

Role of MenACWY and MenB Vaccine in Preventing Meningococcal Disease in *Homo sapiens*

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Abstract

Meningococcal disease is the severe, critical and life-threatening infectious disease which is mainly caused by a bacteria *Neisseria meningitidis*. Globally, there are total 12 to 13 serogroups of *N. meningitidis* but 6 serogroups are considered as major cause of meningococcal disease. These serogroups are (serogroup A, B, C, W-135, X and Y). *N. meningitidis* can be transmitted from person to person by coughing or by exchange of nasal as well as respiratory secretions or droplets. This disease can increase death rates and can cause complications among people. Sometimes infectious diseases are incurable. Moreover, prevention is better than spending money on expensive cure. Now many cost-effective vaccines are available throughout the whole world against different diseases. These vaccines play important role in preventing and controlling deadly diseases. To prevent meningococcal disease some vaccines are being used. As, MenB-4C vaccine is a multicomponent vaccine that is effective in controlling serogroup B. While, Meningococcal tetravalent vaccines are effective in controlling meningococcal disease serogroups A, C, W-135 and Y.

Keywords: Meningococcal disease, MenACWY, MenB, Meningococcal vaccines, *Neisseria meningitidis*

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Introduction

Meningococcal Disease

Meningococcal disease is considered as main cause of two deadly diseases 1) meningitis (severe infection of protective layers of brain and spinal cord) 2) septicemia (severe infectious disease of blood). Although there are many antibiotics that are being used for meningococcal disease, still severe complication and mortality rates are increasing (Greenwood et al., 1987). Pathogens that are major reason of meningococcal disease (MD) are *N. meningitidis*, *S. pneumoniae* and *H. influenzae* type b (Pollard et al., 2009).

Meningitis

A severe infection of brain and spinal cord (CNS) can be caused by bacteria and viruses known as meningitis. Death rates and complications among people are increasing day by day due to meningitis or meningococcal disease. Major threats to human health status are due to bacterial meningitis, there are almost 5 lakh cases that are reported each year globally and 50 thousand deaths occur due to damage or infection of nervous system (Girard et al., 2005).

Septicemia

Meningococcal septicemia is considered as lethal and deadly infectious. More deaths occur due to septicemia (Van Deuren et al., 2000). This disease can cause failure of multiple organs and even can also leads to death. Almost 40% infected people can die due to Meningococcal septicemia while 10% can die due to other conditions of IMD (Goldacre et al., 2003).

Generally, IMD (invasive meningococcal disease) is considered as cause of either meningitis (infection or inflammation of meninges) or septicemia (it is basically infectious disease of bloodstream), it may cause these both infectious diseases. Some severe and long-term physical and nervous system infection have been seen in survivors of IMD (Pelton et al., 2016). Most common infectious conditions caused by *Neisseria meningitidis* are shown in Fig. 1.

Health Problems in IMD Patients

Surgical removal of limbs has been observed in more than eight percent cases, while almost nineteen percent IMD survivors have been suffered from hearing issues (like inability to hear), these cases of IMD were seen in those survivors who suffered from this deadly disease in early childhood (Olbrich et al., 2018). From previous 20 decades, MD is considered as the main cause of major health issues, disease outbreak is badly affecting the health of infants and adults. Death's rate and MD cases among people's increased continuously, severe brain or nervous system damage also have been observed due to this infectious disease (Van Deuren et al., 2000).

Some severe health problems have been observed in 20% IMD patients. These health problems can be nervous system disorders and removal of limbs (arms, legs and hands).

Most Common Infectious conditions caused by *Neisseria meningitidis*

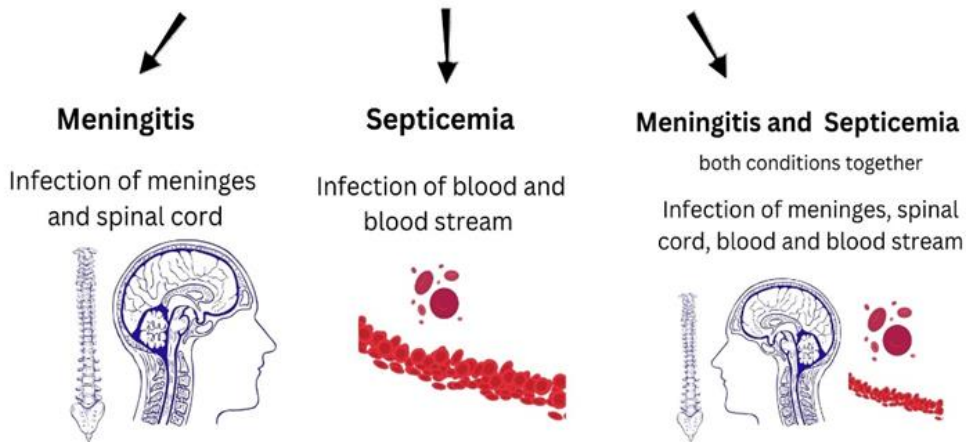


Fig. 1: Common infectious conditions caused by *Neisseria meningitidis*

In some cases, severe mental and chronic physical disorders or disabilities also have been observed due to this deadly disease (Olbrich et al., 2018). In some cases, it may cause pericarditis (inflammation or infection of pericardium), severe infection of joints and pneumonia (Campbell et al., 2019). Health problems observed in 20% IMD patients are shown in Figure 2.

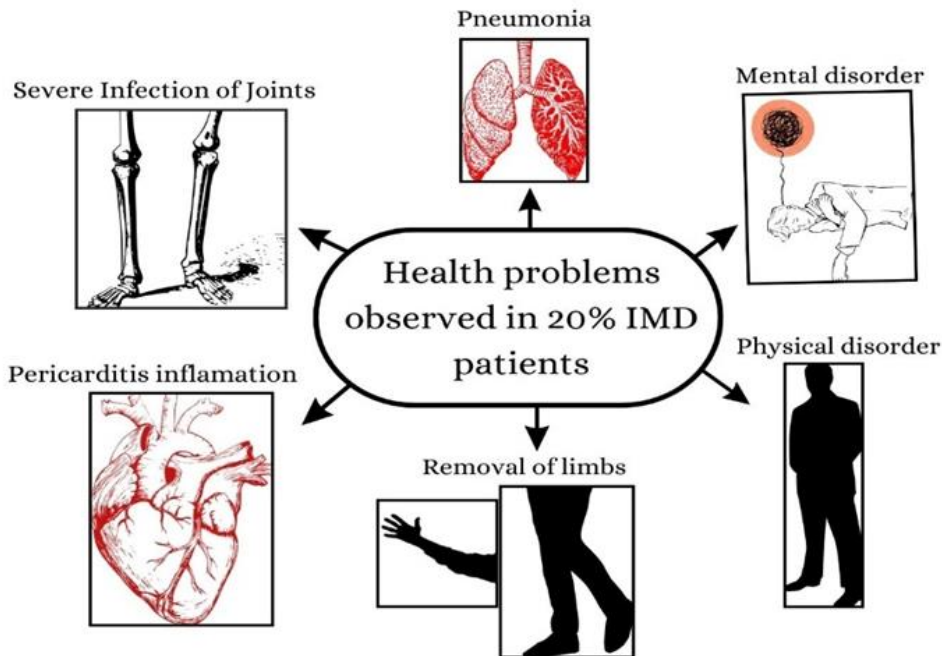


Fig. 2: Health problems observed in 20% IMD patients

Meningococcal Disease Outbreaks

In Brazil four times MD outbreaks occur 1) From the year 1920 to 1925, this disease outbreak was caused by serogroup A (sA) (2) From the year 1945 to 1951, this disease outbreak was caused by serogroup A (sA) (3) From the year 1971 to 1977, this, disease outbreak was caused by 2 serogroups A and C (4) From the year 1988 to 2002, this disease outbreak was caused by serogroup B and serogroup C. Among these epidemics, outbreak that occur in 1971 considered as deadly dangerous outbreak of MD (Moraes, 2005).

Currently, MD outbreak that occur in America was due to serogroup W (sW) but still serogroup (B and C) is considered as main reason of disease outbreak in South America (Sáfadi et al., 2015). MD outbreak in different areas or regions mainly occur due to overcrowding, like in Mediterranean areas disease outbreak were occur due to overcrowding at Hajj, currently this disease outbreak occurs due to serogroup W135 (Jafri et al., 2013).

Mortality Rate due to Meningococcal Disease

IMD is badly affecting people of different age groups, highest number of IMD cases are observed in newborns, children's and elder peoples. Mortality rate among IMD patients is higher due to occurrence of two chronic or specific conditions together (Beebeejaun et al., 2020). According to Trotter et al. (2007) death rate among meningococcal patients in European countries is 8%. Even after proper treatment, 4-20% deaths occur due to this infectious disease (Wang et al., 2019).

Symptoms of Meningococcal Disease

Some early signs or symptoms of MD are pyrexia, headache or cephalalgia and neck stiffness but this disease may cause severe health issues like inability to hear. MD can cause complete loss or damage of cranial nerves, it can also be reason of severe cognitive disorders (Rosenstein et al., 2001). Initial signs of Meningococcal septicemia this disease are fever and pain in muscles, due to these common symptoms it's not easy to diagnose this infectious disease (Goldacre et al., 2003).

Risk Factors of Meningococcal Disease

Disease transmission can occur from one people to another by transfer of bacteria *N. meningitidis*. This bacterium can easily be transmitted by close connections or through coughing and sneezing (Nelson, 1996). Chances of bacterial transmission from person to person increases in reserved or closed areas like boarding schools and army camps. Bacterial transmission rate in these closed areas can be 100% (Olcéan et al., 1981).

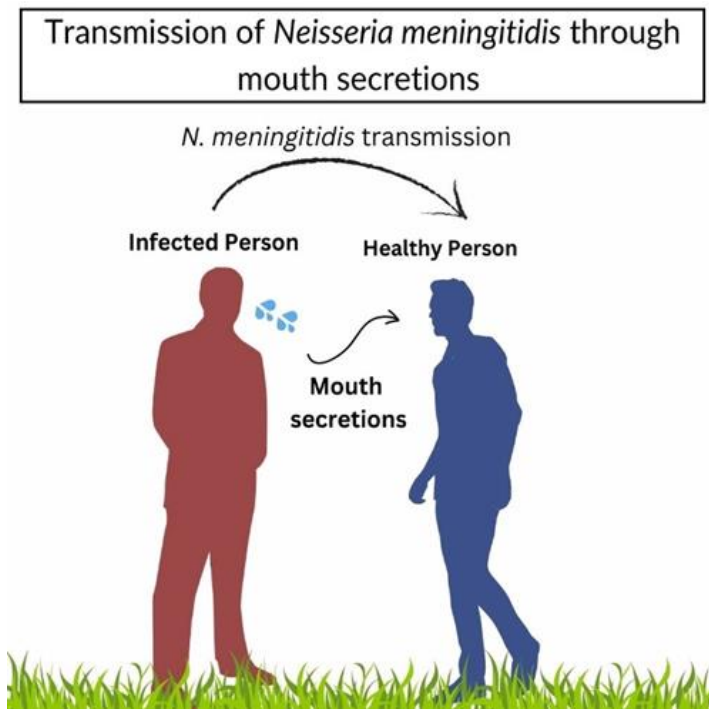


Fig. 3: Transmission of *Neisseria meningitidis* through mouth secretions

Overcrowding in cricket matches, concerts, deaths and other events is considered as main reason of IMD outbreak (Gautret, 2016). Transmission of *Neisseria meningitidis* through mouth secretion are shown in Figure 3. Outbreak of this deadly infectious disease occur in a specific area (Achtman, 1995). During disease outbreak, among population of 1 lakh people, this infectious disease can cause severe infection in almost thousand peoples of that area (Riedo et al., 1995).

Neisseria meningitidis

Neisseria meningitidis is disease causing bacteria which is covered by polysaccharide capsule. This polysaccharide capsule work as protection shields for bacteria, this capsule increases the survival rate of this harmful bacteria throughout the period of deadly disease. Moreover, polysaccharide capsule protects bacteria from antibodies and also increases the chance of disease outbreak by bacterial transmission (Stephens et al., 2007). According to Dwilow (2015) *N. meningitidis* can cause two deadly infectious diseases 1) meningococcal meningoenphalitis 2) meningococemia. Reason of IMD is a gram-negative bacterium named as *N. meningitidis* (Stephens, 2009).

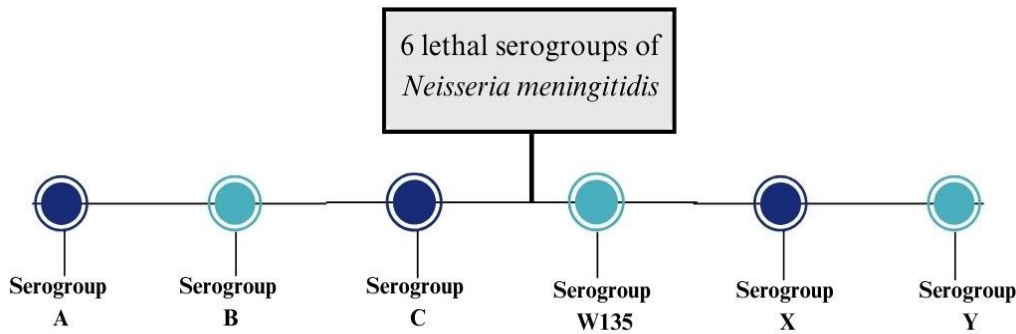
Serogroups of *Neisseria meningitidis*

As polysaccharide capsules of bacteria are considered as main reason of many bacterial diseases. In accordance to polysaccharide capsule of *Neisseria meningitidis*, there are total twelve serogroups (Bijlsma et al., 2014). But six meningococcal serogroups are thought to be main reason of meningococcal disease, these serogroups are (serogroup A, B, C, W, X and Y) (Nadel, 2018).

Rouphael (2012) described that total 13 different serogroups of *Neisseria meningitidis* are present, out of these 6 serogroups are considered as main cause of deadly infectious diseases and these serogroups are A, B, C, W135, X and Y. 6 lethal serogroups of *Neisseria meningitidis* are shown in Figure 4.

More cases of this disease have been observed in young ones or children's and carriage rate of *N. meningitidis* is more in youngsters, almost 55 percent carriage rate of infectious bacteria have been reported in young student of United Kingdom (Ala'Aldeen et al., 2011). Caugant et al. (2007) described that carriage rate of *N. meningitidis* is rare in children's. Generally, children are badly affected by this deadly disease (Olbrich et al., 2018). More cases of invasive meningococcal disease or IMD were observed in children's younger than five years old (Peterson et al., 2019).

Fig. 4: Lethal serogroups of *Neisseria meningitidis*



While, meningococcal serogroup B is considered as main reason of mortality among children with age group less than 1, even more cases of MenB have been observed in that age group (Ladhani et al., 2012). Pace (2012) described that it's quite difficult and time taking to recognize the nature of IMD but this deadly infectious disease can cause death within twenty-four hours. More number of meningitis cases occurred in winter or in spring season (Rosenstein et al., 1999).

Importance of Vaccines

Many infectious and contagious diseases can be prevented and controlled by vaccines (Orenstein, 2017). Modern vaccines are very effective in controlling the disease outbreak, vaccine produce antibodies against foreign substances or infectious bacteria. Now vaccines can also reduce the rate of incidence caused by serogroup B (sB) and protects from MD (meningococcal disease) (Giuliani et al., 2006).

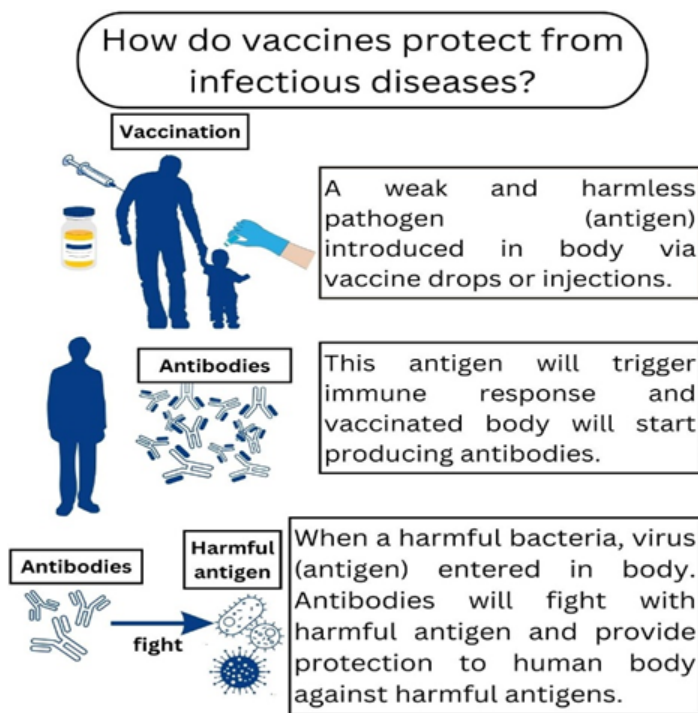


Fig. 5: How do vaccines protect from infectious diseases?

Due to their affordable price and effective results, polysaccharide vaccines are also used by many underdeveloped and poor countries (Ali et al., 2014). These highly effective vaccines are capable of increasing immunity, reducing the rate of occurrence of disease among people as well as these are harmless (Blanchard-Rohner, 2011). The action of vaccines providing protection from infectious diseases is shown in Figure 5.

Impact of Vaccine in Prevention of Meningococcal Disease

MD can be controlled by vaccination (Cartwright et al., 2001). Vaccination is important in preventing bacterial meningitis. Polysaccharide-protein conjugate vaccine has great importance in reducing the rate of occurrence of life-threatening bacterial disease (McIntyre et al., 2012). Vaccines are beneficial and highly effective in controlling meningococcal disease (Stefanelli, 2016). Vaccines for MD can create antibodies that are used in protection against harmful bacteria *N. meningitidis* (Jones et al., 2000).

Meningococcal vaccine (MV) project was started in Africa by association of two organizations (WHO and PATH), the main purpose of this project was to reduce number of IMD cases. In this project, a cost-effective vaccine for serogroup A was introduced (LaForce et al., 2009). MenAfriVac (vaccine) was approved and suggested by WHO in June 2010 due to its positive outcomes (Frasch et al., 2012).

Polysaccharide Vaccine

When different vaccines were introduced for different serogroups ultimately huge reduction in number of MD cases were observed (Pelton et al., 2016). Vaccines provide protection against many infectious diseases. From previous forty years, polysaccharide vaccines (PV) are being used against single or several meningococcal serogroups (Tan et al., 2010). Because of their cheap price, these vaccines are also available in many underdeveloped and poor countries (Ali et al., 2014).

Meningococcal Conjugate Vaccine

According to (Hellenbrand et al., 2013) (meningococcal conjugate vaccine) MCV was introduced and suggested by United Kingdom in the year 1999, this vaccine was used to provide protection against serogroup C (SC). Then in the year 2000, tetravalent conjugate vaccine (TCV) was approved against four serogroups (A, C, W and Y) and another conjugate vaccine was approved against serogroup A in 2010. Conjugate vaccine against serogroup A was actually introduced and approved to overcome the meningitis disease outbreak in Africa (Hellenbrand et al., 2013). In the year 1999, conjugate vaccine for meningococcal serogroup C was firstly approved in United Kingdom. This vaccine reduced mortality rate and also reduced number of incidents caused by meningitis or meningococcal disease (Balmer et al., 2002).

Polysaccharide-protein Conjugate Vaccine

There are many monovalent, quadrivalent and polyvalent vaccines that have been used for different meningococcal serogroups (A, C, W, and Y) since years, but polysaccharide-protein conjugate vaccine (P-PCV) is more beneficial as compared to polysaccharide vaccine. More demand of P-PCV is due to its benefits like it is capable of inducing satisfactory immune responses and it also provides protection against MD (World Health Organization, 2011).

Meningococcal serogroup B

According to (Cohn et al., 2010) almost 33% cases of meningococcal disease in United State are due to serogroup B. Harrison et al. (2009) described that in Europe many people suffered from serogroup B strain. Meningococcal disease outbreak in New Zealand (Baker et al., 2001) and currently disease outbreak in France (Rouaud et al., 2006) occurred due to these strains, these strains are extremely dangerous for public health status and can increase mortality rate. Number of people suffering from serogroup B meningococcal disease has been changing continuously in United State but now the percentage of all MD cases is 30% to 40% (Rouphael, 2012).

Meningococcal Vaccine for serogroup B

Vaccine to overcome meningococcal serogroup B was firstly accepted in Europe, MenB-4C (Bexsero, GSK) vaccine was specifically introduced for children's. Now this vaccine is available for infants in almost thirty-nine countries (Toneatto et al., 2017).

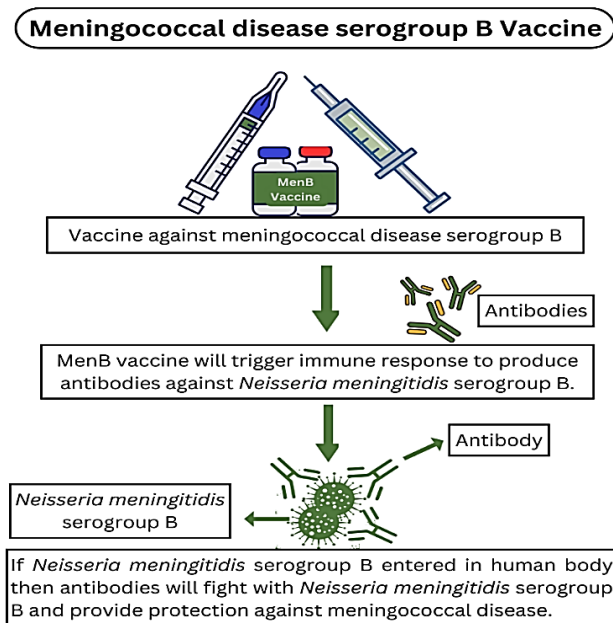


Fig. 6: Meningococcal disease serogroup B vaccine

Because of difficulty in recognition of target antigens, vaccine for serogroup B (sB) have been approved and suggested in the year 2013 (Kuhdari et al., 2016). Meningococcal disease serogroup B vaccine is shown in Figure 6.

OMV Vaccine for serogroup B

Since 1980s, in many countries including France, Chile and Brazil OMV (outer membrane vesicle) vaccines are being used against serogroup B (sB) and since 2004 to 2008 OMV vaccines are also available in New Zealand (Holst et al., 2013). In the Norway and Cuba meningococcal serogroup B cases have been decreased just after availability of effective MenB OMV vaccine (Holst et al., 2013).

MenB-4C and MenB-FHbp

Two other newly approved vaccines against Men (sB) are MenB-4C and MenB-FHbp. In United State, these vaccines can be used to reduce the risk of disease outbreak (Soeters et al., 2017). MenB-4C vaccine is considered as most beneficial vaccine for elders and children's. Reduction in 88% meningococcal (sB) cases have been observed in countries like Wales and England due to this vaccine (McGill et al., 2016).

Meningococcal serogroup A, C, W and Y

According to (Zhu et al., 1995) almost 95% meningococcal disease cases are caused by serogroup A (sA), while rare cases of this infectious disease are caused by serogroup B and C. In U.S. almost 33.33% cases are caused by serogroup C (sC), while other disease cases occur due to serogroup B (sB) and other serogroups (Racoosin et al., 1998).

Quadrivalent Vaccine for Meningococcal Disease

Quadrivalent or tetravalent vaccines are used to provide protection against 4 viruses, bacteria or microorganisms.

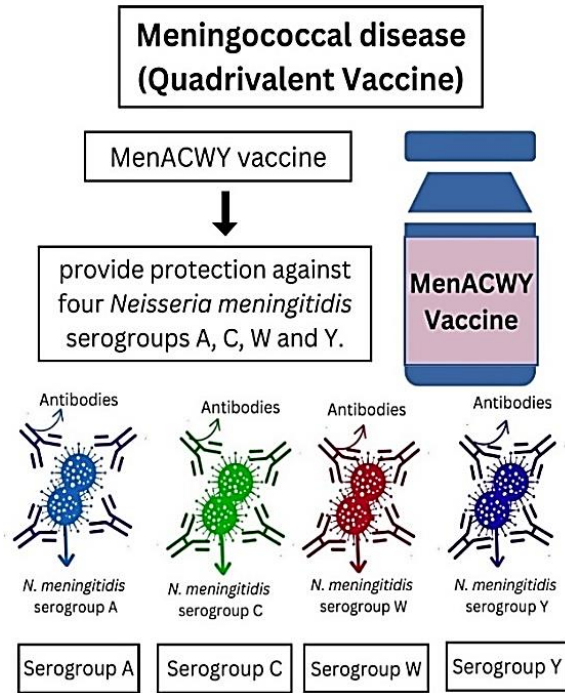


Fig. 7: Meningococcal disease Quadrivalent vaccine

In the year 2005, first tetravalent conjugate vaccine against meningococcal disease was approved and suggested by experts of (CDC, Center for disease control and prevention) in United State. This tetravalent vaccine is specifically used by teenagers to provide protection against 4 meningococcal serogroups A, C, W and Y (Bilukha, 2005). Meningococcal disease quadrivalent vaccine is shown in Figure 7.

Polysaccharide Vaccines for MenACWY

According to (Chang et al., 2012) from the year 1970 and 1980, polysaccharide vaccines (PV) were being used for prevention of four meningococcal serogroups A, C, W135 and Y but these vaccines were not effective and results of these vaccines were not good at all, specifically in children's. But recently many effective conjugate vaccines for single serogroup (serogroup A and serogroup C) and for 4 different serogroups (A, C, W and Y) have been approved (Chang et al., 2012).

Effective Tetravalent Conjugate Vaccine

Although, first tetravalent conjugate vaccine was highly effective but it was quite difficult to assess the results of this vaccine in United State. As initially receipts of tetravalent vaccine was not that much but still a sudden decrease in meningococcal cases was observed (Pichichero, 2005). Now-a-days many monovalent, bivalent as well as quadrivalent conjugate vaccines are approved to prevent meningococcal disease (Halperin et al., 2010).

Conclusion

Meningococcal disease is deadly infectious disease that may leads to death and severe complications. Even after expensive treatment, this disease may remain incurred. Spending money on such diseases can be useless. Now-a-days, there are many cheap and affordable vaccines that are being used for prevention of this disease. Many effective monovalent, bivalent and tetravalent vaccines conjugate vaccines are available that provide protection from MD. These vaccines can reduce mortality rate among peoples and provide protection from chronic diseases like bacterial meningitis and septicemia. Hence, it's better to protect ourselves from this disease by vaccination rather than wasting money on expensive cure.

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