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Type-specific Carbohydrate Antigens of Pathogenic Bacteria. Part 2

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ABSTRACT

*This review summarises the recently elucidated structures of the carbohydrate antigens of gram-negative (*Haemophilus influenzae, Neisseria meningitidis, Pseudomonas aeruginosa *and* Vibrio cholera*) and gram-positive bacteria (*Streptococcus pneumoniae *and Group B* Streptococcus*). The use of carbohydrate antigens as vaccines is discussed.*

INTRODUCTION

The continued prevalence of serious bacterial infections, despite the development of antimicrobial agents, has led to a renewed interest in the structure and immunogenicity of bacterial polysaccharides. The number of structurally determined bacterial polysaccharides has increased dramatically in recent years. This review (in two parts) summarises the recently elucidated structures of type-specific polysaccharides as such information is central to the development of an understanding of the relationship between structure, conformation and the immunological properties of these carbohydrates. The first part of the review (which appeared in the previous issue of Carbohydrate Polymers) dealt with the gram-negative Enterobacteriaceae. This second part covers other pathogenic gram-negative bacteria and pathogenic gram-positive bacteria.

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GRAM-NEGATIVE BACTERIA

Haemophilus influenzae

H. Influenzae have been classified serologically into six groups (a to f). Most serious disease is caused by type b. It is a leading cause of bacterial meningitis in infants and also causes conjunctivitis (particularly in children), otitis media, epiglotitis (inflammation of the pharynx and larynx), pericarditis and pneumonia (Lee, 1987). An *H. influenzae* type b polysaccharide vaccine has been developed and licensed in the USA. However, it is ineffective in young infants (less than 18 months old) and confers only short-lived immunity in older infants (Smith *et al.*, 1973). These are the age groups at greatest risk. *H. influenzae* b-protein conjugate vaccines and the use of cross-reacting organisms (e.g. *Escherichia coli* K100 strain in which the K-antigen differs from type b polysaccharide by a single linkage position) are being investigated as possible routes to the production of an effective vaccine for infants (Lee, 1987).

K-Antigens (Table 1)

The six K-antigens are high-molecular-weight, negatively charged polymers, containing either phosphodiesters or 2-acetamido-2-deoxy-D-mannuronic acid as their acidic component. With the exception of strain e, all the capsular polysaccharides are linear and composed of disaccharide repeating units.

Neisseria meningitidis

N. meningitidis causes meningococcal meningitis and meningococcaemia. It occurs both in endemic and epidemic forms. Fifty percent of cases occur in children aged between 2 months and 4 years. Serogrouping is based on the antigenic capsular polysaccharides (A, B, C, 29E, H, I, K, L, W135, X, Y, Z). Almost all strains isolated from blood or cerebrospinal fluid can be serogrouped but non-encapsulated (non-groupable) strains are often isolated from the nasopharynx of healthy carriers. Serotype differences can be seen in the O-antigens and specific serotype proteins.

A, C and A, C, Y, W135 polysaccharide vaccines have been licenced but have generally only been used amongst civilians for the control of outbreaks (Frasch, 1987). However, the group C polysaccharide is ineffective in children below 18–24 months of age and group A polysaccharide is ineffective in children under 6 months.

TABLE 1
K-Antigens of *Haemophilus influenzae*

K-antigen	*Repeating unit*[a]	*Reference*
a	-4)-β-D-Glc*p*(1→4)-D-RibOH(5-Ⓟ-	Branefors-Helander *et al.* (1977)
b	-3)-β-D-Rib*f*-(1→1)-D-RibOH(5-Ⓟ-	Crisel *et al.* (1975); Branefors-Helander *et al.* (1976)
c	-4)-β-D-Glc*p*NAc-(1-3)-α-D-Gal*p*-(5-Ⓟ- 3 | OAc	Branefors-Helander *et al.* (1979); Egan *et al.* (1980*a*)
d	→4)-β-D-Glc*p*NAc-(1→3)-β-D-Man*p*NAcA-(1→	Branefors-Helander *et al.* (1981*a*); Tsui *et al.* (1981*a*)
e	→3)-β-D-Glc*p*NAc-(1→4)-β-D-Man*p*NAcA-(1→ 3 ↑ 2 β-D-Fru*f*	Branefors-Helander *et al.* (1981*b*); Tsui *et al.* (1981*b*)
f	→3)-β-D-Gal*p*NAc-(1→4)-α-D-Gal*p*NAc-(1-Ⓟ- 3 | OAc	Branefors-Helander *et al.* (1980); Egan *et al.* (1980*b*)

[a]GalNAc = *N*-acetylgalactosamine; GlcNAc = *N*-acetylglucosamine; MaNAcA = 2-acetamido-2-dexoy-mannuronic acid; RibOH = ribitol.

Group B polysaccharide (a homopolymer of $\alpha(2\rightarrow 8)$-*N*-acetyl neuraminic acid, identical to *E. coli* K1) is poorly immunogenic, probably due to its similarity to human glycosaminoglycans. Antibodies directed to an altered B polysaccharide might also react to human glycosaminoglycans; therefore, serotype proteins, found in the outer membrane of meningococcal strains, may provide the best prospect for vaccine control of group B meningococcal disease (Frasch, 1987).

O-Antigens

Eight lipopolysaccharide serotypes have been identified but it is not known whether these determinants are located in the core region or on O-side chains (Lee, 1987).

K-Antigens (Table 2)

The structures of all the presently identified K-antigens have been determined. The polysaccharides are linear and acidic; the acidity derives from either phosphodiester groups or glyculosylonic acid residues.

Pseudomonas aeruginosa

P. aeruginosa is an opportunistic pathogen which causes frequent infections in immunologically compromised patients and those suffering from severe burns or cystic fibrosis, or after surgery. It commonly causes outbreaks of nosocomial infections and is the most frequent cause of death in neutropenic patients (Lee, 1987). *P. aeruginosa* clinical isolates produce a number of extracellular and somatic antigens which have been considered important virulence factors (e.g. flagella, pili, O-antigens, mucoid exopolysaccharides). Two distinct cell-surface polysaccharides are expressed by different strains of *P. aeruginosa*. These are the serotype determinant (O-antigen) and a mucoid exopolysaccharide. The O-antigen-containing lipopolysaccharide has been detoxified by deacylation under alkaline conditions to remove the lipid A moiety. This modified lipopolysaccharide could elicit a specific antibody response when joined to a protein carrier (*P. aeruginosa* pili or tetanus toxoid) (Seid & Sadoff, 1981; Sadoff *et al.*, 1982; Tsay & Collins, 1984). A high-molecular-weight O-antigen has also been isolated from the lipopolysaccharide by mild acid hydrolysis (Pier, 1988). This polysaccharide will produce an immune response in humans (Pier, 1982; Pier & Bennet, 1986) although it is less immunogenic than lipopolysaccharide (Pier *et al.*, 1981, 1984).

P. aeruginosa isolates from cystic fibrosis patients, which express mucoid exopolysaccharide antigen, appear to lack serotype determinants

and are non-typeable. These strains are lipopolysaccharide rough strains (Pier, 1988).

O-Antigens (Table 3)

P. aeruginosa strains are serotyped on the basis of their O-antigens. A number of classification systems exist. The most common serotypes identified in clinical isolates in Britain are O6, O11, O16 and O10 (Habs typing) (Pitt, 1981).

Serotypes O2ab and O2ac have as their O-antigen the same trisaccharide repeating unit, differing only in the presence or absence of an *O*-acetyl group (Knirel *et al.*, 1982*a*). The O-antigens from serotypes O3ab, O3ad, O3ac and O3ade also make up a series. O3ab and O3ad contain 2,3-diacetamido-dideoxy-D-mannuronic acid and an imidazoline derivative of this sugar. O3ab has a α-D-linked 2-acetamido-2-deoxy-D-fucopyranosyl residue whereas in O3ad it is β-D-linked. O3ac and O3dae contain a 2,3-dideoxy-α-L-gulopyranosyluronic acid residue.

P. aeruginosa strains of serotype O4 (O4ab, O4ac, O4ad), O6, immunotype 1 (Fischer classification) and group G (Homma classification) produce very similar O-specific polysaccharides. They are all tetrasaccharide repeating units containing 2-acetamido-2-deoxy-D-galacturonic acid, 2-deoxy-formamido-galacturonic acid, 2-acetamido-2,6-dideoxy-D-glucose and L-rhamnose. Variation exists between these serogroups only in the extent and position of amidation and *O*-acetylation (Vinogradov *et al.*, 1987).

Series 5 (O5abc, O5abd, O5ad, Lányi classification) and immunotype 6 (Fischer classification) have a trisaccharide repeating unit which consists of D-xylose, 2-acetamido-2,6-dideoxy-D-galactose, and a sialic-acid-like di-*N*-acyl derivative of 5,7-diamino-3,5,7,9-tetradeoxy-L-glycero-L-manno-nonulosonic (pseudominic) acid. Structural variation is provided through the *N*-acyl substituents (acetyl or (*R*)-3-hydroxybutyryl) and in the presence or absence of an *O*-acetyl group at position 4 of the *N*-acetyl fucosamine (Knirel *et al.*, 1987).

Vibrio cholerae (Table 4)

V. cholerae serogroup O1 causes Asiatic cholera. This is an acute diarrhoeal disease which can cause pandemics. It is a gram-negative, non-invasive, pathogen which resides in the gut lumen and attaches to the gut mucosa during infection. The production of an enterotoxin is mainly responsible for the disease symptoms.

V. cholerae are typed on the basis of their O-antigens. Serogroup O1 exists as two strains, Inaba and Ogawa, which share a common O-

TABLE 2
K-Antigens of *Neisseria meningitidis*

K-antigen	*Repeating unit*[a]	*Reference*
A	-6)-α-D-Man*p*NAc-(1-Ⓟ- 3 | OAc	Bundle *et al.* (1974)
B	→8)-α-D-Neu*p*5Ac-(2→ (and OAc varient)	Bhattacharjee *et al.* (1975)
C	→9)-α-D-Neu*p*5Ac-(2→ 7/8 | OAc	Bhattacharjee *et al.* (1975)
29E	→3)-α-D-Gal*p*NAc-(1→7)-β-KDO*p*-(2→ 4/5 | OAc	Bhattacharjee *et al.* (1978)
H	-4)-α-D-Gal*p*-(1→2)-Gro-(3-Ⓟ-	Van der Kaaden *et al.* (1984); Michon *et al.* (1984)

I	→4)-α-L-Gul*p*NAcA-(1→3)-β-D-Man*p*NAcA(1→ 4 | OAc	Michon *et al.* (1985)
K	→3)-β-D-Man*p*NAcA-(1→4)-β-D-Man*p*NAcA-(1→ 4 | OAc	Van der Kaaden *et al.* (1985)
L	-3)-β-D-Glc*p*NAc-(1→3)-β-D-Glc*p*NAc-(1→3)-α-D-Glc*p*NAc-(1-Ⓟ-	Jennings *et al.* (1983*a*)
W135	→6)-α-D-Gal*p*-(1→4)-α-Neu*p*5Ac-(2→	Bhattacharjee *et al.* (1976)
X	-4)-α-D-Glc*p*NAc-(1-Ⓟ-	Bundle *et al.* (1974)
Y	→6)-α-D-Glc*p*-(1→4)-α-Neu*p*5Ac-(2→ (contains OAc groups)	Bhattacharjee *et al.* (1976)
Z	-3)-α-D-Gal*p*NAc-(1→1)-Gro-(3-Ⓟ-	Jennings *et al.* (1979)

[a]GalNAc = *N*-acetylgalactosamine; GlcNAc = *N*-acetylglucosamine; GlcNAcA = 2-acetamido-2-deoxy-guluronic acid; Gro = glycerol; KDO = 2-keto-3-deoxy-D-mannooctulonic acid; ManNAc = *N*-acetylmannosamine; ManNAcA = 2-acetamido-2-deoxy mannuronic acid; Neu5Ac = *N*-acetyl-neuraminic acid.

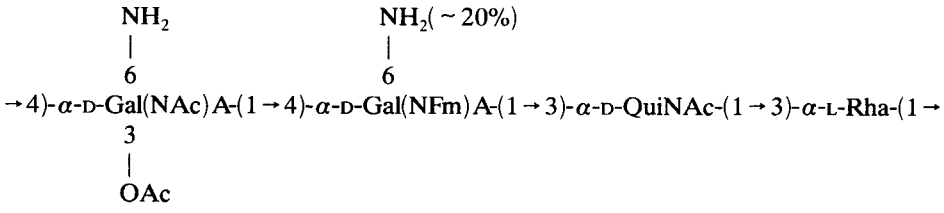
TABLE 3
O-Antigens of *Pseudomonas aeruginosa*

O-antigen	*Repeating unit*[a]	*Reference*
O2 (O2ab is acetylated, O2ac is not)	→4)-α-L-Gal*p*NAcA-(1→3)-α-D-Qui*p*NAc-(1→3)-α-L-Rha*p*-(1→ 2 | OAc	Knirel *et al.* (1982*a*)
O3ab	→4)-β-D-Man*p*ImA-(1→4)-β-D-Man*p*$(NAc)_2$A-(1→4)-α-D-Fuc*p*NAc(1→	Kenne and Lindberg (1983)
O3ad	→4)-β-D-Man*p*ImA-(1→4)-β-D-Man*p*$(NAc)_2$A-(1→4)-β-D-Fuc*p*NAc(1→	Knirel *et al.* (1982*b*)
O3ac	→4)-β-D-Man*p*ImA-(1→4)-α-L-Gul*p*$(NAc)_2$A-(1→4)-α-D-Fuc*p*NAc(1→	Kenne and Lindberg (1983)
O3ade	→4)-β-D-Man*p*ImA-(1→4)-α-L-Gul*p*$(NAc)_2$A-(1→4)-β-D-Fuc*p*NAc(1→	Knirel *et al.* (1983)
O4ab	→4)-α-D-Gal(NAc)A-(1→4)-α-D-Gal(NFm)A-(1→3)-α-D-QuiNAc-(1→2)-α-L-Rha-(1→ NH_2 (6) NH_2 (~10%) (6) 3 | OAc	Vinogradov *et al.* (1987)

O4ac

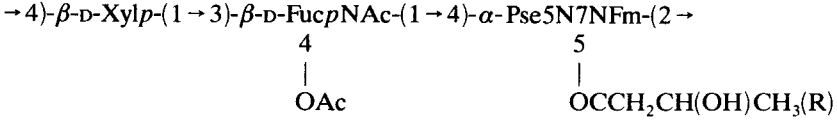
Vinogradov *et al.* (1987)

O4ad



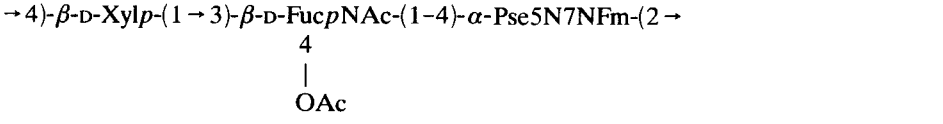
Vinogradov *et al.* (1987)

O5abc



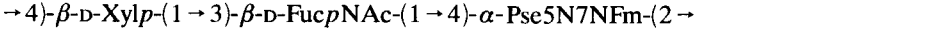
Knirel *et al.* (1987)

O5abd



Knirel *et al.* (1987)

O5ad (Fischer Immunotype 6)



Knirel *et al.* (1987)

TABLE 3 — *contd.*

O-antigen	*Repeating unit*[a]	*Reference*
O6 (Habs)	$\rightarrow$4)-α-D-Gal(NAc)A-(1$\rightarrow$4)-α-D-Gal(NFm)A-(1$\rightarrow$3)-α-D-QuiNAc-(1$\rightarrow$3)-α-L-Rha-(1$\rightarrow$ NH$_2$ at 6 of Gal(NAc)A; OAc at 3 of Gal(NFm)A	Vinogradov *et al.* (1987)
O7 (Fisher Immunotype 2)	$\rightarrow$3)-α-L-Fuc*p*NAc-(1$\rightarrow$3)-β-D-Fuc*p*NAc-(1$\rightarrow$2)-β-D-Glc*p*-(1$\rightarrow$	Horton *et al.* (1981)
O11 strain 170021	$\rightarrow$2)-α-L-Rha-(1$\rightarrow$3)-α-L-FucNAc-(1$\rightarrow$3)-α-L-FucNAc-(1$\rightarrow$3)-β-D-QuiNAc(1$\rightarrow$	Knirel *et al.* (1985)
strain 170040	$\rightarrow$2)-α-L-Rha-(1$\rightarrow$3)-α-L-FucNAc-(1$\rightarrow$3)-α-L-FucNAc-(1$\rightarrow$3)-β-D-FucNAc-(1$\rightarrow$	Knirel *et al.* (1985)
Immunotype 1 (Fischer)	$\rightarrow$4)-α-D-Gal(NAc)A-(1$\rightarrow$4)-α-D-Gal(NFm)A-(1$\rightarrow$3)-α-D-QuiNAc-(1$\rightarrow$2)-α-L-Rha-(1$\rightarrow$ NH$_2$ at 6 of Gal(NAc)A; NH$_2$ at 6 of Gal(NFm)A; OAc at 3 of Gal(NFm)A	Vinogradov *et al.* (1987)

Immunotype 4 (Fischer)	→4)-α-D-Gal*p*NAc(1→4)-β-D-Glc*p*$(NAc)_2$A-(1→3)-α-D-Fuc*p*NAcA-(1→3)-α-D-Qui*p*NAc(1→	Pier and Pollack (1989)
Immunotype 5 (Fischer)	→3)-α-L-Rha*p*-(1→3)-α-L-Rha*p*-(1→3)-α-D-Qui*p*NAc-(1→ 2 2 4 | | | OAc OAc OAc NH_2 NH_2(~50%) | | 6 6	Horton *et al.* (1981)
Group G (Homma)	→4)-α-D-Gal(NAc)A-(1→4)-α-D-Gal(NFm)A-(1→3)-α-D-QuiNAc-(1→3)-α-L-Rha-(1→	Vinogradov *et al.* (1987)

[a]FucNAc = 2-acetamido-2,6-dideoxy galactose; GalNAc = 2-acetamido-2-deoxy galactose; Gal(NAc)A = 2-acetamido-2-deoxy galacturonic acid; Gal(NFm)A = 2-formido-2-deoxy galacturonic acid; Glc$(NAc)_2$A = 2,3-diacetamido-2,3-dideoxy glucuronic acid; Gul$(NAc)_2$A = 2,3-diacetamido-2,3-dideoxy guluronic acid; Man$(NAc)_2$A = 2,3-diacetamido-2,3-dideoxy mannuronic acid; ManImA = 2,3-(1-acetyl-2-methyl-2-imidazolino-5,4)-2,3-dideoxy mannuronic acid; Pse5N7NFm = 5-amino-3,5,7,9-tetradeoxy-7-formamido-L-glycero-L-manno-nonulosonic acid (7-N-formylpseudoaminic acid); QuiNAc = 2-acetamido-2,6-dideoxy glucose.

TABLE 4
O-Antigens of *Vibrio cholera*

O-antigen	*Repeating unit*[a]	*Reference*
O1	→2)-α-Per*p*N-(1→ | C=O | CHOH-CH_2-CH_2OH	Kenne *et al.* (1982)
O2	→4)-β-D-Qui*p*NAc-(1→4)-Sug*p*-(2→4)-β-D-Gal*p*-(1→ α-L-Rha*p* 1 ↓ 3	Kenne *et al.* (1988)
O21	→3)-β-D-Glc*p*NAc(1→7)-Hep*p*-(1→ 4 ↑ 1 β-D-Gal*p*NAc	Ansari *et al.* (1986)

[a]GalNAc = *N*-acetylgalactosamine; GlcNAc = *N*-acetylglucosamine; Hep = D-glycero-D-manno-heptose; PerN = 4-amino-4,6-dideoxy-D-mannose (perosamine); Sug = 5-acetamido-7-acetamido-3,5,7,9-tetradeoxy-L-glycero-β-L-manno-nonulosonic acid; QuiNAc = 2-acetamido-2,6-dideoxy-glucose.

antigen. The Ogawa strain possesses an additional determinant (Sakazaki *et al.*, 1971; Redmond *et al.*, 1973). Genes for the synthesis of O1 antigen have been cloned and expressed in *E. coli* K-12 and such strains have proved an effective vaccine in an infant mouse model (Manning *et al.*, 1986; Manning, 1987). There are at least 72 non-O1 serogroups (Kenne *et al.*, 1988), and a few of these structures have been determined (Table 4).

GRAM-POSITIVE BACTERIA

The major cell wall component of gram-positive bacteria is peptidoglycan. The cell wall is boarded by an inner cytoplasmic membrane. Gram-positive bacteria do not possess lipopolysaccharides of the type present in gram-negative bacteria, but do produce other cell wall polysaccharides which are covalently linked to the peptidoglycan. These include both true polysaccharides and teichoic acids. Capsular polysaccharides can also be produced by gram-positive bacteria.

STREPTOCOCCACEAE

Streptococcus pneumoniae

S. pneumoniae is a major cause of pneumonia, meningitis, otitis media and bacteraemia. It generally occurs as an endemic infection but localised outbreaks can occur in communities living in overcrowded conditions. Pneumococcal infections are amongst the most frequent causes of admission to hospital in many developing countries (Greenwood, 1987).

Capsular polysaccharide types (83) have been differentiated on the basis of their serological properties. In the Danish system of nomenclature, serologically cross-reacting types are given a common group number, each member of a group being distinguished by a single letter. In the American system of nomenclature each serotype is given a unique number (Lund, 1970). Danish type 35A is divided into two serotypes (47 and 62) in the American system. The Danish system of nomenclature has been widely adopted and is used in this review article.

Capsular polysaccharide vaccines can be used to induce serum antibodies which confer resistance to pneumococcal infections. Two multivalent vaccines have been formulated to provide maximum protection against the types most prevalent in the USA and Europe. The 14- and

23-valent vaccines contain types 1, 2, 3, 4, 6A, 7F, 8, 9N, 12F, 14, 18C, 19F, 23F, 25F, and 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20A, 22F, 23F, 33F, respectively.

The comparative frequency of different serotypes changes with both age and geographical location. Many types commonly occurring in Asia (e.g. 15A, 23A and 24F) are not included in either formulation. Groups 6, 14, 18, 19 and 23 are responsible for approximately 60% of all childhood pneumococcal infections (Robbins *et al.*, 1983). This may be related to the inability of many children to develop antibodies to these serotypes before they reach 4–6 years of age. The same serogroups continue to cause a significant, though reduced, proportion of pneumococcal infections in other age groups.

Extensive cross-reactions are observed between antibodies raised to pneumococcal capsular polysaccharides. This is often related to the possession of common structural features. Group 9 capsular antigens (9N, 9A, 9L and 9V) (Table 5) have linear pentasaccharide repeating units with several conserved residues. Variation exists in certain component glycoses and the presence of *O*-acetyl groups. Antigens 9A and 9V differ only through differences in *O*-acetylation.

The K-antigens of serotypes 11F, 11B and 11C have a common tetrasaccharide repeating unit but differ in the phosphodiester substituent and position of *O*-acetyl substitution. In type 11A polysaccharide the phosphodiester-substituted *N*-acetylglucosamine residues are replaced by glucose residues.

Four group 15 antigens exist (15F, A, B and C). They all have a pentasaccharide repeating unit which contains the same component sugars. However, the sugars are assembled to give either a branched (15B and 15C) or a linear (15F and 15A) repeating unit.

The structures of 17F and 17A antigens contain a common pentasaccharide sequence but are, in other respects, dissimilar polysaccharides. Type 17A polysaccharide has an octosaccharide repeating unit whereas type 17F has a heptasaccharide repeating unit with a teichoic-acid-type structure.

Three group 18 capsular polysaccharides (18F, 18A, 18C) have a pentasaccharide repeating unit containing a glycerol phosphate moiety. Variation exists through the substitution of a glucose residue with *N*-acetyl glucosamine (18A) and the position of *O*-acetyl groups.

Antigens 19F and 19A differ only in the position of a single glycosidic linkage.

Cross-reactivity also occurs between *S. pneumoniae* and other bacterial species and genera. For example, *S. pneumoniae* type 14 polysaccharide cross-reacts with Group B *Streptococcus* type III polysaccha-

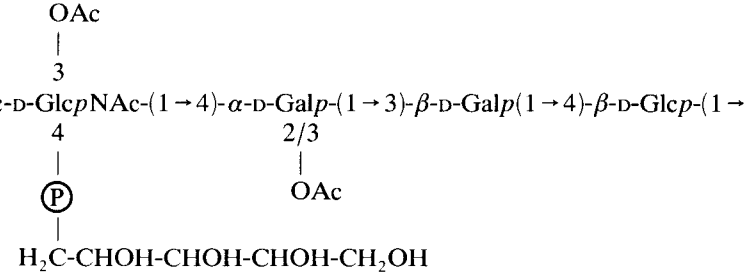
TABLE 5
K-Antigens of *Streptococcus pneumoniae*

K-antigen[a]	*Repeating unit*[b]	*Reference*
2	→4)-β-D-Glc*p*-(1→3)-α-L-Rha*p*-(1→3)-α-L-Rha*p*-(1→3)-β-L-Rha*p*-(1→ 2 ↑ 1 α-D-Glc*p*A-(1–6)-α-D-Glc*p*	Jansson *et al.* (1988*a*)
4	→3)-β-D-Man*p*NAc-(1→3)-α-L-Fuc*p*NAc-(1→3)-α-D-Gal*p*NAc-(1→4)-α-D-Gal*p*-(1→ 2 3 H_3C CO_2H	Jones and Currie (1988)
5	→4)-β-D-Glc*p*(1→4)-α-L-Fuc*p*NAc-(1→3)-β-D-Sug*p*(1→ 3 ↑ 1 α-L-Pne*p*NAc-(1→2)-β-D-Glc*p*A	Jansson *et al.* (1985*b*)
7F(51)	OAc | 2 →6)-α-D-Gal*p*-(1→3)-β-L-Rha*p*-(1→4)-β-D-Glc*p*-(1→3)-β-D-Gal*p*NAc-(1→ 2 4 ↑ ↑ 1 1 β-D-Gal*p* α-D-Glc*p*NAc-(1→2)-α-L-Rha*p*	Moreau *et al.* (1988*a*)
9N (9)	→4)-α-D-Glc*p*A-(1→3)-α-D-Glc*p*-(1→3)-β-D-Man*p*NAc-(1→4)-β-D-Glc*p*-(1→4)-α-D-Glc*p*NAc-(1→	Jones *et al.* (1985)

TABLE 5 — *contd.*

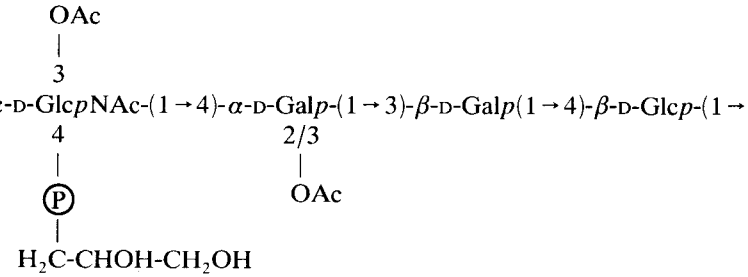
K-antigen[a]	*Repeating unit*[b]	*Reference*
9A (33)	→4)-α-D-Glc*p*A-(1→3)-α-D-Gal*p*-(1→3)-β-D-Man*p*NAc-(1→4)-β-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→	Richards and Perry (1988*a*)
9L (49)	→4)-α-D-Glc*p*A-(1→3)-α-D-Gal*p*-(1→3)-β-D-Man*p*NAc-(1→4)-β-D-Glc*p*-(1→4)-α-D-Glc*p*NAc-(1→	Richards *et al.* (1984*a*)
9V (68)	→4)-α-D-Glc*p*A-(1→3)-α-D-Gal*p*-(1→3)-β-D-Man*p*NAc-(1→4)-β-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→ OAc (3) and OAc (4)	Perry *et al.* (1981)
11F (11)	→6)-α-D-Glc*p*NAc-(1→4)-α-D-Gal*p*-(1→3)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→ 4: Ⓟ-H_2C-CHOH-CHOH-CHOH-CH_2OH; 2: OAc; 3: OAc (50%); + 50% OAc (undetermined location)	Richards *et al.* (1985)
11A (43)	→6)-α-D-Glc*p*-(1→4)-α-D-Gal*p*-(1→3)-β-D-Gal*p*-(1–4)-β-D-Glc*p*-(1→ 4: Ⓟ-H_2C-CHOH-CH_2OH; 2/3: OAc	Richards *et al.* (1988)

11B (76)



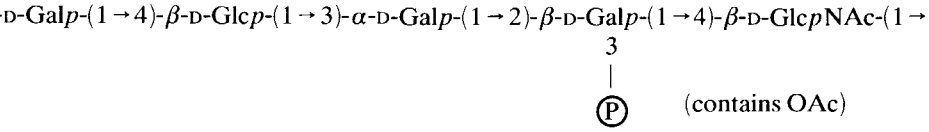
Richards *et al.* (1988)

11C (53)



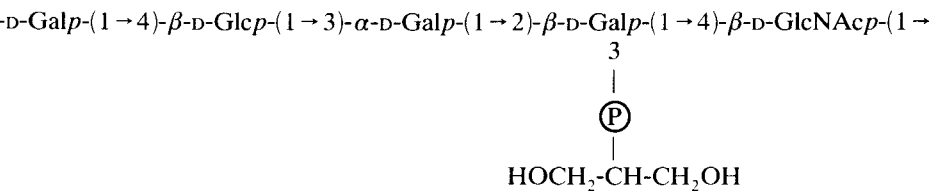
Richards *et al.* (1988)

15F (15)



Perry *et al.* (1982)

15A (30)

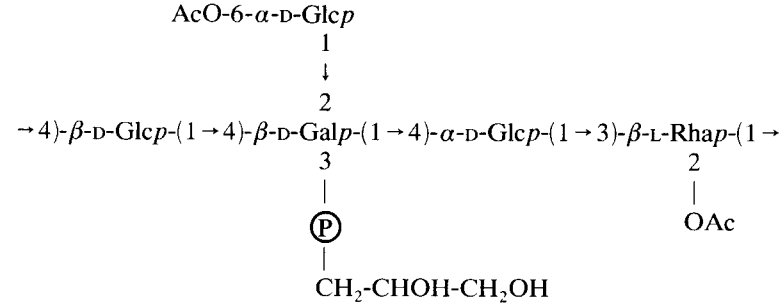


Caroff and Perry (1984)

TABLE 5 — *contd.*

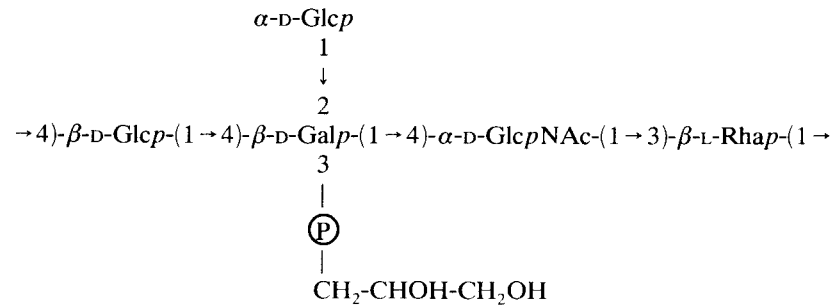
K-antigen[a]	*Repeating unit*[b]	*Reference*
15C (77)	→3)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-β-D-Glc*p*NAc-(1→ 4 ↑ 1 α-D-Gal*p*-(1→2)-β-D-Gal*p* 3 | Ⓟ | R R = H (80%) or $CH_2CH_2N^+Me_3$ (20%)	Jansson *et al.* (1987)
15B (54)	(As 15C with OAc group(s))	Jansson *et al.* (1987)
17F	→4)-β-D-Glc*p*-(1→3)-α-D-Gal*p*-(1→3)-β-L-Rha*p*-(1→4)-α-L-Rha*p*-(1→2)-D-AraOH-(1-Ⓟ-4)-α-L-Rha*p*-(1→ 4 ↑ 1 D-Gal*p* OAc | 2	Kenne and Lindberg (1983)
17A (78)	→3)-β-D-Glc*p*-(1→3)-α-D-Gal*p*-(1→3)-β-L-Rha*p*-(1→4)-α-L-Rha*p*-(1→4)-β-D-Glc*p*A-(1→3)-β-D-Gal*f*-(1→ 4 2 ↑ ↑ 1 1 β-D-Gal*p* α-D-Glc*p*	Jansson *et al.* (1983)

18F (18)



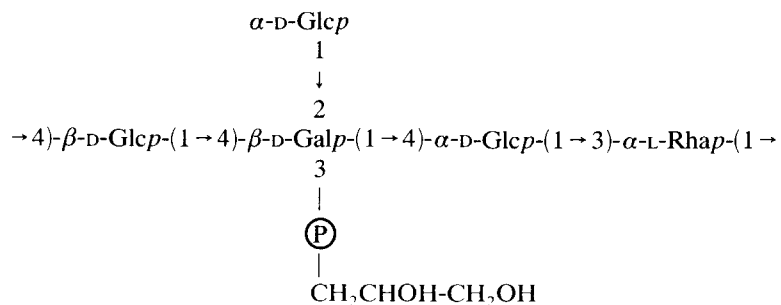
Jansson *et al.* (1988*b*)

18A (44)



Jansson *et al.* (1988*c*)

18C (56)



Lugowski and Jennings (1984)

TABLE 5 — *contd.*

K-antigen[a]	*Repeating unit*[b]	*Reference*
19F (19)	-4)-β-D-Man*p*NAc-(1→4)-α-D-Glc*p*-(1→2)-α-L-Rha*p*-(1-Ⓟ-	Jennings *et al.* (1980); Ohno *et al.* (1980)
19A (57)	-4)-β-D-Man*p*NAc-(1→4)-α-D-Glc*p*-(1–3)-α-L-Rha*p*-(1-Ⓟ-	Katzenellenbogen and Jennings (1983)
20	-6)-Gal*f*-(1→3)-Gal*f*-(1→3)-Glc*p*-(1→6)-Glc*p*-(1→4)-Glc*p*NAc-(1-Ⓟ-	Roy and Roy (1984)
23F (23)	α-L-Rha*p* 1 ↓ 2 →4)-β-D-Glc*p*-(1→4)-β-D-Gal*p*-(1→4)-β-L-Rha*p*-(1→ 3 | Ⓟ | $HOCH_2$-CH-CH_2OH	Perry *et al.* (1978); Richards and Perry (1988*b*)

29	→4)-β-D-Gal*p*NAc-(1→6)-β-D-Gal*f*-(1→3)-β-D-Gal*p*-(1→6)-β-D-Gal*f*-(1→1)-D-RibOH-(5-Ⓟ-	Kenne and Lindberg (1988)
31	→2)-β-L-Rha*p*-(1→3)-β-D-Gal*f*-(1→3)-β-L-Rha*p*-(1→4)-β-D-Glc*p*A-(1→3)-β-D-Gal*f*-(1→	Batavyal and Roy (1983)
33F (70)	→3)-β-D-Gal*p*-(1→3)-α-D-Gal*p*-(1→3)-β-D-Gal*f*-(1→3)-β-D-Glc*p*-(1→5)-β-D-Gal*f*-(1→ 2 2 ↑ | 1 OAc (40%) D-Gal*p*	Richards *et al.* (1984*b*)
37	→3)-β-D-Glc*p*-(1→ 2 ↑ 1 β-D-Glc*p*	Adeyeye *et al.* (1988)
45 (72)	→3-α-D-Gal*p*-(1→3)-α-L-Fuc*p*NAc-(1→3)-β-D-Gal*p*NAc-(1→2)-α-L-Rha*p*-(1→ 6 4 ↑ ↑ 1 1 α-D-Gal*p* β-D-Glc*p*NAc 6 | Ⓟ | CH_2-CHOH-CH_2OH	Moreau *et al.* (1988*b*)

[a] American nomenclature in parentheses where different from Danish.

[b] AraOH = arabinitol; FucNAc = *N*-acetylfucosamine; GalNAc = *N*-acetylgalactosamine; GlcNAc = *N*-acetylglucosamine; ManNAc = *N*-acetylmannosamine; PneNAc = 2-acetamido-2,6-dideoxy-talose (pneumosamine); Sug = 2-acetamido-2,6-dideoxy-xylo-hexos-4-ulose.

ride (Crumrine *et al.*, 1979) and *Neisseria gonorrhoea* R-type lipopolysaccharide (Diena *et al.*, 1979). Other cross-reacting organisms include *E. coli* (Heidelberger *et al.*, 1968), *Klebsiella* (Lee & Koizumi, 1981; Lee & Wang, 1985) and non-groupable streptococci (Robbins *et al.*, 1983).

Group B *Streptococcus* (Table 6)

Group B *Streptococcus* is a major cause of meningitis (Anthony & Okada, 1977; Baker, 1977). It can also cause septicaemia and infections of the bone, ears, eyes, joints, kidneys and lungs. Group B infections of adults are usually less severe than those in infants.

Group B streptococci produce a carbohydrate group antigen and one of several type-specific capsular polysaccharides. All of the structurally determined type-specific antigens (types 1a, 1b, 11, 111) contain a common trisaccharide repeating unit (β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→4)-β-D-Glc*p* (Table 6). Types 1a and 1b differ only in the position of a single residue linkage. The type-specific polysaccharides of all recognised strains, including three recently identified (IV, V and NT6 — new type candidate), contain *N*-acetylneuraminic (sialic) acid (Ryc *et al.*, 1988).

CARBOHYDRATE ANTIGENS AS VACCINES

Despite the development of antibiotics, pathogenic bacteria continue to present the threat of endemic and epidemic disease. The widespread use of antibiotics has been followed by the emergence of multiply resistant bacterial strains and numerous instances of treatment failure. In addition, certain classes of antibiotics exhibit toxic effects (e.g. nephrotoxicity and ototoxicity) when used in high dosage or for extended periods. The use of broad-spectrum antibiotics may also result in super-infection following the treatment (Cryz, 1987). The use of bacterial polysaccharides as immunoprophylatic or immunotherapeutic agents is therefore being widely researched and should provide a valuable complement to the use of antibiotics. Purified polysaccharide immunogens are non-toxic and, in contrast to whole-cell vaccines, can be chemically and physically defined leading to a greater level of control over their efficacy (Jennings, 1983). Three bacterial polysaccharide vaccines are already available (meningococcal, pneumococcal and *H. influenzae* type b) and many others are undergoing clinical studies (Lee, 1987).

TABLE 6
K-Antigens of Group B *Streptococcus*

K-antigen	*Repeating unit*[a]	*Reference*
1a	→4)-β-D-Glc*p*-(1→4)-β-D-Gal*p*-(1→ 3 ↑ 1 α-D-Neu*p*5Ac-(2→3)β-D-Gal*p*(1→4)β-D-Glc*p*NAc	Jennings *et al.* (1983*b*)
1b	→4)-β-D-Glc*p*-(1→4)-β-D-Gal*p*-(1→ 3 ↑ 1 α-D-Neu*p*5Ac-(2→3)-β-D-Gal*p*(1→3)-β-D-Glc*p*NAc	Jennings *et al.* (1983*b*)
11	→4)-β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→3)-β-D-Gal*p*-(1→2)-β-D-Gal*p*-(1→ 6 3 ↑ ↑ 1 2 β-D-Gal*p* α-D-Neu*p*5Ac	Jennings *et al.* (1983*c*)
111	→4)-β-D-Glc*p*-(1→6)-β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→ 4 ↑ 1 α-D-Neu*p*5Ac-(2→3)-β-D-Gal*p*	Wessels *et al.* (1987)

[a]GlcNAc = *N*-acetylglucosamine; Neu5Ac = *N*-acetyl-neuramininic acid.

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