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Advice for pathologists and anatomical pathology technologists for autopsy of cadavers with known or suspected new/virulent strains of influenza A

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Comments	This document replaces *Guidance for pathologists and anatomical pathology technologists for autopsy of cadavers with known or suspected pandemic (avian) influenza.* **Professor Carrock Sewell** **Director of Communications**

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There is concern about the procedures to be followed in the mortuary if and when there is a request to examine the body of a person who is known or suspected to have died from unusual or novel strains of influenza. The H5N1 strain has caused many deaths in Asia this century. Currently there is concern about a pandemic being caused by swine influenza (H1N1), but it is possible that a further novel influenza virus may give rise to a pandemic. Anatomical pathology technologists (APTs) and pathologists are front line clinical staff in this context.

Although no one knows if there will be a pandemic, in the event of one the Dept of Health and Health Protection Agency (HPA) estimate the likely excess mortality in the UK to be at least 50,000 deaths[1]. The most critical cases will be those occurring early on during an epidemic; once health professionals become proficient at making a clinical diagnosis, the need for confirmatory in vivo laboratory and autopsy diagnosis will diminish. Any such early autopsied cases can potentially provide significant information for clinical pathology and epidemiology.

The Dept of Health, with HPA, has produced guidance[1,2], which includes much useful background information, as well as specific protection advice for those health care workers who may be exposed to aerosols containing the influenza virus - eg in critical care, and during an autopsy examination.

Autopsy pathology

There is now a considerable literature on the pathology, pathogenesis and virology of fatal human cases of avian H5N1 influenza, including a comprehensive account with full literature citation[3]. There is no published information, as yet, on the pathology of H1N1-related fatalities.The key histopathological features include:

- acute lung injury (diffuse alveolar damage);
- lymphopaenia in lymph nodes and spleen;
- haemophagocytosis in lymphoid organs and bone marrow.

The sites where virus can be identified by immunohistochemistry (IHC) and virological molecular diagnostics are:

- lung;
- intestines;
- lymph node lymphocytes;
- blood.

1. Location of the autopsy

The HPA document on the management of unusual illnesses of infectious aetiologies[4] refers to where autopsies are performed. These influenza autopsies can be performed in any suitably equipped mortuary where the APT and pathology staff are practised and comfortable in performing infectious high-risk cases (Hazard Group 3 – see below).
If this influenza infection is first suspected during the actual autopsy procedure, it is safer to continue with the examination, using appropriate protection, than to have the opened cadaver transported, potentially leaking, to another more specialised autopsy location.

2. Personal protection

The influenza A viruses are generically categorised (by the Advisory Committee on Dangerous Pathogens (ACDP)) in Hazard Group 2. However, when a new strain is identified (eg new strains of H5N1 or H1N1) these are categorised as HG3, and the appropriate health and safety precautions apply.
Standard universal precautions for autopsy work (scrub suit, complete cover gown, apron, gloves with cut-resistant undergloves, visor eye protection) pertain. The critical issue concerns respiratory protection for those exposed to aerosols of virus.

Respiratory protection
The recommendation is for a FFP3, disposable or re-usable, respirator. This is not a powered, ventilated-visor head set, but a face mask that fits tight. It is widely available through NHS equipment providers. Several mortuaries already use them as routine face protection for all cases. It is appropriate as protection for viruses (as well as bacteria), but is not protection against chemical toxins.
[The Nov 2007 Guidance on infection control cites HSE advice that a powered respirator should be used. As aerosol-exposed health care workers in critical care units are advised to wear FFP3 masks, not powered respirators, the 2007 advice is not followed here. The Dept of Health is aware of this approach].

Drug prophylaxis
Oseltamivir ('Tamiflu') has been proposed as a treatment for and prophylaxis against swine/avian influenza. Pathologists and APTs should consult with the local occupational health unit whether this drug is appropriate for those exposed in a mortuary setting.

Vaccination
If and when a vaccine against avian/swine influenza becomes available, front line health staff including those who work in mortuaries should be vaccinated via local occupational health units.

3. Specimen sampling

To establish the diagnosis of swine/avian influenza if suspected at autopsy, or to confirm a previously suspected case, the correct samples need to be taken. The HPA has issued guidance for autopsy diagnosis for unusual illnesses from chemical, radiation and biological agents, with emphasis on the agents likely to be used in bioterrorist attacks[4]. Although it did not specify avian/swine/ pandemic influenza, the sample protocol is broadly appropriate for these infections.

The **fresh tissue** samples for the **microbiology departments** include:

- lower airways and lung tissue;
- lymph node (not spleen);
- distal small bowel;
- peripheral whole blood.

These samples are sent in sterile containers, without medium, labelled according to site of origin. As with other high-risk samples, they must be placed within a sealed plastic bag with appropriate sticker.

HOWEVER, experience since the swine influenza epidemic started in the UK has shown that raw tissue samples are NOT the optimum or cost-effective means of establishing the viral infection.
Nasopharyngeal swabs (ie long swabs that are snapped in half after sampling and placed in viral transport medium) are the practical diagnostic procedure. These are the same as used to make the diagnosis in vivo. Two swabs per case are used:
1. to sample the nasopharynx, via the nose, on both sides; this is done before the autopsy dissection
2. to sample to bronchi when the lungs have been removed from the body.

The swabs are analysed on automated PCR machines.

Until there are specified centres for such virological investigations, the specimens go to the usual virology dept, and their networks will function to provide the optimum diagnostic service.

For **histopathology**, with **formalin fixation**, a standard set of samples should comprise all the major organs (including intestine[3,5], and must include lung, trachea and bronchus. Recommended minimum sampling:

- central (hilar) lung with segmental bronchi;
- right and left primary bronchi;
- trachea (proximal & distal);
- pulmonary parenchyma from right and left lung;
- vertebral bone marrow;
- hilar lymph nodes;
- any other organ that indicates a possibly relevant co-morbidity.

Immunohistochemistry for these influenza viruses is not widely available at present, but may become important and complimentary to virological diagnostics if there is a progressive pandemic.

A common mode of death in pandemic influenza is secondary bacterial pneumonia following the viral pneumonitis with ARDS, but other organs are also affected. Haemophagocytosis is particularly noted, and may be a factor that determines the outcome in young subjects.

Co-morbidities (eg ischaemic heart disease, stroke and chronic obstructive airways disease) will also be relevant in determining whether patients, particularly the more elderly, survive or not, and need to be documented.

4. Communication concerning the autopsy and resultant diagnosis

The HPA document indicates the relevant people and authorities who will be concerned - depending on the location of the death. They include the senior clinician in the case, the Trust Pandemic Influenza Lead, the coroner, the local Occupational Health Consultant or Consultant in Communicable Disease Control (CCDC). A list of potentially exposed staff in the mortuary should be kept[4].

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References

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3. Korteweng C & Gu J. Pathology, molecular biology and pathogenesis of avian influenza A (H5N1) infection in humans. *Am.J.Pathol* 2008, **172**: 1155-1170
4. *Initial investigation and management of outbreaks and incidents of unusual illnesses. A guide for histopathologists and APTs*. Health Protection Agency. Version 4.0, Nov 2007. www.hpa.org.uk
5. Uiprasertkul M*, et al*. Influenza A H5N1 replication sites in humans. *Emerg Infect Dis* 2005; **11**, issue 7.

Checklist for pathologists

Is the autopsy a coronial/medico-legal or consented case?

If coronial, has the coroner agreed to the microbiological and histopathological investigations?

Is the autopsy complete or limited? If limited, what organs were not examined?

Check the samples to microbiology:

- lower airways and lung tissue;
- lymph node (not spleen);
- small bowel;
- blood.

Which microbiology dept did these samples go to?

Check the samples for histopathology:

- central (hilar) lung with segmental bronchi;
- right and left primary bronchi;
- trachea (proximal & distal);
- pulmonary parenchyma from right & left lung;
- vertebral bone marrow;
- hilar lymph nodes;
- any other organ that indicates a possibly relevant co-morbidity.

Are there significant co-morbidities in lungs and other organs? If so, note them.

With all the microbiology and histopathology results returned, what is the cause of death sequence?

Was swine/avian influenza the main cause of death?

If not, what was the main cause of death?

Has the CCDC been sent a copy of the autopsy report if influenza was the cause of death?

Has the coroner received the final autopsy report?