Public Health

Laboratory diagnosis of human infection with avian influenza

Box 1: Definitions of influenza-like illness and severe respiratory illness

Influenza-like illness in the general population is defined as acute onset of respiratory illness with fever and cough plus ≥ 1 of the following symptoms — sore throat, arthralgia, myalgia or prostration — that could be due to influenza virus. In children less than 5 years of age, gastrointestinal symptoms may also be present. In children less than 5 and adults 65 years of age or older, fever may not be prominent.

In addition to the symptoms noted above, patients with severe respiratory illness, including severe influenza-like illness, may have radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome. Patients with severe influenza-like illness may have complications such as pneumonia, acute respiratory distress syndrome, encephalitis or other severe and life-threatening complications.

Source: Health Canada. *Early detection of severe or emerging respiratory infections through severe respiratory illness (SRI) surveillance: SARS post outbreak period / SRI alert period.* Ottawa: Health Canada. Available: www.phac-aspc.gc.ca/sars-sras/pdf/hc-ri-enhanced-surveillance-pop_e.pdf.

Background and epidemiology: Human infection with the Asian strain of avian influenza A (H5N1) virus has heightened our awareness of the potential for the emergence of a pandemic strain of influenza A virus. This Asian strain of H5N1 is highly pathogenic, resulting in severe illness and death in the majority of known human cases.

Avian influenza viruses are classified as low or high pathogenic avian influenza (LPAI or HPAI) viruses on the basis of the severity of illness in birds and genetic characteristics of the virus. Most avian influenza viruses cause only mild or asymptomatic illness in birds, but HPAI virus infections can be rapidly fatal in some species. There are 16 known hemagglutinin (HA) subtypes and 9 known neuraminidase (NA) subtypes of influenza A viruses. Many different combinations of HA and NA proteins are possible, and each represents a different subtype. Although all known subtypes of influenza A viruses can be found in birds, the 3 most prominent are H5, H7 and H9.[1]

The highly pathogenic avian influenza A (H5N1) subtype has now spread to wild and domestic birds in parts of Asia, Europe and Africa. Evidence supports bird-to-human and environment-to-human transmission as well as rare, inefficient, nonsustained human-to-human transmission.[2,3] At the time of writing this article, and according to the classification of the World Health Organization, the current situation is pandemic alert phase 3. This phase is characterized by 2 or more confirmed cases of human infection with a novel virus subtype and no evidence of efficient or sustained human-to-human transmission.

Because infected birds shed influenza virus in their saliva, nasal secretions and feces, direct contact with infected poultry or surfaces and objects contaminated by their feces or secretions is currently considered the main route of human infection. Initial symptoms in humans include fever, cough and other respiratory symptoms. Other symptoms of an influenza-like illness (see Box 1) and diarrhea may be present. The incubation period is usually 2–8 days but may be up to 17 days. Severe complications include acute respiratory distress syndrome, multiple-organ failure and sepsis syndrome.[2,4] The case-fatality rate is high, at 55%–60%.[5]

Specimen collection: Standard and appropriate barrier precautions should always be taken when collecting specimens from patients. Specimens should be obtained as soon as possible after the onset of symptoms (1–3 days). In general, a nasopharyngeal swab or aspirate is considered the preferred specimen for seasonal influenza testing; however, recent data suggest that oropharyngeal and lower respiratory tract specimens (i.e., sputa and bronchoalveolar lavage fluid) are superior to nasopharyngeal specimens for the detection of avian influenza A (H5N1) infection in humans.[2] Specimens from multiple sites may yield the best results. In cases of atypical presentations, such as gastroenteritis and encephalopathy, stool and cerebrospinal fluid specimens, respectively, are advised.[2]

Swabs and transport media intended for bacteriologic testing are not suitable for influenza testing. In addition, swabs with calcium alginate or cotton tips and wooden shafts are not recommended. Swabs for influenza testing should have a dacron tip and an aluminum or plastic shaft.

Specimen storage and transportation: Specimens should be collected in the appropriate viral transport medium and shipped immediately to the testing laboratory (on ice, if possible) in accordance with regulations of the Transportation of Dangerous Goods Act. Specimens may be refrigerated at 4°C (± 2°C) for up to 48–72 hours; after that, specimens should be frozen at −70°C.

Specimen testing: Rapid antigen testing is not currently recommended for the detection of avian influenza A (H5N1): a negative result does not exclude avian influenza,[6] and a positive result of an antigen test (including immunofluorescence methods) does not differentiate between seasonal and avian influenza A viruses. Confirmatory testing and subtyping must be performed by molecular methods (e.g., reverse transcriptase polymerase chain reaction), virus culture or both. Culture of this high-risk pathogen is restricted to certified containment level 3 facilities.[7] All speci-

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mens that test positive for influenza A (H5N1) must be confirmed by the National Microbiology Laboratory or its designate.

Given the increased likelihood of seasonal influenza infections, these guidelines for H5N1 testing in humans should be applied only to patients who have a history of travel, or contact with a traveller, to areas affected by outbreaks of avian influenza[8] *and* a significant clinical and exposure history. The need exists for increased vigilance for the surveillance, recognition, reporting and prompt investigation of patients with severe influenza-like illness or severe respiratory illness (see Box 1).

To establish your patient's risk of avian influenza A (H5N1) infection based on travel and exposure history and for guidance on further actions, contact your local medical officer of health. For additional information on avian influenza testing, contact your provincial public health laboratory.

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Clinical Vistas

Silent menace: septic abdominal thrombophlebitis

A 69-year-old man presented with fever and chills of acute onset without any localizing complaints. He was previously generally well, but had a history of dyslipidemia and benign prostatic hypertrophy. The findings of his examination and laboratory tests were normal, and he was discharged.

He was admitted again after 3 days, during which he felt only lassitude and experienced recurring severe shaking chills. His vital signs were normal except for elevated temperature (38.5°C) and heart rate (103 beats per minute). A meticulous examination again revealed little except for the discovery of a moderate, non-tender enlargement of the prostate. The findings of electrocardiography, chest radiography and abdomi-

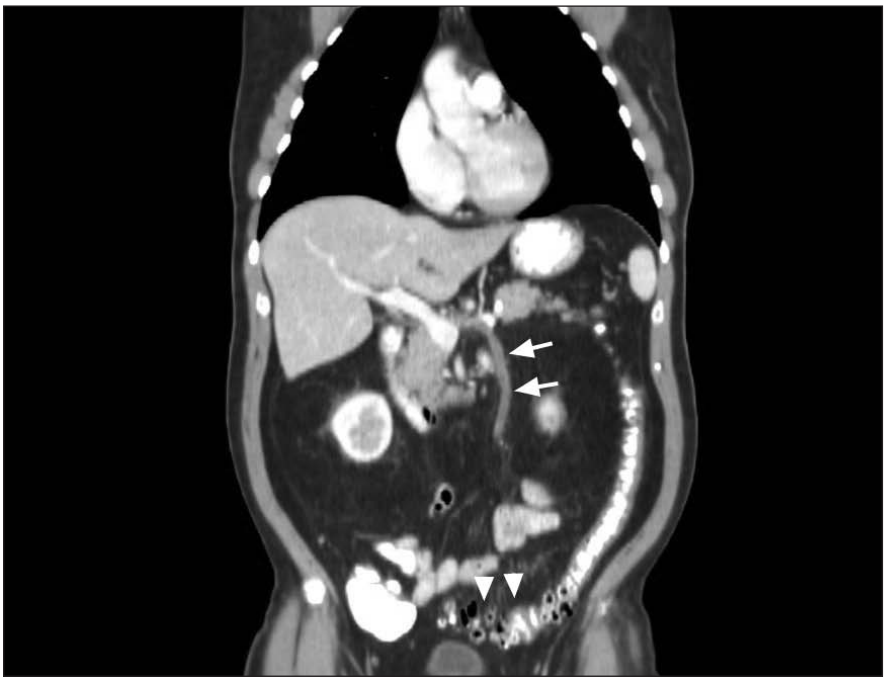

Fig 1: Coronal contrast-enhanced computed tomographic image of the abdomen showing a filling defect within the inferior mesenteric vein (arrows) projecting into the splenic vein lumen with adjacent diverticulosis (arrow heads).

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