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Outbreak Investigation at a Vermont Community Hospital

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Contents

Lesson Plan

TITLE: Outbreak Investigation in a Community Hospital

SUBJECT AREA: Biology, environmental science

OBJECTIVES: At the end of the module, the student will be able to:

- Use the distribution of cases of a cluster of health-related events (disease) to generate hypotheses about the cause
- Recognize the characteristic features of a common source outbreak
- Critically judge the evidence supporting or refuting a particular hypothesis about the cause of the outbreak
- Appreciate the role of the environment constructed by humans in contributing to environmental health problems

TIME FRAME: One or two 45-minute lessons

PREREQUISITE KNOWLEDGE: None

MATERIALS NEEDED: Calculator; handouts or overhead projector

PROCEDURE: This accessible example of outbreak investigation focuses on an actual outbreak that occurred in 1980 among employees of a hospital in Vermont. The story unfolds in stages, as students are given the story in pieces, just as the original investigators would have uncovered it. After receiving each new part of the story, students are asked to reflect on the implications of the new information and to consider what information they would seek next. For students who have been introduced to the steps involved in an outbreak investigation and who have studied the difference between association and causation, the lesson could be done as a written exercise, with handouts distributed sequentially (see Written Exercise). In that case it might be done in one 45-minute lesson. However, for students who have not yet been introduced to outbreak investigation and to the various types of outbreaks (common source, person to person, vector borne) and who are not familiar with distinguishing association from causation, it would work better as a general class discussion, with an introduction to outbreak investigation presented with the teacher and then each installment of the story presented with use of an overhead projector (see Class Presentation and Discussion). Taught this way, the first 45-minute lesson might include the introductory presentation and some portion of Section A; the second lesson would cover the remainder.

ASSESSMENT: To be determined

LINK TO STANDARDS:

NATIONAL SCIENCE EDUCATION STANDARDS

Content Standard A: Science As Inquiry

- Abilities necessary to do scientific inquiry

Students Should:	Performance Indicators
• Identify questions and concepts that guide scientific investigations.	• Students should formulate a testable hypothesis and demonstrate the logical connections between the scientific concepts guiding a hypothesis and the design of an experiment. • They should demonstrate appropriate procedures, a knowledge base and conceptual understanding of scientific investigations.
• Design and conduct scientific investigations.	• Students must use evidence, apply logic and construct an argument for their proposed explanations.
• Formulate and revise scientific explanations and models using logic and evidence.	• Student inquiries should culminate in formulating an explanation or model. • In the process of answering questions, students should engage in discussions and arguments that result in the revision of their explanations.
• Recognize and analyze alternative explanations and models.	• Students should be able to use scientific criteria to find the preferred explanations.

- Understandings about scientific inquiry. Students should understand that:
  - Scientists conduct investigations for a wide variety of reasons. For example, they may wish to discover new aspects of the natural world, explain recently observed phenomena or test the conclusions of prior investigations or the predictions of current theories.
  - Scientific explanations must adhere to criteria such as the following: A proposed explanation must be logically consistent; it must abide by the rules of evidence; it must be open to questions and possible modification; and it must be based on historical and current scientific knowledge.

Content Standard E: Science and Technology

As a result of activities in grades 9–12, all students should develop awareness that:

- Scientists in different disciplines ask different questions, use different methods of investigation and accept different types of evidence to support their explanations. Many scientific investigations require the contributions of individuals from different disciplines, including engineering. New disciplines of science, such as geophysics and biochemistry, often emerge at the interface of two older disciplines.

Content Standard F: Science in Personal and Social Perspectives

As a result of activities in grades 9–12, all students should develop understanding of:

- Personal and community health
  - Hazards and the potential for accidents exist. Regardless of the environment, the possibility of injury, illness, disability or death may be present. Humans have a variety of mechanisms—sensory, motor, emotional, social and technological—that can reduce and modify hazards.
- Environmental quality
  - Natural ecosystems provide an array of basic processes that affect humans. Those processes include maintenance of the quality of the atmosphere, generation of soils, control of the hydrologic cycle, disposal of wastes and recycling of nutrients. Humans are changing many of these basic processes, and the changes may be detrimental to humans.

Acknowledgment is made to SUNY Upstate Medical University at Syracuse, Case Series: Patient and Population-Based Prevention, Case 2002-7. This project is funded by the Josiah Macy Jr. Foundation and Health Resources Services Administration (HRSA), U.S. Department of Health and Human Services.

Note: The original case was developed for the Epidemiology Teaching Program under the direction of Lloyd F. Novick, M.D., M.P.H., Vermont Commissioner of Health, Director, Epidemiology Program and Professor of Clinical Medicine, College of Medicine, University of Vermont 1978–1984. Dr. Novick also used this case as Director of the Office of Public Health, N.Y. State Department of Health, and Chair of the Department of Epidemiology at the University of Albany School of Public Health from 1986 to 1995. This case continues to be taught at the University of Albany.

Classroom Presentation and Discussion

General Principles of Outbreak Investigation

Some diseases occur in clusters, with their onsets concentrated in time and space. When such clusters are larger than one would expect from the usual rate of occurrence of the disease in a population, such clusters are called **outbreaks** or **epidemics.** The number of cases that constitute an outbreak (or epidemic) varies from disease to disease and from population to population. A single case of smallpox would be an outbreak because we think that smallpox has been eradicated from the world. One hundred cases of the common cold in a middle-sized town in January might not be called an outbreak, as the common cold is so, well, common at that time of year. The key criterion is a distinct increase in incidence about the expected rate.

When outbreaks occur, public health scientists often investigate them in the hope of finding a cause that can be neutralized. The cause may be a single common source of exposure that can literally be turned off (like John Snow and the Broad Street pump, which caused cholera in London in the mid-nineteenth century; see the Huang/Bayona module on disease outbreak investigation), person-to-person spread (like SARS, or sudden acute respiratory syndrome, which was halted in 2003 by isolating exposed and ill people so they could not expose the next round of people) or vector-borne diseases (like malaria, which can be controlled by keeping down the mosquito population).

When scientists investigate an outbreak, they follow a sequence of steps that corresponds to the scientific method but is adapted to the particular circumstances, most notably that the scientist does not control the conduct of the experiment. The first step is to gather information about the illness in order to judge what kind of illness it is (e.g., infection) and what the agent might be (e.g., *Vibrio cholerae*) because that may give clues as to the source and mode of spread. Moreover, gathering information about the cases allows the scientist to create a working, objective definition of a case, so that consistency is ensured in judging which illnesses constitute cases and which do not. For each illness that meets the definition of a case, basic information is collected about time, place and person: when the illness began, where the ill person lived or worked, and who (in terms of age, sex, occupation, etc.) fell ill. The times of onset are plotted in a histogram (an epidemic curve) in order to look for evidence of the mode of spread. Diseases that are spread from person to person tend to spread out over time, sometimes with increasingly large waves of cases separated by the average incubation period (the time from exposure to onset of illness). For example, SARS is spread person to person with an average incubation period of 6 days and a maximum of 10 days. Figure 1 shows the distribution of SARS cases in

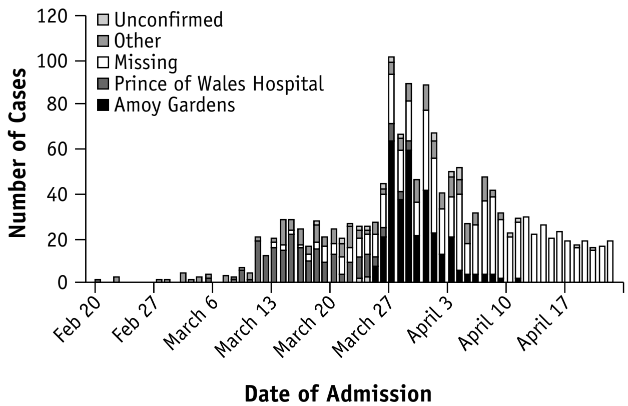


Figure 1: Cases of Severe Acute Respiratory Syndrome (SARS) in Hong Kong by date of hospital admission, 2003 (1).

Hong Kong in 2003.[1] The cluster in Amoy Gardens was suspected to have been spread via some other route, as 60% of those ill had diarrhea (an unusually high rate of occurrence).

Common source outbreaks, on the other hand, tend to have a rapid upswing of cases and a somewhat slower tailing off, reflecting the variation possible within one incubation period of the disease.

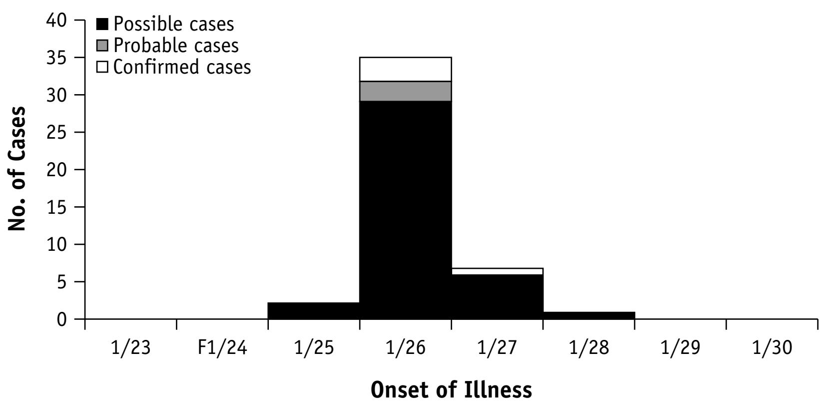


Figure 2: No. of confirmed, probable, and possible cases of Pontiac fever, by date of onset of illness (month/day), among guests who stayed at Wisconsin hotel A during 23–25 January 1998 (2).

Pontiac fever is spread from a common source through droplets, with an incubation period of 6–48 hours. The outbreak shown in Figure 2 was traced to the use of a whirlpool spa.[2]

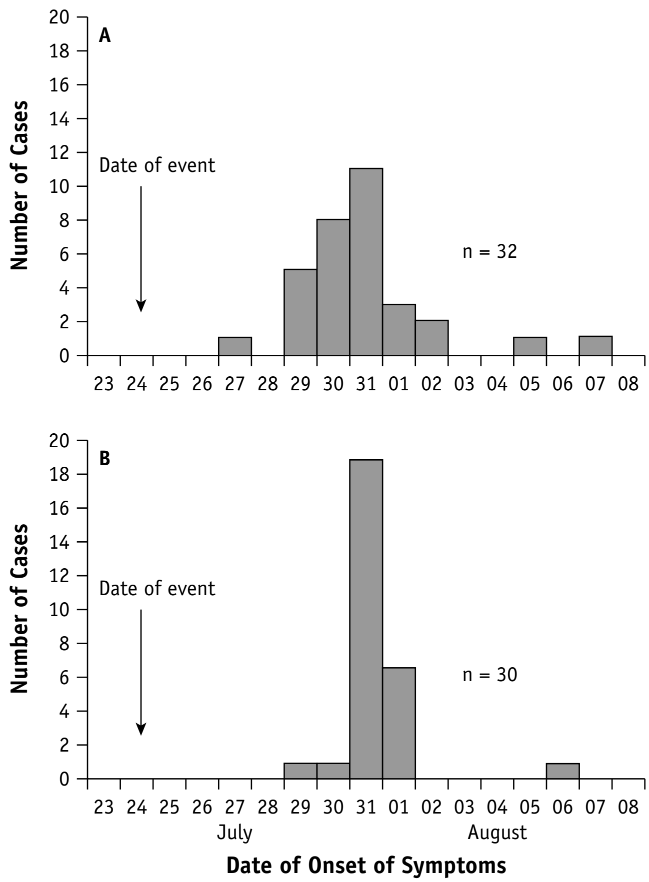


Figure 3: Dates of onset of symptoms among case patients who attended event A *(A)* or event B *(B),* which were associated with clusters of cases of cyclosporiasis (3).

Cyclosporiasis is a parasitic disease that can be spread from a common source with an incubation period of 3–14 days. Figure 3 shows the distribution of cases in two outbreaks traced to contaminated basil in salads.[3]

In general the range between the shortest and the longest incubation period of a disease gives a first-order approximation of the average incubation period (e.g., staphylococcal food poisoning has incubation periods that range from 30 minutes to 7 hours, with an average of 3–4 hours; legionnaires' disease has incubation periods that range from 2 to 10 days, with an average of 4–5 days). Vector-borne diseases may also be spread out but still cluster in the season when the vector density is high. West Nile virus infection is vector borne (spread by mosquitoes) with an incubation period of 3–15 days. Figure 4 shows the 1999 outbreak in New York.[4]

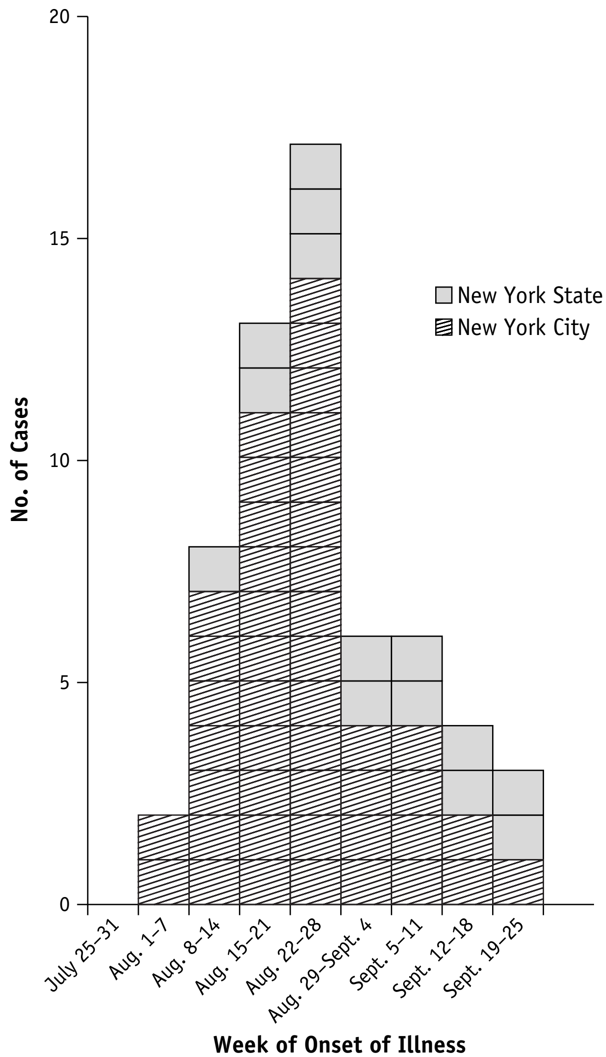


Figure 4: Number of Patients Hospitalized with West Nile Virus Infection (Epidemic Curve) in the New York City Metropolitan Area in 1999.

Hatched boxes represent patients who resided in New York City, and light gray boxes represent patients who resided in other parts of New York State (4).

Places of work or residence are plotted on a map to look for geographic clustering. Because clustering of cases may merely reflect clustering of the population in space, one must seek to make adjustments on the basis of the distribution of the population. The same challenge arises in interpreting the age, sex and occupation distribution of the ill people. By looking at time, place and person, suitably corrected for the characteristics of the underlying population, one conducts what is called **descriptive epidemiology.** From information about the clinical characteristics of the cases and from the descriptive epidemiology, scientists attempt to generate a hypothesis about the cause of the outbreak. On the basis of the hypothesis, scientists attempt to structure a study that mimics as closely as possible the conditions of an experiment to test that hypothesis. Generally such a study involves (1) comparing people with cases with a group of people who might have fallen ill but did not in order to compare rates of exposure to the hypothesized cause (a case–control study) or (2) comparing people who were exposed to the hypothesized cause and those who were not exposed in order to compare rates of illness (a cohort study). This study to test a hypothesis is called **analytical epidemiology.** If analytical epidemiology uncovers an association between exposure to the hypothesized cause and occurrence of disease, one tries several ways to test whether the association is causal. Associations that are causal tend to be stronger; generally show a dose response (so that higher degrees of exposure are associated with higher risks of illness); always have the exposure occur before the onset of illness; tend to be consistently found, regardless of the manner in which they are looked for; tend to be specific (so that illness occurs only when the hypothesized cause is present); and are biologically plausible. If no association is found or if the association found does not appear to be causal, the scientists generate another hypothesis and conduct an additional study. Once an association is found that is thought to be causal, one takes the appropriate specimens for laboratory analysis or otherwise gathers additional evidence to confirm the hypothesis and then institutes control measures, based on the evident cause. The control measures constitute the ultimate test of the hypothesis, so one must monitor the occurrence of the illness after instituting the control measures to be sure that the outbreak stopped.

References

1. Donnelly CA, Ghani AC, Leung GM, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet*. 2003;361:1761–1766.

2. Fields BS, Haupt T, Davis JP, Arduino MJ, Miller PH, Butler JC. Pontiac fever due to *Legionella micdadei* from a whirlpool spa: possible role of bacterial endotoxins. *Journal of Infectious Diseases.* 2001;184:1289–1292.

3. Lopez AS, Dodson DR, Arrowood MJ, et al. Outbreak of cyclosporiasis associated with basil in Missouri in 1999. *Clinical Infectious Diseases.* 2001;32:1010–1017.

4. Nash D, Mostashari F, Fine A, et al. The outbreak of West Nile virus in the New York City area in 1999. *New England Journal of Medicine*. 2001;344:1807–1814.

Written Exercise (Student's Version)

Section A: An Outbreak of Illness

A local health department is notified by a physician in the Emergency Department (ED) of a small community hospital in northwestern Vermont that on the morning of January 3, 1980, nine hospital employees sought treatment in the ED. Common symptoms, in decreasing order of frequency, included headache, nausea, eye irritation, throat irritation, dizziness and vomiting. On physical examination most of the patients demonstrated normal blood pressure and pulse, hyperactive bowel sounds and mild redness of the conjunctivae. The median duration of symptoms was 36 hours with a range of 2 to 48 hours. The only symptom that lasted longer than 12 hours was headache. No other physical signs or symptoms were identified.

Questions

1. Is this a common source outbreak (with disease transmission from a single source)? What information has been presented to support or refute this?

2. What are some of the possible causes of the illness (in terms of agent and transmission)?

3. What other information do you need to determine the extent of the problem?

Initial investigation by the ED physicians and the local health department yielded the following additional information:

- The hospital had a total of 150 employees. In addition to the 9 employees who were evaluated in the ED, 18 employees were absent and reported ill on January 3. An employee survey by hospital physicians revealed that the majority of this group had symptoms compatible with upper respiratory infections, including fever, cough, malaise and runny nose. Six of the 18 ill employees reported symptoms similar to those who presented to the ED. None of the 70 hospital inpatients reported similar symptoms.
- The hospital has a cafeteria where most employees eat their meals. In the 24 hours preceding the onset of illness, 10 of the 15 employees with these symptoms ate in the cafeteria.
- The hospital is served by the town water system and the town sewer system.
- Surveillance of the community outside the hospital revealed no additional cases.
- Appendix A provides demographic and clinical information on each of the 15 cases. Of the 150 employees, 55 were male and 95 were female. The mean age of all female employees was 38 years and the mean age was 40 years for all male employees. The mean age for the total employee population was 39 years.
- No further cases occurred in the hospital after January 3, 12 noon.

Questions

4. From the information that you now have, what people are most likely to be affected? Summarize your evidence.

5. From all this information, how would you define a case? What are the advantages and disadvantages of your definition?

6. What would you conclude from these findings?

7. What percentage of cases had headaches? Nausea? Vomiting?

8. Create a way to show the distribution of cases in time.

9. What does this display tell you?

Section B: Environmental Investigation

As part of the investigation, the health department sent investigators from the Division of Environmental Health to the hospital. They presented a floor plan of the hospital. Plot the cases' work sites on the diagram of the hospital shown in Appendix B.

Questions

10. Describe the distribution.

11. Now, what are your hypotheses about possible sources and transmission of the agent?

12. What are the next steps you would take?

The investigation further reveals that in 1959 a new centralized air conditioning and ventilating system was installed to serve the pharmacy, central supply, intensive care unit, recovery room, operating room, labor and delivery, and housekeeping office. Areas served by this central air system are shown in Appendix C (cross-hatched areas). At the time of the outbreak, 24 people (2 males, 22 females) worked in departments served by this central unit. Another 126 worked in other areas of the hospital.

Questions

13. Calculate the attack rates of those who worked inside and outside those areas served by this central air conditioning and ventilating system.

14. Has this changed your hypothesis about the etiology of this outbreak and transmission? What is the most likely hypothesis now?

15. In the areas served by this system are the attack rates for males and females different? How do these attack rates differ from those in the entire hospital? How do you explain the difference?

16. What are important criteria in determining whether a causal relationship exists between an exposure and an outcome? Which of these criteria were met in this outbreak investigation?

Section C: Tests of the Ventilating System

The ventilating system was tested for the presence of carbon monoxide, and the possibility that a toxic substance got into the system through the main courtyard vent was investigated. Neither of these investigations revealed a possible source. An inventory of chemicals stored and used in the hospital was taken. At approximately 8:30 a.m. on the day of the outbreak, staining materials used for the preparation of cervical smears were changed. These chemicals included one liter of xylene, which was discarded down a sink drain in the autopsy laboratory.

Through velometer testing and simulation of conditions at the time of the incident, it was determined that xylene was the probable cause of the outbreak. The fan unit room has a floor drain that connects to a sewer line downstream from the autopsy laboratory. The trap in this floor drain was dry, and xylene vapor was sucked back through that drain into the fan unit room. It was then distributed by the fan to the hospital rooms served by it. (See Appendix D.)

Additional Information

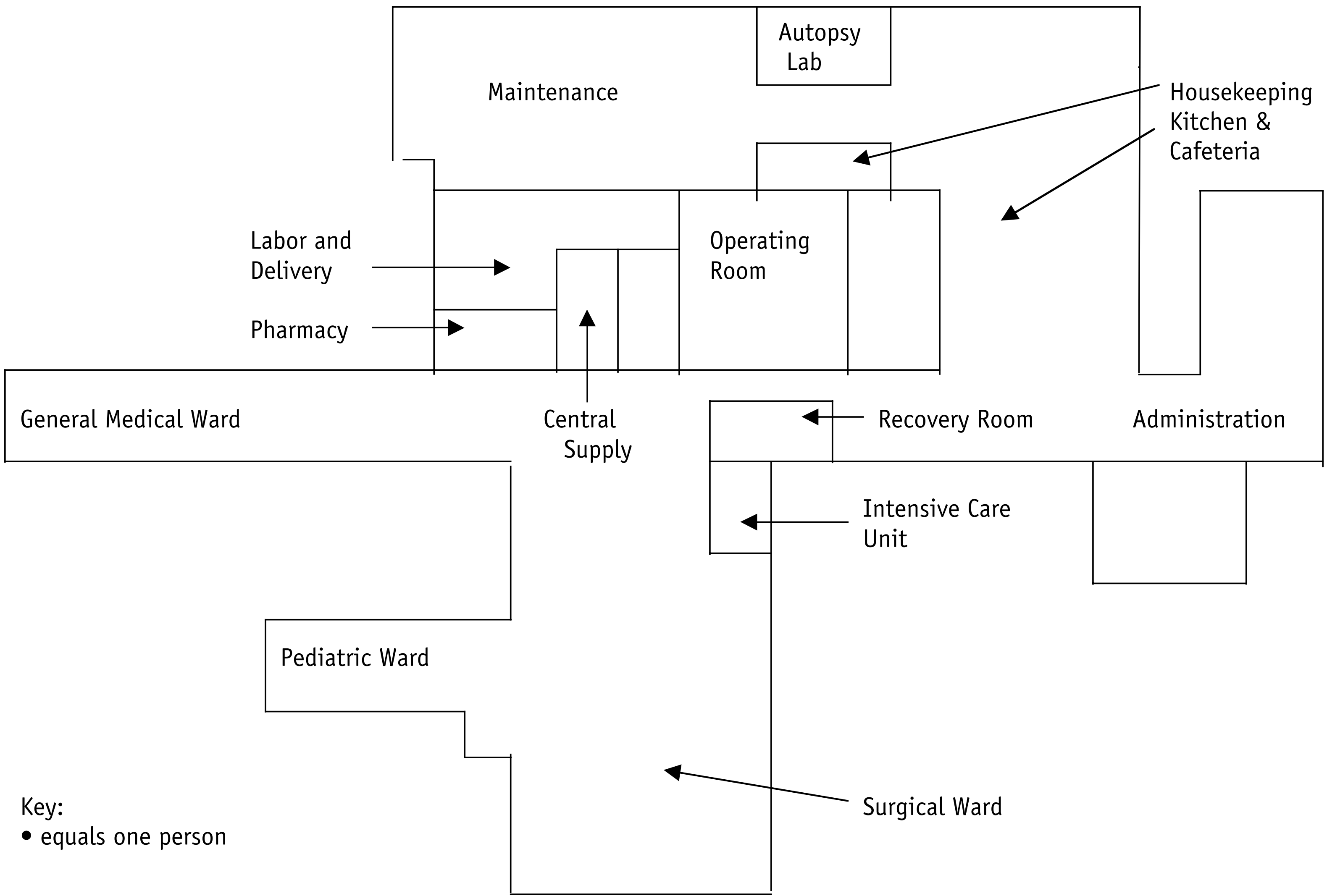
Xylene is an aromatic hydrocarbon similar in chemical structure to benzene and toluene. It occurs in three isometric forms: orthoxylene, metaxylene, and paraxylene. Commercial xylene, frequently referred to as xylol, is a mixture of three isomers. Xylene is colorless, flammable, highly volatile, and insoluble in water, and it has a characteristic odor. The odor threshold is approximately 1 ppm in air. It is used extensively in industry as a solvent and is a component of many common commercial products such as paints, varnishes, inks, dyes, adhesives and cleaning fluids. In hospitals xylene is used by the laboratory as a rinse when preparing cervical Papanicolaou smears and microscopic slides of surgical specimens. Liquid xylene is a skin irritant and causes local erythema, dryness, defatting and characteristic dermatitis. Xylene vapor is a mucous membrane irritant and also has systemic effects, primarily on the central nervous system. (See Appendix E.) In doses, as low as 230 ppm, it causes headache, nausea and vomiting; in higher doses, it can lead to narcosis and death. Fortunately because of the nature of its metabolites, xylene does not have the bone marrow toxicity associated with benzene. Appropriate corrective measures have been taken by the hospital. The inspection door is no longer left open. The floor drains are filled with mineral oil in the dry winter months and are checked periodically for an airtight seal. Xylene is no longer discarded through the hospital sewer system.

Appendix A: Information on the 15 Cases

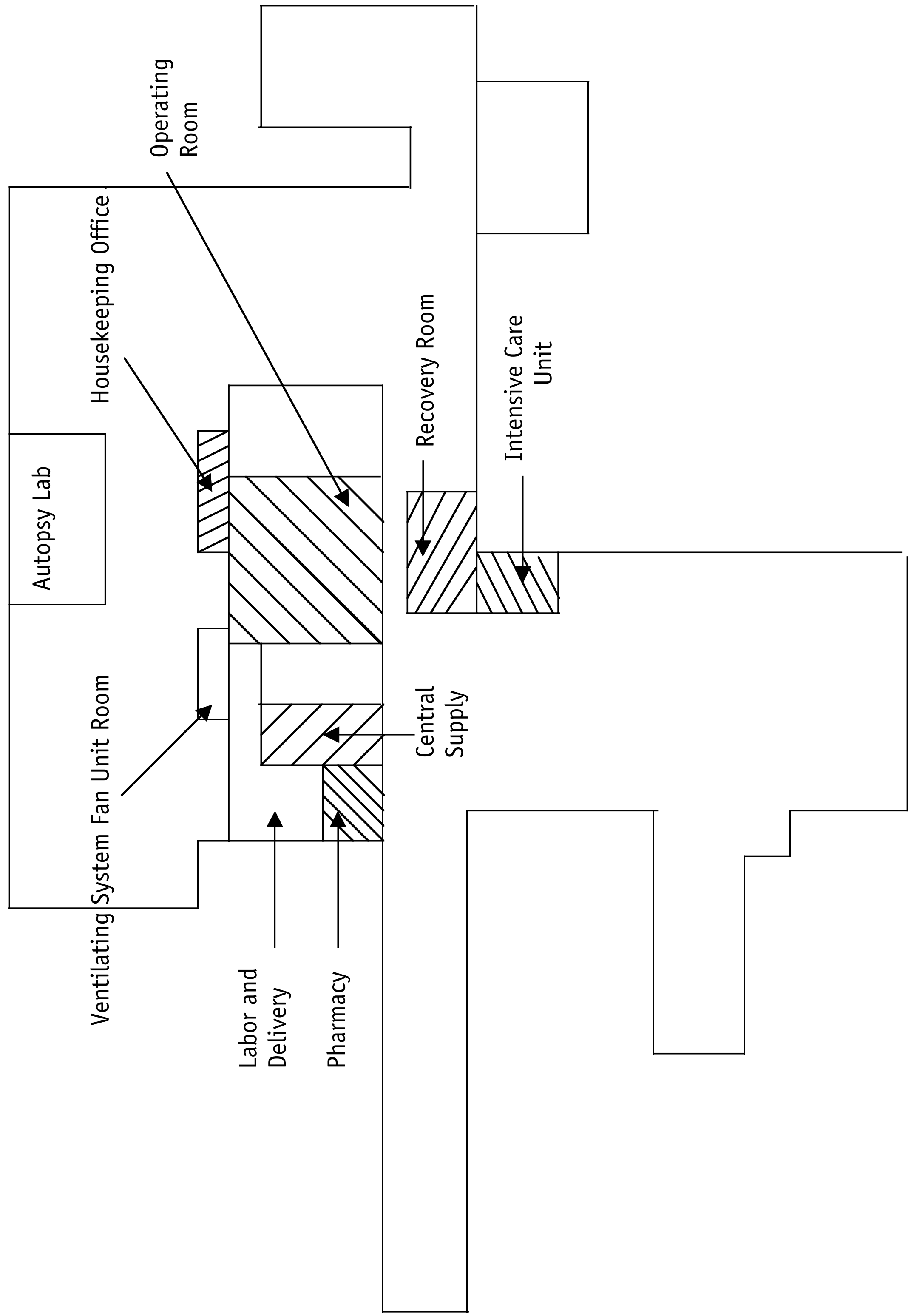
Case #	Sex	Age	Work Location	Time Of Onset	Headaches	Dizziness	Nausea	Vomiting	Duration (Hours)	Time Visited ED
1	F	41	PH	9:00 AM	0	0	+	+	2	10:00 AM
2	F	54	RR	DR	+	0	+	0	48	-
3	F	39	HK	DR	+	0	+	0	12	-
4	F	55	HK	9:15 AM	+	+	+	0	48	10:25 AM
5	F	39	OR	DR	+	+	0	0	DR	-
6	F	28	ICU	9:15 AM	+	0	+	0	DR	-
7	F	21	CS	8:45 AM	+	+	+	+	24	9:45 AM
8	F	52	OR	9:30 AM	+	+	+	+	48	10:30 AM
9	F	39	ICU	9:15 AM	+	0	+	+	24	11:15 AM
10	F	53	OR	9:30 AM	+	+	+	+	48	10:30 AM
11	F	42	CS	9:00 AM	+	+	+	+	24	9:55 AM
12	F	38	RR	9:15 AM	0	+	+	0	48	12:30 PM
13	F	21	PH	DR	+	+	0	0	DR	10:10 AM
14	F	42	OR	DR	0	+	+	0	DR	-
15	M	32	OR	DR	+	0	+	0	DR	-

DR = Don't Remember
HK = Housekeeping
CS = Central Supply
PH = Pharmacy
OR = Operating Room
RR = Recovery Room
ICU = Intensive Care Unit

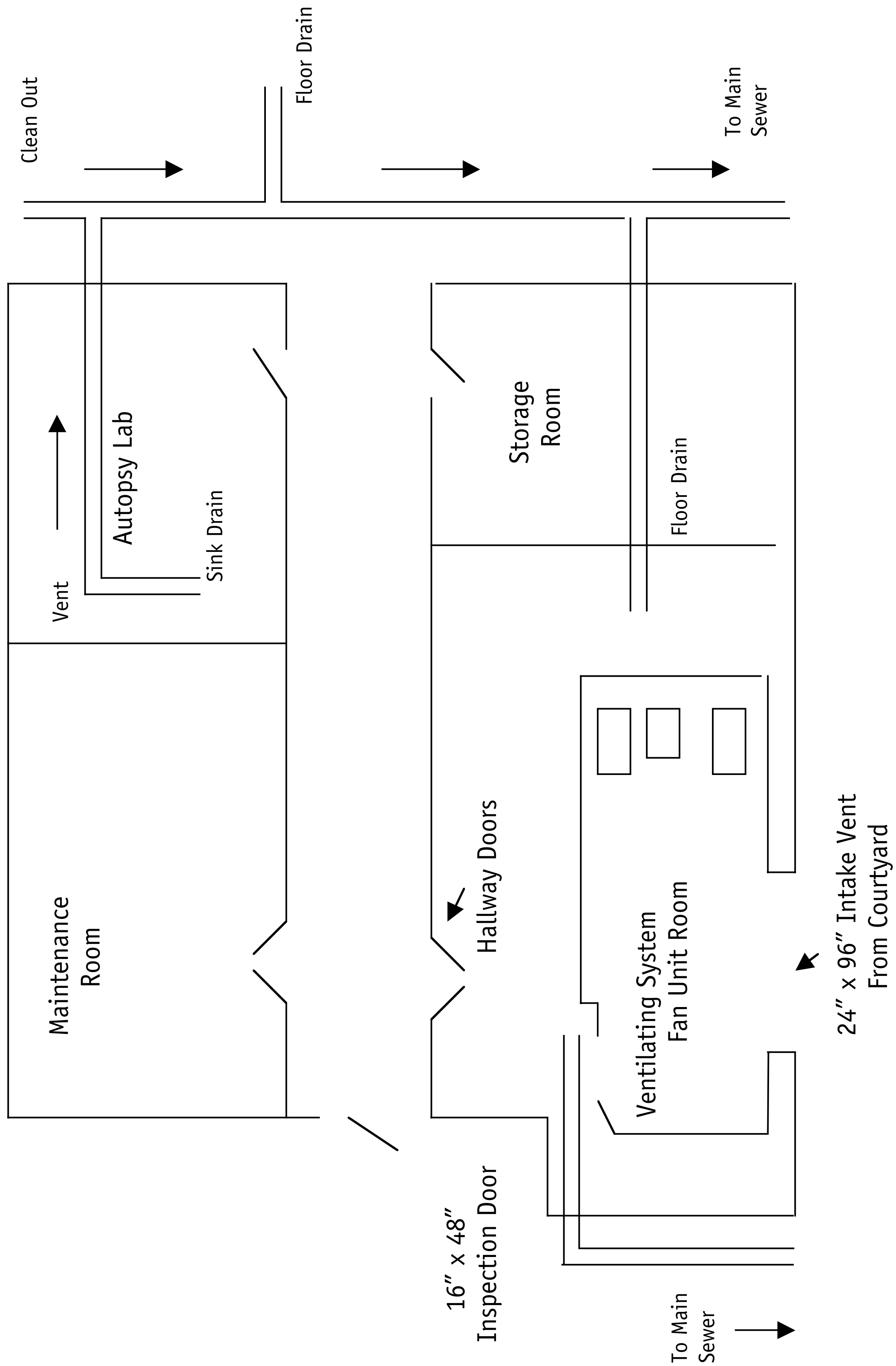
Appendix B: Hospital Floor Plan (Work Sites of Cases)



Appendix C: Hospital Floor Plan (Areas Served by Central Air System)



Appendix D: Distribution of Xylene Vapor



Appendix E: Estimated Threshold Vapor Concentrations for Effects of Xylene on Humans

Effect	**Parts per million (PPM)**
Odor threshold	1.0
Mucous membrane irritation	110–460
Nausea or vomiting	250+
Dizziness	230–690
Taste of threshold	230–690
Narcosis	2,000+
Lethal dose	10,000+
Federal occupational safety standard = 100 ppm	

Written Exercise
(Teacher's Annotated Version)

Section A: An Outbreak of Illness

A local health department is notified by a physician in the Emergency Department (ED) of a small community hospital in northwestern Vermont that on the morning of January 3, 1980, nine hospital employees sought treatment in the ED. Common symptoms, in decreasing order of frequency, included headache, nausea, eye irritation, throat irritation, dizziness and vomiting. On physical examination most of the patients demonstrated normal blood pressure and pulse, hyperactive bowel sounds and mild redness of the conjunctivae. The median duration of symptoms was 36 hours with a range of 2 to 48 hours. The only symptom that lasted longer than 12 hours was headache. No other physical signs or symptoms were identified.

Questions

1. Is this a common source outbreak (with disease transmission from a single source)? What information has been presented to support or refute this?
   The occurrence of multiple cases of an unusual problem, with onsets clustered closely in time, suggests a common source of the outbreak.
2. What are some of the possible causes of the illness (in terms of agent and transmission)?
   The cause could be an infectious agent, allergen or toxin. The occurrence of nausea, vomiting and diarrhea raises the possibility that the agent was ingested, but eye irritation suggests direct contact, perhaps through the air.
3. What other information do you need to determine the extent of the problem?
   One needs to determine whether other employees of the hospital have had the same problem and whether it has occurred in patients or visitors to the hospital, or in people in the surrounding community. One would like to be certain that there were no cases prior to January 3 that may have been unreported. Furthermore, one would like to establish surveillance to detect new cases if they should occur.

Initial investigation by the ED physicians and the local health department yielded the following additional information:

- The hospital had a total of 150 employees. In addition to the 9 employees who were evaluated in the ED, 18 employees were absent and reported ill on January 3. An employee survey by hospital physicians revealed that the majority of this group had symptoms compatible with upper respiratory infections, including fever, cough, malaise and runny nose. Six of the 18 ill employees reported symptoms similar to those who presented to the ED. None of the 70 hospital inpatients reported similar symptoms.

- The hospital has a cafeteria where most employees eat their meals. In the 24 hours preceding the onset of illness, 10 of the 15 employees with these symptoms ate in the cafeteria.
- The hospital is served by the town water system and the town sewer system.
- Surveillance of the community outside the hospital revealed no additional cases.
- Appendix A provides demographic and clinical information on each of the 15 cases. Of the 150 employees, 55 were male and 95 were female. The mean age of all female employees was 38 years, and the mean age was 40 years for all male employees. The mean age for the total employee population was 39 years.
- No further cases occurred in the hospital after January 3, 12 noon.

Questions

4. From the information that you now have, what people are most likely to be affected? Summarize your evidence.

   Hospital employees seem to be the one group at risk, as no cases were found in patients or the general community. Women seem at greater risk than men, as the attack rates were 15 percent (14/95) and 2 percent (1/55), respectively. Age may not be a factor, as the mean age of the ill women is 40 years, close to the 38-year average for female employees. However, without knowing the age distribution of employees, one cannot be certain that attack rates are similar in various age groups. One can draw no conclusions about the cafeteria use as a possible factor in this disease, because we do not know the fraction of unaffected hospital employees who used the cafeteria. One might ask students how they could determine the usage of the cafeteria by unaffected hospital employees.

5. From all this information, how would you define a case? What are the advantages and disadvantages of your definition?

   A case might well be defined as a person who entered the hospital since January 1 and subsequently developed an illness that included at least two of the symptoms of headache, dizziness, nausea and vomiting, but not fever or cough. As advantages, this definition (a) is reasonably unambiguous, (b) distinguishes between what seems to be the outbreak illness and other common health problems, (c) focuses the investigation on the hospital and on a narrow time window, (d) acknowledges the need for exposure to occur before illness, and (e) is based on information that could easily be collected.

As disadvantages, the definition (a) relies largely on subjective symptoms, (b) uses symptoms that can be found with many illnesses, and (c) could result in overlooking a wider problem if one existed beyond the hospital. Other suggested definitions would have different advantages and disadvantages.

6. What would you conclude from these findings?

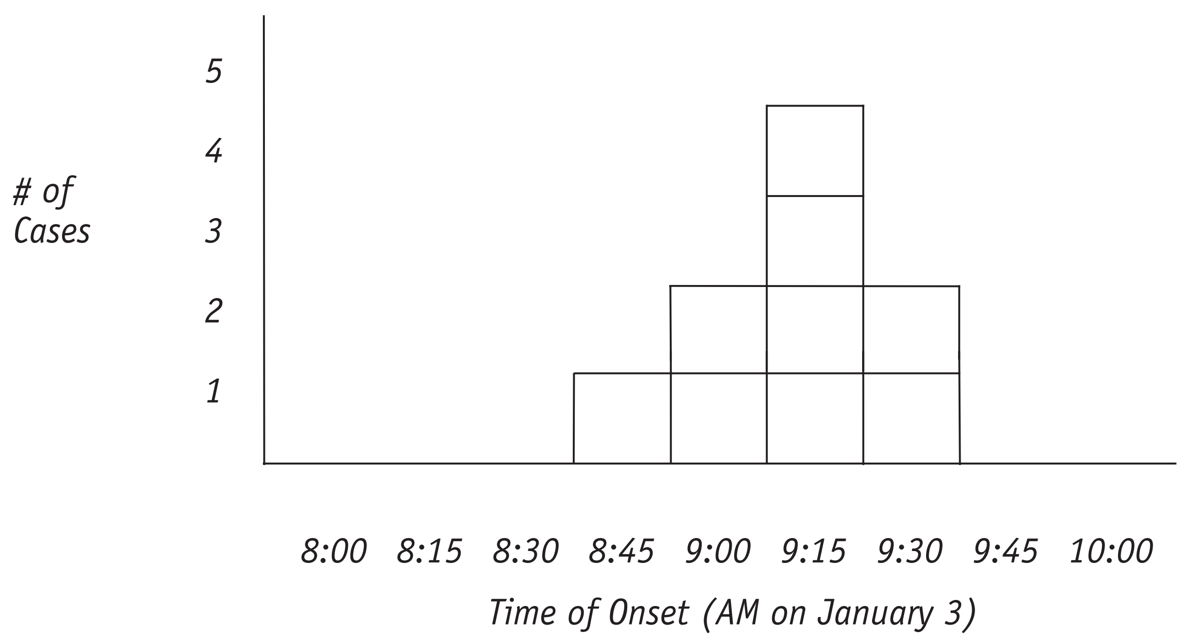
   The tight clustering of cases suggests that exposure occurred around 8 a.m. on January 3 and that most of the people exposed were female employees.

7. What percentage of cases had headaches? Nausea? Vomiting?

   Headache—80%
   Nausea—87%
   Vomiting—40%

8. Create a way to show the distribution of cases in time.

   The epidemic curve that epidemiologists use commonly looks like this:



One wants a scale for the *x*-axis that distinguishes the times of onset but permits one to see the shape of the epidemic curve (as the illustrated version does). One wants a range for the *x*-axis that includes not only the entire duration of the outbreak but also an interval before and after that allows one to see the baseline rate of disease, and therefore to judge whether or not there really has been an outbreak. Epidemiologists favor square boxes for each case so that the height of the epidemic curve is representative of the size of the outbreak.

9. What does this display tell you?

   The steep rise and rapid fall-off of case onsets is typical of a common source outbreak with a very short incubation period. Infectious agents that cause illness by multiplying within the host would not be expected to have such a short incubation period because even under ideal conditions rapidly multiplying organisms double their numbers only every 20 minutes, and concentrations of such organisms need to reach high levels before illness occurs. Toxins and allergens, however, can act very quickly, including toxins produced by some bacteria (which is why staphylococcal food poisoning has such a short incubation period). So this outbreak may be caused by a toxin or allergen.

Section B: Environmental Investigation

As part of the investigation, the health department sent investigators from the Division of Environmental Health to the hospital. They presented a floor plan of the hospital. Plot the cases' work sites on the diagram of the hospital shown in Appendix B.

Questions

10. Describe the distribution.

    All the cases occur in one of six adjacent areas toward the center of the hospital.

11. Now, what are your hypotheses about possible sources and transmission of the agent?

    Geographic clustering of cases suggests a focal exposure to a toxin or allergen. The fact that people from several different administrative units are involved suggests dissemination through some common activity, such as ingestion (e.g., water fountain, coffee urn) or inhalation (e.g., cleaning fluid, paint, laboratory chemical). The fact that most of the affected people were women suggests that the source may be a material with which women are more likely to come in contact or a location where women are more likely to work or visit.

12. What are the next steps you would take?

    One needs to examine the area where ill people worked in order to identify common activities and potential common exposures. One should look at the air handling system to determine whether the distribution of cases is consistent with movement of air within the hospital.

The investigation further reveals that in 1959 a new centralized air conditioning and ventilating system was installed to serve the pharmacy, central supply, intensive care unit, recovery room, operating room, labor and delivery, and housekeeping office. Areas served by this central air system are shown in Appendix C (cross-hatched areas). At the time of the outbreak 24 people (2 males, 22 females) worked in departments served by this central unit. One hundred twenty-six employees worked in other areas of the hospital.

Questions

13. Calculate the attack rates of those who worked inside and outside those areas served by this central air conditioning and ventilating system.

    Inside—63% (15/24)
    Outside—0% (0/126)

14. Has this changed your hypothesis about the etiology of this outbreak and transmission? What is the most likely hypothesis now?

The dramatic clustering in units served by the central ventilation system strongly suggests that an airborne agent was introduced into and disseminated by that ventilation system.

15. In the areas served by this system, are the attack rates for males and females different? How do these attack rates differ from those in the entire hospital? How do you explain the difference?

    Within the area served by the central ventilation system, attack rates for men (50% [1/2]) and women (64% [14/22]) were not much different. Both were much higher than the attack rate of 0% in the rest of the hospital. Both results are consistent with an airborne toxin, which commonly affects a large fraction of the people exposed. Allergens usually affect a smaller proportion of people.

16. What are important criteria in determining whether a causal relationship exists between an exposure and an outcome? Which of these criteria were met in this outbreak investigation?

    (a) Exposure should have occurred in a larger fraction of people who became ill than in those who stayed well. (b) The difference in attack rates in exposed and unexposed people should be large. (c) More intense exposure should have been associated with a higher attack rate. (d) Exposure should have preceded onset of disease. (e) Exposure should consistently be followed by the disease. (f) The disease should not be caused by factors other than the exposure. (g) The disease should have characteristics that make it biologically plausible that the exposure could cause it.

    In this investigation (a) and (b) have been demonstrated, but information has not yet been presented in regard to (c)–(g).

Section C: Tests of the Ventilating System

The ventilating system was tested for the presence of carbon monoxide, and the possibility that a toxic substance got into the system through the main courtyard vent was investigated. Neither of these investigations revealed a possible source. An inventory of chemicals stored and used in the hospital was taken. At approximately 8:30 a.m. on the day of the outbreak, staining materials used for the preparation of cervical smears were changed. These chemicals included one liter of xylene, which was discarded down a sink drain in the autopsy laboratory.

Through velometer testing and simulation of conditions at the time of the incident, it was determined that xylene was the probable cause of the outbreak. The fan unit room has a floor drain that connects to a sewer line downstream from the autopsy laboratory. The trap in this floor drain was dry, and xylene vapor was sucked back through that drain into the fan unit room. It was then distributed by the fan to the hospital rooms served by it. (See Appendix D.)

Additional Information

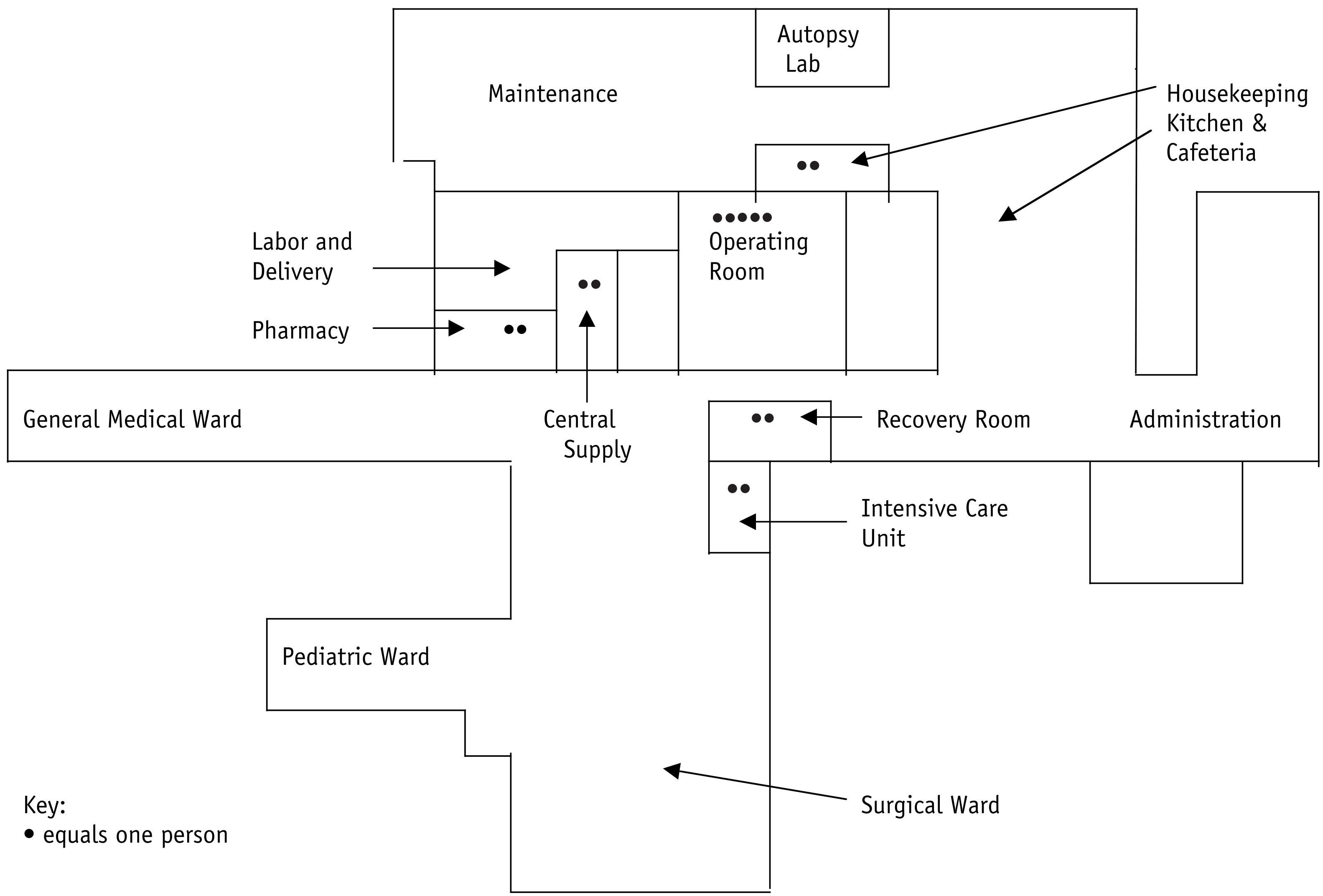
Xylene is an aromatic hydrocarbon similar in chemical structure to benzene and toluene. It occurs in three isometric forms: orthoxylene, metaxylene and paraxylene. Commercial xylene, frequently referred to as xylol, is a mixture of three isomers. Xylene is colorless, flammable, highly volatile and insoluble in water, and it has a characteristic odor. The odor threshold is approximately 1 ppm in air. It is used extensively in industry as a solvent and is a component of many common commercial products such as paints, varnishes, inks, dyes, adhesives and cleaning fluids. In hospitals xylene is used by the laboratory as a rinse when preparing cervical Papanicolaou smears and microscopic slides of surgical specimens. Liquid xylene is a skin irritant and causes local erythema, dryness, defatting and characteristic dermatitis. Xylene vapor is a mucous membrane irritant and also has systemic effects, primarily on the central nervous system. (See Appendix E.) In doses as low as 230 ppm, it causes headache, nausea and vomiting; in higher doses it can lead to narcosis and death. Fortunately because of the nature of its metabolites, xylene does not have the bone marrow toxicity associated with benzene. Appropriate corrective measures have been taken by the hospital. The inspection door is no longer left open. The floor drains are filled with mineral oil in the dry winter months and are checked periodically for an airtight seal. Xylene is no longer discarded through the hospital sewer system.

Appendix A: Information on the 15 Cases

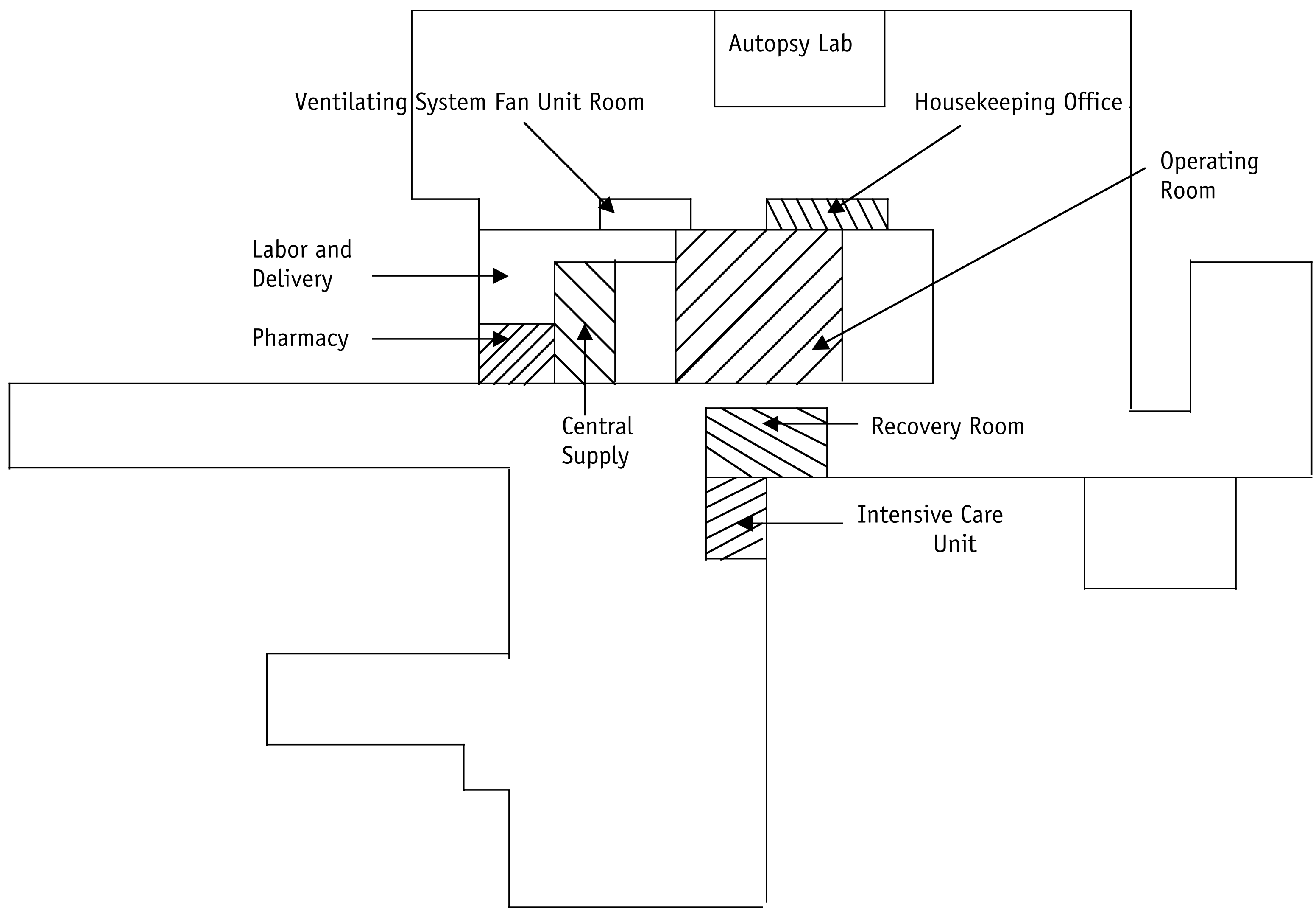
Case #	Sex	Age	Work Location	Time Of Onset	Headaches	Dizziness	Nausea	Vomiting	Duration (Hours)	Time Visited ED
1	F	41	PH	9:00 AM	0	0	+	+	2	10:00 AM
2	F	54	RR	DR	+	0	+	0	48	-
3	F	39	HK	DR	+	0	+	0	12	-
4	F	55	HK	9:15 AM	+	+	+	0	48	10:25 AM
5	F	39	OR	DR	+	+	0	0	DR	-
6	F	28	ICU	9:15 AM	+	0	+	0	DR	-
7	F	21	CS	8:45 AM	+	+	+	+	24	9:45 AM
8	F	52	OR	9:30 AM	+	+	+	+	48	10:30 AM
9	F	39	ICU	9:15 AM	+	0	+	+	24	11:15 AM
10	F	53	OR	9:30 AM	+	+	+	+	48	10:30 AM
11	F	42	CS	9:00 AM	+	+	+	+	24	9:55 AM
12	F	38	RR	9:15 AM	0	+	+	0	48	12:30 PM
13	F	21	PH	DR	+	+	0	0	DR	10:10 AM
14	F	42	OR	DR	0	+	+	0	DR	-
15	M	32	OR	DR	+	0	+	0	DR	-

DR = Don't Remember
HK = Housekeeping
CS = Central Supply
PH = Pharmacy
OR = Operating Room
RR = Recovery Room
ICU = Intensive Care Unit

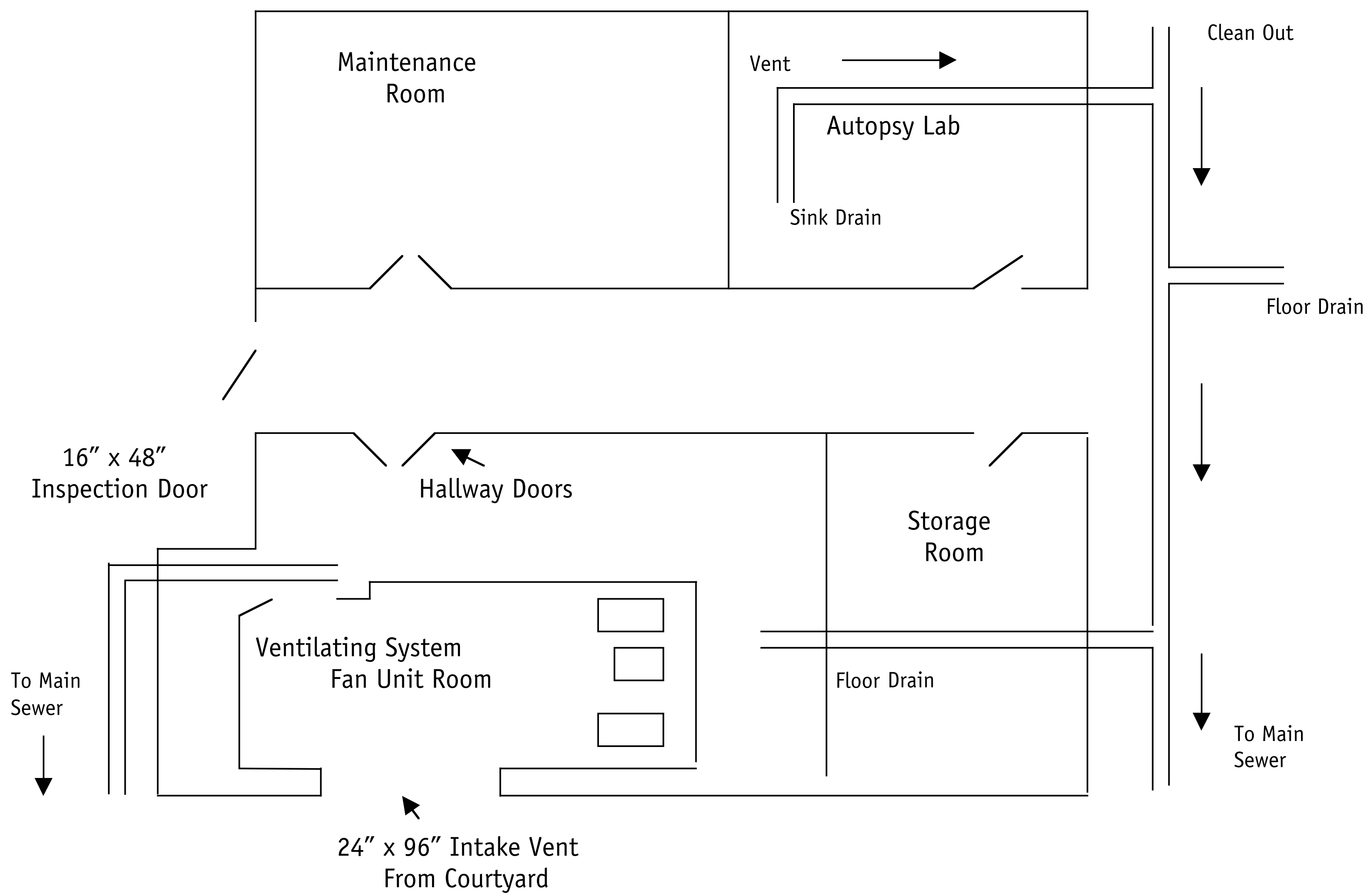
Appendix B (Teacher's Version): Hospital Floor Plan (Work Sites of Cases)



Appendix C: Hospital Floor Plan (Areas Served by Central Air System)



Appendix D: Distribution of Xylene Vapor



Appendix E: Estimated Threshold Vapor Concentrations for Effects of Xylene on Humans

Effect	**Parts per million (PPM)**
Odor threshold	1.0
Mucous membrane irritation	110–460
Nausea or vomiting	250+
Dizziness	230–690
Taste of threshold	230–690
Narcosis	2,000+
Lethal dose	10,000+
Federal occupational safety standard = 100 ppm	