GUIDELINES FOR THE MANAGEMENT OF PATIENTS IN CRITICAL CARE WITH CONFIRMED INFLUENZA

Diagnosis

Critical influenza in adults commonly presents as secondary bacterial pneumonia or acute exacerbations of COPD or asthma. Primary pneumonitis is less common. Influenza infection should be considered as a differential for any of the following presentations in critical care:

- Community acquired pneumonia
- Hospital acquired pneumonia
- Severe acute respiratory infection
- Exacerbations of chronic lung conditions
- Sepsis
- Encephalopathy/encephalitis, aseptic meningitis, transverse myelitis, Guillain-Barré syndrome
- Myocarditis
- Rhabdomyolysis

Influenza virus and other viral or bacterial infections may occur concurrently with a difficulty in differentiation. Detection of a bacterial infection does not exclude the possibility of active influenza infection.

Vaccination does not guarantee protection, and a patient's vaccination history should not influence a decision to test or commence empirical antiviral therapy.

In the absence of a negative influenza PCR, if a patient has presented with respiratory failure and markers of infection, then empirical antiviral therapy should be started until PCR is resulted.

Sampling

Appropriate samples (see below) should be obtained as soon as influenza is suspected.

Table 1.0: Sampling for detection of influenza virus

Non-intubated	**Intubated**
Viral throat swab	Viral throat sab
AND	**AND**
Lower respiratory tract (LRT) if there is evidence of LRT involvement (eg productive cough) i.e. sputum	Preferably deep sample (BAL/mini-BAL) although endotracheal tube aspirate also acceptable. . Samples should also be sent for microbiological and fungal analysis. Lower respiratory tract samples remain important in critical care as viral throat swabs can become negative over time while LRT samples remain positive.

PCR can also be undertaken on CSF if CNS involvement suspected.

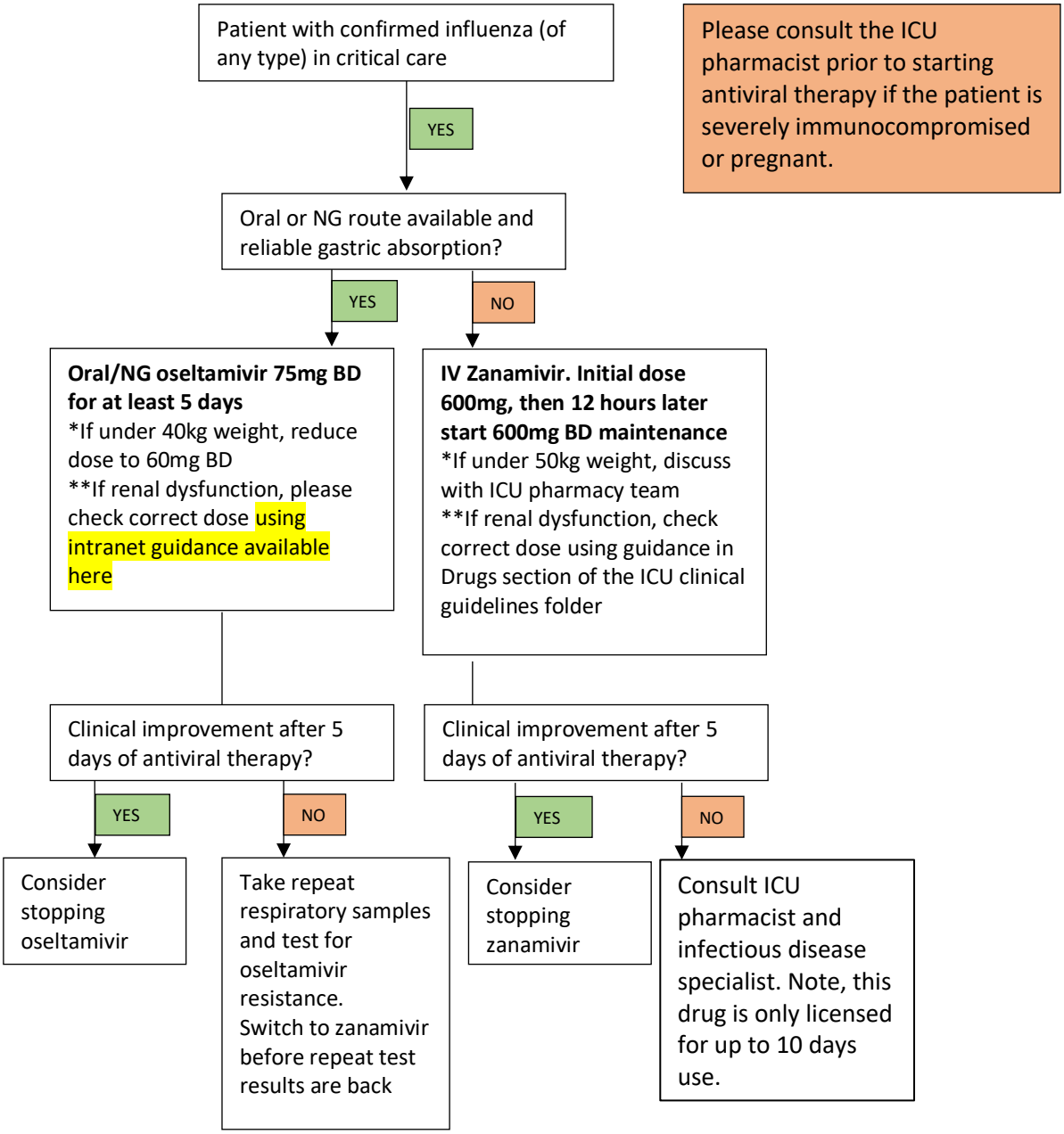
The role of repeat sampling
If an initial influenza test result is negative, but clinical suspicion remains high, diagnostic tests should be repeated and advice sought from local microbiology/virology specialists.

In patients with confirmed influenza, there is no reliable data to support routine serial testing to assess either response to treatment or to inform step-down of infection prevention and control measures.

In a patient with confirmed influenza on antiviral therapy either clinically deteriorates or has non-resolving illness despite at least 5 days of antivirals, follow up PCR testing can be considered with a request for antiviral resistance testing if it remains positive. This may inform an extended duration of antiviral treatment.

For guidance on stepping down contact precautions and moving convalescing patients out of side-rooms, refer to the latest IPCT guidance.

Antiviral therapy



Current national guidance advises that all adults hospitalised with a diagnosis of influenza should receive a neuraminidase inhibitor(i.e.oseltamivir or zanamivir) The limited evidence is strongest for delivering this in the first 48 hours. Where possible, patients should be included in randomised controlled trials.

Inhaled Zanamivir has no utility in critical care, as it is not well-absorbed from the respiratory tract to suitable systemic concentrations. IV zanamivir no longer needs to be prescribed on a named patient basis.

Special considerations for antiviral therapy

- *Patients with renal dysfunction require altered dosing of both enteral oseltamivir or IV zanamivir. Guidance for oseltamivir and zanamivir dosing can be found in the drugs folder of the ICU Guidelines.*

- **Patients with significant immunocompromise** should receive neuraminidase inhibitors in line with the above standard protocol and dosage unless the dominant circulating influenza strain at the time has a higher risk of oseltamivir resistance. In this case, use intravenous zanamivir in critical care as a first line agent.

- **Pregnant patients in critical care with influenza** can have oral/NG oseltamivir in line with the above guidance. If a pregnant patient in critical care requires intravenous zanamivir, this should be discussed with a local infection specialist.

Antiviral resistance
Infections with antiviral resistant influenza can occur in any patient, but are more likely in the following groups:

- Severely immunocompromised
- Acute illness developed while taking antiviral prophylaxis
- Contact with known resistant cases
- Patients experiencing changes of antiviral therapy, especially if gaps between therapies
- Clinical deterioration while receiving antiviral therapy

Viral mutations conferring resistance to both oseltamivir and zanamivir can occur in Influenza A(H1N1)pdm09, A(H3N2), and B infections. If oseltamivir resistance is suspected, consider switching to intravenous zanamivir. If zanamivir resistance is suspected, do not switch to oseltamivir as there is significant likelihood of resistance to both medications.

Corticosteroids
The use of adjunctive corticosteroid therapy is not recommended for management of influenza in critical care. Corticosteroids should not be withheld if there is any other indication (eg adrenal insufficiency, refractory septic shock).

Common complications of influenza infection

Bacterial infection
Bacterial superinfection is very common in critical influenza. In the event of clinical deterioration, a co-infection should be suspected, and repeat respiratory samples (preferably via BAL) should be taken.

These may occur concurrently with influenza infection or after clearing of the virus. Common causes are *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenzae*. Invasive Group A strep and *Neisseria meningitidis* are also recognised complications.

Fungal infection
Invasive aspergillosis is the most common form of fungal co-infection with influenza. This most commonly presents as pulmonary aspergillosis, however tracheobronchitis and extra-pulmonary disseminated disease may also occur. A BAL or blood sample should be sent for detection of aspergillus antigen OLM AspLFD to detect this. Empirical antifungal therapy according to local guidance should be started before samples are resulted if clinical suspicion is high.

Special circumstances

Pregnancy
Pregnant patients are at particular risk of severe respiratory failure in influenza.
See the above section on antiviral therapy for specific guidance on use in pregnant patients.

These patients are at increased risk of premature labour and should have regular monitoring for PV bleeding or ruptured membranes.

Immunocompromise
The absence of fever, myalgia, or cough is common in transplant patients. If infected with a circulating strain at higher risk of oseltamivir resistance (eg Influenza A H1N1) then such patients should be started on IV Zanamivir as first line therapy. If not, oral/NG oseltamivir is an acceptable first line.

Co-infection with other viruses, bacterial, or fungal is more common in the immunocompromised. A high index of suspicion for co-infection should be maintained if a patient is not responding as expected to routine intervention. If these patients do contract invasive aspergillosis, any immunosuppressants being received should be reviewed and reduced wherever possible after discussion with a relevant specialist.

Infection prevention and control measures

Please see the most up to date IPCT guidance and NIPCM appendix on managing respiratory pathogens. Step down criteria for winter viruses can be found here.

Deaths from Influenza

All deaths from influenza should be reported to public health.
In hours: 0131 465 5420 or 0131 465 5422
Out of hours: via switchboard public health on call

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