

Background:

Legionella is a genus of over 60 species of gram negative intracellular bacteria. In endemic areas, legionella are found in low concentrations in most freshwater sources like lakes, rivers, and sewers. In their natural habitat, legionella live inside bacteria eating amoeba and protozoa. All species are considered pathogenic, but Legionella pneumophila is the most common disease causing agent. Legionella spreads through aerosolized droplets and multiply inside alveolar macrophages in the body. They are capable of causing a severe pneumonia known as Legionnaires' disease and a less severe form called pontiac fever. Legionnaires disease has an incubation of 2-10 days. Symptoms always include fever, myalgia and pneumonia and commonly include shortness of breath, headache, confusion, nausea, diarrhea. Hospitalization is common in cases of Legionnaires' disease and the mortality rate is around 10 percent. However, only around 5% of those exposed actually develop the infection. Pontiac fever is theorized to be a reaction to Legionella endotoxins and occurs 24-72 hours after exposure. Though cases lack pneumonia, they still retain symptoms of fever and myalgia. Pontiac fever is self limiting to slightly less than a week. Some risk factors of Legionnaires' disease are:

- Age ≥50 years
- Smoking (current or historical)
- Chronic lung disease (such as emphysema or COPD)
- Immune system disorders due to disease or medication
- Systemic malignancy
- Underlying illness such as diabetes, renal failure, or hepatic failure
- Recent travel with an overnight stay outside of the home, including stay in a healthcare facility
- Exposure to hot tubs
- Travel to hospital, nursing home or cruise within the last 10 days

Legionella is treated with with antibiotics but they must have high intracellular penetration. The incidence of legionella is increasing, with about 1.8 cases per 100,000 pop reported in 2016. However, many epidemiologists believe Legionnaires' disease is underreported.

1. Define and provide 2 examples of a chronic and acute disease (6pts)

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

2. According to your definitions, what is pontiac fever? (1pt)

- a. acute
- b. chronic

3. According to your definitions, what is legionnaires' disease? (1pt)

- a. acute
- b. chronic

4. List the steps in the chain of transmission (6 pts)

5. Acanthamoeba, an ubiquitous freshwater bacterivore differs little on the cellular level with mammalian cells. Acanthamoeba are commonly found with legionella like endosymbionts. Bacteria isolated from Acanthamoeba are often associated with higher efficacy in invading human tissue and resistance to antibiotics. What would Acanthamoeba be to legionella? Explain why (4 pts)

- a. A reservoir
- b. A biological vector
- c. A mechanical vector
- d. A host

TB1: Acanthamoeba is also a human pathogen, List some diseases it causes, symptoms or risk factors (up to 6 points)

6. Droplets of legionella are around (1pt)

- a. 100-10 μm
- b. 10-5 μm
- c. Less than 5 μm

Pneumonia outbreak at [REDACTED]

It is July 12th, 2014, the dog days of summer, your family is on vacation in Singapore but you're stuck working at your local health office in the sleepy town of [REDACTED], population . You receive a call."we would like to report a case of Legionnaires' disease" says hospital clerk."Ok" you say, "tell me about the case". The hospital clerk happily obliged. "2 days ago, a 17 year old hispanic male was admitted to our hospital. The patient was brought in by his mother after he experienced coughing and a fever of 39.7 degrees celsius. His mother said that he started complaining of chest pains on the 9th. When we performed a radiograph on him, we

found he had pneumonia. He was attending the summer school at [REDACTED] high school. We issued a culture , but the results are not yet conclusive. However, the urine antigen test we performed yesterday turned out positive. The patient is still in our ICU, receiving treatment.” “keep us updated you say, we’ll give you [DATA EXPUNGED] in return” you say. You put down your phone, surprised, immediately your mind begins to race.

7. Please fill out the case report (the case report is attached next to the test files) (10 points)

<https://www.cdc.gov/legionella/downloads/case-report-form.pdf>

8. According to the case report, is this patient a probable or confirmed case? (1 point)

9. Please define both terms (2 points for each)

10. Define sensitivity (2pts)

11. If the urine antigen test for legionella has a 73.2% sensitivity rate, how many false negatives would you expect to find in a sample of 829 cases? Show work (3pts)

12. Using the above information, find the PPV, if possible. (3pts)

13. What type of error would be a false negative be? (2pts)

The CDC prefers 2 methods to diagnose legionella: culture or a urinary antigen test, Here are some pros and cons to these tests:

Culture:

+	-
Can detect all serotypes and species of legionella	Takes longer to get a confirmation
Slightly higher specificity	Lower sensitivity
Can be taken anywhere	More expensive

Urinary test:

+	-
Cheaper	only detects legionella pneumophila
Quicker	serogroup 1
Higher sensitivity	slightly lower specificity

For questions 14-19 (1pt each), say which test would be better to use

14. An immunocompromised patient who already has all the clinical symptoms of Legionnaires' disease, including pneumonia

15. A patient reporting symptoms of Legionnaires' disease without a immediately identifiable cause of infection

16. Someone who insists he or must have gotten Legionnaires' disease because he or she visited a place where an outbreak occurred.

17. An air conditioning cooling tower suspected to have caused an outbreak of legionella

18. A patient that tested positive in paired serology (another diagnostic test) who you want to compare to other patients and environments.

19. An elderly person who attends a nursing home which recently had an outbreak of Legionella pneumophila serotype 1 and who has been complaining of coughing.

20. According to the above information, would this be considered an outbreak? List 2 reasons why or why not. (5pts)

21. Define active and passive surveillance and provide an example (6pts):

TB2: define either sentinel, public health or syndromic surveillance and provide an example (up to 2 pts, ONLY DO 1)

22. The hospital themselves reported the first case, is this active or passive surveillance (1pt)?

23. By offering [DATA EXPUNGED] what have you done to the mode of surveillance (2pts)?

24. What type of surveillance, active or passive is more likely to underreport cases and why? (3pts)

25. Why would you want to investigate this? Give 3 reasons (3pts):

Your team decides to investigate further. You make calls to arrange an investigation. Soon, your assistant returns with some papers. "Sir, I have bad news. We found 9 more cases of Legionnaires disease and 11 cases of Pontiac fever, additional reports might still be coming in, All cases seem to have occurred at [REDACTED] high school".

26. Which step of an outbreak investigation are you on now? (1pt)

27. After 5 more steps, which step would you be on? (2 pts)

28. Is a general or specific case definition better right now? Please explain why (3pts)

Cases of Legionnaires' Disease

Case #	Date of onset	Chest pain	coughing	Diarrhea	fever	gender	age	occupation	culture
1	7/9	y	y	n	y	m	17	student	+
2	7/9	y	y	y	y	f	15	student	+
3	7/10	n	y	n	n	f	39	teacher	+
4	7/10	y	y	n	y	m	73	Substitute teacher	-
5	7/10	n	n	y	y	m	25	Teaching assistant	+
6	7/11	y	y	y	y	m	56	School counselor	+
7	7/11	n	y	n	y	m	56	administrator	+
8	7/11	y	y	n	y	f	45	SRO	+
9	7/12	y	y	y	y	m	61	teacher	+
10	7/13	n	y	y	y	f	14	Student	-

Cases of pontiac fever

Case #	Date of onset	headache	Muscle aches	Diarrhea	fever	gender	age	occupation	+
1	7/8	y	n	n	y	m	43	teacher	+
2	7/9	y	y	n	y	m	29	Teaching assistant	+
3	7/10	y	y	n	y	f	17	student	+
4	7/10	n	y	n	y	f	15	student	+
5	7/11	y	y	n	y	f	38	administrator	+
6	7/11	n	n	n	y	f	35	teacher	+

7	7/11	n	n	n	n	m	18	student	+
8	7/11	n	n	n	y	f	60	administra tor	+
9	7/12	y	n	n	n	m	16	student	+
10	7/12	y	y	y	y	m	15	student	+
11	7/13	y	y	n	y	f	17	student	+

New cases of Legionnaires disease and pontiac fever

	2010	2011	2012	2013 (current)
Legionnaires disease	8	0	1	10
pontiac fever	9	1	2	11

Census data of the town of [REDACTED] (in 100,000)

* In the year of 2011, the town of [REDACTED] was split in two to deal with the booming population

	2010	2011	2012	2013
population	1.1	0.4		0.47

29. What are the 4 components of a case definition (4pts)?

30. What are the 3 components of the epi triad? (3pts)

1. _____
2. _____
3. _____

31. What are the 3 components of the *descriptive* epi triad? (3pts)

1. _____
2. _____
3. _____

32. What part of the descriptive epi triad would column 2 of the graph be? (1pt)

33. What part of the descriptive epi triad would column 9 of the graph be? (1pt)

34. .Based on your current knowledge, write a case definition for this outbreak: (6 pts)

35. What are the first and second graphs called? (2pts)

36. Please construct an epi curve for cases of Legionnaires' disease. Label the axes and the title. (10pts)

37. Define an epi curve (2pts)

38. What type of epicurve is this? (2pts)

39. What does this type of epi curve tell you about the exposure period of the outbreak? (4pts)

40. What do the cases of pontiac fever tell you about the outbreak? (4pts)

41. Calculate the incidence of Pontiac fever in 2010 (per 100,000 people) (2pts)

42. If the incidence of Legionnaires disease in 2012 was 2.3 per 100,000 people, what was the population at the time in 100,000s? Round to the nearest hundredth. (3 pts)

43. What is the period prevalence of Pontiac fever between 2010-2012 (3pts)

As you gaze over your results, you see the majority of the outbreak seems concentrated at [REDACTED] high. You order an investigation quickly. You need to hire some people: To the left are the positions you need. To the right are the people you are considering hiring or recruiting. Match the candidates to their jobs (6pts):

person		role
44. sanitarian		A. interviews cases and provides first aid
45. School officials		B. Tells of the general school layout and student activities
46. janitor		C. informs and enforces relevant health related legislation
47. Lab technician		D. informs the public of necessary health measures
48. nurse		E. has extensive knowledge of cleanliness in the school
49. reporter		F. Cultures and performs diagnostic tests
		G. provides medication to cases

After a long day of calling and hiring, you dive to your empty apartment and slump down on the couch. You see that your wife has sent pictures from their vacation in Singapore. As you scroll through the photos you absentmindedly turn on the tv to your favorite channel. Instead, you are met with the blare of a news jingle, "Deadly outbreak of Legionella at [REDACTED] high school, are health officials doing enough!?!?" says the news anchor with too much hairspray in her hair. You audibly groan.

50. What are 2 benefits of widespread news coverage of an outbreak (2pts)?

- a. _____

- b. _____

51. What are 2 disadvantages of widespread news coverage of an outbreak (2pts)?

- a. _____

- b. _____

The next morning, you arrive bright and early to the school. The school Principal, Dr. Vasich, greets you. "I promise to do everything I can to aid in your investigation. He says as sweat forms on his brow." "Tell me about your school, you say". "[REDACTED] high school is one of the biggest high schools in the region." Vasich begins. "As such it is the perfect campus for summer school. Students from schools across the county come here to attend our prestigious summer school which began on Monday July 7th. Before then the school had been closed down for repairs. [REDACTED] high has a North and East campus. Each campus has separate amenities like plumbing, air conditioning and electricity though they all come from a single underground pipe. The east campus has been used extensively for summer school while our sports teams have also been utilizing the north. Teachers usually go between the buildings to relax at the several teachers lounges we have scattered through the building. he finishes. "Thank you" you say

At this point you are considering closing the school

52. What are 2 benefits of closing the school? (2pts)

- a. _____

- b. _____

53. What are 2 downsides of closing the schools (2pts)?

- a. _____

b. _____

A day later your assistant briefs you on the current status of the outbreak. "After narrowing our reach to the school we've sent out a custom questionnaire to everyone attending the school." she says. "There have been 2 additional cases of Legionnaires' disease and we've discovered 117 probable cases of Pontiac fever. Parents of those hospitalized filled out the cases forms to the best of their ability". I'm happy to say that we only have 2 non responses! Next up is the sanitarian "I've reviewed the school and found many unsanitary places." he says, straightening his glasses "First, there are stagnant pools in the greenhouse that the biology teachers use for breeding fish, secondly there is an open fountain in the school's atrium that students used to toss coins into but is now scummy with biofilms, there is also a hot tub in the north teacher's lounge which the janitor ahs told me is not regularly emptied." his look of disdain at the school shines clearly through his forced neutrality. "Tomorrow I'm going with the janitor to take samples and start an environmental investigation".

54. Why would a custom questionnaire be more beneficial than a general form? List 2 reasons (2pts)

a. _____

b. _____

55. Why would Pontiac fever likely be underreported as seen above? (3pts)

Here are a list of the risk factors your assistant included on the questionnaire:

- Attended class in the east campus
- Attended class in the north campus
- Ate lunch in the atrium (has an uncovered bird bath)
- Had class in the greenhouse (uncovered fish breeding pools)
- Bathed in the hot tub (teachers only)
- Visited a hospital within the last 10 days
- Washed themselves in the river (sports teams)

55. Please write a hypothesis supporting eating lunch in the atrium as the cause of the outbreak. (4pts)

56. Please write a null hypothesis for washing themselves in the river being the cause of the outbreak . (4pts)

Cases of Legionnaires' disease at REDACTED high by exposure

	Sick	Not sick	total
Attended east building	10	116	126
Attended north building	3	34	37
Exposed to covered atrium fountain	10	69	79
Entered the greenhouse	1	11	12
Visited a hospital within the last 10 days	1	16	17
Bathed in river	3	23	26
Visited hot tub	7	23	30

Note: [REDACTED] high has 153 students in total, there are 12 total cases of Legionnaires' disease.

57. Please define and provide the pros and cons of a case control study (5pts):

+	-

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57. Please define and provide the pros and cons of a cohort study (5pts):

+	-

58. For this case which study design would you choose and why? (6 pts):

59. For this study, how would you measure association? (1pt)

- a. Odds ratio
- b. Fisher's exact test
- c. ANOVA
- d. Relative risk

60. Calculate the risk associated with visiting the greenhouse (show work) (3pts):

61. Calculate the attributable risk of eating in the atrium (show work) (3pts):

62. List the top 3 risks most likely to have caused the disease, ranked lowest to highest (6pts):

1. _____
2. _____
3. _____

63. Please calculate the chi square values for those 3 (with Yates correction) (show work) (12 pts)

1. _____
2. _____
3. _____

Percentage Points of the Chi-Square Distribution

Degrees of Freedom	Probability of a larger value of χ^2								
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05	0.01
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84	6.63
2	0.020	0.103	0.211	0.575	1.386	2.77	4.61	5.99	9.21
3	0.115	0.352	0.584	1.212	2.366	4.11	6.25	7.81	11.34
4	0.297	0.711	1.064	1.923	3.357	5.39	7.78	9.49	13.28
5	0.554	1.145	1.610	2.675	4.351	6.63	9.24	11.07	15.09
6	0.872	1.635	2.204	3.455	5.348	7.84	10.64	12.59	16.81
7	1.239	2.167	2.833	4.255	6.346	9.04	12.02	14.07	18.48
8	1.647	2.733	3.490	5.071	7.344	10.22	13.36	15.51	20.09
9	2.088	3.325	4.168	5.899	8.343	11.39	14.68	16.92	21.67
10	2.558	3.940	4.865	6.737	9.342	12.55	15.99	18.31	23.21

64. Using the above p value table, please determine if the chi square values you calculated above are statistically significant (use 95%) (3pts)

1. _____
2. _____

3. _____

What does this mean? (4pts)

65 The health data gathered in your investigation was from a voluntary survey. What bias may this have caused? (3pts)

66. This type of bias has a tendency to _____ estimate incidence. (2 pts)

- a. Over
- b. under

67. Though the hot tub showed the highest risk, you don't trust the results completely. Why so? (3pts)

- a. Selection bias
- b. Confirmation bias
- c. Congruence bias
- d. Confounding
- e. Recall bias

68. Explain your reasoning:

69. You decide to do something about this and separate those who visited the hot tub above age 55 and above with those under 55

<55 yrs

≥ 55 yrs

	Case	control		Case	control
Entered hot tub	1	5	Entered hot tub	6	18
Did not enter hot tub	0	100	Did not enter hot tub	5	18

70. Now calculate the mantel haenszel test for you risk entry (show work) (4pts)

71. What seems to be the cause of the outbreak (2pts)?

72. Provide 3 reasons why you believe so (use Hill's criteria) (6pts)

- a. _____
- b. _____
- c. _____

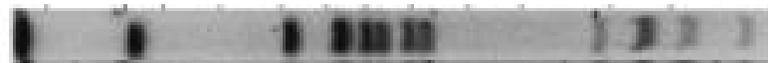
74. List Hill's criteria (4pts):

While you have been investigating the outbreak, the lab tech has fervently been culturing samples that you collected from around the school. Soon he calls you back with results "we've completed our environmental study" he says, I'll fax you the results!

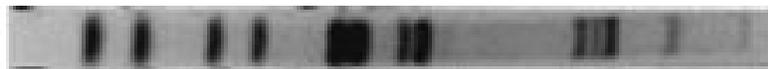
75. When the lab tech was culturing the bacteria, what step of Koch's postulates would he be on? (2pts)

76. List Koch's postulates (4pts):

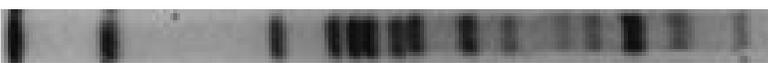
Results from the Lab



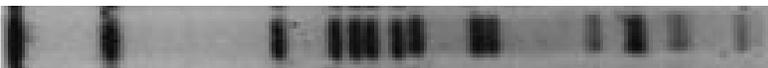
Lake strain



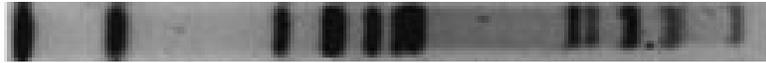
Hospital strain



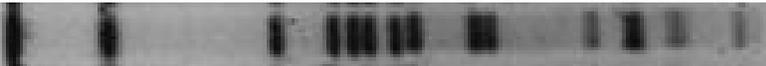
Sewer strain



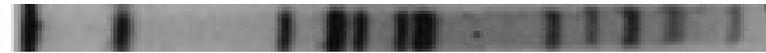
Fountain strain



Index case



Case 5



Case 8

TB3. What is this technique called and what is its purpose? (4pts)

77. Do the lab results support or contradict your investigation? Explain. (3 pts)

78. What strain looks seems to me the original strain that contaminated the fountain? (2pts)

- a. Lake
- b. Hospital
- c. sewer

79. List up to 5 control methods to deal with the outbreak

- a. _____
- b. _____
- c. _____
- d. _____
- e. _____

Finally the investigation concludes, you smile. Helping save people's lives is so great, you think. It's days like this that you're proud to be an epidemiologist.

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And that's all I wrote