Outbreak Investigation

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This lecture contains material from lectures previously taught by
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By the end of this lecture students should be able to

- Understand what constitutes to an outbreak
- To differentiate between endemic and epidemic
- Learn the importance of investigating an outbreak
- Be familiar with the steps for an outbreak investigation
- list types of studies used to investigate an outbreak
- Read an epidemic curve and use it in estimating the incubation period
- To calculate the attack rate from outbreak investigation data

Endemic, Epidemic, Pandemic, Outbreak

- **Endemic:**
  - The constant presence of usual prevalence of a disease in a given geographic area
- **Epidemic:**
  - The sudden increase in the number of cases for a certain disease above what is normally expected in that population
- **Pandemic:**
  - When an epidemic spreads over several countries usually affecting a large number of people
- **Outbreak:**
  - It is an epidemic that occurs in a limited geographic area (e.g. an institution, a home facility, a neighbourhood, a village…)

Source: *U.S. Department of Health and Human Services. Principles of Epidemiology in Public Health Practice (third Ed). 2008. Available at: https://www.cdc.gov/ophss/csels/dsepd/ss1978/ss1978.pdf*

What is a cluster?

- A cluster is the aggregation of cases in a given area over a particular period without regard to whether the number of cases is more than expected*

- **Why is this important?**

Because detecting unusual clusters of disease can hint to the occurrence of an outbreak in that population

** U.S. Department of Health and Human Services. Principles of Epidemiology in Public Health Practice (third Ed). 2008. Available at: https://www.cdc.gov/ophss/csels/dsepd/ss1978/ss1978.pdf*

How are Outbreaks Detected?

- *Analyzing surveillance data*:
  - reviewing exposure information from reports of infectious diseases cases sent by laboratories and healthcare providers
- *Health Ministry*
  - *conducts periodical routine surveillance* for infectious disease cases in the community, and detect an unusual increase in the number of reported cases
- *Infection and control at the hospital*
  - review microbiological isolates of organisms from patients and wards to detect any unusual increase in number of infections
- *Vigilant physician*
  - notices an unusual cluster of patients with the same symptoms and reports to health authorities

Factors that may affect the decision to investigate an outbreak

- Number and pattern of people involved (cluster of cases)
- Type of disease (ease of transmission; type of causative agent)
- Severity of disease; unusual presentation
- Availability of effective control measures
- If the disease needs prompt control measures to prevent fast spread to others (or is it already over?)
- Availability of staff and resources to conduct investigation

Reasons for conducting an outbreak investigation

- Control and prevention
- Research opportunity
- Learning and training "an experiment of nature waiting to be analyzed"
- Public or legal concerns

Steps for conducting an outbreak investigation

Table 6.2 Epidemiologic Steps of an Outbreak Investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Construct a working case definition
5. Find cases systematically and record information
6. Perform descriptive epidemiology
7. Develop hypotheses
8. Evaluate hypotheses epidemiologically
9. As necessary, reconsider, refine, and re-evaluate hypotheses
10. Compare and reconcile with laboratory and/or environmental studies
11. Implement control and prevention measures
12. Initiate or maintain surveillance
13. Communicate findings

** U.S. Department of Health and Human Services. Principles of Epidemiology in Public Health Practice (third Ed). 2008. Available at: https://www.cdc.gov/ophss/csels/dsepd/ss1978/ss1978.pdf*

Example: Botulism in Argentina

- On January 13, 1998, an infectious diseases physician at a Buenos Aires hospital telephoned the Directorate of Epidemiology of the Argentine Ministry of Health (MOH) to report two possible cases of botulism.
- The patients, both men, presented with drooping eyelids, double vision, difficulty swallowing, and respiratory problems.
- One patient had onset of symptoms on January 5 and the other on January 6.
- The physician had drawn sera and collected stool specimens from the men to test for botulinum toxin but no results were available

1-Prepare for field work

- Do you have the knowledge, resources and staff for the field?
- Will you need any laboratory tools?
- Do I need equipment to protect myself?
- Do I have an action plan?
- Identify team members (who will do what?)
- Is it a zoonotic disease? (will I need a veterinarian?)

Botulism in Argentina: is it worth investigating?

- Could this possibly be an outbreak? is it worth investigation?
- Seriousness of the disease?
- Food-borne from a possible manufacturer (contaminated products) could spread to many people

2-Establish the existence of an outbreak

- Is the number of cases higher than the usual?
  - Compare the current situation with the expected number from past weeks or months; hospital data; neighboring cities; background of disease in community
- Is there a cluster of cases with the same complaints?
- Is the increase in reporting due to actual increase in number of cases or due to improvement of diagnosis and surveillance methods?
- Severity of the disease? availability of control measure? dose this need prompt response?

Back to the Botulism example..

- The epidemiologists established that this is a public health emergency because people may contract the disease from the same source and the complications of the disease is severe.

- However, the results from the lab were still not available, but they still have to *verify the diagnosis* before continuing.

3-Verify the diagnosis

- This is required to:

1. To ensure that the disease has been properly diagnosed
2. To rule out that increase in disease diagnosis was due to laboratory error

- Review clinical findings (are they consistent with the disease?)
- Laboratory methods used
- Frequency tables for clinical findings (are they all presenting with same symptoms?)

Back to the Botulism example..

- The clinical syndrome of botulism is dominated by neurologic signs and symptoms.
- If respiratory muscles are involved, ventilatory failure and death may result unless supportive care is provided.
- The average incubation period for botulism is 18-36 hours, but symptoms can occur as early as six hours or as late as 10 days after exposure.

4-Construct a working case definition

- **Case definition:** This is a set of criteria needed to classify an individual as having the disease or not
- Identify and count cases
- criteria should be objective measures
- DO NOT include the risk factor of interest in your case definition: e.g. if symptoms started after eating in restaurant A, do not make your case definition exclusively for people who ate at rest A
- Instead, define cases within a certain time period
  - who had symptoms from month X to month Y
- Different categories: *confirmed*, *probable*, *possible*, *suspect*
- Start loose and then tighten your definition later on

5-Find cases systematically and record information

- Ask local health facilities if they have patients with similar history and symptoms
- Ask the patients if other members they know have the same symptoms
- Review ER admission log
- Contact laboratory and ask to inform you about any orders for testing for the disease in question
- Contact media to ask community to be vigilant for the symptoms and contact health facility if they experience them

What information should we collect from each case?

- Name
- Demographic data
- Risk factors; exposures. If food borne ask about meal history in the past few days depending on incubation period of the disease
- Symptoms and signs
- Who reported the information
- Confirmed or pending lab results

Perform Line lists

Line Listing of reported suspect cases, page 1

Case #	Initials	Date of Report	Date of Onset	Diagnostic: MD Dx	Signs and Symptoms: N	V	A	F	DU	J	Lab: HA IgM	Other	Age	Sex
1	JG	10/12	10/6	Hep A	+	+	+	+	+	+	+	SGOT↑	37	M
2	BC	10/12	10/5	Hep A	+	–	+	+	+	+	+	ALT↑	62	F
3	HP	10/13	10/4	Hep A	±	–	+	+	+	S*	+	SGOT↑	30	F
4	MC	10/15	10/4	Hep A	–	–	+	+	?	–	+	HBs Ag -	17	F
5	NG	10/15	10/9	NA	–	–	+	–	+	+	NA	NA	32	F
6	RD	10/15	10/8	Hep A	+	+	+	+	+	+	+		38	M
7	KR	10/16	10/13	Hep A	±	–	+	+	+	+	+	SGOT = 240	43	M
8	DM	10/16	10/12	Hep A	–	–	+	+	+	–	+		57	M
9	PA	10/18	10/7	Hep A	±	–	+	±	+	+	+		52	F
10	SS	10/11	10/11	R/o Hep A Hep	+	+	+	[illegible]	+	–	pending	HBsAg [illegible]	31	M

S* = scleral F = fever

Perform a Line List

- A line list is a document that contains key information about each case
- Each row in the line list represents the information about one case
- You include: ID info, demographic info, symptoms, date of onset, PE, any lab results
- There are templates available for line lists on the CDC, but they should be modified to fit the disease outbreak

Table 1. Characteristics of cases of botulism, Buenos Aires, January 1998.

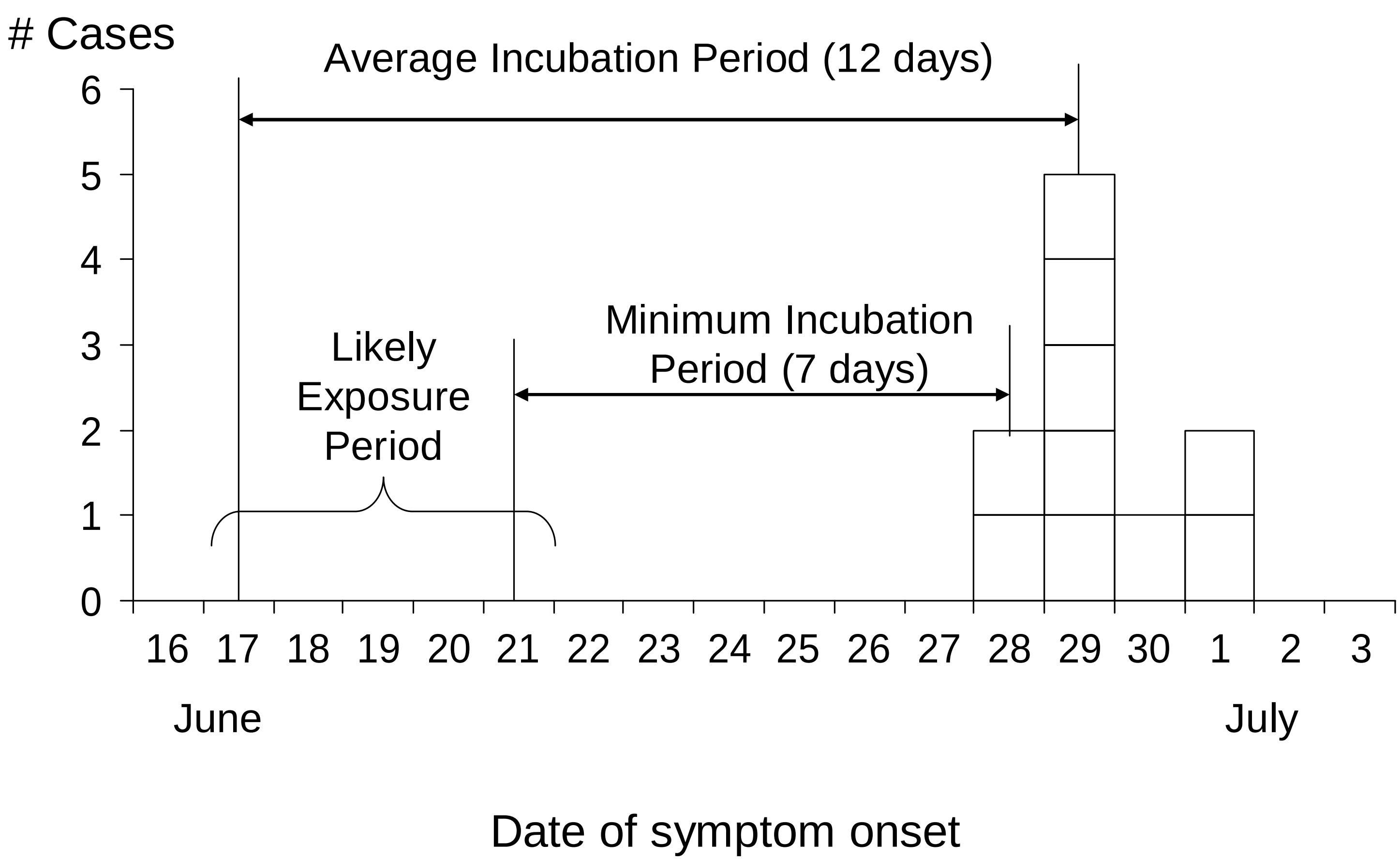
Patient No.	Age (years)	Gender	Work shift	Onset of neuro-logic symptoms	Symptoms
1	42	M*	Morning	January 6	blurred vision, double vision, drooping eyelids, upper and lower extremity weakness, respiratory difficulty, fatigue
2	31	M	Morning	January 5	blurred vision, double vision, drooping eyelids, upper and lower extremity weakness
3	23	M	Morning	January 9	blurred vision, drooping eyelids, upper extremity weakness, fatigue
4	46	M	Morning	January 8	drooping eyelids, difficulty speaking
5	54	M	Morning	January 5	blurred vision, double vision, drooping eyelids, difficulty speaking, respiratory difficulty
6	49	M	Morning	January 10	blurred vision, drooping eyelids, difficulty speaking
7	31	M	Morning	January 15	blurred vision, double vision, drooping eyelids, upper and lower extremity weakness, respiratory difficulty, fatigue
8	44	M	Morning	January 14	respiratory difficulty, fatigue, drooping eyelids,
9	24	M	Morning	January 12	drooping eyelids, fatigue

*M=male gender

6-Perform descriptive epidemiology

- Important to observe time trends (epidemic curve), distribution by geographic area and other demographics
- Try to infer the risk of the disease
- Provides clues about the possible etiology and risk factors in order to generate hypotheses
- Shows <u>where</u> and <u>among who</u> the disease is in order to begin intervention
- Helps identify the likely period of exposure (from epidemic curve)

Example of an epidemic curve



How to identify exposure period from epidemic curve?

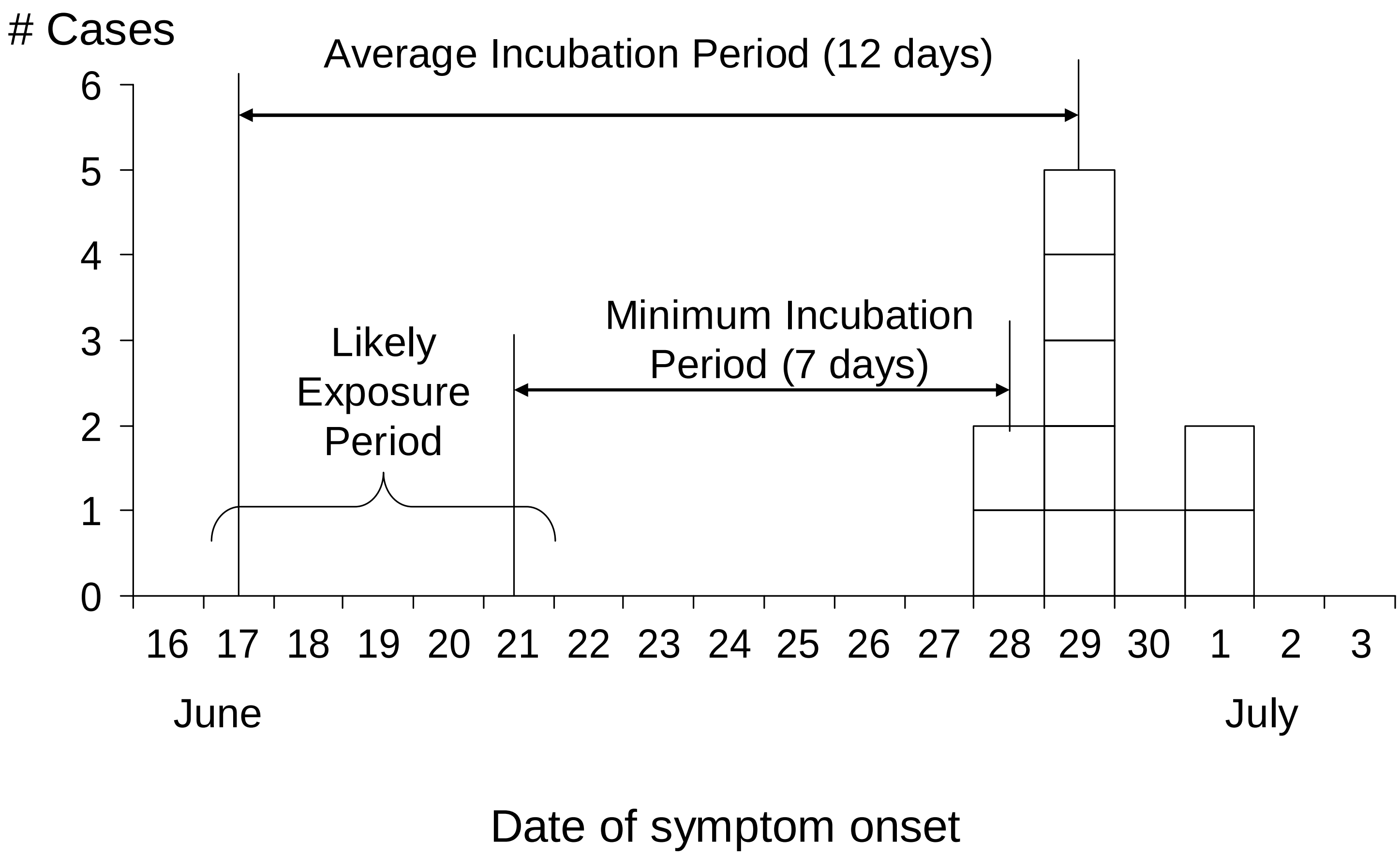
If patients cluster at a certain point:

- Identify the peak of the outbreak Or the median case
- From that point, count back on the x-axis one *average incubation period* => note this date
- Start from the earliest case and count back one *minimum incubation period* => note this date as well

If no cluster of cases (continuous common source):

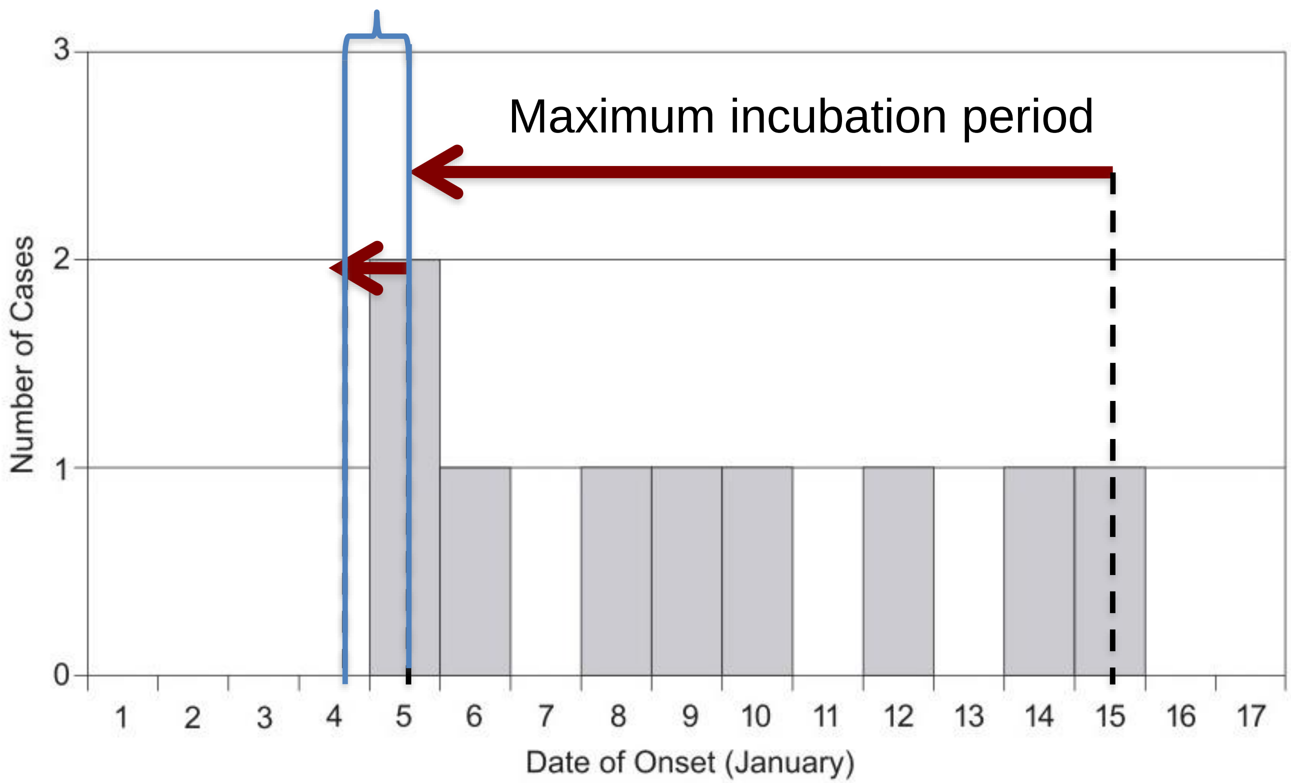
- Earliest case count backwards a minimum incubation period
- Last case count backwards one maximum incubation period

Example of identifying period of exposure from epidemic curve



Epidemic Curve form the botulism example

Figure 1. Onset date of neurologic symptoms among patients with botulism in Buenos Aires, Argentina, January 1998. (N=9)



Incubation period for Botulism:

average 18-36 hrs

Can range from 6 hrs-10 days

Source: U.S. Department of Health and Human Services. Botulism in Argentina. Available at: https://www.cdc.gov/epicasestudies/downloads/bot_ins_eng.pdf

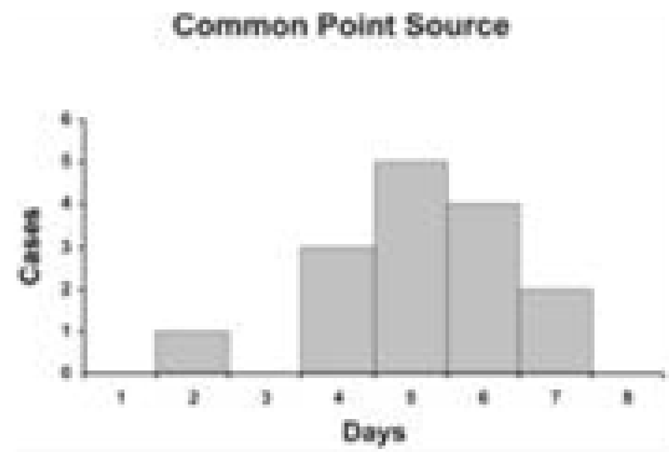
Can you estimate the possible period of exposure?

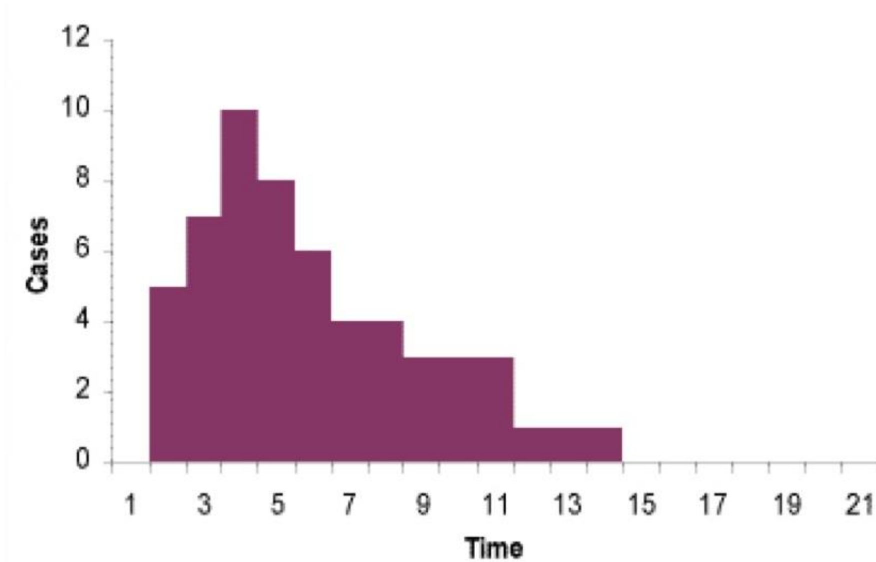
Types of epidemics from epidemic curve

1. Common Point Source

People are usually exposed to the same risk factor over a limited and defined period of time (usually one incubation period)

Shape: rapid rise, with a sharp peak, then gradual decline



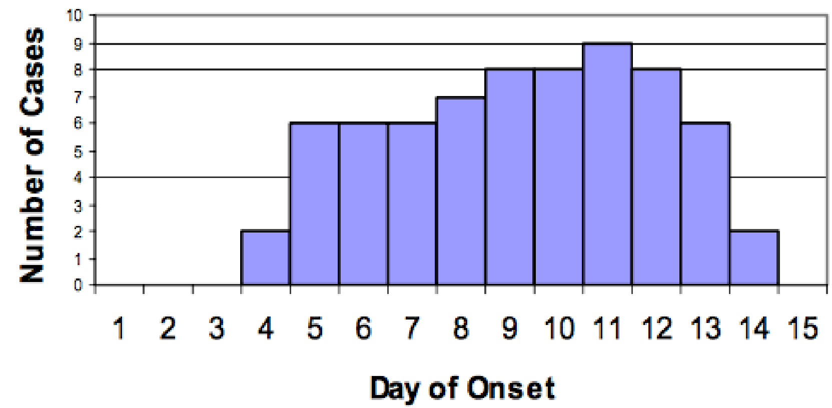


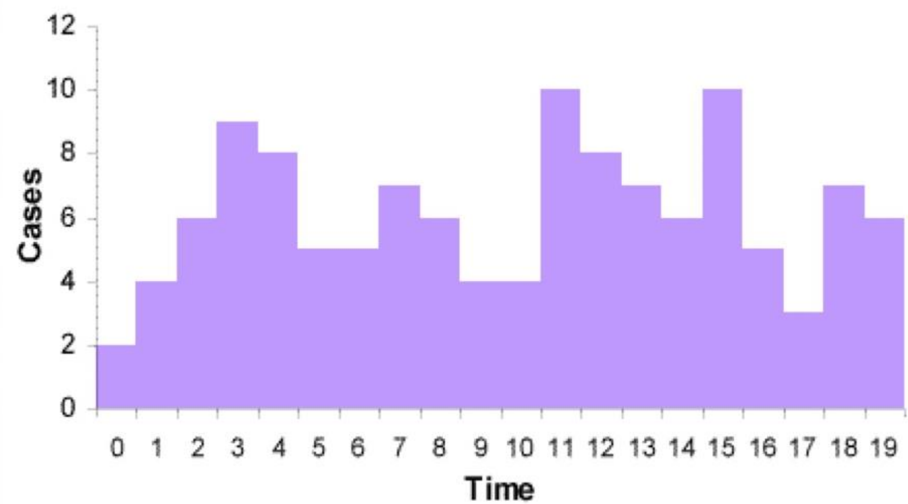
Types of epidemics from epidemic curve

2. Continuous Common Source (intermittent source)

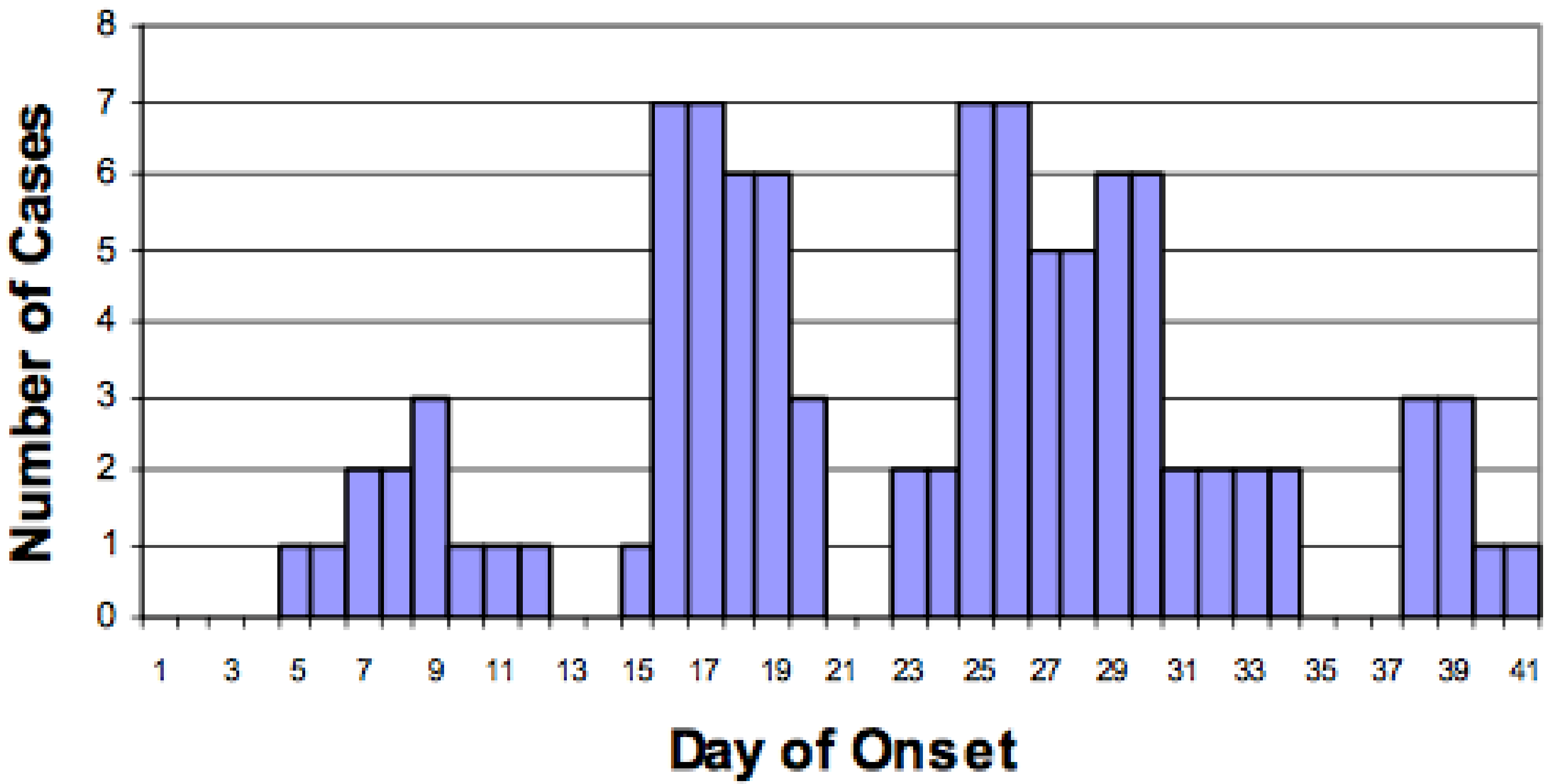
- Exposure occurs over prolonged period (>one incubation period)
- People are exposed continuously or intermittent to a common source

Shape: has several peaks without a clear incubation period





Another Example for Intermittent common source



Source: Torok M. Epidemic curves ahead. Focus on Field Epidemiology 2003;1(5). Available at: https://nciph.sph.unc.edu/focus/vol1/issue5/1-5EpiCurves_issue.pdf

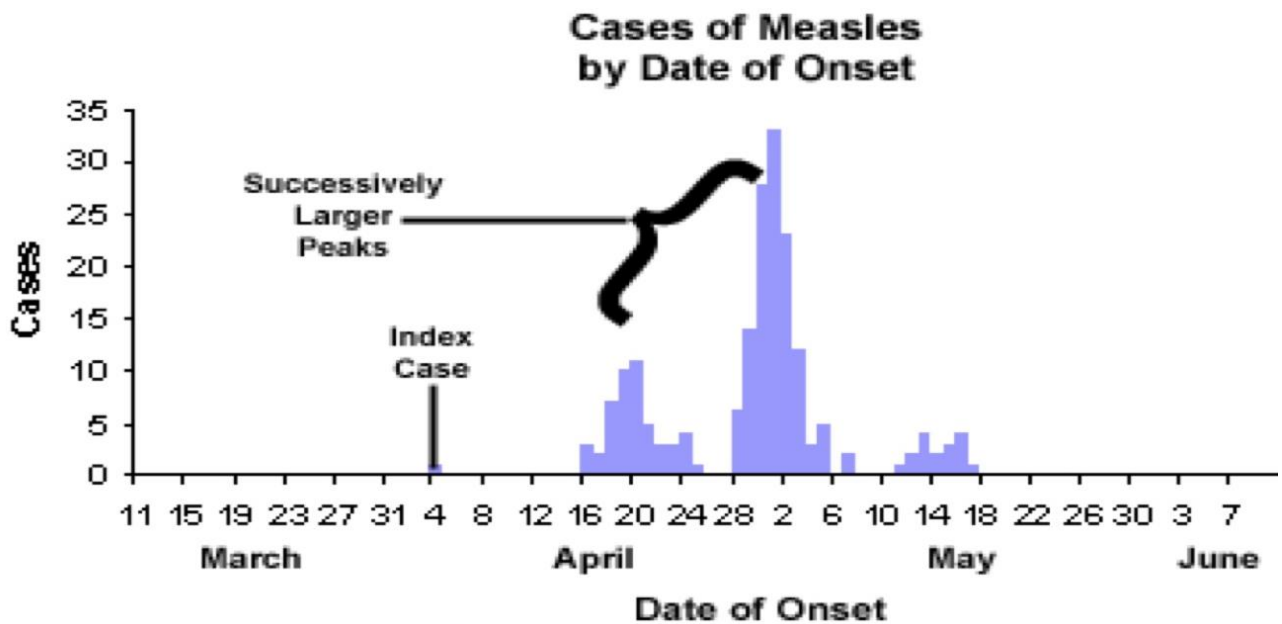
Types of epidemics from epidemic curve

3. Propagated Source (progressive source)

Here cases serve as sources for subsequent cases, and subsequent cases serve as source for later cases.

Reflects a disease transmitted from person to person.

Shape: A series of successively larger peaks



Questions we ask ourselves after looking at the epidemic curve

- Is the outbreak from a single source? or multiple sources?
- Is it spread from person to person?
- Is the exposure continuing or did it just occur at one event?
- Is there a vector involved?
- Is it chemically transmitted or airborne?
- Is the source of infection unapparent?

These help us develop our hypotheses!

Back to the Botulism Example

- What epidemic curve is this?

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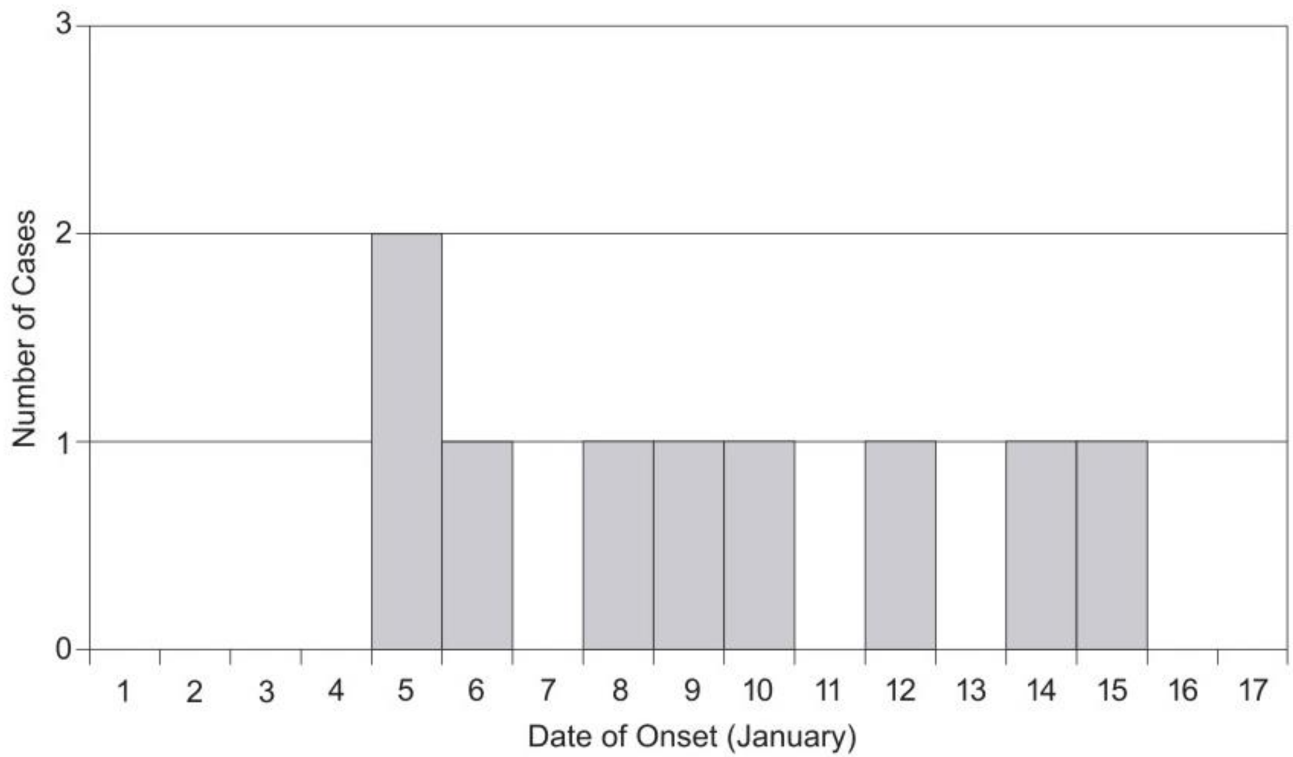


Back to the Botulism Example..

- After some investigation, the epidemiologists found that the cases were all bus drivers who worked at the morning shift, and ate at the same restaurant in the morning.
- Investigators <u>hypothesized</u> that:
  - Exposure was at the restaurant
  - During the morning shift
  - Intermittent exposure to the same source (based on epidemic curve)

7-Develop a hypothesis

The hypotheses may address:

- Source of the agent => What is the reservoir?
- Mode of transmission => vehicles? vectors?
- Exposure and risk factors =>
  - Ask cases about what they think could be possible exposure?
  - *Epidemic curve may trigger the question:* What common exposure happened during the possible period of exposure?
  - What special CCCs do the cases have? (age, sex, risk factors)
  - Why do people in a specific area have the highest attack rate?

8-Evaluate the hypothesis

We evaluate our hypotheses:

1. Compare with established facts=>
   - laboratory testing
   - Environmental assessment
   - Epidemiologic evidence

If findings are not straightforward……..

2. Analytical epidemiological study =>
   - Compare two groups to look for association between the disease and exposure to the hypothesized source

Analytical Epidemiology in Outbreak Investigations

Retrospective Cohort Study

- Suitable when the number of cases is small in a well defined population
- We divide the whole people in that defined population into people exposed vs. people not exposed to the source -> and assess their disease status
- We then estimate the Attack Rate (Risk) , and then the Risk Ratio (relative risk)

Case-control Study

- Suitable when the number of cases is larger
- We divide the people to cases and controls, then assess their exposure status
- We then estimate the odds ratio

Retrospective Cohort

Food	ate			Did not eat			
	Ill	well	AR	Ill	well	AR	RR
meat	29	17	0.63	17	12	0.59	1.06
spinach	26	17	0.60	20	12	0.62	0.97
potato	23	14	0.62	23	14	0.62	1.00
salad	13	11	0.54	28	19	0.60	0.9
Ice cream	43	11	0.80	3	18	0.14	5.71

AR=Attack rate; RR=Rate Ratio

Case-control Study

Exposure		Case	Control	Total
Ate at restaurant A	Yes	30	36	66
	No	10	70	80
Total		40	106	146

9-Reconsider, refine and re-evaluate your hypothesis

- Sometimes epidemiological analyses does not answer the questions of the investigator
- The investigator may need to conduct further studies, study a different exposure, or refine the population being studied in order to reach answers
- The investigator refines the hypothesis based on the results of epidemiologic analysis and if they were not confirmed by laboratory testing, and conduct further studies

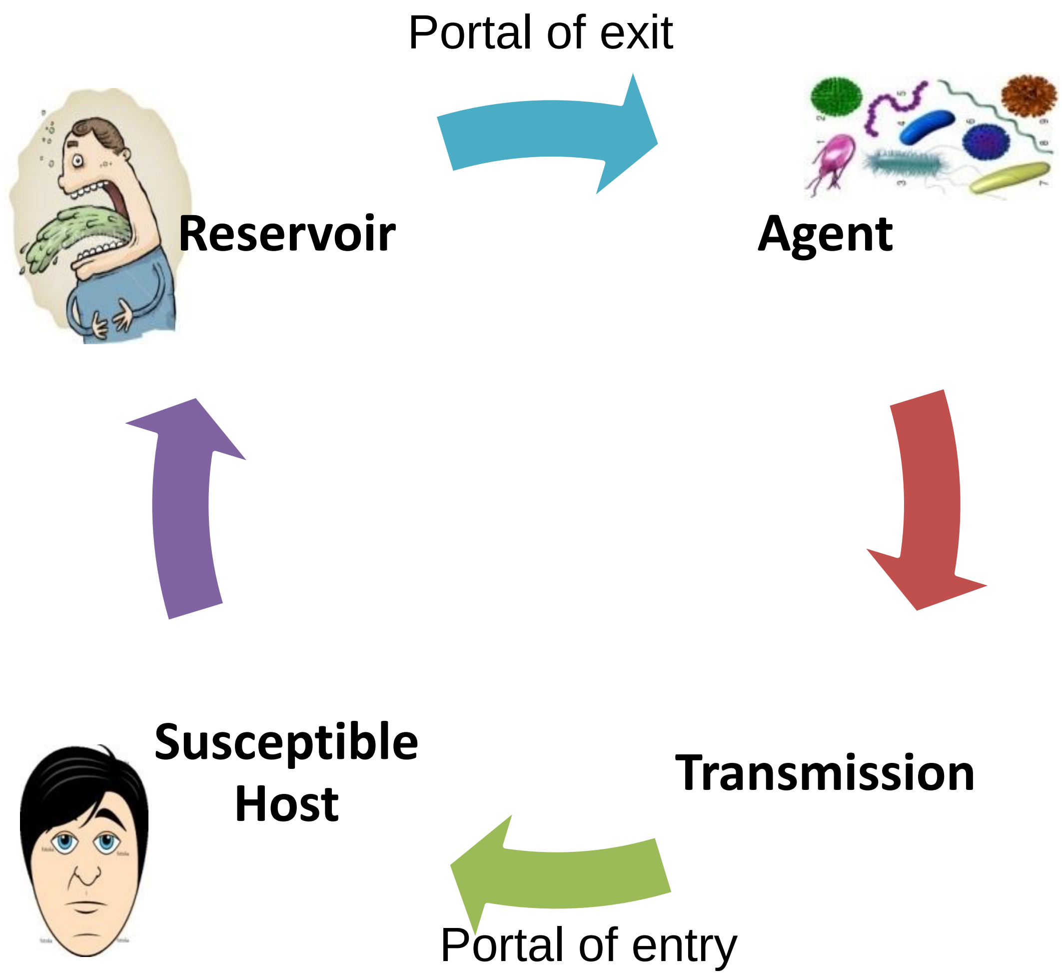
10-Compare with laboratory and environmental studies

- Coordinate results from epidemiological analyses with evidence from laboratory testing and/or assessing the environment
- For example, when a food borne outbreak is suspected, and epidemiologic analyses pointed to a certain food product, the investigator would test that food product and culture it for the infectious agent in question
- If a water-borne outbreak is suspected from epidemiologic study, the investigator would examine the water source for reasons of contamination

11-Implement prevention and control measures

- Prevention and control measures are usually taken from the beginning of the outbreak (prompt treatment of cases; remove the source when identified; isolate cases if needed; prevent spread to susceptible individuals…etc)
- Control measures are implemented in a way that interrupts one or more of the elements in the “chain of infection”

Chain of Infection



12-initiate or maintain surveillance

- Surveillance should be ongoing from the beginning of the investigation
- If not started yet, now is the time for active surveillance and continuing it until we are sure the outbreak has stopped

Reasons for surveillance:

1. To determine that prevention and control measures are working
2. Assured the outbreak did not spread outside the area targeted by the intervention

13-Communicate findings

Summarize everything that happened and what has been done:

- The outbreak (onset, cases involved, symptoms, duration, complications)
- laboratory investigations
- sources detected
- type of epidemiologic study conducted and results of analyses
- coordination of results with evidence (lab and environment)
- prevention and control measures implemented and containment of outbreak

We communicate this summary:

- To local health authority
- written report (scientific format) that is later added to the literature

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