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Short original communication

Veno-occlusive disease (VOD) of the liver in cheetah's and snowleopards

by *T. S. G. A. M. van den Ingh*[1], *P. Zwart*[1] and *A. Heldstab*[2]

Introduction

Veno-occlusive disease of the liver (VOD), a term first used by *Bras, Jelliffe* and *Stuart* in 1954, is pathologically characterized by occlusive lesions of the centrilobular or sublobular hepatic veins. The larger hepatic vein branches are unaffected, in sharp contrast with the findings in the Budd-Chiari syndrome. In the acute disease the intravenous block is caused by loosely arranged connective tissue occupying part or all of the lumen. There is congestion in surrounding sinusoids and the perivenular parenchyma may undergo degeneration and necrosis. At first the reticulin network is intact, but it may collaps and become fibrotic later. In time the connective tissue within affected veins becomes quite dense, whereas collaterals formed from neighbouring sinusoids may relieve the congestion. In more chronic cases cirrhosis may develop and the circulatory changes and further loss of parenchyma may obscure the original perivenular distribution of the fibrosis (*Bras* and *Brandt,* 1979).

Case report

In a retrospective study of autopsy material from cheetah's and snowleopards at the Institutes of Veterinary Pathology at Utrecht and Bern, two respectively three animals showed liver lesions similar to veno-occlusive disease in man. Macroscopically four livers were congested and covered by a fibrinous exsudate with local organisation by connective tissue. The surface of these livers had an irregular appearance due to nodules varying in size from 2–5 mm's (Fig. 1). Whereas two livers seemed to be enlarged, two seemed to be reduced in size. The fifth liver was enlarged resembling cirrhosis with focal fibrous thickening of the liver capsule.

Histologically the livers showed somewhat different appearances. In two livers (macroscopically enlarged) the occlusive lesions of centrilobular and sublobular hepatic veins consisted of loosely arranged fibrous tissue (Fig. 2). The surrounding sinusoids were congested and the parenchyma showed only minor loss of liver cells and slight perivenular fibrosis. In two livers (macroscopically reduced in size) the liver parenchyma was separated by bands of collapsed reticulin with secondary fibrosis

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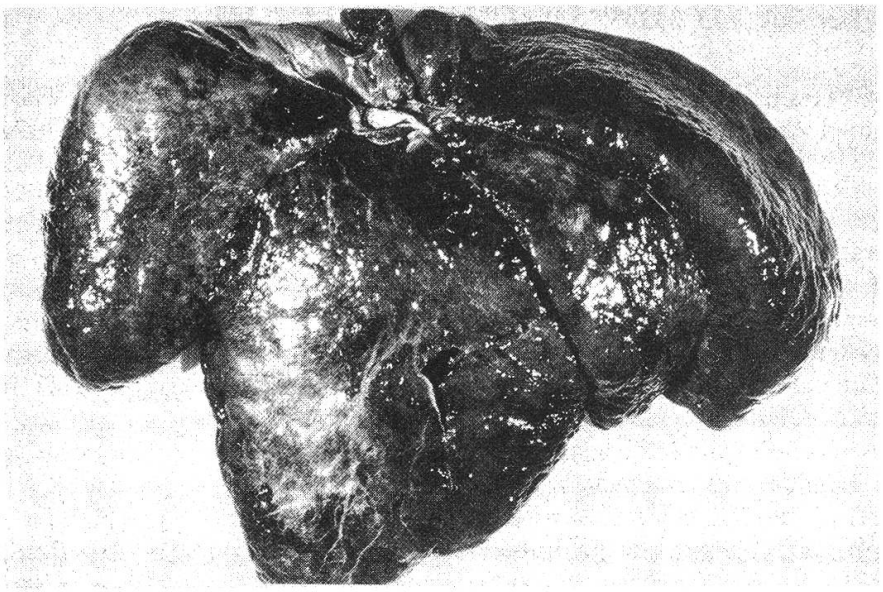

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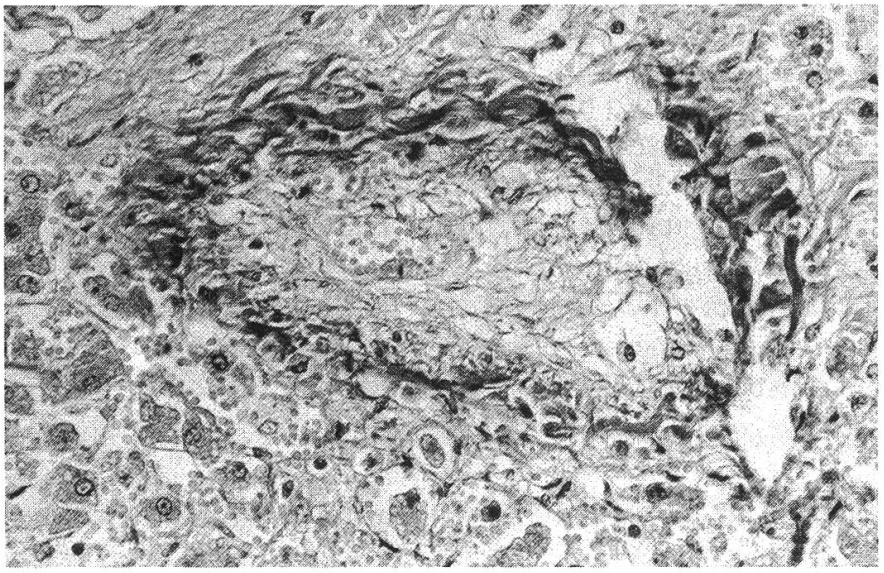

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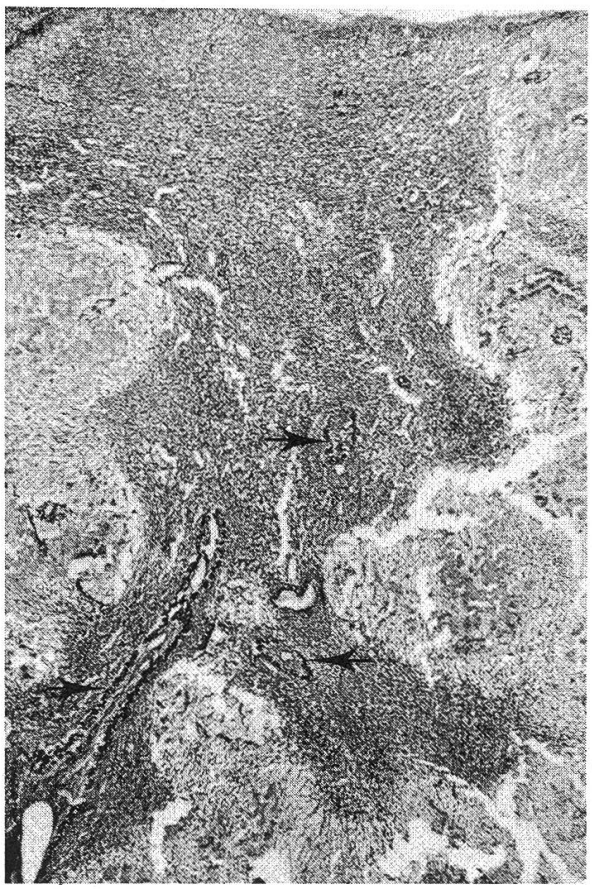

Fig. 3 *Cheetah:* Veno-occlusive disease of the liver. Area of collapsed reticulin with secondary fibrosis; occluded centrilobular and sublobular hepatic veins (arrows). Reticulin 36 ×.

(Fig. 3). In these fibrous bands occluded centrilobular and sublobular hepatic veins with quite dense connective tissue were situated; locally collateral channels had been formed (Fig. 4). In the cirrhotic liver similar bands of connective tissue mainly as centricentral bridging fibrosis and containing occluded centrilobular and sublobular hepatic veins were found; in the nodules, however, hyperplastic parenchymal changes were seen. In all cases the larger hepatic vein branches as well as the posterior caval vein were unaffected, nor could any changes be found suggesting central circulatory failure.

Fig. 1 *Snowleopard:* Veno-occlusive disease of the liver. Swollen and congested liver with an irregular surface.

Fig. 2 *Snowleopard:* Veno-occlusive disease of the liver. Obliteration of a centrilobular hepatic vein by loosely arranged fibrous tissue; congestion in the surrounding parenchyma. Van Gieson 360 ×.

Fig. 4 *Cheetah:* Veno-occlusive disease of the liver. Occlusion of a centrilobular hepatic vein by quite dense connective tissue and perivenular fibrosis; locally collaterals are present (arrows). Van Gieson 360 ×.

Discussion

In man pyrrolizidin alkaloids from Crotalaria and Senecio species are important etiological factors (*Bras* et al., 1957). The disease occurs naturally in animals feeding on these plants and has been produced experimentally (*Bras* and *Brandt,* 1979; *Allen* et al., 1967). The toxic factors responsible for veno-occlusive disease of the liver act probably by degeneration and necrosis of the sinusoidal endothelial lining with insudation of plasma and erythrocytes in Disses's space and loss or necrosis of liver cells. From here the plasma and erythrocytes spread towards the intima of the centrilobular and sublobular veins. As in contrast to the sinusoids these venules have a continuous endothelium and an endothelial basement membrane, exchange of fluid and cells between the wall and the lumen is not possible anymore. This leads to subendothelial fluid accumulation and subsequent narrowing of the lumen (*Brooks* et al., 1970). Besides the changes described above, other kown effects of these alkaloids are megalocytosis of liver cells and severe hepatocellular centrilobular necrosis (*Allen* et al., 1967; *Brooks* et al., 1970; *Jubb* and *Kennedy,* 1970). The effect to be found is both dose and species dependent (*Brooks* et al., 1970); the veno-occlusive lesions always seem to be the result of a single toxic dose (*McLean* et al., 1964). Moreover, veno-occlusive disease of the liver has been reported due to medicinal drugs, aflatoxin and also due to radiation injury (*Zimmerman* and *Ishak,* 1979; *Reed* and *Cox,* 1966).

Liver lesions possibly similar to the lesions described here, have been mentioned in two cheetah's and a tiger housed in zoos in the United States (*Reynolds* and *Peeters,* 1975). So the disease perhaps has been overlooked until now and may be really a serious problem in wild felines. As these animals are carnivores, the uptake of vegetable material in their diet is not likely and other toxic factors should be looked for. In our material no conclusive evidence for a specific etiology could be obtained.

Summary

In a retrospective study of autopsy material, 2 cheetah's and 3 snowleopards showed occlusive lesions of the centrilobular and sublobular hepatic veins. These consisted of a loosely arranged or quite dense collagen and reticulin network. Secondary changes in the surrounding liver parenchyma were congestion, collaps and fibrosis. Because the larger hepatic veins and the posterior caval vein were unaffected, and no changes could be found suggesting central circulatory failure, this resembles veno-occlusive disease of the liver in man. No conclusive evidence for a specific etiology could be obtained.

Zusammenfassung

Im Verlaufe einer retrospektiven Studie von Gepard- und Schneeleoparden-Autopsiematerial hat man durch Bindegewebszubildung verursachte Stenosen in Zentral- und Sublobularvenen nachweisen können. Das umliegende Leberparenchym war gestaut und unterschiedlich massiv fibrosiert. Diese Veränderungen sehen der Veno-Occlusive Disease des Menschen ähnlich. Die Ätiologie dieser Veränderungen ist unklar.

Résumé

Au cours d'une étude rétrospective du matériel d'autopsie de guépards et léopards des neiges, nous avons pu prouver la présence de sténose des veines centrales et sublobulaires dues à la formation de tissue conjonctif.

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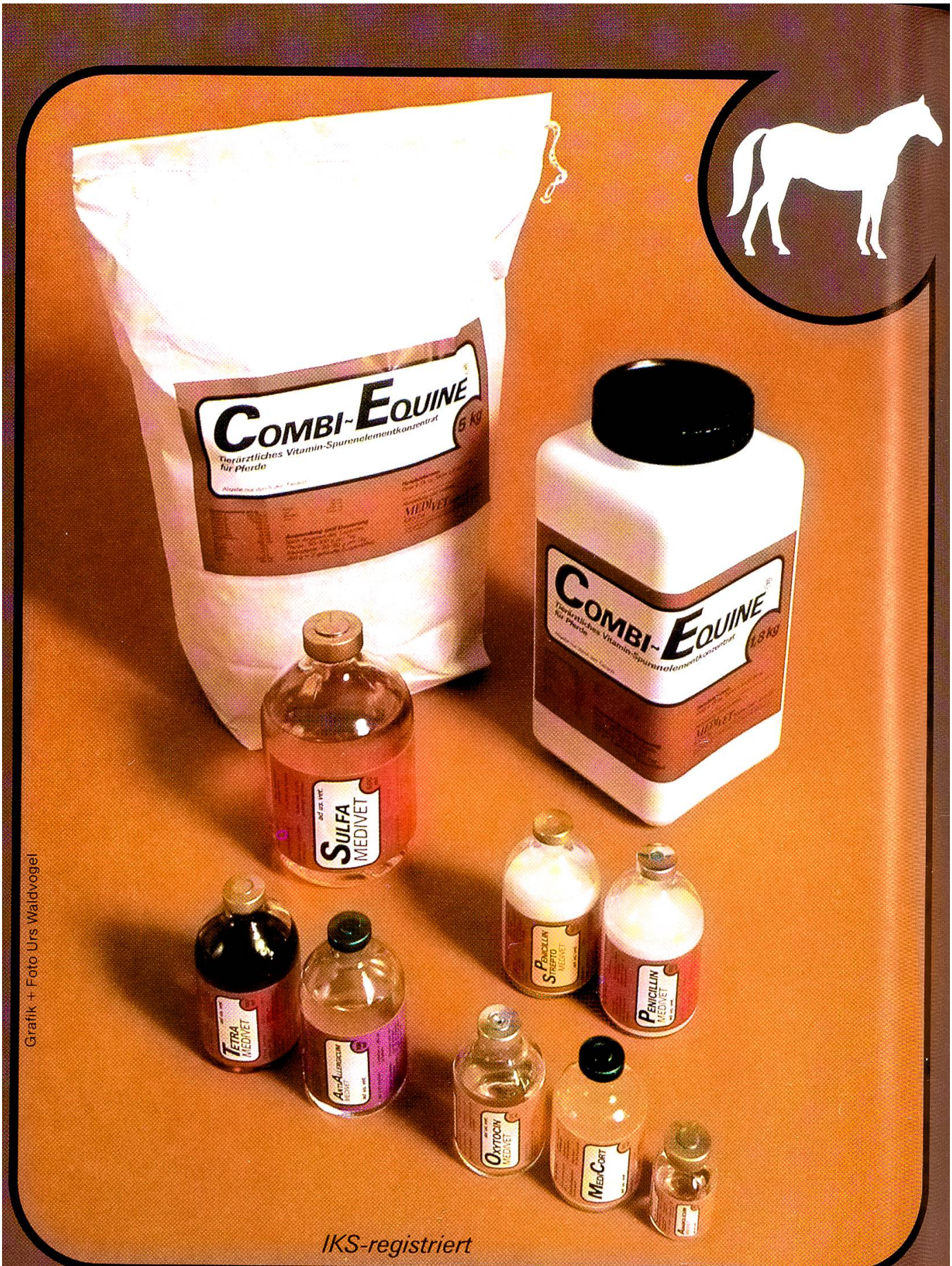

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Le parenchyme hépatique voisin était congestionné et fibrosé de façon plus ou moins massive. Ces altérations sont semblables à celles observées lors de la maladie veino-occlusive chez l'homme. L'étiologie de ces altérations est peu claire.

Riassunto

Nel corso di uno studio retrospettivo relativo a materiale autoptico proveniente da ghepardi e leopardi delle nevi, è stato possibile mettere in evidenza stenosi nelle vene epatiche centro- e sublobulari, causate da proliferazioni di tessuto connettivo. Il parenchima adiacente era congestionato e presentava rilevanti fenomeni fibrotici. Queste lesioni sono simili a quelle presenti nella «Veno-Occlusive Disease» dell'uomo. L'eziologia della forma patologica non è chiara.

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REFERAT

Heilkräuter – nicht mehr heilsam?

Die europäische Vereinigung für biologische Landwirtschaft und Hygiene, «Nature et Progrès» hat einen recht belastenden Bericht über die Verseuchung der Heilkräuter in Europa veröffentlicht. Sie macht auch Angaben über Analyseresultate aus Heilpflanzen, die von schweizerischen Firmen vertrieben werden, unter Übernahme der «vollen Verantwortung für die Veröffentlichung der Namen und betroffenen Marken». Wir geben nachfolgend die deutsche und französische Version der Analyseresultate wieder, die sich auf Stichproben von Produkten zweier Firmen beziehen, welche in je einer Genfer Apotheke, bzw. Drogerie gekauft worden sind.

Die tierärztliche Relevanz scheint auf den ersten Blick gering. Dies nicht nur, weil es sich gerade beim Nutztier meist nicht um Langzeitbehandlungen dreht, sondern auch weil die Verwendung pflanzlicher Heilmittel – das nostalgische Trankmischen – stark in den Hintergrund getreten ist. Aber vielleicht gibt die Stichprobe einen Hinweis auf die Kontamination von Futterpflanzen, die nun allerdings einen nachhaltigeren Effekt auf die «Recyclage» der Giftstoffe über den tierischen Körper haben könnte...