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IMMUNOLOGIC ASPECTS OF DENTAL CARIES. MENINGOCOCCAL POLYSACCHAR--ETC(U)
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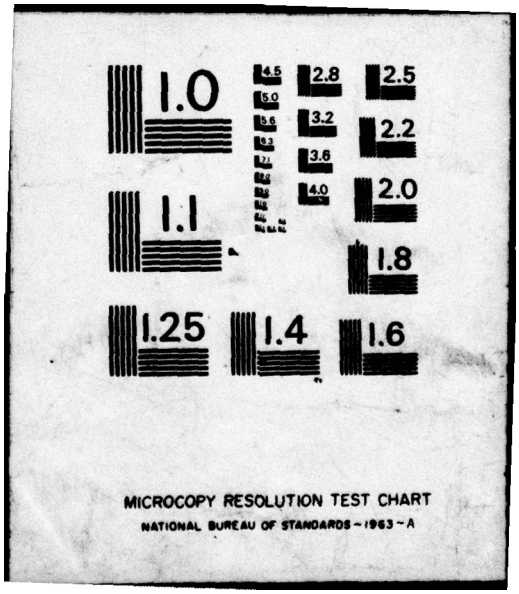
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Meningococcal polysaccharides

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The bacterium, Neisseria meningitidis can be classified into serogroups on the basis of capsular polysaccharides. However, not all serogroups (especially group B strains) have easily demonstrable capsules. Nevertheless, chemical extraction procedures have demonstrated the presence of polysaccharides (4; Table 1).

Capsular polysaccharides of serogroups A, B and C have been tested for safety and immunogenicity in man. Except for a rare local reaction from highly purified polysaccharides no adverse effects have been noted in millions of adults and children who have been vaccinated. An exception to this statement has been those lots of vaccine used in trials in children in Finland in which newer extraction methods were used. This might be a result of the fact that as standards for endotoxin (rabbit fever method) have been relaxed to allow more rapid and less costly extractions, an increased number of local reactions have occurred.

Current regulations of the FDA recommend storage of group C lyophilized vaccine in final containers for up to 18 months at 5 C. Group A vaccine (lyophilized) must be stored at -20 C for no longer than 18 months to prevent breakdown of high molecular weight polysaccharides to lower MW polymers which are much reduced in immunogenicity. Vaccine should be used within 8 hours of rehydration. It should be made clear that these standards are subject to change and, indeed, existing data indicate that the group C vaccine can be stored well over two years.

In animals, meningococcal polysaccharides are essentially lacking in immunogenicity. In humans, humoral immune responses vary. This is due to a variety of factors such as increased antibody levels with increasing age, the molecular size of antigen and the assay technique used (Table 2). Also, there are a number of other factors that are not understood. For example, it is unknown why group B polysaccharides failed to induce an antibody response (8) nor is there an explanation for the apparent induction of tolerance by the group C antigen (2).

Field trials of vaccine efficacy have been carried out in U.S. Army recruits with group C vaccine. An 89.5% reduction in group C disease occurred (3) (Table 3). From a preliminary description of a field trial of group C vaccine in children in Brazil, it would appear that there was no protection at all in the age group immunized at less than two years of age, and only a moderate protective effect in children ages two-three years. Group A vaccines have been tested successfully in Egyptian school children, ages six to 15 years (6), and also in Finnish Army troops (5). The duration of protection is not known for either A or C vaccines. The U.S. Army studies encompassed only an eight to ten week period of recruit training, while in Egypt and Finland the follow-up period was about six months.

Table 1. Chemical characterization of capsular polysaccharides of Neisseria meningitidis [a]

Serogroup	Chemistry
A	N-acetyl, O-acetyl, D-mannosamine phosphate
B	N-acetyl neuraminic acid
C	N-acetyl, O-acetyl neuraminic acid
X	2-acetamido-2-deoxy-D-glucose 4-phosphate
Y	Glucose
Bo [b]	Glucose 50%; neuraminic acid 50%
Z	Not characterized
29E	3-deoxy-D-manno-octulosonic acid (53%) 2-acetamido-2-deoxy-galactosamine (47%)
135	Not characterized

[a] Adapted from Griffiss and Artenstein, J. Mt. Sinai Hosp., 1976, in press.

[b] Y and Bo may designate the same serogroup. There is strong immunologic cross reaction between them and they are usually used interchangeably. The presence of neuraminic acid in their capsules is a matter of dispute.

A recent unpublished report of a group A vaccine trial in Finnish children, ages three months to six years, suggested complete protection from disease in this group compared to young and older unvaccinated individuals in which group A meningitis cases continued to occur. The great majority of vaccinees received a booster dose three months after the primary immunization.

Local antibodies have been measured in nasal secretions following parenteral inoculation of group C vaccine, but their characterization as IgA has not been definitively shown (1). In group C vacinees, protection against nasopharyngeal acquisition (carrier state) of the homologous serogroup of N. meningitidis has been clearly shown in a number of studies (Table 4). Intranasal administration of group C vaccine has resulted in increased humoral antibody levels, but local antibody could not be measured. However, this may be the result of the insensitive assay (hemagglutination) used to measure the local antibody (7).

Table 2. Assays for meningococcal antibodies in humans [a]

Assays	Antigen specificity	Immunoglobulin detected
Passive Hemagglutination	Polysaccharide Protein Lipopolysaccharide	IgM (predominant)
Latex agglutination	Polysaccharide	IgM (probable)
Complement-fixation	Broad crossing among meningococcal serogroups	IgM, IgG (probable)
Precipitin (double diffusion in gel)	Polysaccharide	All classes
Immunofluorescence	Whole organism	IgM, IgG, IgA
Bactericidal	Whole organism with serogroup and also subtype specificities	IgM, IgG, IgA [b]
Opsonization	Polysaccharide	IgG, IgM
Antigen binding (radioactive)	Polysaccharide Other antigens	All classes IgG, IgM, IgA

[a] Adapted from Griffiss and Artenstein, J., Mt. Sinai Hosp., 1976, in press.

[b] IgA binds to organism but does not lyse it, causing diminished effectiveness of IgM and IgG.

Table 3. Field trials of meningococcal polysaccharide vaccines

Vaccine category	No. cases	Total immunized	Remarks
1. Group C	2	28,390	U.S. military recruits
controls	77	114,964	
2. Group A	0	62,295	Egyptian school children
controls	12	62,054	

Table 4. Reduction in group C meningococcal carrier rates by group C polysaccharide vaccine [a]

Company	Carrier rate (%) vaccinated/controls	% reduction
B-6-3	24/42	43
E-5-3	4.6/38	88
E-2-3	31/69	55
B-4-2	15/31	52
C-4-2	12/13	8
A-4-3	12/42	71
C-4-3	21/38	45

[a] Data from Gotschlich et al. and Artenstein et al.

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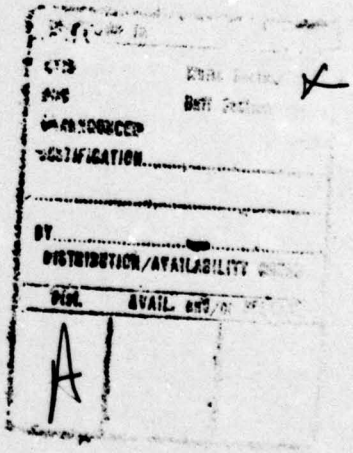

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CAPSULAR POLYSACCHARIDES OF SEROGROUPS A, B AND C HAVE BEEN TESTED FOR SAFETY AND IMMUNOGENICITY IN MAN. EXCEPT FOR A RARE LOCAL REACTION FROM HIGHLY PURIFIED POLYSACCHARIDES NO ADVERSE EFFECTS HAVE BEEN NOTED IN MILLIONS OF ADULTS AND CHILDREN WHO HAVE BEEN VACCINATED. AN EXCEPTION TO THIS STATEMENT HAS BEEN THOSE LOTS OF VACCINE USED IN TRIALS IN CHILDREN IN FINLAND IN WHICH NEWER EXTRACTION METHODS WERE USED. THIS MIGHT BE A RESULT OF THE FACT THAT AS STANDARDS FOR ENDOTOXIN (RABBIT FEVER METHOD) HAVE BEEN RELAXED TO ALLOW MORE RAPID AND LESS COSTLY EXTRACTION S. AN INCREASED NUMBER OF LOCAL REACTIONS HAVE OCCURRED

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