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Serum and Nasal Secretion Immune Response in Meningococcal Disease

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Nasal antibodies to meningococcal organisms were demonstrable by the indirect fluorescent-antibody test in three patients. Serogroup cross-reactions were usual.

Although a higher meningococcal carrier rate is seen in military personnel than in civilians, the relationship of carriage rates to disease outbreaks is uncertain (10). Within weeks of acquiring the organism in the nasopharynx, an adult carrier develops serum antibody (5), which protects against group-specific illness (4). Recently it has been shown that A and C meningococcal polysaccharide vaccines also induce protective levels of group-specific serum antibodies (1, 6, 7, 9). Still unknown, however, is the role, if any, of host nasal secretory antibody. This note reports our observations of the immunologic response of five Marines with varied meningococcal illness seen at Camp Lejeune, N.C., from November 1970 through March 1971.

Serum antibodies were measured by the method of Edwards and Driscoll (3). For nasal antibody studies, 60-ml nasal washes (0.15 M NaCl) were obtained from five patients. Each wash was thoroughly mixed, dialyzed at 0 C with three changes against distilled and deionized water (36–48 hr), dehydrated against a 40% carbowax solution (5–6 hr) to a final volume of 10 to 20 ml, lyophilized, and then suspended to 3 ml with sterile distilled water containing penicillin and streptomycin.

The nasal secretions were tested against the B, C, and Y serogroups of *Neisseria meningitidis* with the indirect fluorescent-antibody (FA) test with fluorescein-conjugated antihuman gamma A goat serum and antihuman gamma G goat serum (Hyland Laboratories). The serum samples were tested in a like manner with fluorescein-conjugated antihuman gamma G and gamma M goat serum (Hyland Laboratories). The method for the identification of *N. meningitidis* has been described (2).

Table 1 illustrates the group-specific passive hemagglutination serologic response to varied forms of meningococcal illness. One also notes the detection of antibody in the synovial fluid (PME, case 5) but not in the spinal fluid (MGM, case 6) by this method.

TABLE 1. *Serologic response to meningococcal infection with the passive hemagglutination test*

Case	Clinical illness	Meningococcal serogroup cultured	Serologic[a] response to PHA			
			Serogroup C		Serogroup Y	
			Acute	Conv.	Acute	Conv.
WPS, case 1	Meningitis	Y	<1:2	<1:2	<1:2	1:64
DAP, case 2	Meningitis	C	<1:2	1:128	<1:2	<1:2
RWG, case 4	Bacteremia	C	<1:2	1:256	<1:2	<1:2
PME, case 5	Arthritis	C	1:32	1:512	<1:2	<1:2
	(Knee fluid on day 4)			1:1,024		<1:2
MGN, case 6	Meningitis	C	1:16	1:256	<1:2	<1:2
	(Spinal fluid on day 16)			<1:2		<1:2

[a] Acute serum was obtained on admission. Convalescent (Conv.) serum was obtained 14 to 17 days after admission. PHA, passive hemagglutination test.

Use of the FA technique also demonstrates good serologic response after infection (Table 2). However, serogroup cross-reactivity is present in all immunoglobulin classes, although the anti-immunoglobulin M (anti-IgM) antibody by indirect FA test was higher against the homologous serogroup than against heterologous serogroups. The synovial fluid of PME (case 5), who had arthritis, showed antibody of all three main classes of gamma globulin. In patient MGM (case 6), who had meningitis, antibody of classes immunoglobulin G (IgG) and immunoglobulin A (IgA) was detectable in the spinal fluid at low titers 16 days after he was admitted. No immunoglobulin M (IgM) was found in his spinal fluid.

Nasal secretory antibody was studied by the

TABLE 2. *Serologic[a] response to meningococcal infection with the indirect FA test*

Case	Globulin tested	Clinical illness	Meningococcal serogroup cultured	Serologic response					
				Serogroup C		Serogroup Y		Serogroup B	
				Acute	Conv.	Acute	Conv.	Acute	Conv.
WPS, case 1	γM	Meningitis	Y	<1:4	1:64	<1:4	1:256	1:4	1:256
	γG			<1:4	1:256	1:4	1:1,024	<1:4	1:256
DAP, case 2	γM	Meningitis	C	<1:4	1:256	1:16	1:64	1:4	1:16
	γG			<1:4	1:64	<1:4	<1:4	1:4	1:256
RWG, case 4	γM	Bacteremia	C	<1:4	1:256	<1:4	1:16	1:4	1:16
	γG			<1:4	1:64	<1:4	1:64	1:16	1:256
PME, case 5	γM	Arthritis	C	1:64	1:1,024	<1:4	1:64	1:4	1:64
	γG			1:64	1:1,024	1:4	1:4,096	1:16	1:1,024
Knee fluid (day 4)	γA				1:16		1:4		<1:4
	γM				1:16		1:16		1:16
	γG				1:256		1:64		1:64
MGN, case 6	γM	Meningitis	C	1:4	1:256	1:4	1:4	1:4	1:64
	γG			1:16	1:1,024	1:16	1:4,096	1:16	1:256
Spinal fluid (day 16)	γA				1:4		<1:4		
	γG				1:4		1:4		
	γM				<1:4		<1:4		

[a] Acute serum was obtained on admission. Convalescent (Conv.) serum was collected 14 to 17 days after admission.

TABLE 3. *Fluorescent-antibody titers of the γA and γG classes in the nasal secretions of patients with meningococcal disease*

Patient/ Serogroup cultured	Serogroup	γG[a]		γA	
		(3 mg/100 ml, day 2)	(35 mg/100 ml, day 9)	(3 mg/100 ml, day 2)	(12 mg/100 ml, day 9)
DAP/C, case 2	C		1:2		1:16
	Y		1:8		1:8
	B		1:2		1:4
		(35 mg/100 ml, day 26)	(40 mg/100 ml, day 41)	(21 mg/100 ml, day 26)	(120 mg/100 ml, day 41)
RWG/C, case 4	C		1:4	1:2	1:4
	Y				1:2
	B				1:2
		(5 mg/100 ml, day 10)	(12 mg/100 ml, day 18)		
WPS/Y, case 1	C				
	Y				
	B		1:4		

[a] γA and γG are from Radial Immunodiffusion (Hyland Laboratories).

FA technique at various times after admission in five patients (Table 3). Low titers of both IgA and IgG could be detected after infection in two men. A third man had local antibody detectable in the IgG class only. In two additional cases, no local antibody was seen.

That no synovial fluid barrier to immunoglobulins exists has been shown before (8) and is confirmed with reference to specific meningococcal antibodies in patient PME (case 5). Low levels of antibody were detected in the spinal fluid of a man with meningitis using the FA test only. The PHA method primarily tests IgM, which was not demonstrable in the spinal fluid by the FA test. The blood-spinal fluid barrier, even with infection, may prohibit the very large (molecular weight 1,000,000) IgM, yet allows smaller molecules of IgG (molecular weight 150,000) and IgA (molecular weight (180,000) to cross.

More studies employing the FA technique for nasal secretory antibody are warranted. Prospective studies of those who become carriers and future monovalent vaccine trials in which nasal secretions are obtained may better evaluate the possible protective role of secretory antibody.

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