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## Septicaemia with a Dysgonic Fermenter-2 (DF-2) Bacterium in a Compromised Host

**Summary:** Dysgonic fermenter-2 (DF-2) is a newly described gram-negative bacterium that can produce serious infections in the compromised host. We are reporting a case of DF-2 septicaemia in a splenectomized patient with chronic lymphocytic leukaemia. The clinical spectrum of infections due to the DF-2 bacterium, the difficulties in establishing the diagnosis and the preferential treatment are discussed.

**Zusammenfassung:** Sepsis durch ein dysgonisches Fermenter-2-(DF-2)-Bakterium bei einem abwehrgeschwächten Patienten. Der dysgonische Fermenter-2 (DF-2) ist ein vor kurzem beschriebenes gramnegatives Bakterium, das ernsthafte Infektionen bei abwehrgeschwächten Patienten hervorrufen kann. Wir berichten über einen Fall von DF-2-Septikämie bei einem splenektomierten Patienten mit einer chronischen lymphatischen Leukämie. Dabei werden sowohl das klinische Spektrum der durch DF-2 verursachten Infektionen als auch die diagnostischen Schwierigkeiten und die günstigste Behandlung besprochen.

### Introduction

Dysgonic fermenter-2 (DF-2) is a newly described gram-negative bacterium that can produce serious infections in the compromised host. About 28 cases have been reported in the literature (1-13). Its occurrence is associated with cellulitis, meningitis, endocarditis, bacteraemia and fulminant septicaemia. A history of a recent dog bite in most patients suggests that it is a zoonotic infection. There appears to be a clear predilection for patients with defective host defence. Commonly associated disorders include splenectomy, alcoholism and chronic lung disease (1).

We are reporting the first documented case in The Netherlands of DF-2 infection in a splenectomized patient with chronic lymphocytic leukaemia and hypogammaglobulinaemia.

### Case Report

A 54-year-old man was admitted to our hospital on November 8, 1980 because of fever and chills. Eight years earlier the diagnosis of chronic lymphocytic leukaemia had been established. In 1977 he had developed auto-immune haemolytic anaemia, and therapy with prednisone and chlorambucil was started. As severe haemolysis had re-occurred, splenectomy was performed in 1978. Because of axillary and cervical lymph node enlargement, treatment with chlorambucil and prednisone was started in 1979 with a satisfactory clinical response. Subsequently, maintenance

therapy with chlorambucil 2 mg daily, five days weekly was given.

Several hours prior to admission the patient became acutely ill with chills, fever, nausea and vomiting. There was no history of recurrent infection. The patient reported no headache, cough, chest or abdominal pain, dysuria or diarrhea. On admission he was taking prednisone 12.5 mg, chlorambucil 6 mg and isoniazide 300 mg daily.

On physical examination the patient appeared moderately ill. The axillary temperature was 39°C, the pulse 120/min and respiration 20/min. Blood pressure was 85/55 mmHg. Bilaterally, enlarged cervical lymph nodes were palpable. Physical examination was otherwise negative. Haemoglobin was 6.8 mmol/l, haematocrit 33.0%. The white cell count was  $100 \times 10^9/l$  with no band forms, 1% neutrophils, and 99% lymphocytes. Serum biochemistry was normal except for a gammaglobulin of 2 g/l. The urine gave a negative test for protein; the sediment contained 16-20 white cells, 1-3 red cells and a sporadic red cell cast per high power field. An electrocardiogram demonstrated sinus tachycardia at a rate of 120/min, but was otherwise normal. An X-ray film of the chest and abdomen was normal.

A presumptive diagnosis of pyelonephritis was established. Cultures from blood and urine were obtained and treatment with cefotaxime 4 x 1 g i. v. was started in the context of a clinical trial with that drug. Shortly after admission, clinically overt shock with anuria developed. Plasma and dopamine infusions were given. Diuresis returned and the blood pressure became normal. In the subsequent days the patient recovered completely and fever subsided. Urine cultures taken on admission were sterile and treatment with cefotaxime was discontinued after 10 days. The patient was discharged from the hospital on day 14. On the eighth hospital day, one initial blood culture was reported to contain a gram-negative bacterium that could not be identified by existing systems for determination.

Subsequent determination was performed at the R.I.V.M. (National Institute of Public Health and Environmental Hygiene, Bilthoven, The Netherlands) by *J. Borst* and subsequently confirmed by *R. E. Weaver* at the Centers for Disease Control (Atlanta, Ga., U.S.A.). The isolate met the criteria for DF-2 bacterium as described by *Butler et al.* (1).

### Discussion

In 1976 *Bobo and Newton* (2) reported the first case of

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septicaemia and meningitis following a dog bite, caused by a previously undescribed gram-negative bacterium. *Butler et al.* (1) described 17 patients with bacteraemia, caused by the dysgonic fermenter-2 bacterium, as it was designated by the Centers for Disease Control because of its slow growth and fermentation of carbohydrates. Five patients had undergone splenectomy before becoming ill. Alcoholism was noted in another four cases. Only two patients were reported to have previously been in good health. The organism, therefore, seems to be an opportunistic pathogen. In accordance with these observations in humans, experimental DF-2 infection in rabbits appears to be enhanced by administration of methylprednisolone (14). Our patient suffered from chronic lymphocytic leukaemia with hypogammaglobulinaemia and had undergone splenectomy three years earlier.

Ten patients in *Butler's* series had a dog bite or a history of recent animal exposure, suggesting an animal reservoir. *Bailie et al.* (15) examined the oral and nasal fluids of 50 dogs to determine the prevalence of aerobic bacteria associated with bite wounds. DF-2 was isolated from four of the dogs. *Martone et al.* (3) reported the only case of DF-2 septicaemia in which the organism could be isolated from the dog implicated in the transmission of infection. Our patient had a dog that frequently caused superficial skin lesions. However, we were unable to culture DF-2 from the dog's gingiva.

The spectrum of clinical disease caused by DF-2 shows great variety. In *Butler's* series cellulitis was the most common finding (seven cases). Primary bacteraemia without focal signs, purulent meningitis and endocarditis were seen in four cases each. In two of the patients fulminant septicaemia developed with hypotension, thrombocytopenia, purpura and oliguria. *Findling et al.* (4) reported a case of DF-2 septicaemia associated with disseminated intravascular coagulation and adult respiratory distress syndrome. At present, about 28 cases of DF-2-associated in-

fections have been described (1-13). In the ten post-splenectomy cases (1, 3, 4, 6, 10, 11) fulminant bacteraemia occurred in seven with a fatal outcome in three, while the remaining three patients developed meningitis. Bacilli were visible in the peripheral blood smear in three of the patients with bacteraemia (1, 3). It therefore appears that post-splenectomy patients are particularly prone to severe DF-2 infections.

Following dog bites, many physicians administer penicillin G prophylactically in order to prevent wound infection caused by *Pasteurella multocida* and mouth anaerobes. Since DF-2 is also susceptible to penicillin G, infections caused by this organism may also be treated. Furthermore, the prophylactic administration of penicillin after splenectomy may prevent DF-2 infections. Since it is so fastidious, DF-2 may be easily overgrown on the culture plate. In addition, identification may be impossible if cultures are discarded too quickly. It should be noted that blood cultures obtained in our patient on admission did not yield the organism until the eighth day!

*In vitro* susceptibility testing suggests that most antibiotics, including penicillin G, chloramphenicol, tetracyclines and carbenicillin, are effective in treating the infection. At present, penicillin G is considered the therapy of choice and should be administered in initially high dosages (1).

The clinical relevance of this microorganism appears to be restricted to febrile immunocompromised hosts, particularly splenectomized patients. The clinician should be aware of the DF-2 bacterium when blood cultures in such patients are initially sterile.

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#### Literature

1. *Butler, T., Weaver, R. E., Venkata Ramani, T. K., Ujeta, C. T., Bobo, R. A., Ji So Ryu, Kohler, R. B.*: Unidentified gram-negative rod infection. *Ann. Intern. Med.* 86 (1977) 1-5.
2. *Bobo, R. A., Newton, E. J.*: A previously undescribed gram-negative bacillus causing septicemia and meningitis. *Am. J. Clin. Pathol.* 65 (1976) 564-569.
3. *Martone, W. J., Zuehl, R. W., Minson, G. E., Scheld, W. M.*: Postsplenectomy sepsis with DF-2: report of a case with isolation of the organism from the patient's dog. *Ann. Intern. Med.* 93 (1980) 457-458.
4. *Findling, J. W., Pohlmann, G. P., Rose, H. D.*: Fulminant gram-negative bacillemia (DF-2) following a dog bite in an asplenic woman. *Am. J. Med.* 68 (1980) 154-156.
5. *Chaudhuri, A. K., Hartley, R. B., Maddocks, A. C.*: Waterhouse-Friedrichsen syndrome caused by a DF-2 bacterium in a splenectomized patient. *J. Clin. Pathol.* 34 (1981) 172-173.
6. *Hinrichs, J. H., Dunkelberg, W. E.*: DF-2 septicemia after splenectomy: epidemiology and immunological response. *South. Med. J.* 73 (1980) 1638-1640.
7. *Ofori-Adjei, D. P., Blackledge, P., O'Neill, P.*: Meningitis caused by dysgonic fermenter type 2 (DF-2) organism in a previously healthy adult. *Br. Med. J.* 285 (1982) 263-264.
8. *Schlossberg, D.*: Septicemia caused by SF-2. *J. Clin. Microbiol.* 9 (1979) 297-298.
9. *Schoen, R. T., Wohlgelemerter, D., Barden, G. E., Swartz, T. J.*: Infection with CDC group DF-2 gram-negative rod. Report of two cases. *Arch. Intern. Med.* 140 (1980) 657-658.
10. *Shankar, P. S., Scott, J. H., Anderson, C. L.*: Atypical endocarditis due to gram-negative bacillus transmitted by dog bite. *South. Med. J.* 73 (1980) 1640-1641.
11. *Boyce, F., Price, R. F.*: Splenectomized patient with fatal DF-2 septicemia. *Clin. Microbiol. Newsletter* 2 (1980) 4.
12. *Smith, C., Rubin, S. J.*: DF-2 Septicemia. *Clin. Microbiol. Newsletter* 5 (1983) 90-91.
13. *Rubin, S. J.*: DF-2: A fastidious fermentative gram-negative rod. *Eur. J. Clin. Microbiol.* 3 (1984) 253-257.
14. *Butler, T., Johnston, K. H., Gutierrez, Y., Aikawa, M., Cardaman, R.*: Enhancement of experimental bacteremia and endocarditis caused by dysgonic fermenter (DF-2) bacterium after treatment with methylprednisolone and after splenectomy. *Infect. Immun.* 47 (1985) 294-300.
15. *Bailie, W. E., Stowe, E. C., Schmitt, A. M.*: Aerobic bacterial flora of oral and nasal fluids of canines with reference to bacteria associated with bites. *J. Clin. Microbiol.* 7 (1978) 223-231.