Epidemiologic Investigation of Outbreaks

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What is an outbreak/epidemic?

- An **outbreak** or an **epidemic** exists when there are *more cases of a particular disease than expected in*
  - *a given area, or among a specific group of people,*
  - *over a particular period of time.*
- Many epidemiologists use the terms "outbreak" and "epidemic" interchangeably;
  - some restrict the use of "epidemic" to situations involving large numbers of people over a wide geographic area.
- The public is more likely to think that "epidemic" implies a crisis situation.

10 Steps of outbreak investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Define and identify cases
5. Describe and orient the data in terms of time, place, and person
6. Develop hypotheses
7. Evaluate hypotheses
8. Refine hypotheses and carry out additional studies
9. Implement control and prevention measures
10. Communicate findings

2. Establish the existence of an outbreak

- Does the observed cases exceed the expected number?
  - Notifiable disease, use health dept. data
  - Other local data, hospital discharge records, mortality records etc
  - If local data not available, *guesstimates* from neighboring cities, countries
  - Conduct your own survey of local physicians, telephone etc

3. Verify the diagnosis

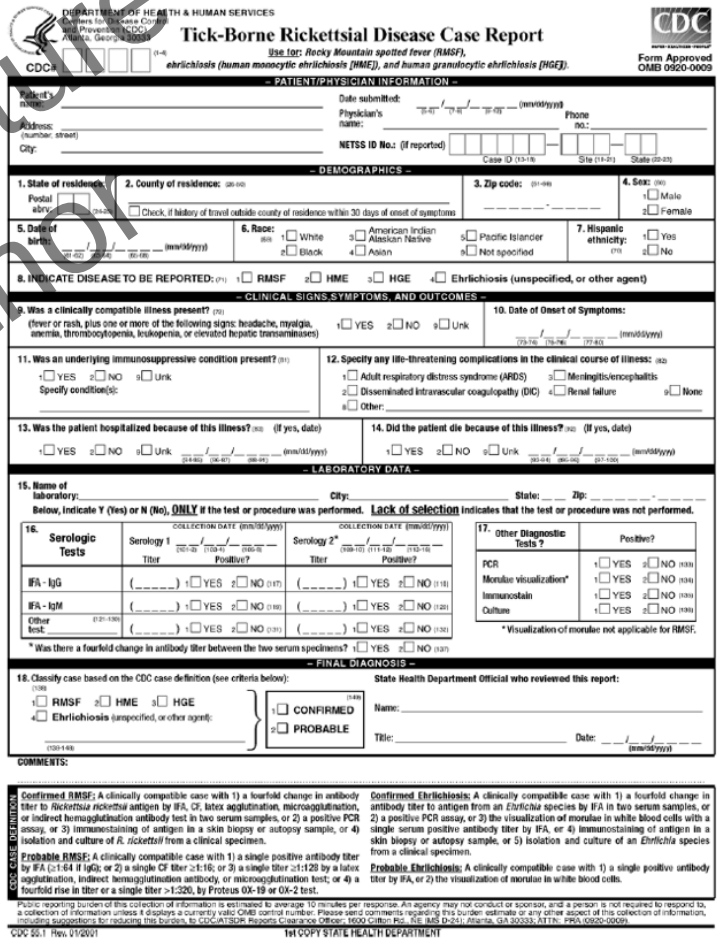
- Identify as accurately as possible the specific nature of the disease
  - The disease is what is said to be
- Collaborate closely with the lab
- Visit people who became ill
  - Gain a better understanding of the disease from those who are affected

4. Define and identify cases

- Establish a case-definition
- Be explicit and inclusive
  - Any geographic limits?
  - Fever?
  - How many loose stools?
  - What level of antibodies?

Still step 4: More details and count cases!

- Collect information on standard CRFs
  - Identifying information
  - Demographic
  - Clinical
  - Risk factor



DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
Atlanta, Georgia 30333

CDC

Form Approved
OMB 0920-0009

Tick-Borne Rickettsial Disease Case Report

Use for: *Rocky Mountain spotted fever (RMSF), ehrlichiosis (human monocytic ehrlichiosis [HME]), and human granulocytic ehrlichiosis [HGE])*

CDC#

– PATIENT/PHYSICIAN INFORMATION –

Patient's name:
Address: (number, street)
City:
Date submitted: (mm/dd/yyyy)
Physician's name:
Phone no.:
NETSS ID No.: (If reported) Case ID (13-18) Site (19-21) State (22-23)

– DEMOGRAPHICS –

1. State of residence: Postal abbr.
2. County of residence:
Check, if history of travel outside county of residence within 30 days of onset of symptoms
3. Zip code:
4. Sex: 1 Male 2 Female
5. Date of birth: (mm/dd/yyyy)
6. Race: 1 White 2 Black 3 American Indian or Alaskan Native 4 Asian 5 Pacific Islander 9 Not specified
7. Hispanic ethnicity: 1 Yes 2 No
8. INDICATE DISEASE TO BE REPORTED: 1 RMSF 2 HME 3 HGE 4 Ehrlichiosis (unspecified, or other agent)

– CLINICAL SIGNS, SYMPTOMS, AND OUTCOMES –

9. Was a clinically compatible illness present? (fever or rash, plus one or more of the following signs: headache, myalgia, anemia, thrombocytopenia, leukopenia, or elevated hepatic transaminases) 1 YES 2 NO 9 Unk
10. Date of Onset of Symptoms: (mm/dd/yyyy)
11. Was an underlying immunosuppressive condition present? 1 YES 2 NO 9 Unk
Specify condition(s):
12. Specify any life-threatening complications in the clinical course of illness: 1 Adult respiratory distress syndrome (ARDS) 2 Disseminated intravascular coagulopathy (DIC) 3 Meningitis/encephalitis 4 Renal failure 8 Other: 9 None
13. Was the patient hospitalized because of this illness? 1 YES 2 NO 9 Unk (If yes, date) (mm/dd/yyyy)
14. Did the patient die because of this illness? 1 YES 2 NO 9 Unk (If yes, date) (mm/dd/yyyy)

– LABORATORY DATA –

15. Name of laboratory: City: State: Zip:
Below, indicate Y (Yes) or N (No), **ONLY** if the test or procedure was performed. **Lack of selection** indicates that the test or procedure was not performed.

16. Serologic Tests	Serology 1 Collection Date (mm/dd/yyyy) Titer	Positive?	Serology 2* Collection Date (mm/dd/yyyy) Titer	Positive?
IFA - IgG	( )	1 YES 2 NO	( )	1 YES 2 NO
IFA - IgM	( )	1 YES 2 NO	( )	1 YES 2 NO
Other test:	( )	1 YES 2 NO	( )	1 YES 2 NO

* Was there a fourfold change in antibody titer between the two serum specimens? 1 YES 2 NO

17. Other Diagnostic Tests ?	Positive?
PCR	1 YES 2 NO
Morulae visualization*	1 YES 2 NO
Immunostain	1 YES 2 NO
Culture	1 YES 2 NO

* Visualization of morulae not applicable for RMSF.

– FINAL DIAGNOSIS –

18. Classify case based on the CDC case definition (see criteria below): 1 RMSF 2 HME 3 HGE 4 Ehrlichiosis (unspecified, or other agent):
1 CONFIRMED 2 PROBABLE
State Health Department Official who reviewed this report:
Name:
Title: Date: (mm/dd/yyyy)

COMMENTS:

CDC CASE DEFINITION

Confirmed RMSF: A clinically compatible case with 1) a fourfold change in antibody titer to *Rickettsia rickettsii* antigen by IFA, CF, latex agglutination, microagglutination, or indirect hemagglutination antibody test in two serum samples, or 2) a positive PCR assay, or 3) immunostaining of antigen in a skin biopsy or autopsy sample, or 4) isolation and culture of *R. rickettsii* from a clinical specimen.

Probable RMSF: A clinically compatible case with 1) a single positive antibody titer by IFA (≥1:64 if IgG) or 2) a single CF titer ≥1:16; or 3) a single titer ≥1:128 by a latex agglutination, indirect hemagglutination antibody, or microagglutination test; or 4) a fourfold rise in titer or a single titer >1:320, by Proteus OX-19 or OX-2 test.

Confirmed Ehrlichiosis: A clinically compatible case with 1) a fourfold change in antibody titer to antigen from an *Ehrlichia* species by IFA in two serum samples, or 2) a positive PCR assay, or 3) the visualization of morulae in white blood cells with a single serum positive antibody titer by IFA, or 4) immunostaining of antigen in a skin biopsy or autopsy sample, or 5) isolation and culture of an *Ehrlichia* species from a clinical specimen.

Probable Ehrlichiosis: A clinically compatible case with 1) a single positive antibody titer by IFA, or 2) the visualization of morulae in white blood cells.

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Create line listings

Case#	Initials	Date of Report	Date of Onset	Physician Dx	Signs and Symptoms						Lab			
					N	V	A	F	DU	J	HAIgM	Other	Age	Sex
1	JG	12-Oct	6-Dec	Hep A	+	+	+	+	+	+	+	SGOT ↓	37	M
2	BC	12-Oct	5-Oct	Hep A	+	-	+	+	+	+	+	Alt ↓	62	F
3	HP	13-Oct	4-Oct	Hep A	+	-	+	+	+	S*	+	SGOT ↓	30	F
4	MC	15-Oct	4-Oct	Hep A	-	-	+	+	?	-	+	Hbs/ Ag-	17	F
5	NG	15-Oct	9-Oct	NA	-	-	+	-	+	+	NA	NA	32	F
6	RD	15-Oct	8-Oct	Hep A	+	+	+	+	+	+	+		38	M
7	KR	16-Oct	13-Oct	Hep A	+	-	+	+	+	+	+	SGOT = 240	43	M

5. Describe and orient the data in terms of time, place, and person

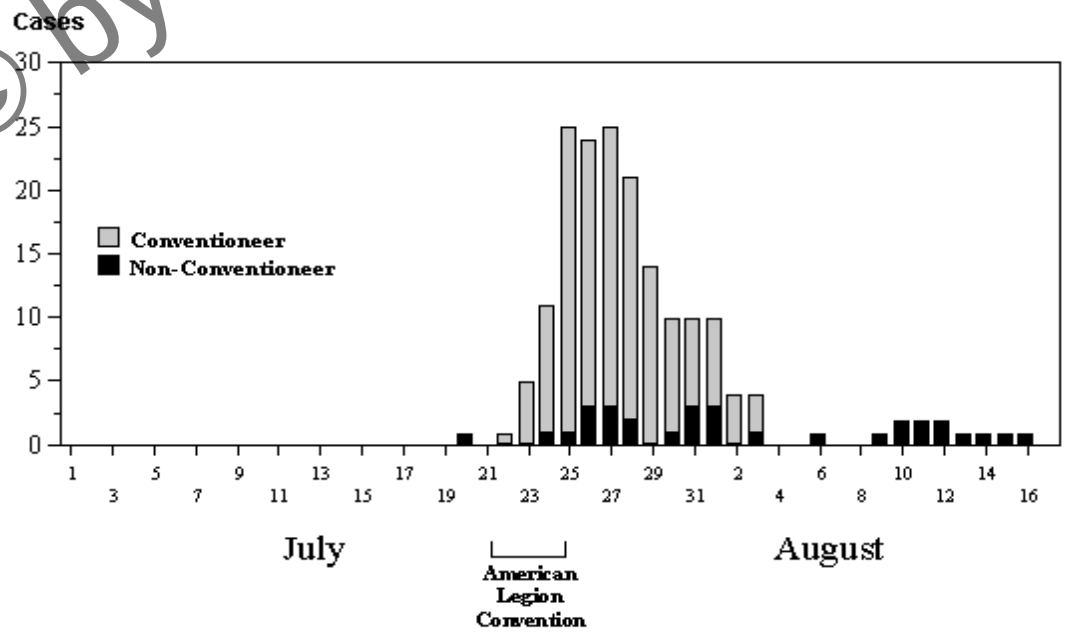
- Characterize the outbreak,
  - Trend over time (epidemic curve),
  - Geographic extent
  - Population affected

- Help you in evaluating the source, mode of transmission, risk factors

The epidemic curve

Helps in:

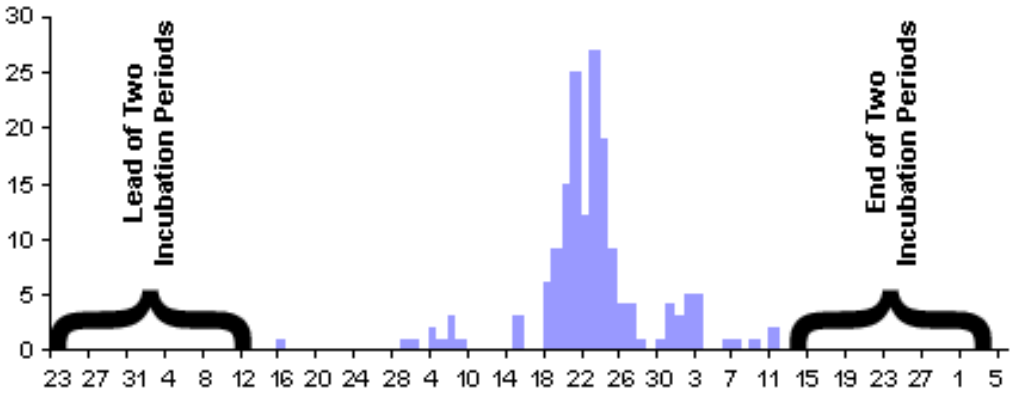
- Confirming the existence of an epidemic
- Where you are in the course of epidemic
- Project future course
- Determine the probable time period of exposure
- Draw inference about epidemic pattern
  - Common source
  - Person-to-person
  - Both
  - None

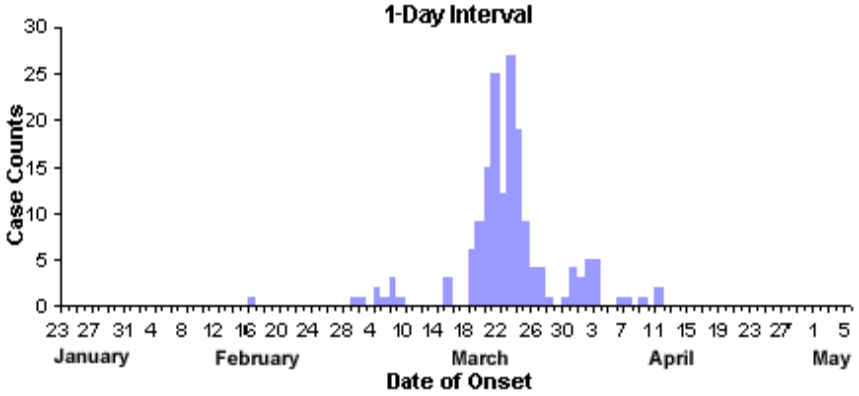


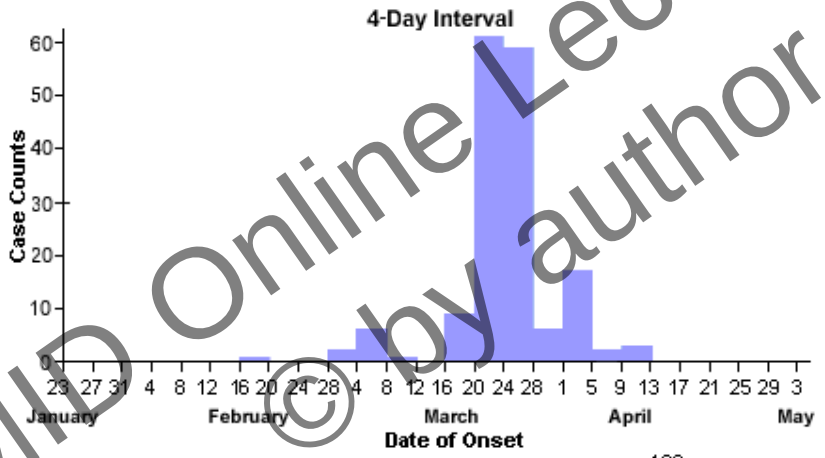
How to draw an epi curve

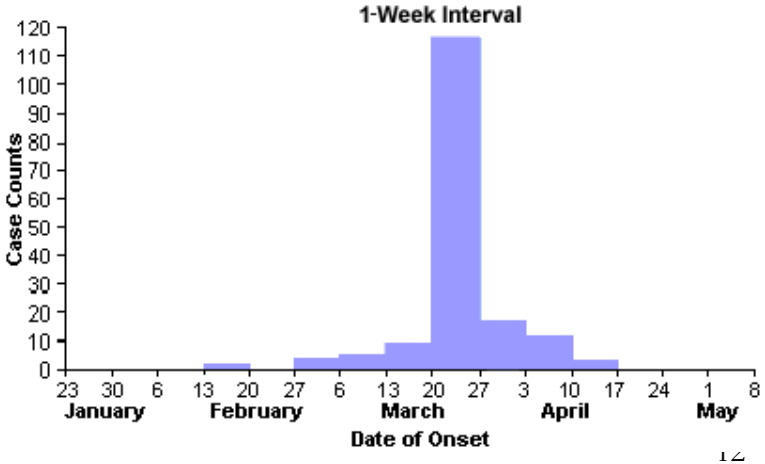
- Date of onset, sometimes hours of onset
- Number of cases on the y-axis
- The unit of time on the x-axis
- Rule of thumb: select a unit not longer than 1/3-1/4th of the incubation time
- If you don't know incubation, draw several
- Include lead-time and end-time periods = Twice the incubation period

Smallpox incubation
Min-max=7-17days
Average=12-14 days

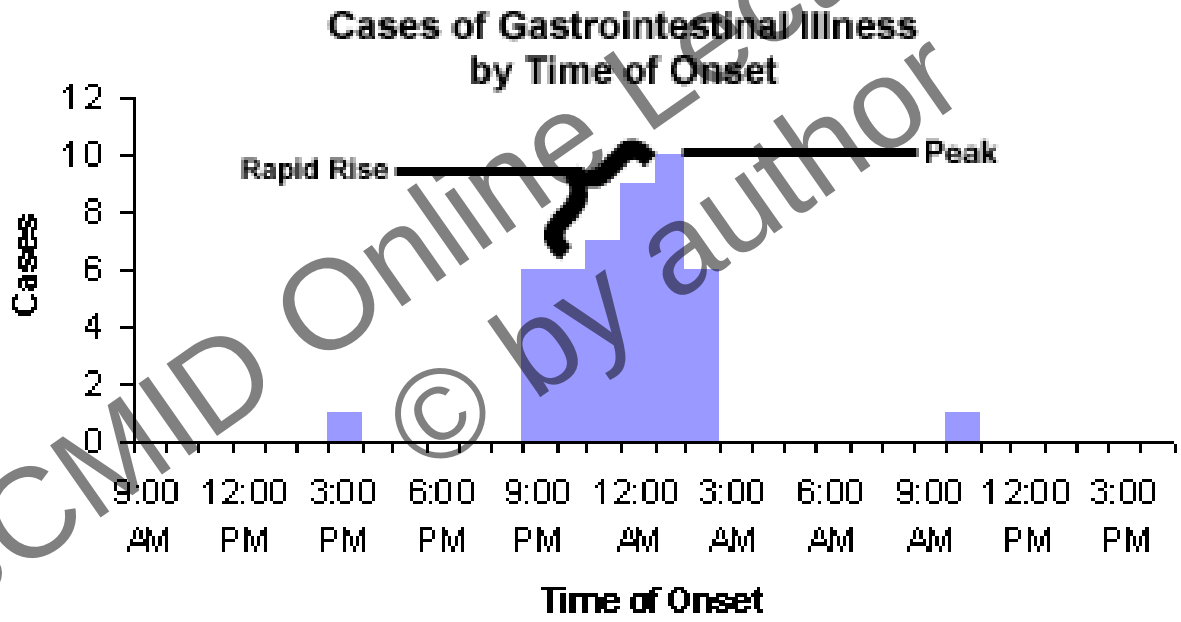




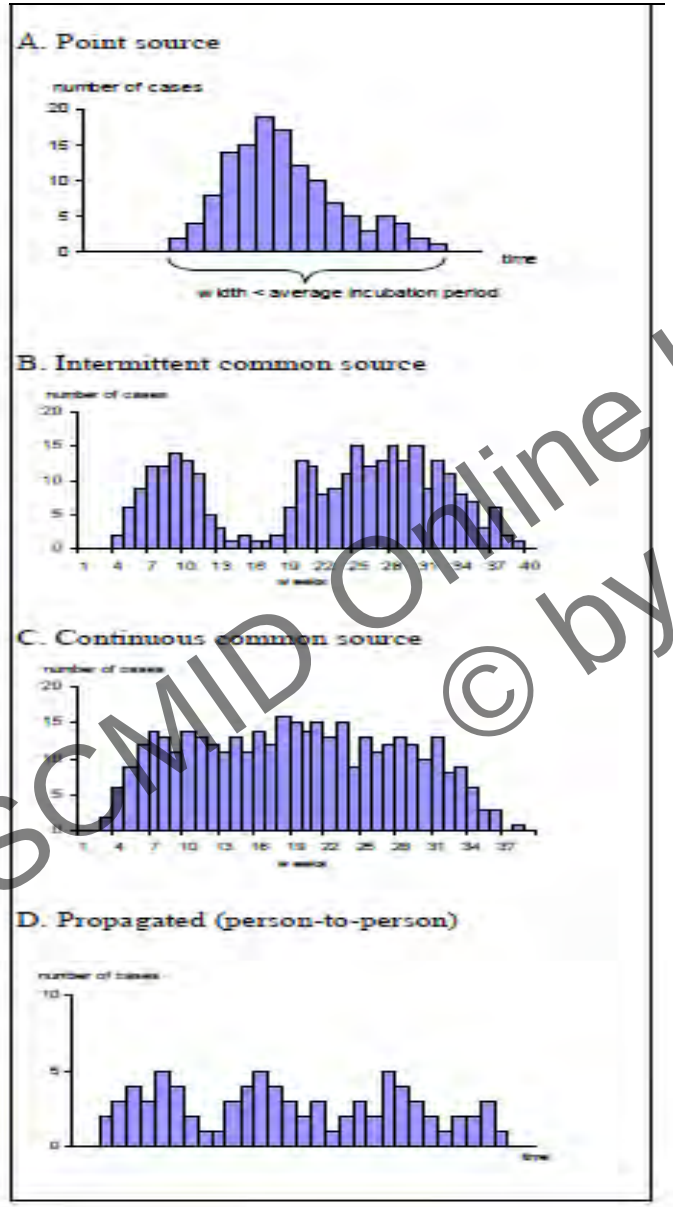




Shape of the epi curve
Point source outbreak



Common-source outbreaks



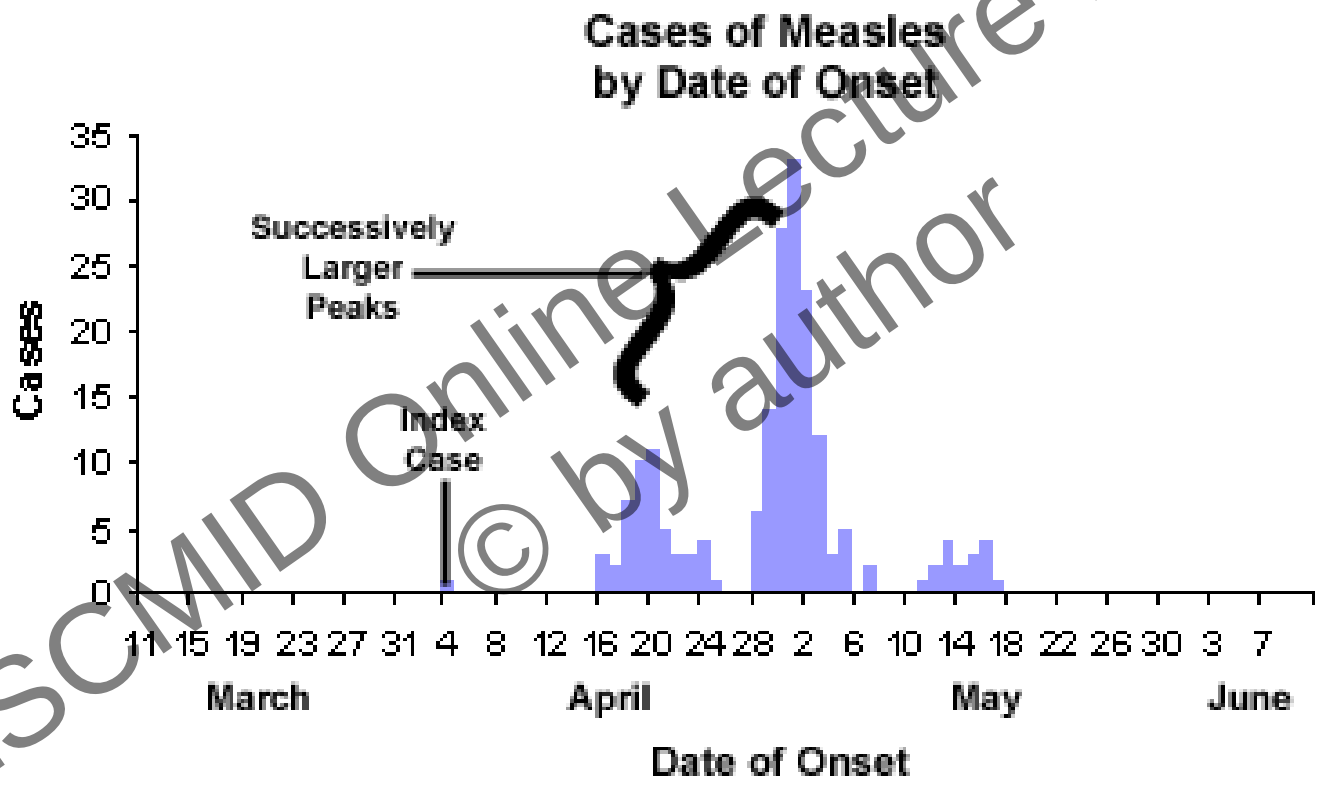
Single common-source

Intermittent common-source

Continuous common-source

Propagated epidemic-mixed pattern

Propagated source (Progressive source)



Pure person-to-person transmission
Measles=incubation ~10days (7-14)

6. Develop hypotheses

Why and how the outbreak occurred?

- Talking to affected people is always helpful
- Develop testable hypotheses

6 &7. Develop and Evaluate Hypotheses

Why and how the outbreak occurred?

- Talking to affected people is always helpful
- Develop testable hypotheses
  - If evidence is too strong no need to test

1. Analytical epidemiology
   1. Cohort study
   2. Case-control study

Odds Ratio in a Case-Control Study

$$\frac{\text{Odds of exposure cases}}{\text{Odds of exposure non-cases}} = \frac{\dfrac{\text{Odds of being exposed}}{\text{Odds of NOT being exposed}}}{\dfrac{\text{Odds of being exposed}}{\text{Odds of NOT being exposed}}}$$

Calculation of odds ratios

Ate strawberries imported from country A?	Cases	Controls	Total
Yes	a = 30	b = 40	70
No	c = 10	d = 80	90
Total:	40	120	160

Odds of strawberries Cases = 30/10

Odds of strawberries Non-cases = 40/80

Odds ratio= ad/bc

Odds ratio= 30x80/40x10 = 6

P-value=95%CI

8. Refine hypotheses and carry out additional studies

- Additional epi studies
- Lab studies
  - Epidemiology can implicate vehicles and guide appropriate public health action, lab evidence can clinch the findings
- Environmental studies
  - Help explain why an outbreak happened

9. Implementing control and prevention measures

- Although it is step 9, do this ASAP!
- You can target the suspects even if you don't know the real source
  - Destroy possibly contaminated food
  - Sterilize contaminated water
  - Infectious person stay away from food handling
  - Cohorting
  - Immunization

10. Communicate findings

- Clear communication with local authorities
- Always work with the authorities and prepare an action plan of how to inform the public