Caught in the air

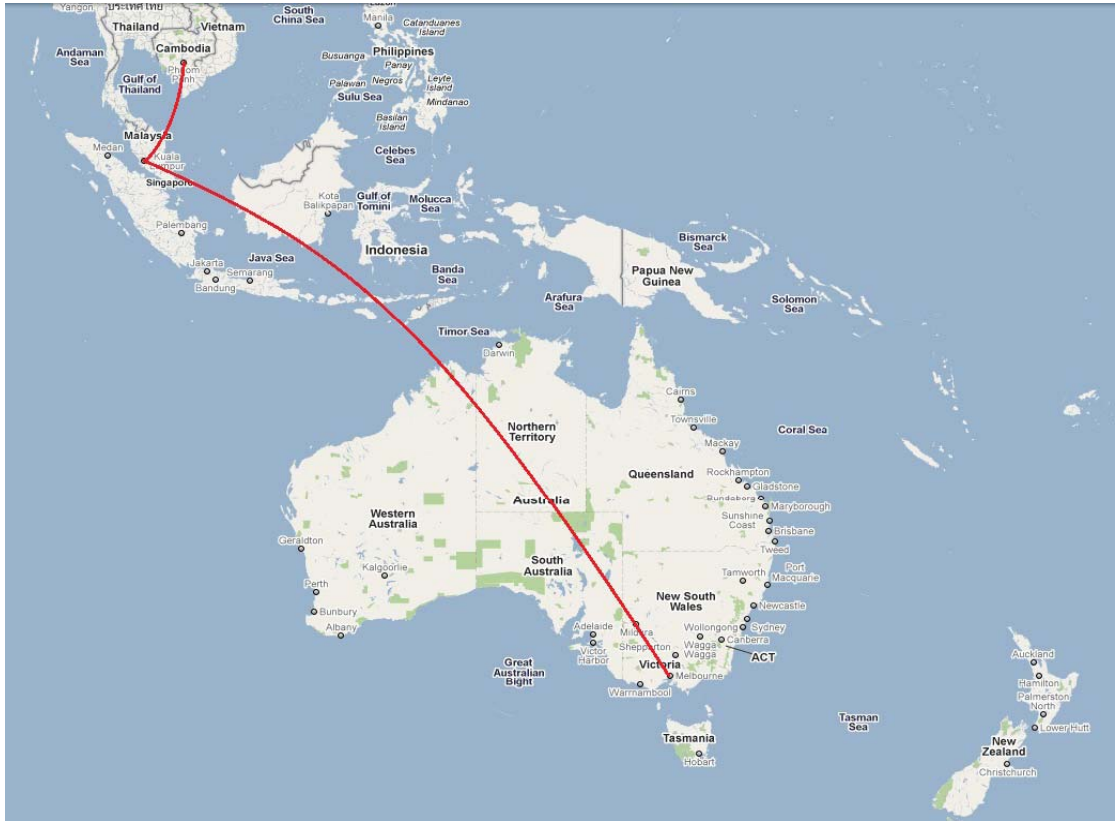
An April Fools' Tale

Jason Kwong

Austin Health

Case

- 47yo female
  - Return 2 weeks ago from Cambodia
    - Fever
    - Headache
    - Myalgia
    - Dry cough



Source: Google Maps

Past Medical History

- Post-operative pneumothorax
- Smoker

- Nil regular medications
- No known allergies

- Nurse

Further information

- Cambodia 14/3/11 – 1/4/11
  - Returned 2 weeks prior to presentation – well
  - Phnom Penh, Siem Riep, Sihanoukville beach
  - Travelled with husband
    - flu-like illness 1 week ago
  - Had not taken any malaria prophylaxis or received pre-travel vaccinations/advice

Progress

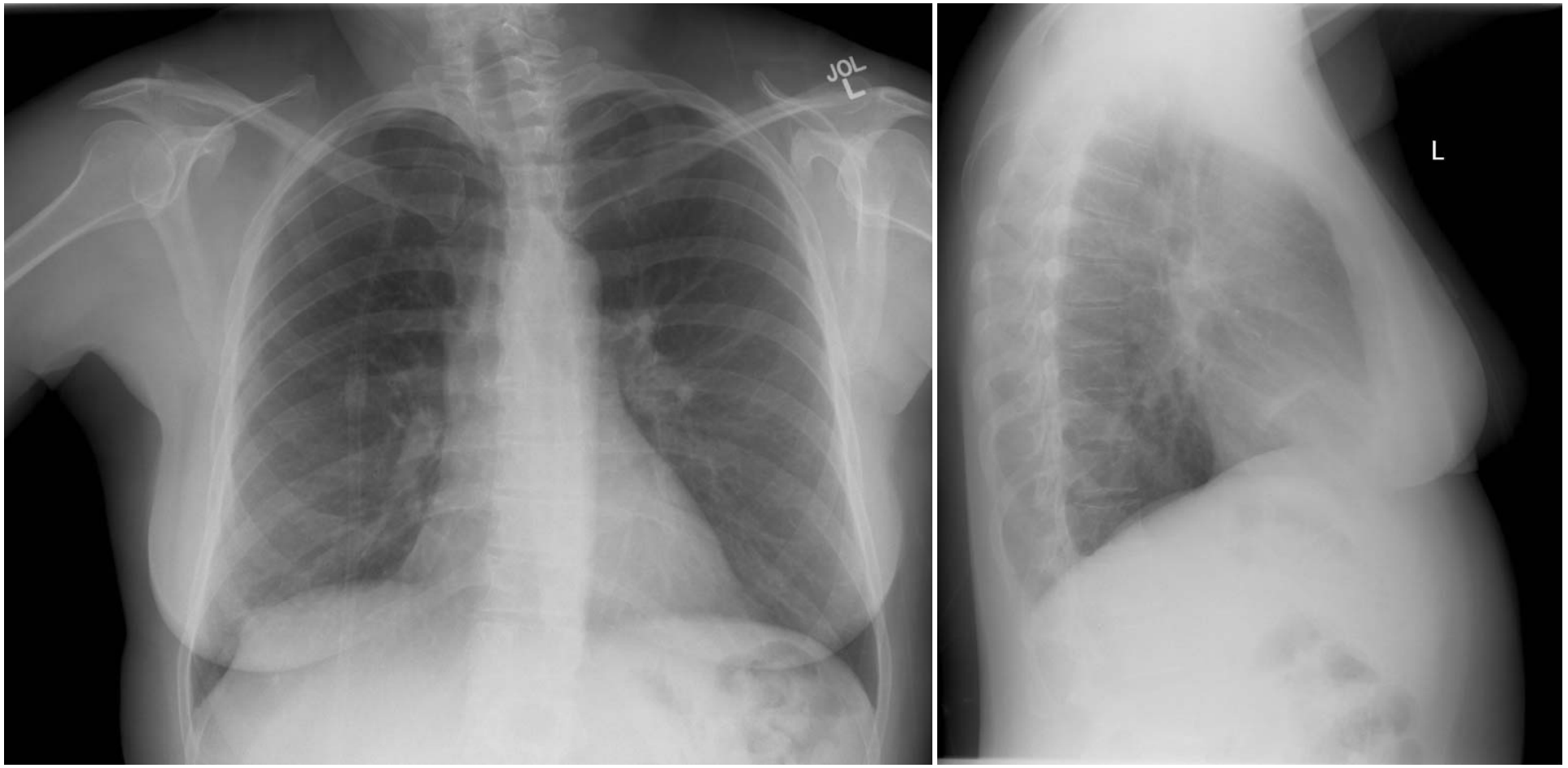
- 8 days following return “flu-like symptoms”
  - Dry cough, nil haemoptysis / SOB
  - Generalised myalgia
  - Frontal headache, nil meningism
  - Chills and sweats
- 11 days following return
  - LMO – clarithromycin
- 13 days following return
  - Austin ED

Examination

- Febrile **39.4**
- **RR 28**, 97% RA, **HR 100**, BP 130/80

- Mild throat erythema
- Blanching erythema on neck/shoulders?
- No lymphadenopathy
- Chest clear

CXR



Investigations

- FBE
  - Hb 131; WCC 5.5; Neut 4.7; **Lymph 0.5**; Plat 238
- normal electrolytes; Cr 71 (eGFR 77)
- LFT
  - Alb 35; BR 12; **ALP 253**; **ALT 313**; **GGT 223**
- **CRP 70**

Emergency Department

- “Respiratory tract infection”?
- “Viral illness”?
- “Infectious disease acquired in Cambodia”?

- Placed in single room
- 3 x sets Blood Cultures
- 2g IV ceftriaxone stat dose
- Referred to Infectious Diseases

Photos obtained and reproduced with patient's permission

Differential Diagnoses?

- Influenza / Resp viral infection
- Mycoplasma
- Rickettsial
- Leptospirosis
- Dengue

Detour ...

- Middle-aged Australian man
  - Recent travel to India
  - Returned via KL to Melbourne 1/4/11
  - Admitted to hospital
    - Fever
    - Dry cough
    - Maculopapular rash on face and upper body
  - No previous vaccinations due to mother's conscientious objection

Differential Diagnoses?

- Influenza / Resp viral infection
- Mycoplasma
- Rickettsial
- Leptospirosis
- Dengue

- ??? Measles ???

Management

- Moved to negative pressure room
- Nose & throat swab
- Serology
- Commenced on doxycycline 100mg bd

Our patient – Day 2

Photos obtained and reproduced with patient's permission

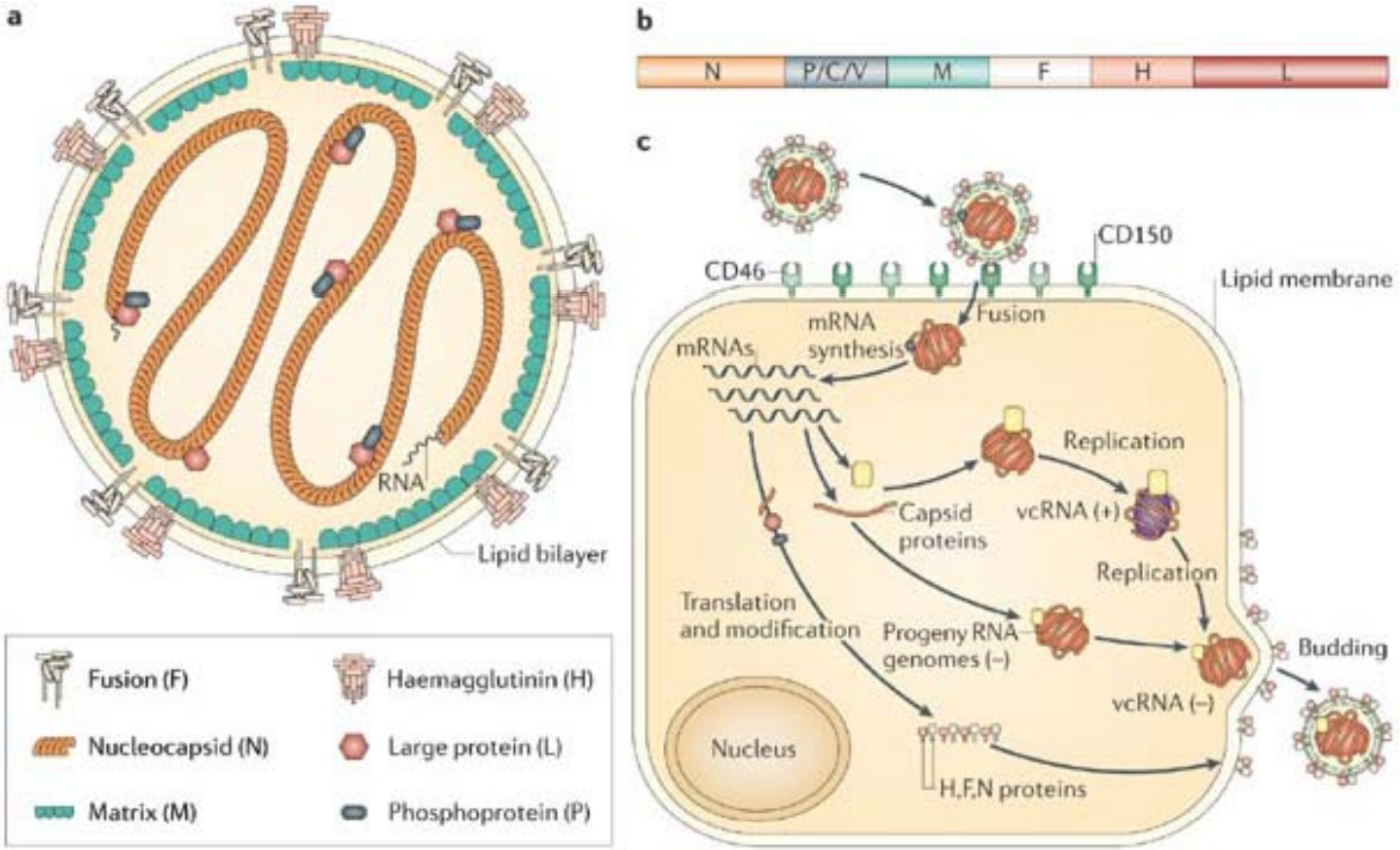
Progress

- Measles IgM positive (IgG –)
- Measles PCR positive
  - Nose / throat

- Inpatient for infective period
- Full recovery
- Returned to work

Measles

- Rubeola virus, genus Morbillivirus



Source: Nature Reviews – Microbiology 2006.

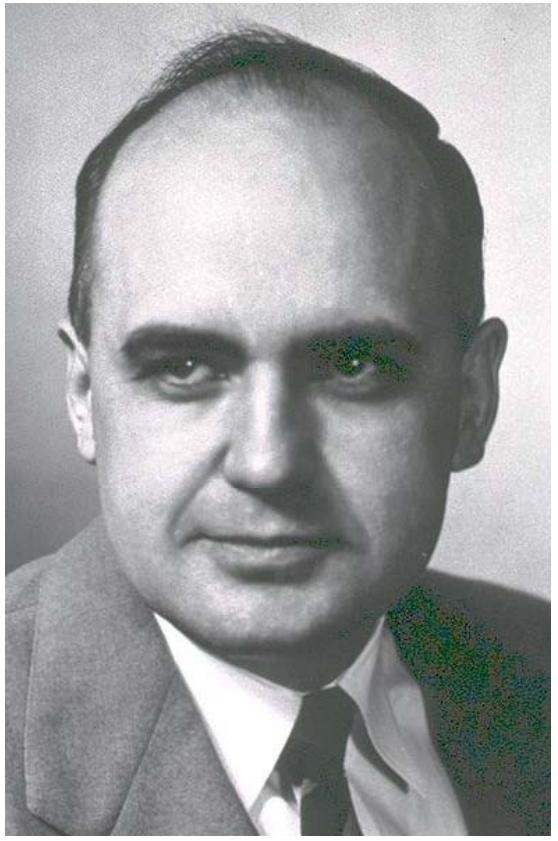
History of measles

- 2000 years of measles
  - Plague of Galen 165-180 AD
  - 1529 Cuban outbreak (two-thirds of native population)
  - 1875 Fiji (one-third population)

  - 1954 Peebles & Enders
    - Propagated wild measles virus in human tissue culture
  - 1963 measles vaccine developed

Source: Centres for Disease Prevention & Control

History of measles



- 2000 years of measles
  - 1971 Maurice Hilleman
    - MMR
  - 1969
    - Measles vaccine licensed in Australia
    - 1983 – Measles / Mumps
    - 1989 – Measles / Mumps / Rubella

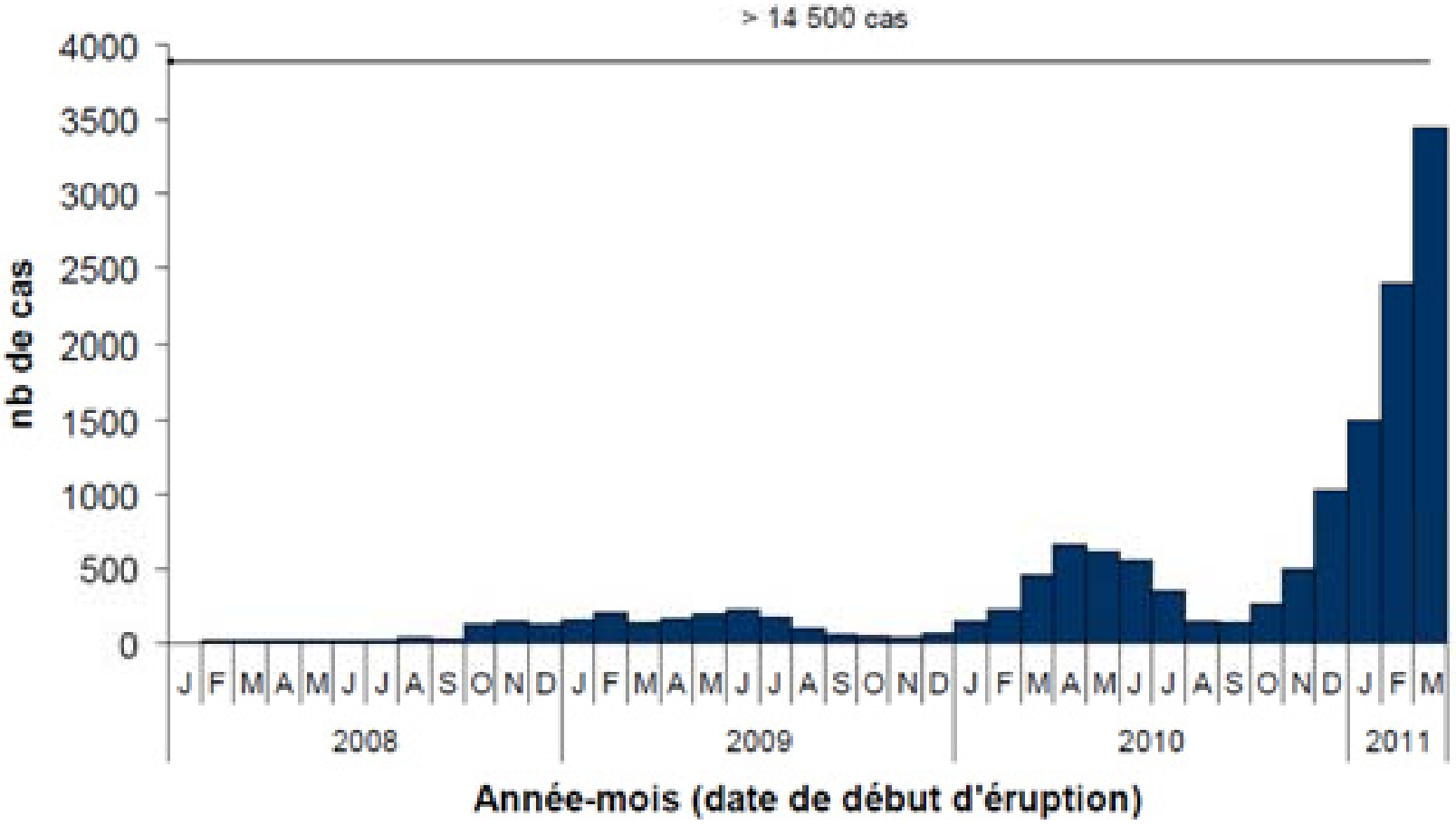
Source: Department of Health, Victoria

Global Impact

- 2000
  - 733 000 deaths worldwide
- 2008
  - 164 000 deaths worldwide
  - Estimated 22.7 million infants and children missed receiving vaccination

Source: World Health Organization

France notified cases 2008-2011



Source: European Center for Disease Prevention and Control 2011

Measles cases Jan-Mar 2011

- UK – 345
- Germany – 276
- Switzerland – 390
- Belgium – 231
- Spain – 786
- France – > 7500
  - 12 encephalitis; 1 myelitis
  - 360 cases severe pneumonia
  - 6 deaths

Source: European Center for Disease Prevention and Control 2011

Renewed commitment to measles and rubella elimination and prevention of congenital rubella syndrome in the WHO European Region by 2015

World Health Organization
REGIONAL OFFICE FOR Europe

Regional Committee for Europe
Sixtieth session

Moscow, 13–16 September 2010

Retraction—Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

Following the judgment of the UK General Medical Council's Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by Wakefield et al[1] are incorrect, contrary to the findings of an earlier investigation.[2] In particular, the claims in the original paper that children were "consecutively referred" and that investigations were "approved" by the local ethics committee have been proven to be false. Therefore we fully retract this paper from the published record.

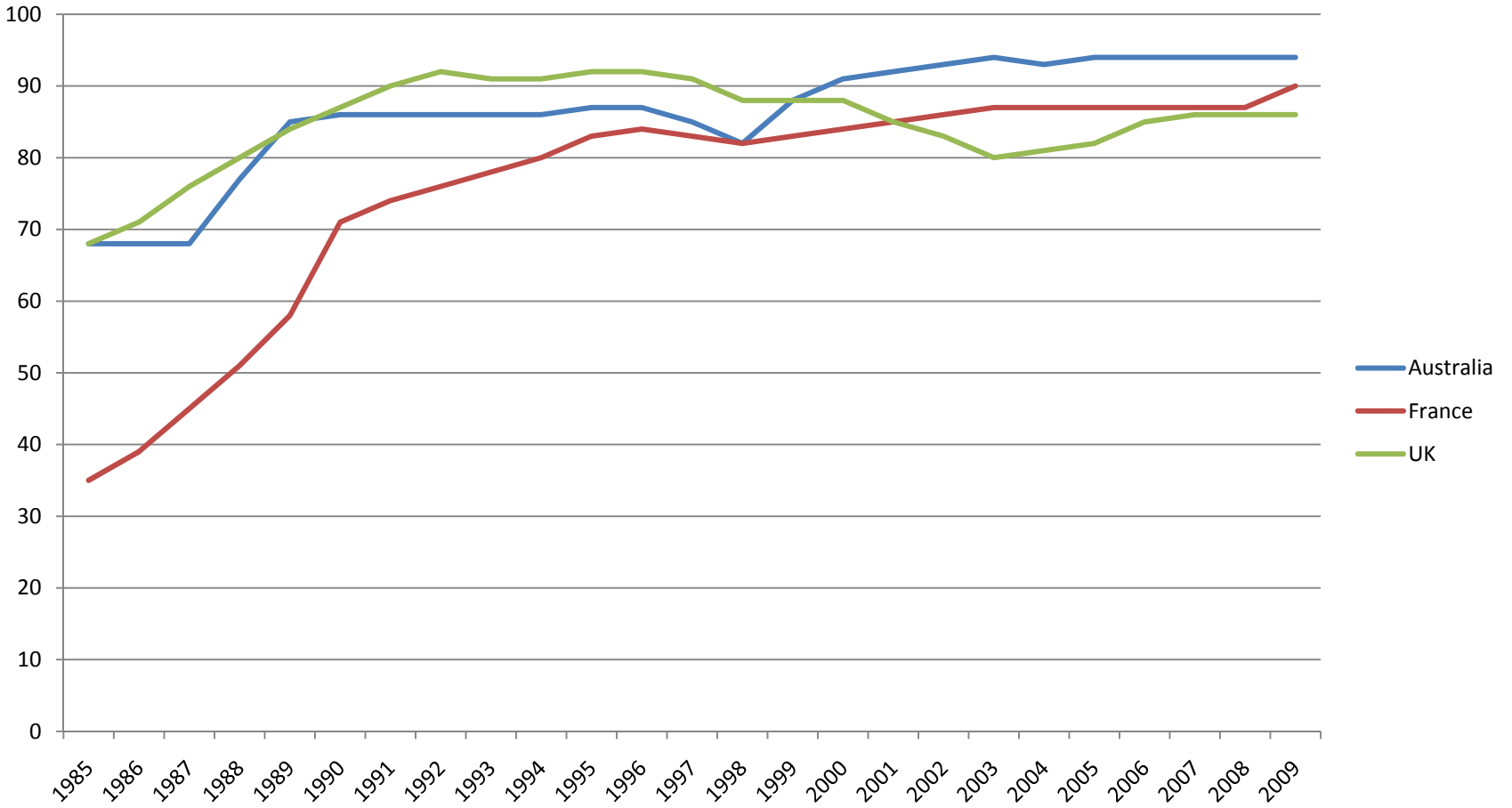
The Editors of The Lancet
The Lancet, London NW1 7BY, UK

1 Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; **351**: 637–41.

2 Hodgson H. A statement by The Royal Free and University College Medical School and The Royal Free Hampstead NHS Trust. *Lancet* 2004; **363**: 824.

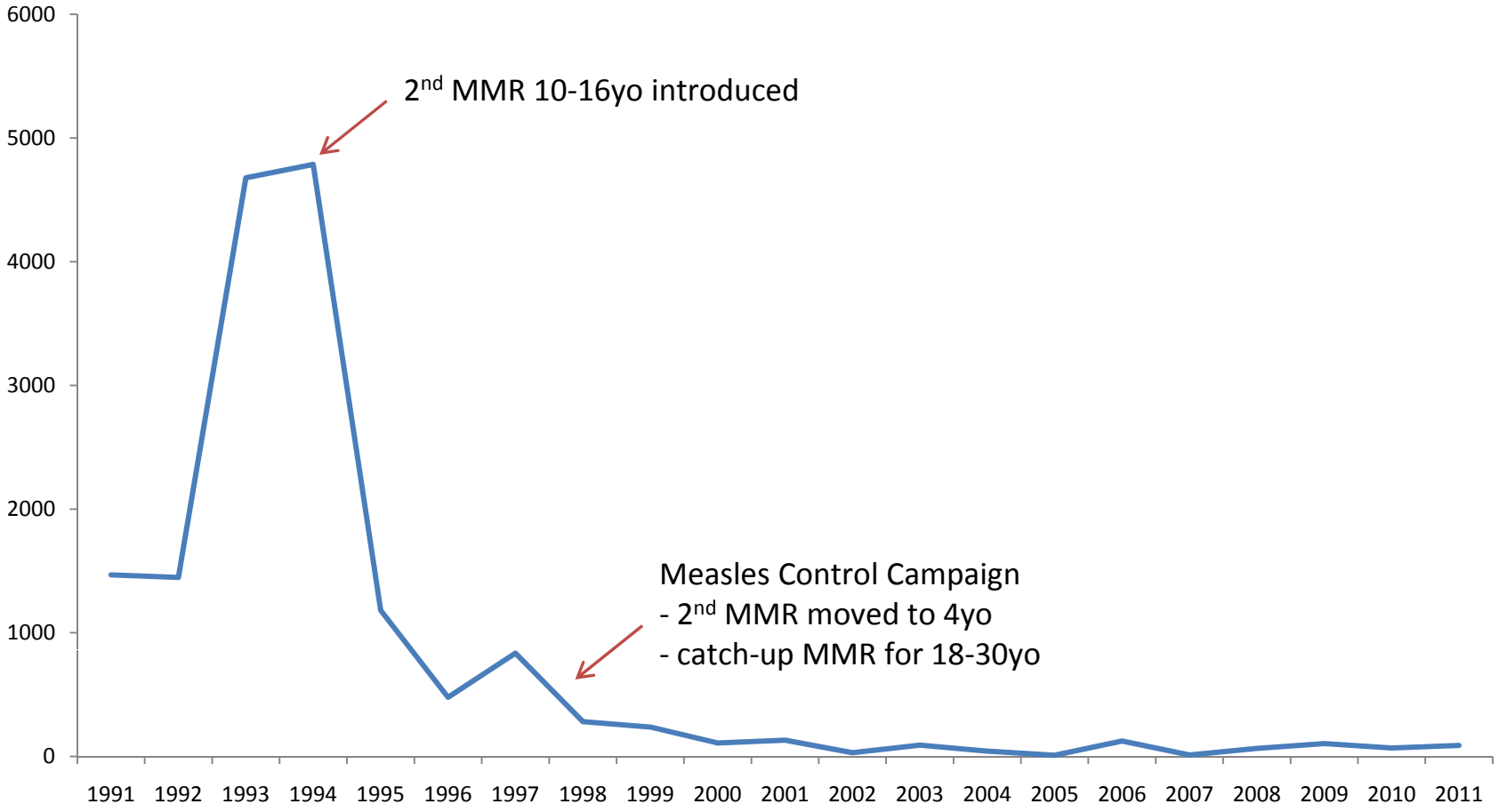
Published Online
February 2, 2010
DOI:10.1016/S0140-6736(10)60175-4

Measles vaccination rates



Source: WHO & UNICEF, 2011

Australia
Cases per year – 1991-2011



Source: National Notifiable Diseases Surveillance System, Dept of Health & Ageing

Clinical features

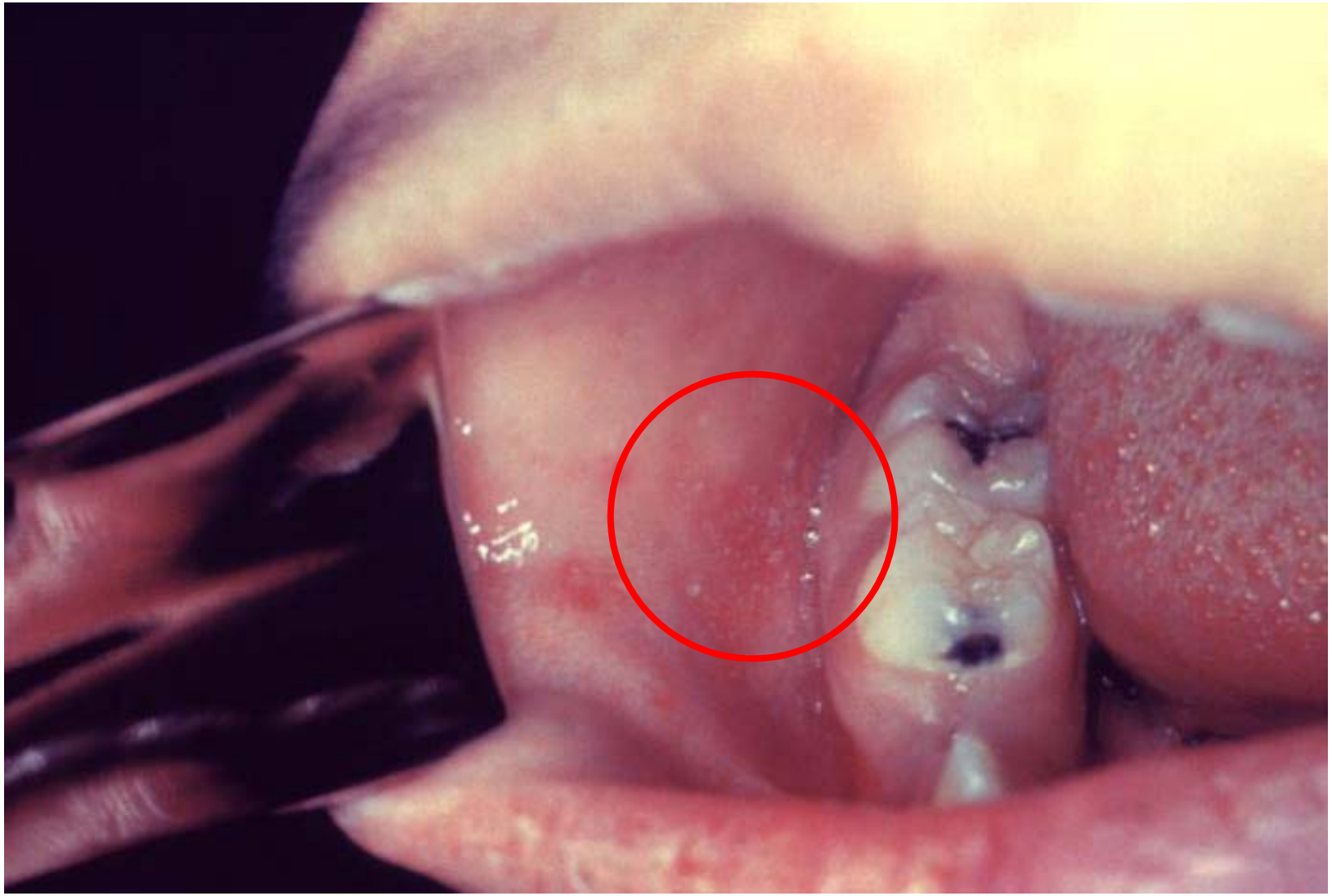
- Prodrome
  - Fever, malaise
  - Cough, coryza
  - Conjunctivitis
- Maculopapular rash

Source: Centres for Disease Prevention & Control

Rash

Source: Centres for Disease Control and Prevention

Koplik spots



Source: Centres for Disease Control and Prevention

Diagnosis

- Clinical
- Serology
  - Increase in total measles Ab titre in convalescent sample
  - ELISA specific IgM
- RT-PCR
  - Throat / nasal / urine / serum / NP aspirate
- Viral culture

Diagnosis

- Hong Kong cohort 2006-2009
  - Sensitivity of testing
  - 360 samples

Days after rash onset	IgM	NP Asp culture	Serum PCR	NP Asp PCR	Nose/Thr PCR	Urine PCR
0 – 3	91%	82%	81%	94%	100%	94%
4 – 7	99%	74%	78%	100%	100%	100%
> 7	100%		50%	N/A	100%	100%
Overall	**95%**	**80%**	**76%**	**96%**	**100%**	**97%**

Source: Woo et al. J Med Virol, 2010

Complications

- Respiratory tract
  - Pneumonia / ear infections
- Neurologic (1/1000)
  - Encephalitis
  - Acute disseminated encephalomyelitis (ADEM)
  - Subsclerosing panencephalitis (SSPE)
- Other
  - Hepatitis / gastroenteritis / stomatitis / diarrhoea
  - Myocarditis / pericarditis

Source: Centres for Disease Prevention & Control

Vaccination

- Combination vaccine
  - MMR (Priorix; also Trimovax, MMR II, Tresivac)
  - MMRV
- Live attenuated measles virus
  - Not transmissible after vaccination
- 95% seroconversion after single dose
  - >99% after 2 doses
  - “Long-term” immunity
  - Secondary failure rate <0.02%

Source:
Australian Immunisation Handbook, 2008.
“The Blue Book”, Department of Health, Victoria

Treatment

- Supportive
- Bacterial superinfection
- Vitamin A
  - Reduction in mortality in children
  - Recommended in developing countries where Vitamin A deficiency is prevalent
  - No trials in developed countries
- Ribavirin?
  - Case reports in severe pneumonitis; SSPE

Source: Centres for Disease Prevention & Control

Measles infectivity

- Highly infectious
- Basic reproduction rate (R_0)
  - Average number of people infected by single case
  - Measles R_0 = 10-15
    - Swine flu R_0 = 1.5
- Vaccine coverage required to prevent
  - $1 – (1/R_0)$
  - 90-93%

Source: Centres for Disease Prevention & Control

Australian Immunisation Register

State	Age Group	Number In State	DTP	POLIO	HIB	Hep B	MMR	Fully	% DTP	% polio	% HIB	% Hep B	% MMR
ACT	60-<63 Months	1,226	1,122	1,124	0	0	1,118	1,116	91.52	91.68	0	0	91.19
NSW	60-<63 Months	23,390	20,936	20,916	0	0	20,879	20,792	89.51	89.42	0	0	89.26
VIC	**60-<63 Months**	**17,458**	**15,970**	**15,974**	**0**	**0**	**15,931**	**15,878**	**91.48**	**91.5**	**0**	**0**	**91.25**
QLD	60-<63 Months	14,761	13,312	13,306	0	0	13,292	13,233	90.18	90.14	0	0	90.05
SA	60-<63 Months	4,584	4,021	4,019	0	0	4,004	3,993	87.72	87.67	0	0	87.35
WA	60-<63 Months	7,252	6,272	6,265	0	0	6,267	6,215	86.49	86.39	0	0	86.42
TAS	60-<63 Months	1,632	1,480	1,478	0	0	1,479	1,472	90.69	90.56	0	0	90.63
NT	60-<63 Months	860	759	758	0	0	756	752	88.26	88.14	0	0	87.91
AUS	**60-<63 Months**	**71,163**	**63,872**	**63,840**	**0**	**0**	**63,726**	**63,451**	**89.75**	**89.71**	**0**	**0**	**89.55**

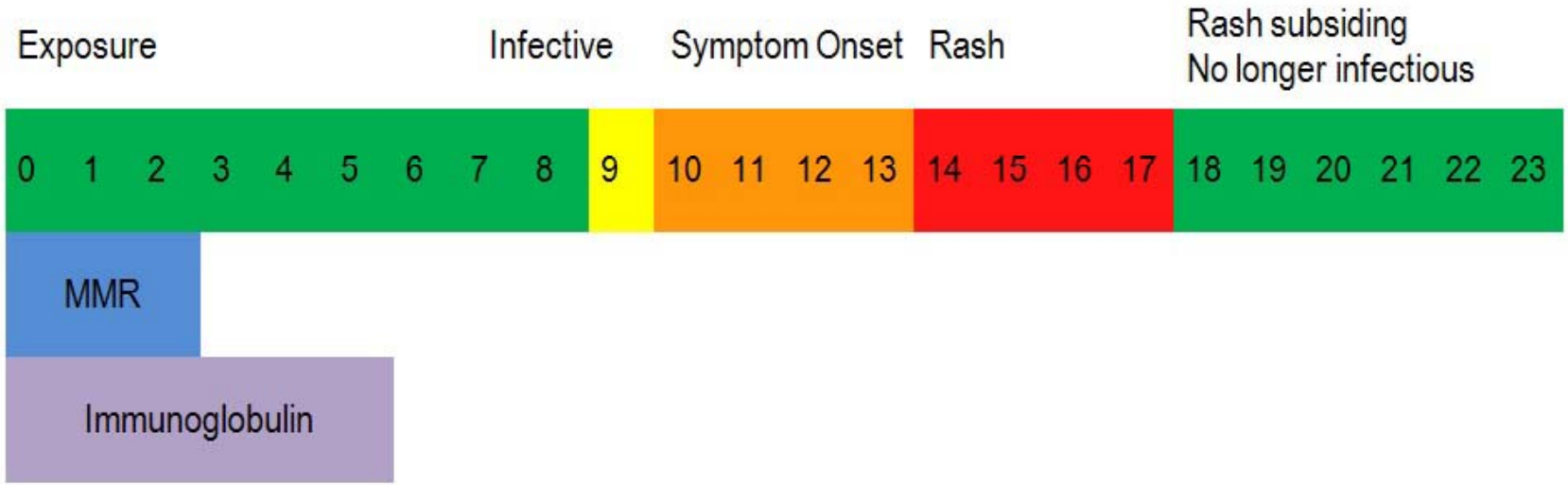
Source: Department of Health, Victoria

Infectivity

- Spread
  - Respiratory secretions
  - Aerosolised droplets
- Incubation period
  - Approx 10 days (7-18)
- Infectivity period
  - Beginning of prodrome
  - Up to 4 days after appearance of rash

Source: Department of Health, Victoria

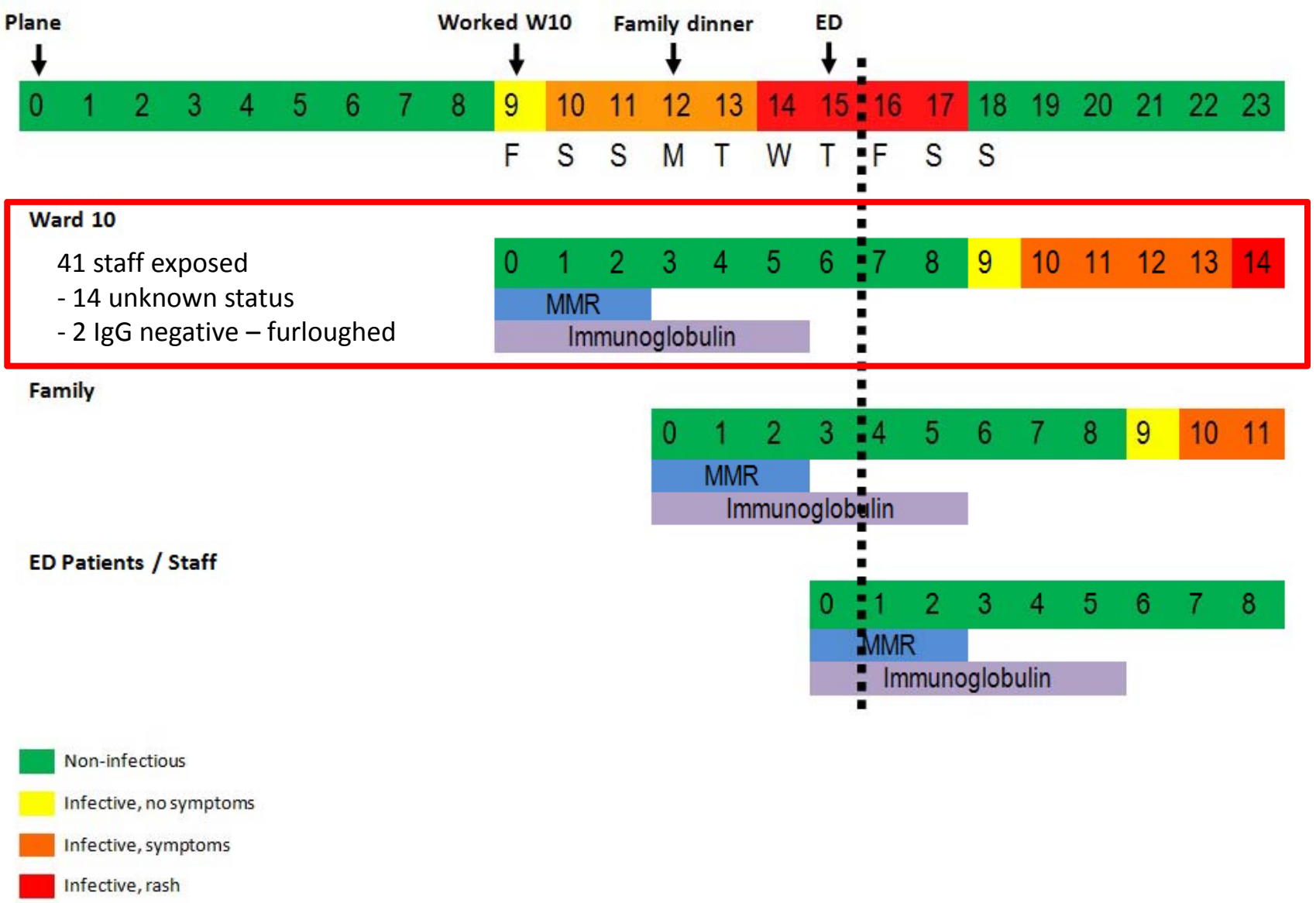
Timeline

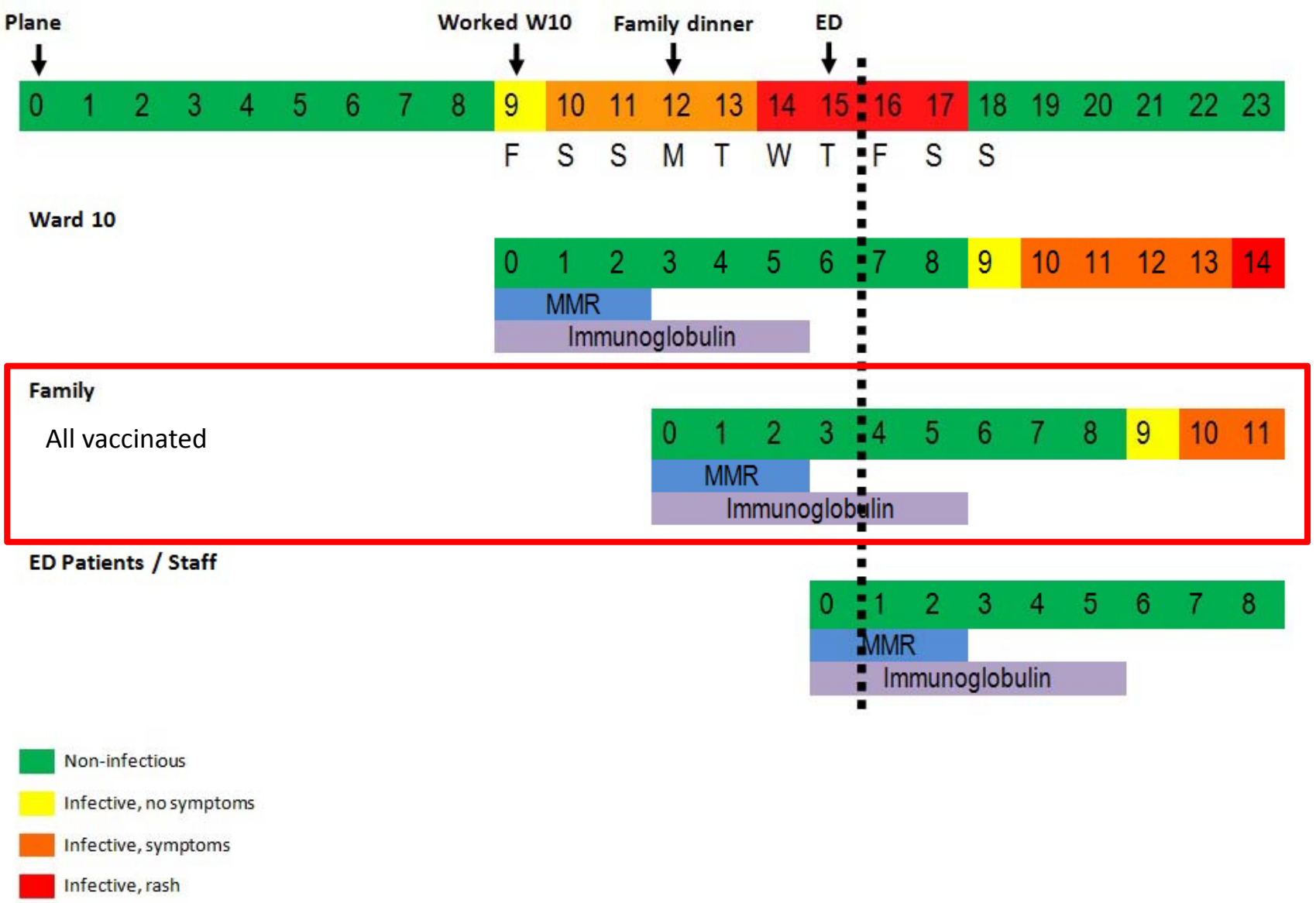

Exposure
Infective
Symptom Onset
Rash
Rash subsiding
No longer infectious
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
MMR
Immunoglobulin

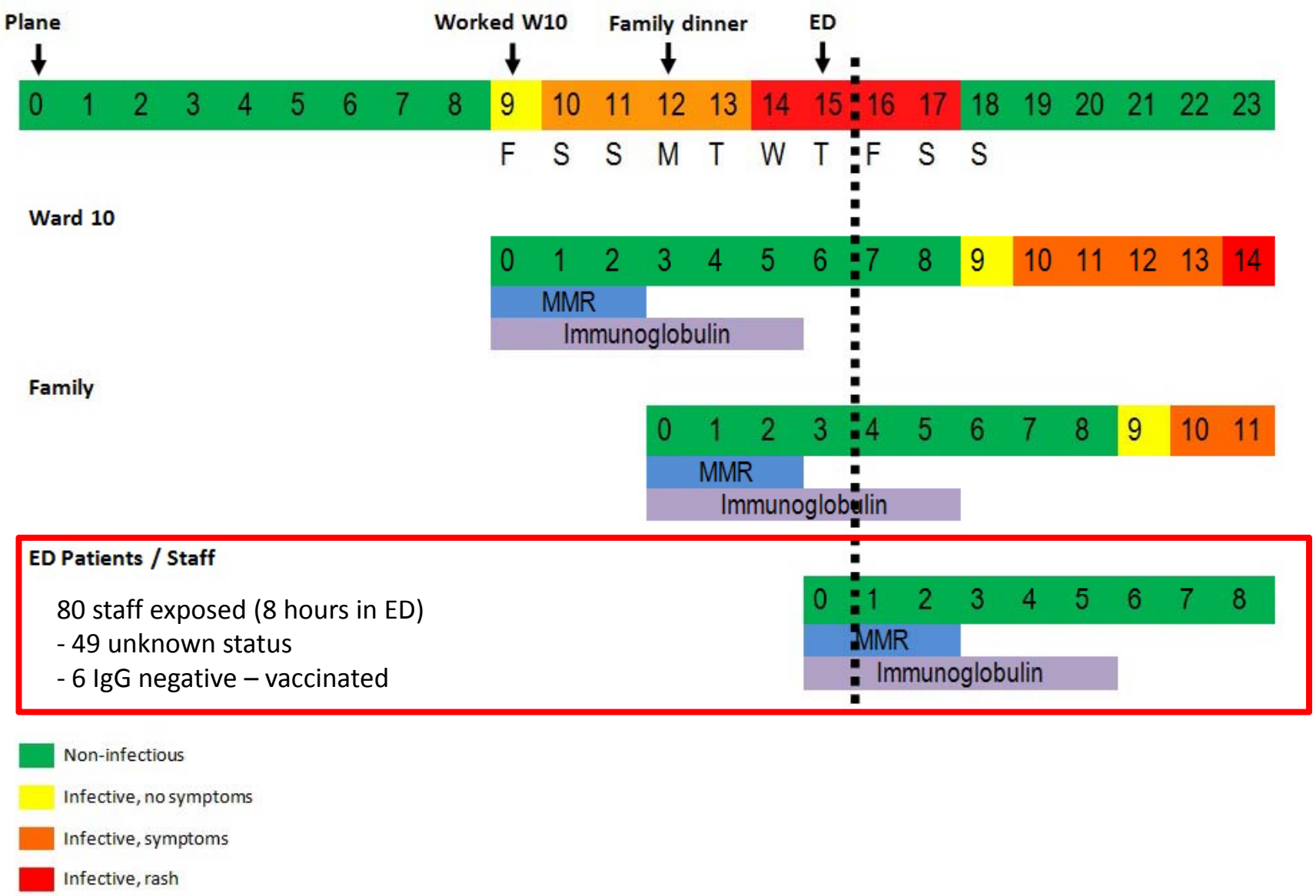
Infection Control Procedures

- Negative pressure isolation
- Identification of susceptible contacts
- Protection of susceptible contacts
  - Vaccination if within 72 hours of contact
  - Immunoglobulin if >72 hours, within 6-7 days
    - 0.2mL/kg IM (max 15 mL)
    - MMR three months later
  - Immunoglobulin if unable to have MMR

Source: Department of Health, Victoria


Plane
Worked W10
Family dinner
ED
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
F S S M T W T F S S
Ward 10
41 staff exposed
- 14 unknown status
- 2 IgG negative – furloughed
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
MMR
Immunoglobulin
Family
0 1 2 3 4 5 6 7 8 9 10 11
MMR
Immunoglobulin
ED Patients / Staff
0 1 2 3 4 5 6 7 8
MMR
Immunoglobulin
Non-infectious
Infective, no symptoms
Infective, symptoms
Infective, rash


Plane
Worked W10
Family dinner
ED
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
F S S M T W T F S S
Ward 10
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
MMR
Immunoglobulin
Family
All vaccinated
0 1 2 3 4 5 6 7 8 9 10 11
MMR
Immunoglobulin
ED Patients / Staff
0 1 2 3 4 5 6 7 8
MMR
Immunoglobulin
Non-infectious
Infective, no symptoms
Infective, symptoms
Infective, rash


Plane
Worked W10
Family dinner
ED
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
F S S M T W T F S S
Ward 10
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
MMR
Immunoglobulin
Family
0 1 2 3 4 5 6 7 8 9 10 11
MMR
Immunoglobulin
ED Patients / Staff
80 staff exposed (8 hours in ED)
- 49 unknown status
- 6 IgG negative – vaccinated
0 1 2 3 4 5 6 7 8
MMR
Immunoglobulin
Non-infectious
Infective, no symptoms
Infective, symptoms
Infective, rash

Other contacts

- Non-Austin staff eg. Ambulance personnel
- 108 Patients exposed in ED
  - Visitors

- 102 staff / patients / visitors returned for follow-up
  - 70 vaccinated
  - 13 given NHIG

Efficacy of post-exposure prophylaxis

- NHIG
  - Endo et al. J Pediatrics, 2001
    - Immunocompetent unvaccinated exposed children
    - Variable depending on measles Ab titre
      - 43% efficacy if low titres < 16 IU/mL
      - 100% efficacy if titres > 40 IU/mL

Source: Endo et al. J Pediatrics, 2001

Efficacy of post-exposure prophylaxis

- Vaccine
  - Barrabeig et al. Pediatr Infect Dis J, 2011
  - 54 exposed unvaccinated children who received PEP vaccine
    - 91% vaccine effectiveness if < 72 hours

Source: Barrabeig et al. Pediatr Infect Dis J, 2011

Efficacy of post-exposure prophylaxis

- NSW outbreak 2006
  - MMR 100% effective
  - NHIG 75% effective

	Contacts identified	Secondary cases identified	Rate (per 1000)
MMR	82	0	0
NHIG	183	2	10.9
Refused	93	3	32.3
Too late	195	10	51.3
Total	553	15	27.1

MMR: measles-mumps-rubella vaccine.
NHIG: normal human immunoglobulin.

Source: Sheppeard et al. NSW Public Health Bulletin, 2009

Measles contact tracing

- Born before 1966 – assumed immunity
- Born during or after 1966
  - 2 doses of MMR – assumed immunity
  - 1 dose of MMR / unsure
    - Vaccination
    - Serology
  - Not vaccinated – vaccination

Source: Department of Health, Victoria

Infect Control Hosp Epidemiol 2010

Seroprevalence of Measles Antibodies among High-Risk Healthcare Workers in Auckland, New Zealand: Additional Justification for Assumption of Age-Determined Immunity Based on Local Data

Deborah Williamson, MD; Joshua Freeman, MD; Paul Austin; Caroline Allum, MD; Sally Roberts, MD

NZ seroprevalence in HCW

- Search through pre-employment screening tests
  - 2527 born after 1969
    - 335 (13%) no immunity
  - 912 born before 1969
    - 19 (2%) no immunity
  - Overall 10% had no immunity

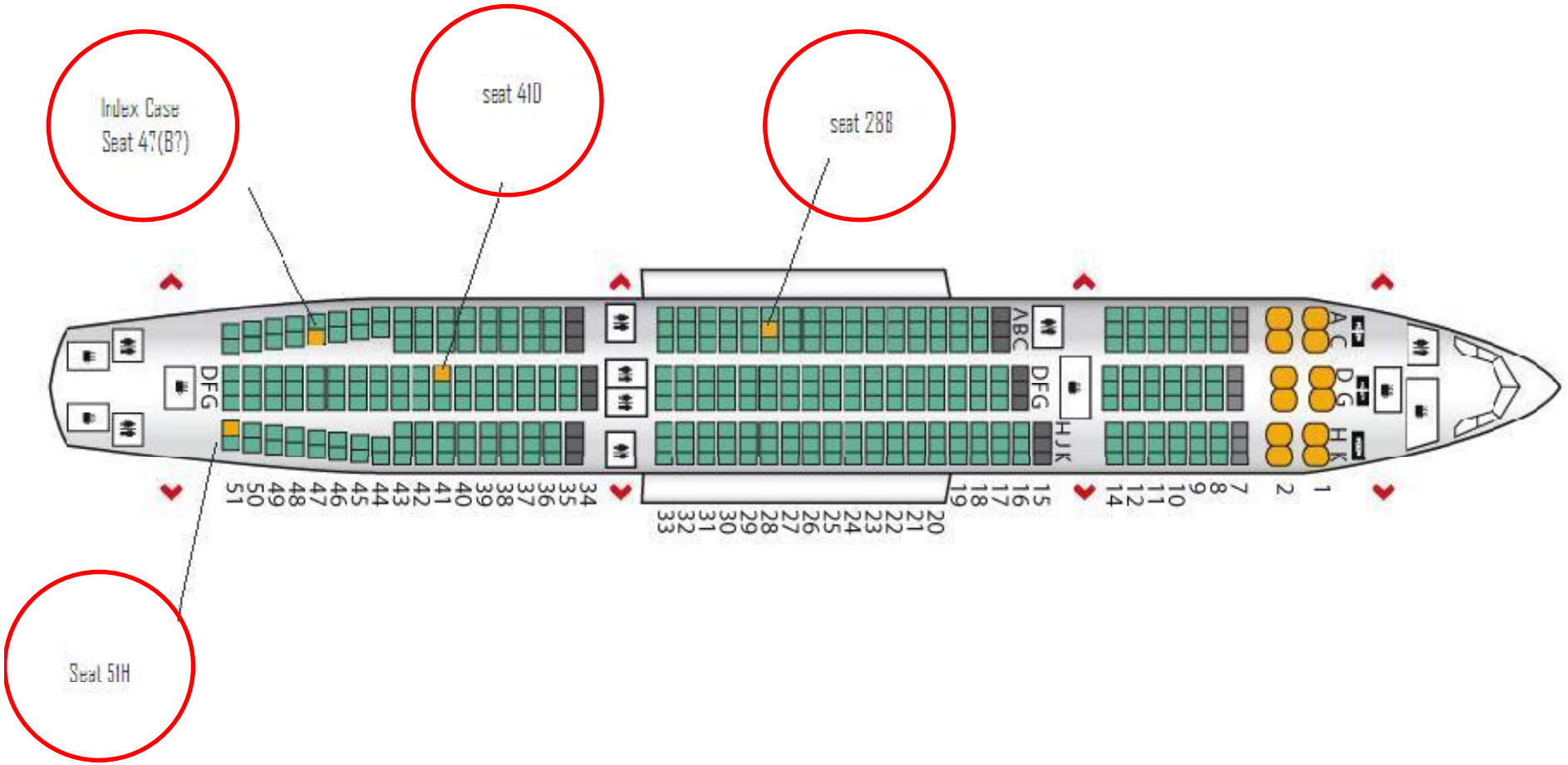
HCW vaccination

- Vaccination *recommended* for all HCW
  - DHS guidelines
- Austin Health
  - Information regarding screening and pathology request form for all new staff
  - Responsibility of individual HCW
    - Know status
    - Request vaccination
  - No staff database

Back to the case …

- Initial exposure
  - Sister of “Plane Index Case”
    - Plane Index Case (seat 47B)
    - Sister in Australia

Seating plan



Source: Victorian Department of Health, 2011

Department of Health Role

- Screening of plane contacts
  - Previously 2 rows in front, 2 rows behind

- ? needs adjusting
- ? notification to hospitals

The follow-up

- 6 cases in Melbourne linked
  - 4 patients admitted to hospital for measles in Melbourne
  - 1 admitted to hospital in Tasmania
- 2 patients diagnosed in Auckland after departing Melbourne airport
  - 5 further cases in Auckland

Cost of measles outbreak

- Arizona 2008
  - 14 linked cases
  - Approx $800,000
- Iowa 2004
  - Index case + 2 secondary cases
  - Total estimated cost $142,000

CSIRO PUBLISHING
www.publish.csiro.au/journals/hi
Research
Healthcare Infection, 2010, **15**, 43–46

The costs of containing measles within a health care service

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- 12 cases
- 365 staff exposed
  - 68 required vaccination (19%)
  - None furloughed
- At least $10,300 (underestimate)

Cost

Phone calls	$600
Blood tests @ $10/test	$1800
MMR vaccines @ $20/vaccine	$1500
Immunoglobulin	$1000
Miscellaneous consumables	$1200
Extra staffing / overtime / furloughed	$10000
Inpatient stay	$2400
TOTAL	$18,500
Each individual vaccinated (herd immunity)	Priceless

Take home messages / comments

- Consider measles in the returned traveller
- Cost of measles outbreak is significant
  - Prevention much easier/more effective than follow-up
- Public vaccination rates are marginally above required rate for herd immunity

- Staff screening / surveillance programs?
- Hospital notification?

“What a fool does in the end, the wise do in the beginning”

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- Rhea Martin, Donna Cameron (Austin Infection Control)
- Hana Wellington, Pascal Gelperowicz (Austin Health)

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http://www9.health.gov.au/cda/Source/CDA-index.cfm

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http://www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-home

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http://www.health.vic.gov.au/ideas/bluebook

World Health Organization (WHO)
http://www.who.int/en/