



Centers for Disease Control and Prevention Case Studies in Applied Epidemiology

Influenza A(H5N1) in Humans: Outbreak Investigation Part 2 (International Setting)

Facilitator's Guide: September 15, 2008

Learning Objectives

After completing this case study, the participant should be able to:

- ❑ **Describe key outbreak management issues** that need to be addressed related to supplies, team composition, WHO policy and epidemiologic data management during an internationally located A(H5N1) outbreak investigation.
- ❑ **List appropriate practices and procedures related to each of the following:** specimen collection and transport, epidemiologic investigation, identification of transmission mechanisms, contact tracing, isolation/quarantine policy, treatment/control policy, risk communication priorities, recommended laboratory specimen protocols methods, and ethical considerations.
- ❑ **Identify critical coordination priorities** involving the interface between animal and human health sectors, key stakeholders such as WHO, CDC and Ministries of Health and communication processes between CDC field staff, CDC Headquarters and relevant subject matter experts.

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service



JULY 17:

The hospitals in Dava Ghar and Pelu Jaghai both have suspected or probable cases of influenza A (H5N1) in their wards. Understandably, the hospital physicians and nurses are concerned about health care worker safety. You review infection control practices, respiratory hygiene and worker safety issues with the staff doctor.

Question 18—Estimated Time: 15 Minutes

What specific advice about infection control would you provide to the hospital?

Note: The guidance described below is taken from the WHO Avian Influenza Interim Infection Control Guideline for Health Care Facilities, 10 May 2007.

http://www.wpro.who.int/NR/rdonlyres/EA6D9DF3-688D-4316-91DF-5553E7B1DBCD/0/AI_Inf_Control_Guide_10May2007.pdf

- **Standard precautions should be practiced at all times.**
 - Is there constant use of gloves and hand washing (plus face-shields, masks, eye protection, or gowns if splashes are anticipated) for any contact with blood, moist body substances (except sweat), mucous membranes or non-intact skin?
 - Are gloves removed and discarded immediately after completion of a task, and hands washed every time gloves are removed?
 - Are appropriate administrative policies and practices in place; for example, posted signs, available hand sanitizers, tissues, and waste receptacles in clinic waiting rooms and emergency departments?
 - Is staff educated in respiratory hygiene and cough etiquette?
 - Is cohorting or spatial separation (ideally > 3 feet) of persons with respiratory infections being implemented?

- **Contact and droplet precautions should be implemented during routine care of suspected/probable/confirmed influenza A (H5N1) cases.**
 - Is there a private room or room shared for all influenza A(H5N1) cases?
 - Does staff wear disposable gown and gloves when entering the patients' rooms?
 - Are disposable gown and gloves removed and discarded inside the patients' rooms?
 - Are hands washed immediately after leaving the patients' rooms?
 - Is the patient's room cleaned daily using a hospital disinfectant, with attention to frequently touched surfaces (bed rails, bedside tables, lavatory surfaces, blood pressure cuff, equipment surfaces)?
 - Is there use of disposable equipment or patient-dedicated use of such equipment if possible (e.g. blood-pressure cuffs, stethoscopes)?
 - Are a face shield or goggles, and a surgical mask (not N-95) worn to prevent droplets from reaching the mucous membranes of the eyes, nose and mouth when within 1 meter of the patient?
 - Does the patient wear a surgical mask when outside of the patient room?

- **Airborne precautions should be implemented whenever performing aerosol-generating procedures on influenza A (H5N1) cases.**
 - Are aerosol-generating procedures being undertaken in an airborne infection isolation room?
 - This is a single-patient room equipped with special air handling and ventilation capacity that meets specific standards. This may be improvised to create negative pressure in low resource environments. If the facility has no negative air pressure rooms, negative pressure can be engineered by installing an exhaust fan and directing air from the inside of the room to an outside open area with no person movement. If the facility has no air conditioning, consider opening windows in isolation areas (but keep doors closed).
 - Is there a surgical mask on the patient?
 - Do personnel inside the negative pressure room wear a N-95 particulate respirator (or higher)?
 - Is isolation room air not re-circulating in the building?

KEY POINTS: Available evidence suggests that transmission of human influenza viruses occurs through multiple routes including large droplets, direct and indirect contact, and droplet nuclei. However, observational studies conducted in health-care facilities suggest that droplet transmission is the major mode of transmission in that setting and standard precautions plus droplet precautions are recommended for the care of patients infected with human influenza.

Currently, no sustained efficient human-to-human transmission of avian influenza A H5N1 is known to have occurred, and there is no evidence to suggest airborne transmission from humans to humans. These transmission properties may not apply to a future pandemic virus. WHO Guidelines do, however, recommend that Airborne precautions should be implemented whenever performing aerosol-generating procedures on suspect, probable or confirmed cases.

You are intrigued by the possibility that there may be a possible epidemiologic connection between this 11 year old boy (TMU) in Pelu Jaghai and the 10 year old boy (AAJ) in Dava Ghar through a potential Murg market exposure. Through additional interviewing you also learn that the two boys played a local children's' game—'hu-tu-tu' called 'chasing after the chicken'—at the live-market. During this game they enjoyed chasing what appeared to be a very "slow and unsteady" chicken. You oversee the appropriate collection and transport of respiratory specimens from this 11 year old (TMU). You get the history that it was the uncle (JRO) of the 10 year old (AAJ) who took him to the live-market.

You return to Dava Ghar on the late afternoon of the 17th, tired and anxious that there are possibly other suspected cases of influenza A(H5N1) that you are missing.

JULY 18:

On the morning of the 18th, you go with the staff doctor to make rounds on the ward to see the grandmother (JAM) and to conduct active case surveillance for any interim cases of respiratory illness. You find that she is coughing copious amounts of yellow

sputum with occasional hemoptysis; and though she is laboring to breathe, she is not progressing to respiratory failure. She is still in isolation; you are given the results of the laboratory testing of specimens and much to your relief, the results are negative for influenza A(H5N1). One of her sputum specimens was positive for Acid Fast Bacilli. Her chest x-ray, which you had not been able to see initially, now shows evidence of an upper lobe cavitory lesion.

As part of the team’s daily updates, you are also told that the grandfather now has been documented to have a new fever and complaints of myalgias. Being frail and very anxious about JAM’s condition, he hadn’t really ventured out of her hospital room. He wore an N-95 respirator nearly all of the time he sat by her bedside. He has concomitant congestive heart failure due to hypertension (chronic). Though he had been already been started on chemoprophylaxis with Oseltamavir, his clinical status is rapidly worsening. He is hospitalized.

Later on the 18th, you intend to get your team members together and create a more detailed summary of the ‘cases’ to date and to tally any data that they have acquired from their active case surveillance efforts. Your team also informs you that the throat swab specimen from the 11 year old child (TMU) is positive for H5 influenza by real-time RT-PCR.

A cloacal swab from the (now deceased) infected chicken that was collected during a parallel Ministry of Agriculture investigation has also tested positive for H5 influenza. The Murg market is closed until further notice. A radius for culling and surveillance has been created around its perimeter and active surveillance for illness among poultry is underway on source farms. Both the probable case (AAJ) and the confirmed case (TMU) have been reported to WHO which is mobilizing resources to assist in the investigation.

Question 19—Estimated Time: 5 Minutes

Update the line list - as of July 18th p.m.

KEY POINTS: As of July 18 p.m. this line list shows the grandfather (AWM) is now ill. Given his exposure to the index case at the family vigil (and not due to his exposure to JAM), AWM can now be considered a suspect CASE. Also, the grandmother (JAM) has TB, and not influenza A(H5N1) infection; so she actually becomes a ‘CONTACT’. The 11 year old boy (TMU) at Pelu Jaghai hospital is the first confirmation of influenza A(H5N1) infection. Moreover, it should be noted that it seems more likely that he did not acquire the infection from his playmate (AAJ) at the live market but rather had an independent exposure to the infected chicken while they played the ‘hu-tu-tu’ game.

As you take a short walk to collect your thoughts you receive an urgent message on your cell phone from the Director of Epidemiology. He has just been notified that a reporter from the regional newspaper is pursuing a story on the ill patients in the

adjacent province. Somehow the reporter has learned of the ‘potential’ exposure at the July 8th live-market and wants to write an article notifying the public. The Director of Epidemiology repeatedly states that he wants to talk directly with the reporter and maybe even conduct a press event. He asks you for a list of talking points’ to share with the Public Information Officer (PIO) who works with the MOH.

Question 20—Estimated Time: 10 Minutes

What are three communication messages that could be used to provide the public an update of the current situation? What needs to be conveyed in these messages?

- **“Empathy and understanding”**. The Pegu Government understands the concern that the public must feel about this situation. We will give you regular updates. Here are the facts we know to date:
 - One laboratory confirmed case of influenza A (H5N1) “bird flu” (in an 11 year old boy) has been identified in Pelu Jaghai.
 - Another 10 year old boy who died in Dava Ghar is considered a probable case.
 - Both were playing with a chicken at the Murg Market in Pelu Jaghai that has been confirmed to have been infected with Influenza A (H5N1) “bird flu”.
- **“We are working on this”**. An official investigation, involving collaboration between the Pegu MOH, Ministry of Agriculture, and the World Health Organization is underway.
 - It’s early in our investigation and the complete scope of the infection among humans is unknown at this time
 - There is currently no evidence of widespread infection or human to human transmission.
 - The Murg Market is closed until further notice and we continue to actively search for additional human and animal cases.
- **“What you can do”**. The Government of Pegu is committed to identifying the extent of this outbreak and rapidly controlling it. You can help!
 - Wash your hands after contact with poultry or other birds.
 - Cook all poultry and poultry products well before eating.
 - Don’t let your poultry mingle with other birds, keep your birds confined to avoid exposure and contamination.
 - If you have a fever and sore throat and you have been around sick or dying birds, notify your village health volunteer.
 - Do not eat any bird that was sick or dying before slaughter.
 - Immediately report any ill or dead poultry to the toll-free hotline at +01-65-244-675
 - For more information about this investigation, or to report suspected cases of influenza A (H5N1) in humans or animals, please do not hesitate to contact the Pegu Public Information Officer at +01-65-244-675.

Question 21—Estimated Time: 5 Minutes

Who are the specific people that must receive regular situation reports from your team? How might this change based on who you are deployed with?

- The Ministry of Health will be the final authority on reporting channels and chain of command in their country. The MOH will share situational updates with the WHO IHR focal point in the country office.
- Any CDC person that is serving as a short term consultant to WHO must also communicate through the WHO chain of command. Permission must be received from WHO to share official information with its external partners such as CDC.
- If deployed by CDC, then one can report to CDC under the auspices of the MOH.

Question 22—Estimated Time: 15 Minutes

What are the essential components of a situation report?

Instructions: Brainstorm these key categories with the team. For the purposes of time do not have the group fill out a situation report.

Rapid Response Team Daily Situation Report

Date: July 18th, 5pm

Location: Dava Ghar Province, Pegu

1. Rapid Response Team Composition

2. Surveillance/Epidemiology

2a. Update on human cases

There is 1 Confirmed Human Case of Influenza A (H5N1):

As of 18 July there is one confirmed human case of Influenza A(H5N1). This is in an 11 year old boy from Pelu Jaghai. This boy had a symptom onset date of July 12 and had contact with an “unsteady chicken” at the Murg Market on July 8th.

There is 1 Probable Human Case of Influenza A (H5N1):

A 10 year old playmate of the confirmed case who lived in Dava Ghar also had contact with the same chicken at the live bird market on July 8th, died of respiratory illness on July 16th, and was buried by his family before specimens could be collected. This 10 year old decedent remains classified as a probable case.

There is 1 Suspected Human Case of Influenza A (H5N1):

The grandfather of this 10 year old child is now currently hospitalized in Dava Ghar with fever, shortness of breath and myalgias and is also classified as a suspected case.

2b. New cases and changes in classification since the last report

1) Since the last report at 5pm on July 16th, the 11 year old boy from Pelu Jaghai has received PCR confirmation of H5N1 infection and his status has been changed from a “probable case” to a “confirmed case” according to the WHO case classification.

2) On July 16th The grandmother of the 10 year old probable case from Dava Ghar was classified as a “person under investigation”. Since that time her respiratory symptoms have been confirmed to be the result of active tuberculosis and she is now classified as a “contact” below.

3) The grandfather of this 10 year old child is now currently hospitalized in Dava Ghar with fever, shortness of breath and myalgias and is also classified as a suspected case rather than as a contact.

2c. Contacts and exposed persons being monitored

Four contacts are currently being closely monitored for symptoms and are under voluntary quarantine. These contacts include:

1) The grandmother of the 10 year old decedent (probable case from Dava Ghar) that is known to also have active tuberculosis.

2) The mother of the 10 year old decedent (probable case from Dava Ghar), who also attended the live bird market on July 8th

3) The uncle of the 10 year old decedent (probable case from Dava Ghar), who also attended the live bird market on July 8th.

4) The mother of the confirmed case from Pelu Jaghai, and his caretaker while ill.

Workers from the poultry farms and owners of backyard flocks that provided birds to the Murg Market are under surveillance for fever or respiratory symptoms. They are also under voluntary quarantine for 7 days. These flocks were identified through an ongoing joint MOH/MOA investigation.

2d. Update on human surveillance

Active surveillance for suspected human cases is being undertaken in all health care facilities in Pelu Jaghai and Dava Ghar provinces. Active surveillance for fever and respiratory illness is also being undertaken among poultry workers and backyard flock owners that supplied birds to the Murg Market. Door to door active surveillance is being undertaken every other day by local health workers in the villages of the confirmed and probable cases. The community health workers and local health care providers are receiving refresher training in human case definitions and appropriate reporting channels.

2e. Evidence of human-to-human transmission

To date there is currently no evidence of sustained human to human transmission.

3. Pending laboratory results

No clinical specimens could be obtained from clinical specimens taken from the 10 year old probable case from Dava Ghar prior to his burial. RT-PCR analyses confirmed H5N1 infection in the 11 year old child from Pelu Jaghai. Oropharyngeal and nasopharyngeal swabs collected from the grandfather of the probable case from Dava Ghar have been sent to the National Laboratory and are pending. All specimens have also been forwarded to the WHO reference lab for diagnosis of Influenza A/H5N1.

4. Clinical management/Infection control

Non-hospitalized contacts have been advised to remain at home for 7 days after their last contact probable or suspected case. The hospitalized contact is in isolation and has been started on prophylaxis with a neuraminidase inhibitor given her underlying active tuberculosis. Non-hospitalized contacts have been educated about risk factors/risk behaviors of exposure, and the signs/symptoms of AI illness. All contacts have received instructions on how to self-monitor for fever post-exposure. During this period,

contacts have been instructed to stay at home voluntarily. If contacts have fever, they have been told to immediately report their symptoms to health authorities and/or the RRT and remain in voluntary home quarantine. All probable and confirmed cases are currently in isolation and are receiving treatment doses of neuraminidase inhibitors.

5. Update on animal health and surveillance

The animal health representative to the RRT has undertaken several field visits in Dava Ghar and Pelu Jaghai Provinces to investigate the occurrence of illness among birds and: To date he has inspected:

- the case patient's home and its surroundings, backyard poultry areas
- local poultry farms (commercial or backyard farms) near the case patient's home
- local places frequented by wild birds (e.g. lakes)

The live bird market has been closed. Farms providing poultry to the market and all farms within a 10 mile radius of the Murg market are under active surveillance by the Ministry of Agriculture. Respiratory and cloacal specimens are being collected from samples of well birds and all birds with signs of illness. Specimens are being sent to the National Animal Health Laboratory.

6. Planned activities

The team plans to visit (or telephone) each contact daily for at least 7 days following a known exposure to a suspected, probable or confirmed H5N1 case. Investigation and contact tracing will continue and all suspected cases will be reported to the appropriate authority.

Efforts to identify additional cases beyond close contacts will focus on:

- persons who may have been co-exposed to the same source as the case patients
- persons with bird and animal exposures (see section 2)
- clusters of socially and geographically linked persons with respiratory illness
- persons with unexplained severe acute lower respiratory infection with fever

7. Requests for assistance and resources

Request policy on recommendation for prophylaxis of attendees at live bird markets with stated exposure to sick or dying birds.

8. Other

You may want to include your epidemiologic curve and line listing here but take care to maintain the confidentiality of the cases under investigation. In addition, issues you may want to discuss here are the recent press conference, security, and other concerns.

Now that you have handled these media coverage and reporting issues, you return to the team on the late afternoon of July 18 to summarize the investigation to date as you had originally planned. Instead your team says that there is a problem that has arisen with some of the family members of the little boy (AAJ). You are told that the mother (NJC) and the uncle (JRO) are the only exposed persons to date who have refused MOH attempts to implement a voluntary quarantine. Although they both report feeling "weak and tired with aches", they have no other symptoms.

Question 23—Estimated Time: 7 minutes

If a person with known exposure to a confirmed human case of Influenza A(H5N1) refused to accept voluntary quarantine, how would you respond ?

This is another decision that must ultimately be made by local authorities. The goal of quarantine is to protect the public by separating persons exposed to a communicable disease from the general population. It is based on utilitarian concepts of protecting the common good (the greatest possible good for the greatest number of individuals). Imposition of quarantine or other liberty limiting measures needs to be balanced with protection of individual rights, such as the protection of quarantined individuals' privacy, protection against stigmatization, and avoidance of unequal burden being placed on specific individuals or groups. Whenever possible, voluntary measures should be used.

KEY POINT: Review that quarantine is for asymptomatic persons and isolation is for symptomatic persons. The following points might help you to provide advice in the current situation. Ethical justification of quarantine or isolation requires that:

- 1)** There must be a possibility of person-to person spread of disease and the necessity of quarantine as a containment measure.
- 2)** The least restrictive measures proportional to the goal of achieving disease control must be used. Voluntary quarantine should be used before more restrictive measures are enacted.
- 3)** Society must be able to provide necessary support services for those in quarantine (e.g., provide, food, water, household and medical supplies, etc) and to ensure the long-term psychological impact and stigmatization of persons quarantined or isolated is minimized.
- 4)** Public health officials must communicate clearly the justification for their actions and allow for a process of appeal (transparency principle).
- 5)** Quarantined individuals should be closely monitored to detect onset of symptoms. Those with symptoms should be moved to isolation or a cohort of symptomatic persons in order to ensure that other persons placed under quarantine are not put at increased risk.

You personally visit NJC and JRO, who finally agree (with the help of local religious leaders) to a voluntary home quarantine. They have now become more concerned over their own health and promise to self-monitor for presence of fever. When you again ask NJC of any other family members who may have been around the 10 year old (AAJ), she now tells you that there is one 19 year old brother (DKS), who is a university

student in the city of Anawrahta. He came to town just to take care of his little brother during the family vigil on July 12-13. He had gone back on the 14th for exams.

JULY 19:

You are awoken late at night to learn that the 11 year old boy (TMU) is intubated. You are also surprised to hear that the mother (NJC) of the boy who died (AAJ), and AAJ’s uncle, (JRO) have now been admitted to the hospital with cough, fever, shortness of breath, and signs of pneumonia noted on chest x-ray. Additionally the mother also had myalgias, diarrhea and mild sore throat. NJC reports that her symptoms worsened dramatically at 3 am on July 19th. JRO began to fell ill 10 hours later while taking care of NJC.

NJC provides more history that she in fact did care for her boy while he was sick at home; she recalls she and her parents (JAM and AWM) were close by the boy during the 48 hours prior to his admission to Dava Ghar Provincial Hospital.

JULY 20:

You begin the day getting updates from the MOH team. You are also told that the 19 year old student sibling (DKS) now has fallen sick (onset of symptoms – July 20th) – with fever and cough. He returned to his home province because he was not feeling well. He strongly denied having attended any live-markets and any contact with dead or ill poultry as he was either at his brothers bed-side, or at school.

Later that morning you receive word that the grandmother (JAM) was released from the hospital, but the grandfather (AWM) has died with multiple complications, including renal failure, encephalitis and ventricular arrhythmias. You are not surprised to learn that he died of Influenza A (H5N1) infection – as confirmed from the PCR testing.

Question 24—Estimated Time: 5 Minutes

Update the line list - as of July 20th afternoon

KEY POINTS: As of July 20th, this line list shows that the grandfather (AWM) has died and confirmed to be an A(H5N1) CASE. This provides additional evidence that AAJ also likely dies from Influenza A(H5N1) infection. In the interim, the mother (NJC) and the uncle (JRO) of the “index” case (AAJ) have been hospitalized as probable cases, and a 19 year old sibling of AAJ who is a student from out-of-town (DKS) is also hospitalized as a suspect case.

You don’t have the appetite given all the tension but you manage to eat a bowl of rice and vegetables. Before you finish you are approached by some scared health care workers (HCWs), including the respiratory technician (HCW-RT) on duty when the 10 year boy (AAJ) who died. He reports having worn PPE but he states he “felt droplets

touch his face”. He is now running a fever and is very worried. Additionally there are two other HCWs who are demanding something be done about their potential exposure to the virus. There was a nurse (Nurse #1) who took care of the grandfather’s body during the last hour of his life and helped in taking care of the body post-mortem. She is unsure if she wore all of the required PPE at all times. There was also a traveling nurse (Nurse #2) who recalls how scared she was even though she had adhered to contact and droplet precautions when briefly taking a meal tray into the grandfather’s hospital room.

Question 25—Estimated Time: 7 Minutes

The respiratory therapist who took care of the 10 year old (AAJ), Nurse #1 who treated the grandfather (AWM) and handled the body post-mortem, and Nurse #2 who brought the grandfather a meal all request antiviral therapy. Assuming Oseltamivir is available, who do you recommend should receive antiviral therapy and at what doses?

The recommendations below are based on the *WHO Rapid Advice Guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus*

http://www.who.int/csr/disease/avian_influenza/guidelines/pharmamanagement/en/index.html

1) Respiratory Therapist (HCW-RT): The respiratory therapist was likely involved in high-risk procedures, at a stage when he didn't know that the patient was likely to have influenza A(H5N1). There may have been a breach in his PPE based on his report that he felt droplets touch his face. He also has a fever and should be considered for empiric treatment with neuraminidase inhibitors. The recommended dose of Oseltamivir for the treatment of influenza, in adults and adolescents 13 years of age and older, is 150 mg per day, given as 75 mg twice a day for at least five days. Oseltamivir is not indicated for the treatment of children younger than one year of age. The respiratory therapist should undergo appropriate diagnostic testing.

2) Nurse # 1: The nurse who attended to the grandfather and took care of the body may have had exposure to infectious aerosols and secretions and should receive prophylaxis doses of Oseltamivir given as 75 mg once per day for 7 days (or up to 10 days) after the last exposure. She should self-monitor her temperature twice daily and report any febrile event to a designated contact.

3) Nurse # 2: The nurse who took the meal tray into the grandfather's room likely had no significant exposure and cannot be considered a close contact given the transient nature of the visit. She should not receive prophylaxis doses of Oseltamivir. In order to comfort her she could also be asked to self-monitor temperature twice daily and report any febrile event to a designated contact.

KEY POINTS: It is important to point out that anti-virals are not infallible and there is little data on their efficacy. *Consistent and appropriate use of PPE is the first line of defense against infection.*

Later that evening (July 20th), your colleagues return from Pelu Jaghai having completed their case investigation and contact tracing. You learn that DKS now has radiographically confirmed pneumonia. The two teams find a room in the hospital to update their line lists and review all of the epidemiologic data.

The complete line listing for these cases and contacts as of July 20th evening: should be provided

Question 26—Estimated Time: 20 Minutes:

Make an epidemic curve of the cases as of July 20th evening. What can be learned from the epidemic curve?

Note: For those in the group who have never made an epidemic curve, get a volunteer to draw the curve of suspect, probable and confirmed cases and to then describe its axes. Coach this person to add arrows that indicate the two known exposure locations (the Murg Market , and the start and end of the 48 hour vigil) on the X-axis.

Provide completed curve to the group after this is completed for further

EXPOSURE:

Notice that besides showing the number of cases, the two far left arrows on the timeline indicate the two potentially different exposure sources:

- The live-market on July 8th. This could represent a predominantly zoonotic exposure to influenza A(H5N1).
- The family vigil, lasting almost 48 hours from July 11-13th. This could represent a exposure to an infected human.

CASE BY CASE FINDINGS:

- The 10 year old boy who died (AAJ) was likely infected with A(H5N1) at the live-market
- 11 y/o (TMU) is within plausible incubation period for exposure at live-market and likely did not acquire the infection from the 10 year old playmate (AAJ).
- When considering the epidemic curve in the context of known exposure histories, the following interpretations can be made regarding mode of transmission for additional cases
 - The mother (NJC) may have been exposed at the live-market although that incubation is outside the normal range for to Influenza A(H5N1) (11 days). She more likely became infected as a result of close contact with her son (AAJ) which would make her incubation period a more plausible 6-8 days.
 - The grandfather (AWM) was likely exposed to A(H5N1) as a close contact

- with his grandson (AAJ) as he had no reported poultry exposure
- The uncle (JRO) was likely exposed to A(H5N1) at the live-market event, but his symptom onset was 12 days after that reported exposure. However he could possibly have been infected by NJC whose symptom onset was one day earlier than his. He was reportedly not around the boy (AAJ) after the boy’s onset of symptoms. He may also have an as yet to be determined alternative source of exposure.
 - The 19 y/o (DKS) may have been infected at the time of the family vigil.

In a real-life situation, there may well be many more individuals who could have been exposed to A(H5N1) (e.g., at the live market event, occupational exposures etc...), and many more possible exposures to consider.

Update:

Over the next several days, the mother (NJC), the uncle (JRO), and the 19y/o (DKS) are all confirmed positive for Influenza A(H5N1) by RT-PCR and specimens are sent to a WHO H5 Reference laboratory. You also learn that all of the remaining individuals who were considered ‘contacts’ tested negative for influenza A(H5N1). The respiratory therapist tested positive for Influenza A(H3N2).

Question 27—Estimated Time: 20 Minutes

Make a graphical representation of the cases with known onset dates, sources of exposure and incubation periods. Using this and the WHO criteria for determining human-to-human transmission, make an assessment of the likelihood that each case was infected via human-to-human transmission?

NOTE: Coach the class through making this graphic. After discussion, provide the example graphic included with the final line-listing. Then create a column on the case line list called “human-human transmission”. Label each case as “likely”, “not likely”, or “possible” using the WHO criteria mentioned below, the graphic, and the final line-listing.

There is an uncertain risk of human-to-human spread of avian influenza. Suspicion of human-to-human transmission is increased when the time of onset between two cases falls within a single incubation period (~2 to ~7 days), and when no alternative source of exposure is found. In practice it can be very difficult to differentiate between human-to-human transmission and a common source exposure. Human-to-human transmission may be indicated in the setting of:

- Well documented exposure to a confirmed, probable, or suspect human case
- and
- The time interval between contact with a human case and illness onset is 7 days or less
- and
- Absence of an alternative source of exposure such as exposures to birds, animals,
 - feathers, droppings, fertilizers made of fresh bird droppings, contaminated
 - environments, or laboratory specimens
- OR
- Several generations of transmission linked to a primary case

Thus a comprehensive epidemiologic case investigation is essential to make this determination. In line with the International Health Regulations (2005), WHO should be notified if the investigation suggests that human-to-human transmission is occurring as described above.

HUMAN to HUMAN transmission?

ID #	INITIALS	LOC	STATUS – Case vs. Contact	Human-to- human transmission?	Possible Sources of Exposure
1	AAJ	DG	Probable CASE	Not likely	Live-Mkt: July 8
3	AWM	DG	Confirmed CASE	Likely	Caretaker of # 1, no reported poultry exposure.
4	NJC	DG	Confirmed CASE	Possibly- Likely	Caretaker of # 1; Live-Mkt: July 8
5	JRO	DG	Confirmed CASE	Possibly- Likely	Live-Mkt: July 8, Exposure to NJC may be more likely source given incubation periods
6	TMU	PJ	Confirmed CASE	Not likely	Live-Mkt : July 8. Exposed to AAJ, prior to AAJ’s symptom onset.
8	DKS	DG	Confirmed CASE	Likely	Caretaker of # 1. Exposed at vigil, denies poultry exposure.

KEY POINTS: Review criteria for establishing human to human transmission above. Clearly establishing human-to-human transmission may be possible although difficult. There may be instances in which it is relatively clear but given the common sources of zoonotic exposure, or exposure to unknown fomites that may be present in the environment, it is nevertheless challenging to confidently conclude such modes of transmission. If the epidemiologic team is not thorough enough in its assessment of possible poultry exposures, an erroneous conclusion of human-human transmission may be reached. Similarly lack of appropriate human contact tracing could miss important second generation human cases.

Over the next 10 days you, the Rapid Response Team, the Director of Epidemiology and the relatives of many of the patients are saddened to see the demise of the mother (NJC) of 10 year old boy (AAJ). The uncle (JRO) and the 19 year old (DKS) survive though they received the same intensity of early intervention and medical care as the mother. The 11 year old boy at Pelu Jaghai (TMU) also dies during this time period.

You reflect on the investigation findings and the ongoing passive and active surveillance activities in the region. You are glad to hear that no more acute unexplained respiratory infections with an underlying epidemiologic link to cases, contacts or sick poultry have arisen.

Question 28—Estimated Time: 3 Minutes

What would you do at this stage? How long must you wait before you and your colleagues consider this investigation closed and the outbreak(s) over?

You need to wait for at least the passage of 2 incubation periods, e.g., approximately 2 weeks to allow for any sub clinical infection to manifest among those exposed to influenza A(H5N1) either through direct contact with ill poultry and/or ill human cases.

The most important measures at this point are:

- to enhance ongoing active surveillance for influenza A(H5N1) in humans and animals (there is never a stronger indication for active surveillance than at this point in an investigation);
- to enhance biosecurity measures in farms, backyard flocks and markets;
- to provide effective prevention and control measures for managing contacts and cases in both community and health care facilities;
- to continue to offer strong, sustainable public health risk communication messages, and;
- to review and improve pandemic plans for interagency coordination and resource allocation.

By July 31st, you and your team receive information from the WHO H5 Reference Laboratory that all of the H5N1 viral isolates that were obtained from infected patients were identical and were classified as Clade 2 virus strains. Sequence analysis also revealed that the H5N1 viruses that were isolated were sensitive to the neuraminidase inhibitors Oseltamivir and Zanamivir, but resistant to the adamantane drugs amantadine and rimantadine. You finally pack your bags and return home to your family after a long and eventful stay in Pegu.

NOTE: All referenced Line Lists (by date in scenario), Epidemic Curves and Graphics are included on the following pages

July 15th mid-day.

The line list (for the cases and contacts) so far is presented below:

ID #	Initials	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	Child (exposed at live market)	Child	F, C, S	10	Live-Mkt: July 8 Grandmother: July 9	No lab specimen	Probable CASE	Hospitalized on ventilator, pneumonia, respiratory failure
2	JAM	DG	65	F	Grandmother of # 1	Retired	F, C, S	9	Caretaker of # 1 ?Timing	Pending	Person Under Investig.	Hospitalized

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

**DG: Dava Ghar
PJ: Pelu Jaghai**

July 16th a.m.

The line list (for the cases and contacts) so far is presented below:

ID #	Initials	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	'index' case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Pending	PUI/ CONTACT	Hospitalized
3	AWM	DG	70	M	Grandfather (# 1)	Retired			Caretaker of # 1		CONTACT	
4	NJC	DG	36	F	Mother (# 1)	Home-maker			Caretaker of # 1; Live-Mkt: July 8		CONTACT	
5	JRO	DG	27	M	Uncle (# 1)	Farmer			Live-Mkt: July 8		CONTACT	

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

**DG: Dava Ghar
PJ: Pelu Jaghai**

July 16th p.m.

The line list (for the cases and contacts) so far is presented below:

ID #	Initials	LOC	AGE	SEX	EPI relation	OCC.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	‘index’ case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Pending	PUI/ CONTACT	Hospitalized
3	AWM	DG	70	M	Grandfather (# 1)	Retired			Caretaker of # 1		CONTACT	
4	NJC	DG	36	F	Mother (# 1)	Home-maker			Caretaker of # 1; Live-Mkt: July 8		CONTACT	
5	JRO	DG	27	M	Uncle (# 1)	Farmer			Live-Mkt: July 8		CONTACT	
6	TMU	PJ	11	M	Playmate (# 1)	Child	F, C, D, M	12	Live-Mkt: July 8	Pending	Suspect CASE	Hospitalized
7	AMC	PJ	29	F	Mother of # 6	Mother			Caretaker of # 6		CONTACT	

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

**DG: Dava Ghar
PJ: Pelu Jaghai**

July 18th p.m.

The line list (for the cases and contacts) so far is presented below:

ID #	Initials	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	‘Index’ case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Negative H5N1	CONTACT	Hospitalized
3	AWM	DG	70	M	Grandfather (# 1)	Retired	F, S, M	18	Caretaker of # 1	Pending	Suspect CASE	Hospitalized
4	NJC	DG	36	F	Mother (# 1)	Home-maker			Caretaker of # 1; Live-Mkt: July 8		CONTACT	
5	JRO	DG	27	M	Uncle (# 1)	Farmer			Live-Mkt: July 8		CONTACT	
6	TMU	PJ	11	M	Playmate (# 1)	Child	F, C, D, M	12	Live-Mkt: July 8	Positive H5N1 - PCR	Confirmed CASE	Hospitalized
7	AMC	PJ	29	F	Mother of # 6	Mother			Caretaker of # 6		CONTACT	

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

DG: Dava Ghar

PJ: Pelu Jaghai

July 20th afternoon

The line list (for the cases and contacts) so far is presented below:

ID #	Initials	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	'Index' case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Negative H5N1	CONTACT	Recovered
3	AWM	DG	70	M	Grandfather (# 1)	Retired	F, S, M	18	Caretaker of # 1	Positive H5N1 - PCR	Confirmed CASE	Died (7/20)
4	NJC	DG	36	F	Mother (# 1)	Home-maker	F, C, S, M, D, URI	19	Caretaker of # 1; Live-Mkt: July 8	Pending	Probable CASE	Hospitalized
5	JRO	DG	27	M	Uncle (# 1)	Farmer	F, C, S	19	Live-Mkt: July 8, NJC	Pending	Probable CASE	Hospitalized
6	TMU	PJ	11	M	Playmate (# 1)	Child	F, C, D, M	12	Live-Mkt: July 8	Positive H5N1 - PCR	Confirmed CASE	Hospitalized
7	AMC	PJ	29	F	Mother of # 6	Mother			Caretaker of # 6		CONTACT	
8	DKS	DG	19	M	Sibling (#1)	Student	F, C	20	Caretaker of # 1	Pending	Suspect CASE	Hospitalized

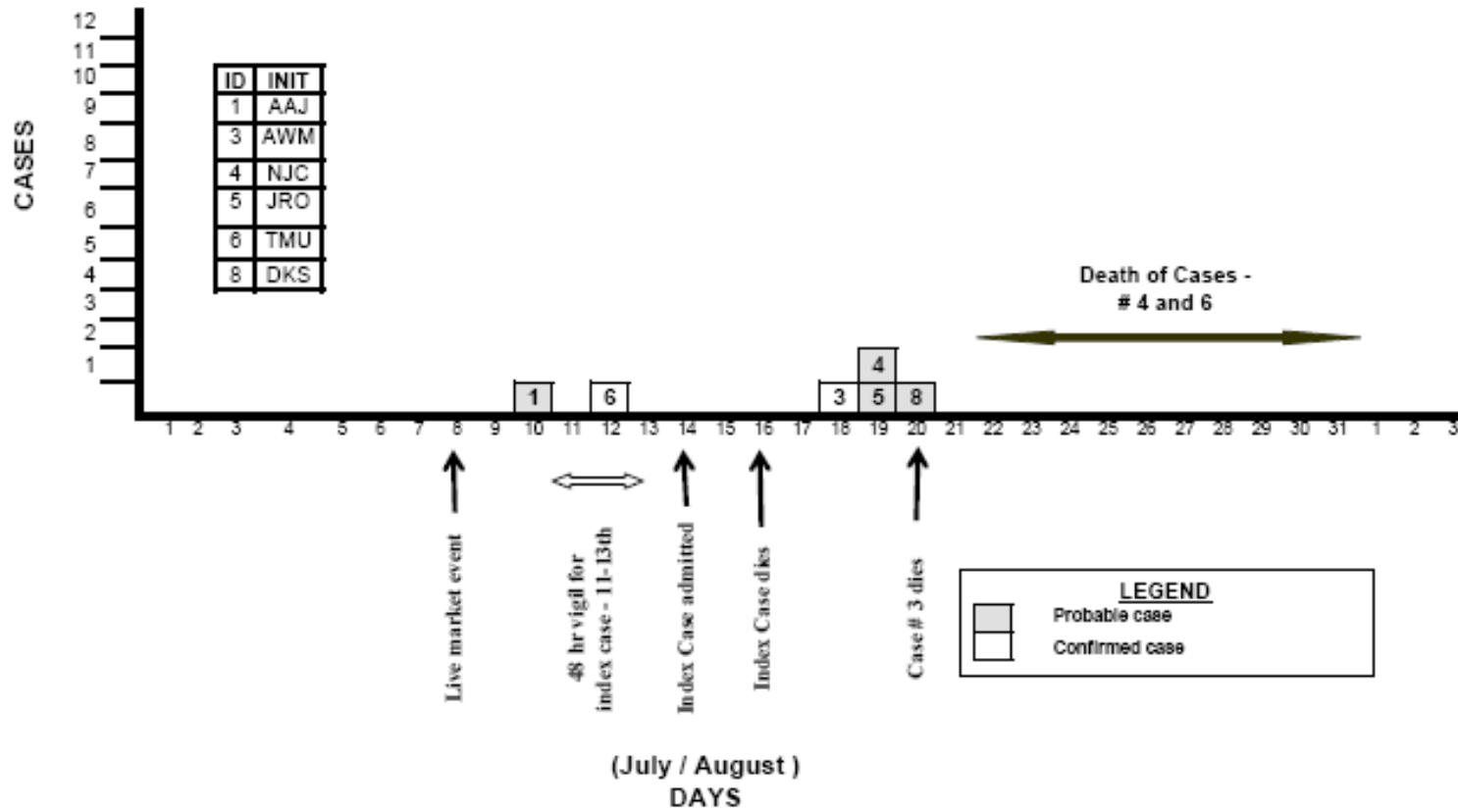
F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

DG: Dava Ghar

PJ: Pelu Jaghai

Epidemiologic Curve of Cases

Epidemic Curve, by date of onset of H5N1 infected persons in Dava Ghar and Pelu Jaghai Hospitals, July 2006



The complete line list for cases and contacts—July 20th, Evening:

ID #	INITIALS	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	‘index’ case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Negative H5N1	CONTACT	Survived
3	AWM	DG	70	M	Grandfather (# 1)	Retired	F, S, M	18	Caretaker of # 1	Positive H5N1 - PCR	Confirmed CASE	Died (7/20)
4	NJC	DG	36	F	Mother (# 1)	Home-maker	F, C, S, M, D, URI	19	Caretaker of # 1; Live-Mkt: July 8	Pending	Probable CASE	Hospitalized
5	JRO	DG	27	M	Uncle (# 1)	Farmer	F, C, S	19	Live-Mkt: July 8, NJC	Pending	Probable CASE	Hospitalized
6	TMU	PJ	11	M	Playmate (# 1)	Child	F, C, D, M	12	Live-Mkt : July 8	Positive H5N1 - PCR	Confirmed CASE	Hospitalized
7	AMC	PJ	29	F	Mother (# 6)	Home-maker	-----	n/a	Mother of # 6	Pending	CONTACT	Survived
8	DKS	DG	19	M	Sibling (# 1)	Student	F, C	20	Sibling of # 1	Pending	Probable CASE	Hospitalized
9	HCW-RT	DG	34	M	Not relative	HCW-RT	-----	n/a	Caretaker of # 1	Pending	PUI	Survived
10	HCW-N	DG	23	F	Not relative	HCW-nurse	-----	n/a	Caretaker of # 3	Pending	CONTACT	Survived

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

DG: Dava Ghar
PJ: Pelu Jaghai

Final Line List:

ID #	INITIALS	LOC	AGE	SEX	EPI relation	OCCUP.	SYX	ONSET - July	POSS. EXPOS.	LAB STATUS	STATUS – Case vs. Contact	OUTCOME
1	AAJ	DG	10	M	'index' case	Child	F, C, D, S	10	Live-Mkt: July 8	No lab specimen	Probable CASE	Died (7/16)
2	JAM	DG	65	F	Grandmother (# 1)	Retired	F, C, S	9	Caretaker of # 1	Negative H5N1	CONTACT	Survived
3	AWM	DG	70	M	Grandfather (# 1)	Retired	F, S, M	18	Caretaker of # 1	Positive H5N1 - PCR	Confirmed CASE	Died (7/20)
4	NJC	DG	36	F	Mother (# 1)	Home-maker	F, C, S, M, D, URI	19	Caretaker of # 1; Live-Mkt: July 8	Pending	Confirmed CASE	Hospitalized
5	JRO	DG	27	M	Uncle (# 1)	Farmer	F, C, S	19	Live-Mkt: July 8, NJC	Pending	Confirmed CASE	Hospitalized
6	TMU	PJ	11	M	Playmate (# 1)	Child	F, C, D, M	12	Live-Mkt : July 8	Positive H5N1 - PCR	Confirmed CASE	Hospitalized
7	AMC	PJ	29	F	Mother (# 6)	Home-maker	-----	n/a	Mother of # 6	Pending	CONTACT	Survived
8	DKS	DG	19	M	Sibling (# 1)	Student	F, C	20	Sibling of # 1	Pending	Confirmed CASE	Hospitalized
9	HCW-RT	DG	34	M	Not relative	HCW-RT	-----	n/a	Caretaker of # 1	Pending	PUI	Survived
10	HCW-N	DG	23	F	Not relative	HCW-nurse	-----	n/a	Caretaker of # 3	Pending	CONTACT	Survived

F: Fever; C: Cough; D: Diarrhea; S: Shortness of breath; M: Myalgias; URI – upper respiratory syx

DG: Dava Ghar
PJ: Pelu Jaghai

