TREATMENT OF CASEOUS LYMPHADENITIS: WHAT ARE WE DOING AND WHY?

How Did This All Start?

We started this line of research and investigation with a clinical question. Would tulathromycin have efficacy against caseous lymphadenitis in sheep and goats? However, our very first thoughts of using this drug in an extra-label manner also included its potential use in respiratory disease. The pneumonic form of Pasteurellosis in small ruminants is one of the most common causes of respiratory disease and includes as etiologies, both *Mannheimia haemolytica* and *Pasteurella multocida*. Mycoplasma spp. have been implicated as well in many cases.

While ceftiofur is approved for use in goats and does have reported efficacy against many isolates of *M. haemolytica* and *P. multocida*, there has been reported resistance to *Mycoplasma spp.* Further, the frequent dosing required to establish consistent therapeutic concentrations in these animals can be problematic due to handling and herding of these goats. Therefore, another “tool” would be desirable that would be both efficacious and long-acting.

After visiting with some folks at NRSP-7, it was clear that research was underway, including elucidating the pharmacokinetics of this drug in goats, to seek such a label and approval. So we decided to turn our focus back to CL. There are many properties of tulathromycin that we felt would make this drug particularly useful for treatment of CL lesions.

**Tulathromycin Properties**

- In a subclass of the macrolide family – active against gram positive organisms
- Efficacy reported for primary pathogens of BRDC including *Mycoplasma spp.*
- Long-acting
- Highly lipid soluble and large volume of distribution

So we set out to compare our current treatment of these lesions with treatment with tulathromycin. However, there were some other important considerations we thought should be investigated first. In talking with some of our CLIENTS, this drug was already being used extra-label in sheep and goats for respiratory disease at the dose for cattle and swine. This, we felt was bold considering there was no data on safety to non-target animal species. Why the concern? Tilmicosin (macrolide) is labeled for sheep, but is reportedly cardiototoxic to goats and pigs. Safety studies were only performed in target animal species (10 x the labeled dose), so is the molecule different enough to be safe for goats? Further, what about genotoxicity? Erythromycin and tilmicosin, both traditional macrolides, have been extensively studied and found to be non-toxic to the genome (non-carcinogenic), but, what about tulathromycin?

**Safety Study**

The objective of our study was to determine if the administration of tulathromycin to goats at ten times the label dose for cattle and swine resulted in adverse effects.

Ten goats were enrolled in the study and randomly assigned to treatment or control groups with five animals each. Tulathromycin or an equivalent volume of saline was administered subcutaneously to treatment and control groups, respectively. Samples were obtained from both groups prior to and at pre-determined times following administration for hematology, serum chemistry, urinalysis, genotoxicity analysis and fecal floatation. In addition, goats were observed daily for clinical evidence of adverse effects post-dosing over a seven-day study period.

All goats survived until the end of the study, and although all goats in the tulathromycin treated group experienced periods of transient pain following administration, laboratory data and clinical observations indicated no significant differences in parameters of clinical relevance between treatment and control goats. Overall, findings were similar to those of previously performed safety studies performed in cattle and swine. However, the numbers of changes in genomic material were significantly greater for treatment goats as compared to controls. No significant gross or microscopic lesions were observed in either group upon post-mortem examination that could have been attributed to tulathromycin administration.

In conclusion, this study suggested that administration of tulathromycin to goats at ten times the label dose for cattle and swine results in clinically mild and transient effects. Further studies are needed to explore potential long-term effects in light of the genotoxicity results.
After these results we felt comfortable turning our attention to whether or not tulathromycin could be efficacious in the treatment of CL in sheep and goats.

Caseous Lymphadenitis and Client Owned Animal Study

Caseous lymphadenitis is a chronic disease caused by *Corynebacterium pseudotuberculosis*. One prevalence study looking at culled sheep from 9 Western States found the prevalence to be 42.41%. It has also been reported as the third leading cause of economic loss to the sheep industry in the Western United States. Although prevalence studies such as these are lacking in goats, with the reportedly marked increase in numbers of goats in the Western and Southwestern US, we can assume the prevalence of caseous lymphadenitis in these populations is also rising. Various forms of treatments have been examined, with the best, most obviously being prevention. Culling these animals from the herd is the next most logical means of preventing spread and stopping outbreaks. However, many to most of our clients utilize these goats as pets, show animals or valuable breeding does and bucks, therefore, they frequently chose to “live” with the disease rather than cull them from the herd. Intralesional injection with formalin has been proposed to be efficacious, however, the legal ramifications of injecting a known carcinogen into a food producing animal are limiting. Surgical excision is an effective means of removing lesions, however, it requires a higher cost due to general anesthesia and post-operative complications can be significant. Lancing and flushing these lesions has been a standard form of care, but the down-side to this modality is that during the convalescent period, there is opportunity for the lesion to drain infectious material into the environment. Systemic treatment with antimicrobials has been reported, however, the ability of an antibiotic to penetrate the encapsulated lesions is questionable. Erythromycin and rifampin in combination have been used to treat the disease, however, this requires daily, long-term therapy and failures still occur. Due to tulathromycin’s high lipid solubility, large volume of distribution and ability to reach sustained concentrations in infected tissues in cattle for long periods of time make it an attractive product to attempt treatment of this disease. Following our safety study, we were convinced that this drug, at the label dose of 2.5 mg/kg, would be safe to administer to goats. Therefore, we set out to investigate this drug for caseous lymphadenitis treatment.

The objectives of our study were to evaluate and compare treatments of caseous lymphadenitis in small ruminants, and to investigate in vitro susceptibility of *Corynebacterium pseudotuberculosis* to tulathromycin. We started by comparing how we currently were treating CL versus treatment with tulathromycin. Our treatment at the time was to lance these lesions, drain them and flush them thoroughly with diluted betadine solution, then administering a one-time dose of procaine penicillin G at 22,000 IU/kg SQ.

Client-owned cases were enrolled based on the presence of a peripheral, subcutaneous mass and were randomly assigned to one of three treatment groups. From all cases, lesions were aspirated for bacterial culture and antimicrobial susceptibility, and blood was collected for serum hemolysin-inhibition testing. Treatment groups were as follows: opening, draining and flushing the lesions (A), 2.5 mg/kg intralesional tulathromycin after intralesional lavage (B), and 2.5 mg/kg subcutaneous tulathromycin and intralesional lavage(C). Animals were discharged to owners with specific instructions regarding biosecurity and parameters that warranted re-examination or constituted treatment failure. All cases were re-examined approximately one month from enrollment, unless treatment failure was observed. If lesions were unresolved, they were re-cultured, opened, drained and flushed (A).

Forty-eight cases were identified, forty-three of which culture positive for *C. pseudotuberculosis*. Proportions of resolution one month post-treatment were 92.9% (95% CI = 69.5-99.6%), 83.3% (54.9-97.1%) and 82.4% (59.1-95.3%) for Groups A, B and C, respectively (95% CI). These proportions were not significantly different between groups (P = 0.775). All of the case-obtained isolates had a MIC<sub>90</sub> of ≤ 2.0 µg/mL and 71% had a MIC<sub>90</sub> of ≤ 1.0 µg/mL. Disk diffusion results indicated zones of inhibition ranging from 21-33 mm in diameter after 24 hours.

In conclusion, our data indicate that clinical isolates of *C. pseudotuberculosis* have low MIC’s to tulathromycin, and there may be acceptable alternatives to treatment of caseous lymphadenitis rather than opening, draining and flushing lesions. So, we began treating these cases with intra-lesional and/or parenteral tulathromycin rather than lancing, flushing and draining. Even though the percentage resolution was highest for lancing them, we felt like it would be in the best interest of the farm and animals to leave these lesions intact if at all possible as there continues to be drainage of the organism into the environment for variable lengths of time following lancing. But, several questions remained. Is this an acceptable way to handle the disease in large number herds/flocks? Could this replace culling as a means to eliminate the disease from herds/flocks? Does the drug reach adequate levels in the abscesses? Does the drug work in the face of purulent material? We
were unable to have controls in this study because they were client owned. An ideal control would have been one in which the lesions were lavaged only. For all we knew to this point, that treatment may have worked as well. Information as to the answers to those questions was gained in the next two studies we performed which will be discussed in the next period.

References


HOW DOES TREATMENT OF CASEOUS LYMPHADENITIS IMPACT THE PREVALENCE OF DISEASE? (DOES IT WORK?)

Prevalence Study, Large Herd Management Study

We did a study that recently came out in JAVMA in which we attempted to determine the seroprevalence of C. pseudotuberculosis, the external culture positive prevalence of CL and the effect, if any, treatment of a subset of these animals had on the prevalence over a 13 month period.

The study animals were 3 herds of goats and sheep in West Texas. Pedigrees were available for one of these groups. The goats and sheep in these herds occasionally shared the same pastures, pens and working facilities, therefore, we are compelled to sample them all. The main advantages to this study, over our previous clinical trial are the large numbers, the ability to have control animals, the ability to evaluate susceptibility in offspring and within family lines and the ability to follow them in a natural herd setting for over one year. These herds had managed CL in previous years by “culling” animals with suspect lesions from the herd. They did not vaccinate for CL.

In herd one, all mature sheep and goats were bled for the synergistic hemolysin inhibition test to determine titers on the initial visit. All were examined for evidence of clinical external CL suspect lesions. Any active lesions on these animals were cultured. These “cases” were separated from the rest of the herd and randomly assigned to treatment or control groups. Treatment animals had their lesion flushed via intralesional lavage with saline, then they were administered 2.5 mg/kg tulathromycin directly in the lesion and 2.5 mg/kg subcutaneously in the neck. Control animals in this herd had their lesions flushed via intralesional lavage with saline, then they were administered an equivalent volume of saline to a 2.5 mg/kg dose of tulathromycin directly in the lesion and administered the same volume of saline subcutaneously in the neck. These cases were
were collected for histopathology at tissues around each cage were collected for histopathology. Further, both left and right prefemoral lymph nodes bact

tulathromycin concentrations as well as the plasma. Furthermore, the tissue chamber fluid was cultured for the plasma were obtained at set times up to 360 hr post administration. The tissue chamber fluid was analyzed for tulathromycin concentrations as well as the plasma. Furthermore, the tissue chamber fluid was cultured for the bacteria. At 360 hr post-administration immediately following sample collection, all goats were euthanized and tissues around each cage were collected for histopathology. Further, both left and right prefemoral lymph nodes were collected for histopathology and bacterial culture.

In herd two, all mature sheep and goats were bled for the synergistic hemolysin inhibition test to determine titers. All animals were examined for clinical evidence of CL suspect external lesions. Any active lesions on these animals were cultured. These “cases” were separated from the rest of the herd and randomly assigned to treatment or control groups. Treatment animals had their lesion flushed via intralesional lavage with saline, then they were administered 2.5 mg/kg tulathromycin subcutaneously in the neck. Control animals in this herd had their lesions flushed via intralesional lavage with saline, then they were administered an equivalent volume of saline to a 2.5 mg/kg dose of tulathromycin subcutaneously in the neck. These cases were monitored for one month. At the end of the one month period, if the lesions were resolved they were returned to the herd. If resolution did not occur, they were removed from the herds or euthanized and necropsied.

In herd three, all mature goats were bled for the synergistic hemolysin inhibition test to determine titers. Any active lesions on these animals were cultured. These “cases” were removed from the herd and not treated.

All three herds were visited every 6 months for re-examination for the presence of CL suspect external lesions. Each time, suspect cases in each of the Herds were handled with the same protocol as prescribed above. In total including the initial visit, 3 visits were made to these Herds over a 12 month visit. Further, one month after each of the 3 examination visits, the Herds were followed up by checking for resolution.

Findings

Initial serologic prevalence ranged from 7.52 to 69.54% and culture positive prevalence of external CL ranged from 0 to 6.12%. At the end of the study (13 months), the culture positive prevalence of external CL ranged from 0 to 9.56%. We were unable to compare treatments between the herds, and were unable to evaluate efficacy for several factors that were beyond our control. The primary reason, being that although we had control animals and treated animals, and they were isolated from the rest of the herd/flock following treatment, these animals ran together and were unable to be separated. Therefore, treated and control animals were together during the periods between treatment and evaluation. We were able to evaluate the ability of the SHI test as a predictor of whether or not serologically positive animals free of lesions at the beginning of the study would develop lesions during the study period, versus those that were serologically negative without clinically detectable external CL suspect lesions. By doing so, it was possible to evaluate the use of this SHI test as a tool in culling animals from the herd. We discovered that the SHI test serology results were poor predictors of the development of CL lesions during the study period. An animal with a positive SHI test serologically was not any more likely to develop a CL lesion during the 13 month period than an animal that was negative on the SHI test. If a producer was using this to eliminate animals from a herd, they could potentially eliminate genetically valuable individuals who would not develop a CL lesion. We did elucidate from all the data in this study that the management of two of these herds by treatment with tulathromycin did not significantly result in a rise in overall culture positive prevalence. We regret not being able to evaluate treatment efficacy or comparing between herds, however, these results prompted our latest study.

Tissue Cage Study

So after this study in the large herds, we decided the only way to evaluate treatment efficacy and answer many of the questions we still had regarding using tulathromycin as a treatment for CL, was to create our own abscess model with controls. The questions that remained after the client owned animal study and the study in the large herds with our two treatments included the following: does the drug get into the lesions? does the drug do anything when injected directly into the lesion? is the drug active against the bacteria?

We used surgically implanted tissue cages to create an abscess model in goats. A tissue cage was implanted into each paralumbar fossa of 12 goats that were healthy and free of CL lesions. These tissue cages are constructed of plastic with a silicone membrane covering. On chamber on one side of the animal was inoculated with Corynebacterium pseudotuberculosis, while the chamber on the opposite side was not. This chamber served as our negative control. We then administered 2.5 mg/kg tulathromycin subcutaneously in the neck of half of these goats, while the other half received the tulathromycin directly into infected chambers. Samples of chamber fluid and plasma were obtained at set times up to 360 hr post administration. The tissue chamber fluid was analyzed for tulathromycin concentrations as well as the plasma. Furthermore, the tissue chamber fluid was cultured for the bacteria. At 360 hr post-administration immediately following sample collection, all goats were euthanized and tissues around each cage were collected for histopathology. Further, both left and right prefemoral lymph nodes were collected for histopathology and bacterial culture.
Following a single SQ administration concentrations of tulathromycin were detected inside the infected and non-infected tissue cages. Inside the chambers that were infected that were injected with tulathromycin, concentrations of tulathromycin were well above the MIC of the bacteria for the entire 15 day period. As for bacterial counts, overall, these declined in all infected chambers until the end of the study. In 6 of the 12 infected chambers, no growth of Corynebacterium pseudotuberculosis was found (3 after SQ injection of the drug and 3 after intra-chamber injection into the infected chambers). Six of the lymph nodes were positive for bacterial culture. All but one of these were on the same side as the infected chamber, while the remaining positive lymph node was on the side opposite the infected chamber. Interestingly, 3 lymph nodes were positive when there was no growth of bacteria in either chamber. Grossly, the tissue cages were surrounded by a fibrous capsule and filled with fibrin and purulent material. Histopathologic examination of the tissues and lymph nodes indicated there was inflammation in these tissues representative of a walled off site of infection.

Our Interpretation of All of This Data

Tulathromycin does reach concentrations inside these isolated cores of infection following subcutaneous injection. Further, this drug does seem to display antimicrobial properties when injected directly into the lesions and it also reaches outside these regions. The fact there was growth inside some chambers in which drug levels reached well above the MIC indicates there are other “factors” involved that protect this organism in vivo, or allow it to avoid the killing properties of the drug. The fact there was no growth inside some chambers that did not have drug concentrations above the MIC indicate the in vivo MIC may not entirely always agree with in vitro results. Further, based on the fact we had some positive lymph nodes when no bacteria was cultured from the chambers indicates the organisms may not be completely eliminated from the body. There are other questions that need to be answered still. What would multiple treatments a week apart do? What would other drugs that the organism is susceptible to do in this model? How would they perform?

So After All This, Does It Work?

This is by no means a cure of CL. We have had successes and failures, however, I feel as it is a viable alternative in herds that choose to manage the disease by “living with it”. Our data in the latest study, although we didn’t stamp out all the bacteria in all animals, went a long way toward what we see clinically. Some animals have lesions that resolve and don’t come back. Some don’t respond and some resolve, but develop other lesions sometimes months later. Our current treatment is to administer two doses at 2.5 mg/kg tulathromycin, one directly into the lesion following intra-lesional lavage, and the other SQ in the neck. We do this one time and recommend they follow isolation protocol until the lesion either resolves or runs its course depending upon the response. We have been using a 34 day withdrawal period based on recent research.1

Reference

ETIOLOGY
Struvite - Ca, Mg, ammonium phosphate – concentrate feeds have high levels of P
Calcium carbonate – legume/clover pastures, high Ca in diets?
Calcium oxalate – some plants precipitate this (very small portion of what we see)

PATHOGENESIS
Formed by interaction between organic matrix and solute
Matrix – protein, mucoprotein, peptide
   Mucoprotein content affected by pelleted feed, implanting, concentrate feed
Organic matrix
   5% organic matrix in struvite stones
Solute – struvite
   Ca:P04 imbalance
   PO4 >0.5% with low Ca in ration
Solute precipitate around matrix
   pH = alkaline urine favors struvite, while acidic urine favors silicious calculi

LOCATION OF OBSTRUCTION
Sheep/goats = urethral process, distal sigmoid flexure
Occasionally at the urethral diverticulum

EPIDEMIOLOGY
Struvite
   Occurs late in feeding period
Calcium carbonate
   Sporadically

CLINICAL SIGNS
Urethral obstruction
   Stranguria (goats tend to vocalize)
   Colic signs
   Urinary bladder distention
Partial obstruction
   Stranguria (goats tend to vocalize)
   Dribble urine
   Hematuria
   Ruptured urethra
   Water belly
   Cool, pitting edema in preputial area and ventral abdomen due to urine leakage
   Ruptured bladder
      Abdominal distention
      Abdominocentesis and/or ultrasound is beneficial

LAB FINDINGS
CBC – dehydration
   Serum chemistry – low Cl, Na, K may be normal depending on duration!
   Urinalysis – hematuria if partial obstruction

ANCILLARY DIAGNOSTICS
   Abdominocentesis
   Creatinine in fluid vs. creatinine in serum
   Ultrasound
   Check kidneys!
      Compromised kidneys very much affects prognosis
      Remember: small ruminants have multiple stones, therefore, recurrence is likely if steps are not taken to dissolve/remove them.
PROGNOSIS

Urethral obstruction/rupture – short term good (if no renal damage present)
  Long term – guarded
  Ruptured bladder
    Fair with treatment, 50% survive

DIAGNOSIS

History
Clinical signs/lab findings

THERAPY

Urethral obstruction
Medical
  Extend penis (good luck sometimes)
  Pass urinary catheter while flushing
  Urethral diverticulum prevents catheterizing urinary bladder
  Place in walpoles buffer solution via cystocentesis (not if urethra is compromised )

WALPOLES THERAPY

We have greatly reduced the number of surgical procedures we have had to do by employing this therapy. It must be mentioned, however, that the population we use this technique on is primarily the young show whether that is trying to make it to the show. Therefore, for this population, surgical procedures are not economically justifiable, nor practical in most instances. On the other hand, it has “spared” a fair number of pets and more expensive breeding animals surgical intervention.

Protocol:
  a. examine urinary bladder and abdomen for free fluid, and degree of bladder distension
  b. sedate with xylazine? I sometimes use valium at 0.25 mg/kg IV
  c. extend the penis and remove urethral process
  d. attempt to pass catheter as far as possible and lightly flush (don’t get too aggressive here)
  e. using the ultrasound probe while the animal is in lateral recumbency, visualize the urinary bladder.
  f. using a 1 ½ inch, 18 ga needle (sometimes for bigger goats we’ll use a 3 inch needle), and while watching with the ultrasound, pass the needle into the urinary bladder
  g. draw off some urine and check pH
  h. draw off 50 to 100 mL of urine
  i. we usually have a stopcock on the end of an extension set so that we can draw off urine, close the stopcock and infuse walpoles
  j. infuse 50 to 100 mL walpoles
  k. continue to draw out contents and instill walpoles while checking the pH before more more walpoles is introduced
  l. when the pH is less than 5 or 6, stop
  m. repeat in 6 to 8 hours if necessary

Sometimes, (maybe more frequently than we know) we will find free fluid outside the urinary bladder the day after treatment. If the animal is passing urine and acting normally, this free fluid has not been a problem. We have drained this off sometimes, realizing that rather than having a tear, we probably have movement of fluid through a leaky bladder, including the hole we made with the needle.
We start the animal on 200 mg/kg ammonium chloride BID orally until we get acidification of the urine.
We control this by pulsing the ammonium chloride to them after the episode.

Surgical therapy
  Perineal urethrotomy/urethrostomy – salvage procedures (re-stricture, other stones come down and re-block)
  Tube cystotomy
  Urethral rupture – combine above with ventral drainage
  Urinary bladder rupture
    Provide abdominal outflow
Repair bladder?
Marsupialization – becoming one of our better long-term options for pets (marsupialize to the prepuce?)
Supportive care – renal damage?

PREVENTION
Important to have uroliths analyzed as to composition (some labs will give you %’s of contents)
Struvite
  Acidify urine
  Ammonium chloride at 200 mg/kg orally BID 3 days on, 3 days off
  Ca:P ratio >2:1
  No more than 0.3% P in diet! (sometimes, the best you can do is get close)
  Provide water all the time that is fresh, clean!

OUR STUDY
A review of a retrospective study we did using treatment with Walpoles solution will be discussed. This paper was published recently (Janke J, et al.. J Am Vet Med Assoc 2009 234(2):249-252).

Latest Study on Chlortetracycline
PLASMA CONCENTRATIONS OF CHLORTETRACYCLINE FOLLOWING ORAL ADMINISTRATION TO SHEEP FOR EIGHT DAYS. K. Washburn1, V. Fajt1, P. Plummer2, J. Coetzee2, S. Washburn1. 1. Texas A&M University College of Veterinary Medicine, College Station, TX. 2. Iowa State University College of Veterinary Medicine, Ames, IA.

The objectives of this study were to determine plasma concentrations and pharmacokinetic parameters of chlortetracycline (CTC) in adult sheep after oral administration of either 40 or 250 mg/head twice a day. These doses represent the FDA-approved feed additive dose and the commonly used but unapproved dose, respectively, for the prevention of ovine infectious abortion.

Sheep were orally dosed with 40 mg or 250 mg of CTC twice a day for 8 days (final dose range was 0.4-0.7 mg/kg and 3.0-3.9 mg/kg, respectively). Plasma samples were collected just prior to dosing on days 1, 1.5, 2, 4, 5 and 8 to assess drug accumulation. Samples were also collected 4, 8, 12, 24, and 36 hrs after the last dose to investigate the apparent elimination half-life of CTC.

Mean observed maximum CTC concentrations (Cmax) were 20.0 ng/mL after 40 mg and 101 ng/mL after 250 mg dosing. Mean apparent elimination half-life was 18 hrs (40 mg dose) and 20 hrs (250 mg dose).

Although published data do not exist to estimate plasma CTC concentrations necessary for the prevention of ovine abortion from Campylobacter spp., concentrations reached in our study are far below the minimum inhibitory concentrations (MICs) reported in the literature for isolates from abortion outbreaks. This suggests that either these dosages are not high enough or that the pharmacodynamic parameter relating preventive dose to pathogen MICs is yet to be determined.

Blood Transfusions of Ruminants

Why?
Anemia
  Blood loss
  Hemolytic event
Failure of passive transfer
Bovine plasma is expensive and is difficult to harvest due to the nature of the ruminant blood. Whole blood has the IgG necessary to provide protection for the calf. Calves greater than 24 hours of age that have not received colostrum, or those that are diagnosed by other means to be failure (sodium sulfite test/refractometer)

Who is the best donor?
Adult from the same farm is ideal for either instance
  For FPT, mother of calf has low circulating IgG
  Adult ensures you can collect enough most of the time
  Biosecurity issues – don’t want something from someone else’s herd (BLV, anaplasmosis, BVD, etc.)
How much blood do we give?

\[
\text{BW(kg) x 0.1 x PCV desired – PCV patient} \quad \text{= L of whole blood} \\
\text{PCV donor}
\]

What about for failure of passive transfer?

\[
\text{BW(kg) x 0.1 x TP desired – TP patient} \quad \text{= L of whole blood} \\
\text{TP donor}
\]

For your average 100 lb. calf, this works out to be about 2 L.

How do we collect it?

Catheterize animals (donor and recipient) with 10 to 12 ga needle in cattle and 14 to 16 ga in small ruminants. Glass bottles, ACD bags, commercial collection kits (don’t require catheter)

10 – 15 mL/kg can be safely removed from donor acutely

(About 20% of total blood volume)

Sodium citrate is the anticoagulant of choice if you will use it within hours

1 part sodium citrate; 9 parts blood

Acetate citrate dextrose required for longer storage of blood

1 part ACD, 9 parts blood

How do we give it?

Catheter placed, then blood is run through a transfusion set (filter).

Transfusion reactions are rare

Ruminants don’t have the tendency to form autoantibodies to red blood cells

However, I start at a slow rate for the first 10 to 15 minutes

0.5 mL/kg over this time

Signs:

Tremors

Tachypnea

Tachycardia

Then give at rate of 10 mL/kg/hr

What to expect?

Transfused cells only last about 4 days

If another transfusion is required, the same donor can be used as long as it is not after about day 5. If after day 5, a different donor should be used to prevent a reaction.

SMALL RUMINANT CASE DISCUSSIONS

CASE 1
Signalment: 3 year-old male intact Boer goat
History: One week history of coughing, labored breathing, depression. On pelleted feed. Treated 3 days prior to admission with tulathromycin.
Physical examination abnormalities: Intermittent cough and abdominal efforts upon expiration.

CASE 2
Signalment: 3 year-old intact Boer goat
History: One month history of worsening lameness of right rear limb. Referring had radiographed stifle and found effusion. Goat placed on phenylbutazone and rest but had not improved.
Physical examination abnormalities: Pain upon manipulation of stifle and right coxofemoral joint.
Diagnostics: Radiographs of stifle and coxofemoral joint
CASE 3
Signalment: 3, 3 to 4 year-old cross breed does
History: These were 3 does from a group of 15 that were kept in a 20 acre pasture. This pasture was one of 4 similar sized pastures and the owner rotated these goats with two other groups of about 15 in each (always had one pasture open). All 3 of these were from same pasture and none of the others in the other two pastures were affected. One other goat in the same pasture was left as she had become recumbent after a three day period of ataxia and weakness.
Physical examination findings: Two of the does were recumbent and one was ambulatory but had significant deficits. All three were bright, alert, eating, drinking and essentially normal upon physical examination.
Neurologic examination findings: The two down does had no cranial nerve deficits, however, one doe had markedly depressed withdrawal reflexes and patellar reflexes while the other had a depressed patellar reflex of the left rear limb. The video depicts the deficits in the ambulatory goat.
Lesion localization: Lower motor neuron disease with a lesion or lesions in the spinal cord, asymmetrical distribution suggesting possible multiple lesions.

CASE 4
Signalment: 2 year-old intact male Hampshire ram
History: Owner had noted him breathing heavily and had not seen him urinate in the last 24 hours. Anorexic for about last 3 days. Depression.
Physical examination findings: The patient seems depressed and walks stiff in the rear legs. He has bilateral serous nasal discharge with increased respiration rate and effort. Crackles are present in the right dorsal lung field.
Diagnostics: Radiographs; serum chemistry, abdominal ultrasound

CASE 5
Signalment: 2 year-old intact male Boer goat
History: Presented for vocalizing, straining and lack of urination for approximately 10 hours. On pelleted feed.
Physical examination abnormalities: Vocalizing frequently, stranguria.
One week later, here he came again with another obstruction. It was determined he needed a tube cystotomy. Came back 5 days later, still very painful upon urination. Was urinating, but small stream. Ten days after this, re-admitted. Physical examination revealed urethra-rectal fistula and he was dribbling urine from anus. Treatment this time was with urinary bladder marsupialization. Tissue around anus sloughed, but urinary problem was solved!

CASE 6
Signalment: 1.5 year-old Dorper sheep, intact
History: enlarging mass in scrotal area
Physical examination: picture is worth a thousand words

CASE 7
Signalment: Boer doe with swollen limbs and lethargy
History: anorexia and lethargy
Physical examination: dull, bilaterally distended abdomen

CASE 8
Signalment: one of 3 kids from doe affected with lesions of about 10 days duration
History: kids are normal in every way except skin condition
Physical examination: (pictures)
Diagnostics: full thickness skin biopsy, skin scraping

CASE 9
Signalment: one year-old Boer cross female
History: three week history of worsening skin condition
Physical examination: dry, crusty lesions with alopecia distributed generally over entire body. Lesions are pronounced around both eyes, are non-puritic and in some areas fissured.
Differentials: external parasites, superficial pyoderma, pemphigus foliaceous,
Diagnostics: skin scraping, skin biopsies
BOVINE CASE DISCUSSIONS

CASE 1
4 year-old Angus cow presented for weight loss of one month’s duration and what the owner described as ‘inability to eat’ for about one week’s duration. The cow was out on pasture with others and at least two other cows were experiencing similar clinical signs. The region this herd was located was experiencing a “100 year” drought. Physical examination abnormalities included excessive salivation, a dropped jaw and poor body condition score. The rumen was large and doughy.

CASE 2
4 year-old crossbred cow presented for lethargy, weakness and weight loss of one week’s and one month’s duration, respectively. Out on pasture with a large herd along the Gulf Coastal region of Texas. The cow was raised from a calf on the farm. Physical examination findings included pale mucous membranes, mild ataxia, poor body condition and decreased rumen contractions.

CASE 3
2 week-old Brangus calf presented for a 24 hour history of being off by herself, not nursing and having difficulty standing and walking. Physical examination abnormalities included a stiff, stilted gait, an enlarged umbilicus with purulent material present on the opening, retracted ears and a raised tail.

CASE 4
4 month-old Hereford cross calf presented for head tilt and circling of approximately one week’s duration. The calf was one of approximately 5 to 6 calves that displayed these clinical signs on this farm every year for the past 5 years. No previously affected calf had been necropsied. This was a 3,000 cow herd on several thousand acres in South Texas. Physical examination abnormalities included bilateral conjunctivitis, some corneal edema/opacity on the right eye and mild nasal discharge bilaterally. Neurologic abnormalities included a head tilt to the right and circling. The calf circled primarily to the left, but occasionally would change directions. The calf reportedly nursed normally and was bright and alert. This calf reportedly represented the others over the years very well.

CASE 5
2 year-old Brahman bull presented for a one week history of lethargy, anorexia and increasing abdominal distension. The owners had not noted urination over the last 24 hours. The bull was out on pasture with cows for his first breeding season. Physical examination abnormalities included weakness, lethargy and a “pear” appearing abdominal contour from the rear. Rectal examination abnormalities included a large doughy rumen and the absence of feces.

CASE 6
3 year-old Angus cow presented for recumbency of three day’s duration. Cow was out on ryegrass containing pasture. Calved 3 months prior. Owner had fertilized heavily and then rain fell on these pastures. Owner had been lifting with hip lifts twice daily and had administered dexamethasone, flunixin meglumine and vitamin B complex in the days preceding presentation. The owner administered one bottle of CMPK the morning of presentation (about 6 hours prior). Physical examination findings included recumbency, dehydration and profound depression. Initial therapy included IV hypertonic saline followed by crystalloid solutions for rehydration and stabilization.

CASE 7
3 year-old cow found out in pasture in lateral recumbency. Estimated to have been down for no more than 24 hrs. Cow had a 2 month old calf at side that was normal. Pasture was primarily ryegrass. Physical examination abnormalities included lateral recumbency, tonic-clonic like seizures, opisthotonus and excessive salivation. The area around the cow was disturbed as if paddling had occurred.

CASE 8
3 year-old bull presented for weight loss, chronic diarrhea of about one month’s duration and some blood in the stool for the past week. The bull was on pasture with cows and had maintained a good appetite throughout. He had been dewormed one month prior to presentation. Vaccinations were current. The pasture was heavily wooded. No other animals affected. Raised from calf on farm. Physical examination abnormalities included bloody, watery diarrhea containing black flecks of a hard material, oral and preputial erosions and a roughened, inflamed rectal mucosa upon palpation.

CASE 9
5 year-old Brahman female presented for recumbency of 36 hours duration. She had calved 6 days prior to parturition. Two weeks prior to presentation, she was presented to the referring veterinarian for udder edema and vulvar edema. She was treated with isoflupredone and a diuretic for one week until she calved. The owner noted the edema went away completely. Calving was uneventful. Three days after she calved, the cow was noted to be down and reluctant to stand. She progressively got weaker up to the point of presentation. She had continued to eat...
and drink normally throughout. Physical abnormalities included recumbency, moderate dehydration and her head and neck were flexed to the left toward her flank. Neurologic examination was unremarkable.

**BOVINE NEUROLOGY**

When presented with neurologic signs in the bovid, my approach begins with two basic questions: is it a primary neurological disease and is it rostral or caudal to foramen magnum? Etiologies that can cause neurologic signs include almost every category and consist of bacterial, viral, toxic, metabolic/nutritional, traumatic, neoplastic, congenital or hereditary and degenerative disease. This discussion will focus on answering the question of lesion localization. Lesion localization is the best way to get a grasp on a potential etiology, treatment and prognosis.

Taking a history is an even more crucial step in deciphering the cause of these signs. Investigative questions should include the

Environment ie: hogs nearby?, junkyard?, plants?, feeding practices?, silage?
Past disease? ie: pneumonia?, diarrhea?, navel infection?, BVD?
Age of onset
Breed ie: Brown Swiss, Charolais, Saler
Length of illness
Therapy and response
Past vaccinations, dehorning, castrations, spraying

**Signs Associated With Lesions in the Head**

Cerebral lesions in cattle, as in other species, can be diffuse or local and include commonly:
- seizures
- depression – Reticular Activating System
- change in mentation
- cortical blindness (normal PLR)
- compulsive circling
- opisthotonus
- head pressing
- yawning
- bellowing (abnormal vocalization)

Cerebellar lesions in cattle most commonly display some of the following signs:
- ataxia w/o paresis
- intention tremors
- wide based stance
- hypermetria
- strong muscle tone
- falling over backwards
- no conscious proprioception (CP) deficits
- may lack menace reflex, but have normal vision (swelling in the cerebellar region)

Vestibular apparatus lesions manifest as peripheral or central signs. Signs of peripheral disease include:

- Usually no depression
- head tilt – to the side of the lesion
- eye drop - to the side of the lesion
- leaning – to the side of the lesion
- circling – to the side of the lesion
- nystagmus – fast phase away from lesion – usually horizontal
- ataxia w/o weakness
- bright, alert, good appetite

Signs of central disease include
- depression or change in behavior
- head tilt
- eye drop
Lesions of the thalamus or hypothalamus consistently display one or more of the following signs:

- Change in behavior
- Temperature regulation difficulties
- Endocrine dysfunction

Moving to the brain stem, in general signs of this region are characterized by ataxia and paresis, depression to mania along with the more identifiable signs of cranial nerve deficits at the nuclear level. A review of the cranial nerves and deficits follows as well as whether these nerves are sensory or motor or both.

1. **Olfactory** – can’t smell smoke (Sensory)
2. **Optic** – loss of vision (Sensory)
3. **Oculomotor** – pupil dilation, ventrolateral strabismus (Motor)
4. **Trochlear** – dorsomedial strabismus (Motor) ie: polio
5. **Trigeminal** – loss of sensation to head/tongue (Sensory), dropped jaw due to loss of muscles of mastication, atrophy (Motor)
6. **Abducens** – medial strabismus, protrusion of eye (Motor)
7. **Facial** – loss of motor to the head (Motor), loss of sensation to tongue (taste) (Sensory) – otitis interna/media
8. **Vestibulo-Cochlear** – loss of hearing, loss of equilibrium (Sensory)
9. **Glossopharyngeal** – loss of motor to the muscles of pharynx (Motor), loss of sensation of pharynx, loss of parotid and zygomatic salivary glands (Sensory)
10. **Vagus** – loss of motor to pharynx, GI tract, heart, lungs, larynx (Motor), loss of sensation to pharynx, larynx, esophagus, trachea, part of external ear (Sensory), loss of afferent limb of many visceral reflexes
11. **Accessory** – loss of motor to trapezius, sternocephalicus, brachiocephalicus, larynx, pharynx (Motor)
12. **Hyoglossal** – loss of motor to muscles of tongue (Motor)

Now, moving caudal to the foramen magnum, we examine neurologic lesions of the spinal cord. These can be focal, multifocal or diffuse. General examples of conditions that disrupt the cord focally include: vertebral trauma, vertebral body abscess, vertebral fractures – ie: spondylosis in old bulls, malnutrition in young (Cu deficiency, high P/low Ca, lymphoma and congenital malformation. General examples of conditions that lead to multifocal cord damage include: CAEV, Parelaphostrongylus tenuis and Hypoderma bovis. Diffuse disease examples that may manifest as cord signs include rabies, pseudorabies, delayed O-P toxicity, botulism, tetanus, copper toxicity and progressive ataxia of Charolais and Brown Swiss (spinal muscle atrophy).

Gait deficits are probably the most common clinical signs we see in cord lesion(s). It is important to make some distinctions in order to determine the most likely localization. Paresis can be exhibited as flexor weakness in lesions involving the brain stem white matter or spinal cord or extensor weakness in lesion of the spinal cord gray matter (upper or lower motor neuron, respectively). Examples of gait deficits with paresis of flexor or extensor involvement include limb dragging, worn hooves, buckling and trembling when bearing weight. Animals can be ataxic with or without weakness with cord signs as well (cerebellar lesions have the classic ataxia without “weakness”). Ataxia takes the form of incoordination, swaying, abducted or adducted limb placement, limb crossing and pivoting on the inside limb and circumducting the outside limb when circling. Also, ataxia may manifest as a hypermetric or hypometric gait.

Although problematic in an adult bovid, when given the opportunity (downer animal, small calf), neurologic examinations should include an evaluation of spinal reflexes. Some of the most useful include the panniculus reflex, crossed extensor reflex, withdrawal reflex and the patellar reflex. Taking a closer look at how the bovine segments of the cord are divided according to signs we see the following breakdown:

- C1-C6 – Altered head and neck movements
  - Superficial sensation loss
  - CP deficits
Increased reflexes
Ataxia to all four
Recumbent

C6-T2 – Hyperactive rear limb reflexes
Depressed fore limb reflexes
Fore limb CP deficits- knuckle, stumble
Superficial sensation loss

T2-L3 – Normal fore limb reflexes
Hyperactive rear limb reflexes
CP deficits in hind limbs
Superficial sensation loss
Ataxia – hind limbs most severe and may dog sit

L4-S2 – Normal fore limb reflexes
Depressed rear limb reflexes
CP deficits in rear
Superficial sensation loss
Ataxia – hind limbs

S1-S2 – Bladder distention, loss of anal tone
“LMN Bladder” dribbles

S3-Cd5 – Flaccid tail, anus, loss of sensation to penis, vulva, perineum (caudal epidural)

Ancillary diagnostics that can be commonly employed such as advanced imaging are most of the time not practical in cattle medicine. However, examination of CSF can be rewarding. We typically NEVER take this from the cisterna magnum. Lumbosacral taps are the most practical to perform and the safest! As a matter of interest, here are some reference values for normal bovine CSF:

- Protein: < 40 mg/dl
- Nucleated cells: < 10/microliter – monocytes
- Pandy: neg. for globulin
- Glucose: 60-80% of blood
- CPK: < or = 20 IU/dl
- Sodium: 134-144 mEq/L

Obviously, other diagnostic tools such as a CBC and chemistry panel can help to some degree answer the question, is it primary neurologic disease?

In summary, the endpoint to this discussion has been, when presented with signs of neurologic dysfunction, we ask, is it primary neurologic disease and is the lesion rostral or caudal to the foramen magnum. Lesion localization, even if you believe it is a disease you can’t treat, goes a long way toward directing treatment (treat the treatable) and determining prognosis.

References are available by the author.

**Diseases Causing Generalized (Diffuse) Brain Signs**

**Polioencephalomalacia (thiamine deficiency and hydrogen sulfide toxicity forms)**

**Thiamine deficiency form**

**Etiology/Predisposition**
Primarily occurs in young cattle, sheep, goats, antelope, deer
Usually animals on a high concentrate, low roughage diet.
Low thiamine decreases the activity of transketolase in the RBC’s which is the rate limiting enzyme in the pentose phosphate pathway. This leads to a decreased utilization of glucose by tissues. Thiamine is also needed for alpha ketoglutarate and pyruvate promotion of the Krebs cycle (responsible for ATP prod. in brain). Without adequate ATP, the ATP dependent transport mechanisms for Na and water are impaired leading to neuronal swelling.
Factors of thiamine deficiency:
1. disturbances in thiamine metabolism
   a. low intake
   b. increased demand ie: increased thiaminase activity in the rumen
- *Clostridium* species – proliferates with increased grain intake
- *Bacillus* sp. – proliferates with increased grain intake
- Ingestion of thiaminase producing plants ie: “horsetail” (*Equisetum*)
- Drugs – piperazine, levamisole, thiabendazole, acepromazine

2. decreased rate of synthesis - molasses- decreases amount of proprionate (glucose precursor) – high in S
3. increased excretion
4. thiamine antimetabolites such as amprolium (40x treatment dose)

Feeds and/or plants that may predispose:
- a. Corn gluten
- b. Turnips
- c. Kocia

Stages of disease occur in 3 stages:
1. spastic, uncoordinated movement/convulsions when excited/may or may not be blind, hyperesthesia
2. blind/opisthotonus/star gazing (4th CN)/circles/head press/diarrhea
3. lateral recumbency/paddling/death/head tilt/nystagmus

Sudden onset with cortical blindness (intact PLR)
-trochlear nerve damage leads to dorsomedial strabismus (medial part of pupil rotates dorsally)
-normal rumen function
-these may be only signs

**Diagnosis:** transketolase activity in blood – levels of mean erythrocyte transketolase ▲

**Postmortem:**
-moist, swollen, yellow cortical gyri, cerebellar coning
-may fluoresce under UV light due to lipofuscin

**Treatment:**
-thiamin 5mg/# QID on day 1, then BID for a couple more days
-vitamin B complex
-DMSO may help scavenge free radicles
-transfaunation to replace thiamin producing organisms

Treatment response may be diagnostic! ie:no animal should die of CNS signs without thiamine on board
If animal does not respond, it may still be polio, but the brain is so necrotic, the damage is non-repairable. May be a “dummy” and survive.

**Prevention:**
-Brewer’s yeast provides extra source of thiamine
-increase roughage in diet selects for favorable rumen bacteria
-check sulfate levels in diet/water to be sure it’s not the following

**Hydrogen sulfide toxicity (high sulfates)**

High Sulfates in the Diet – causes polioencephalomalacia as well via hydrogen sulfide toxicity

**Pathogenesis:**
High levels of S in ration, forage or water. Two types of bacteria are present in the rumen. The assimilatory type uses S for assimilating S containing amino acids. The dissimilatory type uses S as part of its own respiration and in turn produces hydrogen sulfide gas. This gas is eructated and inhaled. Inhaled hydrogen sulfide is absorbed and is thought to exert its toxicity via disruption of the cytochrome oxidase (P450) enzyme necessary for cellular electron transport.

**Predisposition:**
High levels of S in diet.
High concentrate feed leads to lower pH in the rumen which favors the dissimilatory bacteria. This process usually takes about 2 weeks of intake.

**Diagnosis:**
History and clinical findings of cortical blindness with acute onset.
CHECK WATER AS A POTENTIAL SOURCE
Lesions on necropsy are identical to thiamine responsive polioencephalomalacia.
On a herd basis, levels of S in cattle can be measured via chute side rumen gas cap test.
**Treatment:**
Thiamine – somewhat responsive at same dosages that thiamine responsive polio is treated with Diazepam to control seizures, convulsions.
Transfaunate.

**Lead**

Only a small amount of ingested lead is absorbed, the rest is excreted in the feces.
Metallic lead is less absorbable than the lead salts.
- absorbed lead is stored in bone
- becomes mobilized during periods of metabolic acidosis or treatment with CaEDTA

**Pathophysiology:**
- lead combines with RBC and increases its fragility
- lead inhibits utilization of Fe and biosynthesis of heme
- inhibits delta-aminolevulinic dehydratase (d-ALAD) and ferrochetalase enzymes of heme synthesis, leads to a build up of porphyrins as well.

**Presentations:**
- encephalopathy
- gastroenteritis
- peripheral neuritis
- liver and kidney failure
- abortion
- anemia
- immunosuppression

**Sources:**
- batteries!
- lead arsenate
- grease/used motor oil/lead based paints
- roofing felt/linoleum
- oil field pipe dope (on the ends of old sticks of drilling pipe)

**Toxic Dose:**
Acute lethal dose – in calves 400-600mg/kg one time, in adults 600-800mg/kg
Minimal daily intake - 6mg/kg/day

**Signs: (These are definitely rabies suspects)**

**Acute**
- young (CNS and GI)
- takes 12-24hrs to develop
- cerebral signs include seizures, champing of jaws and frothing, rhythmic contractions of ears and eyelids
- rumen atony and dead protozoa
- blind with normal PLR

**Subacute:**
- older
- blind with normal PLR
- anorexia
- bruxism
- dull but alert eye and ears

**Chronic:**
- lead stored in bone
- normocytic normochromic anemia
- basophilic stipling
- weight loss

**Postmortem:**
May not see anything early, but late you may see abomasitis or kidney and liver swelling.

**Diagnosis:**
- basophilic stippling with a normocytic, normochromic anemia
- levels of aminolevulenic acid
- blood lead (purple top!) > or = to 0.35PPM
- liver and kidney > or = to 10PPM
- fecal 0.35PPM
- reticular radiographs (metallic foreign body – Diehard)

**Treatment:**
- cathartic like magnesium sulfate 1-2 g/kg orally
- CaEDTA 6.6% solution – 73mg/kg daily divided into 2-3 doses for 5 days, then repeat if necessary (may cause secondary zinc deficiency, therefore when the skin starts to scale, be prepared)
- thiamine 5-10mg/kg daily
- rumenotomy (remove Diehard)
- supportive with fluids
- oral alimentation (transfaunate)

Can we eat it doc? Takes several months to be removed from the bone. (personal note to self, don’t eat soup or pot roast)

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**Rabies**

**Cause:** Rhabdovirus

**Pathophysiology:** Enters the epidermis or SQ via bite or salivary/CSF fluids contamination – replicates locally – travels via peripheral nerves, spinal rootlets or spinal cord to brain – travels to saliva and nasal epithelium

Incubation period: 3 weeks to 3 months – may shed virus before clinical signs

Clinical signs appear more quickly if animal is bitten or infected on the head or extremities.

**Transmission:**
- bite – most common
- nervous tissue/CSF fluid exposure
- aerosol
  Bat caves?
- milk

**Reservoirs:**
- fox in north
- skunk or raccoon in south
- bats

Three forms:
1. Furious
2. Dumb
3. Paralytic

**Signs – furious**
- hyperexcitable, fear, rage
- early tenesmus, bellow but may not make normal noise, aggressive
- paraphimosis, hypersexuality
- die in 2-4 days

**Signs – dumb**
- depressed, anorexic, febrile, tenesmus
- flaccid tail, anus, bladder, tongue
- salivate, head press, circle
- base wide stance, ataxic, CP deficits, dropped head/neck

**Signs – paralytic**
- 1st often see unexplained ataxia or shifting leg lameness
- spinal reflexes are depressed
- recumbency, flaccidity
- down after 3-5 days, then die about day 10

**Diagnosis:**
FA stained hippocampus and cerebellum, Negri bodies with a non-suppurative encephalitis, mouse inoculation

**Prevention:**
Vaccinate all farm dogs, cats etc.
Vaccinate cattle?
Water Deprivation/Salt Water Toxicity

Either get too much salt or not enough water.
- see this in show pigs that are held off water to make weight, then transported, then allowed to drink
- seen also in pigs in winter on automatic water supplies that freeze
- winter – due to frozen water for any species
- calves that are scouring that the owner has treated with incorrectly mixed oral electrolyte solutions – creates very high levels of Na in blood which normalizes with brain Na ion
- calves fed exclusively milk without access to fresh water – weaned and offered water

Maximum tolerable salt level in feed is 4% for lactating cows and 6% for non-lactating cows. Water 5,000PPM is the maximum tolerable level for all classes of livestock.

Pathophysiology (water deprivation):
- Na ion concentration becomes higher in the brain tissue than the CSF and blood due to hyperosmolar CSF and brain tissue created during times of water deprivation. The high Na in these regions inhibits the normal mechanisms in place to pump Na out.
- formation of “idiogenic osmoles’ in the cerebrum
- when water is offered to these animals, the Na content of the water is lower than the ion content of the CSF and tissues
- water moves from area of greater concentration to lesser concentration (from blood to CSF and brain)
- cerebral swelling

Signs:
- cerebral, from brain swelling
- can get GI signs from high salt intake, causes a severe diarrhea that may even be bloody (omasitis)

Postmortem:
- inflammation of omasum, abomasal and omasal surfaces may be hemorrhagic and dark
- cerebral edema (coning)
- in swine only – eosinophilic meningoencephalitis

Diagnosis:
- clinical signs (pigs sit and spin)
- history
- CSF Na > than serum Na or serum and CSF Na > than 160 mEq/l
- cerebral Na 1800PPM or >
- histopathology

Treatment:
- frequent small amounts of water
- IV mannitol to decrease edema
- diazepam to control seizures
- IV sodium containing fluid such as hypertonic saline
- if giving a scouring calf fluids and CNS signs develop, think Na ion toxicity, then provide IV fluids HIGH in sodium as to slow the movement of water into the brain

Prevention:
- access to fresh water all the time
- check salt levels in water/feed

Nervous Coccidiosis

Seen most commonly following or during outbreak of scours from coccidia. (bloody)
Current thinking is that signs come from a toxin liberated from the gut due to invasion of coccidia.
Eimeria sp.

Signs:
- at first are intermittent with periods of normalcy between episodes that get shorter and shorter as the disease progresses
- convulsions
- muscle tremors
- opisthotonus with forelimb extension
- strabismus
- tetanic spasms
**Diagnosis:**
- clinical signs and fecal flotation

**Treatment:**
- Albon (sulfamethazine) boluses, vitamin A
- One time and then leave alone

**Prevention:**
- coccidiostats in feed and/or water
  a. sulfamethazine
  b. decoquinate (Deccox)
  c. amprolium
  d. ionophores (rumensin and lasolocid)
- break fecal oral cycle

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**Urea Toxicosis**

- Urea = 45% nitrogen and is = to 281% protein
- Protein is 16% nitrogen
- Usually added as about 1% of total dry matter of ration (0.5% for dairy cattle)
- Non-protein nitrogen source

**Toxic Dose:**
- cattle – 1-1.5g/kg but as little as 50 g can be toxic to animals that have not been consuming urea
- sheep – 2g/kg b.w.

**Sources/Causes:**
- fed to hungry animals that have not been eating urea in feed
- improper mixing
- high concentrations in low energy diets
- soybeans fed with urea (soybeans contain urease)
- screw-up! (wrong product in salt feeder)

**Pathophysiology:**
- urea is split by urease in the rumen to produce ammonia and then ammonium (urea to NH3 and H ions via urease, then to NH4)
- as more NH4 is produced, the pH of the rumen climbs
- at the higher pH, more NH4 converts back to NH3
- NH3 is absorbed through the rumen wall and carried to liver
- normally in the liver, NH3 is converted to urea and excreted, but if excessive NH3 is presented to the liver than can be processed, NH3 goes systemically (brain)

**Signs:**
- salivation
- bruxism
- abdominal pain
- dull
- muscle tremors
- hyperirritability
- tetany
- prostration/death (1-4hrs)

**Diagnosis:**
- ammonia smell of rumen contents
- rumen pH > 8 (have to sample quickly after death to be accurate)
- freeze blood and take rumen content immediately after death NH3 > 2mg/dl in blood or >80mg/dl in rumen content
- establish source

**Treatment:**
- 1-2 gallons of vinegar plus cold water (5 gallons) if not tetanic (vinegar decreases pH, cold water decreases temp. thereby decreasing urease activity
- sheep 1 quart vinegar
- rumenotomy to empty contents
Bacterial Meningitis

Young calves, lambs, kids and pigs
Highly associated with failure of passive transfer!
CNS is infected via hematogenous route (OMPHALITIS)
Clinical signs associated with
a. omphalitis
b. hypopyon
c. arthritis (swollen joints)
d. enteritis
e. pneumonia
f. physisis

In adults (cows) associated with mastitis caused by Pseudomonas aeruginosa
Calves that seem to be improving clinically from septicemia/bacteremia, but maintain elevated rectal temperature may signal impending CNS signs!
Cause:
- E. coli – most common organism isolated!
- Pasteurella, Actinomyces pyogenes, Salmonella

Signs:
- may or may not be febrile
- hyperesthesia (nerve root involvement)
- head extension
- opisthotonus
- convulsions
- muscle rigidity
- exaggerated spinal reflexes
- abnormal vocalization when stimulated

Clinical Pathology/Diagnosis:
- low glucose?
- may or may not see elevated WBC count, neutrophilia, high fibrinogen
- protein might be low (never got colostrum)
- CSF tap is diagnostic! (protein > 40 mg/dl, neutrophilia, pandy pos., glucose < 50% of blood, CK > 20 IU)

Pathophysiology:
Inflammation of the arachnoid trebecula and choroid plexus leads to decreased absorption of CSF fluid which leads to hypertensive hydrocephalus

Postmortem:
- cloudy meninges
- cloudy CSF

Differentials:
- hypoglycemia
- congenital abnormality
- toxins (lead)
- IBR

Treatment:

a. antibiotic
   - Naxel (ceftiofur sodium) 2-4 mg/lb IV TID
   - Nuflor (florfenicol) 20 mg/kg IV q 24 hrs
b. NSAID’s
   - banamine 1.1 mg/kg IV BID
c. Sedative if needed
   - valium .5 – 2 mg/100 lb
d. Whole blood – failure of passive transfer
e. IV fluids
f. Milk
Thrombotic meningoencephalitis (TEME)

**Cause:**
*Histophilus somni*

**Pathophysiology:**
Vasculitis with thrombus formation and septic infarcts in various organs. Endothelial cells slough and expose collagen which starts the clotting cascade.

**Signs:**
- usually see concurrent manifestations of *H. somni* ie: pneumonia or arthritis
- very high fever initially (108 F)
- acute – blind, nervous signs, depression, weakness ataxia, paralysis, coma, death, accompanied by swollen joints.

**Syndromes associated with Histophilus:**
- CNS
- Arthritis
- Pneumonia (BRD)
- Otitis externa/interna
- Abortions

**Diagnosis:**
- clinical signs/history
- hemorrhages on retina, hyphema
- culture from TTW fluid or chest tap – very fragile bug
- CSF – xanthochromia, increased neutrophils, total protein > 100 mg/dl

**Postmortem:**
- brain – multifocal areas of hemorrhage and necrosis
- pleural thickening

**Treatment:**
- oxytetracycline 5 mg/lb IV BID
- florfenicol 20 mg/kg IV SID
- naxcel initially 2mg/lb IV BID, then 1mb/lb IV BID x 4 days
- NSAID’s (banamine 1 cc/100 lbs IV or IM SID)

**Prevention:**
- vaccine may reduce severity and incidence of CNS disease
- need new vaccine
- mass medicate LA 200 or Aureomycin in feed (5-10 mb/lb/cow/day)
- lower stress

**Listeria**

**Cause:**
*Listeria monocytogenes*
- G positive flagellated coccobacillus
- lives in soil, vegetation and fecal material (spoiled silage)
- intracellular organism

**Its Favorite environment:**
- pH > 5.5
- oxygen supply
- moisture

- occurs when stored silage is disturbed and spoils ie: broken door on the bottom of a silo allows moisture and oxygen to get in, pH goes up (normally silage cures under acidic pH) and bacteria multiplies

**Pathophysiology:**
- enters via mucous membranes of mouth or conjuctiva or nares and migrates centripetally up the trigeminal nerve
- seen commonly in young cattle during tooth eruption
- affects cattle, sheep and goats
Signs:
- fever early then normal
- depression
- encephalitis, meningitis, ophthalmitis, septicemia, abortion and mastitis
- trigeminal nerve involvement – loss of sensation to face, dropped jaw on same side as lesion
- abducens – medial strabismus
- facial – droopy lip, eye (secondary keratitis, deviated nares)
- vestibulocochlear – head tilt
- glossopharyngeal and vagus – dysphagia and salivation (may lead to acidosis)
- hypoglossal – decreased tongue tone

**Hallmark of listeria is multifocal cranial nerve signs with depression and acute onset.**

**Diagnosis:**
- clinical signs/history
- CSF – increased monocytes and protein (MONONUCLEAR PLEOCYTOSIS)
- illness > 4 days (usually excludes rabies)

**Postmortem:**
- multifocal microabscesses in the brain

**Treatment:**
- correction of acidosis
- PPG (40,000 IU/kg BID for 7 days, then SID for 14 days) Float them in PPG!
- oxytetracycline (5mg/lb BID x 7 days)

**Zoonotic potential:**
Organisms in milk may withstand pasteurization!

### Cerebellar Disease

**BVD (Cerebellar Hypoplasia)**

**Cause:**
BVD infection in the dam generally between day 100 and 200 of gestation

Virus attacks rapidly dividing cells, and the cells of the cerebellum are doing just that during this stage of gestation

This in utero viral infection is also associated with
- cataracts
- retinal hemorrhages

**Signs:**
- cerebellar (hypermetria, head tremors, whole body tremors, ataxia without weakness)
  - present at birth
- some animals compensate and live to make slaughter weight
- if you find calves born with cerebellar signs, best rule out BVD before moving on to a zebra (inherited disorder)

**COMMON DISEASES OCCUR COMMONLY**

**Diagnosis:**
- pre-suckle titer to BVD? This just indicates exposure.
- BVD ELISA pre-suckle or after maternal antibodies have waned
- virus isolation from tissues
- may be very difficult to pin this on BVD as the virus is already gone when we see these cerebellar signs

**Storage Diseases**

**GM1 Gangliosidosis** – decreased Beta-Galactosidase activity
- Fresian cattle (not cold cattle!)
- cerebellar signs start during first few weeks of life (not birth)
- unsteady gait
- dead by 1 year

**Glyconeogenesis** – Beef Shorthorns and Brahmans

**Mannosidosis** – **Alpha mannosidase** deficiency
- Angus, Murray Grey, Galloway, Simmental
- first few weeks of life (not birth)
- ataxia, head tremor, poor doing
- abortions, neonatal death, poor doers
- homozygous or heterozygous (complete or partial deficiency, respectively)
- blood test available to detect carriers
- acquired form of alpha mannosidase deficiency in cattle, sheep and horses comes from consumption of Loco Weed (Astragalus, Oxytropis) swainsonine is the toxin

**Beta mannosidase deficiency – Saler**
- autosomal recessive
- can’t stand at birth
- domed calvarium, narrow palpebral fissures
- dilated ventricles, loss of cerebral and cerebellar white matter
- blood test for enzyme to pick out carriers

**Claviceps Paspali (Dallis Grass Staggers)**

**Cause:**
- fungus attacks ovary of several different grasses (bermudagrass, canary grass, rye grass, Dallis grass)
- signs are a result of an ergot – occurs in winter after wet, humid summer

**Signs:**
- resemble cerebellar disorder due to tremors of head, whole body
- ataxia, neurological derangement, shaking
- otherwise bright, alert and responsive to surroundings
- usually continue to eat and drink normally

**Treatment:**
- get off offending pasture
- mow to remove seed heads

**Spinal Cord Disease**

**Trauma**

Trauma directly to cord caused from compression created by vertebral fractures

**Causes:**
- riding during estrus
- chute injuries
- nutritional secondary hyperparathyroidism (young calves on high grain, low roughage diet without Ca supplementation)
- secondary to vertebral body abscess
- copper deficiency

**Signs:**
- localization to area of cord
- acute onset
- CSF fluid may or may not have evidence of hemorrhage (erythrophagocytosis)

**Treatment:**
- salvage if you can (no drugs)
- dexamethasone 0.5 mg/# one time
- banamine
- phenylbutazone 10 mg/kg orally on day one, then 5 mg/kg orally every 48 hrs (long withdrawal time and illegal in dairy cattle older than 30 months)

**Vertebral Body Abscess**

**Cause:**
- Archanobacterium pyogenes most common.

**Pathophysiology:**
- hematogenous spread usually from navel which may invade the meninges
- usually in animals over 2 weeks of age

**Signs:**
- alert, afebrile, good appetite
- localize to cord segment (some calves may have just a head tilt without ataxia – look in ear)
Diagnosis:
- increased serum globulins/fibrinogen?
- CSF may or may not have increased WBC’s, or protein – CPK is usually increased
- acute to subacute onset

Treatment:
- these calves die

Epidural Abscess
Caused by ascending myelitis from
- tail docking
- epidural injections
- trauma and infection

Signs:
- febrile
- localize cord segment
- inflammatory leukogram

Treatment:
- antibiotic (oxytetracycline, florfenicol, ceftiofur, sulfas)

Prognosis:
- depends on duration

Parasites
Causes:
- Hypoderma bovis (northern cattle grub)
- Paralephostrongylus tenuis – meningeal worm of white tailed deer – larvae passed in feces, then penetrates footpad of mollusks which are then ingested by sheep, llama, goats-parasite migrates to and in CNS. Even though this larvae migrates in the spinal canal in the white tailed deer, it does NOT cause clinical signs in this species. Signs are only observed in an un-natural host.

Signs:
- ataxia
- depends on location in cord – may be multifocal or non-symmetrical
- acute onset that may progress
  - usually progresses to recumbency

Treatment:
- dexamethasone SP may help early
  - fenbendazole (10 mg/kg) once a day for five days along with flunixin meglumine

Prevention:
- deworm regularly with ivermectin, fenbendazole or valbazen in goats/llamas for P. tenuis
  - ivermectin or systemic insecticide before entrance to CNS occurs

Neoplasia
Cause:
Bovine lymphosarcoma commonly invades the lymph nodes near the spinal canal. Also, this tumor occasionally invades the canal and spinal cord itself.
- usually in lumbar area – epidural space or within cord itself

Diagnosis:
- history (3-6 years old)
- may be acute onset and mislead you to think signs are trauma induced
- rectal palpation – enlargement of internal lymph nodes (sub-lumbar)
- positive BLV titer (p-24 may be helpful if positive)

Treatment:
- another plot in the cemetery

Tetanus
Cause:
Clostridium tetani
Three toxins (exotoxins)
- tetanospasmin – inhibits impulse transmission of the spinal motor inhibitory cells (Renshaw cells) by inhibiting the release of glycine and GABA
- tetanolysin – causes tissue necrosis thereby contributing to favorable environment for multiplication
- non-spasminogenic toxin – overstimulates sympathetic nervous system

**Source:**
- wound (deep puncture that sets up anaerobic environment)
- uterus (post partum, prolapse?)

**Signs:**
- may take 1-2 weeks to develop
- stiff gait
- elevated third eyelid
- "pump handle tail" (elevated, stiff)
- off feed
- erect ears – retracts ears, lips
- bloat
- exaggerated movements
- hyperesthetic

**Treatment:**
- keep in a quiet place (patches over eyes, darkened, cotton in ears)
- debride wound, flush uterus etc.
- PPG (40,000 IU/kg SID or 20,000 IU/kg BID for 7 days)
- tetanus antitoxin (Cattle: 20,000 IU IV first day, then 10-15,000 IU SID until improvement is noted) (dose varies widely from 1000 to 5000 units/500kg to 1000 to 5000 units/kg)
- diazepam – may neutralize unbound toxin
- acepromazine-activates inhibitory spinal cord tracts
- guaifenesin – IV to effect – blocks impulse transmissions at interneurons of spinal cord
- mephenesin – polysynaptic blocking agent
- dantrolene – muscle relaxant

**Prevention:**
- tetanus toxoid

**NEUROLOGIC DISEASE: CASES**

**CASE 1**
Herd of 150 Angus crossbred cows, gave birth to these calves. A calf with similar signs was born last year and died due to misadventure (fell into a ravine and was cast). There had been two other cases in previous years that were chalked up to "bad luck". Cows of these calves have been normal in every way. One of the calves of the past that survived slowly improved. Postmortem on calf last year was grossly unremarkable. Work-up on these is non-specific.
Physical examination: within normal limits
Neurologic examination: see video
Lesion localization?

**CASE 2**
Group of 60 Holstein heifers raised as replacements out on pasture. Two heifers are recumbent on farm, these were presented for examination. Nothing has died. Recumbent heifers still eat, drink normally. On physical examination, no other remarkable findings were noted. Cranial nerves were normal. These heifers still had an appetite. No significant laboratory abnormalities were noted.

**CASE 3**
6 month old doe presented for "stumbling" and 'weakness" for about a 1 week duration
Lesion Localization?

**CASE 4**
4-month old show heifer prospect presented for gradually worsening “lakeness” or ataxia of 10 days duration. No other abnormalities noted.
Lesion localization?
CASE 5
Calf presented for acute onset clinical signs. The calf was 4-months old, and was out with dam on pasture. No history of abnormal birth, or other disease problems prior to presentation. No other calves affected. The cow was normal. Physical examination parameters were normal. Neurologic examination revealed blindness with intact papillary light reflex, champing of the jaws, preferred to stay recumbent and ear twitching.
Lesion localization?
CASE 6
These twin calves were presented at 10 days of age. The signs you see were present at birth according to the owner. The dam of these twins was part of a group of cows purchased over the past 2 years. Supposedly, the cattle herd of origin was well vaccinated. Physical examination calves were normal with the exception of bilateral cataracts in one twin. Neurologic examination revealed a “hypermetric” gait in the other calf.
Lesion localization?
CASE 7
This yearling heifer was presented for a two day history of ataxia. The owner thought she may have been blind for a short period of time. When we got her off the trailer, however, she appeared to have vision, although it was possibly limited. Another heifer at the farm was recumbent and had been similarly affected prior to her progression to recumbency. The owner treated with LA 200 on the first day they noticed clinical signs.
Lesion localization?
CASE 8
14 day-old calf born uneventfully. Herd is well vaccinated. Calf nursed and is bright and alert otherwise. No abnormalities noted on physical examination (no swollen joints, navel, scleral injection).
Lesion localization?
CASE 9
Three week-old calf presented for the major clinical sign you see in the video after it was noticed 2 weeks ago. The calf was a product of dystocia, as it was “hip locked” for a period of time. The calf did nurse and is normal in every other way.
Lesion localization?
CASE 10
Yearling heifer presented for history of recumbency for 7 days duration. Prior to going down, heifer appeared healthy but was noted to be becoming weaker. Heifer maintained good appetite and drank water throughout the course of illness. The owners had been slinging her twice daily. They reported she would stand for short periods of time, but then would collapse and not try much after that. Physical examination was unremarkable with the exception of a “dull” demeanor. She was a show heifer, however, so this was difficult to interpret. Neurologic examination revealed slow palpebral reflexes and corneal reflexes bilaterally, an intact papillary light reflex and generalized hypotonia and hyporeflexia. No cranial nerve abnormalities noted and she was visual. The overall interpretation was generalized weakness.
Lesion localization?