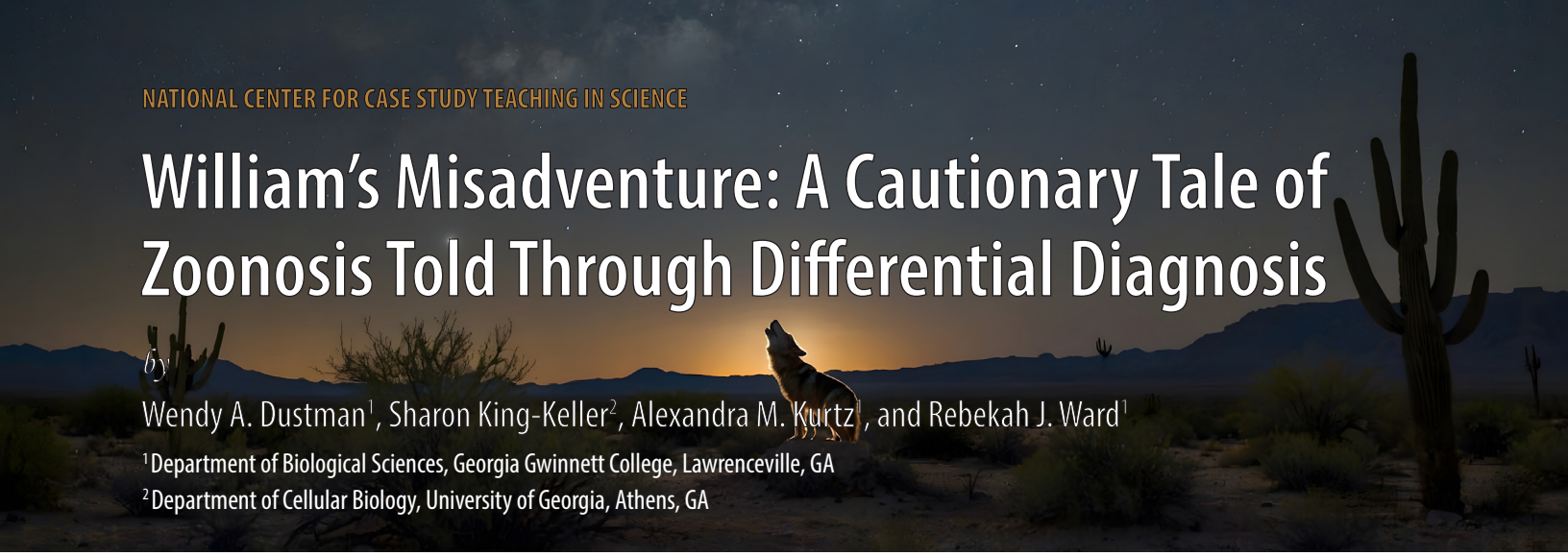
NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

William's Misadventure: A Cautionary Tale of Zoonosis Told Through Differential Diagnosis



by

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Part I – Sick Pups

William was a twenty-year-old college student from New York City. As a rising junior majoring in biology, he hoped to enter a veterinary science program after graduation. Needing preparation for his future career, he had applied for a summer internship with the Mexican Wolf Recovery Program through the U.S. Department of Fish and Wildlife Services. A "city kid" all of his life, William was thrilled to be working in the New Mexico desert. He would get to help with data collection on the Mexican wolf populations that were being re-introduced to an area where they were once among the top predators, although they had not occupied that position for the last 10 years.

William learned his duties quickly and took on extra tasks to make the most of his summer experience. On July 5, the biological station was short-staffed, so William volunteered to check one of the study areas by himself. His supervisor was impressed with William's knowledge and abilities, so she approved William's plan, but she required him to maintain radio contact every 15 minutes with the biological station operator.

William drove his jeep to the assigned study area while tracking signals from the wolves' radio collars. He was trying to observe them and look for signs of new pups in the pack. He tracked a signal from a young female that he knew was ready to deliver pups, but he soon realized she wasn't moving. He feared she was in distress, so he parked as near as possible without disturbing her den, then hiked towards her signal for about 10 minutes before he saw her laying on the ground lifeless. She had two young pups next to her who were crying and trying to suckle unsuccessfully.

He made a quick decision to radio the base station and explain the situation. He guessed the pups were only a couple of weeks old. Aside from starving, they also exhibited respiratory distress (labored breathing), sneezing, and even some bloody sputum from coughing. William reported that he had carefully observed the mother and pups from a distance, making sure not to disturb them. William also reported that the den was covered with the carcasses of several small animals, which looked to be rabbits and various rodents, animals he knew to be common small prey of Mexican wolves.

The station operator told William to come back to base immediately, and then arranged for the station veterinary team to retrieve the sickly pups for emergency treatment. The recovery team was also directed to retrieve the deceased mother so a necropsy could be performed to help pinpoint the cause of the disease.

Upon his arrival at the base, the chief scientist met with William for a short debriefing of the encounter. Because William reported that he had only observed the wolves from a distance, he was directed to return to his normal assigned duties, and to watch himself for any signs of fever or cough and to report these to the base physician immediately.

Question

1. Identify five bacterial pathogens (disease names and their causative agents) that are most likely to have caused the wolves' infectious disease and that could also pose a threat to William. Explain your reasoning for each suspect using the symptoms and signs presented in the narrative.

Part II – Sick William

Approximately 24 hours after his return to the base, William felt feverish, experienced minor chills, and had begun coughing. He immediately reported to the station's medical clinic as the chief scientist had directed. On his way to the clinic, he passed the veterinary isolation ward and became anxious when he saw that the veterinary staff treating the pups were wearing Level C PPE (personal protective equipment).

During the exam, the station's doctor, knowing the health status of the wolf pack, asked William if he had had any direct contact with either the pups or the mother wolf. William confessed that he had originally reported having only observed them from a distance, when in fact this was not true. He had been too embarrassed to admit to the chief scientist that he had handled the pups without any protective gear and had been afraid of being dismissed from the program and the potential negative impact on his future vet school admissions. The doctor specifically asked William, in addition to the fever and chills, if he had experienced coughing (with or without blood) in the sputum, and if he had experienced any chest pains or difficulty in breathing. The doctor recorded his vitals and patient history, then ordered the following lab work: a differential CBC (cell blood count), a Gram stain of his sputum, an acid-fast stain of his sputum, a chest X-ray, and bacterial blood cultures of William's blood. For the last, if any sign of bacterial growth was observed, the orders indicated to follow up with isolation of bacteria on sheep blood agar plates for hemolysis observation.

William was directed to remain in a patient isolation room while tests were performed. The lab technicians who came to draw William's blood, take sputum samples, and take his chest X-ray, also wore Level C PPE. Unbeknownst to William, after the doctor left the exam room, he immediately headed to the decontamination area for treatment.

The base doctor administered antibiotic therapy to William as soon as his exam was complete. William was given an intramuscular injection of antibiotics to jump-start antibiotic therapy, which was then supplemented with oral antibiotic therapy for seven days. William was advised to remain in isolation for 48 hours with bed rest, after which he could resume contact with others if he wore a surgical mask.

Several hours later, after several preliminary test results were available from the mother wolf's necropsy, the doctor added one additional analysis to William's blood sample that would help to either confirm or rule out a potential root cause of the mother wolf's death. Since the lab already had enough samples collected, the doctor issued orders to add an F1 antibody agglutination test on both William's sputum and blood samples.

Doctor's Notes on William

> *Patient was in contact with flea-infested wild wolf pups that displayed dyspnea and minor hemoptysis. Patient noted presence of rabbit and rodent carcasses in the den as well. Patient's blood pressure is elevated (possible anxiety) but within normal ranges. Temperature is elevated at 100.5 °F with occasional chills, which are increasing in frequency. Patient complained of increasing dyspnea and frequency of cough. Sputum produced is slightly cloudy, but there is no indication of hemoptysis.*

Laboratory Reports for William

Table 1. Complete blood cell (CBC) count.

Component	*Patient Value*	*Normal Range*
Total leukocytes	15.6×10^3 per μL	$4.5–11.0 \times 10^3$ per μL
Neutrophils	13.1×10^3 per μL	$1.8–7.7 \times 10^3$ per μL
Monocytes	0.6×10^3 per μL	$0–0.8 \times 10^3$ per μL
Eosinophils	0.3×10^3 per μL	$0–0.5 \times 10^3$ per μL
Basophils	0.1×10^3 per μL	$0–0.2 \times 10^3$ per μL
Lymphocytes	1.5×10^3 per μL	$1.0–4.8 \times 10^3$ per μL
Erythrocytes	5.45×10^6 per μL	$4.0–5.9 \times 10^6$ per μL

Table 2. Sputum staining results.

Component	*Patient Sample*	*Normal*
Gram stain	Short pink bacilli (coccobacilli) with presence of white blood cells	No bacteria and no white blood cells present.
Acid-fast stain	Short blue bacilli (coccobacilli) with presence of white blood cells	No bacteria and no white blood cells present.

Table 3. Blood culture results.

Patient Sample	*Normal*
Growth	No growth

Table 4. Sheep blood agar hemolysis results of isolated colonies from positive blood cultures (24 hr incubation at 35 °C).

Observations	*Interpretation*
Pinpoint grey-white colonies that are translucent. No discoloration or breakdown of sheep's blood.	Gamma hemolytic (i.e., non-hemolytic).

Table 5. Chest radiographs (X-rays).

Patient's Appearance	*Normal Appearance*
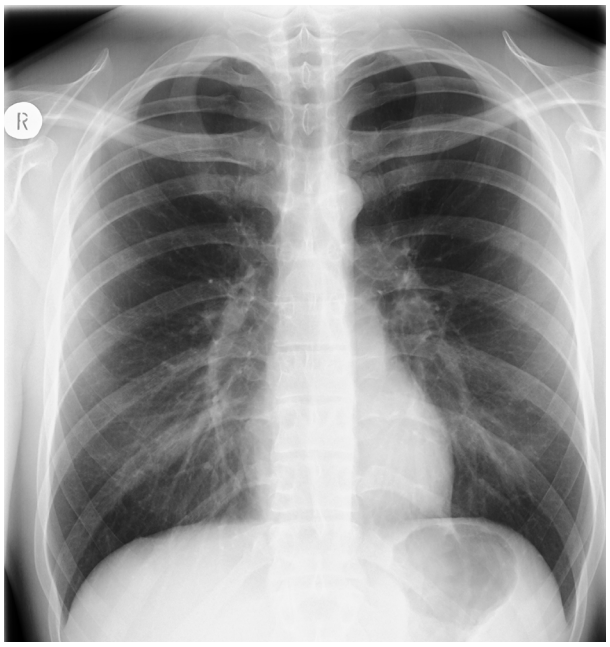	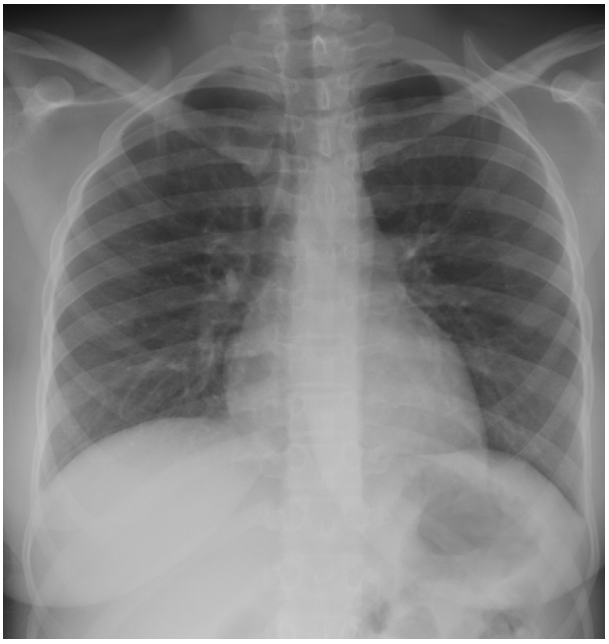
Figure 1. Patchy infiltrates observed. *Credit:* Radiologische Praxis in Ärztehaus Friedrichshain, Flickr, CC BY 2.0.	*Figure 2.* No patchy infiltrates observed. *Credit:* Yale Rosen, Flickr, CC BY-SA 2.0.

Table 6. F1 antibody test.

Component	*Patient Sample*	*Normal*
Sputum	Strong agglutination	Non-reactive / no agglutination
Blood	Non-reactive / no agglutination	Non-reactive / no agglutination

Questions

1. Do the given results help you identify a definitive pathogen? If so, why, and how? Explain how each of the test results (patient symptoms and vitals, CBC, Gram stain, acid-fast stain, hemolytic activity of isolated colonies on blood agar, F1 antibody tests, and X-ray) helped you confirm your diagnosis.

2. This pathogen can manifest infection in its hosts in three different clinical forms, depending on its transmission route and area of the body infected.
   a. Name the three clinical forms of this disease and briefly differentiate them from one another.

   b. What treatment(s) would you prescribe after confirming your original diagnosis? How does each part of your proposed treatment work? If using antimicrobials, explain the associated mechanism of action. Justify your choice. What, if any, supportive therapy would you use and why?

3. Regarding the Level C PPE worn by the hospital staff, was it justified or was it an unnecessary caution? Support your answer in detail.

Part III – Follow-Up

As you have determined by now, the bacterial culprit in this case study is called *Yersinia pestis*, the causative agent of plague, a potentially life-threatening disease affecting humans and other mammals. Plague is rare but persists predominantly in rural areas of the Western United States where it causes small outbreaks from time to time. Plague is a zoonotic disease capable of several different transmission routes. It is easily treated with antibiotics, but they must be administered very quickly to be effective, especially in the case of pneumonic plague.

Once diagnosed, it is important to review the data that are available and determine the form of the disease and the transmission route(s) by which an individual was infected and the transmission route(s) by which it could be passed to others. A descriptive summary of the data from the investigations of the deceased mother wolf and the pups is presented below along with a follow-up on the pups' and William's treatments and recovery.

During the necropsy of the deceased mother wolf, it was determined that she had a severe flea infestation indicated by an extremely high number of flea bite marks. Abnormal lymphadenopathy was detected in the lymph nodes of both axillary and inguinal regions (axillary: in the armpit where front legs meet the chest; inguinal: in the groin where the rear legs meet the abdomen.) Due to the condition of the corpse, it was not possible to obtain blood or sputum samples. However, samples from the infiltrated areas of the lungs were obtained and cultured for bacterial presence, followed by isolation. Isolated colonies were subjected to Gram stain, and acid-fast stain, revealing the isolates were Gram negative bacilli and non-acid fast.

The infected wolf pups underwent similar laboratory testing to William's and showed very similar results: elevated leukocytes (particularly neutrophils), Gram negative bacilli (non-acid-fast) in the sputum, and a positive agglutination test for the F1 antibody only in the sputum. X-rays of the wolf pups also showed the presence of patchy infiltrates in their lungs. The pups were provided with antibiotic therapy by IV upon their arrival at the station and though they responded slowly in the first 12 hours, after 36 hours the pups showed remarkable visible improvement. IV antibiotic therapy continued for a full seven days. After seven days, all symptoms and signs of infection were absent, and the pups were considered healthy. They were reared by staff in the Mexican Wolf Recovery Program until they could be released safely back into the wild.

At the end of William's oral antibiotic therapy, he no longer exhibited a fever, cough, or chills and was released from isolation for light duty for an additional week before resuming his normal duties. As a side note, the doctor and all the vet staff who tended to the wolf pups were administered the same intramuscular and oral antibiotic therapy that William was prescribed. Administration of the therapy began on the same afternoon as William's did, which was a precaution to prevent infection after likely exposure to the infectious bacterium. Thankfully, no medical staff developed signs or symptoms of a *Yersinia pestis* infection.

Questions

Disease transmission can proceed through several routes. Examples include from one human to another, from a natural reservoir (like soil) via an insect vector bite, and also from an unaffected animal where the microbe is normal flora to a human where it is a pathogen.

1. What potential type(s) of transmission are involved in Wiliam's case? Include characteristics of the causative agent and how these could be involved in transmission.

2. Given the case scenario, identify and discuss the role of any vectors, reservoirs, and carriers that could be involved in transmission of this disease. How does the pathogen interact with the vector that facilitates transmission?

3. How did William most likely become infected? How did the female most likely become infected? The pups? Support your answer for each one, citing information from the narrative or the diagnostic results.

Part IV – Extension Activity

Part of any prevention initiative includes education about the disease including the cause, the symptoms, the ways in which the disease is spread, and the ways to prevent infection. Imagine you are a good friend of William's and would like to spread awareness about this disease. Create an info-graphic flyer highlighting this information. Adhere to the following guidelines:

- The flyer is no more than one page in length.
- The format is flexible.
- The flyer should not contain text only, but should also contain graphics, charts, tables, etc.
- The more creative you are with the infographic flyer, the more likely it is that those in the community will pay close attention to your announcement.
- Make sure to provide the following information:
  - disease cause,
  - transmission route(s),
  - symptoms,
  - treatment,
  - potential preventative measures, and
  - a list of references.