#### The Most Commonly Asked Questions Concerning Bovine Pulmonary Hypertension (Brisket Disease) And Pulmonary Arterial Pressure Testing (PAP testing) Western Veterinary Conference Las Vegas, 2022

## 1. Why are cattle the most commonly affected animal and do other animals such as Yaks, Camelids, horses, sheep and goats get the disease?

The bovine pulmonary response to hypoxia pulmonary vascular shunting is seen in all animals under hypoxic conditions. Shunting of pulmonary blood flow is seen in cattle to a much greater degree than in other species. The vasoconstriction mechanism of shunting is a means of distributing pulmonary blood flow away from poorly oxygenated lung tissue to more oxygen-rich areas. This exaggerated shunting mechanism, the anatomic pattern of the bovine lobulated lung, and the small lung-size/body-weight ratio all contribute to a severe loss of functional pulmonary capacity. Pulmonary vascular shunting is initially mediated through pulmonary arteriole constriction in the acute stages of hypoxia. Hypertrophy and thickening of the medial layers of the pulmonary arterioles (medial hypertrophy) and adventitial tissues occur with chronic hypoxic exposure. Vascular remodeling with loss of peripheral pulmonary arteries (rarefaction or pruning) also contributes to increased pulmonary resistance. As indicated earlier, the ensuing pulmonary arterial hypertension results in cor-pulmonale (heart disease secondary to pulmonary hypertension) and RV hypertrophy, followed by RV dilation and right-sided congestive heart failure. It appears that this maladaptive response of vasoconstriction, shunting, arterial medial and adventitial hypertrophy, and vascular pruning resulting in pulmonary hypertension is characteristic of cattle and is a highly heritable characteristic in this species. Some cattle appear to be more naturally resistant to this process, whereas other animals develop these pathologic changes very rapidly and die of HMD in a short period of time. Other ruminants including sheep, goats, camelids, yaks and bison all go through the same response to hypoxia but to a lesser degree. Anatomy of the lungs from gross size to microscopic level are different giving rise to more lung space, to body size and a more elastic type lungs tissue

# 2. What PAP measurement/score should I buy when the test is taken at 4900 feet, I read in a bull catalog that the PAP test was actuate at this elevation if the bulls was 16 months old, is this correct?

Brisket Disease, in review, (High Mountain disease, HMD) results in death due to congestive right heart failure secondary to an increase in blood flow resistance in the lungs. This resistance is a result of chronic (most commonly but not rule) low oxygen tension experienced in high altitude. A PAP test is a means to measure Pulmonary Hypertension or blood flow resistance making it possible to predict an animals' welfare in high altitude. Lung resistance and pulmonary arterial hypertrophy is brought about by a chronic exposure to low oxygen tension. The term chronic is most commonly used, but to define what is chronic is difficult. There appears to be an extreme individual difference in disease resistance. Some animals appear to be very prone to the congestive heart failure while others can live at high altitude and an elevated PAP test for years with no problems. It is for this reason the elevation of the test is important. It has been determined that the low oxygen stress (chronic hypoxia) needed to stimulate problems is not present until approximately 5000 feet elevation. This factor makes it impossible to accurately PAP measure an animal lower than 5000 feet. It is also important that this Pulmonary Artery Hypertrophy secondary to high altitude hypoxia is chronic in nature making it a necessity for the animal to be in altitudes greater than 5000 feet for a minimum period of 3-4 weeks prior to testing. The longer the animal is in high altitude prior to testing the more reliable the test is.

It has been demonstrated that a PAP score will go up as the animal is taken to a higher altitude. It is for this reason elevation of the test site must be considered. For simple guidelines, the animal should be tested at an elevation of at least 5000 feet. The higher the elevation of the PAP test the more accurate the results. Look at the PAP score and the elevation at which it was taken and consider the elevation the animal will be living. It has been determined that the expectation of the PAP score is to increase approximately 1-1.5mmHg per 1000 feet elevation climb, if the initial test was taken at elevations greater than 6500 feet. For example, if an animal is purchased, greater than 12 months of age and tested at 6500 feet rise in elevation the animal is transported to. For instance if they are to graze at 10000 feet the true PAP at 10000 feet would be approximately 44-46mmHg which is a moderate risk score, and a moderate risk animal for use at that altitude.

It should also be noted that not all animals follow the above generalizations. In one study conducted in Laramie Wyoming it was shown at a statistically significant level that cattle tested at 5000 feet and moved to 6500 feet for three weeks and retested, averaged an increase in the PAP of 7.2mmHg. This variation is based on the fact that 5000 feet is the absolute minimum for testing and at this elevation the degree of inaccuracy and PAP variability is much higher. It should be recommended to all involved that cattle tested between 5000 feet and 6500 feet elevation, that the degree of variability is unpredictable and retesting is recommended. Evaluating age and elevation together is a must; if an animal less than 12 months of age is tested at elevations lower than 6500 feet the degree of inaccuracy unpredictable. It is best to think of those cattle PAP tested below 6500 feet as a screening test only and not a test validated for genetic breeding potential. A PAP test at this elevation can be accurately used to find those animals already experiencing pulmonary hypertension thus allowing management decisions at this time. The chance of getting a high false PAP reading is very rare at any elevation.

There is no evidence that the older age of animal tested would increase the accuracy of the test at lower elevations but in some ways it may make since. Since the animal is larger at an older age there is more demand on oxygen making the hypoxic effect greater possibly increasing the PAP measurement.

See the below chart for more information!

## 3. What PAP score is too high to sale, I have seen bulls in sells that are over 100 and marked as 50+?

This is a great question without an exact answer. To give only an opinion justified by physiology, any measurement over 49 may give rise to pulmonary hypertension and right ventricular congestive heart failure. Often when we evaluate a PAP measurement we look at the systolic/diastolic measurement to evaluate the functioning condition of the heart. Higher Systolic/Diastolic (S/D) scores give rise to a poorer prognosis for recovery even at low elevations. The higher the S/D is a reflexion of heart cardiac stress. When

the diastolic measurement gets above 30 mmHg then this is correlated to right ventricular hypotrophy and loss of pliability to the pulmonary artery. What we do not know on a scientific basis is which of these animals can survive this condition and which of these cases may have a heritable contribution. So as far as saying one cannot sell an animal over a certain measurement is difficult. I do think this responsibility lies with the producer in that if the animal would die then the new owner could question why a bull with a high measurement was sold to them. We can also justify not selling the animal with a very high measurement in that this animals offspring may be very suitable to the same hypertension and die.

#### 4. How is the PAP score affected by temperature?

Cold environmental temperature can cause pulmonary hypertension in cattle. Temperatures less than 32 F (most commonly there is little affect until the ambient temperatures are below zero and then may be variable form animal to animal) have been shown to increase PAP by 25% to 55%. Animals with elevated PAP before cold exposure showed greater increases in PAP than normal animals. Animals exposed to cold environments showed decreased arterial Po2 and increased arterial Pco2, indicating that hypoventilation-induced hypoxia is, in part, responsible for the pulmonary hypertension observed at cold temperatures. Increased pulmonary blood flow also contributed to the pulmonary hypertension.

#### 5. Are there breed differences?

Based on tests of more than 351,000 head of cattle, it appears that no one breed is resistant to the effects of high-altitude hypoxia. High-PAP animals (>50 mmHg) have been found in all breeds tested. Some breeds, and pedigrees within breeds, appear to be more naturally resistant to the effects of high altitude, lending support to the conclusion that specific genetic factors can be managed to decrease clinical cases of HMD. It is important in the evaluation of any animal originating from a low altitude herd (5000 ft elevation) to realize that it has a higher probability of experiencing high-altitude effects than those raised in higher elevations. This innate resistance to high altitude is secondary to the effects of natural selection and the culling processes by the rancher. By PAP testing all bulls and all replacement heifers, and culling all females that may give birth to an HMD calf, a rancher can develop a more naturally resistant herd. This type of selection is not possible for ranchers at low elevation because the animals must spend some time at high altitude to show the effects of high-altitude pulmonary hypertension. This consideration is important in testing or using animals originating from lowland herds or artificial insemination sires.

## 6. Are there differences in bulls vs. heifers and do I use the same numbers for each in developing my herd?

No physiologic basis exists for a difference in PAP measurements between male and female cattle. The author (TNH) has observed differences in the percent of male and female cattle that have high PAP measurements in specific herds. These differences can often be attributed to husbandry practices and feeding management (see later discussion on body condition), or to breeding practices and breeding management. Selection of low elevation seed stock that have not been confirmed to have a low PAP measurement at altitude can greatly influence the PAP measurements of replacement cattle and may result in a gender difference in PAP measurements.

## 7. I am feeding an Ionophore (rumensin), I have heard that this increases the PAP score, how long should I have them off the rumensin before I test them?

This is an area that without a doubt needs further research. At this time there does not seem to be any consistent repeatable data showing that there is a direct correlation to pulmonary hypertension and the feeding of Ionophores. That being said, Ionophores fed to cattle at high altitude may increase the risk of pulmonary hypertension. In a small pilot study, an ionophore was fed to calves at the labeled dose for 6 weeks in a Colorado feedlot at an elevation of 1500 m (5000 ft). No other changes were made in the cattle's diet or environment. The PAP results at the end of the 6-week feeding trial resulted in 44% being over 50 mmHg and 71% being 45 mmHg or greater. A repeat PAP measurement was taken 1 month after removal of the ionophore and showed a mean decrease in the PAP of 6 mmHg. Further work is needed to evaluate the potential effect of ionophores on pulmonary hypertension when fed to cattle at high altitude.

There is an ongoing study at the University of Wyoming that is looking at the effects of elevation changes and PAP scoring as well as the affects of an Ionophore in the diet. These results are pending and you will be updated as the results come in.

#### 8. Do bulls test different in the feedlot than if they are out on pasture?

This is another good question. When looking at the entire PAP population data there does seem to be some differences from feedlot cattle vs. pasture cattle in wide open space. This may be due only to weight gain and being pushed or possibly crowding with the increase in Co-founding respiratory issues. Overall, keeping cattle on pasture does not eliminate the genetic potential of hypertension. A study carried out in New Mexico by The University of New Mexico in which cattle were brought into the high country of New Mexico and turned out on summer pasture at 8000 feet showed no difference in those housed in a feedlot. By the time the cattle on the range were tested 6 had already died of Brisket Disease and many of them were about to be clinical at the time of testing.

#### 9. Have you ever killed an animal, what are the side effects of testing?

As far as I know there has never been an animal die during the testing. This does not mean that there are not possible complications most being related to chute work. I have listed below a consent form that I use to help all those doing the testing and partaking in the PAP program understand all risks and possible complications.

I, the undersigned, understand the risks involved in performing a Pulmonary Arterial Pressure (PAP) test and accept all risks, those foreseen and those that are not. I accept all responsibility for the animal or animals on which the test is performed and hold no one responsible for any unfortunate accident that may take place. I do not hold those involved in performing the test or those involved with the animal in any other means responsible in any way.

Even though accidents are very rare and all precautions are taken to make the test quick, easy, humane and safe, some accidents are neither preventable nor foreseen. It is therefore the owner or owner's agent who takes all responsibility for the animal and its safety during and after the test.

Below is a list of possible side effects and risks involved. This is not a complete list nor does it represent, in any order, the risks involved. The list includes infection at needle site as well as systemic septicemia and/or endocarditis, chute injury, loss of catheter into vascular system causing pulmonary, cardiac foreign body and emboli, pulmonary cardiac trauma and emboli, acute cardiac failure, catheter malfunction and complications, local abscess formation, acute death or resulting later from one of the above or complications not listed or foreseen.

I do understand all of the above and accept this procedure and all risks involved.

Signature\_\_\_\_\_Date\_\_\_\_\_

#### 10. Does having too much squeeze on the animal affect the PAP score?

Squeezing the animal during the testing can be a problem and the person doing the testing or the help needs to be monitoring the animal during the entire procedure. There needs to be enough squeeze on the animal to eliminate movement and make the procedure safe, but too much squeeze especially in a V type chute can put pressure on the thorax and simply increase pressure mechanically resulting in pulmonary hypertension and a false elevated PAP. The squeeze many times has to be changed during the procedure to accommodate movement, falling in the chutes and normal restraint. The biggest problem I see is not having the bottom of the chute out as wide as it will go. A narrow chute leads to thoracic compression and an artificially elevated PAP measurement.

## 11. What is the thing you keep moving up and down and why are you doing that, how important is that?

After the catheter is inserted into the needle and advanced approximately 8 inches the fluid filled catheter is connected to a fluid pressure transducer. This transducer is what changes the fluid pressure to electrical and transmits it to the computer and PAP machine, This transduce should be at the level of the pulmonary artery where the catheter is picking up the pressure. Since the system is a filled level fluid system to accurately get the correct value the transducer may have to be moved during the procedure to accommodate for animal movement of falling. In some cases depending on the chute the animal may be standing on a bar resulting in moving the transducer up to accommodate for the location of the pulmonary artery. There are many different means in which the person doing your testing knows if the height of the transducer is too high it will cause the PAP measurement to be low and consequently if the transducer is to low then the PAP measurement will be too high. About 2 inches off will result in a 1-2mmHg change in the PAP score.

#### 12. Can we use nose tongs to pull the heads over, the halter is a pain?

Nose tongs should **never** be used in holding or pulling the head over. Nose tongs can result in serious injury and animal pain and discomfort. They will also result in a high PAP score since they obscure the nasal passages and obstruct normal breathing.

#### 13. Does it matter if the animal is pregnant?

It has been reported that pregnant cattle can have higher PAP measurements than nonpregnant cattle. The increased PAP response is greater in animals that already have an elevated PAP. Animals with lower PAP before pregnancy had reduced arterial Pco2 tension during pregnancy, suggesting a compensatory hyperventilatory mechanism that could help offset pulmonary hypoxia. The specific mechanism for the increased pulmonary vascular resistance during pregnancy in susceptible cows is not fully understood. I can add to this by adding that overall there is not a consistent increase in the PAP of pregnant animals. It seems that some may have and increase while others are not affected. Late term pregnancy may affect the PAP simply to loss of space and the inability to inhale and expand the lungs completely leading to a hypoxic condition. As a rule of thumb I do not PAP test any animal, if at all possible, greater than 7 months of pregnancy. The chances of injury to the fetus and abortion just due to chute work make the benefit/risk ratio too high for me to be comfortable. The testing itself would not affect the fetus but the handling could without a doubt.

## 14. Why are so many people starting to test claves at weaning or around weaning? Is this an accurate test at this young age?

In reviewing PAP testing at a young age we will remember that at best the accuracy is about 70%. We have seen in the past 4 years that the accuracy is getting better and is more representative of being about 80% accurate. In short this is most likely secondary to genetic trends causing the calf to be larger and closer to adult ageing than they were 10 years ago. Even with this, the accuracy in predicating what a low PAP will do in time is questionable. The reason most are doing this young age testing is to utilize the PAP test as a culling tool. Many do not want to put effort or money into a calf that already has a high PAP at this age. High PAP pressures at a young age depending on elevation of the test are very accurate. This young age testing allows the rancher to sell anything high and concentrate on those with an acceptable score. These animals are then retested at a year or more of age and the two scores are compared. It is important to remember that the young age test is a screening test only and animals should be retested prior to sale or placed into a herd breeding program.

We have also seen that testing at weaning may cause a slightly elevated PAP measurement secondary to stress and acute sub clinical respiratory disease.

#### 15. Does body condition affect the score?

This is an area that is being researched heavily at this time. It has become apparent that there is a dramatic rise in fat cattle dying of what appears to be congestive right failure and appears to look just like or is Brisket Disease in low elevation feedlots. We do know that the more body condition (or muscle mass) an animal has the greater demand for oxygen just for metabolic demands. Often these larger cattle have chronic respiratory issues due to weight and body size decreasing their ability to breathe affectively, restrictive breathing and poor ventilation. With the larger animal size and increase demand for oxygen and the animal's inability to breathe efficiently can exacerbate the entire pathophysiological mechanism of high altitude disease.

#### 16. Can I vaccinate at the time of testing what about a week or two before?

Since the PAP measurement is actually a measure of lung blood flow resistance, anything causing a decrease in lung space temporary or permanent can cause an increase in the PAP measurement. Any type of respiratory or pulmonary pathology can lead to an arbitrary high PAP measurement. Many of the respiratory diseases cattle experience can lead to this increase in pulmonary hypertension. If an elevated PAP measurement is thought to be secondary to a temporary pulmonary disease then retesting the animal should be done. It should be noted that PAP scores of over 50-55mmHg have a rare chance of dropping to an acceptable level. It appears once the PAP measurement reaches this degree or higher that extensive pulmonary vascular damage has taken place and the animal does not return to a normal pulmonary pressure, making them a high-risk candidate for use in high elevation situations. Even though this animal may not be genetically susceptible to high altitude affects, the lung pathology has made them a risk in acquiring HMD.

#### 17. Does it affect the PAP score to use a hot shot?

Excitement in the chute of any kind can cause a very brief rise in the PAP measurement. Including in this excitement would be the use of hot shots or rough cattle working techniques both of which are highly discouraged. In most cases the rise is very quick and the PAP returns to normal rapidly. This mechanism is known as Pulmonary Vascular Recruitment (PVR). PVR is the physiological response of the lungs to accommodate an increase in cardiac output. The pulmonary vessels within the lung tissue expand and allow for an increase in blood volume. It is for this reason that the excitement in the chute does not affect the PAP measurement to a large degree. Hot shot use and rough handling is discourage for even though it may not lead to a dramatic increase in the PAP measurement it does make the testing much more difficult. The person who is doing the PAP testing should be able to determine in most cases if the increase in the PAP measurement is real or caused by excitement. If the animal is excited the PAP may be increased and the systolic pressure would be very high and the diastolic pressure would be very low, indicating the PVR response. If the evaluator sees this result then care should be taken in giving that animal that PAP score. A retest or patience is required allowing the animal to normalize.

## **18.** How can you get an accurate score when the animal is throwing a fit in the chute, does it make the PAP go up?

This mechanism is known as Pulmonary Vascular Recruitment (PVR). PVR is the physiological response of the lungs to accommodate an increase in cardiac output. The pulmonary vessels within the lung tissue expand and allow for an increase in blood volume. It is for this reason that the excitement in the chute does not affect the PAP measurement to a large degree. Hot shot use and rough handling is discourage for even though it may not lead to a dramatic increase in the PAP measurement it does make the testing much more difficult. The person who is doing the PAP testing should be able to determine in most cases if the increase in the PAP measurement is real or caused by excitement. If the animal is excited the PAP may be increased and the systolic pressure would be very high and the diastolic pressure would be very low, indicating the PVR response. If the evaluator sees this result then care should be taken in giving that animal that PAP score. A retest or patience is required allowing the animal to normalize.

#### 19. I saw a negative number on the screen; can you really have a negative pressure?

The negative number on the screen is a real number. When the negative number is seen this in most commonly an indication that the recovery mechanism of the PVR described about is happening. An example of this would be. An animal has a PAP measurement of 40 60/20, all are well within the normal limits. Then the animal gets excited and the pressure can change to 40 90/-10. This is PVR taking place right in front of your eyes. If given time the scores will return to normal values. As long as the PAP seems stable it can be recorded as a 40mmHg.

#### 20. Can you treat an animal that has Brisket and if so How and what is the success?

Treatment Plan for Animals with Clinically Diagnosed High Mountain Disease:

#### 1. Diuretics;

(Furosemide) at 50mg (1cc of the 5%) per 100 pounds SQ BID until the swelling is 80% or more solved. At that time decrease the frequency to once daily for 5 more days or 5 days past resolution of the peripheral edema present.

#### 2. Limited water and salt intake;

During the treatment phase salt should be removed completely from the diet. A good rule of thumb on water intake is 1 gallon of water per 100-200 pounds body weight every 24 hours to be divided into multiple portions, at least three.

#### 3. Antibiotic Therapy;

Types of antibiotics used are rancher or veterinarian's choice. Since all organs are compromised as well as the immune system antibiotic therapy should be used in attempts to minimized bacterial infection.

#### 4. Environmental control;

All cattle being treated should be given inside climate controlled environment if possible.

#### 5. Oxygen therapy;

Moving to lower elevation or hyperbaric chamber use are always beneficial.

#### 6. Thorocentesis;

Procedure:

-Clean an area on the right side of the chest around the 6-8 rib, just cranial and caudal to the point of the elbow.

-Clip the area if possible and clean with some type of disinfectant. Peroxide, alcohol, Chlorhexidine work well.

-Block the area with lidocaine placing 2-3 cc in the area between the ribs. Block the skin and also direct the needle deep through the intercostal muscles to block the underlying tissue but not into the chest cavity.

-Take a 15 blade and make a stab incision in the blocked area being sure that you penetrate the skin and underlying tissue but do not enter the chest cavity. It is best to

decide where your puncture will be made in the chest wall and slide the skin caudally prior to making the stab incision. By doing this and then working the needle proximal prior to puncturing the chest will allow the skin to seal the puncture hole and prevent a pneumothorax.

-Using a 3 inch plus teat cannula place a three-way stop cock into the cannula. Connect an extension set on the three-way stop cock. This allows you to remove fluid and by utilizing the three-way stop cock never having to remove the syringe from the extension set.

-Place the teat needle into the stab incision and with a hard popping motion push the needle into the chest cavity. A slow push will not work, it must be a fast quick hard snapping push. Once the needle is in the chest cavity move the stop cock to the open position and begin to draw fluid out of the chest with the 60 cc syringe. If you get no fluid move the needle slowly in different directions with continued suction on the 60 cc syringe.

-Continue to draw out as much fluid as possible. Once you are unable to aspirate any fluid remove the needle and rub the area.

Enterprising ranchers have built their own hyperbaric chambers into which they can place calves with HMD. The increased pressure in the chamber effectively takes the animal to sea level pressure that reduces the hypoxic stress and allows the pulmonary hypertension and subsequent congestive failure to subside. Once recovered from HMD, the calves must be taken to a lower altitude to prevent recurrence of pulmonary hypertension.

#### 21. How heritable is this issue?

Evidence is strong that the susceptibility of cattle to hypoxia-induced pulmonary hypertension is inherited. The genetics of susceptibility to hypoxia-induced pulmonary hypertension in cattle appears to be complex. One study suggested a model of an autosomal dominate gene with reduced penetrance. In this study, it was postulated that the variable penetrance could be due to an abnormality in the Y chromosome.

## 22. Is the ideal age to test the same for bulls and heifers? Why do we wait longer to test the heifers?

The ideal age is the same. The reason that the heifers are tested at an older age is due to management only. Most of the time bulls are tested at a younger than desired due to the time of bull sales. It is best to test heifers as old as possible to obtain the most accurate PAP measurement since they will be going into your herd as replacement heifers.

#### 23. Can mooing affect the PAP score?

Mooing can dramatically affect the PAP measurement. Since the moo sound is created by increasing pulmonary pressure during the moo this will be picked up as a very high PAP score. I often will shut the transducer off during the moo so I can start up again as soon as possible.

#### 24. How can you tell if your transducer height is correct?

When the transducer is being set the pulmonary artery is at the level of the point of the elbow and the top of the transducer is set at that level for a close proximity to the correct

location. As the procedure takes place the person doing the testing or their helper watches the screen identifying the wave forms and takes specific note of the jugular pressure. Once in the right ventricle the lowest diastolic pressure should be equal and bounce off the jugular pressure. Fine tuning of the transducer should take place at this point in time. If the animal moves or falls down then the transducer must follow the level of the pulmonary artery.

## 25. If I decide I want to PAP test what things do I need to think about for help and equipment and how long would it take.

The equipment and materials needed to perform PAP testing in cattle are listed below. Good cattle working facility and manual help is a strict requirement. A cattle chute equipped with a squeeze and scissor head catch is best. Other types of head catches tend to bind the head and neck, making passing of the catheter difficult. The animal is secured within the chute with a moderate amount of squeeze applied to reduce body movement. Monitoring the squeeze is very important because too little squeeze allows too much movement, making the procedure difficult. The Cattle chutes must allow securing the head with a halter and turning of the head allowing jugular exposure

-Adequate help for handling cattle efficiently and safely.

-This is best done by having one person running the chute the entire time regardless if it is manual or hydraulic. This person will be in charge of catching the head and applying the desired squeeze to the animal during the procedure. They will make finite adjustments to the chute as needed and also be in charge of monitoring animal wellbeing and stress such as choking in the head catch.

-It is best to have 2 people securing the halter (nose tongs cannot be used) and turning the heads at all times. This allows for one to pull the head while the other tightens the halter safely securing the head into correct positon.

-There should be 1-2 people in charge of moving the cattle into the alley way and into the chute.

-Movement of the cattle should be done in a low stress fashion to the best of their ability. The use of dogs and hot shots should be limited to those animals in a life threating situation or those that have refused movement. Minimal use of these tools is recommended.

-Electric power or generator is required depending on life of the machines internal battery.

-Clean water must be available for cleaning purposes

-All the testing equipment is very sensitive to moisture (rain, snow) so shelter is required in these circumstances. Shelter is advised in situations in which the wind may be blowing. Wind increases the risk of infection due to material contamination. Understanding of the possible complications of testing is a requirement of the rancher and steps should be taken to minimize all possible risk factors.

#### -Record system, recording

-It is best that the rancher supply one or two people that will be in charge of recording the results of the test. This will include recording ear tag number and color.

It is best if the following can be supplied at the time of testing. \*Name and address of owner or owners \*Test Location and elevation. If others bring animals to the testing from other ranches then the location of the cattle's origin and elevation should be noted. \*Breed and color of each animal \*Sex of each animal including identifying steer, bull, heifer and cow \*Age of each individual animal, this can be estimated \*PAP measurement followed by systolic/diastolic measurements. It is a must that three numbers be recorded whenever possible. This allows for better measurement evaluation. \*Sire identification if possible including registration of sire if available. If the animal is pasture bred or this information is not known then this should be noted in the notes region. \*Any notes that the person doing the testing dictates should be listed under the note region on the record sheet. \*Any breeding data available at the time of testing helps to predict trends of the scores. This includes other animals that have been tested previously such as dam and her test score. Sires previous score if tested.

-Summary of Points of consideration prior to testing: -Do not vaccinate within 2 weeks of testing -Evaluate herd management, deworming program, vaccination program, weighing time interval. -Low stress handling at all times -Try to avoid testing just after weaning do to increase stress on the animal

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Everyone involved should have a good understanding of the requirements of taking the PAP measurement, understanding the risk and complications possible, accuracy of the test encompassing elevation of the test, time of the animal at elevation and age of the animal. If there are any questions these things should be discussed and understood prior to the testing.

With the above help and equipment it takes about 3 minutes per head.

## 26. I am concerned that my calves have had some sickness in the past month. If there is some respiratory disease in my calves can that affect the scores?

Because the PAP measurement is actually a measure of pulmonary blood flow resistance, any cause of temporary or permanent pulmonary hypoxia can cause an increase in the PAP measurement. Multiple infectious and noninfectious respiratory diseases, including bovine viral diarrhea virus (BVDV), infectious bovine rhinotracheitis (IBR), parainfluenza type 3 (PI3), Histophilus somni, Pasteurella multocida, Mannheimia hemolytica, lung abscess, lung worm, migrating larva of intestinal parasites, asthma, or even traumatic reticuloperitonitis/pleuritis, can predispose animals to pulmonary hypertension. Hypoxia caused by these conditions can result in pulmonary hypertension and cor pulmonale syndrome, even at elevations lower than 1500 m (5000 ft). However, animals at altitude are much more susceptible to the synergistic effects of concurrent respiratory disease on pulmonary hypoxia and can readily develop acute heart failure in the face of acute respiratory disease. If an elevated PAP measurement is thought to be

secondary to a temporary pulmonary disease, then retesting the animal should be done when the respiratory condition is resolved. It should be noted that PAP scores of more than 50 to 55 mmHg, even when associated with transient respiratory disease, rarely return to an acceptable level. It appears that once the PAP measurement reaches this degree or higher, extensive pulmonary vascular damage has taken place and the animal does not return to a normal pulmonary pressure, making it a high-risk candidate for use in high-elevation situations. This situation is only true if the animal remains at high elevation. Those animals with elevated pressures that are moved to lower elevation often return to a normal PAP, but they are at extreme risk if ever moved again to high elevation. Even though this animal may not be genetically susceptible to high-altitude effects, the lung pathology has made them at risk for acquiring HMD. Gram-negative sepsis may also cause elevation in PAP. Calves experimentally treated with endotoxin show increased pulmonary vascular resistance and elevated PAP. The endotoxinmediated pulmonary hypertension is mediated, at least in part, by prostaglandin F. This effect can be inhibited by indomethacin. These studies suggest that naturally occurring gram-negative sepsis can affect PAP measurements, and thus, PAP values, from animals with concurrent bacterial infections; the tests should be repeated at a later date. In addition, gram-negative sepsis can potentiate pulmonary hypertension in susceptible cattle at high altitude and could increase the risk of clinical HMD in individual animals. Treatment with Flunixin Meglumine may be clinically helpful in blocking the effect of endotoxin on pulmonary hypertension.

## 27. What happens in that rare case a piece of catheter is lost in the animal and how often does this happen?

Extreme caution must be used to not sever the catheter with the needle and allow the catheter to enter into the vascular system. Multiple animals were evaluated between 1980 and 1984 where catheters of varying length were experimentally severed during the procedure. The animals were given antibiotics at the time of the test and monitored over a period of 6 months to 3 years. The animals experienced no acute or chronic problems arising from the foreign body and were kept at high elevation. All pregnant animals calved out without complication. At slaughter, all of the catheters but two were found to be lodged in the right ventricle and main pulmonary artery. One catheter only was found in the pulmonary artery and one was found within the liver. Mild to moderate fibrosis was observed at the catheter location and the surrounding tissue. Fibrosis was most apparent at the papillary muscle. Even though this is encouraging cutting of the catheter can be a fatal consequence of the procedure.

## 28. I noticed that you where trying to stick the jugular on the right and then moved to the left saying the right had no jugular vein, is this possible?

This is possible, even though not common this situation is not rare. We find that about 1:100 calves have either a very small or no jugular on one side. By moving to the other side we often find normal anatomy and can carry on with the procedure. Even more rare we can sometimes find, about 1:200 head, that have no jugular vein on either side. In this case the PAP can't be done and the animal is given a no score. I have not found either situation to be detrimental to the animal's health. When dissecting these animals out many have no jugular vein but a network of small vessels acting as the jugular.

#### 29. What do the numbers mean? What do they correlate to in the animal?

There are three numbers we look at when evaluating the PAP measurement in the animal. They are expressed in mmHg which is the same units as your own blood pressure is expressed in. The numbers you see are the result of a combination of some complex physiological processes. In short they are a means of evaluating blood flow resistance to the lungs and the hearts compensation to overcome this vascular resistance. The resistance in the lungs can be caused by many things as we have discussed including genetic susceptibility to high altitude hypoxia (brisket disease). The first of the three numbers is the mean PAP (mPAP) which is the main number the rancher uses to evaluate which animal they may want to purchase or utilize. The other two are the systolic pressure (sPAP) which is the peak pressure of heart contraction and the diastolic (dPAP) which is the pressure when the heart is filling. Overall the lower the mPAP the better the PAP in general. This is true until the PAP is lower than 34mmHg. At this time technique and repeatability should be evaluated.

#### 30. What's more important, elevation or age?

At this time there has been only one study with controlled circumstances done. There appears to be important aspects to each situation. Testing too young of animals has a low repeatability due to the elasticity of the juvenile lung. In the above mentioned study, 6 month old calves were tested at 8000 feet. At the time of testing, 3 of the animals were showing clinical signs of brisket disease and eliminated from the study, the rest of the scores range from 34 to 55. The animals were then moved to 4800 ft and then tested again at 12 months of age. Even at this lower elevation all of the scores went up and those in the high 40's went up significantly. From this and other testing, we have drawn the conclusion that testing of young animals has very low repeatability and predictive value. We still struggle with the situation that arises often, is it better to test at a younger age at a higher elevation or wait until the cattle are older and test at a lower elevation. Putting this all together the best case scenario is to test at both locations. Using the young test as the screening test and the retest again at the lower elevation. If this is not possible then testing an older animal at the lower elevation appears to be the best option as long as the lower elevation is greater than 5500 feet.

31. What is the score accuracy/repeatability percentage at the different elevations and how do we know what elevation we can use the bull salty compared to where it was tested?

See chart listed below.

#### 32. What is the mean pressure, it does not seem to be the average of the other two numbers?

A summary of pulmonary physiology best describes how the Mean PAP (mPAP) is calculated and what can affect the mPAP. The PAP measurements (mean PAP, systolic PAP; sPAP, and diastolic PAP; dPAP) are associated with many other hemodynamic parameters including cardiac output (CO), pulmonary vascular resistance (PVR), and mean pulmonary artery wedge pressure (PAWP); or Pulmonary Artery Occlusion Pressure. Pulmonary blood pressure is the force of blood against the walls of the pulmonary artery and arterioles as the heart pumps blood throughout the pulmonary vasculature. Less elasticity and thicker arterial walls provide more resistant force to the blood volume resulting in a pressure. Like a water pipe, the resistance on one end of an artery can also cause increased pressure inside the artery. Mean PAWP serves as the resistant force in forming mean PAP. Thus a formula to estimate mean PAP is expressed as.  $mPAP = (CO \land PVR) + mPAWP$ 

The increase in CO, PVR and PAWP will increase mean PAP. The CO measures the amount of blood the heart pumps through the systemic and pulmonary circulation in a minute. Sufficient CO is needed to sustain blood pressure and supply oxygen to the whole body, and it is influenced by heart rate and stroke volume. The PAWP is an indicator for the left atrial pressure, and its increase causes more resistant for blood flow in pulmonary arteries resulting in higher PAP. The PVR is the resistance that the blood flow must overcome to go through the pulmonary circulation. Vasoconstriction and vascular remodeling (e.g. cell proliferation) both influence PVR and therefore blood pressure. Generally, the blood flowing through the pulmonary circulation is essentially the same as the blood flowing through the systemic circulation, but the blood pressure in systemic circulation is about 10 times higher than that in pulmonary vascular resistance. The PVR can be estimated using the modification of equation.

$$PVR = \frac{mPAP - mPAWP}{CO}$$

A simple means of estimating the Mean PAP can be calculated by the following:

$$mPAP = 1/3sPAP + 2/3 dPAP$$

Obviously this does not take in full consideration of the above and a high level of pulmonary vascular resistance can skew the mPAP calculation using this formula.

## **33.** What is the significance of the other two numbers? What affects them and why are they important?

When the PAP measurement is taken the most recognized number recorded is the mean PAP as what we discussed above. The second number is the systolic PAP or sPAP. This is the pressure that is generated when the heart contracts pushing blood into the pulmonary system, This pressure must be high enough to overcome the standing pressure in the pulmonary artery allowing blood to move forward toward the lungs. Thus if there is a significant amount of pulmonary hypertension present this number can and will be significantly high. The normal value for the sPAP with all conditions in the pulmonary vascular system being normal is sPAP=60-90mmHg. The last number is the diastolic PAP or dPAP. This is the pressure at rest or filling process. This number becomes very important as it allows us to evaluate the condition of the heart and pulmonary artery integrity. It also serves as a prognostic indicator and can predict the amount of loss of number vascular elasticity and right ventricular.

can predict the amount of loss of pulmonary vascular elasticity and right ventricular hypertrophy. Normal values of the dPAP are between -10 and 19mmHG. This number is significant in evaluating the degree of change in the heart and pulmonary system with anything over 30mmHg being correlated with significant change and guarded prognosis.

34. My question is this, how can my cow be high when she has lived at this elevation for 6 years? You also said her calf was high yet he spent the entire summer at 9000 feet? Can you explain this?

There is still a lot that we do not totally understand about the effects of altitude on an animal and its correlation to a high or low PAP. We do know that the PAP measurement is an accurate highly suggestive test of pulmonary hypertension. The PAP test can be explained as an indicator of pulmonary hypertension but not necessary explain the etiology behind the hypertensive state. It is important to remember that there are many co-founding factors of pulmonary hypertension making it difficult to evaluate the elevated PAP measurement. The hypertension can result in a slow progressive right ventricular heart failure, acute cardiac collapse or have no clinical significance at all. What we do know although, is that any animal with a high PAP measurement may be and is, prone to the effects of that elevated pressure on the cardiac system, be it genetic or environmental. Animals that are hypertensive and have no clinical signs of it are still very problematic in the sense they can survive but their offspring may not. This seems to be more prevalent on the female side than the male but can affect both sexes. This individual variance may best be explained in looking at humans with systemic and/or pulmonary hypertension. Some humans die of cardiac failure acutely while others never know there is a problem. There appears to be a genetic link to those individuals who can withstand the hypertension compared to those that Secom to it.

35. When is there going to be a DNA test available?

Colorado State (Enns, Thomas) are doing ongoing DNA analysis at this time. There are others joining in with the DNA search as well but at this time this genetic correlation appears to be multimodal and polygenetic. A near DNA solution, even though receiving lots of research and attention may not be in the near future due to the genome complexity and multiple factors involved in the pathogenesis.

36. How do I utilize the PAP EPD?

There will be a great deal of time in the conference spent on the PAP EPD. At this time the EPD is best used with the actual PAP measurement in helping the buyer decide when to buy or not to buy a borderline PAP measurement. For example if a bull has a borderline actual PAP measurement of 43mmHg yet has an EPD at -2.5 then the buyer may select that animal for high altitude use. The opposite may be true for an animal having a positive EPD, regardless of the PAP measurement itself that animal should be considered at risk for high elevation use. The EPD may also be helpful in selecting a sire to be used for AI for high altitude use. The selection of sires with a positive PAP EPD's would not be recommended for high altitude use.

37. If I want to bring a bull to altitude how long does he need to be there to give us an accurate test?

There is work being done on this topic at the present moment. Much of the data suggests that a minimum for 3 weeks is essential to initiate the pulmonary changes to result in an elevated PAP measurement. The elevation in which the animal is being moved to is also important If the animal is going to 9000 feet then 3 weeks would be enough time but if the elevation is 5000 feet then acclimation and clinical change may take 2 months. A rule of thumb would be the longer at altitude the more repeatable and predictive the PAP measurement would be.

38. I heard you say the bull had a trifecta score, what does this mean and what is the prognosis of this situation?

The Trifecta is a term used to note the mPAP, sPAP and dPAP were all in the 100 plus region. For example if an animal measured mPAP=130 with a sPAP and dPAP of 160/110mmH (130, 160/110). These types of measurements are indicative of an extreme case of pulmonary hypertension including changes to the cardiac muscle and the pulmonary vasculature. Conclusions can be drawn that this animal is in a severe hypertensive state and may not survive. The etiology behind these extreme measurements can be all those we have listed but may also be indicative of a congenital abnormality such as a ASD or VSD. When measurements such as these are found special diagnostics are suggested such as auscultation of the heart for the presence of a murmur of possible congenital defect.

**39.** What is the repeatability when an animal is PAP tested at low elevation and then retested at high elevation?

See the chart below:

### Low Elevation Test Chart

PAP test conducted at elevation <4000 ft.

PAP measurements taken at this elevation should be considered screening measurements only identifying hyper-reactive animals and not used for sale purposes

#### (50% Repeatable, Predictive Value)

PAP	Use at Low Elev.	Use at Moderate Elev.	Use at High Elev.	Use at Extreme
Score	(<4000 feet)	(4000-5500 FEET)	(5500-7500 feet)	(>7500 feet)
34-39	Low Risk	Low Risk	Moderate Risk	High Risk
40-45	Low Risk	Moderate Risk	High Risk	High Risk
46-49	Moderate Risk	High Risk	Do Not Use	Do Not Use
<u>&gt;</u> 50	Moderate Risk	High Risk	Do Not Use	Do Not Use

### **Moderate Elevation Test Chart**

### PAP test conducted at elevation 4000-5500 ft.

#### PAP measurements taken at this elevation should be considered screening measurements only identifying hyper-reactive animals and not used for sale purposes

#### (70% Repeatable, Predictive Value)

PAP	Use at Low Elev.	Use at Moderate Elev.	Use at High Elev.	Use at Extreme
Score	(<4000 feet)	(4000-5500 FEET)	(5500-7500 feet)	(>7500 feet)
34-39	Low Risk	Low Risk	Low Risk	Moderate Risk
40-45	Low Risk	Low Risk	Moderate Risk	High Risk
46-49	Moderate Risk	High Risk	Do Not Use	Do Not Use
<u>&gt;</u> 50	Moderate Risk	High Risk	Do Not Use	Do Not Use

### **High Elevation Test Chart**

### PAP test conducted at elevation 5500-7000 ft.

### (75-95% Repeatable, Predictive Value)

PAP	Use at Low Elev.	Use at Moderate Elev.	Use at High Elev.	Use at Extreme
Score	(<4000 feet)	(4000-5500 FEET)	(5500-7500 feet)	(>7500 feet)
34-39	Low Risk	Low Risk	Low Risk	Low Risk
40-45	Low Risk	Low Risk	Moderate Risk	Moderate Risk
46-49	Moderate Risk	Moderate Risk	Moderate Risk	High Risk
<u>&gt;</u> 50	Moderate Risk	Moderate Risk	High Risk	High Risk

### **Very High Elevation Test Chart**

### PAP test conducted at elevation >7000 ft.

#### (95% Repeatable, Predictive Value)

PAP	Use at Low Elev.	Use at Moderate Elev.	Use at High Elev.	Use at Extreme
Score	(<4000 feet)	(4000-5500 FEET)	(5500-7500 feet)	(>7500 feet)
34-39	Low Risk	Low Risk	Low Risk	Low Risk
40-45	Low Risk	Low Risk	Low Risk	Low Risk
46-49	Moderate Risk	Moderate Risk	Moderate Risk	High Risk
<u>&gt;</u> 50	Moderate Risk	Moderate Risk	High Risk	High Risk

These are typical guidelines only. Other consideration should be given to genetics, *EPD* use, Systolic/Diastolic pressures, previous illness, and special consideration should be give to time the animal was housed or has been at elevation. The predictability of the PAP measurement improves over time at elevation (5500 feet minimum).

This chart is base on healthy animals greater than 10 months of age.