epidemi

Outbreak investigations

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Acute public health

- Acute public health
  - Control of spread
  - New knowledge
  - Stimulus for change
  - Hard and very rewarding work
- Never waste a good outbreak!

- This lecture: Examples and theory based on own experience

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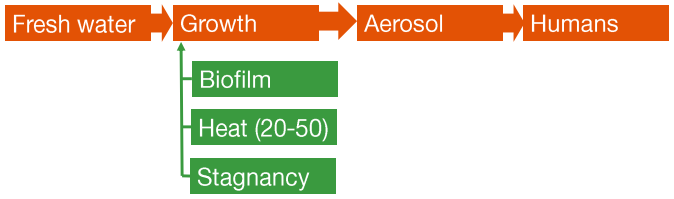
An outbreak of Legionnaires' disease

Legionnaires' disease

- Pneumonia cause by *L pneumophila*
- Incubation period 5-6 (2-10) days
- *L pneumophila's* reservoir is fresh water
- Outbreaks usually caused by aerosolising devices



The outbreak

Sarpsborg and Fredrikstad
- Twin cities along a large river at its junction with the sea
- Industrial area: forest, paper, lignine
- Served by one hospital with its laboratory

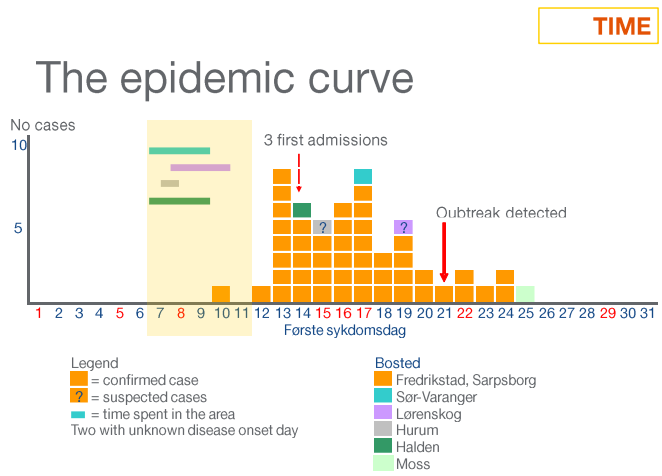
Outbreak warning May 21 2005
11:40 call from local hospital to NIPH 24/7 on call service
18 patients admitted over the last few days with pneumonia
So far 3 positive urine antigen test for Legionella
17:00 Most known cooling towers shut down
19:10 First outbreak meeting
… patient interviews and sampling
… mapping, sampling and inspections of potential sources

Case definition

- Pneumonia with onset in May 2005
  and
- Positive urinary antigen test **or** positive airways secretion culture / PCR
  and
- Having been in Sarpsborg or Fredrikstad in May 2005

- 55 patients (33 men)
- 51 locals, 4 visitors
- 10 died

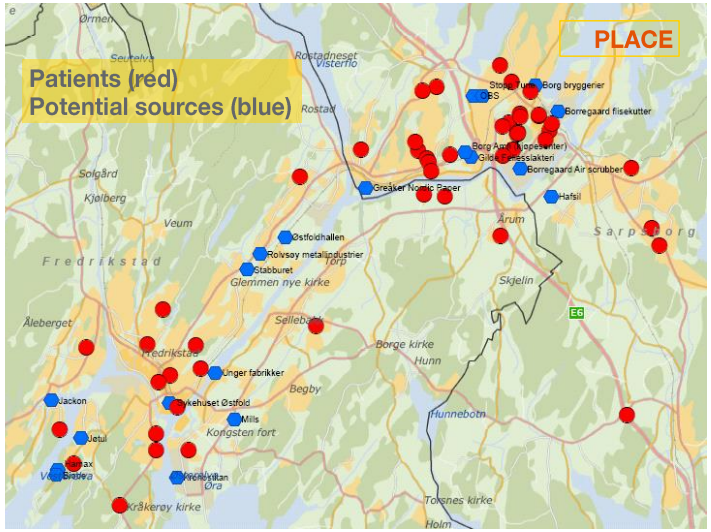
The epidemic curve



PERSON

Attack rates (per 10 000) by age and city

Age group	Fredrikstad	Sarpsborg
30-39		1
40-49	1	4
50-59	4	3
60-69	11	15
70-79	10	**23**
80-89	7	**43**
90-99		**68**
Total	3	6

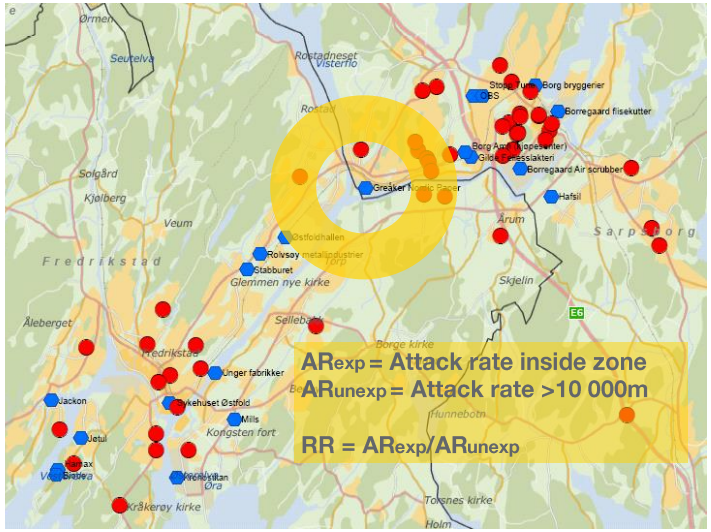


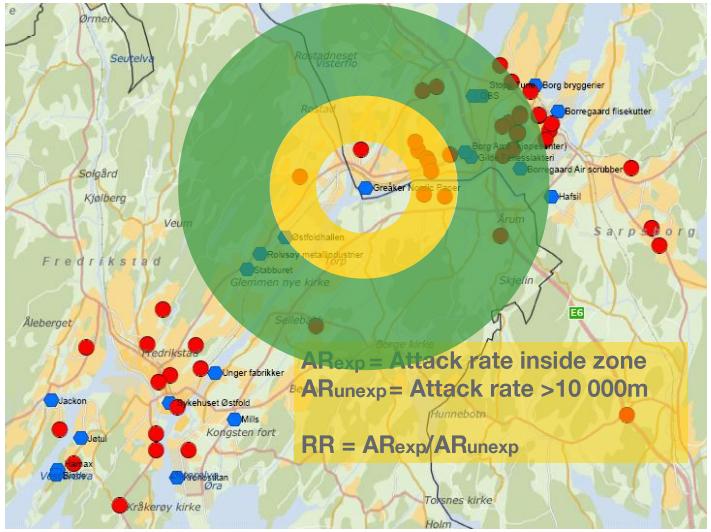
Working hypothesis

- Source active a few days from 7 May
- Source most likely a cooling tower
  - No common indoor location for patients
  - Only cooling tower have spread Legionella so far before; patients have not moved much
- Legionella spread by the wind

→

- *Retrospective cohort study*
- *Microbiological study*





Risk of living close to a plant

Risk ratio for disease for patients living inside a certain concentric zone at given distance from plant compared to living >10 000 m from plant

Plant	Concentric zones around the plant (m)				
	1000	1000-1500	1500-3000	3000-5000	5000-10000
Hafsil (Hafslund Globe)					
Hansa Borg Bryggerier					
Nordic Paper AS					
Rolvsøy Metallindustri					
Østfoldhallen					
Borregaard Industrier Ltd					
Gilde Fellesslakteriet BA					
Stabburet					

Risk of living close to a plant

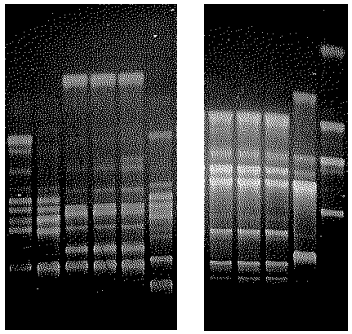
Risk ratio for disease for patients living inside a certain concentric zone at given distance from plant compared to living >10 000 m from plant

Plant	Concentric zones around the plant (m)				
	1000	1000-1500	1500-3000	3000-5000	5000-10000
Hafsil (Hafslund Globe)	0.0	0.0	4.3	1.8	0.4
Hansa Borg Bryggerier	4.0	5.2	1.6	2.6	1.1
Nordic Paper AS	0.0	3.0	4.8	5.0	2.0
Rolvsøy Metallindustri	0.0	0.0	0.9	2.0	4.4
Østfoldhallen	0.0	0.0	1.2	3.6	3.9
Borregaard Industrier Ltd	**9.1**	**5.2**	**2.8**	**1.0**	**0.3**
Gilde Fellesslakteriet BA	2.8	8.1	3.3	0.6	0.6
Stabburet	0.0	0.0	2.4	1.5	5.5

Dose – response relationship

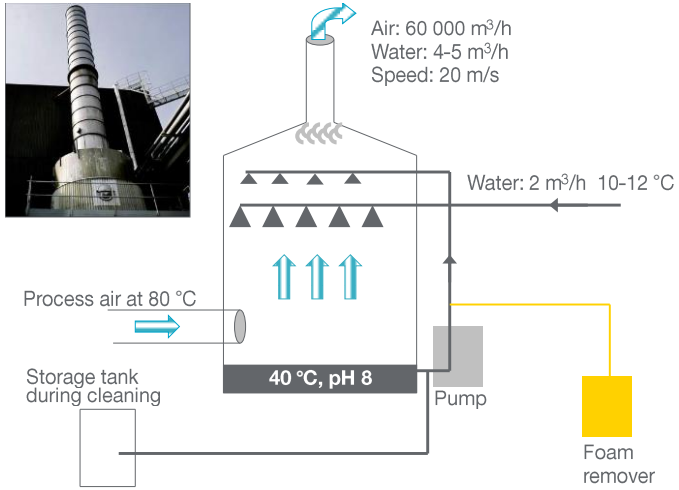
RAPD analyses

1 2 **3 4 5** 6 **7 4 3** 6 K



Primer 1 Primer 2

1. Control L63
2. Control Phil1
3. Patient 1
4. Air scrubber B1
5. Patient 3
6. Cooling tower
7. River Glomma



Lessons

- Work systematically, fast and hard
- Combine methods:
  - Epidemiology
  - Microbiology
  - Environmental science
  - Geography
- Innovate: The doughnut method
- Outbreaks may give new insights:
  - Air scrubbers may cause outbreaks
  - Legionella mya spread > 10 km by air

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Outbreak investigations: theory and practice

TERMINOLOGY

Outbreak, cluster, epidemic

- Epidemic = more than expected
  - Occurrence of cases of an illness in an area clearly in excess of normal expectancy
  - Relative to usual incidence in the same area at the same time of the year
- Outbreak
  - Localised epidemic
- Cluster
  - More cases in space and/or time than expected by chance

TERMINOLOGY

Cause, source, vehicle, reservoir

- Cause = any factor that contributed to the outbreak (proximate and distant)
- Source = a person, animal or object from which the infectious agent is passed to a host
- Vehicle = an object that carries the infectious agent to a host, such as food, water, biologic products or fomites
- Reservoir = the natural habitat of an infectious agent; where it lives and multiplies

Why investigate outbreaks?

- Find the cause(s) to stop the outbreak

Most outbreaks are on the decline or over when we detect them, so why bother?

- Prevent future outbreaks by identifying and neutralising causes
- Increase knowledge about the agent and the disease
- Build confidence among the public
- Train for «the big one»

Detection of outbreaks

- Increase in case surveillance system
- Call from laboratory: unusual number
- Call for clinician: unusual number
- Call for the public: unusal number

Pseudo-outbreaks

- Seasonal variation
- Notification artefacts
- Changes in physician visits or availability of health services
- Diagnostic bias (new methods)
- Diagnostic errors

What is going on?

What is the cause?

How can we stop it?

What can we learn?

Outbreak management

Outbreak investigation	Outbreak communi-cation	Interventions	Research and development
Epidemiology Microbiology (samples from patients, employees, environment, sources) Environmental investigation (homes, serving site, production site, trace back)	With partners, mass media and the public Be: • Proactive • Transparent • Honest • Available • Coordinated	Consider and reconsider based on evolving evidence to decide on: • Closure • Advice • Vaccination • Chemo-prophylaxis	Epidemiology (transmission parameters) Microbiology (phylogeny, virulence, infectiousness, resistance) Clinical (diagnostics, treatments, vaccines)

What is going on?

What is the cause?

How can we stop it?

What can we learn?

Confirm diagnosis, define a case

Confirm diagnosis

- Talk to clinicians and microbiologists
- Provides information on incubation period, usual sources and transmission routes
- Makes specific case defintion possible →

Define a case

- Delineate the outbreak by specifying:
  - Time period
  - Place
  - Person
  - Clinical symptoms
  - Lab-results

Not exposures!

«A person living in Solna, who after October 13 2015 develop diarrhoea and has Salmonella Napoli *isolated from fæces.»*

Find, list, and describe cases

- Find cases
  - Ask doctors, hospitals, laboratories
  - Ask the public
- List cases
  - Line list in e.g. Excel
- Describe cases
  - Time: Epicurve
  - Place: Map, table
  - Person: Table

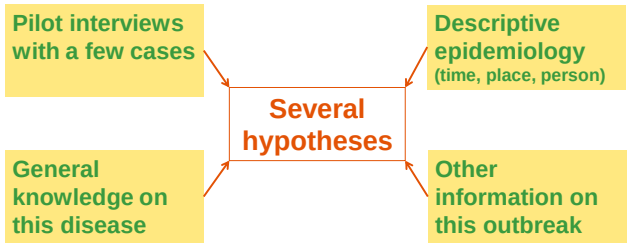
What is going on?

What is the cause?

How can we stop it?

What can we learn?

Forming hypotheses



Estimating associations

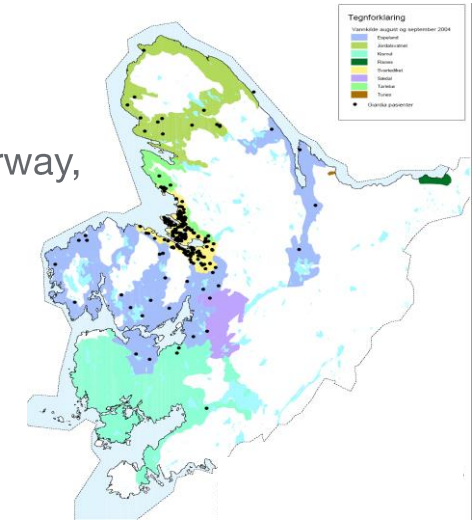
Cohort study

- Compare attack rate in exposed and unexposed groups
- Choose when infromation can be collected on whole or random sample of population

Case-control study

- Compare exposures in cases and controls
- Choose when exposed population is not delineated

Outbreak of giardiasis in Bergen, Norway, 2004



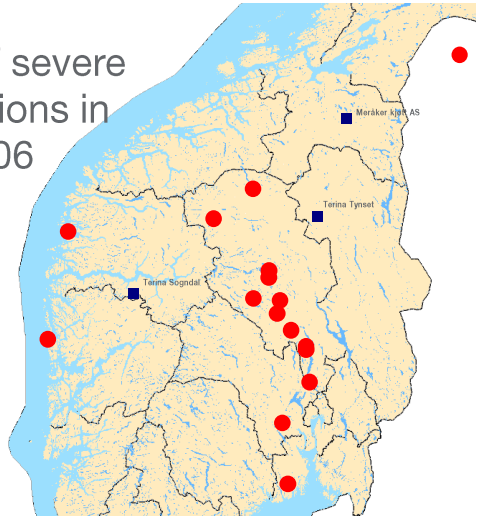
Giardiasis in Bergen, 2004

(attack rate by waterworks)

Waterworks	Cases	N	Attack rate (per 10 000)
Svartediket	637	42 774	148.9
Tarlebø	15	9 685	15.5
Espeland	89	105 440	8.4
Jordalsvatnet	33	34 406	9.6
Sædal	4	14 266	2.8
Kismul	13	23 848	5.5
Sum other	158	194 519	8.1
Svartediket	637	42 774	148.9*

***RR 18.3 95% KI: 15.4 – 21.8**

Outbreak of severe E coli infections in Norway, 2006



The case-control study

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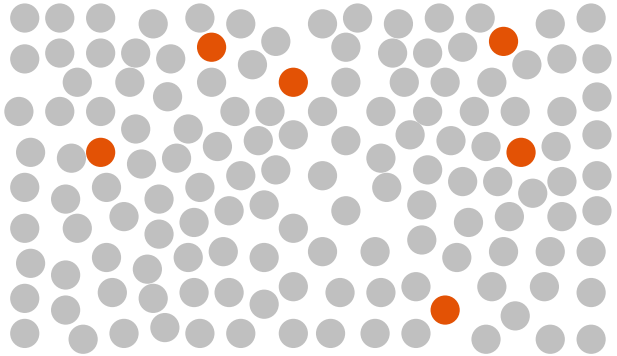

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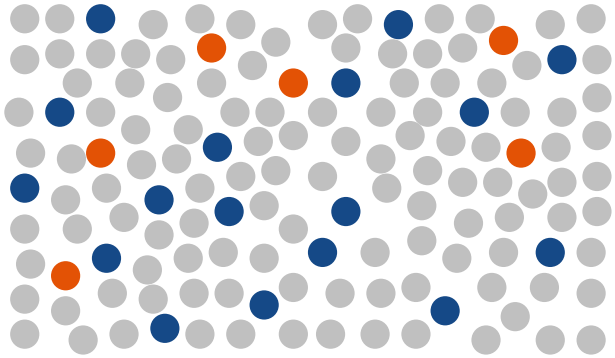
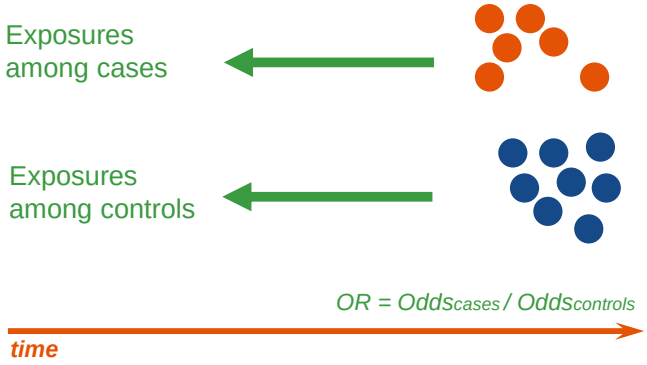


The case-control study



Result for minced meat «G»

Case number	Cases	Controls A	Controls B	Controls C
1	Yes	No	Yes	Yes
2	Yes	No	No	No
3	Yes	No	Yes	No
4	Yes	No	No	Yes
5	Yes	No	No	No
6	Yes	Yes	Unknown	Yes

OR = 8,6

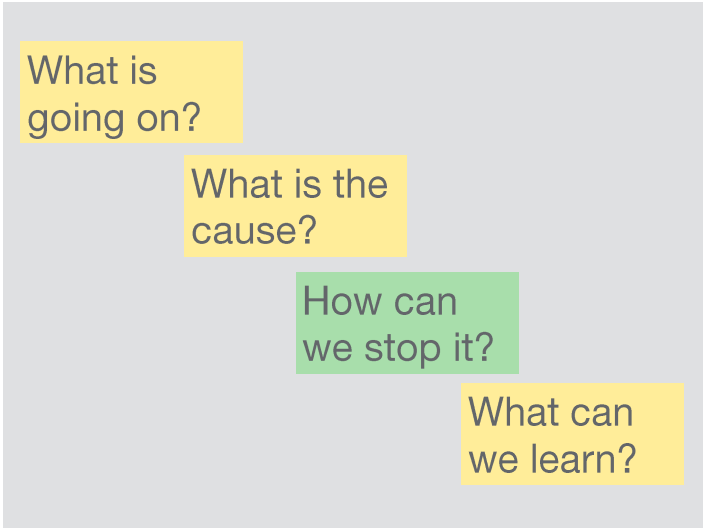
Results for cured sausage «G»

	Cases	Controls A	Controls B	Controls C
1	No	No	No	No
2	Yes	Yes	No	No
3	Yes	No	Yes	No
4	Yes	No	No	No
5	No	No	No	No
6	No	No	No	Yes
7	Yes	No	Yes	No
8	Yes	No	No	No
9	Yes	No	Yes	No
10	Yes	Yes	Yes	Yes
11	Yes	Yes	No	No
12	Yes	No	No	No
13	Yes	No	Yes	No

OR = 17,6 (1,6 – 187)

Other investigations

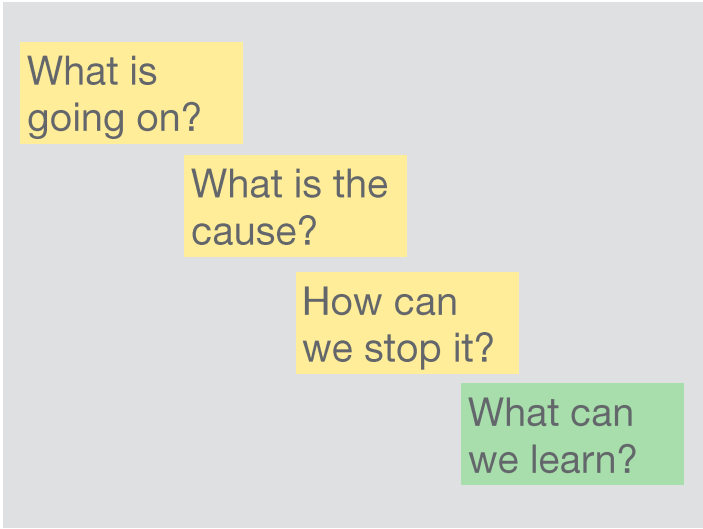
- Microbiological
  - Typing of pathogens from patients, employees, environment, suspected sources
- Environmental
  - Inspection of homes, serving site, production site
  - Tracing of product flow



Control measures

Methods
- Eradicate reservoir
- Eliminate source
- Control vehicle
- Interrupt transmission
- Immunise or provide chemoprophylaxis

Considerations
- Timing
- Level of evidence
- Resources needed
- Legal issues
- «No regret»



Using outbreaks for research

- Epidemiology
  - Transmission parameters
  - Severity measures
- Microbiology
  - Phylogeny
  - Virulence, infectiousness, resistance
- Clinical
  - Diagnostics, treatments, vaccines

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Sources and further reading

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- Giesecke J. Modern infectious disease epidemiology.
- Porta M. A dictionary of epidemiology.
- Gregg MB, ed. Field epidemiology.
- Nygård K et al. An outbreak of Legionnaires' disease caused by long distance spread from an industrial air scrubber. Clin Infect Dis 2008; 46: 61-9.
- Schimmer B et al. Outbreak of haemolytic uraemic syndrome in Norway caused by Escherichia coli O103:H25 traced to cured mutton sausages. BMC Infect Dis 2008; 8: 41.
- Nygård K et al. A large community outbreak of waterborne giardiasis-delayed detection in a non-endemic urban area. BMC Public Health 2006, 6: 141.

Traditional steps of an outbreak investigation

- Confirm outbreak and diagnosis
- Define case
- Identify cases and obtain information
- Describe data collection and analysis
- Develop hypotheses
- Analytical studies to test hypotheses
- Special studies
- Communication, including outbreak report
- Implement control measures

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