

# THE POTENTIAL PROGNOSTIC VALUE OF CERULOPLASMIN TESTING IN RELATION TO THE RESPONSE TO INITIAL ANTIMICROBIAL THERAPY IN BOTTLENOSE DOLPHINS (*Tursiops truncatus*) WITH INFECTED BITE WOUNDS

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## ABSTRACT

Microbiology and management of a bite wound infections represent a significant burden to humans and animals, health care professionals and veterinarian surgeons. While many of these wounds require minimal therapy or no therapy, significant number results in infections, which may even be life-threatening. In addition to local wound infection, other complications may occur.

The bacteria associated with bite-wound infections generally originate from the oral cavity of the biting animal, as well as from the bitten animal's skin flora. Wound management includes the administration of proper local care and the use of proper antimicrobial agents when needed. The clinical presentation and appropriate treatment of infected bite wounds vary according to the causative microorganism.<sup>6</sup>

Adjunctive laboratory data may assist the clinician in supporting the diagnosis of infected wound while awaiting cultural test results. Determination of the concentration of acute phase protein (APP), such as ceruloplasmin, can be used as a direct measure of inflammation activity in the evaluation of adequacy of antibacterial therapy for infected diseases in human and veterinary medicine.<sup>4,7</sup> Ceruloplasmin (Cp) is an  $\alpha$ -glycoprotein that is considered one of the positive acute phase proteins in mammals. Serum levels of ceruloplasmin may be useful marker of infection diseases for cetaceans<sup>1</sup> but its use in the evaluation of response to therapy remains poorly defined.

Serious infections can result from wounds that were caused by bites from aquatic animals. Principal predators of cetaceans include sharks, other cetaceans, polar bears etc. It is known, that male dolphins often have scars that can be attributed as wounds from other male dolphins.<sup>10</sup> A number of oceanaria are involved with rehabilitation programs that result in presentation of injured animals with wounds.<sup>9</sup>

The aim of this study was to define the time course of Cp levels in bottlenose dolphin (*Tursiops truncatus*) with infected bite wounds according to their response to the initial antimicrobial treatment. Three male subadult bottlenose dolphins with infected wounds (5 cases) were examined in our study. Clinical data and complications were registered. Blood samples were obtained before and during treatment weekly for measurement of serum concentration of Cp, and determination of clinical and biochemical analyses. A manual method based on PPD-oxidase assay was used for the determination of ceruloplasmin.<sup>5</sup> Aerobic and anaerobic cultures from the wounds were taken before any treatments. Antibiotic-sensitivity tests were performed. All animals received a broad-spectrum antibiotic for the first seven days. With cultured results, antibiotics were changed if indicated. The

cases were retrospectively classified in two categories: those cases requiring no change of initial administrated antibiotics (group A, 3 cases), and change of antibiotics (group B, 2 cases).

Table 1 shows the weekly-detected concentrations of ceruloplasmin (mg/dl) for affected dolphins. All animals were completely healthy before accidents (level 0). All bottlenose dolphins evaluated in the study had increased concentrations of ceruloplasmin at the time of diagnosis (level 1). Concentrations of ceruloplasmin decreased significantly in all animals at the end of the study period and returned to their initial levels (level 4). Ceruloplasmin concentration decreased more rapidly to initial level in group A than in group B, furthermore Cp concentration slightly increased before change of antibiotic in group B (level 2 and 3).

Table 1. Serum concentration of ceruloplasmin in Bottlenose dolphin

		level 0	level 1	level 2	level 3	level 4
Group A	Case 1	14,43	27,5	23,1	19,6	17,8
	Case 2	17,5	26	22,8	17,8	17,5
	Case 3	18,1	28,1	24,1	20,5	14,8
Group B	Case 4	15,05	27	38	20,1	19,1
	Case 5	14,43	29	31,6	24,7	15,89

Significant increases in Cp were observed in bottlenose dolphins with ineffective initial antibiotic therapy. The inflammatory mechanisms in these infections are similar to those seen in other conditions that lead to systematic inflammatory response and multiple cytokine-mediated organ failure syndromes.<sup>2</sup> Furthermore it is already known that ceruloplasmin is a multicopper plasma protein involved in wound healing through copper-induced vascular endothelial grown factor (VEGF) expression and copper-dependent activation of hypoxia-inducible factor (HIF)-1.<sup>3,8</sup>

Changes in serum concentration of ceruloplasmin in bottlenose dolphins with infected wounds during antibiotic therapy were determined. Overall, measurement of concentrations of selected acute-phase protein, such as ceruloplasmin, can help to evaluate the response to initial antibiotic treatment in infected dolphins.

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## LITERATURE CITED

1. Beal J.E. Jr., and P.T. Cardeilhac. 1979. Elevated ceruloplasmin in a pilot whale with gastritis. *Abstr Proc International Association for Aquatic Animal Medicine*; P. 11.
2. Gruys E., M.J.M. Toussaint, T.A. Niewold, and S.J. Koopmans. 2005. Acute phase reaction and acute phase protein. *J Zhejiang Univ SCI 6B (11)*: 1045-1056.
3. Martin F., T. Linden, D.M. Katschinski, F. Oehme, I. Flamme, C.K. Mukhopadhyay, K. Eckhardt, J. Troger, S. Barth, and G. Cameniseh. 2005. Copper-dependent

- activation of hypoxia-inducible factor (HIF)-1: implications for ceruloplasmin regulation. *Blood* 105(12): 4613-4619.
4. Martinez-Subiela S., L.J. Bernal, and J.J. Ceron. 2003. Serum concentrations of acute-phase proteins in dog with leishmaniosis during short-term treatment. *Am J Vet Res* 64(8): 1021-1026.
  5. Osaki S., D.A. Johnson, and E. Frieden. 1966. The possible significance of the ferrous oxidase activity of ceruloplasmin in normal human serum. *J Biol Chem* 241: 2746-2751.
  6. Robson M.C., D.P. Hill, M.E. Woodske, *et al.* 2000. Wound healing trajectories as predictors of effectiveness of therapeutic agents. *Arch Surg* 135(7): 773-777.
  7. Schmit X., and J.L. Vincent. 2008. The time course of blood C-reactive protein concentrations in relation to the response to initial antimicrobial therapy in patients with sepsis. *Infection* 36(3): 213-219.
  8. Sen C.K., S. Khanna, M. Venojarvi, *et al.* 2002. Copper-induced vascular endothelial growth factor expression and wound healing. *Am J Physiol Heart Circ Physiol* 282: H1821-1827.
  9. Walsh M.T., E. Chittick, and S. Gearhart. 2004. Banding and splinting techniques in marine animals. *Abstr. Proc. International Association for Aquatic Animal Medicine*; Pp. 53-54.
  10. Wells R.S., M.D. Scott, and A.B. Irvine. 1987. The social structure of free-ranging bottlenose dolphins. *In: H. Genoways (ed). Current Mammology, Vol.1, Plenum, NY; Pp. 247-305.*