Influenza virus infection

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Influenza case definitions

- Clinical Criteria
- Laboratory Criteria
- Epidemiological Criteria

Definitions of the ECDC (European Centre for disease Prevention and Control):
http://ecdc.europa.eu/en/activities/surveillance/EISN/surveillance/Pages/influenza_case_definitions.aspx

Influenza - Clinical Criteria

Any person with at least one of the following clinical forms:

- Influenza-like illness (ILI)
- Acute respiratory infection (ARI)

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Influenza-like illness (ILI)

Sudden onset of symptoms AND

At least one of the following four systemic symptoms:

- Fever or feverishness
- Malaise
- Headache
- Myalgia

AND At least one of the following three respiratory symptoms:

- Cough
- Sore throat
- Shortness of breath

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Acute respiratory infection (ARI)

Sudden onset of symptoms AND

At least one of the following four respiratory symptoms:

- Cough
- Sore throat
- Shortness of breath
- Coryza

AND

A clinician's judgment that the illness is due to an infection

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Influenza - Laboratory Criteria

- Pooled bilateral nasopharyngeal and throat swabs rather than nasal wash is the prefered technique in order to obtain respiratory specimen

- Qualitative reverse transcriptase multiplex real time polymerase chain reaction (PCR) of respiratory specimens is the gold standard laboratory method to confirm the diagnosis of influenza and other respiratory viruses. RT-PCR, being multiplex RT-PCR preferably: first level Flu-A/B, RSV, PIV; second level others: MPV, RhV, CoV, EnV if first level negative or progression to LRTI disease

- Subtyping of the influenza isolate should be performed, if possible

- Detection of known mutations causing resistance, such as H275Y mutation can be done using real time PCR

Influenza - Laboratory Criteria

Direct immunofluorescence antibody (DFA), indirect immunofluorescence antibody (IFA) and commercially available rapid diagnostic tests (kits) may be alternatives, when PCR is not available, although these methods have lower sensitivity.

Influenza - Epidemiological Criteria

An epidemiological link by human to human transmission

Definitions of the ECDC (European Centre for disease Prevention and Control):

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Influenza - Case Classification

A. Possible case

- Any person meeting the clinical criteria (ILI or ARI)

B. Probable case

- Any person meeting the clinical criteria (ILI or ARI) and with an epidemiological link

C. Confirmed case

- Any person meeting the clinical (ILI or ARI) and the laboratory criteria

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Risk factors for severe influenza
(to be considered in the following recommendations)

- Older age*
- Lymphopenia*

also:

- First 12 months post HSCT
- GVHD and immunosuppression
- Having an unrelated or mis-matched family donor

*continuous variables (Ljungman et al, Haematologica 2011)

Influenza vaccination to allogeneic/autologous HSCT recipients

- Yearly vaccination with seasonal killed-influenza vaccine is recommended (A-II)
- The vaccine is preferably given prior to the influenza season but not earlier than 3 months post transplant (B-III)
- A second dose of vaccine after 3-4 weeks is advised, although it might have only marginal benefit (B-II)

Influenza vaccinations to household contacts of allogeneic/autologous HSCT patients

- Family members* and close or household contacts of HSCT recipients should be immunized in the first year post-HSCT and continue to be vaccinated annually as long as the recipient is at risk (A-II)

*Influenza vaccine should not be given to infants <6 months old. In some countries it is not recommended for children.

Influenza vaccinations to health care workers caring for leukemia patients and/or allogeneic/autologous HSCT recipients

- Seasonal influenza vaccination is strongly recommended annually for all health care workers (HCWs) of HSCT recipients and non-transplant leukemic patients (A-II)

Post-exposure anti-viral prophylaxis to allogeneic/autologous HSCT recipients

Post-exposure anti-viral prophylaxis, currently with oseltamivir 75 mg (adult dose) once daily for at least 10 days, is advised for HSCT recipients who are less than 12 months after transplant or later and for those who are substantially immunocompromised regardless of vaccination history after exposure to a confirmed or probable case of influenza. (C-III)

Influenza vaccinations to ALL/AML non-transplanted patients

- Vaccination with seasonal killed-influenza vaccine is recommended in the first season after the intensive chemotherapy has been discontinued, as well as for ALL children on maintenance therapy, when the peripheral granulocyte and lymphocyte counts are greater than 500/µL. (B-II)

Influenza vaccinations to household contacts of ALL/AML non-transplanted patients

: Leukemic patients' household contacts* are advised to be immunized with killed influenza vaccine during the period of chemotherapy and shortly after. (C-III)

*Influenza vaccine should not be given to infants <6 months old. In some countries it is not recommended for children.

Post-exposure anti-viral prophylaxis to ALL/AML non-transplanted patients

- Post-exposure anti-viral prophylaxis, currently with oseltamivir 75 mg (adult dose) once daily for at least 10 days, is recommended to all AML/ALL patients during chemotherapy regardless to immunization status of the patient after exposure to a confirmed or probable case of influenza (C-III)

General precaution to avoid transmissions of respiratory viruses

- Good personal hygiene should be observed including frequent handwashing, cover of the mouth when coughing & sneezing, and safe disposal of oral & nasal secretions (A-II)

- Contact with people with symptoms or signs of influenza-like illness (ILI) or acute respiratory infection (ARI) and other community respiratory viruses (CRV), in the hospital and in the community should be avoided (A-II)

Treatment of confirmed or probable case of influenza

• Efforts should be made to confirm all suspected and probable cases of influenza (A-III)

• In all allogeneic/autologous HSCT recipients and ALL/AML patients during chemotherapy therapy and in the following 6 months with confirmed or probable influenza should be treated (A-II)

•Currently preferred first line treatment is oseltamivir, adult dose of 75 mg BID for a mild case and 150 mg BID for severe disease given for at least 10 days (B-II)

• In patients with continuing symptoms, it is advised to repeat PCR tests on respiratory specimens every 5-7 days and to continue treatment until they become negative (C-III)

Treatment of confirmed or probable case of influenza

- In severe or pronged influenza disease, influenza resistance to antiviral drugs should be suspected and tests should be done every 5-7 days until improvement (B-III)

- the current alternative treatment is inhaled zanamivir (B-II)

- In severe influenza when the gut absorption of oseltamivir is impaired and inhalation of zanamivir is not possible, iv peramivir or zanamivir might be alternative options (C-III)

Live attenuated influenza vaccine (LAIV)

- No data exist about LAIV safety and efficacy in leukemic or HSCT patients and it should not be used. (A-III)
- HSCT patients' household contacts and care providers should not be immunized with LAIV, because of the theoretical risk that a live, attenuated vaccine virus could be transmitted to the patients. (B-III)
- Household contacts and care providers, and visitors, of HSCT patients should refrain from contact with the patients for 7 days after immunization with LAIV. (B-III)

Live attenuated influenza vaccine (LAIV)

- Leukemia patients' household contacts and care providers should preferably not be immunized with LAIV, because of the theoretical risk that a live, attenuated vaccine virus could be transmitted to the patients. (C-III)
- Household contacts and care providers, and visitors, of leukemia patients should preferably refrain from contact with the patients for 7 days after immunization with LAIV. (C-III)