Influenza

Influenza is a common respiratory disease. It is spread by the respiratory route only by droplet spread and affects people of all ages. Influenza is highly infectious with a transmission rate of 20–90%. Even when an epidemic is not present some 3000 to 4000 deaths may be attributed to influenza each winter.

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Influenza peaks in the UK in the early months of the year although the virus is present throughout the year. An increasing incidence of influenza has a knock-on effect on other infections spread by droplets. Meningococcus and pneumococcus induced disease rises parallel to the incidence of influenza owing to an increase in the number of people coughing and sneezing.

The highest attack rates are in children with school children playing a major role in the spread of influenza both within their own household and within the local community. In an American study it was found that 33% of children developed influenza in the first year of life with the majority of infections occurring during the period from six months of age.

Influenza is highly infectious with a transmission rate of 20–90%.[1] Even when an epidemic is not present some 3000 to 4000 deaths may be attributed to influenza each winter.[2] Most deaths or worsening of morbidity are secondary to complicating infection following influenza. In the UK, epidemics between 1975 and 1990 resulted in between 5000 and 29,000 extra deaths during each epidemic.[3]

Genetic drift

The influenza virus has the capability of undergoing genetic drift and shift. Genetic drift occurs when the virus genome does not create an exact copy of itself and encodes a different protein structure that is not recognised by host immune systems. Genetic shift occurs when two different strains of flu infect the same cell and major genetic re-assortment ensues. Vaccine manufacture is determined by the World Health Organization in order to prepare the appropriate hemisphere for likely circulating virus and the predictive ability has been excellent in recent years.

Influenza is a major burden to the world's economy and represents a significant workload in primary care each and every winter.

Diagnosis

Diagnosis of influenza in primary care, at present, is usually reliant on clinical history and signs. Laboratory investigation can determine the presence of influenza and can type the disease. Near patient testing is possible to confirm influenza but the rapid diagnostic tests are relatively expensive and use would not be justified. Recent trials comparing diagnosis based on the clinical symptoms against serological confirmation showed that practitioners had an accuracy in excess of 70% in diagnosing influenza on symptoms alone.[4]

The confirmation of circulating influenza is essential for epidemiological analysis of circulating types of influenza in order that vaccine production and pandemic planning may be facilitated. The WHO and the UK Public Health Service constantly monitor the incidence of influenza in order that major epidemics and pandemics are identified at an early stage. Nasopharyngeal washes and aspirates are the sample of choice but are perhaps less practical in primary care. Groups of GP practices (Primary Care Trusts or Local Health Groups or Cooperatives) could facilitate influenza monitoring by agreeing that all patients with suspected influenza from one practice could be laboratory tested.

Box 1: Comparison of influenza and other upper respiratory tract infections

Influenza
Severe malaise
Rapid onset
Profound muscular aches and pains
Marked fever
Severe and early headache
Poor or limited appetite

Colds or "flu-like" illnesses
Mild malaise
Slow onset over days
Minimal aches and pain
Mild intermittent fever
Mild dull headache
Prominent nasal secretions
Normal appetite

In the recent Swine Flu pandemic, spread of the disease was monitored by the insistence on nasal swabs by practitioners suspicious of the patients suffering the disease. Treatment courses of neuraminidase inhibitors were released only on confirmation. This testing was abandoned for the majority of patient once the level of circulating disease had passed a specific incidence and treatment was released based on a checklist of clinical symptoms.

Treatment

Influenza is becoming a manageable disease following the introduction of neuraminidase inhibitors. Neuraminidase inhibitors limit the ability of new influenza A or B virions (which have neuraminidase glycoproteins) to leave the host cell, thus decreasing viral shedding and further damage to the respiratory tract.

Influenza management should now include:

- Effective vaccination policies with shared responsibility between all members of a local health organisation (PCT, LHG, LHCC or Trust), which would protect the vulnerable elderly and high risk patients. Consideration may also be given to vaccinating all school age children to prevent the high transmission rates in the local community
- Early access to neuraminidase treatment for those suffering influenza A or B decreases the infectivity and duration of the disease by one to three days and also reduces the incidence of complications
- Neuraminidase inhibitors may have a role in prophylaxis against influenza at times of epidemic or in institutions where influenza is likely to spread and cause morbidity. This is particularly appropriate to households where there are members in the risk groups
- Symptomatic management of influenza is aimed at maintaining hydration, controlling pyrexia and preventing secondary complications in high risk patients. Secondary bacterial infection usually results from staphylococcus aureus, streptococcus pneumoniae or haemophilus influenzae—a penicillin or erythromycin is the drug of choice.

Prevention

Vaccines against influenza have been available for some 50 years. The vaccine is prepared from virus particles incubated on embryonated hens eggs. The particles are then subjected to chemical solvents or detergents to create either "split virus" vaccines or to remove and use the antigenic haemagglutinin and neuraminidase particles as "suface antigen" vaccines.

Current recommendations in the UK are that all members of the high risk groups should receive an annual vaccination against influenza. Uptake figures in recent years would suggest that far fewer than 50% of such patients under the age of 65 years receive the vaccine.[5] The efficacy of the influenza vaccine is estimated at between 70 and 80%, which would imply that only 40% of the at risk population are likely to have vaccine induced protection in the event of influenza.[5] Such low levels of vaccination need to be addressed to prevent the morbidity associated with flu, particularly in residential institutions. Uptake in the over 65 groups has been maintained at between 70 and 80% in recent years.[5,6]

Annual revaccination

Annual revaccination is necessary to maintain immunity to the antigenic strains of influenza A and B expected to strike each year. Manufacturing the vaccine can take many months and it is not possible to create a new vaccine any sooner than this when a major antigenic shift occurs. Attempts to release the Swine Flu vaccine at the earliest stage possible met

Box 2: Those at risk whom influenza vaccination is recommended

Chronic respiratory disease
- Asthma
- Chronic bronchitis
- Empyhsema
- Other chronic obstructive airways diseases
- Bronchiectasis
- Cystic fibrosis

Chronic heart disease
- Heart failure
- Angina
- Myocardial infarction
- Ischaemic heart disease
- Arrhythmias
- Valvular heart disease

Diabetes mellitus
- Insulin dependent
- Non-insulin dependent
- Insulin resistance syndrome
- Impaired glucose tolerance

Chronic renal disease
- Chronic renal failure
- Long-term dialysis
- Nephrotic syndrome
- Chronic pyelonephritis
- Kidney transplantation

Immunosuppression
- Cancer
- Organ transplantation
- Splenectomy
- Splenic dysfunction
- HIV infection
- Chemotherapy
- Radiotherapy
- High dose corticosteroids

Pregnancy

Long-stay residential accommodation
- Boarding schools
- Residential/group homes for disabled/mental handicap/ visual or hearing impairment
- Nursing homes
- Residential colleges

with resistance from a proportion of patients in primary care as they were led to believe by the lay press that this vaccine was "untested and experimental" whereas in reality it had been prepared in exactly the same manner as the annual influenza vaccine and had been subjected to the same quality controls. The power of the media is never to be underestimated when health matters are concerned and while the press may argue "the right to know" this must be balanced with the "right to prevent spread of communicable disease."

The vaccine is safe and rarely causes systemic upset. Those with anaphylactic reaction to hens egg or egg products should not be given the vaccine. The vaccine cannot cause influenza as it is manufactured from inactivated virus. The commonest adverse reaction is from a systemic immune response similar to that experienced with influenza—fever, malaise, myalgia/arthalgia lasting up to 48 hours. Guillain-Barre syndrome has rarely been reported after vaccination.

The practicalities—past, present and future

Influenza has been a scourge of mankind for centuries, responsible for thousands of deaths when a new strain arises and such pandemics are documented and postulated by historians as the cause of civilisations being cruelly extinguished. The development of medical tools enabling control or limitation of pandemics has been one of the great clinical progresses of the last half century. Vaccination using either killed or subunit vaccines has decreased the excess morbidity linked to seasonal influenza, although the dynamics of administering millions of doses of the vaccine annually to susceptible patients does impact significantly on the activity of primary care in the UK for two to three months at a time when practices are already busy with coughs and colds.

The discovery of the highly effective neuraminidase inhibitors and their commercial development allows a second alternative means of managing influenza. These drugs inhibit the release of virions from infected cells in the respiratory tract, thus decreasing the local damage and spread within the individual and also decreasing the communal infectivity at the same time allowing personal immunity to develop. By administering the drug at the early stage of the disease there is decreased symptomatology in the patient and he/she is able to return to normal functionality very rapidly. The question does need to be raised now that this alternative means of management is available, whether the continuing mass immunisation campaign is still absolutely necessary as the cost and impact of such campaigns could be redirected to the early provision of neuraminidase inhibitors instead.

During the Autumn and Winter of 2009–2010 we all had the experience of the H1N1 (Swine flu) pandemic. This was our first experience since the introduction of neuraminidase inhibitors of a new, highly infective and contagious, influenza virus, which spread characteristically rapidly

Box 3: Complications of influenza

Influenza pneumonitis
Secondary bacterial pneumonia
Otitis media
Exacerbation of chronic lung diseases
Croup and bronchiolitis in children
Febrile convulsions
Myocarditis
Guillain-Barre paralysis
Secondary meningococcal infection
Post viral fatigue

throughout the world following early identification in the USA and Mexico. As with previous pandemics, the virus seemed to kill greater proportions of the young and younger adults than does seasonal influenza. This is probably because of cross immunity allowing some degree of protection in the older population who had either had personal experience of related influenza viruses or persistent immunity from previous vaccination. As was to be expected, there was no immediately available vaccine against this new form of influenza and public health services became organised around the distribution of neuraminidase inhibitors as the first-line of treatment for affected individuals. Access to the drug was regulated by a simple questionnaire administered by non-medically qualified call-centre staff. This process worked by both decreasing the impact on primary health care in comparison to the impact of previous pandemics (1967 and 1981) and also by decreasing the amount of time lost by patients from work.

Another measure, perhaps, of the success of the programme is that of the press reaction to the pandemic—implying that it was the "pandemic that never was" and criticising the costs of the campaign when analysing the numbers of deaths and hospital admissions. In the mind of the lay person, there was a "lot of fuss about nothing".

WHO will no doubt be analysing the relative death rates and morbidity in countries where there was a different level of access to neuraminidase inhibitors and we look forward to reviewing those figures in due course, but from a personal view point I believe that the early use and ease of access to neuraminidase inhibitors probably saved a considerable number of people from dying in 2009–2010 and also maintained the workforce at a time of potential mass sickness.

So what about the future?

At present there are a number of potential developments in respect of influenza prevention and management. Vaccination looks to continue to be the mainstay of influenza management for some years to come although decreasing cost by using intradermal injection (smaller vaccine dose required) is likely to be pushed-forward. Development of more comprehensive vaccines is proceeding which will, hopefully, prevent the need for annual revaccination and allow protection against shift of viral antigen. Neuraminidase inhibitors may be combined with other antiviral activity such as that shown by amantadine, which diminishes the creation of virions within the infected cell in order to decrease further the impact of influenza on the individual.[6] Public health has benefitted considerably from the "wash your hands" marketing, which accompanied the 2009–2010 pandemic and everywhere you go, alcohol gel is abundantly available.

Conclusion

Influenza is a chameleonic mass murderer, which although can be tamed, will forever rear its head. We have effective tools to deal with the disease but we still need to remind the public and the media that influenza is not a simple head cold and needs to be treated seriously at all times.

Conflict of interest: none declared

References

1. Nicholson KG. Human Influenza. In Nicholson KG, Webster RG, Hay AJ; editors; Textbook of Influenza, Oxford, Blackwell Science 1998 219–64
2. JCVI. Advice on the H1N1v and 2010/2011 Seasonal influenza vaccination programmes. Accessed October 2010 www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_118093.pdf
3. Nicholson KG "Managing Influenza in Primary Care" Blackwell Science, Oxford 1999 page 67
4. Miller E, Hoschler K, Hardelid P, et al. *Lancet* 2010; **375**: 1100–8
5. Immunisation against infectious diseases 3rd edition JCVI The Stationary Office Norwich 2006 ISBN 0 11 322528 8
6. Human Virology—2nd Edition — Collier L, Oxford, J. Oxford University Press, Oxford 2000 ISBN 0 19 262820 8