Investigation and response to an outbreak of leptospirosis among raspberry workers, NSW, 2018



Anthea Katelaris

Health Protection NSW & National Centre for Epidemiology and Population Health, ANU

Keira Glasgow, Anthony Zheng, Suhasini Sumithra, Daneeta Hennessy, Stacey Kane, Kerryn Lawrence, John Turahui, Janet Terry, Debra van den Berg, Paul Corben, Vicky Sheppeard, Jeremy McAnulty





Australian National University





Background

NSW

- June 2018 cluster of febrile illnesses among berry pickers presenting to GP/ED on mid-north coast.
- Initial testing negative → lepto PCR+
- *Leptospira* serovar Arborea
 - Rodents predominant reservoir
- Initial case interviews
 - Single large berry farm
 - All raspberry workers
 - Backpackers, migrants, refugees.

Leptospirosis

- Incubation 2-30 days (usual 5-14)
- Acute phase \rightarrow immune phase
- Serology, PCR, (culture)
- Transmission: infected animal urine → skin abrasions, ingestion, mucous membranes.
- Global: endemic tropically
- Nationally notifiable
 - 10-40/yr cases in NSW



Leptospirosis cases at time of outbreak detection, 21 June 2018, by case status (n=42)



Aim

Investigation conducted to identify the outbreak source and risk factors for infection, to guide prevention and control measures.



Case-control study

Population

 Raspberry workers on the Farm (pickers, packers, supervisors)

Cases

- Active & passive surveillance
- Worked in raspberry team in exposure period
- Case definitions based on national criteria
 Confirmed: 4x rise OR 1x ≥400 & IgM+
 Probable: PCR+ OR IgM+
 - **Possible**: clinical
- Interviewed about behaviours during 4 week exposure period



Case-control study

Controls

- Selected from current raspberry workers
- Had to have worked since before outbreak detection
- Serology collected to screen for asymptomatic infection
- Asked about exposures in May (representative period during outbreak)



Outbreak description

84 cases



- 640 raspberry workers \rightarrow crude AR 11% (conf/prob)
- Clinical disease mostly mild

no severe complications or deaths

Leptospirosis outbreak cases, by case status



- Crude & adjusted ORs calculated from logistic regression
- Only confirmed & probable cases with qus (n=67) & asymptomatic seronegative controls (n=69) in 1° analysis

Multivariable model

Cases	(%)	Controls	(%)	Variable	Adj OR*	95% CI	p value**
39/67	(58)	53/69	(77)	Any glove use	0.3	0.1-0.8	0.01
0.54		1		Median years employed	0.8	0.6-0.9	0.02
10/67	(15)	2/69	(3)	Rodent sighting	7.1	1.3-38.9	0.02
32/66	(48)	18/65	(28)	Interpreter required	4.0	1.6-9.9	0.003

Crude association only

Cases	(%) Controls		(%)	Variable		Crude OR	95% CI	p value*
15/67	(22)	26/69	(38)	Scratches:	Never	1		
11/67	(16)	11/69	(16)		Rarely	1.7	0.6-5.0	0.3
13/67	(19)	14/69	(20)		Often	1.6	0.6-4.3	0.3
28/67	(42)	18/69	(26)		Always	2.7	1.1-6.4	0.03
25/55	(45)	17/68	(25)	Mud	contact	2.5	1.2-5.4	0.02
61/67	(91)	54/69	(78)	Drinks wat	er from trailer	2.8	1.0-7.8	0.045
65/67	(97)	60/69	(87)	Raspbe	rry picking	4.9	1.0-23.5	0.048

No association

Cases	(%) Controls		(%)	Variable	Crude OR	95% CI	p value*	
29/67	(43)	31/69	(45)	Any berry eating	0.9	0.5-1.8	0.9	
23/64	(36)	17/69	(25)	Irrigation water contact	1.7	0.8-3.63	0.2	
58/58	(100)	69/69	(100)	Handwashing	†			

*Wald test p value +Odds ratio undefined due to 0 values.

Environmental Investigations

- 3 farm inspections by EHO
 - PPE inconsistent and inadequate
 - No significant opportunities for drinking water contamination identified from source → storage





Environmental Investigations

- Evidence of rodent activity seen around raspberry plants
- Additional rodent traps
- Mice (*Mus musculus*) caught
 - 3/12 MAT+ Leptospira Arborea & PCR+



Cause?

- Workers likely infected through scratches → came into contact with leptospires from mouse urine in environment
- Raspberry workers at increased risk due to thorns + inadequate glove use



Study limitations

- Self reported
- Biases
 - Recall
 - Social desirability
 - Selection biases



Other questions

- ? Leptospirosis in other wildlife on farm
- ? Baseline prevalence in rodents
- ? Environmental changes contributed to outbreak occurring



Public health response

- Multiple control measures implemented (with SafeWork)
 - Enhanced glove use with compliance monitoring
 - Additional rodent control
- Prophylaxis clinic July
 - Weekly doxycycline x4 weeks
 - 114 / 230 raspberry workers administered
 - Limited evidence
 - Ethical considerations



Conclusions

- Largest known outbreak in Australia
- Important occupational risk among raspberry workers, requiring ongoing protective measures.
- PCR assists in early diagnosis → should be included in surveillance case definitions.



Acknowledgements



Health Protection NSW

Enteric & Zoonotic Diseases PHO trainees Emergency Response Coordination Unit

North Coast Public Health Unit

Pathology North

Coffs Harbour Hospital ED

Dr Alison Winning (Tweed Hospital) Dr Mim Morgan (NBM PHU)

GOVERNMENT

SafeWork NSW



Department of Primary Industries



Local Land Dr Ian Poe Services North Coast





Leptospirosis Reference Laboratory, QHFSS

Dr Scott Craig, Ellena Heading, Mary-Anne Burns



Dr Matthew O'Sullivan



Prof Martyn Kirk

Dr Colleen Lau

Supervisors – Prof Robyn Lucas, Dr Stephanie Davis, Dr Rachael Rodney Harris

Dr Michael Walsh (USyd) Prof John Kaldor (UNSW) Local GPs Study participants Farm management

APPENDIX SLIDES

Epicurve of leptospirosis outbreak cases (n=84) by cases status, overlaid with daily rainfall (Glenreagh weather station)



Date of onset

2018, mean and median monthly rainfall, Glenreagh NSW (BoM)

	Jan	Feb	Mar	Apr	Мау	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Annual
2018	49.0	30.8	162.0	48.2	11.4	61.8	20.2	49.6	53.4				
Mean	143.2	124.5	115.6	83.5	77.9	88.2	28.3	51.9	38.1	95.6	108.2	114.1	1245.8
Median	77.2	74.5	104.7	60.2	36.9	53.6	22.1	28.0	24.6	55.8	91.1	81.7	1274.3

Case finding

- Routine lab notifications
- Local GPs contacted & alert to GPs/EDs 1 testing
- Farm alerted
- Other farms asked
- Referred by other cases
- Rapid ED syndromic
 - surveillance alert



Case finding

(raspberry | blueberry | berry | pick* | farm) AND
(Coffs & Grafton ED)

Problem	Nursing assessment
Fever	Fever + headache 2/7. Nil gastro sx. Pt works as raspberry picker . {Temp=40.0}
Pain, back	2/12 pain to back when picking up heavy objects. Nil neuro sx. {GCS=15}

Laboratory investigation



Laboratory investigation

- Serum screened via Leptospira IgM ELISA (Panbio)
- → MAT antibodies against panel of 22 serovars (Leptospirosis Reference Laboratory, Qld)

- PCR (<7 days) Taqman real-time PCR, targets rrs gene
 - not NATA accredited; high sensitivity (96.4%) & specificity (99.5%) vs culture

Leptospiral serovars used in the current routine microscopic agglutination test (MAT)

panel at the WHO/FAO/OIE Collaborating Centre for Reference and Research on

Leptospirosis, Brisbane, Australia.

Species	Serovar	Strain
L. interrogans	Pomona	Pomona
L. interrogans	Hardjo	Hardjoprajitno
L. borgpetersenii	Tarassovi	Perepelitsin
L. kirschneri	Grippotyphosa	Moskva V
L. weilii	Celledoni	Celledoni
L. interrogans	Copenhageni	M20
L. interrogans	Australis	Ballico
L. interrogans	Zanoni	Zanoni
L. interrogans	Robinsoni	Robinson
L. interrogans	Canicola	Hond Utrecht IV
L. interrogans	Kremastos	Kremastos
L. interrogans	Szwajizak	Szwajizak
L. interrogans	Medanensis	Hond HC
L. kirschneri	Bulgarica	Nicolaevo
L. kirschneri	Cynopteri	3522C
L. borgpetersenii	Arborea	Arborea
L. interrogans	Bataviae	Swart
L. interrogans	Djasiman	Djasiman
L. borgpetersenii	Javanica	Veldrat Batavia 46
L. noguchii	Panama	CZ 214
L. santarosai	Shermani	1342K
L. weilii	Topaz	94-79970/3

Lau CL, Skelly C, Dohnt M, Smythe LD. The emergence of Leptospira borgpetersenii serovar Arborea in Queensland, Australia, 2001 to 213. *BMC Infect Dis.* 2015;15:230. doi: 10.1186/s12879-015-0982-0

Course of illness and diagnosis



Levett, PN. Leptospirosis. Clinical Microbiology Reviews. 2001, 14(2)

Case definitions

Confirmed	 Laboratory-definitive evidence of <i>Leptospira</i> infection 4x rise in MAT titre Single high titre (≥400) & IgM+ Isolation
Probable	 Laboratory-suggestive evidence, with clinically compatible symptoms PCR IgM+ (with convalescent serology pending or not available).
Possible	 Clinically compatible symptoms Fever or chills/rigors AND at least one of: myalgia; arthralgia; headache; jaundice; conjunctival suffusion, rash, GI symptoms, aseptic meningitis; pulmonary complications; cardiac arrhythmias; ECG abnormalities; renal insufficiency; haemorrhage; jaundice with acute renal failure. OR Clinical treating team suspicion of leptospirosis for other or unknown reasons.

Inclusion criteria

Case: Any person who

- met any of the outbreak case definitions (since 1st April 2018)
- worked in a raspberry picking team on the Farm in their exposure period

Controls

Selected from current raspberry picking workers (raspberry pickers, packers, carriers, supervisors and QA staff).

Inclusion criteria

Worked in a raspberry picking team since 2 weeks prior to 1st EHO visit (7/6/18)

Exclusion criteria

Reported symptoms (recruit as case)

Full inclusion and exclusion criteria

CASES

Exclusion criteria

Cases will be excluded from the study if:

- They cannot be contacted after: 3 attempts by phone over 3 different days at different times of the day, AND 3 attempts by SMS over 3 different days at different times of the day, AND 3 attempts by phone to next of kin (if available) over 3 different days at different times of the day.
- Treating team think an alternative cause of illness is more likely, or laboratory testing shows strong evidence of an alternative cause of illness.
- They are unable to answer questions or refuse consent, or an appropriate interpreter cannot be located (in person or via translation phone service)

CONTROLS

Control group recruitment inclusion criteria

People will be recruited to be a control if they:

- Are part of the raspberry picking staff on the Farm (including pickers, packers, carriers, supervisors and quality assurance staff)
- Have worked in a raspberry picking team for at least 2 weeks between 14/3/18 (30 days pre- first case) to 20/6/18 (date of first farm visit).
- Consent to participating in the study, including completing the questionnaire, plus/minus having a blood sample collected for serological testing.

Control group exclusion criteria

People will be excluded from recruitment if they:

- They report symptoms that are clinically compatible with leptospirosis, since 1st April 2018, as per the possible case definition (recruit as case)
- They are unable to answer questions or refuse consent.
- An appropriate interpreter cannot be located (in person or via translation phone service)
- They cannot recall if they worked on the farm between 14 March to 9 June 2017
- Did not work as part of the raspberry picking teams for any of their employment period

Number of notifications of Leptospirosis, received from State and Territory health authorities in the period of 2000 to 2017 and yearto-date notifications for 2018 (NNDSS)

	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Aust
2000	1	53	9	133	8	0	36	4	244
2001	0	66	4	127	3	5	37	2	244
2002	0	39	3	94	2	2	18	2	160
2003	0	39	4	69	2	0	8	6	128
2004	0	40	2	121	1	0	8	5	177
2005	0	35	5	71	3	0	10	5	129
2006	0	17	2	115	1	1	6	3	145
2007	0	9	1	76	1	0	16	5	108
2008	0	17	1	88	0	0	4	1	111
2009	2	18	4	105	0	0	11	1	141
2010	1	22	2	85	2	1	14	5	132
2011	1	40	2	155	2	1	10	3	214
2012	0	22	1	64	2	0	13	3	105
2013	0	12	4	58	2	0	9	0	85
2014	0	14	2	56	1	1	7	3	84
2015	1	17	4	40	0	2	7	1	72
2016	0	14	1	90	2	1	16	6	130
2017	0	20	14	94	1	0	15	3	147
2018	0	56	6	54	0	0	13	2	131

Leptospirosis notifications in NSW residents, by quarter of onset. Jan-Mar 2001 to Jan-Mar 2019



Cases	(%)	Controls	(%)	Variable	Crude OR	95% CI	p value*	Adj OR**	95% CI	p value*
39/67	(58)	53/69	(77)	Any glove use	0.42	0.20-0.88	0.022	0.30	0.12-0.75	0.010
0.54		1		Median years employed	0.84	0.71-0.96	0.045	0.76	0.61-0.95	0.015
10/67	(15)	2/69	(3)	Rodent sighting	5.88	1.24-29.93	0.026	7.09	1.29-38.93	0.024
32/66	(48)	18/65	(28)	Interpreter required	2.46	1.19-5.08	0.015	4.00	1.63-9.86	0.003
15/67	(22)	26/69	(38)	Never having scratches	1					
11/67	(16)	11/69	(16)	Rarely	1.73	0.61-4.95	0.31			
13/67	(19)	14/69	(20)	Often	1.61	0.60-4.32	0.34			
28/67	(42)	18/69	(26)	Always	2.70	1.13-6.43	0.025			
25/55	(45)	17/68	(25)	Mud contact	2.50	1.17-5.36	0.019			
61/67	(91)	54/69	(78)	Drinks water from trailer	2.84	1.02-7.79	0.045			
65/67	(97)	60/69	(87)	Raspberry picking	4.87	1.01-23.48	0.048			
29/67	(43)	31/69	(45)	Any berry eating	0.94	0.48-1.84	0.85			
23/64	(36)	17/69	(25)	Irrigation water contact	1.72	0.81-3.63	0.16			
58/58	(100)	69/69	(100)	Handwashing	†					

*Wald test p value **adjusted for all other variables in model (n=120) +Odds ratio undefined due to 0 values.