PHR 250
5/22/06, 6p

INVESTIGATION OF FOODBORNE DISEASES

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It all starts with one or more sick people.

The text (Procedures to Investigate Foodborne Illness, 5th ed., International Association for Food Protection, Ames, IA, 1999) tells how to organize the foodborne disease surveillance system that should already be in place when the illness complaint arrives. Time will not permit covering the "Investigate Outbreaks" section of the text in lecture. **Please read this and the "Seek Sources" section, to provide an orientation for the data analysis activities on which we will focus.** Note that the procedures are heavily oriented to restaurant-associated incidents. All the same, the hazard analysis and flow diagram portions of the procedure will remind you of the HACCP and risk analysis methods that we have already considered briefly. There are also potentially useful instructions for on-the-spot food analyses and for collection of clinical and food samples for laboratory analysis, which will not be part of our epidemiological exercises in class. Here, we focus on the "Analyze Data" aspect. Because the discussion does not coincide with that of the whole text, please note that the numbers of the tables and figure that came from the text have been left as they were, rather than assigning them in the order of citation in this handout.

ANALYZE DATA

The first task is to obtain a (at least preliminary) diagnosis.
The preliminary diagnosis should later be confirmed by a laboratory diagnosis, but this is not always done, and is sometimes not even attempted. Many foodborne disease outbreaks are of "undetermined etiology." The problem with unknown agents obviously does not exist when case-control studies are used to identify risk factors in sporadic foodborne diseases.

The first diagnosis is made based on signs and symptoms reported by the patient(s) — see Table B (pp. 100–124) in the text.

From the reports, a summary is prepared as shown in the following table (Table 3 of text, p. 46) and compared to the known signs and symptoms for various foodborne diseases until a reasonably good match is found.

Table 3. *Frequency of signs and symptoms*

Signs and symptoms	Number of cases	Percent
Diarrhea	260	88
Abdominal cramps	122	41
Fever	116	39
Nausea	105	35
Headache	68	23
Muscular aches	56	19
Chills	55	19
Vomiting	42	14

When a diagnosis has been made, the investigator will know from the literature what the range of incubation times is.

From the disease histories, the time of onset of disease for individual patients is obtained; these are plotted as shown in the figure below (Fig. 3, p. 45, in the text). The time interval on the X axis should be no more than 1/4 of the incubation period of the disease. The incubation time is subtracted from the median time of onset to find the time of exposure.

The reason that the median rather than the mean time is used is that the times of onset usually have a skewed distribution.

The incubation period may have to be estimated from the “span of onsets” (period from the first person’s onset till the last person’s onset) and applied as above, if there is no firm diagnosis. For a single-incident outbreak (i.e., all of those ill were exposed on the same occasion or meal), the span of onsets is likely to be approximately equal to the incubation period of the illness. Obviously, this does not work if, for example, people bought contaminated food at retail and ate it on various days thereafter.

With good luck, the time of exposure will represent a common meal, such as a banquet or picnic shared by the patients — and a number of other people. This may be done with a meal attendance-attack rate table (Table 4, p.48).

Figure 2. *Epidemic curve of a common-source outbreak.* (p. 45)

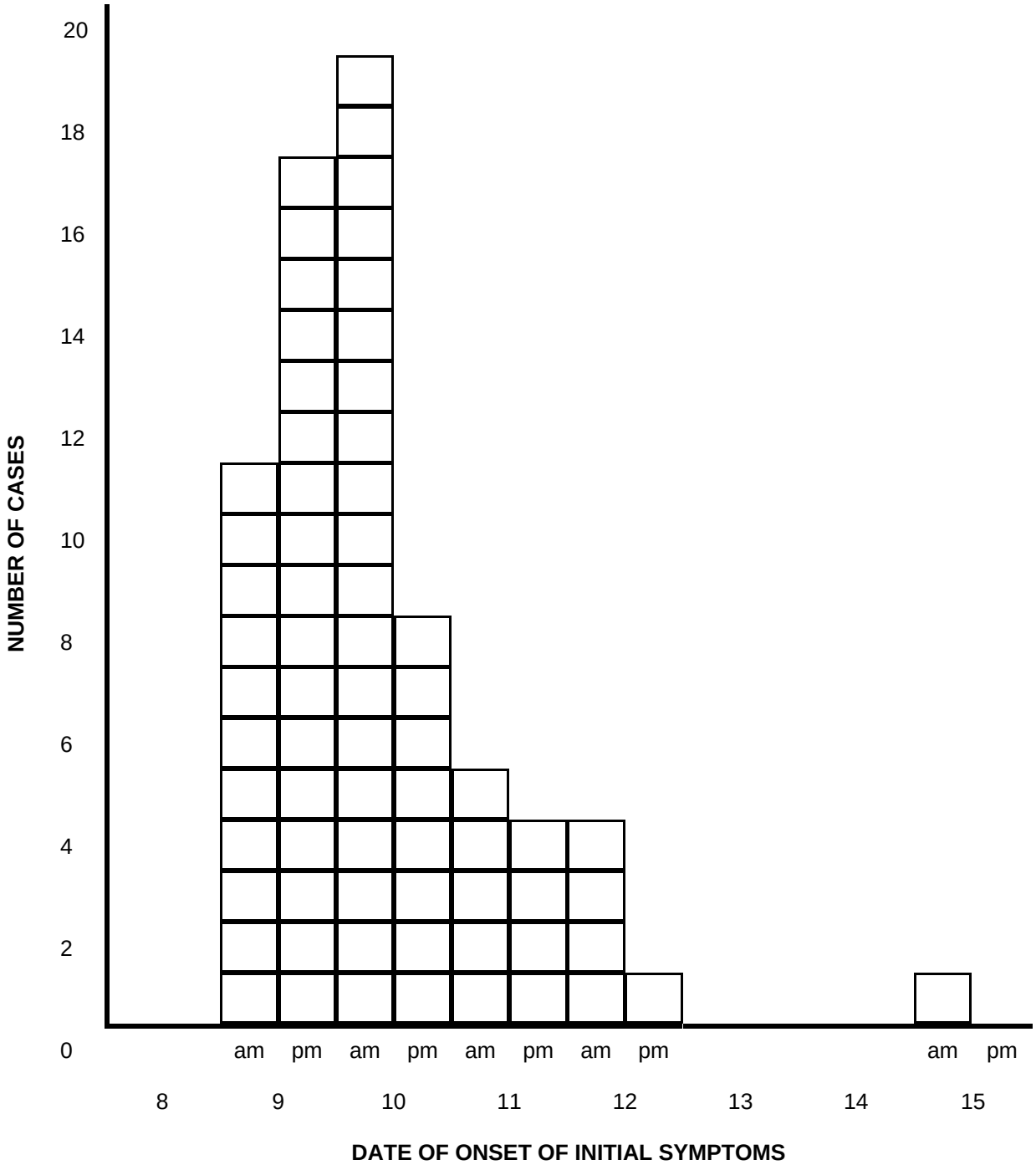

Table 4. *Histories of meal attendance and attack rates*

	Ate/drank				Did not eat/drink						
Day/ meal	Ill (a)	Well (b)	Total (a+b)	Attack rate[a] (%)	Ill (c)	Well (d)	Total (c+d)	Attack rate[b] (%)	Diff. in rates[c]	Rel. risk[d]	*p* val-ue[e]
1/16 B	52	100	152	34	58	94	152	38	–4	0.9	0.55
L	89	150	239	37	21	44	65	32	+5	1.15	0.55
D	87	150	237	37	23	44	67	34	+3	1.07	0.83
1/17 B	56	105	161	35	54	89	143	38	–3	0.92	0.67
L	106	145	251	42	4	54	58	7	+35	6.1	$<10^{-6}$
D	78	130	208	38	32	64	96	33	+5	1.13	0.57

[a] a/(a+b) × 100
[b] c/(c+d) × 100
[c] [a/(a+b)] – [c/(c+d)]
[d] [a/(a+b)] ÷ [c/(c+d)]
[e] *p* refers to statistical significance (see p. 56 et seq. in text)

The next step is to identify as many as possible of the people who participated in the meal and get them to fill out food history questionnaires (e.g., Form C2, p. 75 of the text). If most of those who attended can be identified, the food history data are summarized in a food-specific attack rate table as shown below (Table 5, p. 48 of text; Form K1, p. 88). Differences in attack rates among people who ate and people who did not eat a specified food item are then compared.

One is looking for the greatest difference in or ratio of attack rates. For different reasons, one seldom finds attack rates that are either 100% or 0%.

Table 5. *Food-specific attack rate table*

	Ate/drank				Did not eat/drink						
Food/ beverage	Ill (a)	Well (b)	Total (a+b)	Attack rate[a] (%)	Ill (c)	Well (d)	Total (c+d)	Attack rate[b] (%)	Diff. in rates[c]	Rela-tive risk[d]	*p* value[e]
Turkey	97	36	133	73	2	23	25	8	+65	9.1	<0.000001
Dressing	88	33	121	73	11	26	37	30	+43	2.5	0.000005
Peas	77	28	105	73	22	31	53	42	+31	1.8	0.0002
Rolls	50	16	66	76	49	43	92	53	+23	1.4	0.006
Pumpkin pie	22	14	36	61	77	45	122	63	–2	1.0	0.9
Milk	12	6	18	67	87	53	140	62	+5	1.1	0.9
Coffee	59	39	98	60	40	20	60	67	–7	0.9	0.5

[a,b,c,d,e] See footnotes to Table 4.

If many of the people who attended the meal cannot be accounted for, or for other reasons, it may be necessary to locate controls (well) who match the ill persons according to selected criteria and get food histories from them. Then, one produces a “Case-control vehicle exposure table” (Table 6, p. 50 of text; Form K2, p. 89).

Table 6. *Case-control exposures*

	Cases (Ill)				Controls (Well)						
Food/ beverage	Ate (a)	Did not eat (c)	Total (a+c)	Percent exposed[a]	Ate (b)	Did not eat (d)	Total (b+d)	Percent exposed[b]	Diff. in percent[c]	Odds ratio[d]	*p* value[e]
Turkey	97	2	99	98	36	23	59	61	+37	30.1	<0.0000001
Dressing	88	11	99	89	33	26	59	56	+33	6.3	0.000006
Peas	77	22	99	78	28	31	59	47	+31	3.9	0.0002
Rolls	50	49	99	51	16	43	59	27	+24	2.7	0.007
Pumpkin pie	22	77	99	22	14	45	59	24	–2	1.0	0.98
Milk	12	87	99	12	6	53	59	10	+2	1.2	0.91
Coffee	59	40	99	60	39	20	59	66	–6	0.9	0.5

[a] a/(a+c) × 100
[b] b/(b+d) × 100
[c] {[a/(a+c)] - [b/(b+d)]} × 100
[d] ad/bc
[e] *p* refers to statistical significance (see p. 56 et seq. in text)

Sometimes two or more food items are suspect, like the turkey and dressing in the previous table. If there are enough food-intake histories, one can do a more detailed, stratified analysis by cross-tabulation, as shown in the next table (Table 7, p. 51 of the text). Data for this purpose come from Form D2 (page 77) or Form C2 (p. 75), which permit matching cases as to whether the person ate one food, the other, both, or neither.

Here, people are divided into two groups: those who ate turkey and those that did not; each group is then subdivided into groups of people who ate dressing and those who did not.

Table 7. *Stratified analysis comparing food-specific attack rates for eating and not eating two foods*

		Ate dressing	Did not eat dressing	Totals
Ate turkey	Ill	88	9	97
	Well	33	3	36
	Total	121	12	133
	Percent ill	73	75	73
Did not eat turkey	Ill	0	2	2
	Well	0	23	23
	Total	0	25	25
	Percent ill	0	8	8
Total	Ill	88	11	
	Well	33	26	
	Total	121	37	
	Percent ill	73	30	

One sees that eating turkey was the principal determinant, with quite similar illness rates for those who ate turkey, whether or not they also ate dressing.

Not all outbreaks of foodborne disease occur in connection with common meals. Some result from foods eaten in restaurants by different people at different times; others result from foods bought in retail shops and supermarkets.

If it is possible to identify some suspect foods, a food preference attack rate table (Table 8, p. 52 in the text), as shown on the following page, can be very useful.

Table 8. *Food preference attack rate table*

	Always or usually eat (Purchased within incubation period)				Never eat (Not purchased within incubation period)				
Food	Ill	Well	Total	Attack rate (%)	Ill	Well	Total	Attack rate (%)	Percent difference
Milk, Brand A	17	116	133	12.8	5	20	25	20.0	–7.2
Milk, Brand B	9	85	94	9.6	13	51	64	20.3	–10.7
Cheese, Brand X	22	102	124	17.7	0	34	34	0.0	+17.7
Cheese, Brand Y	20	125	145	13.8	2	11	13	15.4	–1.6
Cheese, Brand Z	17	100	117	14.5	5	36	41	12.2	+2.3

The food preference approach is also used with illnesses such as hepatitis A that have such long incubation periods that most of the victims may not be able to remember exactly what they ate at a given meal more than a month earlier.

In investigating a foodborne outbreak caused by participation in a common, contaminated meal, one is in fact doing a "retrospective cohort study." The attempt is to identify as many exposed and unexposed people as possible and see what the exposure did to them.

When we investigate waterborne, diseases, we generally use a case-control study approach because it is impossible to identify and interview the large number of people involved.

When we study sporadic cases of foodborne disease that mostly are much more common than outbreak-associated cases (cf. CDC vs. CAST statistics), we also use the case-control study approach.

Alternately, pulsed-field gel electrophoresis (PFGE) "fingerprints" from sporadic bacterial infections are now being compared in some states. When fingerprints from multiple cases match, it is sometimes possible to do follow-up interviews that identify a food as a common source of the infections, even though epidemiological evidence to suggest this had otherwise been lacking.

Statistical Calculations

Acquaint yourself with the use and calculation of Relative Risk and Odds Ratio (no confidence intervals). Practice the chi-square and Fisher's Exact Test calculations for a couple of examples.

Note that the last sections of the text address how to try to end an outbreak (public notification) and to use the findings to limit or prevent recurrences. These are important, but will not be discussed.

An Outbreak of Gastroenteritis

On Saturday, May 22, a group of 11 men met at a summer camp for a planning session before the opening of the camp. The wives of four of the men accompanied the group to serve lunch and supper and to spend their leisure time playing bridge. They arrived at the camp about 10:00 a.m. and left immediately after supper.

The lunch consisted of bread, butter, cold turkey, potato salad, milk, and Jell-o and was served at 12:30 p.m. The supper included fruit cocktail, baked ham, cold asparagus, bread, coffee, and ice cream and was served promptly at 6:00 p.m. All foods except the coffee were prepared or purchased on the day before by the wives and carried to the camp mess facilities.

That evening, 8 of the 15 people who spent the day together and shared the common foods became ill. All were recovered within 48 hours. Data on each person are attached. Using these materials, perform the following:

1. Using the Symptom Tally Work Sheet, determine the most commonly occurring symptoms.

2. Prepare, on the Epidemic Curve Tally Sheet, a tally of the times of onset.

   Prepare a graph to illustrate the epidemic curve

3. Using the Attack Rate Work Sheet, calculate the attack rate for each food served.

4. Prepare, on the Incubation Curve Tally Sheet, a tabulation of the possible incubation times.

   On the basis of this additional evidence, what disease is it likely to be?

5. Try to explain how the food became infective (see text of food history).

INTERVIEWS WITH PERSONS ILL & WELL

Person	Foods eaten: Lunch	Foods eaten: Supper	Onset	Symptoms
No. 1 M-23	Cold turkey Potato salad Milk	Baked ham Bread Coffee Ice cream	7:30 p.m.	Abd. cramps Diarrhea
No. 2 M-46	Bread Butter Potato salad Milk	Fruit cocktail Baked ham Bread Ice cream		Not ill
No. 3 M-22	Bread Butter Cold turkey Potato salad Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Bread	8:00 p.m.	Diarrhea Vomiting Headache Abd. cramps
No. 4 F-37	Cold turkey Milk Jell-o	Fruit cocktail Cold asparagus Coffee		Not ill
No. 5 F-29	Cold turkey Potato salad Milk	Fruit cocktail Baked ham Cold asparagus Coffee Ice cream	10:30 p.m.	Diarrhea
No. 6 M-52	Bread Potato salad Jell-o	Fruit cocktail Baked ham Coffee Ice cream Bread		Not ill
No. 7 M-32	Bread Butter Cold turkey Potato salad Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Coffee Ice cream	8:30 p.m.	Vomiting Diarrhea

Person	Lunch	Supper	Onset	Symptoms
No. 8 F-31	Cold turkey Milk	Baked ham Cold asparagus Bread Coffee Ice cream		Not ill
No. 9 M-40	Bread Butter Cold turkey Potato salad Milk Jell-o	Fruit cocktail Bread Coffee Ice cream	10:00 p.m.	Diarrhea Abd. cramps
No. 10 M-30	Bread Butter Potato salad Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Ice cream		Not ill
No. 11 F-28	Cold turkey Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Ice cream	9:15 p.m.	Diarrhea
No. 12 M-38	Bread Butter Potato salad Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Coffee Ice cream		Not ill
No. 13 M-40	Bread Butter Milk Jell-o	Fruit cocktail Baked ham Cold asparagus Coffee Ice cream	8:30 p.m.	Diarrhea Abd. cramps Bloody stools
No. 14 M-35	Bread Butter Milk Jell-o	Fruit cocktail Cold asparagus Coffee		Not ill

Person	Lunch	Supper	Onset	Symptoms
No. 15 M-42	Bread Butter Cold turkey Potato salad Milk	Baked ham Bread Coffee Ice cream	12:30 p.m.	Diarrhea

SYMPTOMS TALLY

SYMPTOM	TALLY	NUMBER %
Abdominal cramps		
Diarrhea		
Vomiting		
Headache		
Bloody stool		
Fever		
TOTAL		

EPIDEMIC CURVE TALLY

TIME OF ONSET	TALLY OF ONSETS	NUMBER
7:00 - 7:59		
8:00 - 8:59		
9:00 - 9:59		
10:00 - 10:59		
11:00 - 11:59		
12:00 - 12:59		
TOTAL		

EPIDEMIC CURVE

Number of onsets in time period

7 - 7:59	8 - 8:59	9 - 9:59	10 - 10:59	11 - 11:59	12 - 12:59

ATTACK RATE WORK SHEET

MEAL	PERSONS EATING FOOD ITEM				PERSONS NOT EATING FOOD ITEM				DIFF.
FOOD	Total	Ill	Well	Attack Rate	Total	Ill	Well	Attack Rate	(%)
Lunch: Bread									
Butter									
Cold Turkey									
Potato Salad									
Milk									
Jello									
Supper: Fruit Cocktail									
Baked Ham									
Cold Asparagus									
Bread									
Coffee									
Ice Cream									

INCUBATION CURVE TALLY SHEET

Person Number	Lunch to onset (h)	Supper to onset (h)