

# CAPNOCYTOPHAGA - AN EMERGING ZONOSIS FROM CANINES

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Capnocytophaga is considered as one of the emerging bacterial zoonotic disease. Numerous infectious diseases are caused by agents that are directly or indirectly transmissible from different animal species to humans. WHO defined Zoonoses as “those diseases and infections, which are naturally transmitted between vertebrate animals and man”. Presently, the zoonotic diseases including the emerging and reemerging pathogens are increasing and more than 700 diseases occurring in man and animals are known to be transmitted mutually.

Emerging zoonoses are the diseases caused by a new microbial agent or by micro organisms previously known but now occurring in areas where diseases was unknown. [Meslin 1992]. The most important factors for emergence of zoonotic diseases are (Brenner *et al.* 1989) change in size and density of human and animal population (Bobo R.A. and Newton E.J.; 1976)) increased movement of man and animals (Conrads *et al.* 1997) increased trade in animal products (Dankner *et al.* 1987) increased handling of animal by-products and waste (Forlenza, S. W.; 1991)) environmental changes due to human activities (Gaastra W. and Lipman L.J.A.; 2010) cultural and anthropological patterns (Goldstein E.J.C.; 1992)) emergence of drug resistance of bacteria (Gomez-Garces *et al.* 1994) close association between man and animals (Griego *et al.* 1995) human behavior food habits and increase in the number of immunocompromised individuals (Greene, C. E.; 1998) handling of contaminated biologicals (Happel K.I. and Nelson S.; 2005) inappropriate waste disposal (Hicklin *et al.* 1987) increased population of stray animals (Job *et al.* 1989) natural disasters. Emerging zoonotic disease agents transmitted by food animals include enteropathogenic *E. coli*, *Salmonella DT104*, *Campylobacter* spp, and *Streptococcus iniae* (from farmed fish). Important viral diseases include Hendra viral disease [1994], Menangle virus [1997], Nipah viral infection [1998], West Nile fever [1999],

SARS [2003] and high pathogenic avian influenza.

Re-Emerging Zoonoses are the diseases with a known zoonotic agent that have re-emerged after many years of its absence in areas where they had been reported before. Few examples are Dengue fever, Meningococcal meningitis caused by *Neisseria meningitides*, Rift valley fever and Neuro cysticercosis.

## Capnocytophaga [CO<sub>2</sub> eater]

*Capnocytophaga canimorsus* was first observed in 1976 by Bobo and Newton from a patient presenting with meningitis and septicemia and was denoted as dysgonic fermenter 2 [DF 2]. Later in 1989, Brenner and colleagues described the organism and proposed the name capnocytophaga. The organism is a member of the normal gingival flora of dogs and cats which will not cause disease in these animals. It causes fulminant sepsis with disseminated intravascular coagulation and multi organ disease in human beings especially in immunocompromised individuals.

## Etiology

It is a fastidious, Gram negative, filamentous nonspore forming facultative anaerobe with tapered ends placed in the family Flavobacteriaceae under the genus Capnocytophaga. Important species under the genus are

- *Capnocytophaga canimorsus*
- *Capnocytophaga cynodegmi*
- *Capnocytophaga gingivalis*
- *Capnocytophaga granulosa*
- *Capnocytophaga hemolytica*
- *Capnocytophaga ochracea*
- *Capnocytophaga sputigena*

Out of these, *C. canimorsus* and *C. cynodegmi* are animal strains and are seen in the oral cavity of the carnivores and had been isolated from 26% dogs and 15% cats. Hence only these two are considered as pathogens of zoonotic importance. *Canimorsus* is the Latin term for dog bite and *cynodegmi* is the Greek

term for dog bite. All other species are seen in the oral cavity of man and have been isolated from dental plaques and periodontitis cases.

### **Epidemiology**

The disease has got world wide distribution. Cases have been reported in the United States, Canada, Europe, Australia and S. Africa. Middle-aged and elderly persons are at greater risk for contraction of disease; more than 60% of sufferers are above fifty years of age or older. In addition, individuals who spend a greater portion of their time with canines and felines are also in a higher risk category. This includes veterinarians, breeders, pet owners and lab workers. Chance of infection after dog bites varies between three and twenty percent and from cats, it may be as high as 50%. Serious infection was reported in immunocompromised individuals and less severe in immunocompetent people. Man to man transmission is not reported. In Finland from 1988 through 1994, several cases of *C. canimorsus* septicemia were identified; 2 cases were associated with sleeping with and/or being licked by a pet. From an 81-year-old woman with cellulitis of the right leg and an ulcer between the fourth and fifth toe, *C. canimorsus* was isolated from blood culture. This patient indicated that she slept with her cat in her bed and that the cat licked her feet and toes. A 60-year-old patient with chronic eczema died of septic shock and renal failure and disseminated intravascular coagulation caused by *C. canimorsus*. In Kansas, USA, a splenectomized 44-year-old man died after infection with *C. canimorsus*.

### **Host range and high risk categories**

Humans, canines, felines and rabbits are the hosts affected with the disease. In addition to those at higher risk of developing complications from *C. canimorsus* due to greater contact with felines and canines, certain pre-existing conditions place individuals in a critically high-risk category. Among these are those who have undergone a splenectomy, alcoholics, and individuals with immunosuppression due to the use of steroids such as glucocorticoids. Individuals with  $\beta$ -Thalassemia and smokers are also listed as high-risk. These individuals, like asplenic and alcoholics, have increased levels of alimentary iron in their bloodstream. *C. canimorsus* requires large amounts of iron to grow, so these conditions are optimal for the bacillus.

Of the cases presented in literature, 33% occurred in asplenic individuals. These individuals have decreased IgM and IgG production. Individuals with asplenia often experience symptom onset within a day of exposure. The infection rapidly progresses toward multiple organ system failures and finally death. The mortality rate in individuals with asplenia is much higher than any other at risk-category for *C. canimorsus* infections.

Alcoholics represent approximately 24% of individuals presenting with *C. canimorsus* infections. Alcoholism has been shown to result in decreased superoxide production in neutrophils as well as declines in neutrophil elastase activity. This results in an increase in predisposition to bacteremia. As a result, people suffering from alcoholism are more likely to suffer from the more dangerous aspects of *C. canimorsus* invasions.

Immunosuppressed patients make up approximately 5% of individuals presenting with *C. canimorsus* symptom.

### **Transmission**

- Through bites and scratches of dogs & rarely cats.
- Licking of cuts & injuries by these animals.
- Accidental parenteral inoculation
- Nosocomial infection through the post operative wound infection

### **Disease In Man**

The incubation period from the dog bite to the onset of systemic symptoms is about 5 days which ranges from 1 to 10 days. Although inconsistent cellulites is the most common finding after bite wound contaminated by *C. canimorsus* and *C. cynodegmi*, in some cases eschariform lesions characterized by formation of purplish black necrotic tissue around the bite site are seen. Splenectomized or immunosuppressed patients including those with advanced age or hepatic cirrhosis develop the most severe illness from septicemia characterized by fever, malaise, myalgia, vomiting, diarrhea, abdominal pain, dyspnoea, hypotension, skin and subcutaneous infection, stiff neck, thrombocytopenia with purpura, symmetric peripheral gangrene, oliguria, disseminated intravascular coagulation and death. Fatality rate is seen over 30% and acute myocardial infarction has been reported in some people, also can lead to meningitis,

endocarditis, septic arthritis and osteomyelitis.

The organism appears to have an affinity for the eye causing angular blepharitis and severe keratitis. Accidental corneal inoculation was reported during a tooth extraction in a poodle causing severe refractory keratitis in a veterinarian.

### Diagnosis

- Clinical signs and symptoms and history
- Microscopic examination of blood smear or buffy coat smears of bacteremic patients with gram stain to detect the organism
- Cultural examination using McConkey's agar, Brain heart infusion agar or Chocolate agar with 5% carbon dioxide and 5% rabbit blood. Organisms are slow growing, may require 8 days of incubation and hence the laboratory should be informed if capnocytophaga is suspected so that specific test can be performed to detect these unusual organisms. Otherwise it would be either discarded or misdiagnosed as contaminant. Both *C. canimorsus* and *C. cynodegmi* are known to induce cytopathic effects in cell culture.
- Polymerase chain reaction assays of species specific genes

### Treatment

Immediate cleansing of wounds caused by canines and felines can be successful in keeping *C. canimorsus* infections at bay. Irrigation of wounds with saline is recommended and individuals are encouraged to seek medical help for the administration of antibiotics.

The organism shows susceptibility to many antimicrobials including penicillin, ampicillin, amoxicillin, clavulanate, cephalosporin, tetracycline, chloramphenicol, clindamycin, erythromycin, quinolone and sulphamethoxazole trimethoprim combination but are resistant to aminoglycosides and polymyxin. Therapy with amoxicillin – clavulanate [875/125 mg two or three times a day or 1000/200 mg two or three times a day I/V] should be initiated immediately when the infection is suspected.

### Prevention and control

- Early initiation of antimicrobial therapy in suspected individuals

- Avoid close contact with dogs and cats
- Thorough washing of bite wounds and scratches with soap and water and then with antiseptic solution.
- Health education.
- The organism is susceptible to 1% sodium hypochlorite, 70% ethanol, 2% formaldehyde and gluteraldehyde. The organism gets inactivated by moist heat at 121°C for 15 min. and dry heat at 160-170°C for one hour.

### Conclusion

*Capnocytophaga canimorsus* and *Capnocytophaga cynodegmi* are the normal inhabitants of the gingival cavity of dogs and cats. These are now considered as emerging zoonotic agents which can cause a wide spectrum of diseases, ranging from mild local wound infections after a dog or cat bite to fulminant, often lethal courses with sepsis, meningitis and disseminated coagulopathy. *Capnocytophaga* is an opportunistic pathogen causing multiorgan disease especially in splenectomised individuals, alcoholics and patients on corticosteroids. The public should be educated properly and they should be made aware of the potential risk of dogs and cats bite and the measures to be taken when such an incident occurs. Any clinician attending patients with a history of dog bite or saliva contact and progressive illness should consider *capnocytophaga* as a possible offender and take special care to elicit an accurate history and immediate therapy with antibiotics.

### References

- Brenner D.J., Hollis D.G., Fanning G.R., Weaver R.E. (1989). *Capnocytophaga canimorsus* sp. nov. (formerly CDC group DF-2) a cause of septicemia following dog bite, and *C. cynodegmi* sp. nov., a cause of localized wound infection following dog bite. *J. Clin. Microbiol*; **27**:231-5.
- Bobo R.A. and Newton E.J. (1976). A previously undescribed gram-negative bacillus causing septicemia and meningitis. *Am. J. Clin. Pathol.*; **65**:564-9
- Conrads G., Mutters R., Seyfarth I., Pelz K. (1997). DNA-probes for the differentiation of *Capnocytophaga* species. *Mol Cell Probes.*; **11**:323-8.
- Dankner WM, Davis CE, Thompson MA. (1987). DF-2 bacteremia following a dog bite in a 4-month-old child.

- Pediatr. Infect. Dis. J.; **6**:695–6.
- Forlenza, S. W. (1991). *Capnocytophaga*: An update. *Clin. Microbiol. Newsletter*, **13**(12), 89-91.
- Gaastra W. and Lipman L.J.A. (2010). *Capnocytophaga canimorsus*. *Vety. Microbiol.* **140**: 339-346.
- Goldstein E.J.C.( 1992). Bite wounds and infection. *Clin Infect Dis*;**14**:633-40.
- Gomez-Garces, J.-L., Alos, J.-I., and Sanchez J. Cogollos, R. (1994). Bacteremia by multidrug-resistant *Capnocytophaga sputigena*. *J. Clin. Microbiol.* **32**:1067-1069.
- Griego R.D., Rosen T., Orengo I.F., Wolf J.E. (1995). Dog, cat and human bites: a review. *J. Am. Acad. Dermatol.*; **33**:1019–29.
- Greene, C. E. (1998). Infectious diseases of the dog and cat, p. 333. W. B. Saunders Company, Philadelphia.
- Happel K.I. and Nelson S. (2005). Alcohol, Immunosuppression, and the Lung. *Proceedings of the American Thoracic Society* **2**(5): 428-432.
- Hicklin H., Verghese A., Alvarez S. (1987). Dysgonic fermenter 2 septicemia. *Rev Infect Dis.*;**9**:884–90.
- Job L., Hormann J.T., Grigor J.K., Isreal E.( 1989). Dysgonic fermenter-2: a clinico-epidemiologic review. *J Emerg Med*; **7**:185-92.
- Other References from which review material has been extracted**
- Jolivet-Gougeon, A., Sixou, J., Tamanai-Shacoori, Z., & Bonnaure-Mallet, M. (2007). Antimicrobial treatment of *Capnocytophaga* infections. *International J. Antimicrobial Agents*, **29**(4), 367-373.
- Krauss, H., Weber, A., Appel, M., Enders, B., Isenberg, H. D., Schiefer, H. G., Slenczka, W., von Graevenitz, A., & Zahner, H. (2003). Bacterial Zoonoses. *Zoonoses: Infectious Diseases Transmissible from Animals to Humans*. (3rd ed., pp. 173-252). Washington, DC.: ASM press.
- Le Moal G, Landron C, Grollier G, Robert R and Burucoa C. (2003). Meningitis Due to *Capnocytophaga canimorsus* after Receipt of a Dog Bite: Case Report and Review of the Literature. *Clinical Infectious Diseases* **36**: 42-46.
- Lindquist D, Murrill D, Burran WP, Winans G, Janda JM, Probert W. (2003). Characteristics of *Massilia timonae* and *Massilia timonae*-like isolates from human patients, with an emended description of the species. *J. Clin. Microbiol.*; **41**:192–6.
- Lion C, Escande F, Burdin JC.( 1996). *Capnocytophaga canimorsus* infections in humans: review of the literature and cases report. *Euro. J. Epidemiol.*; **12**:521–33.
- Morrison G. (2001). Zoonotic infections from pets. Understanding the risks and treatment. *Postgrad Med.*; **110**:24–48.
- Mossad, S. B., A. E. Lichtin, G. S. Hall, and S. M. Gordon. (1997). Diagnosis: *Capnocytophaga canimorsus* septicemia. *Clin. Infect. Dis.* **24**:123, 267.
- Pers C, Gahrn-Hansen B, Frederiksen W. (1996). *Capnocytophaga canimorsus* septicemia in Denmark, 1982–1995: review of 39 cases. *Clin Infect Dis.*; **23**:71–5.
- Sandoe, J. A. T. (2004). *Capnocytophaga canimorsus* endocarditis. *Journal of Medical Microbiol.* **53**(3), 245-248.
- Valtonen, M., A. Lauhio, P. Carlson, J. Multanen, A. Sivonen, M. Vaara, and J. Lähdevirta. (1995). *Capnocytophaga canimorsus* septicemia: fifth report of a cat-associated infection and five other cases. *Eur. J. Clin. Microbiol. Infect. Dis.* **14**:520-523.

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