# Vaccines in the Prevention of Viral Pneumonia

Clementine S. Fraser, BMBS, BSc, MRCP,
Akhilesh Jha, MBBS, BSc, MRCP,
Peter J.M. Openshaw, MBBS, BSc, PhD, FRCP, FMedSci*

**KEYWORDS**

• Influenza • Vaccination • Respiratory syncytial virus (RSV) • Parainfluenza • Adenovirus
• Lower respiratory tract infection (LRTI) • Viral pneumonia

**KEY POINTS**

- Viral pneumonias are a major cause of disease and death across the globe.
- Vaccination is a most effective way of preventing infection, but is only available for a limited (but expanding) number of respiratory pathogens.
- Current seasonal influenza vaccines confer insufficient protection, especially in some high-risk populations (eg, older adults).
- Research into correlates of protection has identified new ways to develop universal influenza vaccines that induce broad and long-lasting humoral and cell-mediated responses.
- Respiratory syncytial virus is a common cause of viral pneumonia and a largely unrecognized killer of frail elderly persons. Many promising vaccines are under development and there are high hopes of effective vaccines in the near future.

## INTRODUCTION

Pneumonia is of huge global public health concern. Viral and bacterial pneumonias are major and leading causes of global mortality, the impact being greatest in children, the elderly and the immunodeficient, and those with comorbidities.[1–3] In 2015, pneumonia was estimated to cause 41.7 deaths per 100,000 population.[4] In 2010, it is thought that there were approximately 15 million hospital admissions for severe acute lower respiratory infections (ALRI) in children less than 5 years old, and that 265,000 of these resulted in death. However only 62% of children with ALRI are admitted to hospital, with most deaths happening in the community (81%).[5]

The introduction of molecular (polymerase chain reaction–based) diagnostics enabled pathogens to be identified in many patients with community-acquired pneumonia, but in many cases the initiating infection remains unidentified. Respiratory viruses are implicated in about 45% of pneumonia cases requiring hospitalization in children[6] but some viruses (rhinovirus and adenovirus in particular) are found both in symptomatic and asymptomatic individuals.[7]

The relative importance of viral infections as a cause of pneumonia has increased not only because of improved diagnostics but also because of the introduction of bacterial vaccines such as the Hib conjugate (*Haemophilus influenzae* type B conjugate vaccine) and pneumococcal

Disclosure: P.J.M. Openshaw holds a Wellcome Trust grant (WP108516) supporting vaccine testing with Mucosis BV, and collaborates with GlaxoSmithKline on RSV disease.
Respiratory Sciences, National Heart and Lung Institute, Imperial College London (St Mary's Campus), Norfolk Place, Paddington, London W2 1PG, UK
* Corresponding author.
*E-mail address:* p.openshaw@imperial.ac.uk

Clin Chest Med ■ (2016) ■–■
http://dx.doi.org/10.1016/j.ccm.2016.11.009

conjugate vaccines.[8] Vaccination is also available for influenza and vaccination against varicella zoster, rubella, and measles helps to prevent additional cases of viral pneumonia and its complications.

The burden of ALRI caused by viral pathogens indicates clearly that additional effective, durable, and affordable vaccines are urgently needed.

## VIRAL VACCINES

Current licensed vaccines include inactivated, subunit, vectored, and live attenuated preparations. Inactivated vaccines may be made up of whole virus, split virus, subunit, or viruslike particles. Whole virus is grown in culture and then inactivated using a variety of methods, including chemical or heat treatments, to render them nonpathogenic. Vaccines containing whole killed organisms are generally cheaper to produce but may have a disadvantageous safety (reactogenicity) or immunogenicity profile. Spilt virus vaccines are a type of inactivated vaccine, split using organic solvents or detergents. Subunit vaccines comprise isolated or biosynthetic viral proteins that are selected to stimulate appropriate protective immune response while avoiding adverse host reactions.

Some vaccines, especially those that are highly purified and refined, may need to be combined with adjuvants and/or require the inoculation of multiple doses to be immunogenic. Adjuvants augment the host's immune response to vaccination, normally by providing a collateral danger signal via the innate immune system and thus boosting the protective acquired immune response. They enhance immunologic memory, allowing greater optimized antigen presentation.[9] Examples of adjuvants include alum (aluminum salts), virosomes, MP59, and AS03.

## EXPERIMENTAL VACCINES

There are many different innovative vaccine approaches that are currently in clinical development and for the most part these focus on directing pathogen genomic material to the target host immune cell (Fig. 1). DNA vaccines involve the injection of DNA encoding specific antigens into muscle leading to de novo antigen expression and the stimulation of both B and T cells. A major advantage of DNA vaccines is the stability,

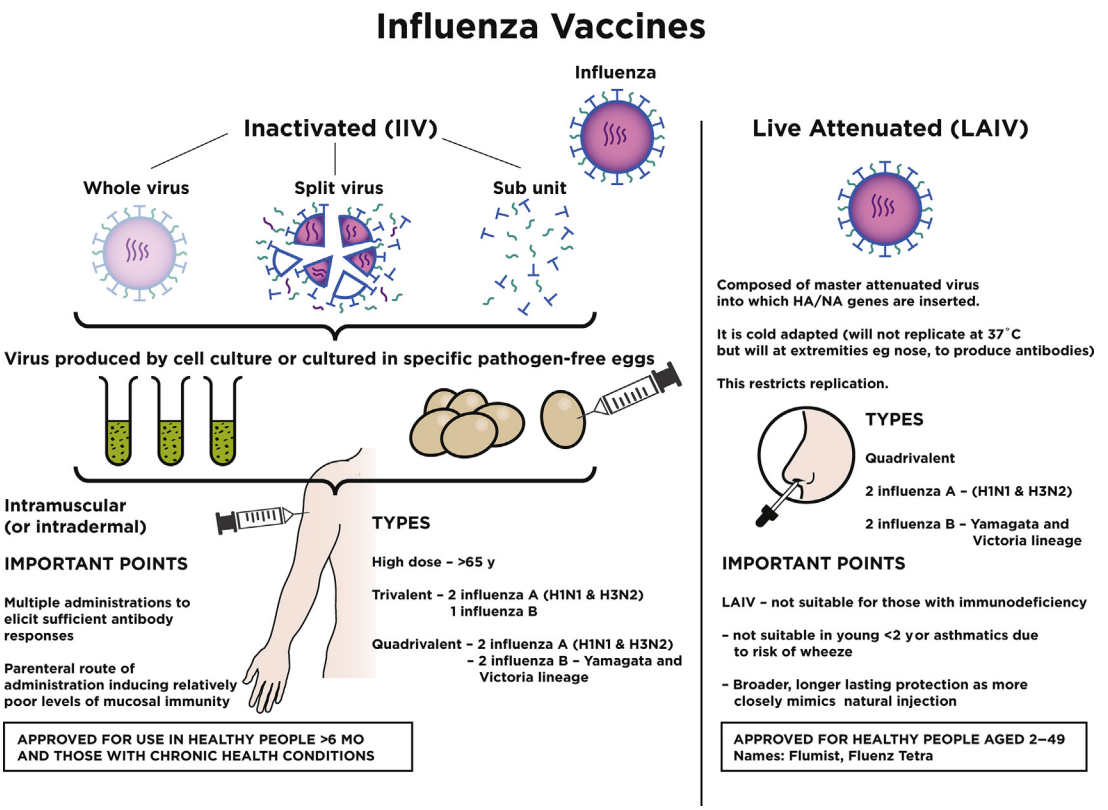


**Fig. 1.** Influenza vaccines. HA, hemagglutinin; IIV, inactivated influenza vaccine; LAIV, live attenuated influenza vaccine; NA, neuraminidase.