

Appendix 1. Hepatic necrosis in neonatal calves: Diagnostic checklist

Background:

An increase in fatal hepatic necrosis has been observed in Western Canadian beef calves. While the number of cases remains small, there is a need to determine the etiology and understand calf and herd characteristics that might be associated with this clinical manifestation. Calves are most often described as "weak" and having icterus or liver lesions on postmortem exam.

Information to include in diagnostic submissions:

For suspect cases of hepatic necrosis in calves, diagnostic laboratory submission forms should be filled out completely. Important information to provide includes:

Herd characteristics
\square Size of the herd and size of any within-herd groups that are managed separately
☐ Calving date range
☐ Housing and bedding management practices
☐ Vaccinations administered to dams and calves
\square Feed and water source(s) during pregnancy, calving, and the neonatal period
Herd history
☐ Mortality and morbidity incidence (e.g., 5 sick and 4 dead within the last 7 days)
☐ General clinical signs observed in the herd
☐ Treatments given at the herd level (e.g., all calves are given "X" product at birth)
\square Other diagnostic testing undertaken and the results
Case history
\square Signalment including breed, age or fetal age, and sex
\square Clinical signs before death including the temperature, pulse, and respiration rate
☐ Treatment(s) (including the product, dose, duration, and route) administered
\square Timing between death and postmortem evaluation (e.g., euthanized, died overnight)
Field necropsy notes
☐ Overall body condition, hydration
☐ Gross internal and external abnormalities
Diagnostic testing for the initial database for suspected cases:

Test	Sample Required
Histology	Full tissue suite, particularly including gross lesions
Bacterial culture	Fresh or frozen liver
Mineral evaluation*	Fresh or frozen liver and kidney
Vitamin A and E	Fresh or frozen liver
Mycotoxin evaluation	1 kg of well-mixed feed

^{*} Should include Cu, Fe, Zn, Co, and Se (e.g., Mineral Panel 1 at Prairie Diagnostic Services)

Additional testing may be required and undertaken with direction from a pathologist.



Table S1. Liver trace mineral and vitamin concentrations, reported in parts per million and parts per billion (Cobalt). Concentration data were reported on a weight basis. Trace mineral concentrations were determined using Inductively Coupled Plasma-Mass Spectrometry. Vitamins were quantified using High Performance Liquid Chromatography.

	Laboratory	Magnesium	Manganese	Iron	Cobalt	Copper	Zinc	Selenium	Molybdenum	Vit E	Vit A
F1.1: PDS2212744	PDS	155.6	2.98	815.1	113.2	59.4	358.3	0.861	0.110	236.1	39.8
F2.1: PDS2213602	PDS	97.3 ¹	0.867	649.7	23.4	69.2	61.6	1.27	0.076	152.8	103.3
F2.2: PDS2213610	PDS	119.5	0.687	322.8	22.1	71.2	26.8	0.948	0.106	151.3	125.2
F3.1: PDS2213104	PDS	128.7	1.28	367.2	15.7	13.2 ¹	18.7	0.798	0.103	N/A	N/A
F4.1: PDS2213105	PDS	114.6	1.07	350.6	28.8	60.9	64.2	0.833	0.156	N/A	N/A
F5.1: PDS2213155	PDS	119.0	1.49	236.3	16.3	49.0	28.4	0.499	0.115	71.6	39.3
F5.2: PDS2213163	PDS	151.1	4.30	168.1	35.6	72.1	152.4	1.00	0.156	99.8	16.5
F5.3: PDS2213173	PDS	134.8	4.89	146.1	61.7	96.3	110.6	0.821	0.170	15.6	12.9
F6.1: UCVM22-292	PDS	127.6	0.643	259.8	17.0	84.4	43.4	0.637	0.107	123.9	33.9
F6.2: UCVM22-293	PDS	139.5	1.90	773.3	27.2	59.8	45.0	0.602	0.083	211.9	82.3
F6.3: UCVM22-296	PDS	143.2	1.45	182.9	19.3	143.9	49.6	1.90	0.089	297.7	63.9
F6.4: UCVM22-297	PDS	156.4	1.50	340.9	34.7	88.5	129.7	0.836	0.112	230.6	57.6
F6.5: UCVM22-301	PDS	108.1	0.827	237.5	21.9	64.1	57.2	0.624	0.058	134.2	42.8
F6.6: UCVM22-302	PDS	157.8	1.89	602.5	19.9	93.4	117.6	0.605	0.091	221.0	93.7
F7.1: UCVM22-335	PDS	146.0	0.921	322.9	15.5	61.7	17.0	1.27	0.051	130.5	72.3
F7.2: UCVM22-346	PDS	139.3	0.991	322.9	15.9	38.2	17.7	0.603	0.106	159.4	203.3
F7.3: UCVM22-397	PDS	121.4	1.29	275.5	16.9	88.0	26.4	0.787	0.079	N/A	N/A
F8.1: UCVM22-570	PDS	126.0	1.08	160.9	38.1	67.2	22.6	1.47	0.141	90.2	N/A
F9.1: PDS2406734	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F10.1 UCVM23-585	AVC	N/A	N/A	352	N/A	88	N/A	N/A	N/A	N/A	N/A
F10.2: UCVM23-638	PDS	125.1	1.49	457.4	21.7	98.2	14.6	2.09	0.071	39.1	40.5
F10.3: UCVM23-639	PDS	115.5	0.552	37.6	15.1	3.22^{1}	15.5	0.698	0.121	184.1	60.9

Reference ranges for hepatic trace minerals for fetal/neonatal calves are described in Puls R. Mineral Levels in Animal Health: Diagnostic Data. 2nd ed. Clearbrook, Canada: Sherpa International; 1994 and Corbett RB. Trace mineral nutrition in confinement dairy cattle. Vet Clin North Am Food Anim Pract 2023;39:425–438. The reported vitamin A reference ranges for stillborn/fetal neonates and calves <9 days old is 1.4-4.3 and 14.2-35.7 ppm wet weight, respectively (converted from dry weight basis using factor of 3.5; the reported vitamin E reference ranges for stillborn/fetal neonates and calves <9 days old is 1.1-2.9 and 3.4-5.7 ppm wet weight, respectively (Puls R. Vitamin levels in animal health: diagnostic data and bibliographies. 2nd ed. Clearbrook, Canada: Sherpa International; 1994). Abbreviation: N/A = not analyzed

1. Interpreted as deficient by a toxicologist.

Table S2. Kidney trace mineral data, reported in parts per million (wet weight basis) and parts per billion (cobalt only).

	Laboratory	Magnesium	Manganese	Iron	Cobalt	Copper	Zinc	Selenium	Molybdenum
F1.1: PDS2212744	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F2.1: PDS2213602	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F2.2: PDS2213610	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F3.1: PDS2213104	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F4.1: PDS2213105	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F5.1: PDS2213155	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F5.2: PDS2213163	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F5.3: PDS2213173	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F6.1: UCVM22-292	PDS	194.5	0.412^{1}	51.5	16.4	33.9^{2}	53.9	0.869	0.222
F6.2: UCVM22-293	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F6.3: UCVM22-296	PDS	138.8	0.611	66.3	13.6	41.7^{2}	43.2	0.831	0.182
F6.4: UCVM22-297	PDS	153.2	0.568^{1}	102.8	26.6	66.4^{2}	89.4	1.31	0.188
F6.5: UCVM22-301	PDS	195.0	0.562	53.5	16.0	52.0^{2}	121.6	1.14	0.302
F6.6: UCVM22-302	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F7.1: UCVM22-335	PDS	176.4	0.706	131.6	13.6	11.8^{2}	24.1	0.985	0.173
F7.2: UCVM22-346	PDS	167.6	1.05	80.9	29.0	3.09	43.5	0.762	0.155
F7.3: UCVM22-397	PDS	170.6	0.530	102.6	11.6	25.5^{2}	41.0	0.812	0.102
F8.1: UCVM22-570	PDS	106.2	0.460^{1}	83.9	34.8	19.9^{2}	25.2	1.41	0.231
F9.1: PDS2406734	PDS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
F10.1 UCVM23-585	AVC	N/A	N/A	105	N/A	4.5^{1}	N/A	N/A	N/A
F10.2: UCVM23-638	PDS	216.7	2.43	855.5	40.8	155.8 ²	26.1	2.69	0.120
F10.3: UCVM23-639	PDS	142.6	1.77	306.8	18.9	107.9 ²	22.3	1.12	0.079

Reference ranges for renal trace minerals for cattle are described in Galey FD, Maas J, Tronstad RJ, Woods LW, Johnson BJ, Littlefield ES, et al. Copper toxicosis in two herds of beef calves following injection with copper disodium edetate. J Vet Diagn Invest 1991;3:260–263. The reported threshold for chronic copper toxicosis in renal tissue in cattle is >10 ppm wet weight. Abbreviations: N/A: not available.

^{1.} Interpreted as deficient by toxicologist

^{2.} Interpreted as toxic by toxicologist