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Aeromonas Infections

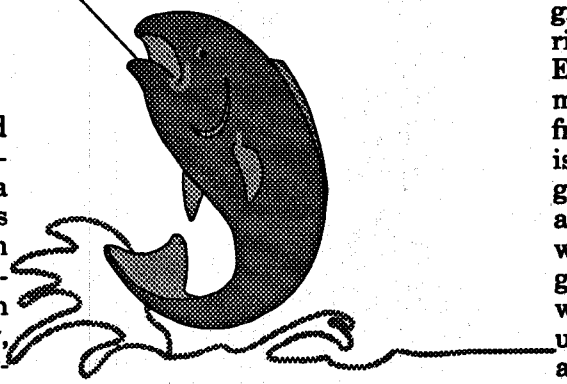
What do furunculosis in fish and mouth rot (ulcerative stomatitis) in snakes have in common with a fisherman's infected leg wound? The answer is they may all be due to aeromonads, gram negative bacilli with a natural habitat in freshwater, estuarine water, and soil. These organisms are a common cause of infection in cold-blooded animals and an occasional hazard for persons exposed to rivers, lakes and streams.

Clinical Manifestations

Aeromonads have been associated with four syndromes in humans. Septicemia, sometimes associated with a slow-moving necrotizing myositis and/or ecthyma gangrenosum skin lesions, is usually seen in compromised hosts, especially patients with cirrhosis or leukemia. Presumably, the organism in these patients is carried asymptomatically in the intestinal tract before invading the bloodstream.

Although its etiologic role has not been fully documented, aeromonads have been isolated from the stools of otherwise healthy patients with diarrhea more often than from control subjects. The diarrhea is described as watery with no white blood cells seen microscopically; a seasonal pattern (summer) has been observed. Both adults and children may be affected. Evidence suggests these patients acquire the organism by drinking untreated water.

Wound infections, usually of the hand or lower extremity, frequently result in a rapidly progressive cellulitis suggestive of Group A streptococcal cellulitis. Osteomyelitis has also been described. History usually reveals the otherwise healthy patient injured himself outdoors and contaminated the wound with freshwater or soil. These injuries have frequently been associated with warm weather recreational activities such as boating, fishing, swimming, and waterskiing.



Miscellaneous other infections have been described, including intra-abdominal abscess, hepatobiliary infection, peritonitis, meningitis, urinary tract infection, and pneumonia.

Epidemiology in Virginia

Although *Aeromonas* infections are not reportable in Virginia, we reviewed the records for 16 isolates referred to the State Lab (Division of Consolidated Laboratory Services) and identified as *Aeromonas* sp. from September 1, 1989 through June 30, 1991. There was no apparent geographic clustering based on the referring hospital for any of these isolates. Eight isolates were from stool specimens from patients ranging in age from 2 months to 69 years. Three isolates were from wounds (hand, groin and leg) of patients ranging in age from 18 years to 55 years; all were submitted in the months of August through October. Five isolates were from miscellaneous other sites: urine (x2), gallbladder, appendix, and perineal abscess. Ages of these patients ranged from 33 to 79.

Special Surveillance

The Office of Epidemiology is interested in receiving, on a voluntary basis, reports of aeromonad-associated infections occurring over the next two years in order to better characterize the epidemiology in Virginia. The Office is cooperating with the Virginia Institute of Marine Science, College of William and Mary, which is conducting a parallel study of *Aeromonas* sp. in the environment and the relationship of organism density to contamination of a water body by sewage and other nutrients. Case reports should be directed to Carl W. Armstrong, MD by calling 804/786-

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6029 or writing the Office of Epidemiology, Virginia Department of Health, Rm123, PO Box 2448, Richmond, Va 23218.

Laboratory Identification

Aeromonads will grow on standard culture media (blood agar and enteric differential agars). Clues to the laboratory identification of *Aeromonas* sp. include growth on MacConkey agar, a positive oxidase reaction, and fermentation of carbohydrates. Performance of the oxidase test is crucial for differentiating the organism from the Enterobacteriaceae (e.g. *Escherichia, Enterobacter, Serratia, Providencia*). If the oxidase test is omitted, *Aeromonas* sp. is most often misidentified as *Enterobacter* sp. There are three recognized species that have been associated with human infection: *A. hydrophila* (the most common), *A. sobria, and A. caviae*.

Treatment

A. hydrophila is usually resistant to ampicillin and other penicillins including the ureidopenicillins (e.g. piperacillin). Antibiotics of choice include trimethoprim-sulfamethoxazole or one of the newer quinolones (ciprofloxacin or norfloxacin).

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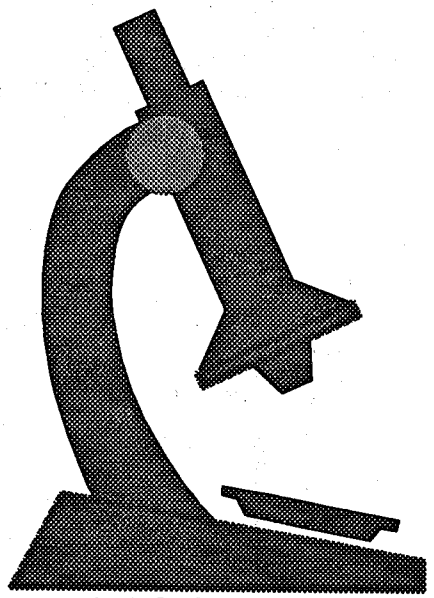
Interpretation of Antibody to Hepatitis B Core Antigen Alone*

The hepatitis B core antigen (HBcAg) is an internal component of the hepatitis B virus (HBV). HBcAg can be detected in the liver during HBV infection and is present in intact hepatitis B virions. No free HBcAg circulates in the blood, and the antigen can be detected only after detergent has been used to disrupt virus particles; there is no commercially available test for detecting HBcAg in serum.

Antibody to HBcAg

In acutely infected persons, antibody to HBcAg (anti-HBc) appears in serum 3-5 weeks after appearance of the hepatitis B surface antigen (HBsAg) and before the onset of symptoms. IgM anti-HBc appears first and



can persist in high levels for 6 or more months; IgM anti-HBc is a reliable marker for recent infection. IgG anti-HBc appears shortly after IgM anti-HBc and persists for life. In persons who recover from infection, HBsAg disappears, and antibody to HBsAg (anti-HBs) develops; the immune state is therefore characterized by detectable anti-HBs and anti-HBc. In HBV carriers, HBsAg persists, and anti-HBs does not develop; the carrier state is therefore also characterized by detectable HBsAg and anti-HBc.

Finding anti-HBcAg alone

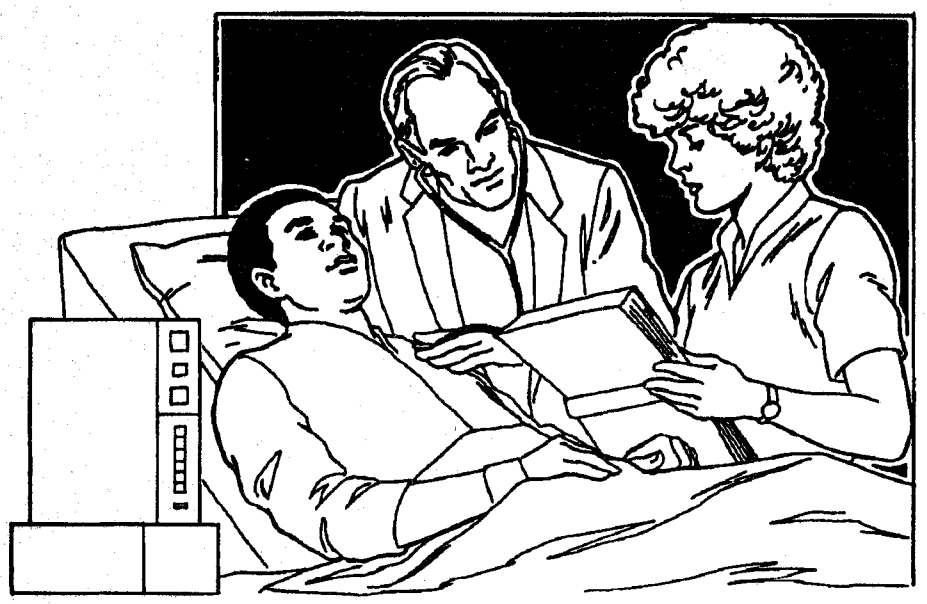
When persons are tested for the three basic markers of HBV infection (HBsAg, anti-HBc, and anti-HBs), a proportion are found to be positive for anti-HBc alone, without detectable HBsAg or anti-HBs. Serologic studies of large groups have shown this pattern in up to 6% or more of those tested. In general, the frequency of this result is directly related to the frequency of prior HBV infection in the population.

The serologic profile of anti-HBc alone has often generated questions in interpretation, particularly whether such persons may be infectious to others or whether they are susceptible to new HBV infection and require hepatitis B vaccine if they are in high-risk groups.

One problem in interpretation has been false-positive results. As with all laboratory tests, false-positive and non-specific results can occur. Studies have shown that positive anti-HBc results near the cutoff of the test are often not repeatable on the same or subsequent specimens. Furthermore, epidemiologic studies have suggested that such low positive results may occur in 0.5% to 2% of specimens irrespective of the prevalence of HBV infection in the group, supporting the concept of nonspecific reactivity.

Most positive anti-HBc results with current assays, however, are likely to be true positives. The pattern of anti-HBc alone is subject to several biological/serological interpretations other than false positive:

- *Early convalescence after acute infection* (the window period). Many persons in whom acute HBV infection is resolving experience a period in which HBsAg wanes to subdetectable levels, anti-HBs has not appeared, and anti-HBc is the only specific HBV marker detectable. This period usually lasts several weeks but can persist for several months or more before anti-HBs develops. IgM anti-HBc is always present during this period.
- *Passive transfer of anti-HBc.* Anti-HBc crosses the placenta; HBsAg does not. Infants born to carrier mothers can be positive for anti-HBc alone from passively transferred antibody; this reactivity can persist for



one year or longer. Adults can also be positive for anti-HBc alone because of the passive transfer of antibody, although there are few instances in which this might happen. Because of the routine screening of blood donations for anti-HBc as a surrogate test for non-A, non-B hepatitis, passive transfer of antibody from blood transfusion should no longer occur. The passive transfer of anti-HBc from clotting factor products (Factors VIII and IX) is possible because these are made from blood that may contain anti-HBc. Hepatitis B immune globulin (HBIG) may have enough anti-HBc to elicit a positive anti-HBc; however, we are aware of no studies in which this has been quantitated. Passive transfer from immune globulin (IG) would be unlikely to occur, since IG would be expected to have low titers of anti-HBc.

- *Remote infection with loss of detectable anti-HBs.* The pattern of anti-HBc alone may result if anti-HBs levels wane after resolved infection. This would usually be expected to occur many years after infection, although recent studies have produced conflicting results.
- *Remote infection with possible low-level HBsAg.* The pattern of anti-HBc alone may persist for an indefinite period after infection without development of anti-HBs. An important subcategory of this group may include persons who circulate HBsAg at levels not detectable by current commercial assays (low-level HBV carriers). Nevertheless, the risk for HBV infection after transfusion of blood positive for anti-HBc alone seems to be low.

Markers to Test For

Current Public Health Service recommendations rarely require testing for all three hepatitis B markers (HBsAg, anti-HBc, and anti-HBs). Screening of HBsAg only is recommended for the universal screening of pregnant women. Anti-HBc or anti-HBs testing is recommended for prevaccination screening. Because diagnostic panels including tests for all three markers are commonly used, however, the situation requiring interpretation of anti-HBc positivity alone will arise. The likelihood that persons with such results will fall into one of the above categories mentioned or have nonspecific antibody will vary with the testing situation and the quality of the diagnostic laboratory.

Further Diagnostic Workup

The need for further work-up to ascertain the cause depends upon the clinical indications; in most circumstances, no further evaluation is needed as such persons are likely immune to reinfection and would be infectious to others only under unusual circumstances. A complete work-up could include repeat testing for anti-HBc and IgM anti-HBc, and testing of a follow-up specimen for anti-HBc and anti-HBs. Persons in the window stage will be positive for IgM anti-HBc and will eventually develop anti-HBs. Those who have non-specific or passively acquired antibody will be negative on follow-up. Those who remain persistently positive for anti-HBc alone are those for whom interpretation is most difficult. It has been suggested that persons with resolved infection who have lost anti-HBs can be identified by the development of a brisk anamnestic anti-HBs response with a single dose of hepatitis B vaccine; however, this method has not been validated and would rarely be clinically indicated. Instead, a more practical approach would be to retest after several months to see whether anti-HBs (or possibly HBsAg) has developed.

Infectivity and Vaccine Use

With respect to infectivity or the need for vaccine, persons in the window phase of infection and persons with remote infection who have lost detectable anti-HBs can be considered noninfectious to others and immune to reinfection, and do not need vaccine. Persons with passively acquired antibody are not infectious but should receive vaccine if indicated; passively acquired antibody does not interfere with vaccine response. Persons with a chronic pattern of anti-HBc alone who are possible low-level carriers are not candidates for hepatitis B vaccine. There is no evidence that they are susceptible to de novo infection, but there is some evidence in animal models that anti-HBc protects against infection. Since their levels of HBsAg (and therefore circulating virus) are not detectable by current assays, these persons are presumably minimally infectious, as evidenced by the low risk of transmission even after transfusing whole units of blood. In settings where small amounts of blood or body secretions are transferred, such as in needlesticks or sexual and household exposures, persons with anti-HBc alone can be considered noninfectious, and their contacts do not need postexposure prophylaxis or vaccine.

**Adapted from: Hepatitis Surveillance Report No. 52. Atlanta: Centers for Disease Control, 1989:2-5.*

Cases of Selected Notifiable Diseases, Virginia, July 1 through July 31, 1991.

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
	State	Regions					This Yr	Last Yr	5 Yr Avg
		NW	N	SW	C	E			
AIDS	59	3	20	6	12	18	353	325	182
Campylobacter	67	15	19	6	18	9	210	243	237
Gonorrhea~	1474	-	-	-	-	-	8674	8971	8074
Hepatitis A	22	3	14	1	4	0	100	153	144
Hepatitis B	13	1	1	5	1	5	106	112	166
Hepatitis NANB	11	0	7	0	2	2	21	24	30
Influenza	0	0	0	0	0	0	684	763	2018
Kawasaki Syndrome	3	0	3	0	0	0	18	13	12
Legionellosis	0	0	0	0	0	0	7	7	5
Lyme Disease	23	0	9	3	5	6	42	32	13
Measles	3	0	1	0	1	1	24	68	54
Meningitis, Aseptic	28	3	7	2	8	8	115	87	71
Meningitis, Bacterial*	10	3	0	2	1	4	65	79	100
Meningococcal Infections	7	1	2	3	1	0	23	33	39
Mumps	5	0	3	0	0	2	38	77	62
Pertussis	0	0	0	0	0	0	10	13	18
Rabies in Animals	28	14	2	2	3	7	141	104	149
Reye Syndrome	0	0	0	0	0	0	1	1	1
Rocky Mountain Spotted Fever	4	0	0	3	0	1	5	2	6
Rubella	0	0	0	0	0	0	0	1	3
Salmonellosis	143	15	69	21	24	14	499	512	535
Shigellosis	43	0	9	31	3	0	189	74	119
Syphilis ~	65	0	22	12	14	17	515	429	260
Tuberculosis	34	2	1	2	12	17	158	159	180

Localities Reporting Animal Rabies: Albemarle 2 raccoons; Augusta 3 raccoons; Charlotte 1 raccoon; Clarke 2 raccoons; Culpeper 1 skunk; Essex 1 raccoon; Fauquier 1 fox; Gloucester 1 groundhog; Goochland 1 raccoon; Isle of Wight 1 raccoon; Loudoun 1 bat, 1 raccoon; Montgomery 2 raccoons; Nelson 1 raccoon; Newport News 1 raccoon; Rockingham 1 raccoon; Southampton 1 raccoon; Sussex 1 raccoon; Warren 3 raccoons; York 1 raccoon.

Occupational Illnesses: Asbestosis 18; Carpal Tunnel Syndrome 42; Coal Worker's Pneumoconiosis 32; Hearing Loss 6; Repetitive Motion Disorder 9.

~Total now includes military cases to make the data consistent with reports of the other diseases.

*Other than meningococcal

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