

A detailed white line drawing on a teal background depicting various microscopic structures, including several large, multi-layered circular cells and a large, spiky virus-like particle on the right side.

Influenza

Last updated: September 5, 2018

This is a summary of WHO global epidemiological surveillance standards for influenza, available at http://www.who.int/influenza/resources/documents/influenza_surveillance_manual/en/



DISEASE AND VACCINE CHARACTERISTICS

Influenza viruses are orthomyxoviruses that cause acute respiratory illness, ranging from mild febrile illness accompanied by body aches, cough and sore throat to severe pneumonia, which can be complicated by bacterial superinfection. Influenza viruses that infect humans are transmitted person to person, mostly by droplets and aerosols from the respiratory secretions of infected people, and occasionally from fomites or animals. Influenza viruses cause seasonal influenza epidemics, mostly in the winter months in temperate climates and with less distinct seasonality in the tropics, with annual attack rates of 5–10% in adults and 20–30% in children (1). Groups at higher risk of severe illness include young children, pregnant woman, the elderly and those with underlying medical conditions. The incubation period is one to four days. In general, the disease burden of influenza in lower- and middle-income countries has been underestimated. A recent modelling analysis estimated that between 291 243 and 645 832 seasonal influenza-associated respiratory deaths occur annually (4.0–8.8 per 100 000 individuals) (2). Global pandemics of novel influenza A subtypes occur every 10–40 years, which can cause high mortality such as that seen during the 1918 “Spanish flu” influenza pandemic, estimated to have caused 20–40 million deaths globally.

Because influenza viruses change rapidly due to antigenic drift, vaccines are reformulated and delivered annually, commonly through seasonal campaigns. Licensed influenza vaccines include inactivated or live-attenuated influenza type A and B viruses, with three or four subtypes per vaccine. Inactivated influenza vaccines (IIV) are administered by injection; live-attenuated influenza vaccines (LAIV) are delivered as nasal spray. Only IIV’s are licensed for children younger than age two years. Two doses of influenza vaccine given four weeks apart are recommended during the first season a child is vaccinated, followed by annual vaccination before influenza season. Maternal influenza immunization during pregnancy can protect infants too young to be vaccinated against influenza disease through transplacental transfer of antibodies. The World Health Organization (WHO) suggests that countries make decisions on influenza vaccines based on local disease burden, resources, capacity and other health priorities (1).



RATIONALE AND OBJECTIVES OF SURVEILLANCE

GENERAL OBJECTIVES

- Provide timely and high-quality epidemiological data on influenza cases to guide policy.
- Provide viral isolates for evaluation and vaccine production.

SPECIFIC OBJECTIVES

- Epidemiological
 - » Describe the seasonality of influenza.
 - » Signal the start and end of the influenza season.
 - » Identify and monitor groups at high risk of severe disease and mortality.

- » Establish baseline levels of activity for influenza and severe influenza-related disease in order to evaluate the impact and severity of each season and of future pandemic events.
- » Generate influenza data that can be used during focused studies to estimate influenza burden and help decision-makers prioritize resources and plan public health interventions.
- » Detect unusual and unexpected events such as outbreaks of influenza outside the typical season, severe influenza among healthcare workers, or clusters of vaccine failures that may herald novel influenza virus.
- » Identify locally circulating virus types and subtypes and their relationship to global and regional patterns.
- » Assist in developing an understanding of the relationship of virus strains to disease severity.
- » Monitor antiviral susceptibility of circulating viruses.
- » Provide a platform for evaluation of vaccine and other intervention effectiveness.

► Virological

- » Provide candidate vaccine viruses (CVV) for seasonal and pre-pandemic influenza vaccine production. In the event of pandemic, a pre-pandemic CVV can be used to develop a pandemic vaccine quickly if matching the pandemic virus.
- » Describe the antigenic character and genetic makeup of circulating viruses.

GEOGRAPHIC FOCUS OF SURVEILLANCE

Influenza is not targeted for global elimination/eradication. Influenza surveillance data are mostly used to support national vaccination strategies and the development of global vaccine composition. Virus isolates from national surveillance programmes can be used to provide strain information for global vaccine formulation. Global and regional networks of influenza surveillance exist, including WHO's Global Influenza Surveillance and Response System (GISRS) (www.who.int/influenza/gisrs_laboratory/en/).



TYPES OF SURVEILLANCE RECOMMENDED

MINIMAL SURVEILLANCE

Minimal suggested surveillance to monitor influenza includes the following characteristics:

- **Facility-based and sentinel site.** Because influenza is endemic and has a high incidence in all regions, influenza surveillance is not expected or designed to capture every case. The site of surveillance is facility-based, both inpatient and outpatient, based on the surveillance syndrome used for case detection. Facilities are selected for surveillance as part of a sentinel site network in most cases.
- **Syndromic.** Influenza surveillance is most often done using syndromic surveillance.
 - » Influenza-like illness (ILI) surveillance monitors persons seeking care in ambulatory facilities.
 - » Severe acute respiratory illness (SARI) surveillance monitors persons with more severe illness who have been admitted to hospital for their respiratory illness.
 - » The balance between ILI and SARI surveillance will depend on the specific information needs and surveillance priorities in each individual country.
- **Laboratory-confirmed.** Patients meeting syndromic case definitions should be laboratory tested for influenza virus because of low specificity of ILI and SARI for influenza infection.
 - » Testing all patients for influenza at a site is ideal, if feasible, but otherwise a sampling strategy should be implemented for selection of patients for testing and data collection.
 - » In settings of very high incidence, such as the 2009 H1N1 pandemic, not all detected cases need to be laboratory confirmed.
- **Case-based.** Case-based data is gathered from SARI and ILI cases from which a sample was collected.
- **Active.** Surveillance officers actively detect cases in health facilities.

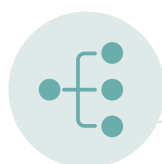
The target population for influenza surveillance is all persons, both children and adults. In temperate climate zones, influenza seasonality is usually well defined. Data collection and reporting should occur at a minimum during the known influenza season and for a short period preceding and following the season. Year-round surveillance is recommended because it adds to general understanding of out-of-season influenza activity and provides essential information about the emergence of novel influenza strains and antiviral resistance markers.

ENHANCED SURVEILLANCE

Enhanced surveillance would be done whenever surveillance activity is increased because something unusual is identified, such as a pandemic, or a new subtype is starting to circulate.

INTEGRATION WITH OTHER PATHOGENS UNDER SURVEILLANCE

Some sites using syndromic ILI or SARI surveillance will test for other respiratory pathogens, including RSV, pneumococcus and pertussis. Multiplex polymerase chain reaction (PCR) testing of upper respiratory tract specimens is becoming more common.



CASE DEFINITIONS AND FINAL CLASSIFICATION

SUSPECTED CASE DEFINITIONS FOR CASE FINDING

- Influenza-like illness (ILI). An acute respiratory infection with the following:
 - » measured fever of $\geq 38^{\circ}\text{C}$
 - » cough
 - » onset within the last 10 days.
- Severe acute respiratory illness (SARI). An acute respiratory infection with the following:
 - » history of fever or measured fever of $\geq 38^{\circ}\text{C}$
 - » cough
 - » onset within the last 10 days
 - » requires hospitalization.

FINAL CASE CLASSIFICATION

- **Confirmed.** Patients meeting the ILI or SARI definitions who have laboratory confirmation of influenza virus infection, using one of the following criteria:
 - » conventional PCR or real-time reverse transcription PCR (RT-PCR)
 - » viral antigen detection by immunofluorescence or enzyme immunoassay methods

- » viral culture with a second identification step to identify influenza viruses (immunofluorescence, hemagglutination-inhibition or RT-PCR)
- » four-fold or greater rise in antibody titre in paired acute and convalescent sera.
- **Probable.** In pandemics of novel influenza A viruses, a probable case is an epidemiologically-linked case, which is a case meeting the suspected case definition and epidemiologically linked to a confirmed case, but for which no confirmatory laboratory testing for influenza virus infection has been performed, or test results are inconclusive for a novel influenza A virus infection. Criteria for epidemiological linkage are that the patient has had contact with one or more persons who either have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked if at least one person in a chain of transmission has had laboratory confirmation.



CASE INVESTIGATION

In general, individual cases of influenza detected in surveillance do not require further investigation, apart from referral for clinical care, if not yet in care.



SPECIMEN COLLECTION

SPECIMEN TYPES

► Nasopharyngeal/oropharyngeal swabs

- » For ILI cases, nasal swabs, nasopharyngeal swabs, nasopharyngeal aspirates, nasal washes, and combined nasal and throat swabs are all acceptable and have higher yield of virus detection than oropharyngeal specimens (throat swabs) alone.
- » For SARI cases, the same specimens as in ILI should be taken. The relative sensitivity of nasal versus oropharyngeal swabs is unknown for SARI. If patient is intubated, endotracheal aspirates or bronchoalveolar lavage (BAL) can be used where clinically indicated
- » It is important to note that if other viruses are being tested in addition to influenza, the optimal specimen type might differ.
- » For RT-PCR, swabs should be collected using swabs with a synthetic tip (such as polyester or Dacron®) and an aluminium or plastic shaft, and should be submitted in viral transport medium. Swabs with cotton or calcium alginate tips and wooden shafts are not recommended.

► Serum

A positive case is a fourfold or greater rise in neutralization antibody titer based on testing of an acute and a convalescent serum specimen. The convalescent neutralizing antibody titer must also be 1:80 or higher. A single serum specimen cannot reliably be used for the diagnosis of seasonal influenza virus infection (3). Collect 3–5 mL whole blood for serologic testing.

TIMING OF COLLECTION

Specimens for the isolation of influenza viruses in cell culture and for the direct detection of viral antigens or nucleic acids should ideally be collected within three

days of the onset of clinical symptoms (4). Acute-phase serum specimens should be taken promptly after onset of symptoms and no later than seven days afterwards. Convalescent-phase serum specimen should be collected two to four weeks later.

STORAGE AND TRANSPORT

Swabs should be collected, stored, and transported using a suitable medium (4). For PCR, if the sample cannot be processed within 48–72 hours, keep it at or below -70°C. Prevent repeated freeze/thaw cycles to maintain RNA integrity and virus viability. Swabs intended for the direct detection of viral antigens by immunofluorescence assay (IFA) should be kept on ice or other coolant at approximately 2–8°C and processed within one to two hours of collection. Specimens should not be frozen except for those sent from remote locations. Specimens may be rejected if they are not kept at 2–4°C (for ≤ 4 days) or frozen at -70°C or below, or if they are incompletely labelled or documented.

For culture, swabs should be placed at 4°C immediately after collection and promptly transported to the laboratory, where they should be inoculated into susceptible cell cultures as soon as possible. If the specimens cannot be processed within 48 hours, they should be kept frozen at or below -70 °C, ideally in liquid nitrogen. In order to prevent loss of infectivity, avoid repeated freezing and thawing.

Sera may be stored at 4°C for approximately 1 week, but should be frozen at -20°C for periods longer than this. The transportation of specimens should comply with current WHO guidance on the transporting of infectious substances. Receiving laboratories in other countries should be notified in advance of specimens being sent to allow them time to arrange an import licence.



LABORATORY TESTING

► **RT-PCR.** RT-PCR has the highest sensitivity for detection and is the minimal recommended test for most laboratories. RT-PCR provides information to:

- » differentiate influenza virus type in symptomatic patients from viral RNA in respiratory specimens or virus culture
- » determine the subtype of influenza A viruses or lineage of influenza B viruses
- » presumptively identify virus in patient respiratory specimens or viral cultures which may be infected with influenza A of subtype H5 (Asian lineage)
- » detect novel or newly evolving influenza A viruses
- » detect antiviral resistance.

► **Viral cultures**

- » Viral cultures are used to complement the findings of RT-PCR, allowing detailed antigenic and genetic characterization of the virus.
- » For labs with resources of both RT-PCR and viral cultures, it is recommended to use a combination of both RT-PCR and virus isolation.
- » RT-PCR-positive specimens can be selected for viral culture for further antigenic and genetic characterization, as well as drug-susceptibility testing if required.

► **Sera.** Haemagglutination (HA) inhibition testing, microneutralization assay and immunofluorescence antibody staining are the tests most commonly done. A four-fold rise in HA antibodies between acute and convalescent sera samples indicates acute infection.

► **Sensitivity and specificity**

- » RT-PCR has high sensitivity and specificity. However, individuals who received nasally administered influenza A vaccine may have positive test results for up to three days after vaccination. Moreover, negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions. Children tend to shed virus more abundantly and for longer periods than adults. Therefore, specimens from adults may have lower sensitivity levels than specimens from children.

- » Positive and negative predictive values are also dependent on influenza prevalence. False negatives are more likely during peak activity when the prevalence of disease is high. False positives are more likely during periods of low influenza activity when prevalence is moderate to low.

ADDITIONAL TESTING

► **Subtype testing.** Subtype testing of confirmed cases of influenza can provide useful information to global decisions regarding vaccine strain composition.

► **Antiviral testing.** Testing of resistance to neuraminidase inhibitors such as oseltamivir or zanamivir can provide useful information (5), including the background rate of resistance in circulating viruses. It can also help with monitoring treatment failures and resistance in high-risk cases.

► **Multiple pathogen testing.** ILI and SARI syndromic surveillance can be used to test for other respiratory pathogens besides influenza. Testing can be done serially, first testing for influenza virus, and if negative, then testing for other pathogens. Alternatively, parallel testing, particularly using multiplex testing platforms, is becoming more common. Take caution in interpreting the presence of pathogens in the non-sterile upper respiratory tract as evidence of etiology of the illness episode. This is particularly true of bacteria that commonly colonize the upper respiratory tract (for example, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*).

SPECIAL LABORATORY CONSIDERATIONS

- Optimum specimen types and timing for peak viral levels during infections caused by a novel influenza A virus have not been determined. The collection of multiple specimens from the same patient may therefore be necessary to detect the virus.
- For Member States that routinely conduct testing, results should be regularly reported directly to FluNet or through regional platforms.
- Viruses found to have resistance to antiviral drugs should be shipped to WHO collaborating centres along with clinical information. If antiviral resistance is detected and confirmed among a circulating viral subtype that is currently predominantly susceptible

to antivirals, it is also important to investigate cases and contacts to determine whether the resistant virus is transmitting human-to-human. If so, this event should be reported immediately through the International Health Regulation focal point of the country.

LABORATORY NETWORKS

Global influenza virological surveillance has been conducted through WHO's Global Influenza Surveillance and Response System (GISRS). National

Influenza Centres (NICs) form the backbone of the GISRS. They collect virus specimens in their country, perform preliminary analyses, and ship representative clinical specimens and isolated viruses to WHO collaborating centres for advanced antigenic and genetic analysis. The results form the basis for WHO recommendations on the composition of influenza vaccine each year, as well as relevant risk assessment activities at WHO.



DATA COLLECTION, REPORTING AND USE

RECOMMENDED DATA ELEMENTS FOR CASE-BASED SURVEILLANCE

- Unique identifier
- Sex
- Age
- History of fever and body temperature at presentation
- Date of symptom onset
- Admitted to hospital and date of hospitalization (for SARI patients only)
- Date of specimen collection
- Exposure to influenza antiviral drugs in the last 14 days. If yes, name of antiviral
- Pregnancy status
- Presence of any chronic pre-existing medical illness
 - » Chronic respiratory disease
 - » Asthma
 - » Diabetes
 - » Chronic cardiac disease
 - » Chronic renal disease
 - » Chronic liver disease
 - » Chronic neurological or neuromuscular disease
 - » Haematological disorders
 - » Immunodeficiency, including human immunodeficiency virus (HIV)
 - » Obesity parameter (body mass index, or BMI)
 - » Tuberculosis
 - » Haematological disorders
- Laboratory testing results: Type of test, result, subtype (if available) and antiviral testing (if available)
- Additional data elements for certain types of surveillance
 - » Patient outcome (death, survival)
 - » Seasonal influenza vaccination status, formulation given (IIV, LAIV), and date of administration
 - » Population of the catchment area for sites doing population-based surveillance
 - » Total number of hospital admissions (if doing SARI surveillance) and outpatient visits (if doing ILI surveillance) by age group

REPORTING REQUIREMENTS AND RECOMMENDATIONS

Apart from novel strains or those with antiviral resistance, individual influenza cases are generally not immediately notifiable to public health authorities. Any case of human infection with a new influenza subtype or with a novel strain needs to be reported immediately to WHO under International Health Regulations. Epidemiological and virological data collected from sentinel sites should be reported to the national health authorities weekly and possibly more frequently in an outbreak or pandemic.

► FluNet

FluNet (www.who.int/influenza/gisrs_laboratory/flunet/en/) collects virological data. The data are provided remotely by NICs and other national influenza reference laboratories collaborating actively with GISRS. These data are also uploaded from WHO regional databases. Public users have real-time access to selected data reports including tables, maps, and graphs at the national level, whereas data providers have full access to all virological information at the national level and by laboratory. The virological data entered into FluNet are critical for tracking the movement of viruses globally and interpreting the epidemiological data reported through FluID.

At the minimum, the following samples should be sent to the WHO collaborating centre (CC) for inclusion in FluNet:

- » viruses that cannot be subtyped locally (these and any new subtype virus should be submitted to a WHO CC as soon as possible for further testing)
- » any virus of a new subtype
- » a representative sample of viruses collected at the beginning, peak and end of each season
- » viruses from particularly severe or unusual cases
- » a sample of viruses isolated from outbreak investigations
- » viruses that are low reactors on the WHO haemagglutination inhibition test.

► FluID

FluID (www.who.int/influenza/surveillance_monitoring/fluid/en/) is the WHO system used to share epidemiological data on influenza on a global level. The system complements the existing FluNet reporting network for virological data. Some WHO

regional offices have created regional data entry tools that link directly with FluID and FluNet and can be used by Member States of those regions. FluID is able to accept data on ILI/SARI and mortality by age group with a consultation or population denominator. It allows near real-time tracking of respiratory disease trends regionally and globally. Summary data collected from FluID is publicly available in graphic form to all Member States through WHO websites. These data are combined with influenza virological data from FluNet.

National aggregated epidemiological data for each age group to be reported to WHO via FluID include:

- » number of new influenza-positive ILI and SARI cases during the week reported
- » number of total new outpatient visits in outpatient clinics where ILI surveillance is being conducted, or the catchment population to the sentinel site, during the week reported
- » number of total new hospital admissions on wards where SARI surveillance is being conducted during the week reported
- » number of ILI or SARI cases sampled during the week reported
- » proportion of ILI and SARI specimens testing positive during the week reported
- » total number of inpatient respiratory deaths during the week being reported.

► International Health Regulations (IHR)

IHR requires that all cases of new subtype human influenza be reported to WHO. Once there is credible reason to believe that an animal or human-animal influenza virus has evolved that is capable of sustained human transmission in a community, the IHR give the Director-General of WHO the authority to determine if the event constitutes a Public Health Event of International Concern. If antiviral resistance is detected and confirmed, it is also important to document through careful investigation of cases and contacts whether or not human-to-human transmission has occurred. If sustained human-to-human transmission of resistant viruses is noted in contexts where the circulating viruses of that subtype have been predominately sensitive, this event should be reported immediately through the IHR focal point of the country.

RECOMMENDED DATA ANALYSES

Minimum data analysis

- The number of SARI/ILI overall and stratified by age; the minimum age groups are < 5 years and ≥ 5 years. However, the following age categories could be used:
 - » 0 to < 2 years
 - » 2 to < 5 years
 - » 5 to < 15 years
 - » 15 to < 50 years
 - » 50 to < 65 years
 - » ≥ 65 years.
- The distribution of SARI/ILI by influenza type and subtype [for example, A(H3N2), A(H1N1) and B] by week
- The distribution of SARI/ILI by etiology, including influenza by week (if testing for other etiologies is routinely done)
- The percentage of SARI/ILI associated with influenza virus (and other respiratory pathogens if tested for), stratified by age
- The percentage of SARI/ILI associated with influenza stratified by week or month of surveillance; typically reporting is more frequent (often weekly) during peak influenza transmission season
- The number of deaths associated with influenza
- Calculation of the above data by year of surveillance

ENHANCED ANALYSES FOR SOME SURVEILLANCE SETTINGS

- Morbidity burden due to influenza-associated respiratory infections and proportional contribution of influenza to respiratory infections (6).
- For population-based surveillance, the rates of ILI and SARI per 100 000 population per year in the surveillance population overall and by age groups. Comparison to historical averages will likely give the first indications of the severity of a pandemic as it unfolds (7).
- Seroprevalence of influenza antibodies in the populations, if serology is being done.

- Spatial differences. Assess the timing of peak influenza activity at the individual surveillance sites in country.
- Case-control study for vaccine effectiveness. The most common method of evaluating vaccine effectiveness is the test-negative control design, which minimizes bias. The test-negative design is described elsewhere (8).

USING DATA FOR DECISION-MAKING

- Monitor the distribution of SARI/ILI cases by age categories to alert healthcare professionals to anticipate disease in clinics and hospitals and to inform disease burden.
- Evaluate the distribution of SARI/ILI by influenza type and subtype to guide vaccine choice and selection of appropriate viruses globally.
- Monitor the disease burden to assess immunization programme strategy, such as timing and type of vaccine.
- Monitor changes in antiviral sensitivity of influenza viruses to inform appropriate use of antiviral therapies.
- Monitor the case-fatality ratio, and if it is high, determine the causes (e.g., poor/late diagnosis, poor case management, poor/late access to care, and underlying conditions).
- Identify the underlying risk factors (co-morbidities) that are associated with severe disease, to improve clinical management and prevention of disease in high-risk patients, as well as to identify those as priority groups for vaccination and treatment.
- Evaluate the distribution of SARI/ILI associated with influenza stratified by epidemiological week and by age categories, to estimate the contribution of influenza to respiratory disease burden nationally and globally, and to establish epidemic thresholds for comparison of disease severity between years and localities.
- Detect unusual events such as outbreaks of influenza outside of the typical season or clusters of vaccine failures, to alert IHR focal points about potential public health events of international concern.



SURVEILLANCE PERFORMANCE INDICATORS

TABLE

1

Surveillance performance indicators for influenza

TIME INTERVAL	PARAMETER	TARGET
TIMELINESS: Describes the success of the programme in meeting targets for several different time intervals in the surveillance and reporting process		
Data reporting from the sentinel site to the next administrative level	Percentage of time that a site achieves target date for data reporting	Individual sites deliver at least 80%* of their reports by the target date
Data reporting from the next administrative level to the national level (if applicable)	Percentage of time that an administrative level achieves targets for timeliness	Individual sites should achieve target date for data transfer at least 80%* of the time.
Shipment of specimens to laboratory	Percentage of time that a site ships specimens by the target number of days after collection	Individual sites ship at least 80%* of specimens within targeted time limit
Date of receipt of specimen in the laboratory until result availability	Percentage of time that a lab has test results available within a target time frame set by the programme	Will vary by lab, depending on capacity; programme should establish time frame and monitor the achievement
Result reporting to health care worker participating in the surveillance system	Percentage of time that the testing facility reports results back to surveillance site within target time frame set by the programme	At least 80%* of the results are reported within target time frame
COMPLETENESS: Monitors both the completeness of sites reporting and the completeness of data entered		
Report completion	Percentage of reports received from each site with complete data	At least 80%* of the reports have all data fields completed
Report transmission	Percentage of data reports that are received	At least 80%* of all sentinel sites deliver every reporting interval
Data collection	Percentage of sampled cases that have data collected	At least 80%* of cases from which specimens are collected have data collected
ABERRATIONS: Any sudden or unexpected change in the observed pattern of the data should be investigated. The following are examples of the kinds of changes that might represent either problems with reporting or a change in behaviour of the disease.		
» Unexpected or sudden increase or decrease in the number of reported cases of SARI and ILI or SARI deaths reported » Unexpected or sudden change in the percentage of specimens testing positive for influenza » Unexpected or sudden shift in the type or subtype of virus detected » Changes in the distribution of risk factors reported » Change in the age distribution of cases reported		

*The use of 80% as a target is arbitrary. Individual countries may want to establish their own more stringent targets.



CLINICAL CASE MANAGEMENT

Treatment of influenza infection includes supportive care such as antipyretics and supplemental oxygen as needed. Antiviral treatment with neuraminidase inhibitors (e.g., oseltamavir, zanamivir, amantadine, and ramantadine)

have been shown to reduce hospitalization and mortality if given early in the course of illness (5). Prophylactic use of antivirals is not recommended due to concerns about resistance development.



CONTACT TRACING AND MANAGEMENT

Contact tracing is not usually done for seasonal influenza. The exception is the detection of a rare or highly virulent strain such as H5N1 or H7N9. In that

case, obtain exposure history and assess and follow up with others at risk. Antiviral prophylaxis of contacts is not routinely used.



SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

DEFINITION OF AN OUTBREAK

There is no standard definition for an outbreak of seasonal influenza, which usually occurs in annual epidemics. The term outbreak is more often used for the appearance of cases of a novel or emerging strain of influenza. A single case of a novel strain should trigger a public health response. Seasonal influenza is usually evaluated as levels of influenza activity (9). Participating countries in FluNet report their influenza activity levels as the following (7):

- **no activity** – no influenza viral isolates or clinical signs of influenza activity
- **sporadic activity** – an isolated case of ILI or laboratory-confirmed influenza cases in a limited area

- **local activity** – ILI activity above baseline levels with laboratory-confirmed influenza cases in a limited area
- **regional activity** – outbreaks of ILI or laboratory-confirmed influenza in one or more regions, with the number of cases comprising less than 50% of the country's total population
- **widespread activity** – outbreaks of ILI or laboratory-confirmed influenza in one or more regions, with the number of cases comprising 50% or more of the country's population.

Alert thresholds are also used to put a seasonal epidemic in historical context, based on average annual incidence (9), and to define the severity in terms of transmissibility, seriousness of disease and impact.

INFLUENZA PANDEMIC

A pandemic is the worldwide spread of a new disease. An influenza pandemic occurs when a new influenza virus emerges and spreads around the world, and most people do not have immunity to that virus. Triggers which should be followed by further investigation are as follows:

- abrupt, unexpected changes in the trend of respiratory disease observed in routine surveillance systems
- clusters of severe respiratory disease or pneumonia in families, work places, or social networks
- an increase in absenteeism in schools or workplace can signal an influenza outbreak
- an unexpected pattern of respiratory disease or pneumonia such as an increase in apparent mortality, a shift in the age group associated with severe influenza, or a change in the pattern of clinical presentation of influenza-associated disease
- persistent changes noted in treatment response or outcome of severe lower respiratory illness
- severe, unexplained lower respiratory illness occurring in healthcare workers who care for patients with respiratory disease
- unusually high levels of sales of pharmaceuticals used for respiratory disease treatment

- respiratory disease in humans that is associated with illness in animals
- outbreaks of death or illness in fowl (domestic fowl or ducks) or other animals (swine, cats, etc.)
- human cases of infection with a respiratory sample that cannot be subtyped, or any influenza virus not currently circulating in human populations.

CHANGES TO SURVEILLANCE IN AN OUTBREAK OF NOVEL OR VIRULENT SUBTYPE VIRUS

Most programmes will need to make enhancements to provide additional critical information in the event of a novel influenza virus with sustained community transmission. These might include the following:

- expanded data collection to include additional risk factors, additional clinical data on signs and symptoms, course of illness, complications and outcome
- admission and discharge diagnoses from severe cases
- additional monitoring of high-risk populations
- specific monitoring of intensive care units (ICUs) and cases requiring mechanical ventilation
- collection of mortality data including cause of death.



SPECIAL CONSIDERATIONS FOR INFLUENZA SURVEILLANCE

ANIMAL SURVEILLANCE

Influenza A, in particular, is a zoonotic virus that infects several animals, including humans, pigs, sea mammals and various bird species (10). While animal influenza viruses do not transmit readily to humans, they can rarely cause disease in humans, either through direct transmission from animals or occasional human-to-human transmission. Some subtypes cause severe disease in humans (for example, H5N and H7N9). Disease in humans from avian influenza usually occurs in the setting of large poultry epidemics. Swine influenza

viruses more rarely can cause human disease from direct transmission. Pigs might also serve as the source of mixed human-animal viruses that can become pandemic strains, as occurred with the 2009 pandemic H1N1 epidemic. The goal of surveillance in animals and birds is to complement the human surveillance network, understand the ecology of influenza viruses that are relevant to human and animal health, detect outbreaks with potential for human spread, and determine the molecular basis of transmission and potential for spread to and between humans.



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