only rational approach to prevention at a population level. Secondary cases are common among household and "kissing" contacts of cases, and secondary prophylaxis with antibiotic therapy is widely recommended for these contacts (see below).

Polysaccharide Vaccines Purified meningococcal capsular polysaccharide has been used for immunization since the 1960s. Meningococcal polysaccharide vaccines are currently formulated as either bivalent (serogroups A and C) or quadrivalent (serogroups A, C, Y, and W), with 50 μg of each polysaccharide per dose. Local reactions (erythema, induration, and tenderness) may occur in up to 40% of vaccinees, but serious adverse events (including febrile convulsions in young children) are very rarely reported. In adults, the vaccines are immunogenic, but immunity appears to be relatively short-lived (with antibody levels above baseline for only 2–10 years), and booster doses do not induce a further rise in antibody concentration. Indeed, a state of immunologic hyporesponsiveness has been widely reported to follow booster doses of plain polysaccharide vaccines. The repeating units of these vaccines cross-link B cell receptors to drive specific memory B cells to become plasma cells and produce antibody. Because meningococcal polysaccharides are T cell–independent antigens, no memory B cells are produced after immunization, and the memory B-cell pool is depleted such that fewer polysaccharide-specific cells are available to respond to a subsequent dose of vaccine (Fig. 180-6). The clinical relevance of hyporesponsiveness is unknown. Plain polysaccharide vaccines generally are not immunogenic in early childhood, possibly because marginal-zone B cells are involved in polysaccharide responses and maturation of the splenic marginal zone is not complete until 18 months to 2 years of age. The efficacy of the meningococcal serogroup C component is >90% in young adults; no efficacy data are available for the serogroup Y and W polysaccharides in this age group.

Group A meningococcal polysaccharides are exceptional in that they have been found to be effective in preventing disease at all ages. Two doses administered 2–3 months apart to children 3–18 months of age or a single dose administered to older children or adults has a protective efficacy rate of >95%. The vaccine has been widely used in the control of meningococcal disease in the African meningitis belt. The duration of protection appears to be only 3–5 years.

There is no meningococcal serogroup B plain polysaccharide vaccine because α-2,8-*N*-acetylneuraminic acid is expressed on the surface of neural cells in the fetus such that the B polysaccharide is perceived as "self" and therefore is not immunogenic in humans.

Conjugate Vaccines The poor immunogenicity of plain polysaccharide vaccines in infancy has been overcome by chemical conjugation of the polysaccharides to a carrier protein (CRM_{197}, tetanus toxoid, or diphtheria toxoid). Conjugates that contain monovalent serogroup C polysaccharide and quadrivalent vaccines with A, C, Y, and W polysaccharides have been developed, as have vaccines including various other antigen combinations (e.g., tetanus conjugates with serogroup C

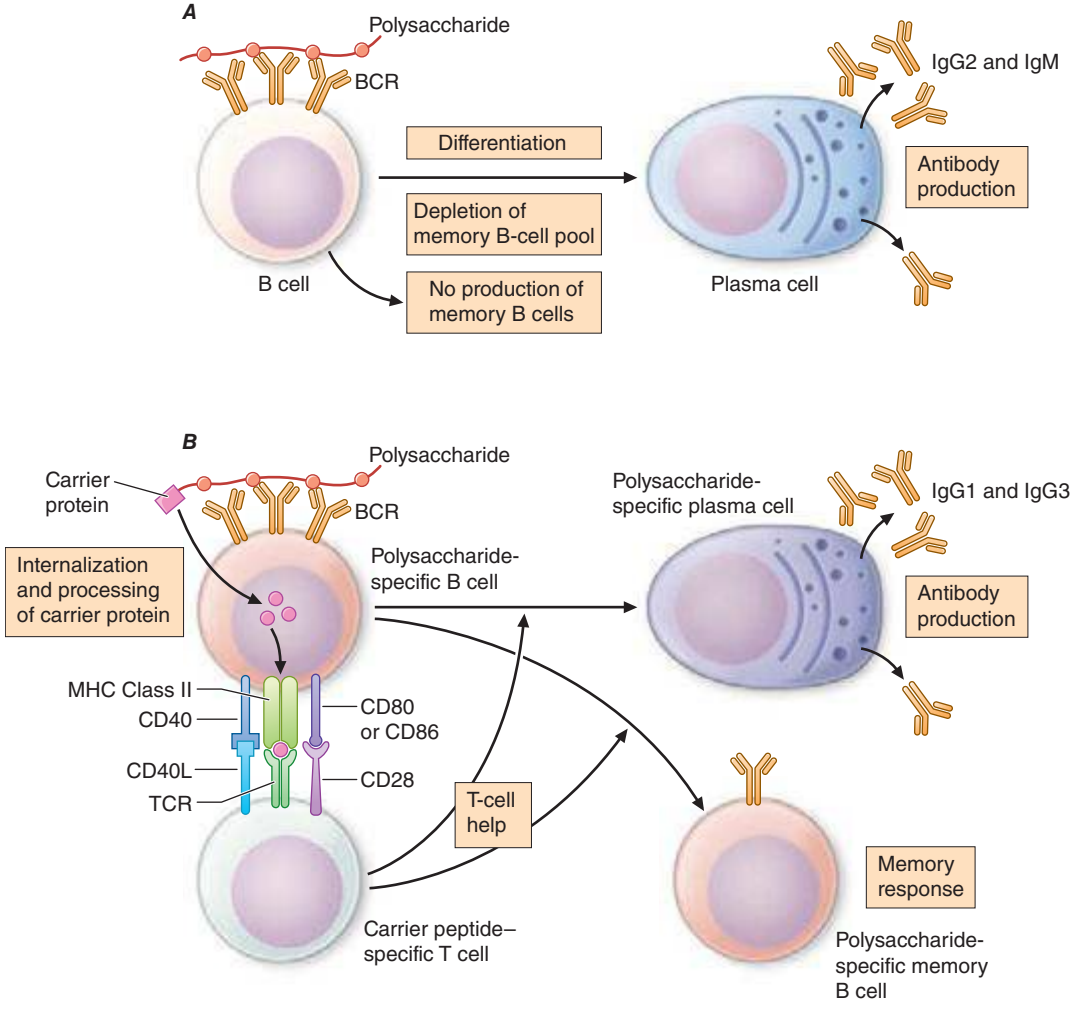

FIGURE 180-6 ***A.*** Polysaccharides from the encapsulated bacteria that cause disease in early childhood stimulate B cells by cross-linking the BCR and driving the production of immunoglobulins. There is no production of memory B cells, and the B-cell pool may be depleted by this process such that subsequent immune responses are decreased. ***B.*** The carrier protein from protein-polysaccharide conjugate vaccines is processed by the polysaccharide-specific B cell, and peptides are presented to carrier peptide–specific T cells, with the consequent production of both plasma cells and memory B cells. BCR, B-cell receptor; MHC, major histocompatibility complex; TCR, T-cell receptor. *(Reprinted from AJ Pollard et al: Nat Rev Immunol 9:213, 2009.)*