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"DOENÇA DO PEITO INCHADO", *Tetrapterys* spp. POISONING, BRISKET DISEASE AND ST. GEORGE DISEASE: A COMPARATIVE STUDY[1]

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Através de revisão de literatura, os principais dados epidemiológicos e patológicos da "doença do peito inchado" (DPI), enfermidade de etiologia obscura que ocorre em bovinos no sul do Brasil, são comparados, em virtude de suas similaridades clínicas, com aqueles observados na intoxicação por *Tetrapterys* spp. (TP), "brisket disease"(BD) e "St. George disease" (SGD). Verifica-se que, epidemiologicamente, a DPI assemelha-se um pouco com a BD, em virtude de ambas ocorrerem em determinadas altitudes. Por outro lado, é provável que a hipóxia crônica secundária à altitude não tenha participação importante na patogenia da DPI, como acontece na BD. A SGD e a TP, causadas por ingestão de plantas, apresentam dados epidemiológicos próprios. Do ponto de vista clínico, as quatro enfermidades são semelhantes. Entretanto, a SGD pode ser diferenciada em função do edema subcutâneo ser mais proeminente na região submandibular e face, enquanto que, à auscultação do coração de animais afetados pela DPI, observa-se o típico "ritmo de galope". À necropsia, a TP é bastante distinta das demais enfermidades, em virtude das lesões do miocárdio serem bem visíveis, ao passo que o hidrotórax é um achado importante na SGD. O exame histológico do coração e do fígado permite diferenciar com facilidade as quatro doenças. A acentuada fibrose intersticial do miocárdio é característica da DPI, enquanto que na TP predominam largamente as alterações degenerativo-necróticas; a SGD e a BD não cursam com lesões histológicas significativas no miocárdio. Por outro lado, a lesão hepática na SGD é típica (peliosis hepatis) e difere do "fígado cardíaco" observado na BD e na DPI. Conclui-se que a DPI é uma doença com características próprias e que, portanto, deve ter uma etiologia diversa das outras três enfermidades.

TERMOS DE INDEXAÇÃO: "Doença do peito inchado", intoxicação por *Tetrapterys* spp., "brisket disease", "St. George disease", bovinos, estudo comparativo.

ABSTRACT.- This review compares the epidemiology and pathology of the following four diseases in cattle: 1) The "doença do peito inchado" (DPI) - a disease of unknown etiology that occurs in southern Brazil, 2) *Tetrapterys* spp. poisoning (TP), 3) brisket disease (BD), and 4) St. George disease (SGD). All four diseases are of similar clinical appearance. DPI bears some resemblance to BD in its epidemiology, both being associated with

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certain high altitude environments. However chronic hypoxia related to high altitudes probably can not be considered an important etiological factor in the pathogenesis of DPI as it occurs in BD, the so-called high-mountain disease. SGD and TP have their own epidemiological features associated with the ingestion of poisonous plants.

It is possible to distinguish clinically SGD from the other diseases by the marked subcutaneous edema of the submandibular and facial regions of affected cattle. The auscultation of the heart reveals a typical sound of "gallop rhythm" that distinguishes DPI. TP differs widely from the other diseases in showing gross lesions in the myocardium at necropsy. Hydrothorax is regarded as an important post-mortem finding in SGD. Histological examination of heart and liver also separates the four diseases easily. A marked and diffuse interstitial fibrosis of the myocardium is characteristic of DPI, whilst degenerative-necrotic changes predominate in TP. No significant microscopic heart lesions occur in SGD and BD. However, SGD presents a specific liver lesion, "peliosis hepatis", that differs from the "cardiac liver" observed in BD and DPI. So it can be concluded that DPI is a disease of yet unknown etiology, as it differs clearly from the other three diseases.

INDEX TERMS: "Doença do peito inchado", *Tetrapterys* spp. poisoning, brisket disease, St. George disease, cattle, comparative review.

I. INTRODUCTION

The authors received information during the last 11 years about the occurrence of an unknown disease affecting mainly cattle in the State of Santa Catarina in southern Brazil. The disease manifests itself as a chronic heart insufficiency and is referred to as "doença do peito inchado" (DPI), translated "swollen brisket disease", because the affected animals develop a pronounced subcutaneous edema of the sternal region (Tokarnia et al. 1989b). In southeastern Brazil, another disease in cattle has been reported a few years ago as being associated with the ingestion of poisonous plants of the genus *Tetrapterys* (Tokarnia et al. 1989a). Both diseases share some common clinical and pathological features. The investigation of DPI in southern Brazil revealed its epidemiological, clinical, macro- and microscopical aspects, however the etiology remains unclear. Using a literature survey and contacts with pathologists from the countries where clinical cases of St. George disease (SGD) and brisket disease (BD) have been reported and appear to have some aspects in common with the two Brazilian diseases, we have tried to gather all available information to differentiate the four diseases and to elucidate the etiology of DPI.

II. RESULTS

The data found in the literature are summarized in Table 1 to 4 according to the epidemiology, clinical pictures, post-mortem and histological changes seen in the four diseases.

III. DISCUSSION

A) *Epidemiology*

The epidemiological aspects of DPI differ widely from those of the other four diseases. It is the only one to affect spontaneously cattle and horses, especially cows over 3 years of age. Only the incidence of DPI has been reported to be higher during gestation and after calving. DPI has been recognized in animals grazing in high areas from 1100 to 1400 m, whereas TP occurs at lower altitudes from 200 to 700 m. The altitude does not influence the occurrence of TP and the disease can be produced successfully by experimentation at altitudes of only 50 m. SGD has frequently been reported at sea level. Most reports of BD refer to animals maintained above 2000 m, although some cases have been reported below 1600 m (Jensen et al. 1976, Bisgard 1977, Alexander 1978) and down to 1200 m (Blake 1967). As DPI only occurs between 1100 and 1400 m, we thought that the disease could be caused by the ingestion of a toxic plant. Many feeding experiments with suspected plants from the area have been carried out without success. Some trials are still in progress.

It is well established that chronic respiratory hypoxia has a great influence on the pathogenesis of BD. It could be considered as the essential etiological factor for the disease to develop, although other causes such as moisture and poisonous plants (*Senecio* and locoweed) might be involved. However plants of the genera *Pimelea*, *Tetrapterys* and *Senecio* that might be related to DPI were not found in the area. *Senecio brasiliensis* and *S. desiderabilis* which occur in the region were found to induce liver cirrhosis in cattle.

The degree to which chronic hypoxia influences the etiology of DPI has not been established yet. Some animals referred to a veterinary hospital situated at an altitude of 900 m were seen to recover partially. This might have been due to reduced physical exercise compared to the great effort required when grazing animals search for food on steep slopes. Moreover, they were better fed in the hospital.

TP may occur throughout the year, whilst SGD is more prevalent during dry periods. DPI and BD have a seasonal incidence however the season of highest prevalence is very different. It is useful to consider other factors such as morbidity and mortality rates to distinghish DPI from the other three diseases. Furthermore, the length of time animals need to stay in the region of occurrence to develop the disease and show clinical symptoms may also help the diagnosis. In DPI, animals require at least 2 years in the area to develop the disease whilst in SGD this period is less than 72 hours. TP onset is seen after 8 weeks in the area, and 10 weeks are necessary for animals to show the classical symptoms of BD. Only animals affected by DPI occasionally partially recover from the clinical illness if removed in time from the enzootic area. DPI, BD and SGD do not induce females to abort but TP does. It is interesting to mention that aborted foetuses show the same cardiac lesions seen in adult animals affected by TP.

B) *Clinical manifestations*

Marked distention and pulsation of the jugular vein is a common clinical sign often observed in all four diseases. Cardiac arrhytmia is more frequent and intense at DPI than in BD and TP. In DPI, auscultation of the heart frequently reveals a characteristic "gallop rhythm". This change in the heart rhythm is not reported in the other three diseases.

Table 1. *A comparison of the major epidemiological aspects of "doença do peito inchado",* Tetrapterys *spp. poisoning, brisket disease and St. George disease*

Epidemiological aspects	"Doença do peito inchado"	*Tetrapterys* spp. poisoning	Brisket disease	St. George disease
Animal species naturally affected	Cattle and probably horses (42)[a]	Only cattle (41,42)	Mainly cattle (4,5,9,17), also sheep in some regions (8 cit. 1, 8 cit. 6, 8 cit.31)	Only cattle (13,16) and perhaps sheep (16)
Age of animals when attacked	Only animals older than 3-4 years (42)	Only animals older than 1 year (41, 42)	Animals under 1 year of age or in older cattle (4, 22, 36)	All ages (27), 7-24 months (14); above 4 months (Seawright, pers. comm.)
Animals particularly affected	Especially cows during gestation and after calving, also older oxen (42)	Any bovine (41, 42)	Any bovine (1, 2, 4, 5, 6, 7, 18, 20, 22, 23, 28, 32, 36, 43)	Any bovine (27); lactating cows more frequently affected than dry cows (14)
Altitudes at which the clinical signs occur	Only at 1100-1400m (42)	200-700m (41)	Usually above 2,000m (1, 2, 6, 7, 9, 36); occasionally below 1,600m (4, 5, 23, 36)	At sea level (Seawright, pers. comm.)
Season in which the disease is more prevalent	Mainly in spring and summer (42)	Throughout the year (41)	Mainly in autumn and winter (1, 5, 23, 36)	Any season (14), especially during dry periods (10, 16)
Morbidity rate	Invariably above 50% (42)	Inconstant (41)	Usually from 0.5 to 2.0% (1, 4, 5, 20, 23), occasionally reaching as high as 5-10% (1, 5, 20, 23)	High, 100% (14), usually from 20 to 50% (10)
Mortality rate of animals that stay in the area	Under natural conditions 100% (42)	Usually high (41)	High, 100% (28)	Many deaths reported (14)
Period of time required for the disease to develop	At least 2 years in the area (42)	Usually from 1 to 2 months in the area (41)	Less than 7 days to 10 weeks (20, 23, 36)	Between 40 and 72 hours (14, 25) to 12 days (19)
Course of the disease	Usually subacute to chronic (42)	Usually subacute to chronic (41)	From 1 to 12 weeks (1, 5)	Several days (14)
Recovery if removed from the area	Some animals show partial recovery (42)	Some animals show recovery (41)	Many animals show recovery if moved to lower altitudes (1, 5, 7, 17, 20, 28, 36)	Many animals recover (37), also chronic cases usually recover (14, 19)
Effects on gestation	Does not induce abortion (42)	Many abortions (41)	No description	No description

[a] The numbers in parenthesis indicate the references.

Similarly respiratory distress has been reported in DPI and BD but not in SGD. All four diseases occasionally may cause "sudden death". Profuse diarrhea may be present during the course of all diseases but with different frequencies. Anemia is known to be a common finding in DPI and SGD. In SGD, pronounced subcutaneous edema starts in the submandibular and facial regions whilst in DPI, BD and TP severe edematous swelling begins in the sternal region.

C) *Necropsy findings*

Dilatation of the heart is an occasional post-mortem finding in TP, but is very common in the other three diseases. Cardiac hypertrophy has been reported only in BD. In TP the cut surface of the myocardium reveals a change in colour from pale red to whitish. However in DPI similar changes are noted in cross sections of the heart, but they are ill-defined and not as conspicuous as in TP to the point that they could even pass unnoticed. Studies on BD and

Table 2. *A comparison of the major clinical signs seen in "doença do peito inchado",* Tetrapterys *spp. poisoning, brisket disease and St. George disease*

Clinical signs	"Doença do peito inchado"	*Tetrapterys* spp. poisoning	Brisket disease	St. George disease
Distention and pulsation of the jugular vein	Invariably present (42)	Occasionally seen (26%) (41, 42)	Usually present (1, 2, 5, 20, 28, 36)	Frequently observed (8, 11, 12, 14, 16, 24, 26, 27)
Cardiac arrhythmia	Frequent, 80% (42)	Occasionally seen, 26% (41, 42)	Present (18, 29)	No description
Respiratory distress	Dyspnoea on exertion (42)	Dyspnoea in terminal stages, labored breathing (41)	Dyspnoea on exertion (20, 36, 43), labored breathing (1, 5, 18, 22, 28)	Severe dyspnoea in chronic cases (24), shallow and rapid breathing (16)
Sudden death	Rarely, on exertion (42)	Rarely, on exertion (41)	It may occur on exertion (1, 5)	It may occur on exertion (14, 27)
Diarrhea	Usually present, 80% (42)	Occasionally seen, 33% (42)	Usually present (1, 2, 4, 5, 18, 20, 28, 36)	Frequently seen (12, 14, 27, 33, 37)
Anemia	Frequently present, 60% (41, 42)	Not present (41)	Not present (14, 17) or only seen rarely (19)	Frequently (37) or invariably present (13, 24, 25, 27, 29)
Primary site of subcutaneous edema	Sternal region (41, 42)	Sternal region (41, 42)	Sternal region (1, 5, 20, 36)	Submandibular space and head (12, 14, 16, 24, 26, 33)

SGD do not describe changes in cross sections of the myocardium although some authors mention flaccidity of the cardiac muscle. DPI and SGD produce severe liver lesions consisting essentially of hepatomegaly due to chronic passive congestion. Subcutaneous edema has already been compared in the previous section on clinical aspect. Cavitary effusions are present in all four diseases but is slightly less common in TP. Ascitis is more pronounced in DPI and BD whereas hydrothorax develops with greater intensity in SGD. In DPI and TP, edema is normally present in the same organs, affecting the mesentery, the folds of the abomasum, the gallbladder wall and the skeletal muscles, in order of decreasing frequency. In BD, edema is said to be confined to the mesentery and digestive tract walls, whilst there is localized edema in the lungs, abomasum and intestines.

D) *Histological alterations*

Histological examination of the heart reveals important differences between the four diseases. In DPI, microscopical lesions show mild regressive changes characterized by diffuse interstitial fibrosis. In addition, very large unusual multinucleated cardiac fibers are occasionaly observed in some of the affected animals. According to Stunzi & Teuscher (1970), the same kind of cells are also present in other diseases, e.g. white muscle disease, "Plötzlicher Herztod" (sudden death of piglets) and "Kardiopathie der Kamele" (cardiomyopathy of camels), in which they are described as "giant myogenic cells". The same authors feel that this type of cell could be explained as "Regenerationserscheinungen" (evidence of regeneration). In animals affected by TP, degenerative-necrotic changes in the heart muscle are more pronounced and there is diffuse interstitial fibrosis of the myocardium. The fibrosis may also be widespread or surround necrotic areas. There are only a few reports mentioning microscopical cardiac changes in BD. Sera & Jensen (1955) and Blake (1965) examined the muscle fibers of hearts from animals with BD histologically. Their morphometrical studies revealed hyperplasia rather than hypertrophy of cardiac myocytes in the affected hearts. These findings contribute to the hypothesis that atypical cells seen in DPI and TP are due to attempts of

Table 3. *A comparison of the major post-mortem findings seen in "doença do peito inchado",* Tetrapterys *spp. poisoning, brisket disease and St. George disease*

Post-mortem findings	"Doença do peito inchado"	*Tetrapterys* spp. poisoning	Brisket disease	St. George disease
Cardiac dilatation	Frequently seen (42)	Exceptionally seen (41, 42)	Present (1, 2, 4, 6, 9 cit. 1, 13, 17 cit. 18, 22, 23, 36, 43)	Present (12, 13, 24, 27, 34, 37)
Cardiac hypertrophy	Not present (42)	Not present (41, 42)	Present (1, 2, 4, 6, 9 cit. 1, 13, 17 cit. 18, 22, 23, 30, 32, 43)	No description
Other cardiac gross changes	White-greyish ill-defined areas on the cut surface of the myocardium (42)	Pallid areas in the heart muscle seen through the epicardium; sharp whitish areas and streaks across most of the cut surface of the myocardium (41)	Flaccidity of the heart (9 cit. 1, 17 cit. 18)	Flaccidity of the heart (14, 16, 37)
Liver lesions	Hepatomegaly, chronic passive congestion (42)	Mild or not present (41, 42)	Hepatomegaly (5, 17 cit. 18, 22, 23) and passive congestion (1, 2, 4, 5, 22, 36, 42)	Hepatomegaly (14, 24, 27 33, 37) and mottled liver on cut surface (13, 14, 24, 37)
Subcutaneous edema	In the sternal region (brisket) exceptionally extending down to the umbilical region and forwards to the intermandibular space (42)	In the sternal region (brisket) exceptionally extending forwards and backwards (41, 42)	In the sternal region, extending forwards (1, 20, 22) and backwards (1, 22, 36)	In the intermandibular space (14, 16, 24) and head (24), it may extend up to the umbilical region (24, 37)
Cavitary effusions	Ascitis (100%) (42) and hydrothorax (60%) (42)	Ascitis (50%) (41,42) hydrothorax (50%) (41, 42)	Ascitis (30) and hydrothorax (20, 43) frequently seen (1, 12, 22, 36)	Ascitis and hydrothorax (16, 26, 27, 29) frequently seen (13, 23, 24, 37), hydrothorax more pronounced than ascitis (10, 11, 13, 19)
Edema in other organs	Mesentery, folds of the abomasum, gallbladder wall, skeletal muscles (42)	Mesentery, folds of the abomasum, gallbladder wall, skeletal muscles (41, 42)	Mesentery, digestive tract wall, skeletal muscles (1), folds of the abomasum (22), mucous membranes of the abomasum and small intestine (23)	Mild edema of the abomasal wall (14, 37), intestines (37) and lungs (10)

regeneration. Epling (1968) studied the ultrastructural aspects of the myocardium from animals suffering from BD and described the following changes: intracellular edema, rupture of myofibrils, sarcoplasmic reticulum and mitochondria, and edema, granulation and hyalinization of the endothelial cells of the myocardium. Individual necrosis of the cardiac muscle fibers accompanied by histiocytes and lymphocytes are occasionally seen in SGD (Seawright & Francis 1971). They are distinctly different from the lesions seen in DPI and TP. In DPI, microscopical lesions in the

Table 4. *A comparison of the major histological alterations seen in "doença do peito inchado",* Tetrapterys *spp. poisoning, brisket disease and St. George disease*

Histological alterations	"Doença do peito inchado"	*Tetrapterys* spp. poisoning	Brisket disease	St. George disease
HEART				
Degeneration and lysis of the fibers	Mild, but constant (42)	Severe (41) and frequent (42)	Not present	Not present
Massive necrosis	Not present (42)	Severe and occasionally seen in natural cases, mild and rarely seen in experimental cases (41)	Not present	Individual necrosis of the fibers
Interstitial areas of fibrosis	Severe, diffuse, constant (42)	Mild to moderate, diffuse, frequently seen (41), focal (42)	Not present	Not present
Extensive areas of fibrosis	Not present (42)	Severe, frequently seen in natural cases; mild, rarely seen in experimental cases (41)	Not present	Not present
LIVER				
Primary centrolobular congestion	Severe, diffuse, constant (42)	Usually mild to moderate (42), moderate to severe in natural cases (41)	Not present	Not present
Fibrosis in the portal triads	Always found, mild (42)	Mild, occasional in natural cases (41), frequent in natural cases (42), absent in experimental cases (41)	Severe (36)	Not present
Centrolobular fibrosis	Not present in cattle but in horses (42)	Mild, occasional in natural cases (41), absent in experimental cases (41), frequent in natural cases (42)	Present (36)	Not present
Peliosis hepatis	Not present	Not present	Not present	Always present (37)
LUNGS				
Medial thickening of the pulmonary arteries and arterioles	Not present	Not present	Present according to most of the authors (4, 5, 7, 22, 30), prominent (4)	Not present
Epithelialization	Seen in 20% of the cases (42)	Not present	Not present	Not present
Failure cells	Many cells present in 20% of the cases (42)	Not present	Not present	Always present (24)

liver are very similar or identical to those in BD since both are attributed to chronic cardiac insufficiency. They are characterized mainly by passive congestion, primarily periacinar, sometimes with an increase in connective tissue in the portal triads. Periacinar passive congestion and fibrosis are occasionally observed in TP, although they are much less intense. Histologically, the hepatic lesions seen in SGD differ widely from those seen in the other three

diseases. Microscopic examination of the liver shows dilatation of the sinusoids, especially in the centro- acinar zones. Seawright & Francis (1971) stated that these lesions were comparable to "peliosis hepatis" previously described in man.

In the lungs, epithelialization accompained by mild fibrosis and the presence of "failure cells" were observed only in one of the animals affected by DPI. However, no noteworthy lesions were seen in the other cases. In TP, mild alveolar congestion and edema are occasionally seen. Muscular hypertrophy of the media of the pulmonary arteries and arterioles was not found in either disease, although there are claims that it has been seen elsewhere in BD (Hull & Anderson 1978). However other investigators (Hecht et al. 1959, Kuida et al. 1963) were also unable to find medial hypertrophy of the arteries in animals affected by BD. They believe that there is a contraction of the arterioles, but it is insufficient to cause hypertrophy of the blood vessels. Previous reports on SGD mentioned alveolar septal thickening, erythrophagocytosis and siderosis as well as compressive atelectasis (Kelly & Seawright 1978).

IV. CONCLUSION

It can be concluded from the epidemiological data that DPI differs markedly from the other three diseases. However a comparison of the clinical features shows that DPI is similar to BD. So it is difficult to distinguish them clearly using clinical information without considering the location. Perhaps the so-called "gallop rhythm" heart sound detected on auscultation of animals affected by DPI could be used to separate it from BD. There are also many points of clinical similarity between TP, DPI and BD. However it is possible to distinguish SGD from the other diseases by considering the clinical evidence, especially the primary site of the subcutaneous edema. With reference to the macroscopical pathology, DPI, BD and SGD are very similar. SGD can be differentiated again from the other diseases by the initial site of the subcutaneous edematous swelling. The marked cardiac lesions and the moderate hepatic changes present at necropsy distinguish TP. Histologically, the four diseases are distinct from one another. Both, DPI and TP, show severe cardiac lesions although these are quite different from each other. In BD noteworthy microscopical changes in the heart are not present whilst in SGD cardiac lesions are characterized by individual necrosis of the muscle fibers accompanied by inflammation. The liver lesions seen in DPI and BD are very similar and hardly to distinguish from each other, whereas those observed in SGD (peliosis hepatis) are easily differentiated from the lesions present in DPI and BD. In naturally occurring cases of TP, periacinar congestion is occasionally seen, but is much less intense than that seen in DPI and BD.

A comparison of the epidemiological information on the four diseases shows that DPI has many unique features that characterize it as a different disease.

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