UNIT NO. 1

VACCINATIONS IN THE ELDERLY

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ABSTRACT

The proportion of the elderly in the population has been steadily increasing globally. In Singapore, it is estimated that a quarter of the population will be older than 65 years in 2030. The elderly are more susceptible to infections and once acquired, the infections are often more severe. Effective vaccination has been the most efficient interventional strategy to reduce the morbidity and mortality of infections in the young and greater attention should be paid to the use of vaccinations in the elderly.

Keywords: Vaccination; Elderly; Immunosenescence;

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INTRODUCTION

With improvements in health care globally, the proportion of elderly will increase markedly. For persons aged 60 years and above, it is estimated that the numbers will double to 2.1 billion in 2050. For those aged >80 years, it is expected to increase from 125 million in 2015 to 434 million in 2050. In Singapore, a quarter of the population will be aged >65 years by 2030. The elderly population will be more susceptible to infections because of waning immunity, poorer response to infection, disabilities (physical and functional) and co-morbidities. The severity of infections will also be higher and many of these infections are associated with long term sequelae including physical de-conditioning, impairment of activities of daily living and loss of independence. The elderly will be exposed to health care institutions in the form of hospitals and nursing homes. Health care associated infections are often associated with multi-drug resistant bacteria and this needs to be considered when antimicrobials are prescribed. Age related changes in the immune system contribute to increased incidence and severity of infections in the elderly. Vaccination is the most effective means to prevent infection. There has been a greater appreciation that vaccinations should continue throughout life and the Ministry of Health has published a set of guidelines on adult immunisation in October 2017.

IMMUNOSENESCENCE

Old age represents a scenario of exhaustion of reserves in our bodies. The aging phenotype is thought to be the result of an imbalance of pro-inflammatory versus anti-inflammatory mechanisms. Immunosenescence is a new concept and came about because of extension of human life span that started since the 19th century. Put simply, it refers to age related changes in the innate and adaptive immune system that results in remodelling of the immune system.

With respect to this article, successful vaccination requires the phagocytosis of vaccine and antigen presentation to naïve T cell and B cells, so that memory T and B cells may be formed. In old age, each step of this process is diminished and weakened. Neutrophils and antigen-presenting cells have impaired phagocytic capabilities. Chronic persistent increased proinflammatory cytokines in old age dampened the host's ability to recognize vaccine targets as danger signals that are required to induce immunity. Consequently, alteration in the administration of some component of the vaccine may be needed to overcome this effect. The age dependent involution of functional thymic tissue means that naïve T cells capable of recognizing presented antigens and differentiating into memory T cells are largely depleted by old age. Moreover, defects in B cell isotype switching and somatic hypermutation in old age critically impair the B cell response to vaccination[1]. Immunosensecence is unfortunately unavoidable. For the purposes of this review, vaccination considerations in the immunocompromised elderly would not be covered as it is beyond the scope of this article.

VACCINES RECOMMENDED FOR THE ELDERLY

For the elderly, most of the current recommendations have focused on vaccination against influenza and pneumococcal infections. Some countries also recommend vaccination against herpes zoster. Despite a reduced response to vaccination in old age, the larger burden of disease and worse outcomes of vaccine preventable infections in old age strongly place vaccination as a worthy healthcare prevention strategy in the elderly.

It is important to highlight that the immunogenecity and efficacy of many vaccines is unknown in the elderly as many of the clinical trials that led to their licensure were performed in younger patients. For example, many of the clinical trials that led to the recent registration of Dengvaxia® were focused on children living in endemic countries.

Influenza Vaccination

Regarding influenza, the elderly bear the greatest burden of disease, manifesting as increased hospitalization, prolonged length of hospital stay, increased admission to ICU and increased mortality. Figures by CDC (Atlanta) regarding the 2015-16 season reported 321 hospitalizations per 100,000 with influenza in those aged 65 years and older. The corresponding rate in the next younger strata (50-64 years old) was 117 per

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100,000[2]. The estimated mortality in the same season in USA was estimated at 477 deaths per 100,000 for those aged above 65 years while the corresponding number for the next younger age strata was 35 per 100,000 cases. Tied inextricably to a greater burden of disease is also a greater justification for effective influenza vaccination. Although the vaccine efficacy decreases in the elderly, the greater severity of disease overcomes the effect of the former and prevents more hospitalizations than vaccinating the younger age groups.

Many variants of influenza vaccines are available in the global market. In Singapore, only the "standard dose", quadrivalent and trivalent, egg-based inactivated vaccines are available. In USA, the live attenuated influenza vaccine was not approved for persons older than 50 years old and is not included in the review.

The main advantage of the quadrivalent vaccine overcomes the difficulty in predicting the endemic influenza B strain for the upcoming influenza season[3]. The quadrivalent hence consists of the 2 influenza A and 1 B strains shared with the trivalent vaccine and an additional influenza B strain. At this time, there has not been direct evidence showing a mortality benefit of the quadrivalent over the trivalent vaccine. Initial trials show non-inferiority of immune response between the 3 strains shared in both vaccine[4]. There has however been modelling data to show cost savings and greater efficacy in using quadrivalent over trivalent vaccine[3].

"High dose" influenza vaccine contains the same influenza strains as the standard dose trivalent vaccine. They have been used in the trivalent vaccine. In the elderly, use of high dose influenza vaccine has reported improved efficacy of up to 36%[5] in preventing influenza related mortality. This is consistent with the concept of requiring a higher dose of antigen to overcome the poorer immune response to vaccination in the elderly or "immunosenescence". These vaccines with higher dose of influenza antigens are not commercially available in Singapore. There is no "high dose" quadrivalent inactivated influenza vaccine.

Our current formulation of influenza vaccine has to be administered annually and protection is only against strains present within the formulation. There may also be loss of efficacy of H3N2 as a result of adaptations of the virus during growth in egg embryo. Studies have shown higher frequency of mutation in the haemagglutinin molecule as the viral isolates are passaged numerous times in egg embryo cultures[6]. This adaptation for growth in eggs compromises the efficacy of the vaccine particle as the haemaglutinin is now slightly different from that of the original circulating strain. In a research study, a new recombinant quadrivalent vaccine containing 45 mcg of heamagglutinin per strain, not grown in eggs but passaged in cells of lepidopteran insects have shown greater efficacy than conventional standard dose quadrivalent vaccine in a group of adults older than 50 years old. The recombinant vaccine has been reported to be 30% more effective and the increased protection stems from greater protection against influenza A strains[7].

As influenza strains are highly variable, vaccine efficacy may vary from year to year. The efficacy of protection from vaccination is thought to last at least 6 months[8] and vaccination more than once a year is generally not needed. In Singapore, where there is minimal seasonal variation in influenza epidemiology, local guidelines[9] have recommended annual vaccination. There remains the concern of a strain change as Singapore is exposed to strains from both northern and southern winter seasons. So far, on the balance of cost effectiveness and practicality, it is recommended to vaccinate with the most updated strains at the time of presentation. Vaccinating twice a year to cover both the southern and northern winter strains though, theoretically covers all predicted circulating strains, can paradoxically result in lower geometric mean titres of protective antibodies after the 2nd influenza vaccine[10].

Pneumococcal Vaccination

Pneumococcal vaccination mainly centres around the pneumococcal conjugate vaccine (PCV13) and the pneumococcal polysaccharide vaccine (PPSV23). The main efficacy of these 2 vaccines is focused on their efficacy to prevent invasive pneumococcal disease(IPD). The efficacy in preventing community acquired pneumonia (CAP) due to pneumococci is less convincing.

Recommendations regarding these 2 vaccines stem from 2 fundamental principles. Firstly, PCV13 induces antigen presentation to T cells and hence generates antibodies in a T cell dependent manner. Memory T cells, thus generated, provide lasting immunity. However, PPSV generates antibodies in a T-cell independent fashion and thus cannot generate long lasting immunity provided by PCV13[11]. Secondly, PPSV23 may compromise the efficacy of PCV13[12]. The exact mechanism of this interference is unclear. Some studies report persistence of PPSV23 antigens as a possible cause of this immune interference. Studies that have demonstrated this effect are done with the 2 vaccines given 6-12 months apart. The duration of this effect has also not conclusively proven but there is data to show that 5 years after PPSV vaccination, it depressive effects on subsequent pneumococcal vaccination would have waned[13].

Taken together, current guidelines recommend PCV13 vaccination in the elderly (more than 65 years old) followed by PPSV23 vaccination 1 year later, with the caveat that this PPSV23 vaccine must be at least 5 years from the previous PPSV vaccination. Should there be a prior PPSV23 given before 65 years old, the PCV13 vaccination must be at least 1 year after the pre-65 years old PPSV23. For example, an elderly who received PPSV23 at 64 years old would, by current recommendation, be advised to receive a PCV13 at 65 years old and his 2nd PPSV23 vaccine at 69 years old.

The efficacy of PCV13 in the elderly came to light in the CAPiTA trial[14] conducted in the Netherlands. In persons ≥65 years old with no previous pneumococcal vaccination history, the cohort receiving PCV-13, when compared to placebo, displayed a vaccine efficacy of 45% against non-invasive

pneumonia and a vaccine efficacy of 75% in invasive pneumococcal disease. In the prevention of non-bacteremic pneumonia, PCV-13 was effective only in the age subgroup who were less than 75 years old. No such age stratification was reported for IPD. In an era of widespread childhood PCV13 vaccination, herd immunity has markedly reduced IPD rates in the elderly suggesting that additional PCV13 vaccination in old age may not be cost effective[15]. At this time, the Advisory Committee of Immunization Practices (ACIP) from US and local guidelines have both continued to recommend the use of PCV13 in the elderly.

Being introduced earlier, PPSV23 has been subjected to many reviews on its efficacy in the prevention of pneumonia and IPD. A Cochrane metaanalysis[16] of 18 RCTs and 7 non-RCTs, totalling an excess of 120,000 patients found that a protective effect against IPD at an odds ratio of 0.26 among the RCTs and 0.48 among the non-RCT. There was no protective effect against CAP in high income countries. This finding was echoed in Israel[17] where retrospective case control study of 470,000 patients found an odds ratio of 0.54 against IPD and no benefit in preventing hospital treated pneumonia.

There has been concern that serotype replacement will undo the benefit provided by these 2 pneumococcal vaccines. A study in UK showed that although the representation of IPD by non-vaccine serotypes have increased in percentage terms, the decrease in total IPD numbers since the introduction of PCV13 remained significant despite the increase in proportion of non-vaccine serotypes[18].

Varicella-Zoster Virus (VZV) Vaccination

VZV vaccination to protect against episodes of herpes zoster and postherpetic neuralgia were one of the first vaccines developed specifically for the elderly. At present, Zostavax® is registered for use in persons aged 50 years and above. The efficacy reported in 2 large trials showed a vaccine efficacy of 70%[19] in the 50-59 age groups, 65.5%[20] in the 60-69 age groups and 55.4% in the ≥70 age group. Although ACIP support the use of VZV vaccines in adults ≥50 years of age, local guidelines support the use in adults ≥60 years of age. This difference in recommendation may arise from the much lower incidence of zoster in the younger age group and hence a greater cost-effectiveness if the vaccine is administered in an older age group. The other consideration is that Zostavax® vaccine that is available in Singapore is slightly less effective in older adults. In the US, ACIP recommends the use of the new adjuvanted subunit VZV vaccine, Shingrix® (see below).

Zostavax® vaccine is a live vaccine containing 19,400 plaque forming units of live Oka strain varicella virus. This is 14 times more than the amount in the usual varicella vaccine administered in children. Hence, the use of these 2 live "varicella" vaccines are not interchangeable. Being a live vaccine, it is contraindicated in immunocompromised adults. Anti-virals that are active against herpesvirus should not be coadminstered between 1 day before to 14 days after zoster vaccine administration. There is no need to test for varicella IgG or document a prior episode of prior chickenpox before Zostavax® vaccination. Elderly more than 60 years old are assumed to have prior varicella exposure. Although there is a concern with the varicella vaccine in persons recently given immunoglobulin-containing products, Zostavax® may be administered safely with antibody-containing products. Shingrix®, an adjuvanted VZV subunit vaccine was recently registered in the United States. ACIP has recommended the use of Shingrix® over Zostavax® in its 2018 guidelines. Shingrix® is not a live virus vaccine, hence, there are considerations for the use of this vaccine for protection of immunocompromised host against VZV. Two trials[21,22] reported over 90% protective efficacy of Shingrix® vaccine in age groups more than 50 years old. Unlike Zostavax®, there seem to be little attenuation of efficacy with increasing age. Shingrix® however has 30-50% increased risk of local injection site reaction when compared to Zostavax®. This increased local reaction probably reflects the effect of the adjuvant in eliciting increased local macrophages and antigen presenting cells resulting in the increase immune response and efficacy of the vaccine.

Travel Vaccines

Japanese encephalitis

Japanese encephalitis(JE) is caused by a Culex mosquito-transmitted flavivirus in Southeast Asia, Japan, Korea, China and India. However, Singapore is an exception and is not considered an endemic country despite being in Southeast Asia. Only less than 1% of people infected with JE virus develop any serious infection. After an incubation period of 5-15 days, fever, headache and vomiting lead to mental state changes, weakness and movement disorders. Parkinsonism features with thalamic involvement are a classical presentation. Acute flaccid paralysis has also been reported. Case fatality rate in symptomatic cases approach 30% and long term neurologic sequelae are seen in 30-50%[23]. In a recent case series from South Korea, the median age of patients affected was 51 years of age.

JE vaccination is recommended for travellers who plan to stay in an endemic country for more than 1 month and have an extensive outdoor or rural itinerary. Since the virus is amplified in pigs and waddling birds, it is predominantly a disease transmitted in agricultural areas. Two Japanese encephalitis vaccine are available in Singapore, Imojev® and Ixiaro®. Imojev® is a live attenuated chimeric viral vaccine. It is to be given subcutaneously 30 days before travel. Seroprotective levels were seen in 99% of vaccinees 30 days after a single dose. Hence, only 1 single dose is recommended for pre-travel vaccination[24]. Being a live vaccine, it should not be administered to any immunocompromised patient. Ixiaro® is an inactivated vaccine and is to be given intramuscularly in a 2 dose schedule 28 days apart. There is data to support a 2nd dose given up to 11 months after the 1st dose. The 2nd dose at least 1 week prior to travel for full protection[25]. If risk of exposure persists after 1 year, a booster is recommended 1-2 years after the primary vaccination[9].

Yellow fever

Yellow fever(YF) is also caused by a mosquito-transmitted flavivirus. It is endemic to sub-Saharan Africa and tropical South America[26]. However, distinct from the JE virus, it is transmitted by the Aedes mosquito in Africa and Haemogogus mosquito in South America. Since the Aedes mosquito is a peridomestic mosquito, transmission in urban areas is possible. Transmission in South America usually occurs in jungled areas as the Haemogogus mosquito predominate in forested areas. An international Certificate of Vaccination or Protection is needed for entry into some endemic countries[27]. Most YF virus infection is asymptomatic. The clinical spectrum ranges from mild undifferentiated disease to severe disease with jaundice and bleeding. The average incubation period is 4.3 days, lasting up to 9 days[28].

The yellow fever vaccine contains a live attenuated virus that is administered subcutaneously or intra-muscularly and must be given at least 10 days before entry into an endemic area[26]. 80-100% of vaccinated persons develop neutralizing antibodies by 10 days after vaccination, but no human studies have been done to document vaccine efficacy. The vaccine is now considered to provide lifelong protection. As a live virus vaccine, it is contraindicated in immunocompromised elderly and also adults with thymus disease or thymectomy. Two serious adverse effects of yellow fever vaccination deserve special mention: yellow fever vaccine associated neurotropic disease(YELAND) and yellow fever vaccine associated viscerotropic disease(YELAVD). They occur with greater frequency in elderly more than 60 years old; 2.3 per 100,000 for YELAND and 2.4 per 100,00 for YELAVD. Both YELAND and YELAVD occur after first vaccination and cases after booster vaccination have not been reported.

YELAND is a serious but rarely fatal adverse event with a usually self-remitting course. It can present as meningoencephalitis, Guillian-Barre syndrome, bulbar palsy, acute disseminated encephalomyelitis (ADEM). Onset occurs 2-28 days after vaccination and causes disease either via direct viral invasion causing meningoencephalitis or via autoimmune mechanism causing GBS and ADEM. In a study of 29 cases of YELAND by CDC, no deaths were reported among the immunocompetent subjects[26]. Deaths from YELAND have been sporadically reported in the literature[29]. YELAVD is a post-vaccination syndrome resembling severe wild type yellow fever infection. Risk factors are age more than 60, thymus disease and prior thymectomy[26]. After an incubation period of 3 days (range 1-8 days), fever, headache, malaise give way to jaundice, bleeding and multi-organ failure, with a mortality rate of 65% in 57 cases reported to CDC. There is no known effective treatment.

All vaccines against arthropod borne diseases should be administered together with advice for mosquito avoidance personal protective measures including the use of protective clothing, insect repellents and permethrin impregnated bed nets where appropriate.

Typhoid vaccine

Enteric fever is caused by *Salmonella enterica* serotype Typhi and *Salmonella enterica* serotype Paratyphi. Humans are the only reservoir for this bacteria and transmission is via fecal-oral routes in settings of poor sanitation, consumption of contaminated food and rarely, sexual practices of men who have sex with men (MSM)[30]. Thorough reviews of typhoid fever have landmarked medical literature through the ages[31]. After an incubation of 6-30 days, dependent on the inoculum load, fever, headache and malaise ensues with hepatosplenomegaly. Untreated, gut perforation and haemorrhage are feared complications after 2-3 weeks of disease.

Internationally, oral live vaccine and inactivated Vi capsular polysaccharide vaccines are both available but only the latter in parenteral form is available in Singapore[9]. It is given as a single intramuscular dose 2 weeks before exposure. Vaccine administration should accompany advice for food and water safety and good hand hygiene practices. Vaccine efficacy is 50-80% and protects only against *Salmonella enterica* serotype Typhi and not serotype Paratyphi[30]. Consistent with the concept of short-lasting immunity invoked in previous sections, a booster every 3-5 years would be recommended if there is repeated risk from travel to countries of high risk.

Meningococcal vaccine

Invasive meningococcal disease caused by *Neisseria meningitides* has an incidence rate of 5-10 cases per year locally[32]. Although not numerically significant, a large number of Haj/Umrah pilgrims from our Muslim community visit holy sites in Saudi Arabia each year, where a valid meningococcal vaccination certificate is required for entry. The meningococcal vaccines that are available locally are the quadrivalent conjugate vaccine and the quadrivalent polysaccharide vaccine. The quadrivalent vaccines protect against serotypes A, C, W-135 and Y. At least 2 meningococcal serotype B vaccines have been registered for use in other countries but are not approved in the elderly and will not be included in this review. Meningococcal disease is endemic in countries in sub-Saharan Africa, also known as the meningitis belt[33]. Meningococcal disease mainly affects children, adolescent and young adults. Hence, the literature on meningococcal disease in elderly population is sparse. Meningococcal vaccine is indicated in those travelling to the meningococcal endemic countries and to Saudi Arabia for Haj/Umrah.

The quadrivalent polysaccharide vaccine is the only meningococcal vaccine licenced for adults more than 56 years old and is given as a 1 dose subcutaneous injection at least 10 days before travel[9]. A booster is recommended every 5 years if exposure risks persists. In a trial measuring vaccine efficacy in an outbreak setting in children 2-15 years old, vaccine efficacy of the quadrivalent vaccine was 97%[34].

The quadrivalent conjugate vaccine is approved for adults less than 56 years old. Despite this, a randomised-controlled trial comparing the quadrivalent conjugate vaccine with the

quadrivalent polysaccharide vaccine in adults older than 56 years old found robust immunogenicity after vaccination with the quadrivalent conjugate vaccine[35]. However the polysaccharides in that study were conjugated to tetanus toxoid and not to the diphtheria toxoid like the formulation available locally. The conjugate vaccine is recommended by ACIP for off-label use in adults over 56 years old in United States who have previously received the polysaccharide vaccine[36]. In the most recent ACIP guidelines, the quadrivalent polysaccharide meningococcal vaccine has been removed from their recommendations.

Dengue vaccine

Dengue fever is endemic locally and the prevalent serotypes vary. After an incubation period of 4-7 days, a febrile phase lasting 5-7 days ensues, giving way to a critical phase where the platelet count will reach a trough level at the onset of defervescence, which lasts 1-2 days. Most complications stemming from plasma leakage and bleeding manifestations occur during the critical phase. This is followed by the convalescent phase where resolution of plasma leakage and thrombocytopenia concludes the natural history.

The landmark publication of the tetravalent Dengue vaccine[37] studied 35,0000 children between 2-16 years old in Dengue endemic countries. Two points deserve mention. Firstly, the vaccine efficacy of serotype 2 was only 47% in children older than 9 years old given the vaccine. Secondly and more importantly, there were more hospitalizations for severe Dengue in the group of children younger than 9 years of age given the vaccine. A plausible reason is that the first wild type infection occurring in these children after vaccination simulated an immunologic milieu analogous to a secondary infection, which is typically more severe.

Vaccine efficacy seem to be related to subjects who are seropositive for Dengue prior to receiving Dengvaxia®. Although elderly in Singapore have a high prevalence of seropositivity, the recent controversial data in young children and the lack of data in the elderly precludes any firm recommendation for Dengue vaccination for the travelling elderly.

NEW VACCINES FOR THE ELDERLY

Our current vaccines against influenza and pneumococcal disease have limitations because they are strain specific. The focus of research has been in developing "universal" influenza and pneumococcal vaccines that provide broad spectrum and long lasting efficacy. The most attractive target currently for a universal influenza vaccine is the conserved stalk region of the haemagglutinin molecule[38]. The remaining challenge is to find an immunogen to induce sufficient protective antibodies in humans. This effort must not only identify suitable target molecules for vaccination, but must also overcome the challenge of immunosenescence. The use of an adjuvant in VZV subunit vaacine and higher doses of antigens in high-dose influenza vaccines have been 2 successful approaches against immunosenescence. Other strategies like heterologous prime-boost vaccination could also play a role to increase the low vaccine efficacy seen in the elderly[39]. The idea behind heterologous prime-boost is to use the same vaccine antigen delivered in 2 different ways in an attempt to induce a more robust immune response.

New intra-dermal delivery methods also hold promise. The potential advantage is to make use of the abundant potent antigen-presenting dendritic cells in the skin to augment the immune reponse[40]. An existing intra-dermal influenza vaccine, Fluzone Intradermal, is licenced in the United States for adults aged 18-64 years old.

The elderly are also one of the target populations for vaccines currently being developed against *Staphylococcus aureus*. At this time, such vaccines are still in the clinical trial stage

Future challenges

Successful aging is the concept of preserving function as long as possible in old age, hence resulting in a shortened number of disease years before demise. Vaccines remain a cornerstone in the prevention of many infectious diseases in old age. The development of improved vaccines still requires effective implementation strategies for the administration of vaccines to the elderly. These strategies include raising awareness amongst prescribers, availability of vaccine to primary care centres and appropriate subsidies for the socially disadvantaged.

Table 1: Summary table of discussed vaccines

Pathogen	Available vaccine locally	Live/inactivated	Schedule	Indication	Route	Duration of immunity
Influenza	Quadrivalent and trivalent standard dose	Inactivated	Yearly	All adults	IM or SC	At least 6 months
Pneumococcus	PCV13 and PPSV 23	Inactivated	PCV13: once after 65 years PPSV: at least 1 year after PCV13 AND at least 5 years after previous PPSV 23	Once after 65 years old	IM	4-5 years for PCV13, likely longer. 5-7 years for PPSV23. Varying data exists.
Zoster	Zostavax®	Live	After 60 years old	Once after 60 years old	SC	8 years [42]
Japanese encephalitis	Imojev® Ixiaro®	Imojev®: live Ixiaro®: inactivated	Imojev®: 1 dose 30 days before travel Ixiaro: 2 doses 28 days apart; 2nd dose to be given 1 week before travel.	Travel to JE endemic countries	Imojev®: SC Ixiaro®: IM	Imojev®: >10 years 42 Ixiaro®: 1-2 years. Booster recommended 1-2 years after primary vaccination if risks persists
Yellow fever	Yellow fever vaccine	Live	1 dose 10 days before travel.	Travel to JE endemic countries	SC	Lifelong
Salmonella typhi	Vi capsular polysaccharide vaccine	Inactivated	1 dose 2 weeks before travel	Travel to south Asia, Africa, Latin America.	IM or SC	3 – 5 years. Booster recommended 3 – 5 years after primary vaccination if risk persists
Meningococcus	Conjugate quadrivalent vaccine Polysaccharide quadrivalent vaccine	Both inactivated. Only polysaccharide vaccine licenced in elderly	1 dose 10 days before travel for both vaccines	Travel to Haj/Umrah, Saudi Arabia	IM	5 years. Booster recommended 5 years after primary vaccination if risk persists

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LEARNING POINTS

- **In elderly, though less immunogenic, vaccinations are indicated and cost effective because of the more severe disease presentation in the elderly.**
- **Specific indications and practice pointers exists for individual vaccines and prescribers should be familiar with them before prescription.**
- **New vaccines created either via novel immunogens, route of administration, vehicle of delivery, methods of manufacture or other means continually invigorate medical science in the pursuit of healthy aging.**