

newsletter

Influenza vaccines

Seasonal influenza (human flu) is one of the most prevalent global infectious diseases and has been in the public focus especially since the epidemic appearance of avian influenza viruses (bird flu), which triggered the scenario of an influenza pandemic.

Introduction

Influenza epidemics occur between December and March in the northern hemisphere and between May and August in the southern hemisphere. They vary in strength from year to year and as a rule persist for 6 to 8 weeks. The associated vaccination campaigns are one of the most common public health measures worldwide. Routine vaccinations are recommended for people as of the age of 60 (in the US as of 50), prophylactic vaccinations for persons with a high health risk or occupational exposure (also for children and juveniles), and the public health authorities may issue special recommendations if there is a known danger of an epidemic. Many influenza vaccines have been approved for administration to children as of 6 months of age. Routine vaccination of children and juveniles is currently not recommended in Germany, Austria and Switzerland. In the US, vaccination has been officially recommended for children since 2004, and this recommendation has been extended to infants as of 6 months for the 2006/2007 season (www.cdc.gov/flu/protect/children.htm). A study published in 2006 now casts doubt on the validity of the findings of previous investigations into the effectiveness of vaccination, particularly for small children (www.bmj.com/cgi/content/short/333/7574/912).

Influenza

Human flu, caused by the influenza viruses A and B, is a socioeconomically significant, endemic, epidemic or pandemic acute infectious disease of the respiratory tract that is transmitted by droplet infection. It usually starts suddenly with a high temperature and severe illness, it takes a long time to recover, and it can lead to life-threatening complications (myocarditis, pneumonia). Infants, elderly people and people with chronic diseases are particularly at risk. About 5-15% of the world's population is infected every year, some 3-5m people become seriously ill, and 250 000-500 000 people, most of them members of high-risk groups, die of influenza or its sequelae (www.who.int/mediacentre/factsheets/en).

Vaccine manufacture

Influenza vaccines have to be re-compiled and administered every year, as the properties of the viruses are constantly changing. The WHO provides information about the composition of the next season's vaccines in February of each year and sends the recommended seed viruses to the manufacturers. The viruses are allowed to reproduce in incubated chicken eggs (it takes one egg to produce one dose of vaccine) before being broken down and the inactivated parts processed into the finished vaccine. The production process is prone to contamination, which makes it necessary to use antibiotics. In all, manufacture takes about 6 months. The vaccine needs to be licensed by the health authorities (eg PEI, EMEA). About 300m doses (some 75 different products) were produced worldwide in 2006. 95 % of these came from nine countries (Australia, Japan, Germany, France, Italy, Canada, the Netherlands, US, UK). Hardly any of the

doses manufactured in the US, Japan or Canada leave the country (www.who.int/wer/2004/wer7940.pdf). An alternative to the conventional method is to produce the vaccine in vero cells. However, this procedure involves reproducing the virus in industrial-scale bioreactors of safety class 3, which is currently not feasible for today's egg-based production facilities. Besides, no egg-culture vaccines have been licensed yet. Some flu vaccines have an adjuvant added to enhance the immune response, which is particularly beneficial for people with an impaired immune system (eg the elderly). Besides the conventional form of vaccine, which is injected into the muscle tissue, a live attenuated vaccine that is administered as a nose spray has been licensed in the US. In Europe, a product of this type had to be withdrawn from the market because of undesired side effects (Switzerland, 2001).

Prophylactic inoculation

One of the cornerstones for combating the disease is annual prophylactic inoculation. This serves to protect the individual against infection, to avoid complications, and to contain the spread of the pathogens within the community (cohort immunisation). Vaccines are also the most important prophylactic against a pandemic. As influenza vaccines have to be adapted to the latest epidemiological situation every year, they offer no protection against other strains of the viruses - nevertheless, they may mitigate the course of the illness. Inoculation with the seasonal influenza vaccine provides no protection against the avian influenza pathogen, but can prevent a double infection (genetic reassortment). Children are considered to be the "fire of the influenza epidemic", as they are one of the main sources of infection for their immediate environment. The US and Canada have recently started vaccinating children as a routine precaution. In a recent project, researchers from the Cochrane Vaccines Field analysed 25 comparative studies on the efficiency and effectiveness of influenza vaccines. According to the findings, there is ample qualitative evidence that vaccines are effective in children as of 2 years of age, but not in children younger than 2. What is more, influenza inoculation is reported to have no influence on hospital admissions, absences from work or mortality rates among otherwise healthy persons below age 65. However, this statement is based on analyses of non-randomised studies and very small data samples. On the other hand, it is well known that 30-50% of elderly people do not respond to the flu vaccine, which makes it all the more important to inoculate their healthy younger contacts, eg staff in nursing homes. One study reports a significant drop in mortality among nursing-home residents if the staff is routinely inoculated in years with a strong flu wave (www.bmj.com/cgi/rapidpdf/bmj.39010.581354.55.pdf). In any case, inoculation remains the only preventive measure, as the possibilities for causal treatment of the diseases are severely limited.

Risks

Reactions to vaccination include local rashes and swelling, aches and systematic reactions with high temperature, headache and nausea. Very rarely, allergic reactions are also observed. There are isolated reports of anaphylactic shocks. As the end product contains chicken protein from the production process, it should not be given to people who are allergic to chicken protein. Additives such as stabilisers, binding buffers or activators and residues may be responsible for undesired responses. Examples are thiomersal, formaldehyde and antibiotics. Some manufacturers therefore offer influenza vaccines that are guaranteed to be free from preservatives and mercury. In Germany, about 1.2% of all recognised inoculation complications are attributable to influenza vaccines (compare: tetanus 2.2%, polio 8.1%, smallpox 64.7%; Bundesgesundheitsblatt 4, 2002). In the US, about 1% of all reported cases are eventually recognised

(www.hrsa.gov/vaccinecompensation). It is extremely rare for permanent harm to be suffered in connection with influenza vaccinations. In many cases, the suspected causal connection between a vaccination and an illness turns out to be improbable. To comply with labelling regulations, manufacturers sometimes mention isolated cases whose causal context has not yet been proven (Epidemiologisches Bulletin 6/2004). Risks may also arise out of the intramuscular administration of the vaccines.

Information for the underwriter

Despite the doubts raised by the Cochrane Vaccines Field about the benefits, prophylactic influenza inoculation is still frequently recommended and performed worldwide and continues to play an important role, especially in national and international pandemic response plans. Furthermore, there are currently calls for a re-think in favour of a universal vaccination strategy and away from risk-group approaches. One aim of this is to increase the inoculation density of the general public and especially among medical staff. There is also debate about reducing the minimum-age recommendation in Europe. As a result, there is still demand for insurance cover for vaccines that could affect product liability insurers. Loss of production due to quality problems, as happened for instance in the UK in 2004, is more likely to be regarded as a traditional entrepreneurial risk and will not normally trigger insurance covers.

Clinical-trials insurance may be affected, eg in the context of testing pilot batches of potential pandemic vaccines. In the event of a pandemic, it is essential that a vaccine be developed quickly. Within the EU, there are procedures for fast-track licensing of pandemic vaccines. The development of innovative vaccines (eg cell-culture vaccines) with a view to enhancing flexibility in production is likewise proceeding apace.

Even if a causal relationship between vaccinations and certain types of harm were to be proven sometime in the future, this would probably not call present-day inoculation recommendations into question. Harm suffered due to vaccinations that are recommended or even prescribed by the public health authorities generally give rise to statutory claims for care and compensation that are usually settled by the authorities themselves. All in all, the number of reported claims is very low compared to the millions of inoculations performed, but isolated instances (eg thiomersal) may still affect insurers.

In the event of a pandemic, hospital liability risks may arise: eg for administrative, treatment, diagnostic or informed-consent-process errors or for inadequate preparation and training in the context of pandemic response plans. Claims may be filed for the cost of curative treatment or for compensation for permanent health impairment suffered by patients.

The morbidity and mortality risk to the individual during an influenza season (or pandemic) is impossible to assess. That makes it all the more important for businesses to engage in all-round risk management, eg by implementing industrial health and safety measures, offering the workforce vaccinations, and expedient contingency planning. It has to be assumed that around 25% of the workforce will be taken ill in a major epidemic and will be temporarily unable to work (www.rki.de). Not many businesses are sufficiently prepared to cope with such situations.

Contact

AssTech GmbH
Postfach 1211
85766 Unterföhring bei München
Telephone + 49 89 3844-1585
Telefax + 49 89 3844-1586
info@asstech.com
www.asstech.com