

# Emergence of a febrile illness of unknown causes among the population and visitors of Upper Egypt

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## **Acknowledgements**

The authors wish to acknowledge the Global Partnership Initiated Academia for Controlling Health Threats (GIBACHT) and their funding body, the German Federal Foreign Office, for their support in developing this case study.

## **Abstract**

This is a fictional case study for training that encourages participants to interact and apply theory into practice. A febrile illness of unknown cause that occurred in Upper Egypt in 2002 was chosen for the events. The location of Aswan was selected to define the climate, topography, and location with the characteristics that support the events. Data obtained from applied research works in Egypt was included. The case study deals with an incidence of severe cases of unknown fever accompanied by neurological and intestinal symptoms, as well as a high percentage of deaths. Most of the symptoms appear in people with direct contact with farm animals especially equines and birds, or those who were near waterways, either tourism workers or tourists. Most of the infected cases or deaths have accumulated in Aswan and some in the neighbouring governorates. This case study focusses on the steps taken during an outbreak investigation, deals with investigative challenges and concepts of biosafety and biosecurity.

## **How to Use the Case Study**

### **General instructions:**

This is a fictional case study and some of its real data was obtained from an applied research work and investigations in Egypt [1]. The details of the original research work have been modified to enhance learning objectives and support the instructional goal.

15 participants should be matched to two facilitators in a training room preferably at a round table. Each participant should be issued a copy of the case study prior to its implementation. The facilitator guide remains with the facilitator. The facilitator introduces the learning objectives of the case study and materials that participants should have at hand before starting the case study. Participants take turns to read the case scenario and the questions or tasks that follow. The participants then discuss and attempt to provide the answer to the question. The facilitator should stimulate participants to discuss and arrive at the correct responses.

**Audience:** Health care providers, epidemiologists, clinicians, Undergraduate/ postgraduate students and public health professionals

**Prerequisites:** Before using this case study, participants should have received lectures or other instruction in outbreak investigation.

**Materials:** Note book, pen, flipcharts, chart papers, markers, calculators and laptops.

**Level of training and associated public health activity:** Novice – Outbreak investigation

**Time required:** The expected time for the case study is about 3 hours

**Language:** English

## **Participant's Guide**

**Goal of Case Study:** the goal of this case study is to understand the challenges that people involved in surveillance systems are facing and to highlight the gaps and explore improvements for disease surveillance systems.

**Learning Objectives:** At the end of the case study, participants will be able to:

1. Understand the dynamic or natural history of a newly emerging disease
2. Distinguish the classification and biological characteristics of the agent causing the disease.
3. Demonstrate the association of the geographical location with the emergence and spread of the disease
4. Explain the role of different host types for spreading of disease.
5. Discuss the proper collection of samples, packing and transportation.
6. Apply the strategies for prevention and control against newly emerging disease.
7. Compare the different technique of mosquito trapping.
8. Demonstrate the suitable schedule for treatment, protection and vaccination if available.

### **Introduction**

The story takes place in Aswan, in Upper Egypt. The Aswan governorate is located in the far south of Egypt just north of the Aswan Dam on the east bank of the Nile at the first cataract, bordered by Qena governorate in the north, the Red Sea to the east, the El wadi El gadeid governorate to the west, and Sudan to the south (see Figure 1) [2].

The capital of Aswan governorate is Aswan city. The province is located 880 km from Cairo. It is divided into 5 administrative centres: Aswan, Daraw, Kom Ombo, Nasr El Nuba and Edfu. It is the link between Egypt and Sudan and the first link with the African continent. Aswan is famous for its history and location, as Egypt's southern gate and is characterised by its beautiful weather and many monuments from different eras [2]. Aswan contains a valley, which stretches across the Nile, is primarily agricultural land while the area in the west of the Nile is a flat and sandy desert.

The population of Aswan is about 1 million people, of which about 56% live in rural areas. The most common economic activities in Aswan are tourism and accompanied activities, rearing of various farm animals such as horses, cattle and poultry, as well as hunting and breeding of wild animals such as Nile crocodiles and wild birds.

The climate is dry, hot in the summer and mild during the winter. The hottest summer periods are in July and August. The coldest winter periods are during December and January.

Rain is rare, but rainfall in the eastern desert may result in seasonal floods in valleys on the eastern bank of Lake Nasser and in the Nile River. Therefore, there are many agricultural drains that are disposed along the Nile and receive all types of wastewater. Foreign tourists and many Egyptians visit Aswan during the holidays, especially in December and January (winter). Horse-drawn cart rides are considered one of the most important tourism activities, which implies close contact between the visitors and equines.

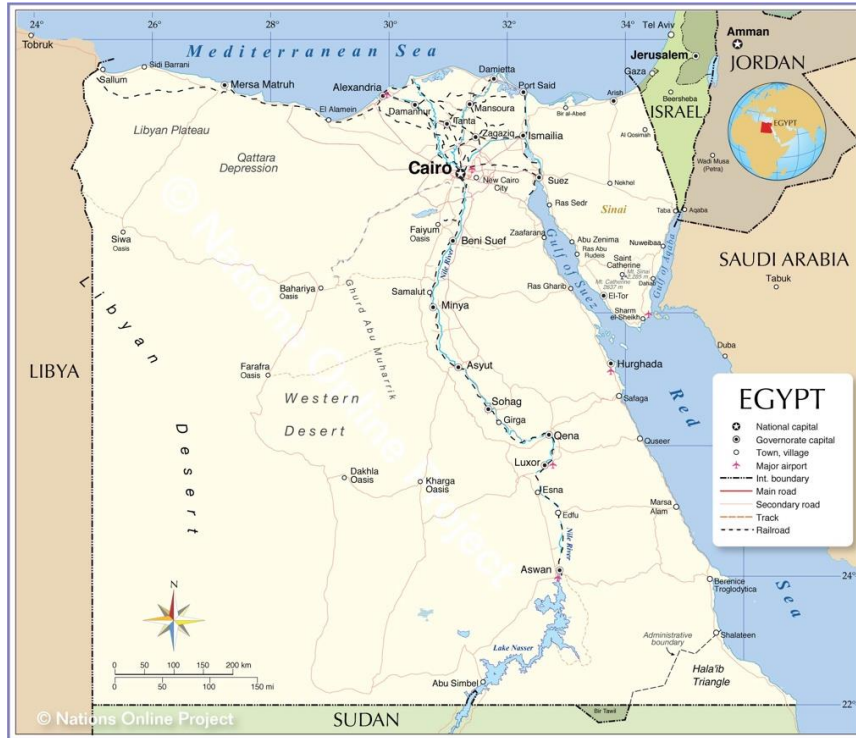


Figure 1: Map of Egypt (Source: Nations Online Project)

**Question 1. What are the factors that make Aswan governorate an interesting area for epidemiological investigations? (Estimated time: 10 min)**

Answer:

## **Part 1**

**Wed, 4<sup>th</sup> December 2002, 11:00 pm:**

22 years old man comes to Aswan Central Hospital (ACH) suffering from high fever, intense headache, muscle weakness, diarrhoea, chills and develops convulsions. He is working in grooming of equines used in cart rides for tourism near the Lake Nasser. He is kept under observation, as he does not respond to treatment. Brain investigations are performed and blood samples are taken and sent to the Ministry of Health central laboratory (MOH- CL) in Cairo, accompanied with a full statement of the case to start an investigation about the cause of unknown fever.

**Question 2. Design a case investigation data form to follow up on onset of disease, exposure-related information, time of sample taken. Show details of affected cases and how they may relate to the sent samples? (Estimated time: 10 min)**

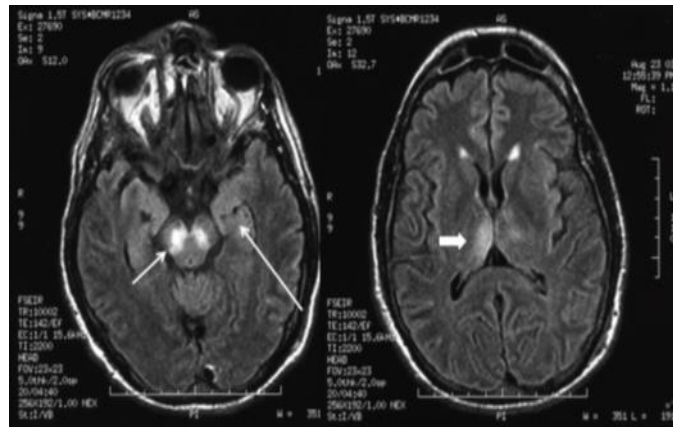
Answer:

**Question 3. What are the clinical and post-mortem investigations that are applied to diagnose the cause of the cases? (Estimated time: 10 min)**

Answer:

**Thu, 5<sup>th</sup> December 2002, 8:00 am:**

Another case of 40-years old woman dies shortly within 4 hours after arrival to ACH. She was suffering from fever and severe nervous manifestation (seizures) in the last 7 days. She was a farmer and reared birds, cattle and horse. Also, she lived beside a huge drain. Brain MRI (Magnetic Resonance Imaging) was performed before her death and showed severe changes in the parenchyma, figure 2.



**Figure 2. Magnetic Resonance Imaging sequence of the brain in a patient with encephalitis [3].**

Post-mortem examinations (PM) are done and tissue samples from liver, lung, gastro intestinal tract (GIT) and brain were taken and sent under high precautionary measures to MOH in Cairo for histopathology. Also, at 1 pm, two brothers of 12 and 15 years old arrive at the central hospital after they developed fever and malaise during a school day. They live near to a small lake and catch different species of wild birds. They develop severe muscular fatigue and need to be admitted to the intensive care unit (ICU) due to ventilatory failure. Blood samples are collected and sent to MOH in Cairo with the note of critical cases and the recommendation to apply further investigation.

**Question 4. What are the recommended samples to collect from patients according to the mentioned symptoms? (Estimated time: 10 min)**

Answer:

**Fri, 6<sup>th</sup> December 2002, 9:00 am:**

Arrival of 45 years Old Italian tourist to ACH, suffering from fever, tremors and muscular weakness, developed within the past 4 days after spending time in a boat on Lake Nasser. He also refers to skin itching of unknown cause and presents a generalised maculopapular rash (Figure 3).



**Figure 3. Diffuse maculopapular rash [3].**

He came to Aswan to visit the Pharaonic antiquities on the banks of the Nile River. He receives symptomatic treatment and is kept under observation. Blood samples are taken and sent to MOH in Cairo. After 3 days, the patient was referred to specified fever hospital in Aswan for further investigations. Another blood samples and different body fluids are taken.

**Question 5. Describe and classify the different suspected causes that may lead to febrile illness symptoms of these cases? (Estimated time: 10 min)**

Answer:

**Question 6. What are the possible ways of transmission of this unknown disease? (Estimated time: 5 min).**

Answer:

**Mon, 9<sup>th</sup> December 2002, 12:00 pm:**

The health status of the two brothers of 12 and 15 years old, and also of the 22 years old man are improving but they are kept under observation and extra blood samples are taken and sent to MOH in Cairo. After 3 days, the 45 years old Italian tourist is discharged from the hospital in good health.

**Sat, 7<sup>th</sup> to Wed, 11<sup>th</sup> December 2002:**

In the course of 5 days, Aswan hospital and its branches receive 100 cases with the following distribution:

- 40 cases suffering from a rise in temperature, headache, muscle weakness, skin itching, diarrhoea, and chills. The age of these cases ranges from 18 to 25 years and these cases are responding to the treatment of antipyretics and symptomatic treatment.
- 50 cases presented with high fever, diffuse maculopapular rash, vomiting, gastrointestinal disorders, seizures, and unspecific neurological symptoms. These cases required intensive care and most began to respond to treatment after 7 to 12 days of symptomatic treatment. However, 5 cases died after 5 days. The ages of these cases ranged from 5 to 12 years.
- 10 cases of ages over 60 years old, 4 of them died shortly after arriving while the other 6 cases died during 3 days of trying to save them. These cases were suffering from high fever and neurological symptoms and did not respond to any treatment.

Blood samples were collected from all cases under treatment to be sent and analysed at MOH in Cairo as well as CSF samples for cases suffering from neurological symptoms, in addition to the PM samples of the deceased cases.

The emergency status has been declared in the governorate and all its hospitals. It has been announced to apply available biosafety and biosecurity measures in dealing with patients, wastes disposal, collecting, and sending more samples for rapid analysis [4].



**Question 7. What type of packaging should be used to transport the samples and why? (We need to organise transportation of the blood samples and tissue) [5] (Estimated time: 15 min.)**

Answer:

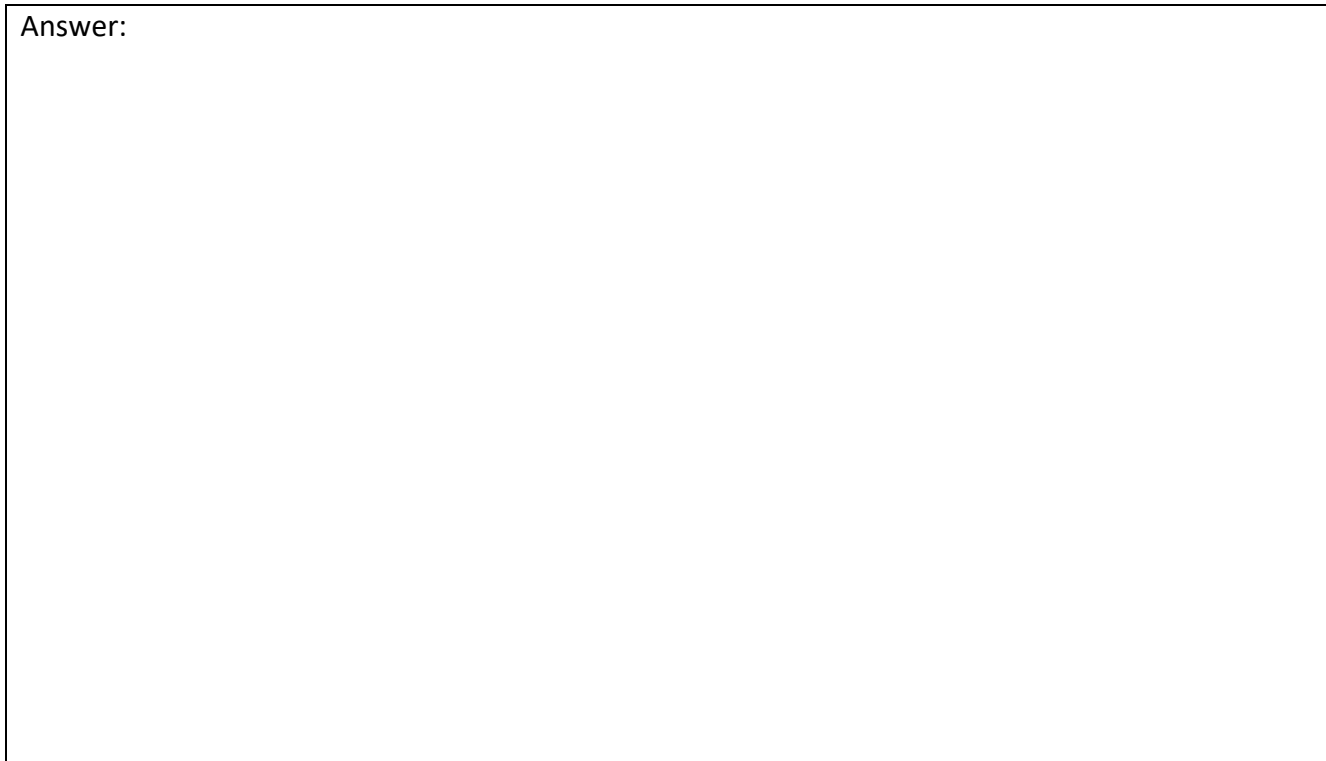
**Question 8. Which type of surveillance technique do you think must be activated and conducted during approach of the case and why? [6-9] (Estimated time: 10 min).**

Answer:



**Question 9. Do you consider this disease outbreak as severe? How do you define this and why?  
(Estimated time: 15 min).**

Answer:



**Sun, 8<sup>th</sup> to Thu, 12<sup>th</sup> December 2002:**

During this period, the environmental centres in Aswan records the death of a large number of wild birds, especially crows, without known causes. Also canters of veterinary surveillance record the death of a large number of animals [6, 7] especially horses, farm animals and some wild animals [10, 11]. The environmental protection stations observe large swarms of mosquitoes densely spread in the area of Lake Nasser and surrounding drains and ponds [8, 9].

**Sun, 15<sup>th</sup> December 2002, 10:00 am:**

The local health authority of Aswan receives a full report about the numbers of febrile cases of the past 7 days and their health status. They call the surveillance officer in Cairo to inform about the obtained data, confirming the importance of the rapid analysis of sent samples and the Case Fatality Rate (CFR) [12].

**Wed, 18<sup>th</sup> December 2002, 8:00 am:**

The local health authority of Aswan received a report from the surveillance officer in Cairo; stating that there were 15 febrile cases recorded without deaths in the neighbouring governorate Qena. In addition, there are 10 cases of Russian tourists in Cairo that just returned from a 10 days tour in Aswan. The surveillance officer requests further investigation and initial assessment for further information; to prepare a report about the history of the diseases in the region, humans, animals and the number of deaths in the region during the last 2 months.

He states that the report must come to his office as soon as possible and asks to prepare a list of people who have been in contact with the patients that showed any symptoms through the last few days. He also tells him that a team of trained personnel are on the way to Aswan for conducting an environmental assessment.

**Question 10. Review and complete this sheet, showing all the details of recorded cases and follow what has been done (Review the cases)? (Estimated time: 20 min).**

#	Date & Period	Location	Case Details			Case Severity	Clinical Investigations	Observations		Notes
			Age	Sex	Occupation	From mild to severe	Observations in MRI, CSF, Tissue	Recovery	Death	
1	4/12/2002	ASWAN G.	22ys	M	Grooming of equines	++	+	+	-	In Risk Area
2	5/12/2002	ASWAN G.	40ys	F	Farmer	+++	+T	-	+	In Risk Area
3	5/12/2002	ASWAN G.	12 & 15ys	2M	Student	++	2& CSF	2+	-	In Risk Area
4	6/12/2002	ASWAN G.	45ys	M	Tourist	++	+	+	-	-
6	7-11/12 /2002	100 Case ASWAN G.	18 – 25ys	22M	Various tourist activities (Wild animals & Nile Tours)	+	-	22+	-	In Risk Area
				18F		+	-	18+	-	In Risk Area
			5 – 12ys	30M		++	-	27+	3+	In Risk Area
				20F		++	-	18+	2+	In Risk Area
			Over 60	4M		+++	4T	-	4+	In Risk Area
				6F		+++	6T	-	6+	In Risk Area
7	18/12/2002	QUNA G. 15 cases	NA	9M	NA	+	-	9+	-	Near Risk Area
				6F		+	-	6+	-	
8	18/12/2002	CAIRO G. 10 cases	NA	4M	Tourist	+	4&CSF	4+	-	-
				6F	Tourist	+	6&CSF	6+	-	-
9	22/12/2002	Different Types of Environmental, Human, Animal and mosquitoes Samples.								
<u>Total Recorded Cases:</u>		...cases	....M			.....		.....		
			...F			... M	... F	... M	... F	
<u>Comments:</u>		M = male (s), F = female (s), Ys. = Years old, G = governorate, CSF = Cerebrospinal fluid, T = Tissue, Number + = Number of Taken Samples								

**Question 11. Draw an epidemic curve and according to its shape, try to assume the pattern of the infection spread in the population (point, intermittent, propagated)? [13-15] What is the importance and characteristics of epidemic curves? (Estimated time: 20 min)**

Answer:

**Question 12. Identify who are close contacts and what is their role in this outbreak investigation. What are the steps of contact tracing? (Estimated time: 5 min)**

Answer:

## **Part 2**

### **Thu, 19<sup>th</sup> December 2002, 7:00 am:**

The team from Ministry of Health, Ministry of Environment, Ministry of Agriculture and epidemiologist arrived in Aswan and start to study and survey all suspected areas and locations of the infected cases, collect the data and take samples for further analysis.

### **Sun, 22<sup>th</sup> December 2002, 1:00 pm:**

The team collects information about the living conditions and behaviour of all recorded cases. The team takes blood samples of the contacts of the cases for analysis. In parallel, they apply a wide environmental assessment and collect samples from sick and dead animals and birds in the affected area. In addition, they trap mosquitoes and sample pond water in the breeding sites according to international methods.

**Question 13. What are the biosafety and biosecurity measures to be applied to avoid the associated risk during working either inside the laboratory or outside? (Estimated time: 5 min)**

Answer:

**Question 14. What are the observations expected by the survey team? (Estimated time: 5 min)**

Answer:

**Question 15. What are the common methods for collecting of various environmental and mosquito samples? [10, 11] (Estimated time: 5 min)**

Answer:



**Tue, 24<sup>th</sup> December 2002, 8:00 am:**

The local health authority of Aswan receives a call from the surveillance officer in Cairo telling him that MOH-CL, the agriculture research centre (ARC), and the veterinary research institutes applied all analytical measures for diagnosis of the main cause of febrile cases, including the Collective Data Sheet (Appendix 1) and a full report will be sent soon.

**Thu, 26<sup>th</sup> December 2002, 10 am:**

Field investigation and laboratory results confirm that the outbreak was caused by a zoonotic arbovirus called West Nile Virus (WNV) [16-18]. The local health authority of Aswan starts the procedures to control the West Nile Fever (WNF) outbreak according to the steps planned by the surveillance officer and authorised personnel from the Ministry of Health, including specialists of veterinary medicine, and the Ministry of Agriculture.

The Minister of Health reassures the population through the media, and informs about the nature and prevention of the disease and announces a hotline (15335) to contact in case of any disease symptoms.

**Question 16: List the laboratory investigations that were applied for diagnosis of the causative agent and precautions during analysis. [5, 19-22] (Estimated time: 5 min)**

Answer:

**Question 17. What are the definitions of zoonotic diseases and arboviruses? (Estimated time: 10 min)**

Answer:

**Question 18. What are the roles of mosquitoes, horses, and wild birds in the transmission of WNV? (Estimated time: 15 min)**

**Question 19. Do you think the Minister of Health managed this outbreak situation well? Explain your answer (Estimated time: 10 min)**

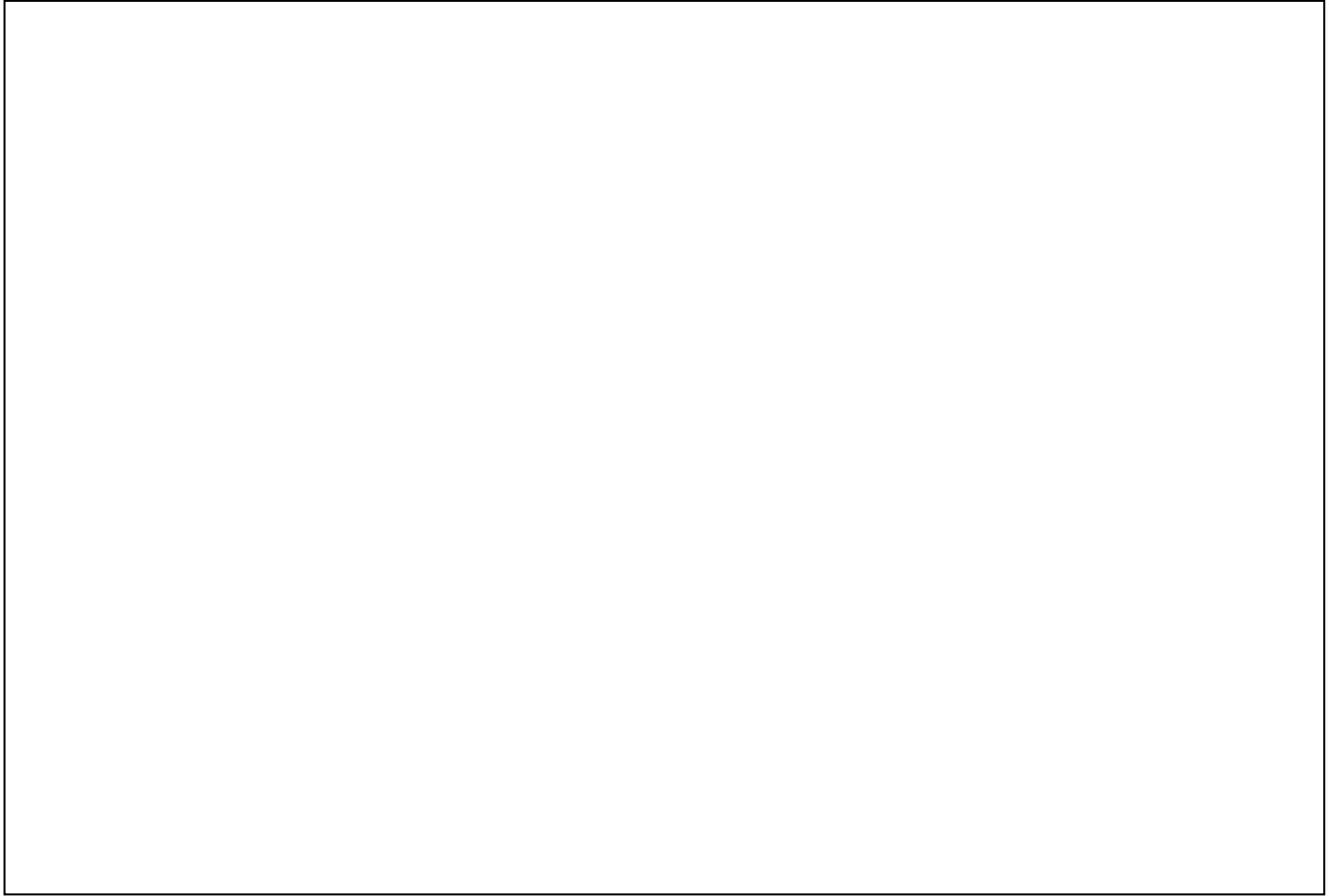
Answer:

**Sat, 28<sup>th</sup> December 2002, 8 pm:**

The President of the Council of Ministers meets with all ministries and disease control agencies to review the future needs required to prevent future disaster. After a month of intensive joint efforts, the team manages to put an end to the outbreak. A risk communication plan to mitigate the possible impact of future outbreaks is out in place.

**Question 20. What are the risk communication elements considered during the disaster preparedness plan? (Estimated time: 20 min)**

Answer:



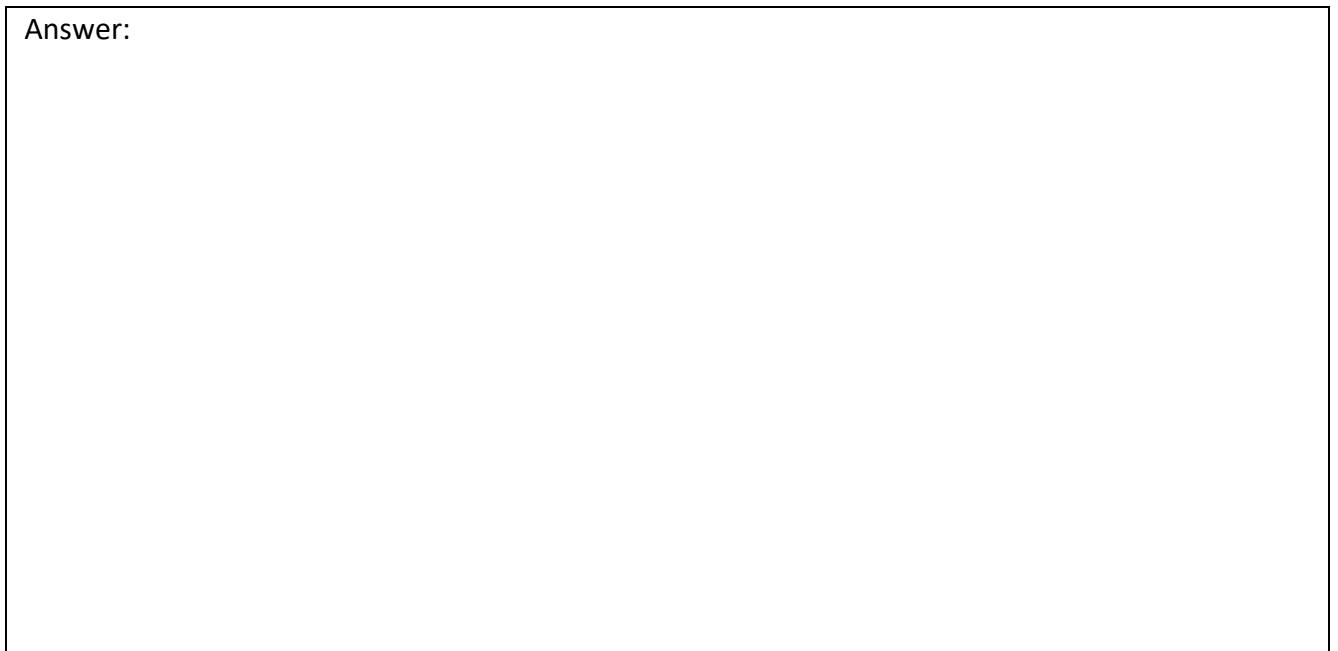
**Question 21. In line with the International Health Regulations (2005), is it necessary to inform the WHO about this outbreak. (Annex 2 IHR 2005 is provided [23]) (Estimated time: 25 min)**

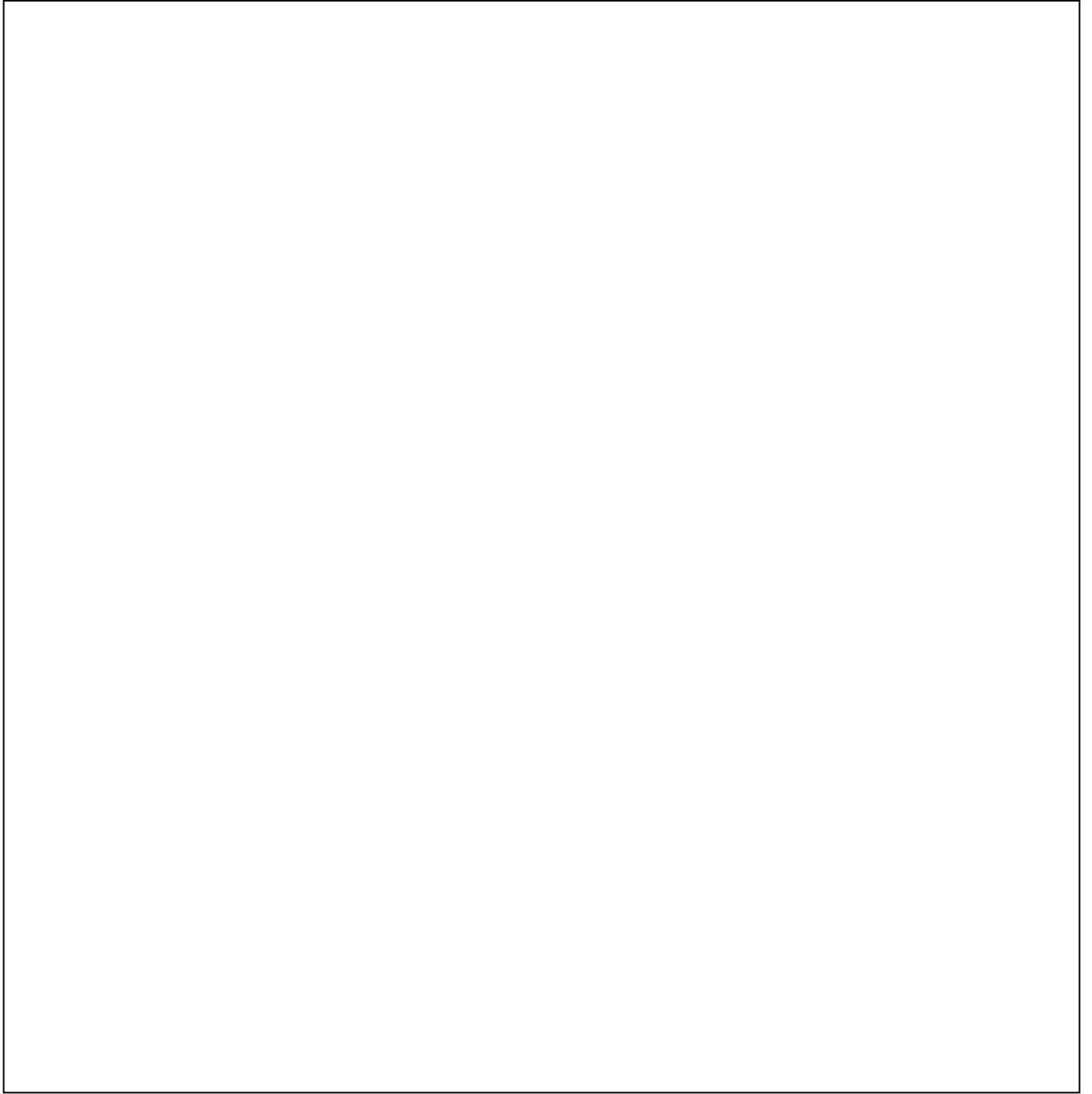
Answer:



**Question 21. What are the recommendations to follow at all levels to resist this pandemic and ensure that it does not recur in the future? [1, 2, 4-6, 12, 19-22, 24, 25]. (Estimated time: 25 min)**

Answer:





## **Conclusion (Epilogue):**

This case describes the prevalence of high fever symptoms with muscle weakness and sometimes-neurological symptoms due to unknown cause. It was observed that most of the infected people either work in rearing of various farm animals such as horses, cattle and poultry, in addition to hunting and breeding of wild animals such as Nile crocodiles and wild birds [10, 11] or live near polluted watercourses where mosquitoes known to spread in Aswan.

The different samples sent to (MOH – CL) in Cairo for conducting the analyses and finding out the cause. Also, the epidemiological team carried out a comprehensive survey of the affected locations and collected different samples of wild live or died birds, horses and samples of mosquitoes that were carefully trapped [26, 27].

The Ministry of Health and specialists in veterinary medicine and agriculture confirmed that West Nile virus (WNV) was the actual cause of all cases. They have been dealing with for elimination of the epidemic through the media on the measures to eliminate the disease, as it is self-limited for people.

During the process of case study and training, we refreshed our knowledge about field epidemiology (outbreak investigation, response and reporting), biosafety / biosecurity and ethical issues besides using of some surveillance studies and find out some scientific facts and using of different illustration. When we finish this created case study, we became able to apply, evaluate, dealing with many complicated data to create a Specific, Measurable, Achievable, Realistic, and Timely (SMART) Solution of real-life cases.

### **See Appendix 1 (report of the surveillance officer in Cairo to the local health authority of Aswan) for further information:**

1- Serum samples were tested by indirect enzyme immune sorbent assay ELISA for IgG and IgM antibodies titres against different febrile causative agents that confirms all samples were positive to West Nile Fever Virus (arbovirus) also ELISA positive samples (defined as positive at dilution  $\geq 1:400$ ) were confirmed by the plaque reduction neutralisation test (PRNT) using 80% positive criterion [3].

2- Wild birds, crows and chicken sera and mosquito pools processed for virus isolation using three different cell lines (Vero, BHK 21 and C6/36).

The virus was identified by the indirect immunofluorescent antibody test (IFA) using specific anti-WNV antibodies. Identification confirmed by RT-PCR using specific primers that amplify 93 base pair (bp) fragments from the WNV [2].

3- Whole Mosquito and the larvae in drain water analysis show that the prevalent species was *Aedes caspius* and the most prevalent mosquito species overall was *Culex*, mainly (*Cx. pipiens*, *Cx. antennatus* and *Cx. perexiguus*) which has been proven to be the primary vector of WNV, also most of the isolated WNV were from *Culex* species [2, 12, 24, 28-30].



## **Background Reading**

- Centers for Disease Control and Prevention. Section 2: Steps of an Outbreak Investigation. Principles of Epidemiology in Public Health Practice. 3rd ed. Atlanta, GA: CDC; 2012.
- Pan American Health Organization (PAHO/WHO) surveillance reports and Epidemiological Alert / Information Sheets at: <http://www.paho.org>
- Canada's Canada Communicable Disease Report at: <http://www.phac-aspc.gc.ca/publicat>.
- The Centers for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Report (MMWR) at: <http://www.cdc.gov/mmwr>
- WNV Keep it on your Radar - California Department of Public Health (CDPH) [www.westnile.ca.gov](http://www.westnile.ca.gov)
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- West Nile Virus Resource Guide (<http://npic.orst.edu/wnv/>)—National Pesticide Information Center - Virus Pathogen Database and Analysis Resource (ViPR): Flaviviridae (<http://www.viprbrc.org/brc/home.do?decorator=flavi>)
- Species Profile – West Nile Virus (Flavivirus) (<https://www.invasivespeciesinfo.gov/profile/west-nile-virus>),
- National Invasive Species Information Center, United States National Agricultural Library. Lists general information and resources for West Nile Virus.
- ECDC TECHNICAL REPORT - West Nile virus risk assessment tool (provided by European Centre for Disease Prevention and Control, 2013) <https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/west-nile-virus-risk-assessment-tool.pdf>

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## Appendix

### Appendix I: Collective Data Sheet (email attachment)

From: Surveillance officer in Cairo

To: The local health authority of Aswan

#### Sheet of Results & Conclusion

Report of the surveillance officer in Cairo to the local health authority of Aswan								
#	Shipping From	Date	Type	Details	State and preservation	Analysis by	Methods, assays	
1	Aswan Central Hospital	4/12/2002	Blood	*20 ys male	Good	Central Laboratory of Ministry of Health	ELISA and PRNT + RT PCR [14, 15, 27]	
2		5/12/2002	Tissue & Blood	40 ys female	Good		ELISA and PRNT + RT PCR & Histopathology [16]	
3		5/12/2002	Blood	*12,15 ys males	Good		ELISA and PRNT + RT PCR	
4		7 – 11 /12/2002	Blood (90 sample)	100 case with death of 15 cases	Good			
			Tissue (15 sample)					
5		9/12/2002	Blood	45 ys male	Good			
6			Blood	*12,15,20ys males (2 <sup>nd</sup> )	Good			
7	Qena governorate	18/12/2002	Blood	15 different cases	Good	ELISA and PRNT IFA + RT PCR & Chemistry		
8	Cairo governorate	18/12/2002	Blood & CSF	10 different cases	Good			
9	Aswan governorate	19/12/2002 TO 22/12/2002	Blood of disease Contact persons	50 different cases	Good	Veterinary Research Ins.	ELISA and PRNT + RT PCR	
10			Blood of Horses	30 samples	Good			
11			Life Birds & carcasses	10 live Bird 20Carcass	Good			Post mortem Isolation on Tissue Culture
12			Drain Water	1 liter/ 5 sources	Good		Ministry OF Agriculture & Environment	Examination for Larvae
13			Whole Mosquito	30 insects	Good in liquid Nitrogen		Parasitological Exam & Isolation	

**ELISA.** Enzyme Linked Immune Sorbent Assay (For detection of Serum anti-WNV immunoglobulin M and G (IgM and IgG),

**PRNT.** Plaque Reduction Neutralisation Test.

**IFA.** Indirect Immunofluorescent Antibody test

**RT-PCR.** Reverse transcription polymerase chain reaction