

LIVER CIRRHOSIS IN THE SNOW LEOPARD (UNCIA UNCIA): CASE HISTORIES  
OF THREE ANIMALS AND SUGGESTION OF SOME DIAGNOSTIC POSSIBILITIES

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SUMMARY

The case histories of two snow leopards stricken with liver cirrhosis, one animal with chronic liver congestion and, for the sake of comparison, a fourth animal with endometritis are presented together with data referring to laboratory investigations and post mortem findings.

The clinical and pathological picture of the two animals with liver cirrhosis showed similar features like liver cirrhosis and disorder of the central nervous system. In the case of liver congestion, ascites was an additional characteristic symptom.

Repeated determinations of hematological parameters, activities of alanine - aminotransferase (GPT) and aspartate-aminotransferase (GOT) as well as vitamin A concentrations in plasma might be

helpful in detecting these liver diseases at an initial stage and in allowing a prognosis pertaining to the course of the disease.

## INTRODUCTION

Based on our experience, we think that liver fibrosis and cirrhosis maintain a significant position among the diseases of the snow leopards kept in zoological gardens. Further we learnt by personal communication with colleagues from zoological gardens in Praguc, Krefeld, West-Berlin and Hamburg that diseases with similar symptoms and case histories have occurred in snow leopards of their zoos. We therefore feel that it would be valuable to collect and publish all obtainable data pertaining to this type of disease, in order to get a documentation of the basic principles in the responses of the snow leopard to this disease. Conclusions drawn from such data might then allow an early diagnosis of the beginning liver alterations leading to cirrhosis with respect to taking adequate countermeasures before a fatal development is irrevocable.

As a first step we have documented our own experience. This contribution does not presume to be a comprehensive study, but the presentation of a brief history and summary of clinical observations, laboratory investigations (1), post mortem findings (1) and suggestions for interpretation might provide a preliminary means whereby some typical features are demonstrated.

## RESULTS

Snow leopards have been kept in the Basle Zoological Garden since March 11, 1970, but until the present report (July 1978) no breeding has taken place. The first female died at approximately 2 1/2 years of age and the second, 6 1/2-year-old female, which is still alive, produced two still-born cubs at the end of May 1975. The male died on January 30, 1976, at about 8 years of age.

Included in this study is also a further fatal case, namely an approximatively 6-year-old female from Hellabrunn, Munich.

From table 1 it can be seen that the initial symptoms, such as apathy and intermittent inappetence, appeared at the earliest two months before the animals died, while disorders of the central nervous system like weakness of the hind legs, swaying gait and inclined head position with temporary slight tremors, only became apparent about one month prior to death. On the occasion of another immobilization<sup>a)</sup> due to the necessity of removal of an ingrowing claw, the male, Basle I, was examined again two weeks before its death. The palpation of the abdomen revealed an enlarged liver and the recovery from narcosis was obviously prolonged.

At this point it should be mentioned that clinical signs belonging to another syndrome as we suspected, were present in the Basle male and female long before the onset of liver symptoms. They consisted in a serous and later on mucopurulent ocular discharge combined with loss of hair around the eyes and along the incrustated margins of the ears. An infestation with notoedres cati was confirmed by microscopical examination and controlled to some extent by insecticidal dips.<sup>b)</sup>

On April 13, 1976, the new female "Vappu" fell ill. The symptoms of prolonged heat, an enlarged uterus with slight purulent discharge as well as anorexia led to the diagnosis of endometritis with eventually secondary impairment of the liver. Kanamycin<sup>c)</sup> and oxytocin<sup>d)</sup> were administered for a one-week period. The progress of the disease and the response to treatment were closely controlled by hematological and clinical chemical analyses (tables 3,4: figure 1). In contrast to the three other snow leopards the female "Vappu" recovered after about two weeks of illness.

Laboratory investigations were only performed on the male, Basle I, the female, Basle II, and the female "Vappu".

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a) Vetalar, Parke Davis

c) TAD

b) Pervalenum, Pitman-Moore & Co.: Ectoral,  
ASID Bonz & Sohn GMBH; Cyflee, Cyanamid

d) Stricker

As shown in table 2, total hemoglobin and mean corpuscular hemoglobin were clearly decreased in Basle I and Basle II during the terminal phase. The increase in total leukocytes and neutrophils was marginal and eosinophilia was not observed although both snow leopards were infested with notoedres cati. The lymphocyte count stayed on a low number with a tendency to drop further. The normal range in cats is considered to be 1,5 - 7,0 G/l<sup>e)</sup> and appears to be applicable also to other animals of the felidae family (2).

"Vappu" on the other hand demonstrated a perceptible leukocytosis with left shift during the initial, acute inflammation of the endometrium (figure 1). Further, the red blood cell count, total hemoglobin, mean corpuscular hemoglobin and lymphocyte number dropped significantly during the course of the disease. Normal values finally were found to be restored at the time of a routine check-up, one year after the recovery of the animal (figure 1).

In all three snow leopards a slight increase in plasma urea was measured during disease, amounting to 10,2 - 14,1 mmol/l<sup>f)</sup>. In addition, a remarkable increase in the activity of plasma GPT and a high level of plasma GOT were found in Basle I and Basle II (figure 2). In contrast, "Vappu" showed a minimal rise in plasma GPT on May 7, 1976, and plasma GOT activities which practically stayed within the normal range although a temporary slight elevation was recorded (table 3). From our experience with various animals of the felidae family it can be said that plasma GOT activities between 30 and 40 IU/l and GPT activities between 40 and 50 IU/l are suspicious and that GOT levels above 40 IU/l and GPT levels above 50 IU/l appear to reflect pathological conditions (3).

The number of vitamin A determinations in our snow leopards is very small, but the results are nevertheless unequivocal (table 4).

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e) = 1,5 - 7,0 x 10<sup>3</sup>/μl

f) = 60 - 83 mg/100 ml

Low vitamin A concentrations were measured in plasma and liver samples of Basle I and to a lesser degree in the plasma from "Vappu" during disease. After total recovery of "Vappu" its vitamin A level amounted to a value which was three times higher than during illness. For comparison, values determined in adult man and infants are added in table 4.

The post mortem findings in the liver and brain from the male, Basle I, and the Munich female were similar.

Macroscopically a cirrhotic liver with a coarsely nodular surface and a firm consistency was found in both animals. In addition, the liver of Basle I was considerably enlarged. No observations were obtainable on the macroscopic changes of the liver of the female, Basle II.

The macroscopic investigation of the central nervous system on the other hand did not reveal any visible alterations in all of the three snow leopards. Microscopically the liver of the male, Basle I, showed a severe loss of hepatic architecture and disappearance of the central veins was obvious. Well vascularized fibrous strands divided the hepatic cells into irregular groups and lobules. The connective tissue contained disseminated mononuclear infiltrates. Adjacent to the areas consisting of fibrous tissue, teleangiectatically dilated sinusoids were observed. Further, small bile ducts were numerous and prominent and appeared to be due to active proliferation. The scarcely preserved liver tissue was slightly hypertrophic and contained large binuclear cells.

In contrast to these histological findings in the male, the changes in the liver of the female, Basle II, resembled those of chronic liver congestion. Grossly, the liver parenchyma was far better preserved than in the male, Basle I. Blood-filled, congested channels extended between the central veins. The central veins themselves were infiltrated by proliferating fibrous tissue and the surrounding liver parenchyma was atrophic and degenerated. The sinusoids appeared dilated. The liver capsule was partially

intermingled with fibrous tissue and infiltrated by mononuclear cells and varied in its thickness. In some areas, a hypertrophy of the serosa of the capsule was observed and thought to be due to the pressure from the ascites fluid.

No histological results were available from the female snow leopard of Munich. The histological examination of the brain of Basle I revealed a distinct oedema in the border layer between cortex and medulla as well as disseminated necrobiotic foci in the cortex cerebri, in the septal nuclei and in the corpora geniculata.

In the Munich snow leopard oedematous loosening of the white substance was found in the cerebral hemispheres, in the brain stem, in the medulla oblongata and to a lesser degree in the cerebellum. An obvious increase in degenerative processes in astrocytes, which consisted in enlarged nuclei and condensed chromatin and material in the nuclear periphery, was especially observed in the brain stem.

No investigations were performed on brain tissue of the female, Basle II.

## DISCUSSION

The control of any disease is essentially based on the possibility of obtaining a diagnosis at an early stage and also depends on the knowledge of its etiology. In the present study we have shown that laboratory investigations in the snow leopard might provide a valuable means by which clinical observations are supplemented in such a manner as to get a picture of the actual state of reaction of the snow leopard in a certain disease and with respect to obtain more detailed information on the severity of the impairment of a particular organ.

The reaction of the leukocytes for example was extremely poor in the case of liver cirrhosis and chronic liver congestion, whilst acute inflammation of the endometrium produced a very distinct, characteristical change in the white blood cell pattern.

Total hemoglobin and mean corpuscular hemoglobin on the other hand appear to be influenced to some extent by various disease processes.

Destruction of the anatomical integrity of the liver cells during the course of the cirrhosis or chronic liver congestion led to the highly pathological levels of GPT, an enzyme which in cats is known to be specific for the liver (4), and also to elevated plasma GOT activities. Similar findings are reported in humans with liver cirrhosis (5). Endometritis on the other hand was followed only by marginal changes of the enzyme pattern which were most probably due to secondary, minor liver cell alterations occurring during the acute inflammatory stage and during the treatment period.

Low vitamin A levels were found in liver cirrhosis as well as in endometritis, a fact which, as we suggest, points to a breakdown of one of the liver functions, namely the ability to store vitamin A. Liver functions may be disturbed during various diseases and independently from or even prior to the occurrence of anatomical cell damage (6).

Since only very few results of clinical and pathological investigations are available at all, a clarification of the etiology and pathogenesis of these liver diseases in the snow leopard is extremely difficult. The time course, case history and laboratory results from Basle I, of which most data could be gained, and the histological findings of the Munich female, resemble those described in human portal liver cirrhosis (5, 7, 8). Apart from alcoholism, also nutritional deficiencies and malnutrition may contribute either in connection with alcoholism or alone to liver cirrhosis in man. Further, epidemic viral hepatitis is another well-known cause of human liver cirrhosis. Rarely, portal liver cirrhosis may be the result of a long-continued nibbling away of hepatic cells due to prolonged occupational exposure to diethyl ether, chloroform, carbon tetrachloride, phosphorus, lead, arsenic or manganese (5, 7, 8).

In snow leopards kept in zoological gardens, unknown nutritional deficiencies cannot be excluded totally as a factor contributing to liver cirrhosis, since the living conditions and feeding habits in the zoos are quite different from those in the natural environment of these animals.

Also it is generally known that arctic animals living in zoos like Basle, where milder weather conditions prevail than in the country of origin, are highly susceptible to diseases caused by parasites, mycotic, bacterial and viral agents not occurring in their natural habitat. Thus it might be possible that one of these agents favours the development of liver cirrhosis in the snow leopard.

It is known for instance that upper respiratory infections do occur in snow leopards in zoological gardens. Basle I showed symptoms of such an infection in 1974 which, after treatment for feline rhinotracheitis, disappeared again. This infection might have contributed at least to the lesions of the central nervous system. The herpes viruses can affect brain tissue as it is the case in mad itch or other herpes infections in animals and man. Regular vaccino-prophylaxis for important viral diseases in the cat, like panleukopenia and feline coryza, was only applied in the Basle zoo since 1976.

Repeated narcosis and treatment with insecticidal baths can be excluded as a primary cause of the liver cirrhosis of Basle I, since the liver of this animal was already damaged when the first treatment was applied. Pathological GPT and GOT values were found in plasma samples from Basle I on January 5, 1972, when it was just narcotized for its first insecticidal bath.

In the case of chronic liver congestion even less information could be obtained. However, the time course of the disease of the female, Basle II, was much shorter and the progress of the disease much more acute than in Basle I, suggesting a different etiology and pathogenesis than observed in the liver cirrhosis of Basle I. Portal hypertension and heart failure in man are known to cause similar histological features as seen in the liver of Basle II (7, 8).



As demonstrated by the present study, much more data have to be gathered and compiled and repeated thorough investigations will have to be performed on each diseased animal in order to obtain useful and applicable statements on the etiology and pathogenesis of these liver diseases in the snow leopard.

TABLE 1: DATA AND CHRONOLOGICAL APPEARANCE OF THE SYMPTOMS REFERRING TO THE FATAL CASES EXAMINED

Individual	Date of birth or acquisition	Bodyweight	Main observations			Date of death	Post mortem findings
			Apathy Anorexia	Disturbance of the CNS	Ascites		
Basle I (male)	imported adult, 1970	5. 1.72: 40,0 kg 2. 2.72: 40,0 kg 19. 4.73: 43,5 kg 15. 1.76: 38,0 kg	from 23.11.75 onwards	from 5. 1.76 onwards	none	30. 1.76	liver cirrhosis; disseminated necrotic foci in the brain
Basle II (female)	born in 1970	5. 1.72: 33,3 kg 2. 2.72: 33,3 kg <sup>+) </sup> 4.10.72: 28,0 kg	from 8.12.72 onwards	from 8.12.72 onwards	24. 8.72: first drainage 4.10.72: 11 litres drained 12.10.72: 5 litres drained 9.11.72: 5 litres drained	18.12.72	chronic liver congestion
Munich (female)	born approximately in 1965-1967	no data available	from 2. 1.73 onwards	from 8. 1.73 onwards; increased after 20. 1.73	none	2. 2.73	liver cirrhosis; degenerative processes in the brain.

<sup>+)</sup>  animal weighed after drainage of ascites

CNS = central nervous system

TABLE 2: HEMATOLOGICAL DATA OF SNOW LEOPARDS WITH LIVER CIRRHOSIS (BASLE I) AND CHRONIC LIVER CONGESTION (BASLE II)

Individual	Date of sampling	RBC: T/1	Hb: G/1 (mmol/l)	MCH: pg (fmol)	Total WBC: G/1	Neutrophils		Lymphocytes: G/1
						Band: G/1	Segmented: G/1	
Basle I (male)	5.1.72	10.1	138 (8.56)	13.7 (0.82)	6.1	0.8	4.0	1.0
	20.1.72	9.8	128 (7.94)	13.1 (0.79)	8.6	1.4	5.0	2.2
	2.2.72	10.0	136 (8.43)	13.7 (0.82)	6.6	1.5	4.0	0.8
	24.8.72	9.3	129 (8.00)	13.9 (0.83)	8.0	3.0	3.2	1.0
	15.1.76	8.4	112 (6.94)	12.2 (0.73)	13.0	1.7	10.0	0.6
Basle II (female)	5.1.72	9.9	153 (9.49)	15.4 (0.92)	14.8	2.9	8.4	1.7
	20.1.72	10.3	157 (9.73)	15.3 (0.91)	16.3	3.3	8.4	4.3
	2.2.72	10.2	152 (9.42)	14.8 (0.89)	16.7	3.9	9.1	2.4
	24.8.72	10.7	127 (7.87)	11.9 (0.71)	17.7	5.7	10.0	1.1

RBC = Red blood cells

T/1 =  $10^6$ /  $\mu$ l

Hb = Hemoglobin

G/1 =  $10^3$ /  $\mu$ l

MCH = Mean corpuscular hemoglobin

WBC = White blood cells

TABLE 3: PLASMA ENZYME ACTIVITIES OF THE FEMALE "VAPPU" AT ILLNESS AND DURING AND AFTER THERAPY.

Date	GOT: IU/1	GPT: IU/1	Glucose: mg/100 ml (mmol/l)	Urea: mg/100 ml (mmol/l)	Comments
13.4.76	11	10	135 (7.42)	24.8 (4.22)	Endometritis
21.4.76	33	15	137 (7.53)	52.0 (8.84)	Therapy
27.4.76	20	23	109 (5.99)	67.1 (11.41)	Therapy
7.5.76	34	56	80 (4.40)	83.2 (14.10)	After therapy
25.6.77	12	20	70 (3.85)	44.7 (7.60)	Check-up

GOT = Aspartate-aminotransferase (EC.2.6.1.1.)

GPT = Alanine-aminotransferase (EC.2.6.1.2.)

Enzyme activities were determined in an optimized, kinetic test at 340 nm and 25°C (Centrifichem System).

IU/1 =  $\mu$ moles/minute/1000 ml.

TABLE 4: VITAMIN DETERMINATIONS IN PLASMA AND LIVER SAMPLES FROM SNOW LEOPARDS  
 COMPARED WITH THOSE FOUND IN MAN AND INFANTS.

Species	Vitamin A concentration <sup>+) )</sup>		Date of sampling	References
	Plasma: IU/100 ml	Liver: IU/g		
<u>Man (adult)</u>				(9,10)
healthy	150 - 280	800 (up to 7000)	-	
deficient	below 80	-	-	
<u>Infants (up to 1 year)</u>				
healthy	100 - 200	550 (up to 900)	-	
deficient	below 50	-	-	
<u>Snow leopards</u>				own results (1)
Basle I (male), diseased	66	12	15.1.76	
"Vappu" (female), diseased	81	-	27.4.76	
healthy	242	-	3.1.78	

+) 1 IU = 0.300 µg all-trans-vitamin A<sub>1</sub> = 0.344 µg all-trans-vitamin A<sub>1</sub>-acetate.

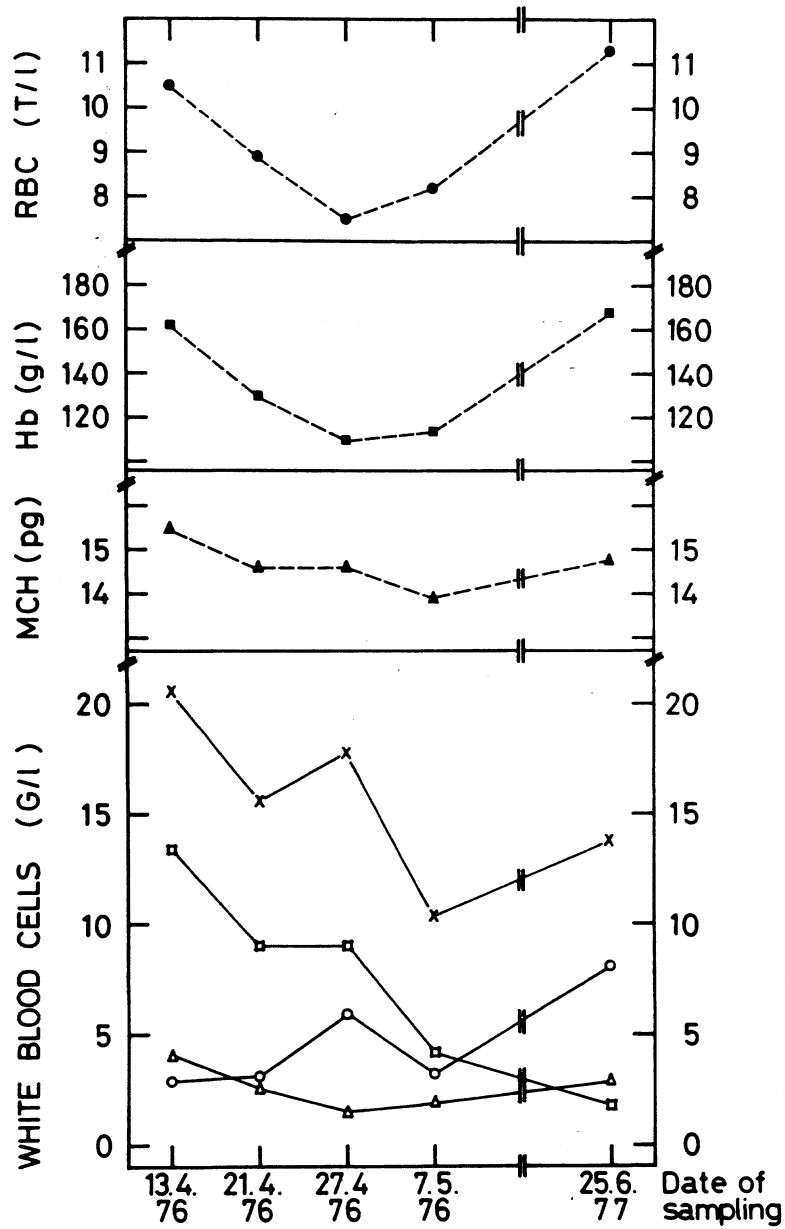


Figure 1: Hematological parameters of "Vappu" at illness and during and after therapy.

White blood cells:

- x — x total leukocytes
- — □ band neutrophils
- o — o segmented neutrophils
- Δ — Δ lymphocytes

RBC = red blood cells; Hb = hemoglobin concentration;

MCH = mean corpuscular hemoglobin.

T/l =  $10^6/\mu\text{l}$  ; G/l =  $10^3/\mu\text{l}$ .

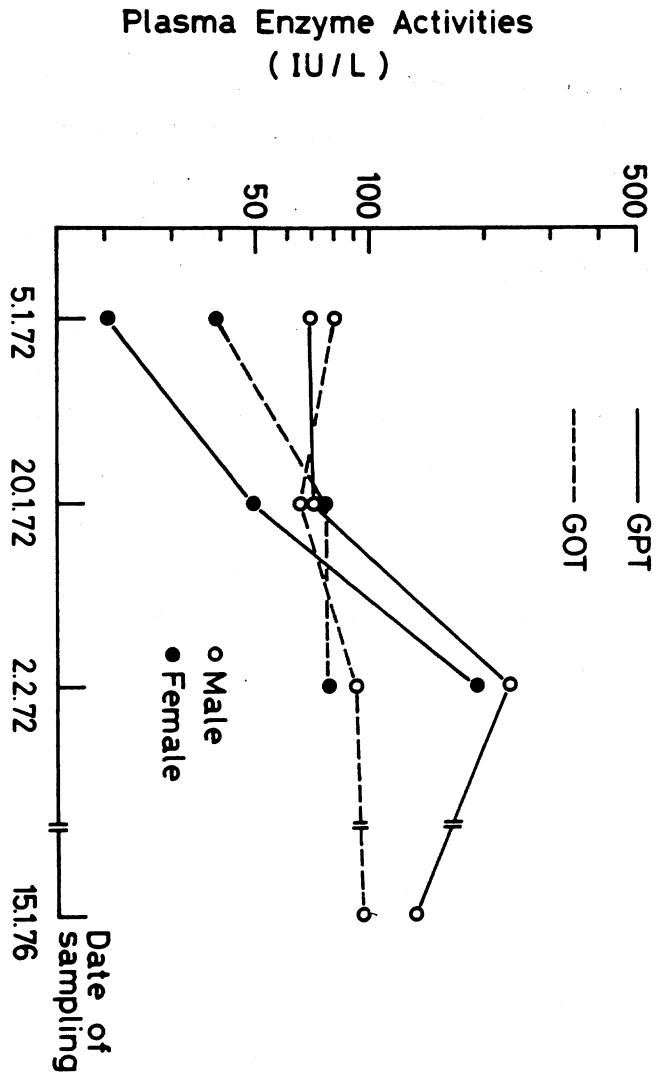


Figure 2: Plasma enzyme activities of the male (Basle I, o) and the female (Basle II, ●) snow leopard during liver disease.

GPT (——) = alanine-aminotransferase (EC.2.6.1.2.)

GOT (-----) = aspartate-aminotransferase (EC.2.6.1.1.)

Enzyme activities were determined in an optimized, kinetic test at 340 nm and 25<sup>o</sup>C (Centrifichem System).

IU/l = μmoles/minute/1000 ml.

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APPENDIX

QUESTIONNAIRE RE. RESULTS OF CLINICAL AND PATHOLOGICAL  
EXAMINATIONS ON SNOW LEOPARDS

On the occasion of the 1st International Symposium on the Snow Leopard from March 7 - 8, 1978, I was commissioned to continue my work on recognizing liver changes in the snow leopard at an early stage. I would therefore ask you kindly to let me have the following results on healthy, ill and dead snow leopards:

Blood investigations

- Red and white blood cells (incl. mineral, glucose, urea)
- Liver enzyme, specially GOT, GPT
- Protein electrophoresis
- Vitamin A examinations in the liver<sup>+</sup> and blood

Clinical investigations

- All experiences with narcosis
- Clinical observations on sick animals

Pathological investigations

- Complete post-mortem reports, transparencies of liver in pathological condition
- Histological preparations of the liver, brain and further interesting organs.

<sup>+</sup>Deep frozen pieces of liver (as large as possible) can be sent for Vitamin A analysis to:

Dr. D. Rüedi  
Basle Zoological Gardens  
CH-4054 Basel

You will naturally be informed about the results of the examinations.  
In advance many thanks for your cooperation and kind regards.

Yours sincerely

Dr. D. Rüedi  
Dr. D. Rüedi  
Zooveterinarian and  
Curator of Mammals  
BASLE ZOOLOGICAL GARDENS