information sheet will focus on the trace elements of colbalt, copper, selenium and iodine.

The main cause of trace element deficiencies is deficiency in rocks and soils and this is particularly likely to occur in management systems where the ration is largely grass and conserved forages. Sandy soils and free draining soils have lower trace element levels than clay soils and deficiencies shown by free draining soils are likely to be exacerbated by recent heavy rainfall. Poorly drained soils and soil on acid rocks such as granite also have low trace element levels. Analysis of soil should form part of the appropriate management of pastures in preparation for grazing livestock.

Four overlapping phases have been used to define the increasing deprivation of trace elements in an animal's diet. Depletion occurs when stores of the trace element in tissues and/or body fluids fall. Deficiency occurs when trace element levels, normally homeostatically retained within restricted limits in pools such as plasma, start to fall. Dysfunction occurs when trace element-dependent functions (usually enzyme related) in tissues or body fluids become rate-limited due to a reduction in the trace element. Disorder (clinical disease) occurs when livestock appear abnormal or perform poorly as a consequence of trace element restriction. Trace element testing usually involves picking up the deficiency stage, thus preventing the onset of dysfunction.

Cobalt

Cobalt is an essential trace element required for the production of vitamin B_{12} in the rumen; the latter is required for the metabolism of propionic acid via a number of coenzymes.

Cobalt deficiency therefore results in vitamin B_{12} deficiency. This may present as inappetance, ill thrift, hepatic lipidosis, anaemia, immunosuppression, reduced reproductive performance and increased neonatal mortality. Gastrointestinal nematodes also reduce the absorption of vitamin B_{12} from the gut and therefore may precipitate or exacerbate vitamin B_{12} deficiency.

Cobalt deficiency is seen particularly in unsupplemented lambs grazing pastures on cobalt deficient soils; adult sheep, calves and adult cattle are progressively less affected. Soils have much higher cobalt levels than pasture, so soil contamination of the forage/grazing can be an additional source of cobalt. Vitamin B_{12} is secreted in milk so cobalt only becomes a requirement in calves and lambs once the rumen develops.

Measurement of cobalt status in sheep and cattle at least historically has been through measurement of serum vitamin B_{12} levels. However, there are plasma proteins that bind to vitamin B_{12} and potentially prevent its detection by laboratory assays. This is more of a problem in cattle than in sheep and explains why the reference interval used for bovine vitamin B_{12} is lower than that for sheep. There are also analogues of vitamin B_{12} produced in the rumen that have no biological activity, particularly in cattle on concentrate diets, and some of these analogues will be picked up by vitamin B_{12} assays. As a result, measurement of serum vitamin B_{12} status particularly in milking dairy cows may be unreliable. Even in sheep, results need to be interpreted with caution. Furthermore, vitamin B_{12} levels take some time to drop in lambs grazing vitamin B_{12} deficient pastures as reserves become depleted.

Liver cobalt concentration is likely to be a better indicator of an animal's overall vitamin B_{12} status and the most reliable indicator is assessment of response to vitamin B_{12} supplementation.

Copper

Copper is an essential component of enzymes which form part of the antioxidant defence

system. It is also involved in the formation of collagen and elastin and is necessary both for the formation of haemoglobin and the reutilisation of iron freed by the normal breakdown of haemoglobin.

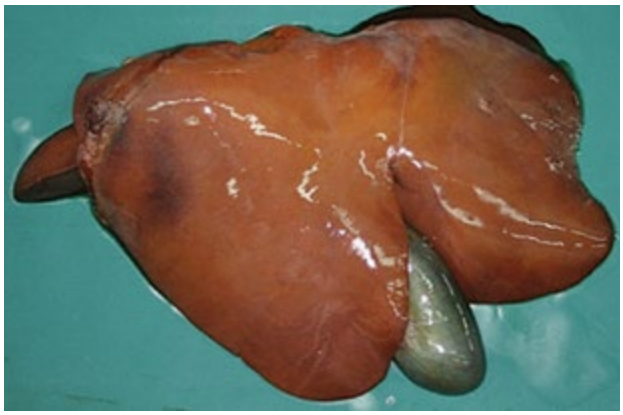
Copper deficiency may present as ill thrift, changes in hair colour, scour, chronic lameness and anaemia in cattle and swayback, fleece abnormalities and possibly ill thrift in sheep. Deficiency may be primary, when intake is inadequate, or secondary, when utilisation of copper is prevented principally by molybdenum, often in combination with inorganic sulphate leading to the formation of thiomolybdates. These reduce the absorption of copper by binding to copper in the rumen and may also reduce the availability of plasma copper when they are present in circulation. Iron is also a significant antagonist of copper absorption.

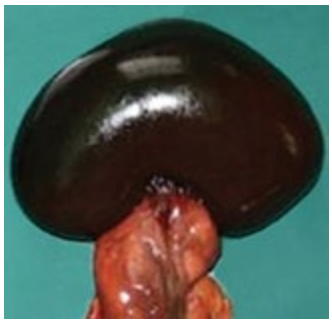
Measurement of copper status in the live animal has been traditionally carried out using plasma copper concentrations. During copper depletion, these are maintained homeostatically while the liver copper store is depleted and plasma copper levels are usually well below the stated reference interval when copper responsive disease occurs. Serum copper is a less useful means of assessing copper levels in circulation than plasma copper, as significant but variable levels of copper are taken out of the sample during the clotting process; this is at least in part due to copper being bound to the acute phase protein, caeruloplasmin. Measuring liver copper levels gives a more accurate measure of an animal's copper status and this can be done via biopsies on live animals and sampling of culled animals.

In secondary copper deficiency, signs of deficiency may still occur when plasma copper levels are within the reference interval if thiomolybdates are present in circulation. There are at present no reliable methods of measuring thiomolybdate levels in plasma.

Assessing response to copper supplementation alongside a control (unsupplemented) group is the most reliable means of assessing copper deficiency. However, both cattle and sheep can be pushed into copper toxicity if excessive copper supplementation is given and it is important to assess copper status before supplementation is considered.

Copper toxicity historically has been considered to be primarily a problem in sheep. Certain sheep breeds are more prone to toxicity, including North Ronaldsay, Charollais, Texel, Beltex, Blue-faced Leicester and Suffolk, and it is also reported more in intensively reared flocks on concentrate rations. Acute toxicity occurs with e.g. ingestion or injection of copper containing drugs or ingestion of copper containing pesticides. Signs may include abdominal pain, scour, vomiting and shock progressing rapidly to death. Chronic toxicity occurs with a period of 'over exposure' to copper, e.g. with excess supplementation. Initially, there is an accumulation phase as liver copper levels rise, followed by clinical disease, with liver degeneration and release of copper into circulation; in some cases a haemolytic crisis also occurs. Signs include anaemia, jaundice and haemoglobinuria.





Yellow-brown colouration of the liver and 'gun metal' colouration of the kidney of a sheep with confirmed copper toxicity

The liver copper level at which clinical copper poisoning occurs is quite variable. The excess copper released into circulation by the liver is filtered out by the kidneys and kidney copper analysis is more useful in the assessment of copper poisoning. Very high plasma copper concentrations are also usually sufficient evidence to diagnose copper poisoning in live animals, particularly when coupled with raised liver enzymes (GGT and GLDH) indicative of liver degeneration. Lower levels may reflect either the accumulation phase of copper poisoning or inflammation, as 90% of plasma copper is present as caeruloplasmin, an acute phase protein which increases during inflammatory responses.

Copper toxicity is not restricted to sheep and

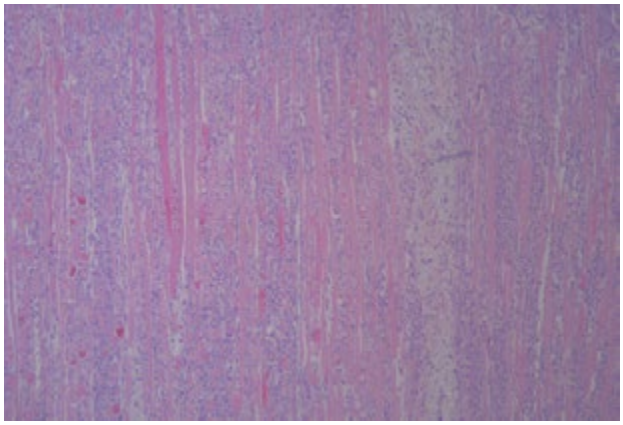
high levels of copper supplementation given particularly to dairy cattle have led to liver copper levels in many animals that are well above reference range, as illustrated in newly published research by the University of Nottingham. Although this may not be associated with clinical disease, a recent report from the University of Guelph suggests that subclinical copper toxicity in high-producing Holstein dairy cows may be associated with infertility and ketosis.

It needs to be remembered that liver copper levels exceeding a certain threshold are potential food safety incidents and should be reported to the APHA.

Selenium

Selenium is a component of the enzyme, glutathione peroxidase (GSH-Px) which, along with vitamin E, is an important anti-oxidant.

Selenium deficiency classically is associated with white muscle disease (enzootic muscular dystrophy), particularly when young animals are turned out for the first time on to lush pasture. It also may cause ill-thrift, poor reproductive performance and, in cattle, retained placentae.



Skeletal muscle from a goat kid confirmed with selenium deficiency: there is evidence of myonecrosis, macrophage infiltration and regeneration with satellite cell proliferation.

There is also evidence to suggest it may be associated with immunosuppression.

There are two methods used to assess selenium levels in circulation. Levels of the selenium containing enzyme, GSH-Px, found in erythrocytes can be measured in whole blood and the activity of this enzyme is directly related to selenium levels in the blood. However, GSH-Px levels change only slowly with changing selenium status (4-6 weeks following a change in selenium intake). Measuring serum selenium provides a better indicator of any recent changes in selenium status as it responds more rapidly to administration of selenium. Historically, this assay has not been commercially available but this is no longer the case. In cases of white muscle disease, additional supportive evidence is provided by measuring muscle enzymes (CK and AST).

Vitamin E has a complimentary but independent role to selenium as a cellular antioxidant and therefore the possibility of vitamin E deficiency needs to be considered alongside selenium deficiency. It has been found that, when selenium levels are low, higher vitamin E levels are required to avoid deficiency and the converse is also reported to be true. Therefore for suspected cases of deficiency where the precise aetiology is not known, both vitamin E and selenium status should be assessed.

Liver selenium measurement is the test of choice to assess selenium status in the dead animal.

Selenium toxicity may occur when excess selenium is provided in the diet or parenterally, or animals are grazing seleniferous pastures or plants. Acute toxicity, e.g. associated with accidental overdose, may be associated with distress, abnormal respiration, recumbency, scour and death within a few hours. Clinical signs of chronic toxicity include dullness, emaciation, coat changes (including alopecia) and lameness, possibly accompanied by hoof sloughing. GSH-Px levels may not rise in parallel with excessive selenium intakes but blood selenium levels will; however they will return to normal following correction of selenium intake so it is difficult to confirm chronic selenium toxicity retrospectively. Acute toxicity can be demonstrated by measuring serum selenium levels. Liver selenium is the most appropriate means of investigating selenium toxicity in the dead animal.

Iodine

Iodine is a component of the hormone thyroxine, which controls energy metabolism and is essential for foetal growth and development. Iodine deficiency may be primary or secondary. Primary iodine deficiency is associated with grazing on iodine deficient soils, such as are found in Derbyshire, Gloucestershire, Nottinghamshire, Somerset, Devon and Oxfordshire. Secondary iodine deficiency is associated with ingestion of goitrogens; these may exert their effect through impairing iodine uptake by the thyroid (e.g. thiocyanates or nitrates found in brassicas and legumes), iodination of tyrosine residues in the thyroid

gland (e.g. thiouracil compounds found in brassicas) and preventing entero-hepatic recycling of thyroxine (e.g. flavonoids from soya).

In cattle, iodine deficiency is most commonly manifested as a high incidence of stillbirths and weak new born calves with characteristic goitre. Other reproductive abnormalities, including decreased bull libido and failure of oestrus expression in cows, have been reported. In sheep, weak, alopecic lambs with goitre are most commonly seen; other reported signs include extended gestation lengths and increased perinatal mortality.

Iodine deficiency can be assessed in a variety of ways. In still births, thyroid weight relative to bodyweight can be used to indicate the likely presence of goitre, confirmed by measuring thyroid iodine content and/or histopathology. These are post mortem tests but they are the most reliable means of investigating possible iodine deficiency in a herd.

In adult animals, Plasma Inorganic Iodine (PII) levels are a sensitive indicator of iodine intake over the previous few days, but are not a measure of an animal's iodine or thyroid status. After an increase or decrease in iodine intake, the PII level rises within hours and falls within days, respectively. What limited data there is suggests that cattle reference intervals can be used successfully in sheep. Cohort samples can be pooled and three samples are probably sufficient from a single management group for initial assessment of recent dietary iodine intake. However, as iodine is effectively stored in the thyroid, it needs to be borne in mind that short periods of low intake picked up by low PII measurements may have no adverse clinical effect. Secondary iodine deficiency also may not become apparent by measuring only PII levels. The common goitrogens affect iodine uptake by the thyroid and also iodine metabolism within the thyroid. Therefore, although the PII level may indicate adequate recent dietary intake, there may be low circulating T4 levels. Similarly, selenium deficiency impairs thyroid hormone availability without depressing plasma PII levels.

Measurement of serum thyroxine (T4) also has been used as an assessment of iodine deficiency. As circulating T4 levels are affected by many factors apart from iodine intake, e.g. stage of lactation, parasitism, season, its sensitivity and specificity are low. Interpreting T4 levels therefore has to be a probabilistic one, using thresholds below which T4 levels are highly suggestive of iodine deficiency and, as levels approach these thresholds, the likelihood of iodine deficiency increases.

As with other trace elements, response to supplementation is a sound means of confirming iodine deficiency and comparison with an untreated control group is useful.

How many animals to sample

The number of animals to sample to assess for trace element deficiency is influenced by several factors. In addition to variations in test reliability, the main factor on farm is the variability in status within the herd of the trace element being tested. Variability will be affected by factors such as age, diet, health status and milk yield. As a rule of thumb, at least six animals should be sampled from each different cohort of animals between which these factors differ. If the results within the cohort are highly variable, more samples may be needed to obtain a reliable mean.

When to sample

Trace elements are usually well supplied by concentrate rations and therefore sampling animals on concentrates may be of little value. Of more value is sampling dry cows, ewes in early to mid-pregnancy and growing animals on grass, trace elements being of importance for the growth and development of the foetus and the growth of young stock.

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