

# Removing the pump handle

Investigating an outbreak

FETP India

## Competency to be gained from this lecture

Successfully investigate an outbreak to propose effective prevention and control measures

## Key areas

- Preparing yourself
- Counting cases
- Generating hypotheses
- Testing hypotheses
- Implementing control measures

# Getting ready to investigate an outbreak

- Passport
- Money
- Travel order
- Blue dart
- SIM card
- Sampling material
- Supervisor's home and cell number

# Steps of an outbreak investigation

1. Determine the existence of an outbreak
2. Confirm the diagnosis
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*Counting cases*

# Determine the existence of an outbreak

- Definition of an outbreak:
  - Increased incidence in a given place and time
- Elements needed:
  - Numerator
    - The number of cases
  - Denominator
    - The size of the population where cases come from
  - Collection of this information over time
    - Baseline

*Counting cases*

# Pseudo-outbreaks not confirmed to be linked with an increase of incidence

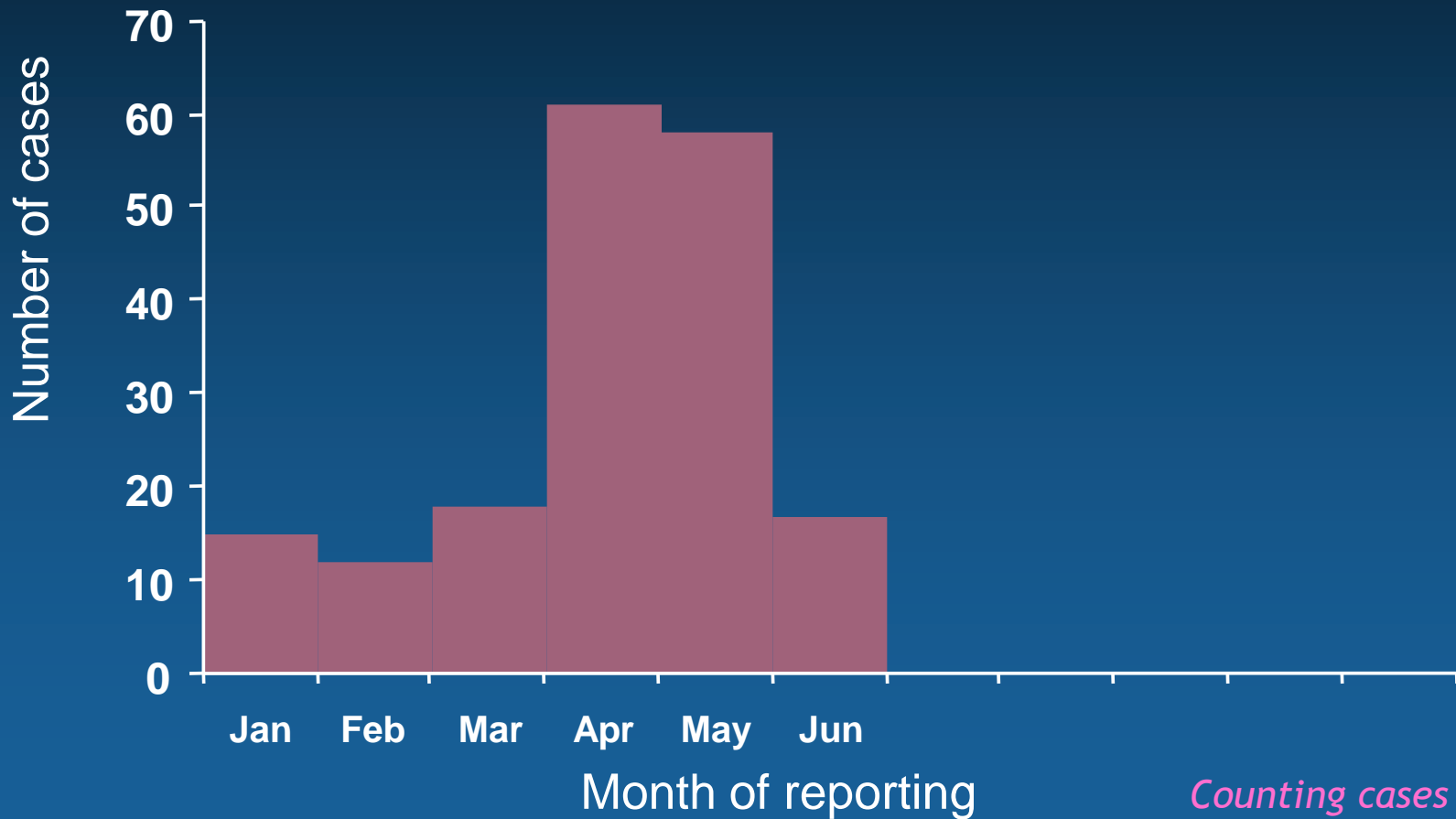
- Artifact in the numerator:
  - Increased awareness
  - Reporting of prevalent cases as incident cases (e.g.; hepatitis C, sleeping sickness)
  - Laboratory error
- Variation of the denominator:
  - Rapidly changing population denominators
    - Hospital patients, migrants, refugees, or expatriates



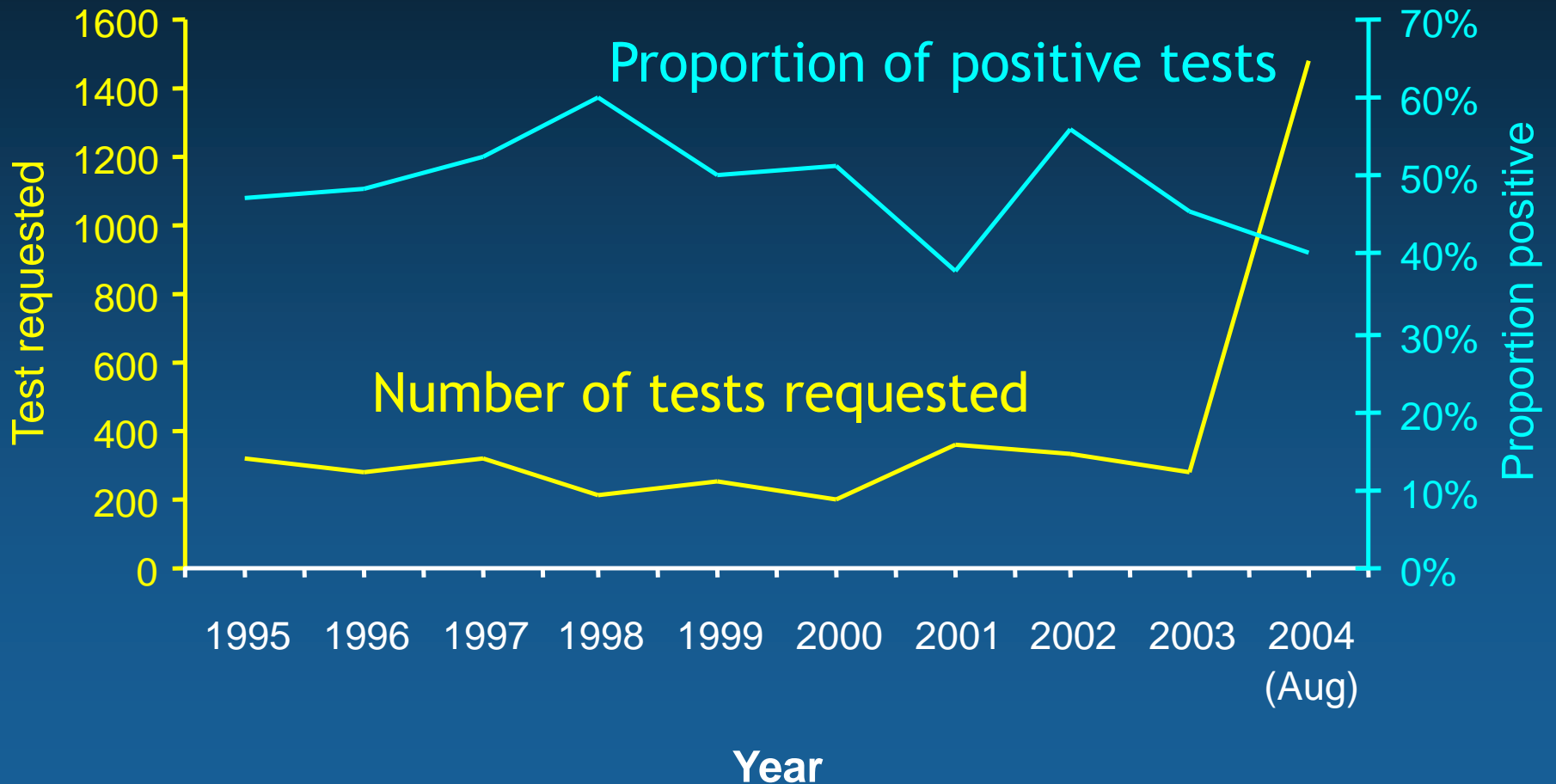
# Kala-azar in Canning, West Bengal, January - June 2004

- December 2003:
  - Newspapers report outbreak and deaths
- Increase in the number of reported cases
- No similar episode in the last 3 years
- April 2004:
  - Investigation in Chatrakhali, one of the villages where most of the cases were identified

# Cases of Kala-azar by date of reporting, Chatrakhali village, West Bengal, India, 2004



# Blood samples requests for Kala-azar, Canning, West Bengal, India, 1995 - 2004



*Counting cases*

# Pseudo-outbreaks of leishmaniasis, Chatrakhali village, West Bengal, India, 2004

- Initial report of cases early in 2004
  - One death
- Increased awareness
- Active case search in the village in April-May
- Identification of many prevalent cases
- The peak in the request for serological tests documents the increased awareness that caused the pseudo-outbreak

# Pseudo-outbreak are not pseudo-problems

- The issue is not acute
- The problem is chronic

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# Confirm the diagnosis

- Gather clinical information
  - Communicate with clinicians, specialists
  - Shortlist a number of probable diagnoses
- Seek laboratory confirmation
  - Communicate with the laboratory
  - Conduct testing for probable diagnoses

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# Being clear about what a case definition is and is not

- A case is an event
- An event is something that happens to:
  - A person,
  - In a given place,
  - At a given time
- A case definition is a set of criteria that triggers reporting
- A case is not a person
- Events do not exist if you lack info:
  - On the person
  - On the place
  - On the onset date
- A case definition is not a diagnosis

# “Cases” versus “case-patients”

## “Case”

- Event
- Used to refer to the event (e.g., counting)
- One case is unique

## “Case patient”

- Person to whom the event happens
- Used to refer to the person (e.g., You interview case-patients, not cases)
- More than one case can happen in a case-patient (e.g., relapse)

*Counting cases*

# Prototype case definition

- A case is the occurrence of [spell out syndrome] in a resident of [ spell out location] between [beginning date] and [end date]
- Use of standardized syndromic case definition is preferable
  - Integrated Disease Surveillance Programme in India
  - WHO
  - CDC

# Various levels of case definition: Rationale

- Different levels of case definition allow:
  - Searching for potential cases widely
  - Narrowing the search subsequently
- Case definitions may differ at the descriptive and analytical stages
  - Descriptive stage (Case-finding)
    - More sensitive
  - Analytical stage (Hypothesis testing)
    - More specific

# Various levels of case definition: Template

- Possible cases
  - Events that can possibly be considered as cases following investigation
- Probable cases
  - Events that are compatible upon clinical assessment
- Confirmed cases
  - Events that are confirmed by laboratory assessment

*Counting cases*

# Various levels of case definition: Measles

- Possible cases
  - Fever with rash
- Probable cases
  - WHO case definition compatible
- Confirmed cases
  - Serological confirmation

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## The case definition frames the criteria to look for cases

- Use time, place and person criteria from the case definition
- Chose a uniform strategy to search for cases
  - Passive surveillance
  - Stimulated, passive surveillance
  - Active surveillance
  - Door-to-door case search
- Search cases everywhere in the same way

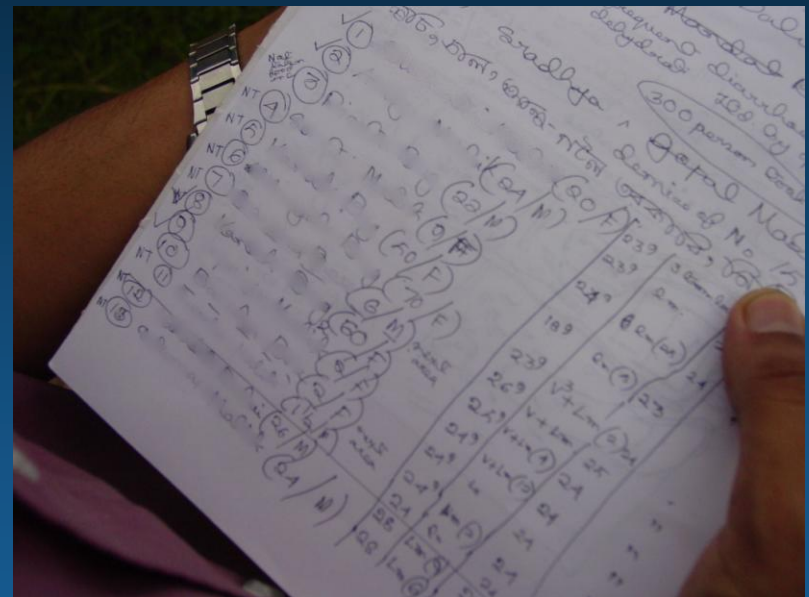


## Example pointing to the danger of heterogeneous case search strategy

- Cluster of disease X identified in primary health centre of village A
- Case search strategy:
  - Door-to-door case search in village A
  - Active surveillance in the district
  - Passive surveillance in the state
- The descriptive epidemiology will indicate that the incidence is highest in village A
  - Artifact

# The line listing

- Constitutes and updates a database of cases
- Protects the confidentiality of the patients
- Prepares an easy, automated, descriptive analysis



Counting cases

# Guiding principles for the line listing

- Is unique
  - Don't confuse yourself and others with multiple versions
- Contains a unique identifier for each record (case)
- Ensures confidentiality
- Contains essential information on each case
  - Time, place, person, other (e.g., clinical picture, laboratory)
- Can be updated as the investigation develops
- Allows regular, automated, computerized analysis
  - Aggregation

*Counting cases*

# Typical line listing for an outbreak investigation

Unique identifier

Time

Place

Person

Outcome

Lab

Uni. ID	OnsetDate	Ward	Block	City	AgeYears	Sex	Hospital	Death	HEVIgM	HAVIgM
1	1-Mar-05	18	2	HYD	12	1	1	2	1	9
2	3-Mar-05	22	1	HYD	25	2	1	2	2	1
3	5-Mar-05	23	3	HYD	36	1	2	9	9	9
4	6-Mar-05	-	-	SEC	23	2	1	1	1	2

*Counting cases*

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# Count, divide and compare (CDC)

- Count
  - Aggregate the cases in the line listing by characteristic (e.g., age, sex, residence)
- Divide
  - Divide the number of cases by the relevant denominator
- Compare
  - Compare incidence across groups

# Using time, place and person information to generate hypotheses

- Time
  - Epidemic curve
- Place
  - Spot map
  - Incidence by area
- Person
  - Incidence by age, sex, etc.
  - Trawling questionnaire of cases
  - Interview of outliers

## TIME: Drawing an epidemic curve

- Bar chart
- Time in X axis
  - Unit:  $1/4$  of the incubation period
- Number of cases in Y axis
- No intervals between bars

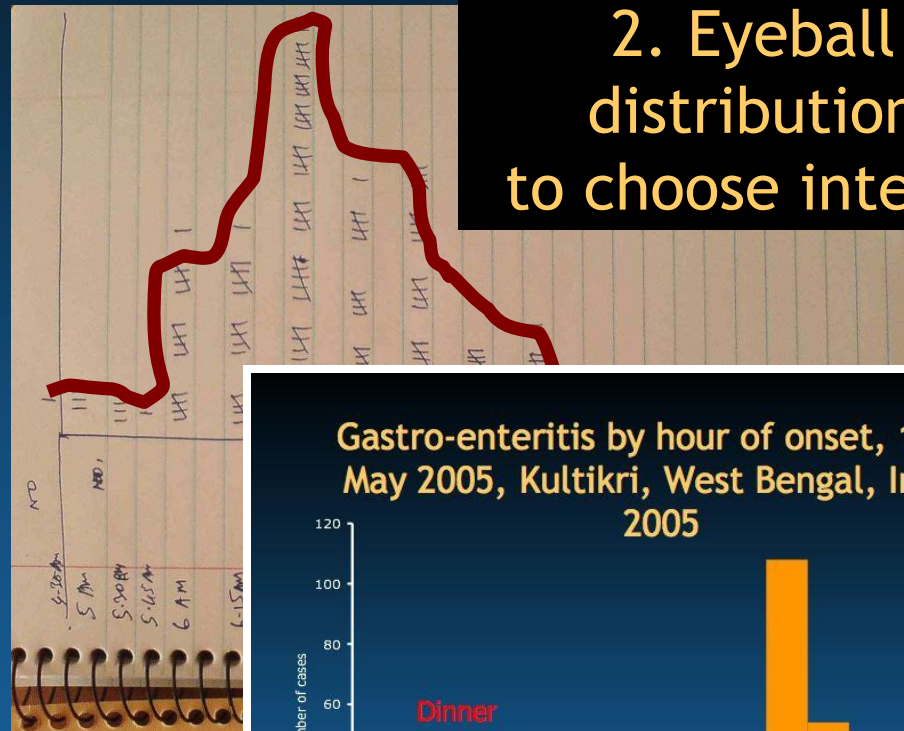


# Drawing the epidemic curve on the basis of the distribution by time of onset

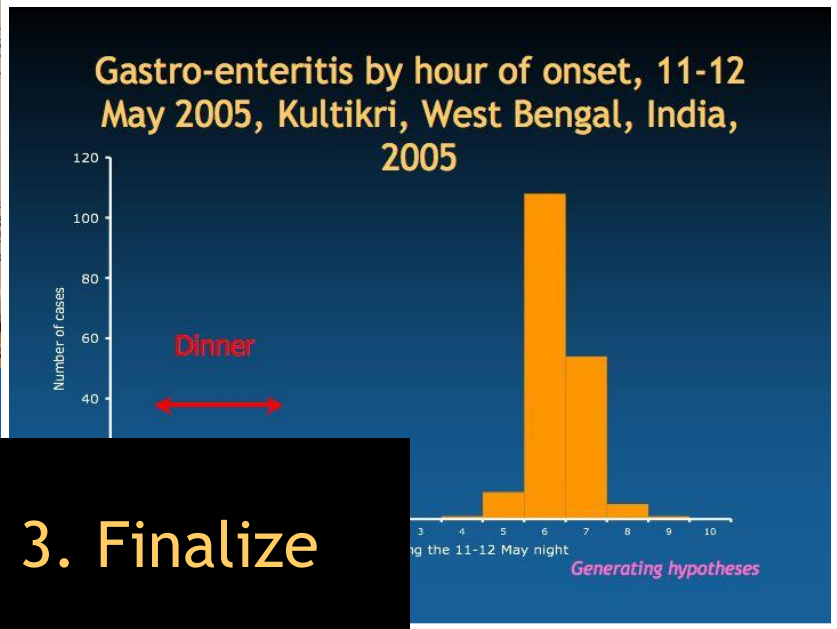
ND

Time	Cases
4-30 AM	1
5 AM	ND, IIII
5-30 AM	III
5-45 AM	I
6 AM	IIII IIII IIII I
6-15 AM	IIII IIII IIII I
6-30 AM	IIII IIII IIII IIII IIII IIII IIII IIII
6-45 AM	IIII IIII IIII IIII I
7 AM	IIII IIII IIII IIII IIII
7-15 AM	IIII IIII
7-30 AM	IIII IIII I
7-45 AM	II
8 AM	II
8-30 AM	I
9-30 AM	I

1. Count cases by time of onset



2. Eyeball distribution to choose interval



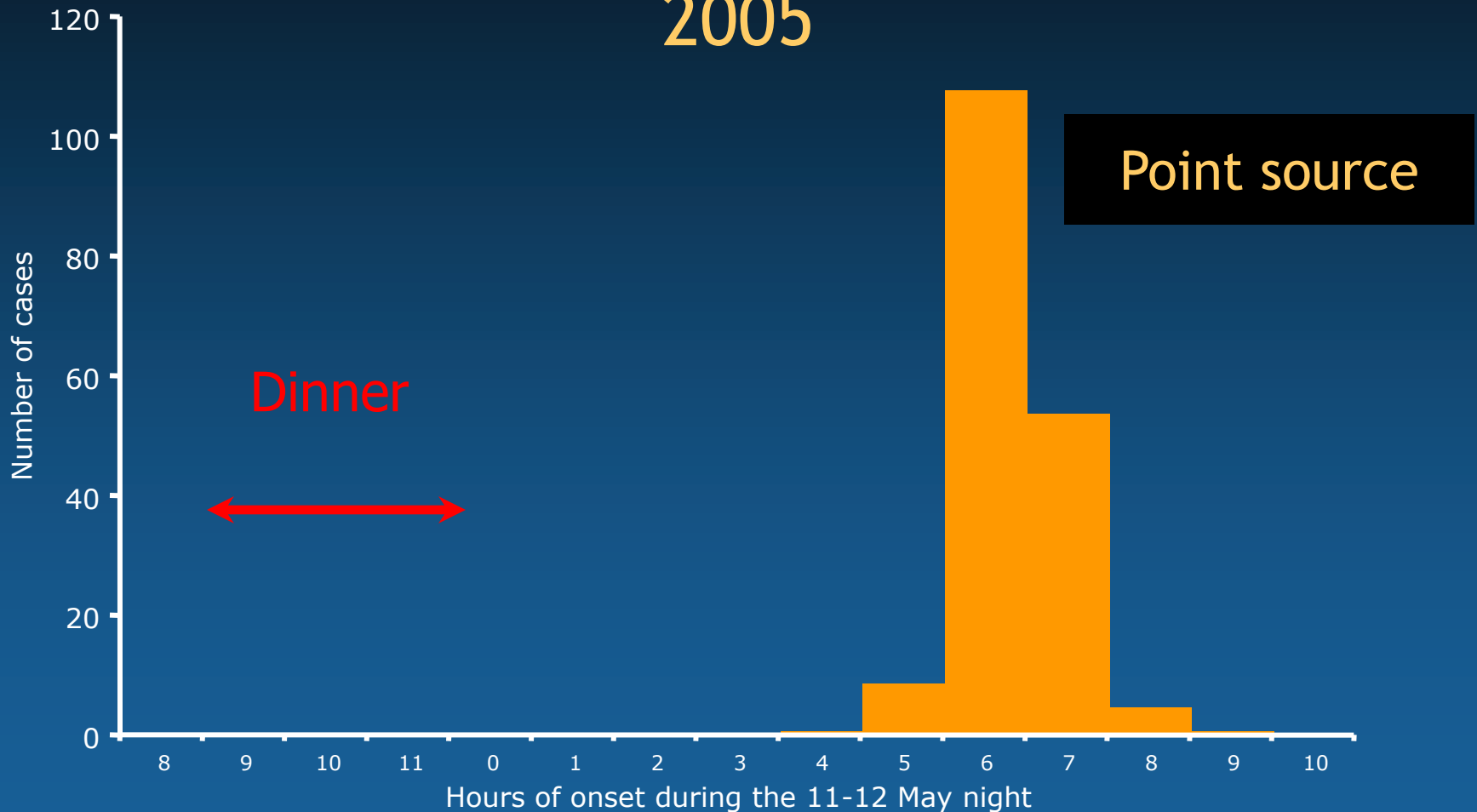
3. Finalize

# Describing and interpreting an epidemic curve

- Description
  - Beginning
  - Peak(s)
    - Number
    - Duration
  - End
- Interpretation
  - Point source outbreak
  - Persisting common source outbreak
  - Person-to-person transmission

*Generating hypotheses*

# Gastro-enteritis by hour of onset, 11-12 May 2005, Kultikri, West Bengal, India, 2005

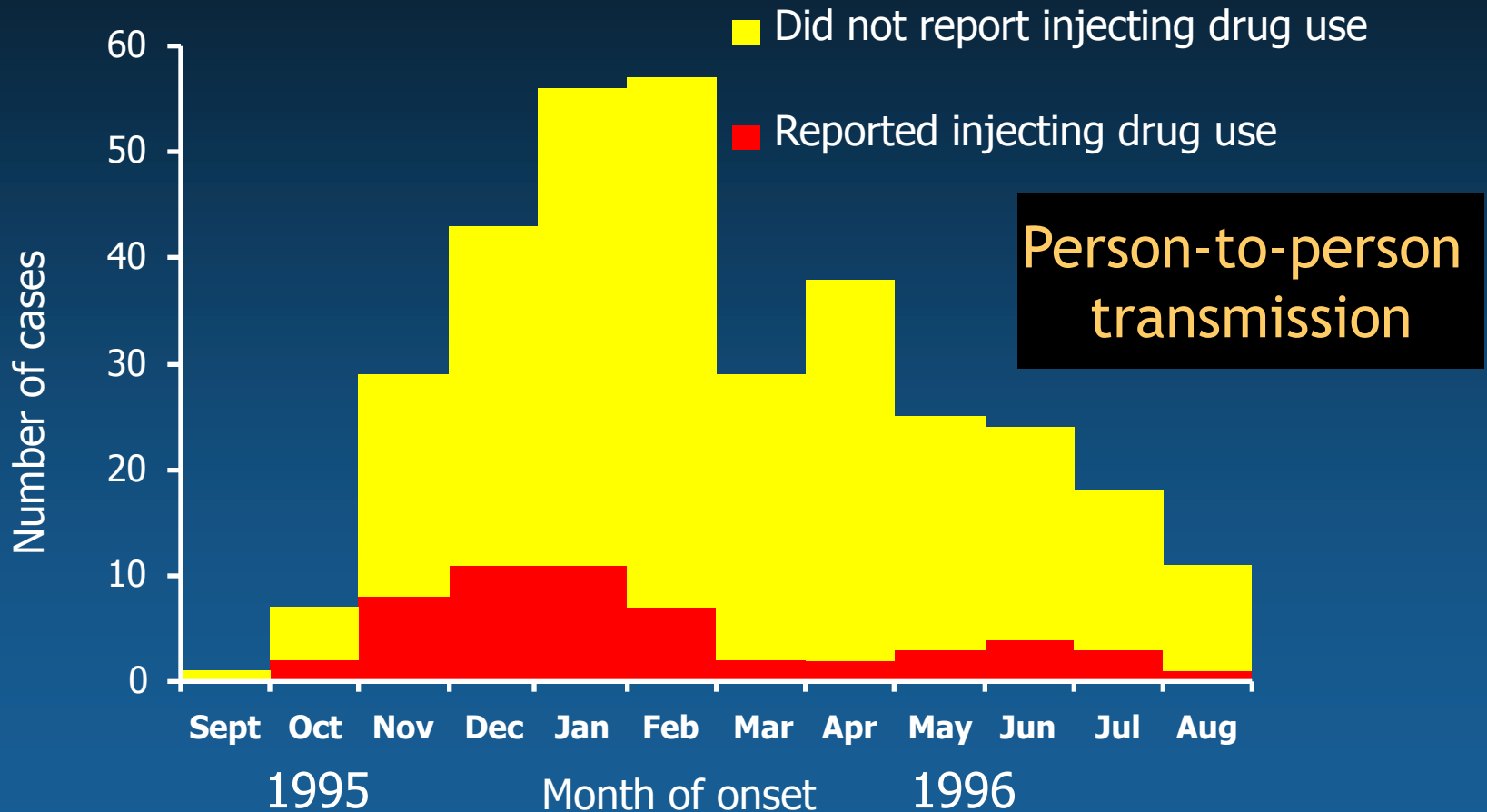


*Generating hypotheses*

# Acute hepatitis by week of onset, Hyderabad and vicinity, Andhra Pradesh, India, 2005



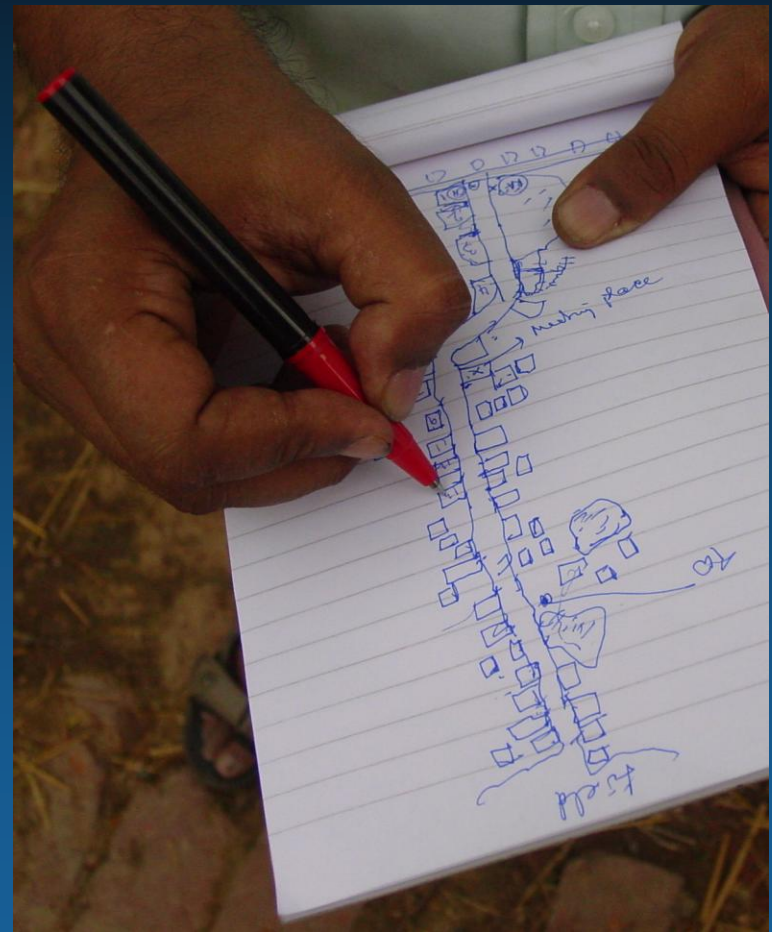
# Hepatitis A cases by month of onset in Siouxland, Iowa, USA, 1995-1996



*Generating hypotheses*

# PLACE: Drawing a map

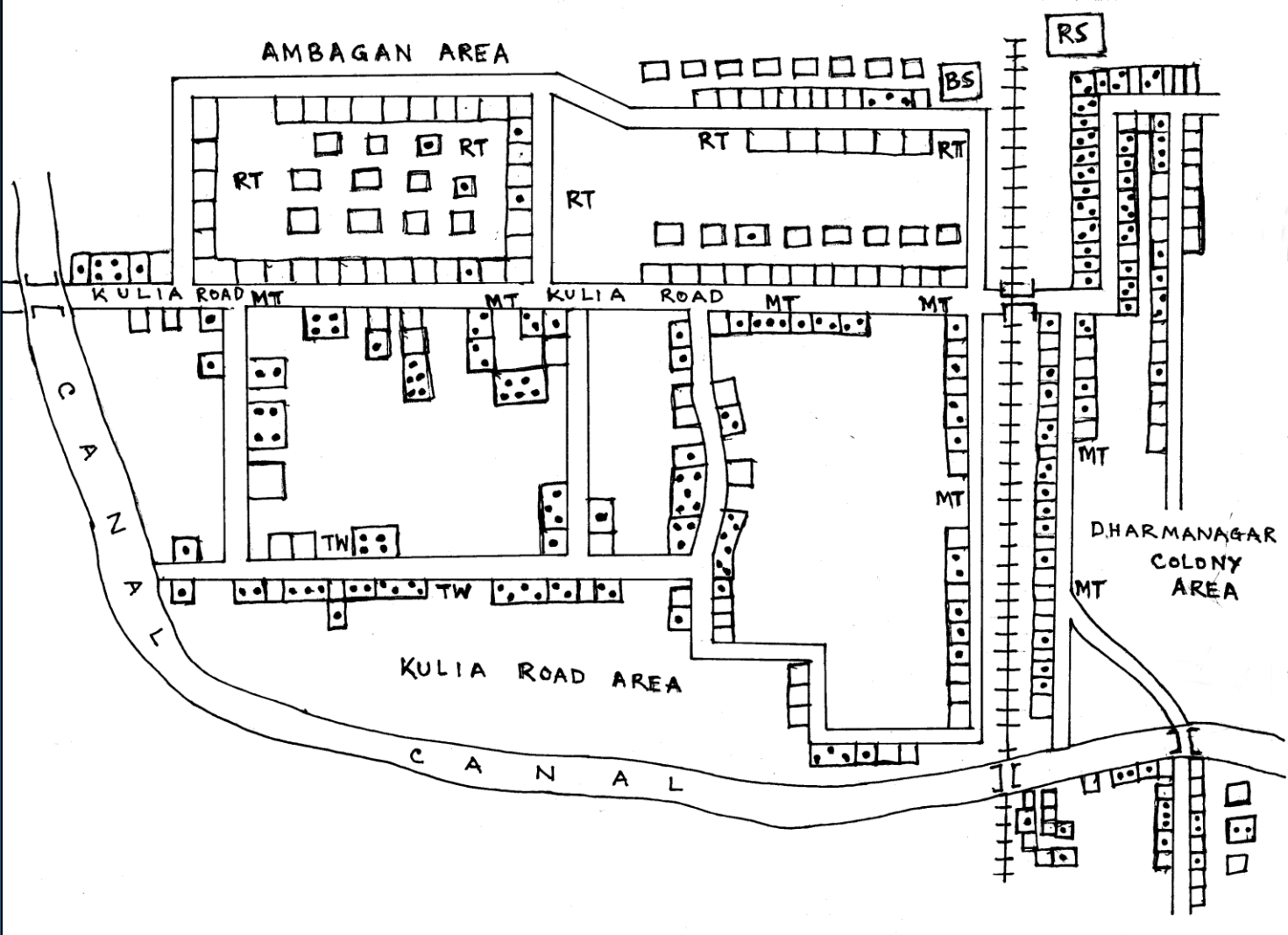
- Spot map
  - Plot of cases (spot) on a rough map in the field
  - Does not account for population density
- Incidence by area
  - Calculate incidence by area (ward, block)
  - Draw map with colour scale proportional to the incidence



*Generating hypotheses*

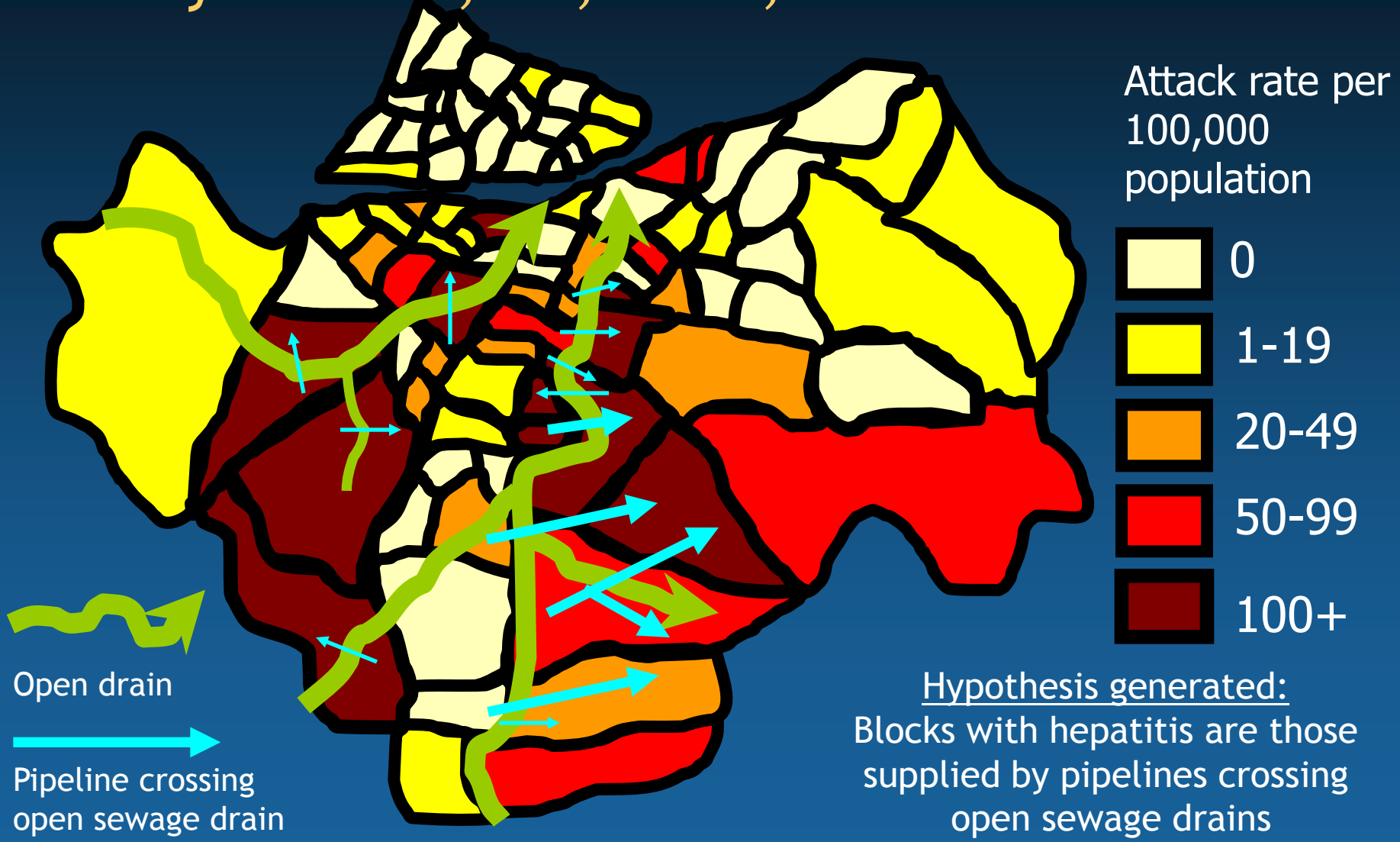
# Spot map

## Cholera cases by residence, Kanchrapara, N-24 Parganas, West Bengal, India, 2004



# Incidence by area

## Incidence of acute hepatitis by block, Hyderabad, AP, India, March-June 2005





# PERSON: Incidence by population groups

- Count
  - Count the cases in each age and sex groups
- Divide
  - Obtain census denominators for each age and sex groups
- Compare
  - Estimate the incidence for each:
    - Age group
    - Sex group

*Generating hypotheses*

# Attack rate of measles by age and sex, Cuddalore, Tamil Nadu, India, 2004-2005

Characteristics		Number of cases	Population	Attack rate per 100,000
Age group	0-4	50	255,755	19.6
	5+	51	1,795,383	2.8
Sex	Male	48	1,032,938	4.6
	Female	53	1,018,200	5.2
Total		101	2,051,138	4.9

*Generating hypotheses*

# Trawling questionnaires to generate hypotheses

- Open-ended questionnaires administered to the case-patients only
- Objective
  - Identify what is common to all the cases
    - Event they participated in?
    - Place they visited?
    - Behaviour they have in common?

# Trawling questionnaire to generate hypotheses, outbreak of hepatitis A among drug users, Iowa, 1997 (1/3)

- Convenience sample of 19 case-patients using illicit drugs, injectors and non-injectors
- Close-ended and open-ended questions regarding:
  - Illicit drug use, including methamphetamine

# Trawling questionnaire to generate hypotheses, outbreak of hepatitis A among drug users, Iowa, 1997 (2/3)

- Opportunities for contamination of the methamphetamine during preparation before use:
  - Hand washing uncommon
  - Handling of methamphetamine and paraphernalia
  - Filters (“cottons”) squeezed to express liquid out
- “Needle sharing” uncommon
- “Indirect sharing” common
- No heating necessary before injection
- ✓ Hypothesis: Fecal-percutaneous route of transmission possible

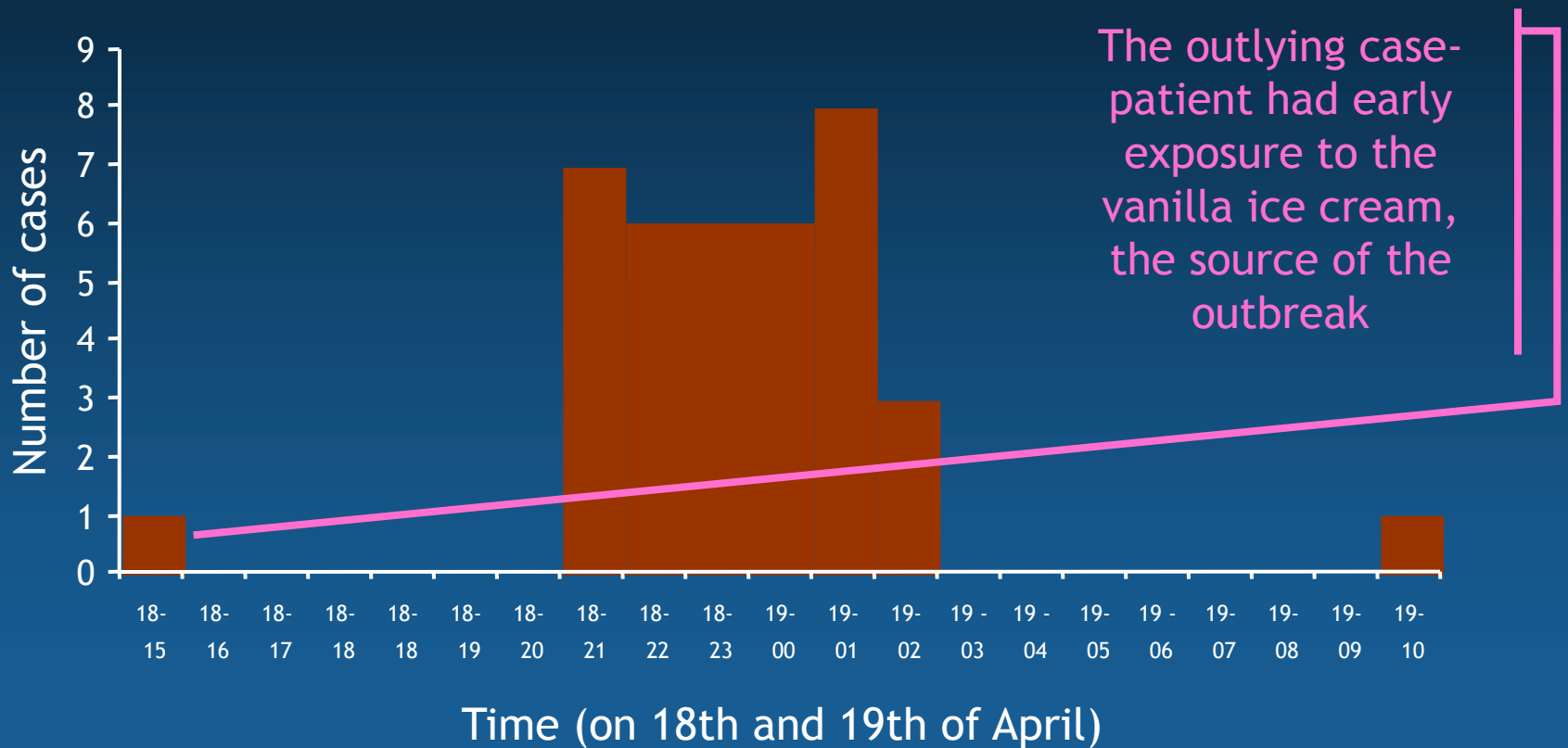
# Trawling questionnaire to generate hypotheses, outbreak of hepatitis A among drug users, Iowa, 1997 (3/3)

- Opportunities for contamination of the locally made methamphetamine after production
  - Poor hygiene in production facilities
  - Methamphetamine handling
- Brown methamphetamine quoted as a possible source among all colours available
- ✓ Hypothesis: A specific batch of methamphetamine may constitute a source

# Using outliers to generate hypotheses during outbreak investigations

- Outliers may have had a different type of exposure to the source of infection
  - Different timing
  - Different intensity
  - Different location
- Outliers may be source patients
- Outliers may correspond to errors in data collection

# Using outliers to generate hypotheses: Cases of gastro-enteritis according to onset time, Oswego, USA, 1940



*Generating hypotheses*



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# From hypothesis generating to hypothesis testing

- Characteristics that are common among cases lead to the generation of hypotheses
- More than one hypotheses may be generated
  - There may be more than one source
  - The investigator may be following a red herring
- Analytical study tests hypotheses to sort out:
  - Characteristics common to all individuals
  - Characteristics specific to cases

# Testing hypotheses using an analytical study

- Define study objectives
  - One hypothesis or multiple hypotheses
- Write mini-protocol
  - Cohort or case control studies, as appropriate
- Define referent exposure period for cases and controls
  - Time - comparability

# Elements to take into account to choose a case control or a cohort study during an outbreak investigation

	Case control	Cohort
Rare disease /large community	+++	-
Common disease/ small community	-	+++
Complete population accessible	+/-	+++
Large amount of resources	+	++
Limited resources	+++	-

*Testing hypotheses*

# Elements of a one-page mini-protocol for outbreak investigations

- Background
- Objectives
- Methods
  - Null hypothesis
  - Study design
  - Study population
  - Sample size
  - Case definition
  - Case ascertainment
  - Recruitment of controls
  - Data collection
  - Analysis plan
- Expected benefit

*Testing hypotheses*

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# Interpreting the results of an analytical study during an outbreak

1. Is the suspected exposure associated with illness?
  - What is the strength of association?
  - Is there a statistical significance?
2. Is there a dose response relationship?
3. If a single source is suspected:
  - Does the source of infection identified explain the majority of cases?

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# Incidence of gastro-enteritis according to food items consumed, wedding dinner, West Bengal, 2005

	Incidence among those who ate			Incidence among those who did not eat		
	Ill	Total	%	Ill	Total	%
Cold drinks	153	186	82%	25	41	61%
Salad	144	189	76%	34	38	89%
<b>Fish Fry</b>	<b>173</b>	<b>195</b>	<b>89%</b>	<b>5</b>	<b>32</b>	<b>16%</b>
Fish Curry	119	149	80%	59	78	76%
Mutton	158	200	79%	20	27	74%
Rosgulla	159	202	79%	19	25	76%
Ice cream	166	211	79%	12	16	75%
Pan	148	181	82%	30	46	65%

Relative risk (fish fry): 5.6

Attributable fraction in the population =  $(173/178) \times 82\% = 80\%$

*Attributable fraction in the population*



# Attack rate of gastro-enteritis by food items, Coochbehar, West Bengal, India, 2005

	Attack rate (%)		Relative risk	95% confidence interval
	Ate	Did not eat		
Raw custard *	90%	51%	1.8	1.3-2.4
Fruits	76%	86%	0.88	0.76-1.0
Sugar candy	75%	88%	0.85	0.74-1.0
Puffed rice	80%	84%	0.95	0.83-1.1
Seasoned rice	67%	84%	0.79	0.60-1.0

87% of cases exposed, population attributable fraction: 38%

The custard does not explain all cases: A raw spoon of contaminated milk used for the custard was served to all guests

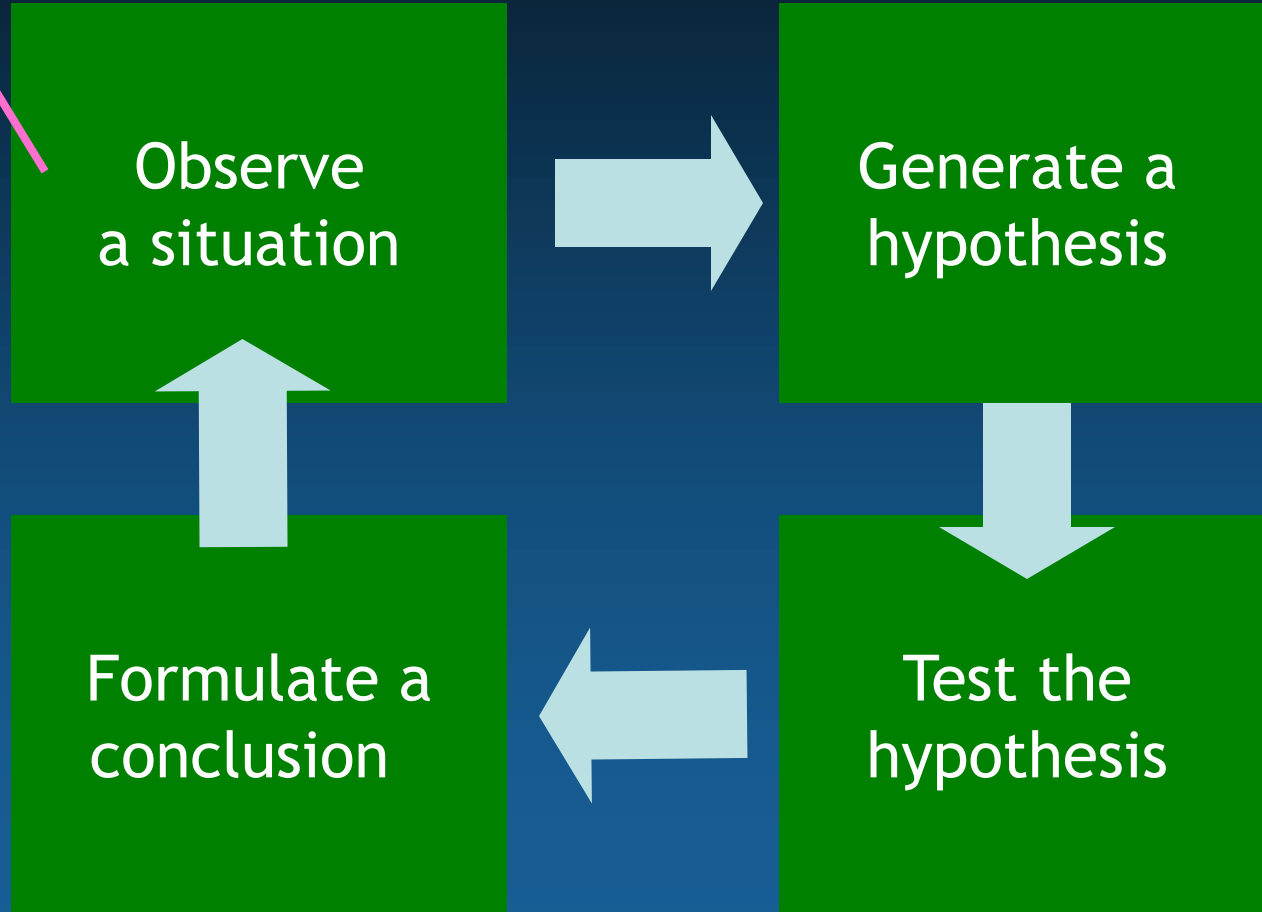
# Drawing conclusions

- Examine whether the source of infection identified explains the descriptive findings
- Follow up on source of infection identified
  - Environmental study
  - Trace back investigation
- Gather laboratory evidence
  - Non-human samples

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Does the conclusion explain the initial observations?

# Generating and testing an hypothesis during an outbreak investigation



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# Compare the conclusion with established facts

- Contacts with headquarters / supervisors
- Literature review
- Medline search
- Internet

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# Planning additional studies

- Laboratory studies
  - Microbiological typing
- Other fields
  - Environmental
  - Anthropological
  - Health economics

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# Possible matrix for the communication of the findings of an outbreak investigation to various audiences

Audience	Medium	Focus of the content	Communication objective
Epidemiologists, laboratory	•Report	•Epidemiology	•Documentation of the source
Public health managers	•Summary	•Recommendations	•Action
Political leaders	•Briefing	•Control measures	•Evidence that the situation is under control
Community	•Press release, interview	•Health education	•Personal steps towards prevention
Scientific community	•Presentation, manuscript	•Science	•Scientific progress

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# Preliminary epidemiological report to conclude an outbreak investigation

- A written report must be left in the field
- It should be:
  - Short
  - Preliminary (disclaimer)
  - Factual
- Several formats can be used:
  - Abstract
  - Slide set
  - Bulleted list
  - Table

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# Proposed final reports for the results of an outbreak investigation

- Oral scientific presentation
- Manuscript
- Epidemiological bulletin report

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# Standard control measures

- May be formulated initially
  - Before the results of the investigations
- Should be different from idealistic blanket recommendations
  - E.g., Provide piped water to all residents of the village
- Should be feasible and focused
  - E.g., Health care workers should wash hands while managing cholera patients in the hospital

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# Executing prevention measures following an outbreak investigation

- Short, medium and long term recommendations
- Characteristics of good recommendations
  - ✓ Evidence based
  - ✓ Specific
  - ✓ Feasible
  - ✓ Cost effective
  - ✓ Acceptable (Discuss with health officials)
  - ✓ Ethical

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# Example: A well that caused an outbreak of cholera in Orissa, India, 2003

- Short term
  - Bar access to the well
- Medium term
  - Protect the well that caused the outbreak
- Long term
  - Ensure that all new wells are protected

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# Well that caused a cholera outbreak, Orissa, India, 2003



Bar access  
to the well

Absence  
of  
platform

Absence  
of  
brims

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# Well that caused a cholera outbreak, Orissa, India, 2003, few months after



Platform

Protective wall

Brim

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# Other public well constructed after the cholera outbreak investigated in 2003 in Orissa, India



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# Evaluating prevention measures following an outbreak investigation

- Input
  - Were the recommendations implemented?
- Process
  - Did the recommendation successfully achieve the objective?
- Outcome
  - Did the recommendation lead to a reduction of mortality and morbidity?

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## Take-home messages

- Get ready!
- Look at cases
- Describe the outbreak by time, place and persons to generate hypotheses
- Test hypotheses in analytical studies
- Find the cause of the outbreak and remove the pump handle