Outbreak Investigation

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Outbreaks: The basics

- **Definition**
  - Occurrence in a region/community of a disease/healthrelated event clearly in excess of normal expectancy
    - Relative to usual frequency
- **Goals of an outbreak investigation**
  - To identify the source of illness
  - To guide public health intervention
- **Ways to recognize an outbreak**
  - Routine surveillance activities
  - Reports from physician and laboratories

Why investigate an outbreak?

- Characterize the problem
  - Extent, impact (including economic)
- Identify preventable risk factors
  - New research insights into disease

Case Study

Initial Call

- Late June, 2007: Calls from 4 Doctors reporting 6 patients with bloody diarrhea and *E. coli* O157:H7 infection

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- Late June, 2007: Calls from 4 Doctors porting 6 patients with bloody diarrhea and *E. coli* O157:H7 infection
- 1 day later: Call from Department of preventive medicine in Jeddah
- Increase in laboratory reports of *E. coli* O157:H7
  - June 2007 = 52

Steps in Outbreak Investigation

1. Verify the Diagnosis

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- *Escherichia coli* O157:H7 first identified as a human pathogen in 1982 in the US
- Sporadic infections and outbreaks since reported from many parts of the world (e.g., N. America, Western Europe, Australia, Asia, and Africa)
- Cattle are the primary reservoir for *E. coli* O157:H7
- Implicated foods are typically those derived from beef, hamburger, raw milk
- Infection has also been transmitted through contact with infected persons, contaminated water, and other contaminated food products.

1. Verify the Diagnosis

- Infection with *E. coli* O157:H7 is diagnosed by detecting the bacterium in the stool.

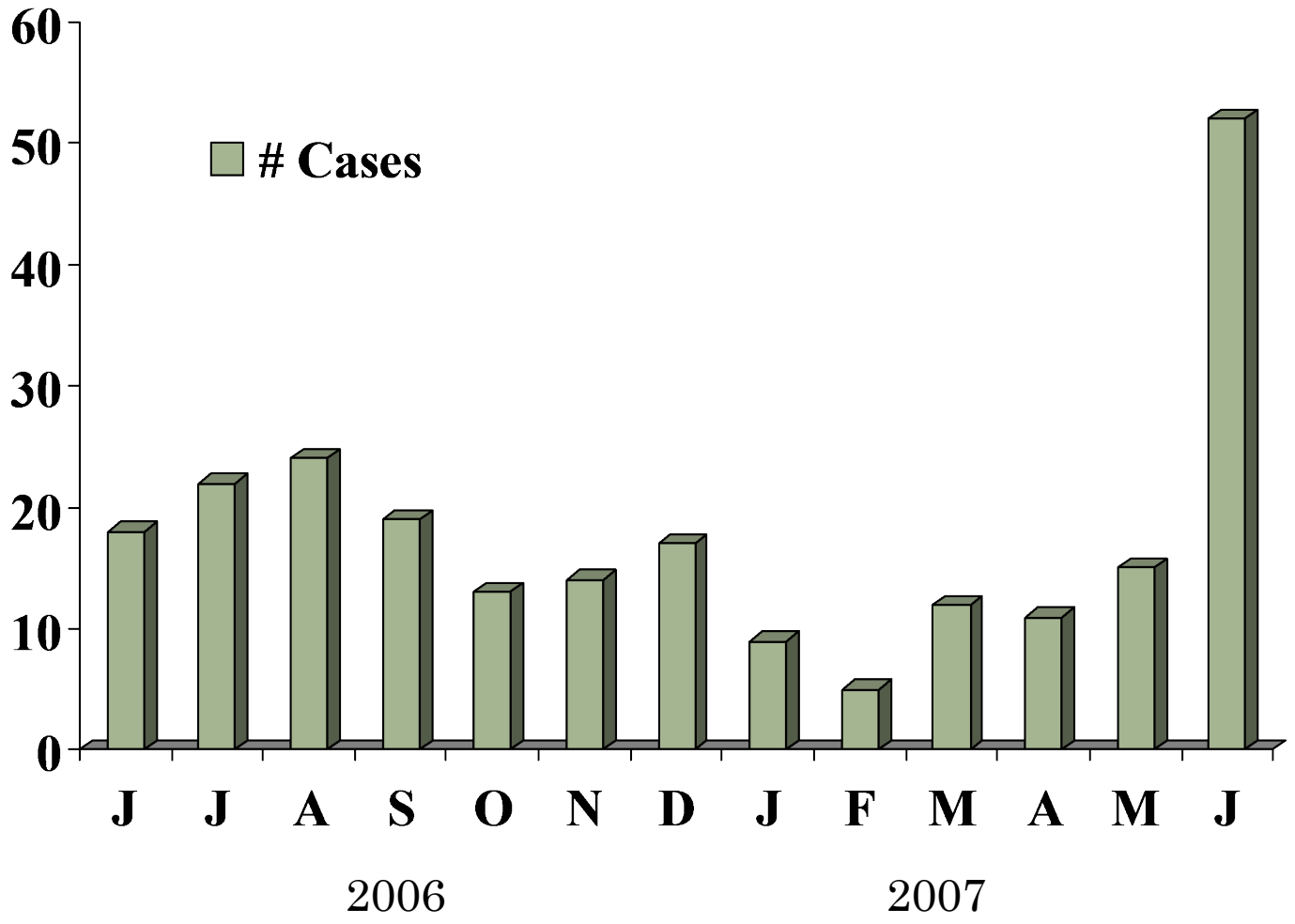
Steps in Outbreak Investigation

1. Verify the Diagnosis

Steps in Outbreak Investigation

1. Verify the diagnosis
2. Confirm the outbreak

Trends in *E. Coli* O157 Cases



What could account for the increase in cases?

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Real increase

- Increase in population size
- Changes in population characteristics
- Random variation
- Outbreak

Artificial increase

- New testing protocol
- Changes in reporting procedures

Initial Investigation

- No substantial changes in population size
- No appreciable changes in the population characteristics
- No laboratory based changes
  - Surveillance / testing
  - Reporting protocol

Initial Investigation

- Any other way to see if there is a relationship between these *E. coli* isolates?

Molecular Epidemiology

- DNA fingerprinting
- Pulsed Field Gel Electrophoresis (PFGE) most common in outbreak investigations
- A cluster of isolates with the same PFGE pattern suggests they arose from the same parent (same source)
- Still need an epidemiologic investigation

Steps in Outbreak Investigation

1. Verify the diagnosis
2. Confirm the outbreak

Steps in Outbreak Investigation

1. Verify the diagnosis
2. Confirm the outbreak
3. Case definition

3. Develop a Case Definition

- Incubation period for *E. coli* O157:H7 ranges from 3-8 days with a median of 3-4 days.
- The infection often causes severe bloody diarrhea and abdominal cramps, but can also cause a non-bloody diarrhea or result in no symptoms.
- In some persons, particularly children under 5 years of age and the elderly, infection can be complicated by hemolytic uremic syndrome (occurs in about 2-7% of infections)

Case Definition?

Case Definition

- Outbreak investigation definition:

  1. diarrhea (>3 loose bowel movements a day) and/or abdominal cramps

  2. resident of Jeddah

  3. onset of symptoms between June 15 and July 15

  4. stool culture yielding *E. coli* O157:H7 with the outbreak strain PFGE pattern.

Steps in Outbreak Investigation

- Verify the diagnosis
- Confirm the outbreak
- Case definition

Steps in Outbreak Investigation

- Verify the diagnosis
- Confirm the outbreak
- Case definition
- Descriptive Epidemiology

Characterization of Cases

Of the initial 38 persons who met the case definition, 26 (68%) were female with a median age of 31 years.

Table 1. Age group and gender distribution for persons with *E. coli* O157:H7 infection (with PFGE pattern), Jeddah, June 15 - July 15, 2007. (N=38)

Age group (years)	Gender		TOTAL
	Male	Female	
0-9	2 (17%)*	2 (8%)	4 (11%)
10-19	2 (17%)	3 (12%)	5 (13%)
20-39	3 (25%)	9 (35%)	12 (32%)
40-59	2 (17%)	8 (31%)	10 (26%)
60+	3 (25%)	4 (15%)	7 (18%)
TOTAL	12 (101%)	26 (101%)	38 (100%)

* percentages refer to column totals.

Cases

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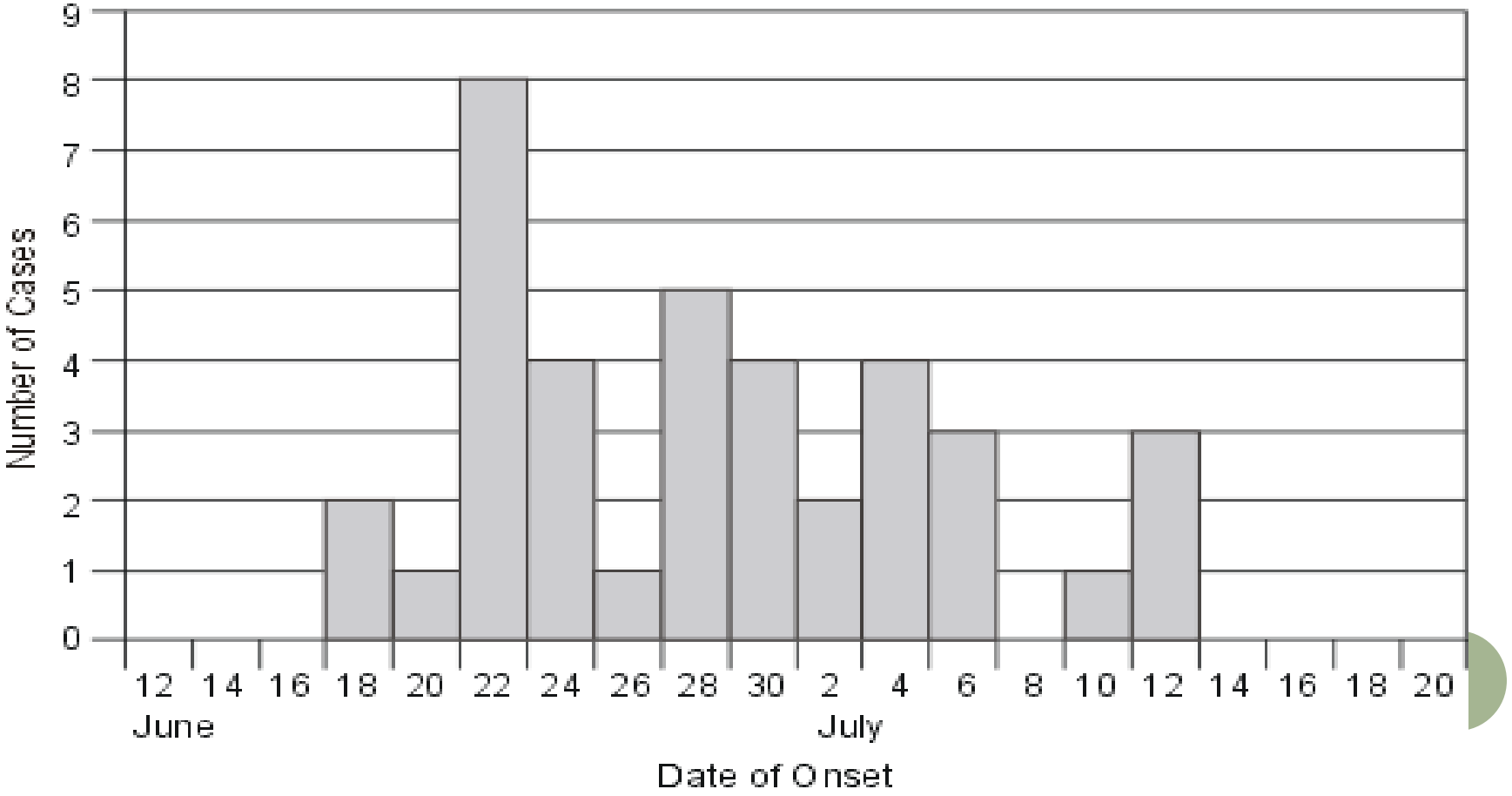
Epidemic Curve

Figure 1. Date of illness onset for persons with *E. coli* O157:H7 infection and the outbreak PFGE pattern, June 15 - July 15, 2007. (N=38)

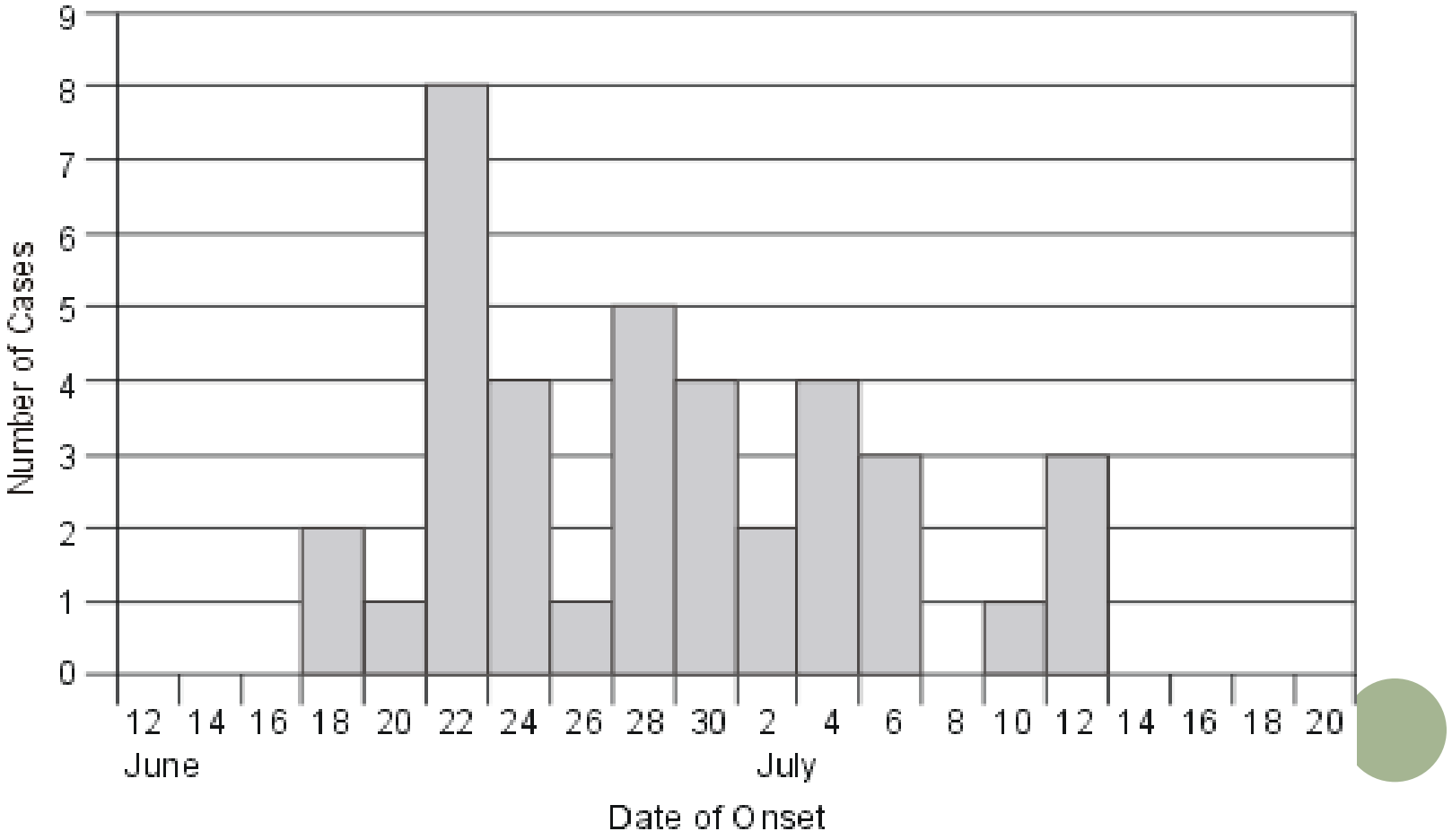


Epidemic Curves

- How to set it up
- What it tells you
  - Mode of transmission
    - Propagated
    - Common source
  - Timing of exposure
  - Course of exposure

Epidemic Curve

Figure 2. Date of illness onset for persons with *E. coli* O157:H7 infection and the outbreak PFGE pattern, June 15 - July 15, 2007. (N=38)



Steps in Outbreak Investigation

- Verify the diagnosis
- Confirm the outbreak
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- Descriptive epidemiology

Steps in Outbreak Investigation

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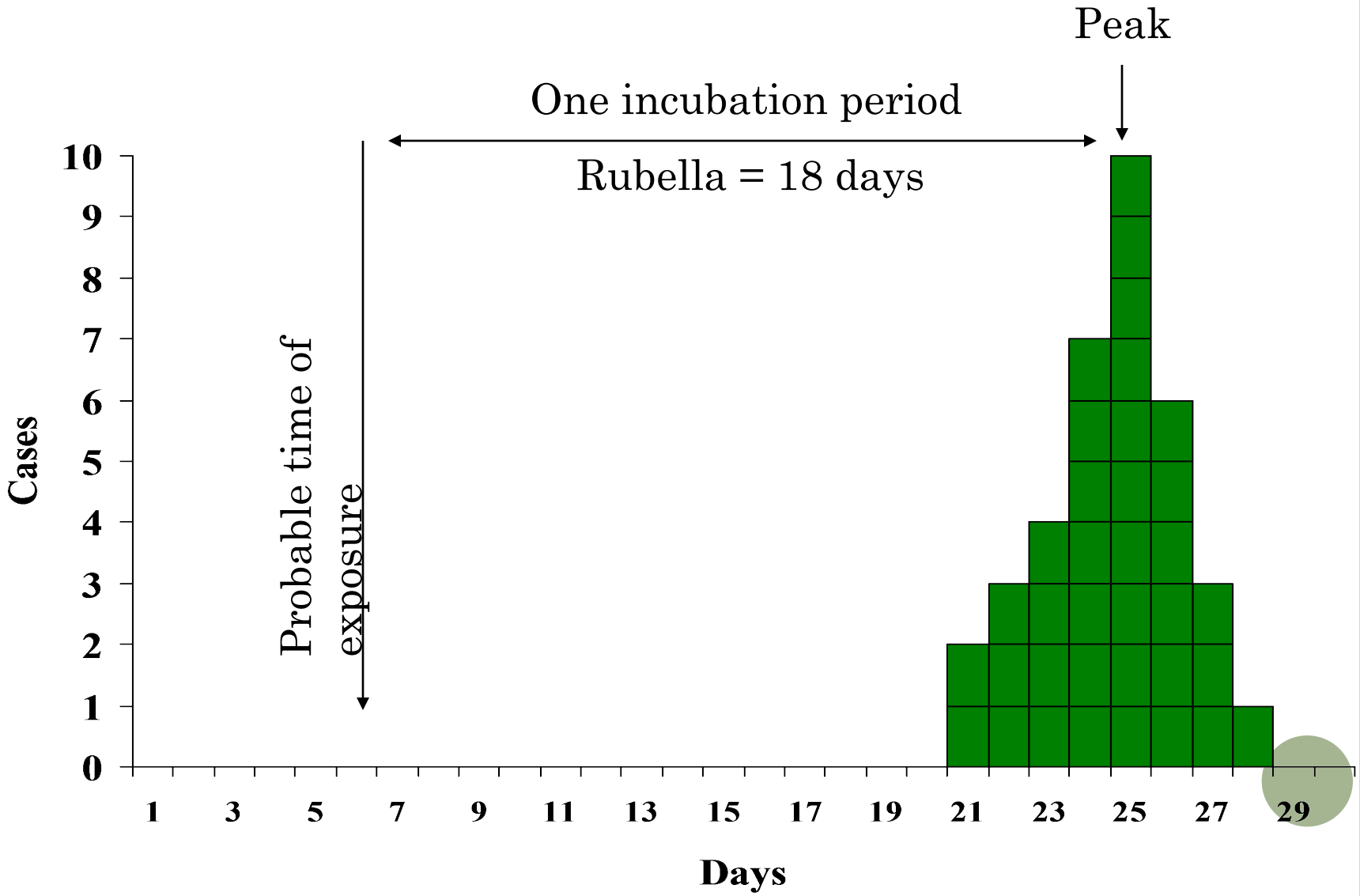
- Develop a hypothesis

Developing a Hypothesis

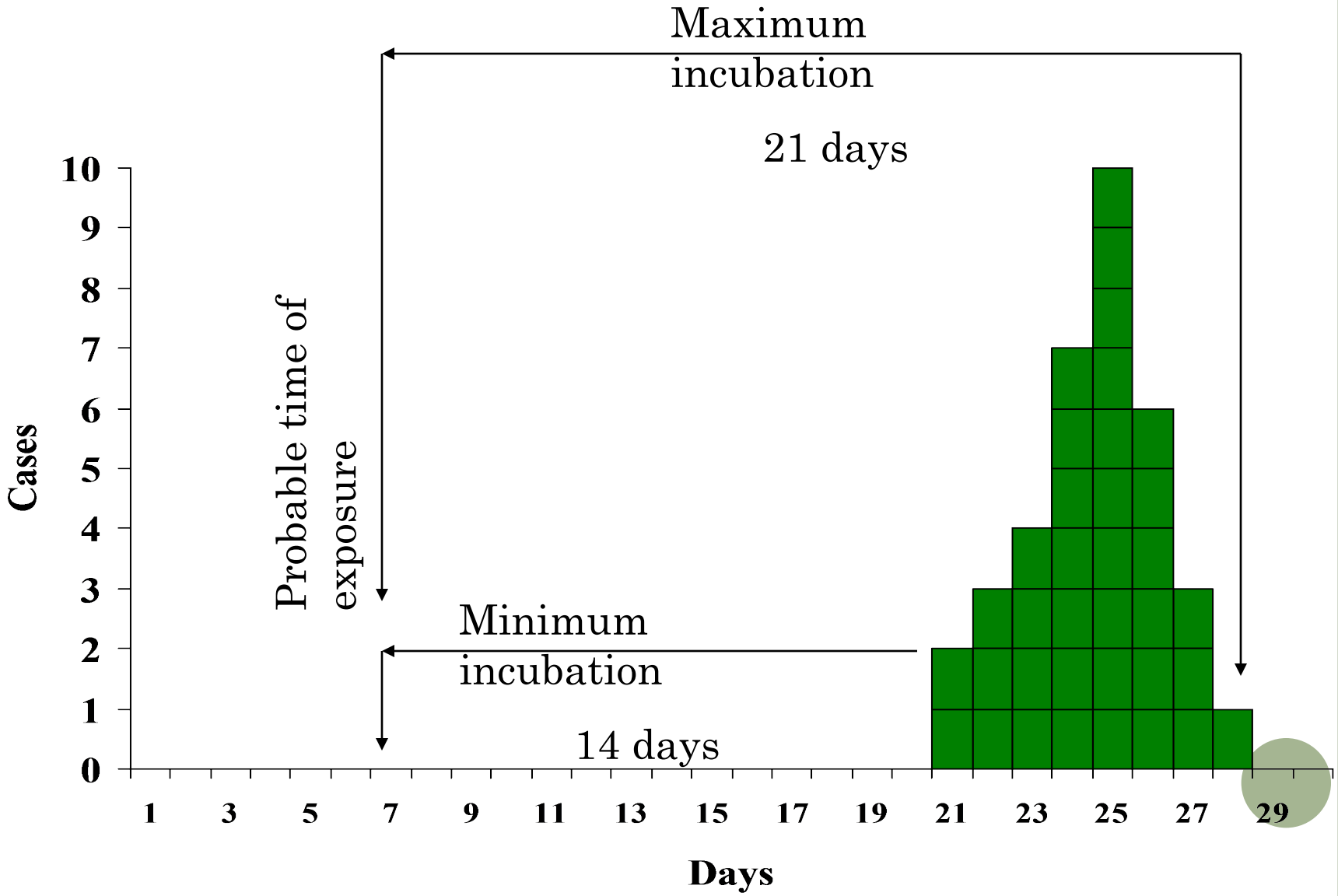
Determining the Probable Period of Exposure

- Mean/Median incubation period
- Minimum/maximum incubation period

Estimating date of exposure

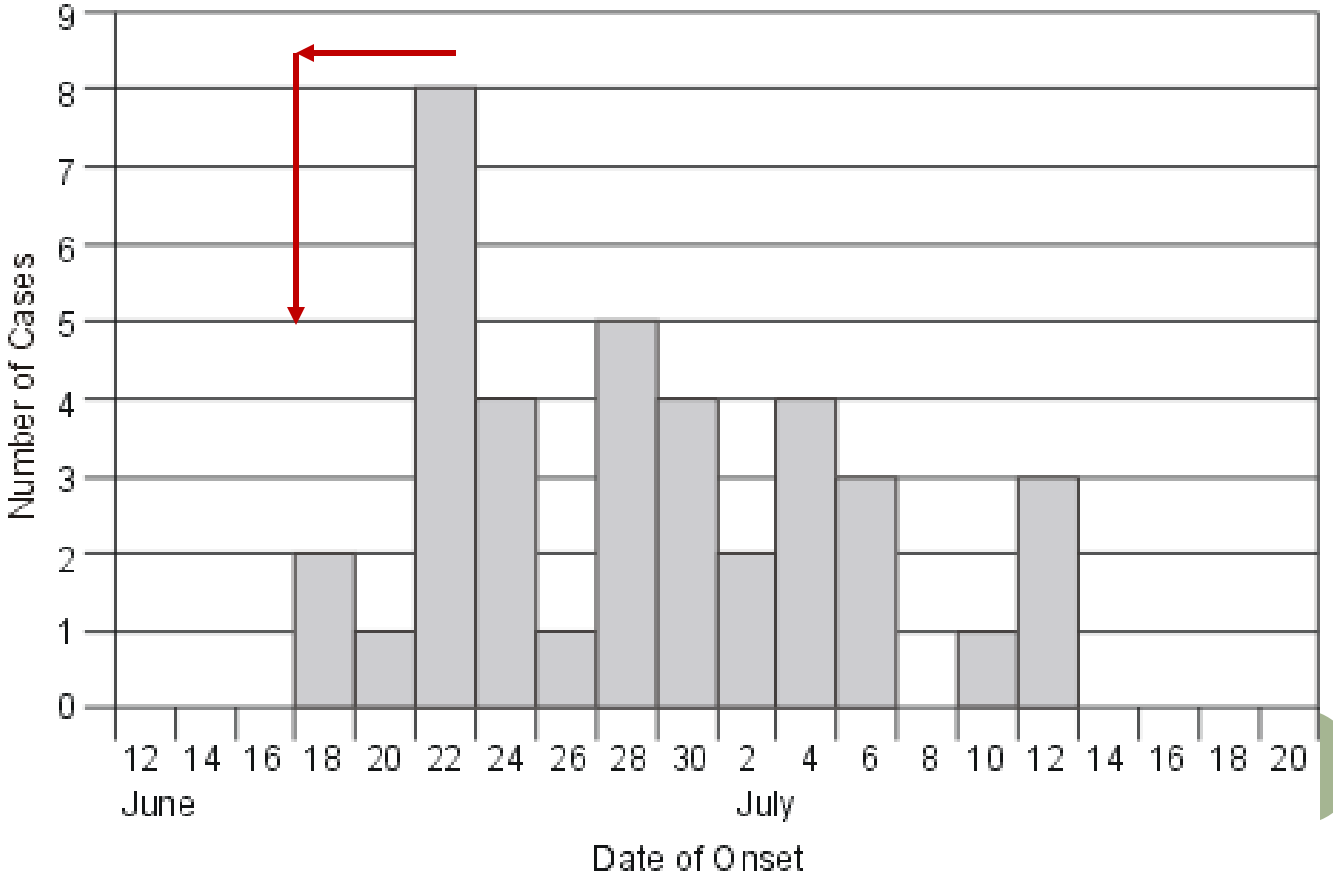


Estimating date of exposure



E. Coli Epidemic Curve

Figure 3. Average incubation period = 4 days (range 3-8 days)



Findings

- The median age of patients is 31 years (range 2 -76); 68% of cases are among females.
- Factors present in over 50% of cases:
  - Female, milk, hamburger, lettuce, alfalfa sprouts
  - water exposure?

Hypothesis?

Hypothesis of Investigators

- Lettuce and/or parsley consumption is associated with *E. coli* infection

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- Case definition
- Descriptive epidemiology
- Develop a hypothesis

Steps in Outbreak Investigation

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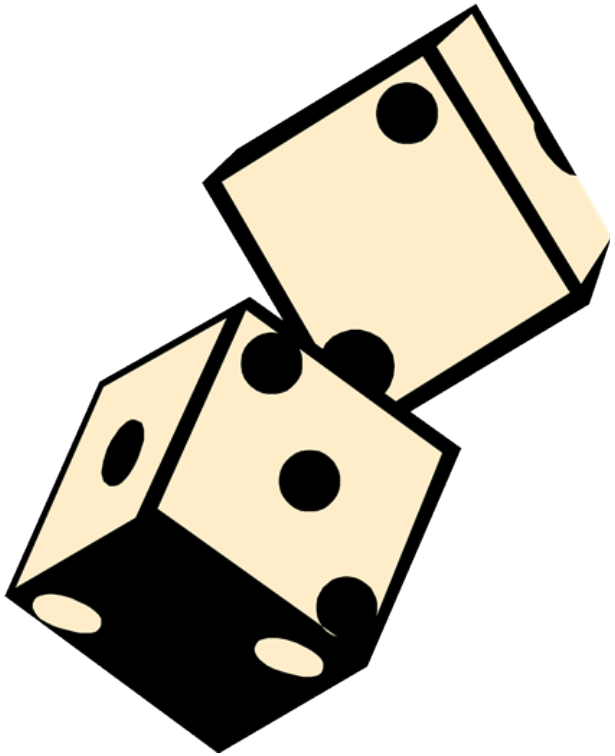
- Test the hypothesis

Pick a Control Group



Controls Selected

- 2 controls selected for every case
- Matched to the case by:
  - Age group
    - (0-<2 years, 2-<5 years, 5-<12 years, 12-<18 years, 18-<60 years, and 60+ years)
  - Sex

Selection of Controls

- Exposure information among cases was collected for the 7 days before onset of illness.
- For controls, exposure information was collected for the 7 days before the interview and for the 7 days before the onset of illness in the matching case.
- Twenty-seven case-control sets were interviewed; the remaining case-patients could not be reached.

Interview Results

Variable	Cases (n=27)	Controls (n=54)
Female	18 (67%)	36 (67%)
Med Age	31	31
Rec water exposure	9 (33%)	21 (39%)
Other Ill person	6 (22%)	9 (17%)
Day care	16 (59%)	33 (61%)
Farm	2 (7%)	2 (4%)
Fair	12 (44%)	24 (44%)
Travel	8 (30%)	13 (24%)
Hamburger	17 (63%)	36 (67%)
Meat	14 (52%)	26 (48%)
Milk	21 (78%)	44 (81%)
Alfalfa sprouts	15 (56%)	4 (7%)
Lettuce	18 (67%)	34 (62%)

E. Coli and parsley?

Variable	Cases	Controls	OR (95%CI)
	15 (56%)	4 (7%)	25 (4-528)

No other food item was significantly associated with

illness.

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- Implement control and prevention measures

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- Develop a hypothesis
- Test the hypothesis
- Refine hypothesis / Execute additional studies
- Implement control and prevention measures
- Communicate findings

Conclusions

- Importance of applying the multi-step approach in outbreak investigation
- Utility of new subtyping methods such as PFGE
- Importance of disease reporting
- Flexibility of hypothesis generation
  - New vehicle for the transmission of *E. coli* O157:H7
- Increasing geographic dissemination of outbreaks