

兒童常見的病毒性腸胃炎



臺中榮民總醫院兒童醫學部兒童感染科

陳伯彥



兒童健康繼續教育講座

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講座時間 108年7月13日(星期六) 13:20 - 17:20

講座地點 金門縣衛生行政大樓3樓 (金門縣金湖鎮新市里中正路1-1號)

時間	項目	講者	主持人
13:20-13:50	報到		
13:50-14:00	貴賓致詞	金門縣衛生局王漢志局長 衛生福利部金門醫院屠乃方院長	
14:00-14:40	麻疹與德國麻疹的防治	長庚醫療財團法人林口長庚醫院兒童內科部感染科 陳志榮醫師	金門縣衛生局 王漢志局長
14:40-14:45	討論		
14:45-15:25	兒童的病毒性腸胃炎	臺中榮民總醫院兒童醫學部 陳伯彥醫師	
15:25-15:30	討論		
15:30-15:50	休息		
15:50-16:30	流感的防治	長庚醫療財團法人林口長庚醫院兒童健康研究部 黃玉成醫師	衛生福利部金門醫院 屠乃方院長
16:30-16:35	討論		
16:35-17:15	人類乳突病毒疫苗的保護效果與安全性	國立臺灣大學醫學院附設醫院兒童醫院 李秉穎醫師	
17:15-17:20	討論		

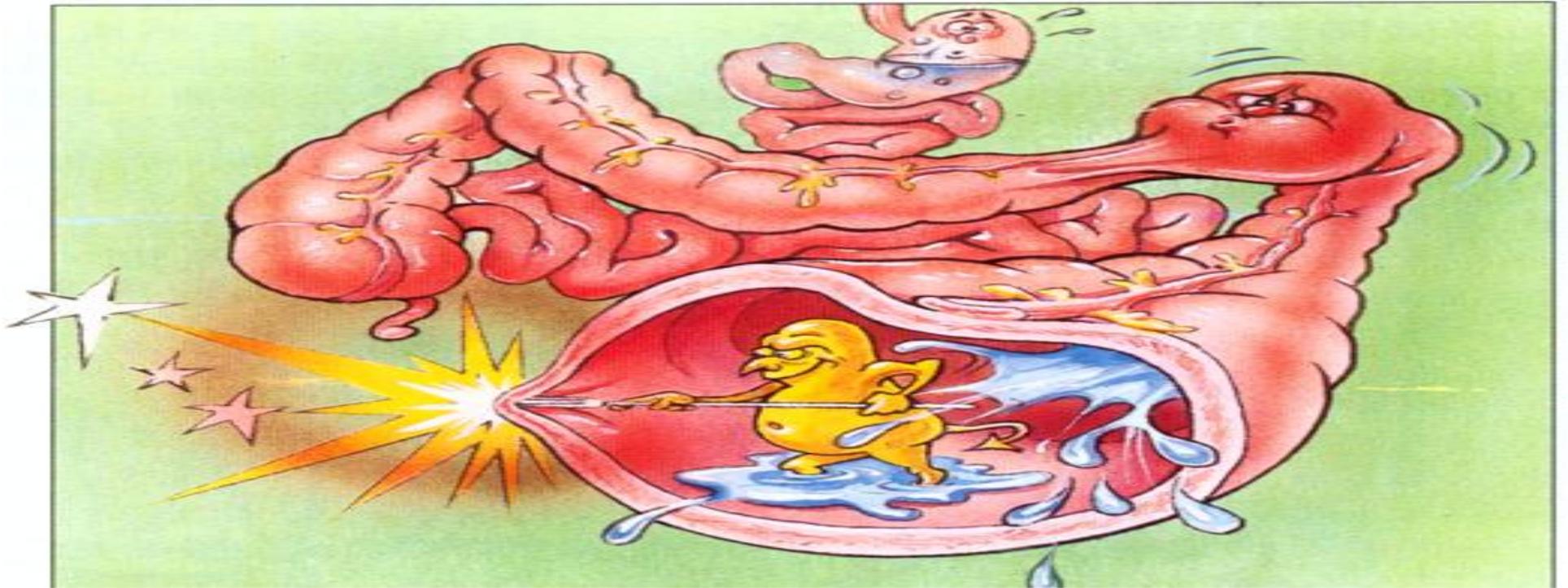
※經費來自菸品健康福利捐

※本講座繼續教育積分認定：臺灣兒科醫學會2學分、台灣新生兒科醫學會1學分、中華民國醫師公會全國聯合會3.2學分、中華民國護理師護士公會全國聯合會3.2學分、公務人員終身學習時數

急性腸胃炎與腹瀉

怎麼回事？

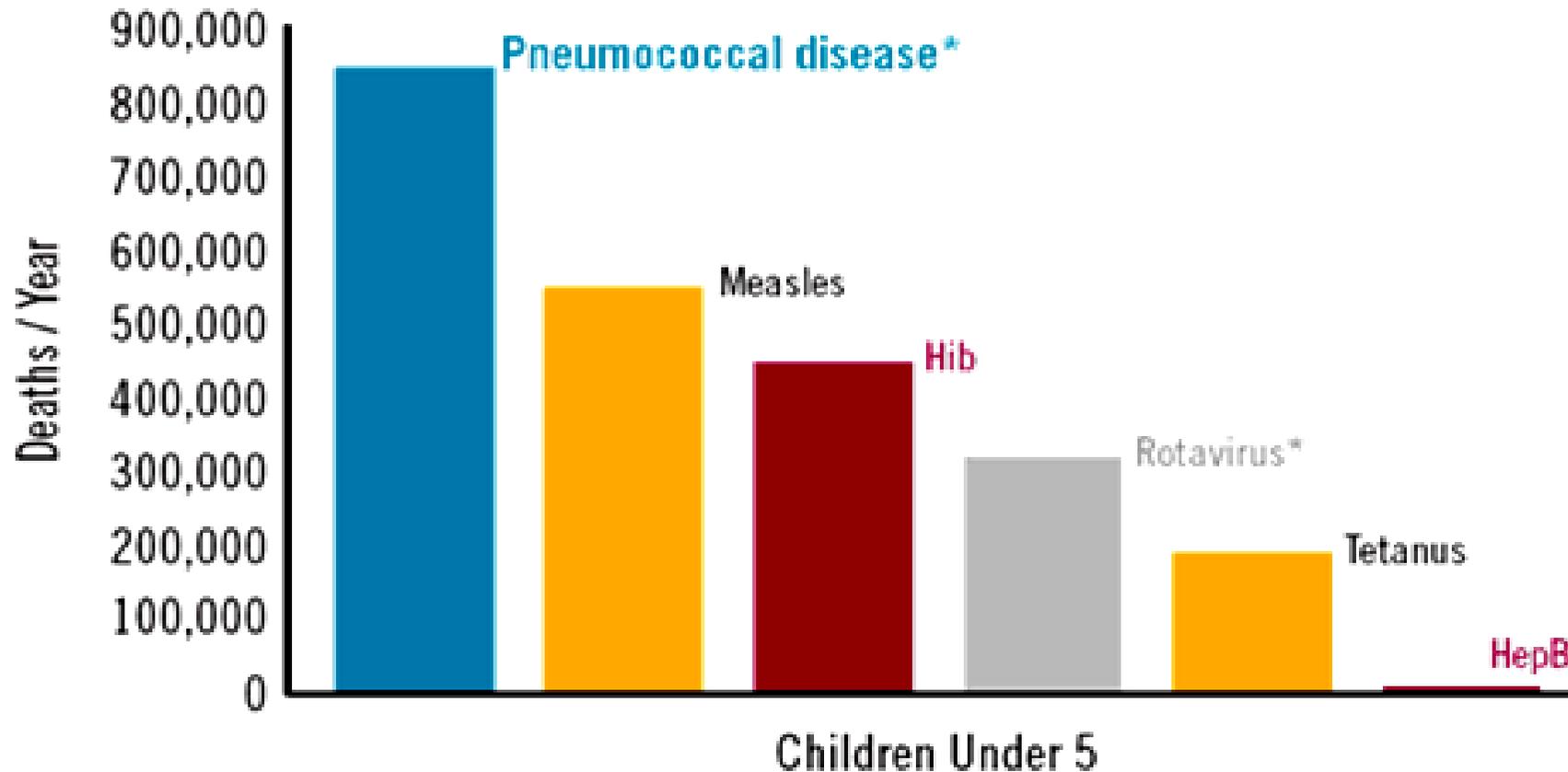
當嘔吐或是腹瀉發生時，身體事實上是試著要從消化道的兩端開口將有害的**病毒**及**細菌**寄生蟲等迅速的排出。然而，**消化不良**也可能只是因為旅途不適、**藥物**或是**吃得太多**、**太興奮**的一種反應而已。在嚴重的情形下，身體會喪失過多的水分而導致脫水的現象。





五歲以下幼童疫苗可預防傳染病

The leading cause of vaccine-preventable child[†] deaths



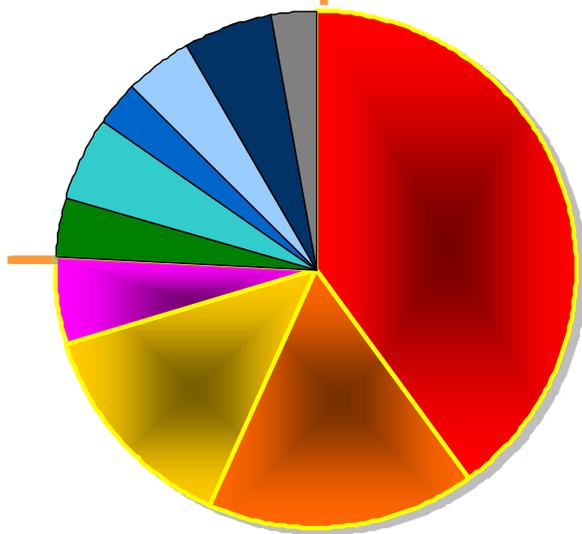
[†] Children < 5 years of age. * Provisional estimates.

WHO official mortality rates. Available at www.preventpneumo.org/diseases_vaccines/ (accessed Jan 2008).

不同國家地區腸道病原的比例

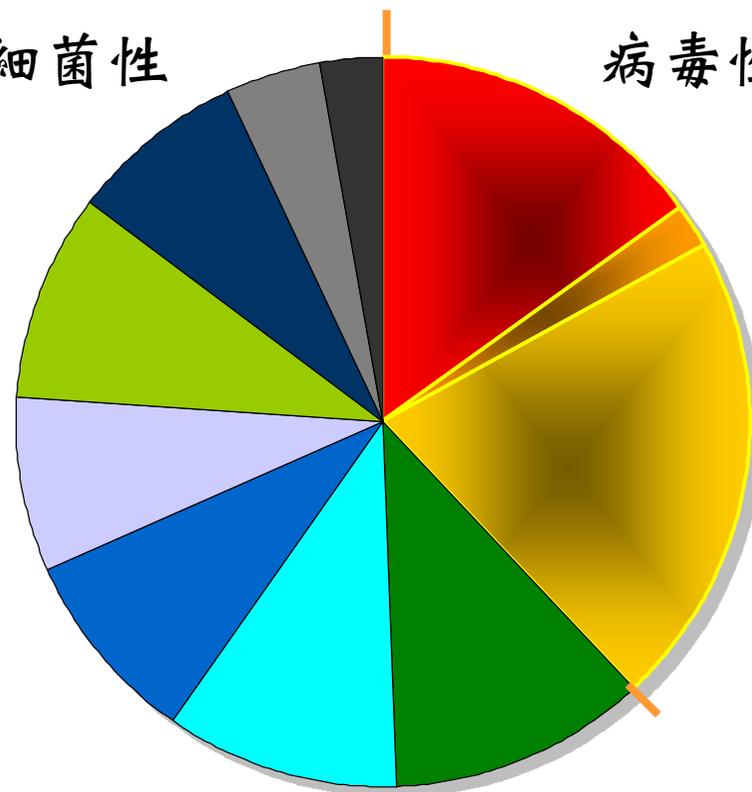
- RotaV
- Ead
- Norwalk
- Other V.
- ETEC
- Campylobacter
- Shigella
- Salmonella
- Vibrio
- Giardia
- Crypopordium
- E. histolytica

細菌性 病毒性



已開發國家(歐美)

細菌性 病毒性



開發中國家(亞非洲)



感染性腹瀉病原特性與危險因子

Pathogens Causing Diarrhea and Associated Risk Factors

Viruses		
Rotavirus	No	Person to person transmission, especially daycare centers
Norovirus	No	Person to person transmission Seafood or shellfish
Adenovirus	No	Immunocompromised
Cytomegalovirus	No	Immunocompromised Organ transplantation

排廢水的潛在風險

Dangers Of Sewage Damage



Negative Effects of Raw Sewage

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Key Notes

- On average, 7 million people suffer from illnesses caused by exposure to raw sewage per year.
- 7% of those 7 million become severely or fatally ill.

Viruses

Norwalk virus, rotavirus, Hepatitis A, Poliomyelitis Virus, Adenovirus

Gastroenteritis

Diarrhea, Vomitting, Abdominal Pain, Nausea, Cramping

Hepatitis A

Jaundice, Fever, Diarrhea, Fatigue, Cramping, Loss of Appetite, Nausea

Poliomyelitis

Sore Throat, Fever, Vomitting, Nausea, Cramping, Constipation, Diarrhea

Bacteria

Campylobacter, E. coli, Leptospria Salmonella, Shigella

Campylobacteriosis

Bloody Diarrhea, Fever, Cramping, Nausea, Vomitting

Escherichia coli (E. coli)

Bloody Diarrhea, Fever, Cramping, Nausea, Vomitting

Leptospirosis

Fever, Headaches, Body Aches, Chills, Diarrhea, Vomitting, Jaundice, Rash

Salmonellosis

Diarrhea, Fever, Cramping

Shigellosis (Bacillary Dysentery)

Bloody Diarrhea, Fever, Cramping

Parasites

Cryptosporidium parvum Giardia intestinalis

Cryptosporidiosis

Diarrhea, Loose Stool, Cramping, Slight Fever

Giardiasis

Diarrhea, Loose Stool, Cramping, Slight Fever



For more information on the dangers of sewage damage or to request sewage damage or biohazard cleanup, visit

www.si-restoration.com

溫度與食物安全

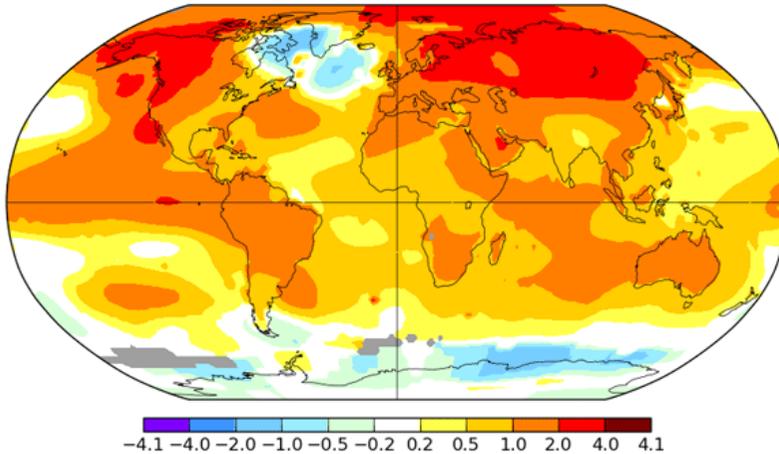
Temperature and food safety



Annual J-D 2015

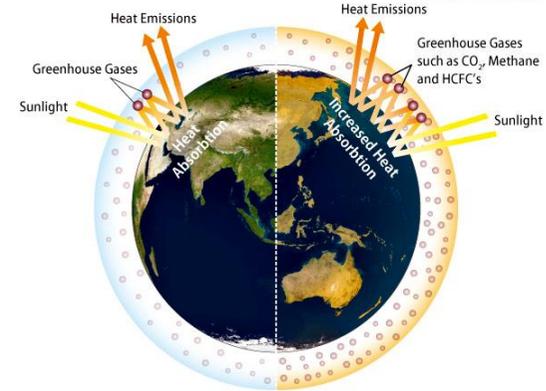
L-OTI (°C) Anomaly vs 1951-1980

0.85

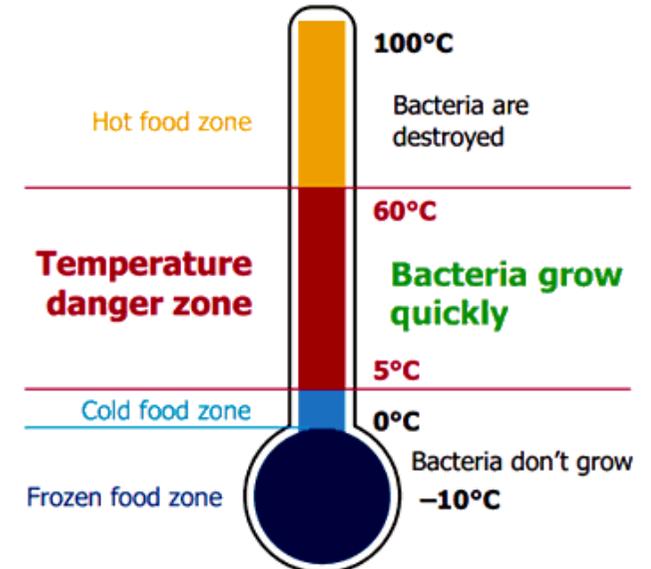


The Earth

The Earth with Increased Greenhouse Gases

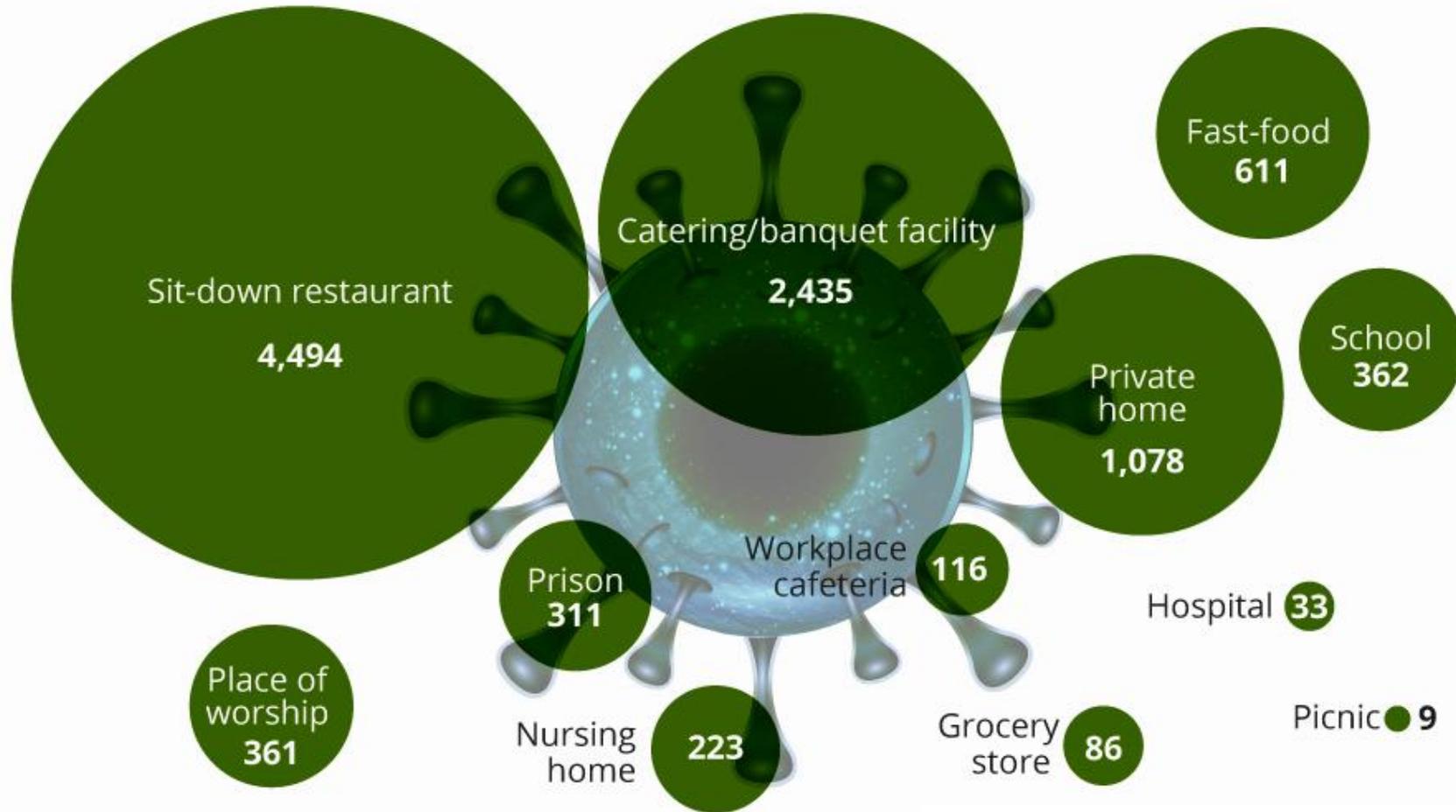


- The temperature danger zone is between 5°C and 60°C, when it is easiest for harmful bacteria to grow in food
- Minimise the time that food spends at these temperatures in order to keep food safe
- Refrigerated food needs to be kept at 5°C or below
- Hot food needs to be kept at 60°C or above



Where Food Preparation Leads To Food Poisoning

Number of illnesses from foodborne disease outbreaks in selected U.S. locations*

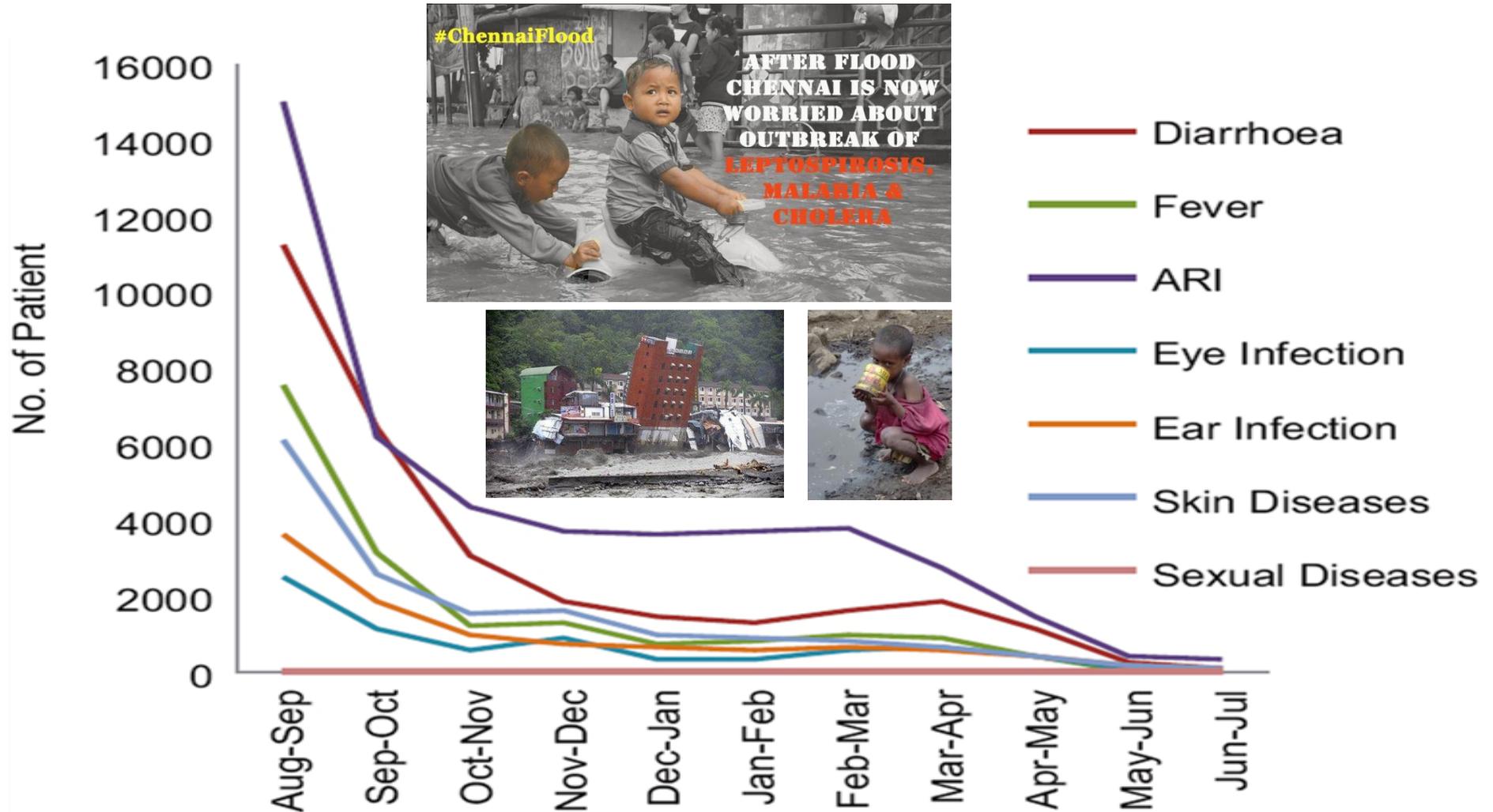


*Reported number of cases in 2013
Source: CDC

食物中毒場所

水災後可能突增的感染症

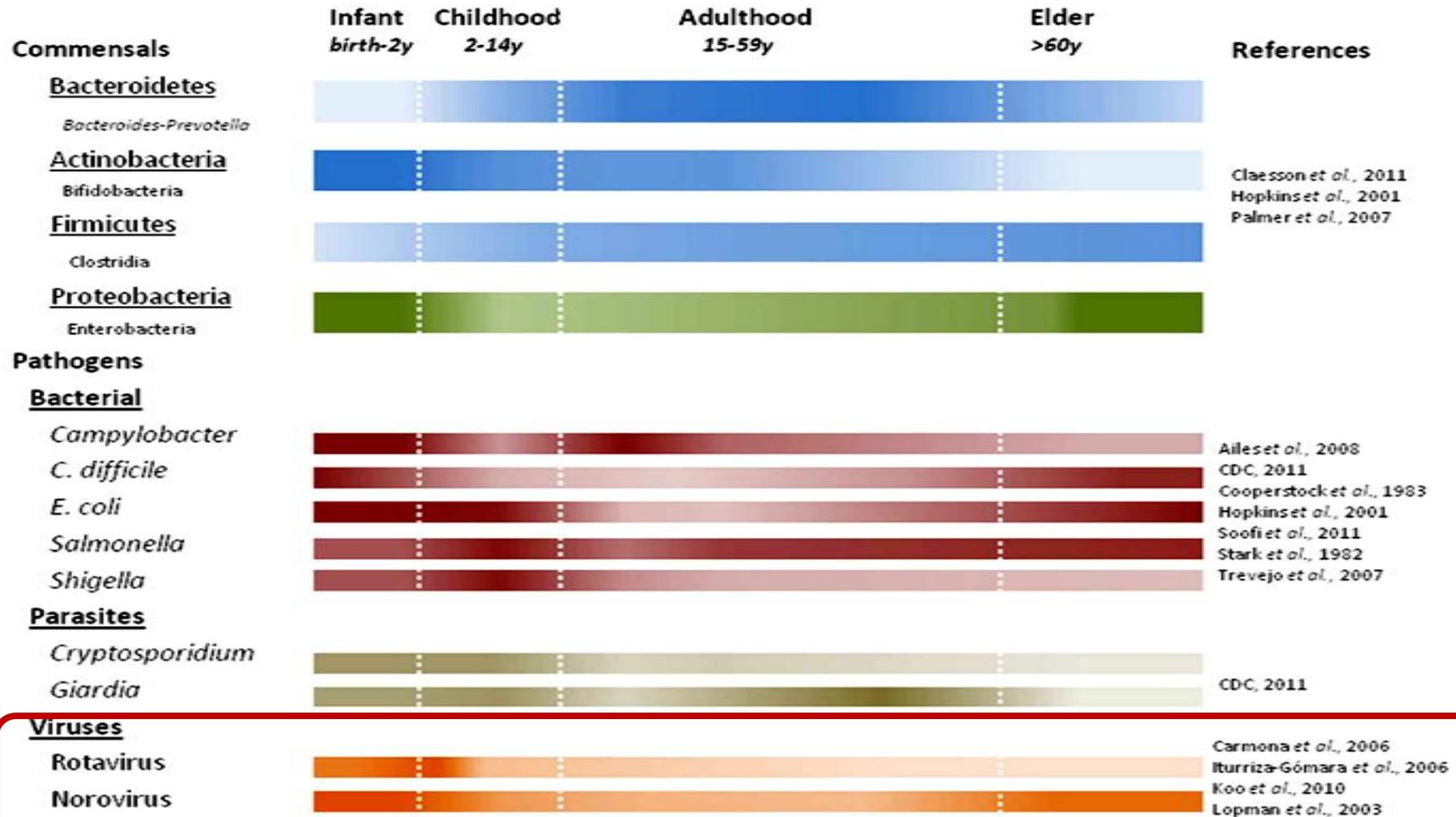
Major diseases during 1st year (2008) following the flood



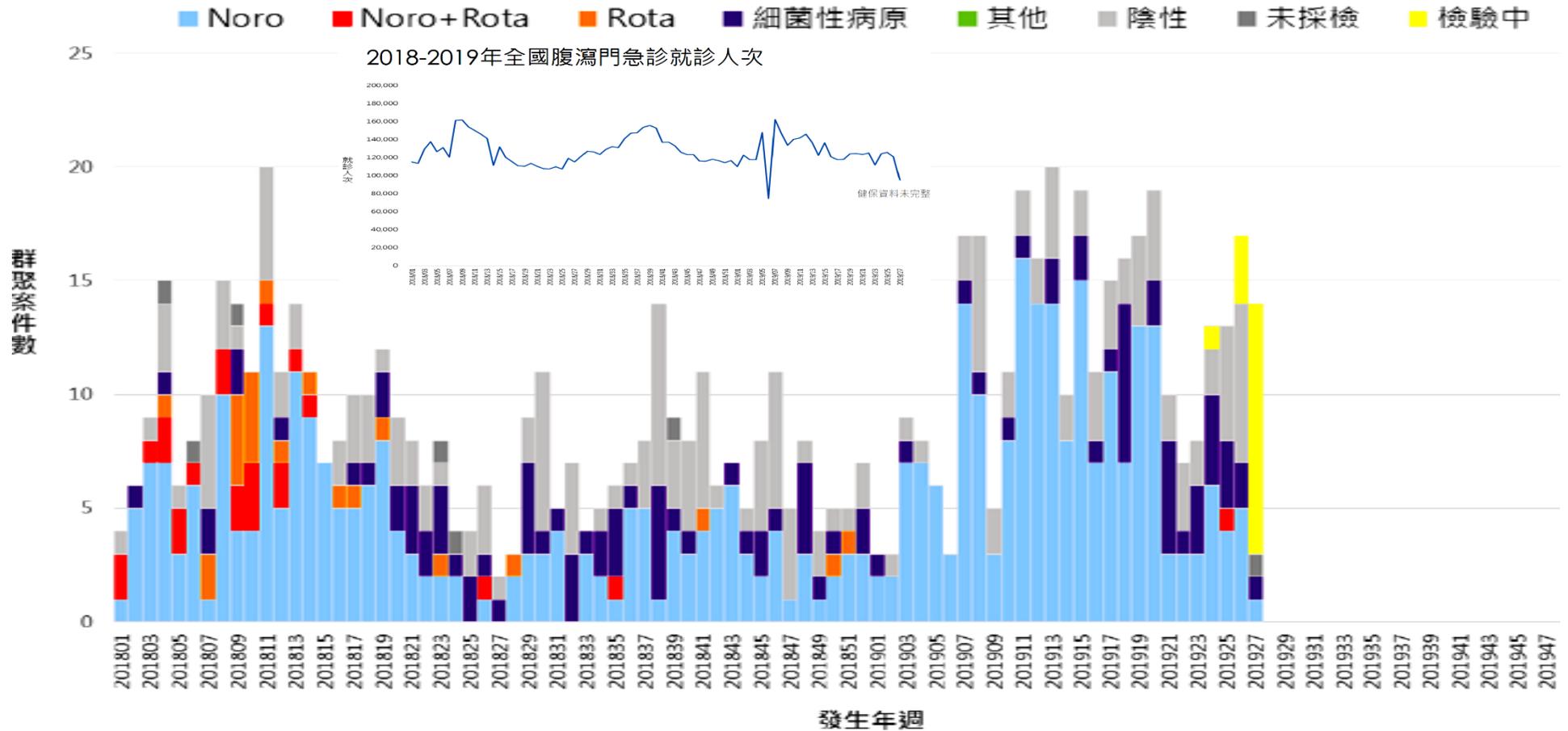


人生腸道共生菌與潛在致病菌的風險

Predominant commensal and pathogenic microbes associated with human life stages



2018-2019 腹瀉群聚通報趨勢~依病原

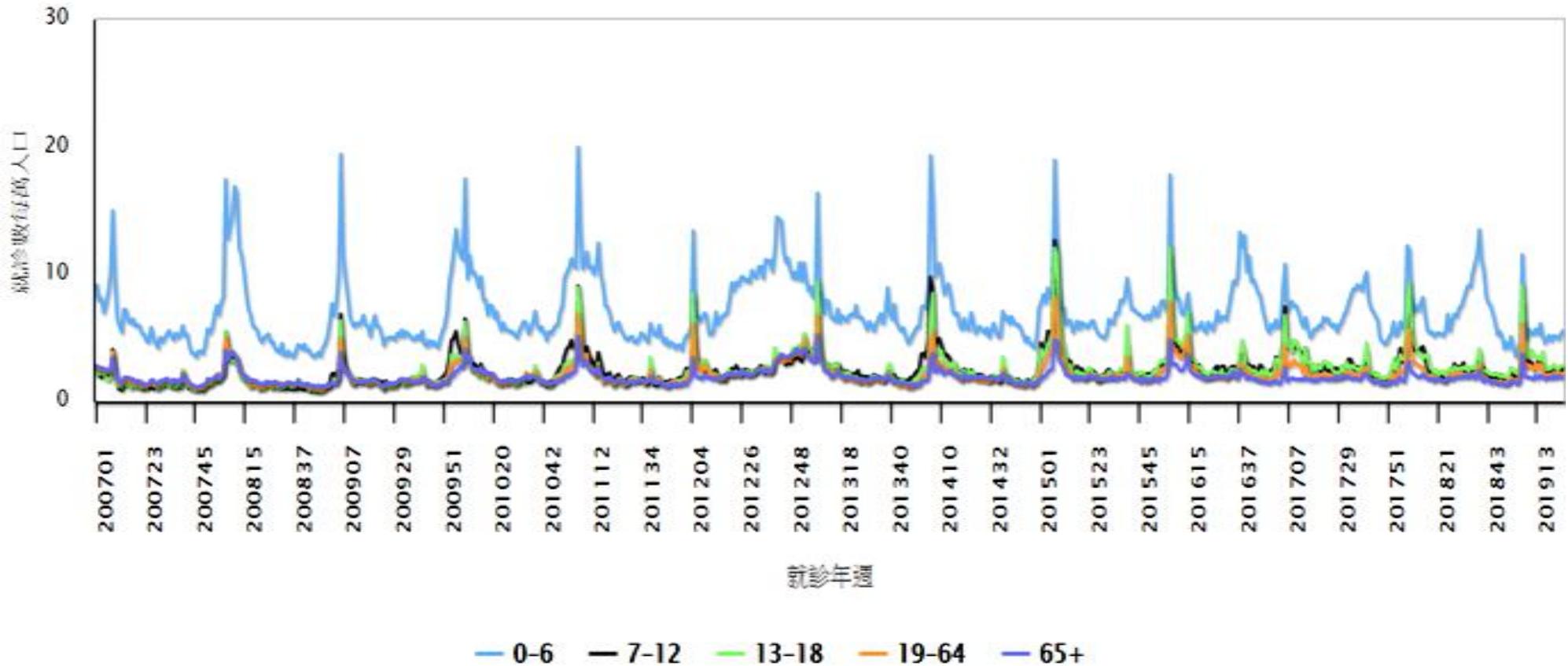


* 案件如同時檢出病毒及細菌性病原，以病毒性病原計算。

* 2019年細菌性病原(共88起)包括：仙人掌桿菌(29.5%)、金黃色葡萄球菌(63.6%)、腸炎弧菌(6.8%)、沙門氏桿菌(15.9%)、霍亂弧菌 Non-O1, Non-O139(0%)、腸道出血性大腸桿菌 Non-O157(1.1%) 等病原。

2007~2019 台灣急診急性腹瀉監測

2007年01週-2019年24週急診急性腹瀉年齡別每週每萬人口就診率趨勢圖

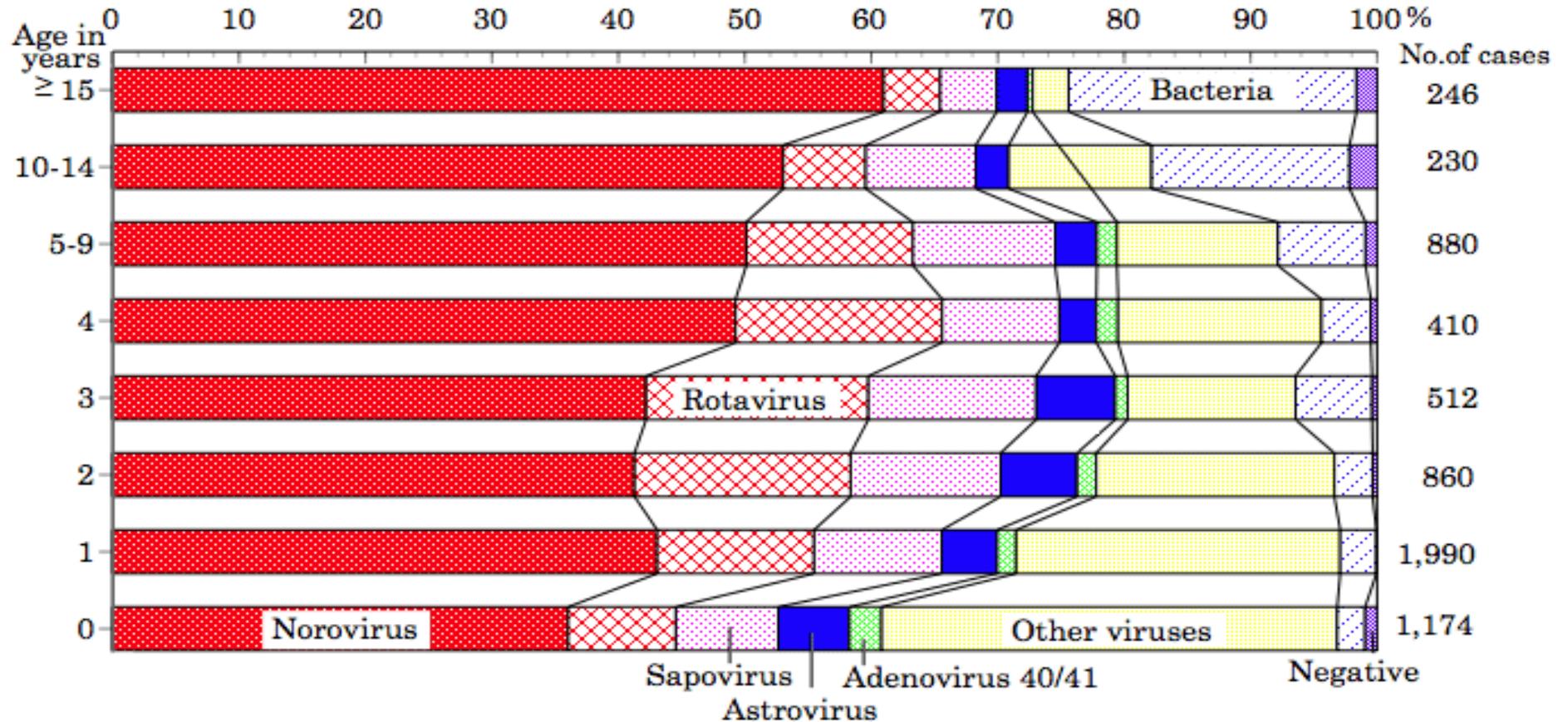


日本腸胃炎病原監測



Distribution of viruses & bacteria detected from sporadic infectious GE by age in Japan

Figure 2. Distribution of viruses and bacteria detected from sporadic infectious gastroenteritis cases, by age, 2014-2016, Japan



(Infectious Agents Surveillance Report: as of December 26, 2016)

病毒性腹瀉

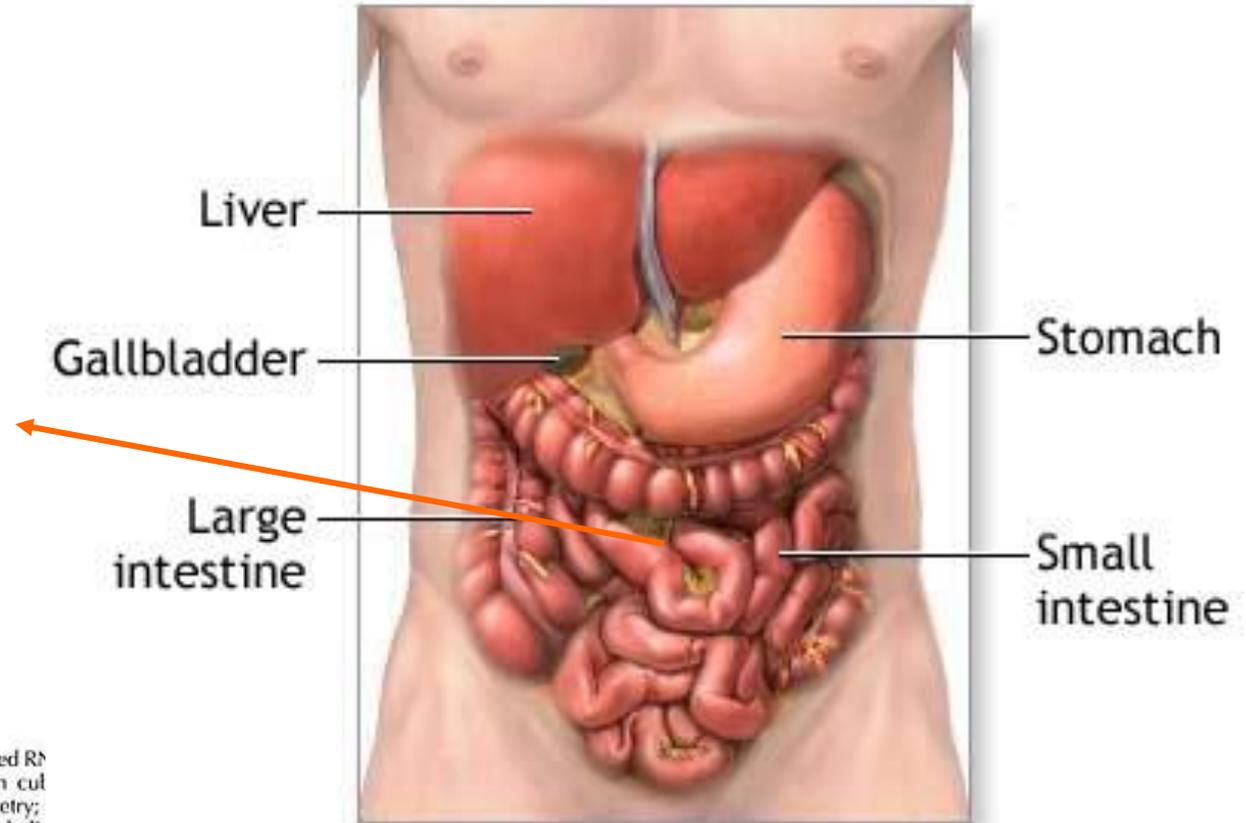
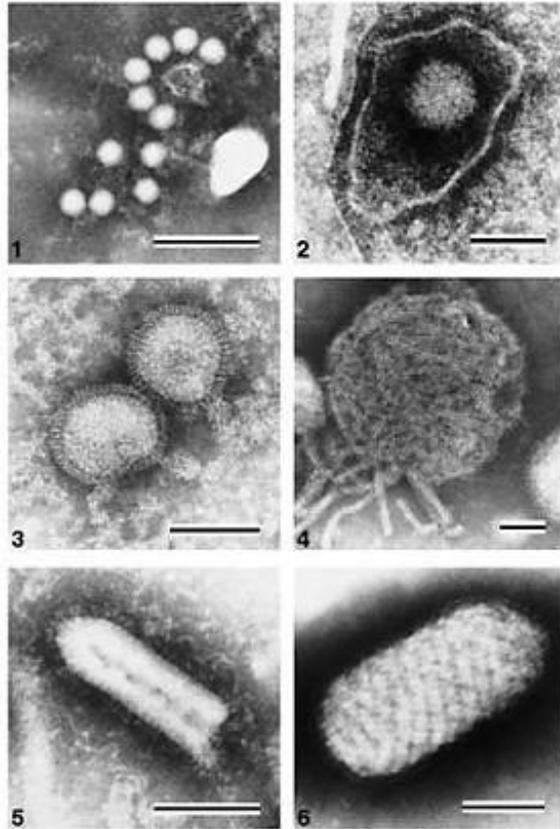


Figure 1.1 MORPHOLOGICAL FORMS OF VIRUSES: 1. poliovirus, naked Rⁿ virus with cubic symmetry; 2. herpesvirus, enveloped DNA virus with cub symmetry; 3. influenzavirus, enveloped RNA virus with helical symmetry; mumps virus, enveloped RNA virus with helical symmetry—the helic nucleocapsid is being released; 5. vesicular stomatitis virus, morphologica similar to rabies virus; 6. orfivirus, also with a complex symmetry. Bars represent 100 nm (Electron micrographs courtesy of E. Kjeldsberg)

常見腹瀉病毒性病原特性

TABLE 1: TYPES OF ACUTE VIRAL GASTROENTERITIS^{7*}

Virus	Incubation Period	Duration	Seasonality	Transmission
Rotavirus	1-3 days	5-7 days	Predominantly in winter and fall	Fecal-oral route and respiratory transmission
Norovirus	12-48 hours	1-4 days	Year-round, but especially in winter	Fecal-oral route, aerosolization, respiratory transmission, food, fomites, and water
Sapovirus	1-2 days	3-4 days	Year-round	Fecal-oral route
Astrovirus	4-5 days	5-6 days	Predominantly in winter	Fecal-oral route and water
Enteric adenovirus (40 and 41)	3-10 days	6-9 days	Predominantly in <u>summer</u>	Fecal-oral route

*This is not a comprehensive list.

Sara Marlow. February 01, 2016

<http://contemporaryclinic.pharmacytimes.com/journals/issue/2016/february2016/best-approaches-to-acute-gastroenteritis>

Newly Identified Viruses in Human Gastroenteritis

Pathogens or Not?

Virus	Family	Identification	Case-control study
Astrovirus BF34	Astroviridae	(41)	-
Astrovirus MLB1	Astroviridae	(42)	(37, 38)
Astrovirus MLB2	Astroviridae	(43)	(38)
Astrovirus MLB3	Astroviridae	(44)	(38)
Astrovirus VA1-3	Astroviridae	(43, 45, 46)	(38)
Astrovirus VA4	Astroviridae	(44)	(38)
Recovirus	Caliciviridae	(47)	-
Gyrovirus 3	Circoviridae	(48)	-
Gyrovirus 5 and 6	Circoviridae	(49)	-
Gyrovirus 9	Circoviridae	(50)	-
Papillomavirus CH2	Papillomaviridae	(51)	-
Bocavirus 1	Parvoviridae	(52)	(29, 32)
Bocavirus 2	Parvoviridae	(53)	(30-32)
Bocavirus 3	Parvoviridae	(31)	(31, 32)
Bocavirus 4	Parvoviridae	(54)	-
Bufavirus 1 and 2	Parvoviridae	(33)	-
Bufavirus 3	Parvoviridae	(55)	-
Tusavirus 1	Parvoviridae	(56)	-
Picobirnavirus group 3	Picobirnaviridae	(34)	-
Picobirnaviruses	Picobirnaviridae	(57)	-
Picobirnavirus D and E	Picobirnaviridae	(58)	-
Human parechovirus 7	Picornaviridae	(59)	-
Human parechovirus 12	Picornaviridae	(60)	-
Salivirus	Picornaviridae	(23)	(10, 22-24)
Kobuvirus	Picornaviridae	(61)	(62, 63)
Cardiovirus	Picornaviridae	(64)	(10, 12)
Cosavirus	Picornaviridae	(17)	(17-20)
MX polyomavirus	Polyomaviridae	(65)	-
MW polyomavirus	Polyomaviridae	(66)	(25)
STL polyomavirus	Polyomaviridae	(67)	(26)

Am I causing
your patient's
diarrhea and
vomiting?

Don't guess. Know.



病毒性腸胃炎的檢驗

GASTRO-ENTERITES VIRALES

Virus Rotavirus et Pararotavirus
 Adenovirus (types 40 -41)
 Calicivirus (Norovirus type Norwalk ...)
 Astrovirus
 Coronavirus
 Enterovirus

Diagnostic

Prélèvements : selles

Diagnostic direct rapide :

EIA Rota

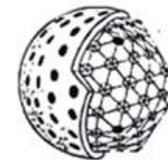
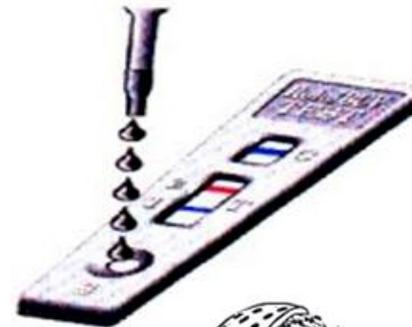
EIA Adeno

EIA Norovirus

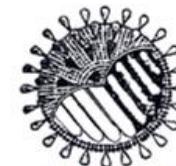
Diagnostic direct :

cultures : Enterovirus

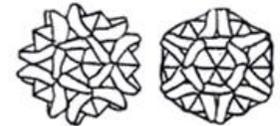
PCR : Calicivirus
 Astrovirus
 Coronavirus



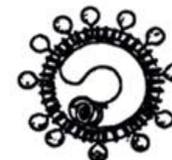
Rotavirus



Coronavirus



Calicivirus



Torovirus



Astrovirus



Adenovirus

免疫檢測與多重病原基因快速檢驗



Clinical Applications Immunoassays and Molecular Biology



Immunoassays



Molecular Biology





多重病原基因快速檢驗~急性腹瀉

T4

Pathogens detected by gastrointestinal panels FDA-cleared for testing stool samples in patients with infectious diarrhea.

ASSAY	ORGANISMS DETECTED	
FilmArray GI (BioFire Diagnostics)	Bacteria	<i>Campylobacter (yeyuni, coli, and upsaliensis)</i> , <i>Clostridium difficile</i> , <i>Plesiomonas shigelloides</i> , <i>Salmonella</i> , <i>Yersinia enterocolitica</i> . <i>Vibrio (parahemolyticus, vulnificus, and cholera)</i> , <i>Diarrheagenic E. coli/Shigella (EAEC, EPEC, ETEC, STEC, EIEC)</i> , <i>Shiga-producing E. coli</i> , <i>E. coli O157</i> .
	Viruses	Adenovirus F40/41, Astrovirus, Norovirus GI/GII, Rotavirus A, Sapovirus.
	Parasites	<i>Cryptosporidium</i> , <i>Cyclospora cayetanensis</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> .
xTAG GPP* (Luminex Molecular Diagnostics)	Bacteria	<i>Campylobacter</i> , <i>Clostridium difficile</i> , <i>Salmonella</i> , <i>Yersinia enterocolitica</i> . <i>Vibrio cholera</i> , <i>Enterotoxigenic E. coli (ETEC)</i> , <i>Shigella</i> , <i>Shiga-producing E. coli</i> , <i>E. coli O157</i> .
	Viruses	Adenovirus F40/41, Norovirus GI/GII, Rotavirus A.
	Parasites	<i>Cryptosporidium</i> , <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> .
Verigene EP (Nanosphere Inc.)	Bacteria	<i>Campylobacter group</i> , <i>Salmonella</i> , <i>Shigella</i> , <i>Vibrio group</i> , <i>Yersinia enterocolitica</i> , <i>Shiga-toxin 1 and 2</i> .
	Viruses	Norovirus GI/GII, Rotavirus A.
	Parasites	None

EAEC: Enteraggregative *E. coli*; EPEC: Enteropathogenic *E. coli*; ETEC: Enterotoxigenic *E. coli*; STEC: Shiga-toxin–producing *E. coli*; EIEC: *Shigella*/Enteroinvasive *E. coli*.

*This assay requires pre-extraction of nucleic acids using the NucleiSENS easyMAG instrument (BioMerieux).



多重病原基因快速檢驗

The BioFire® FilmArray® Gastrointestinal (GI) Panel

Traditional Testing



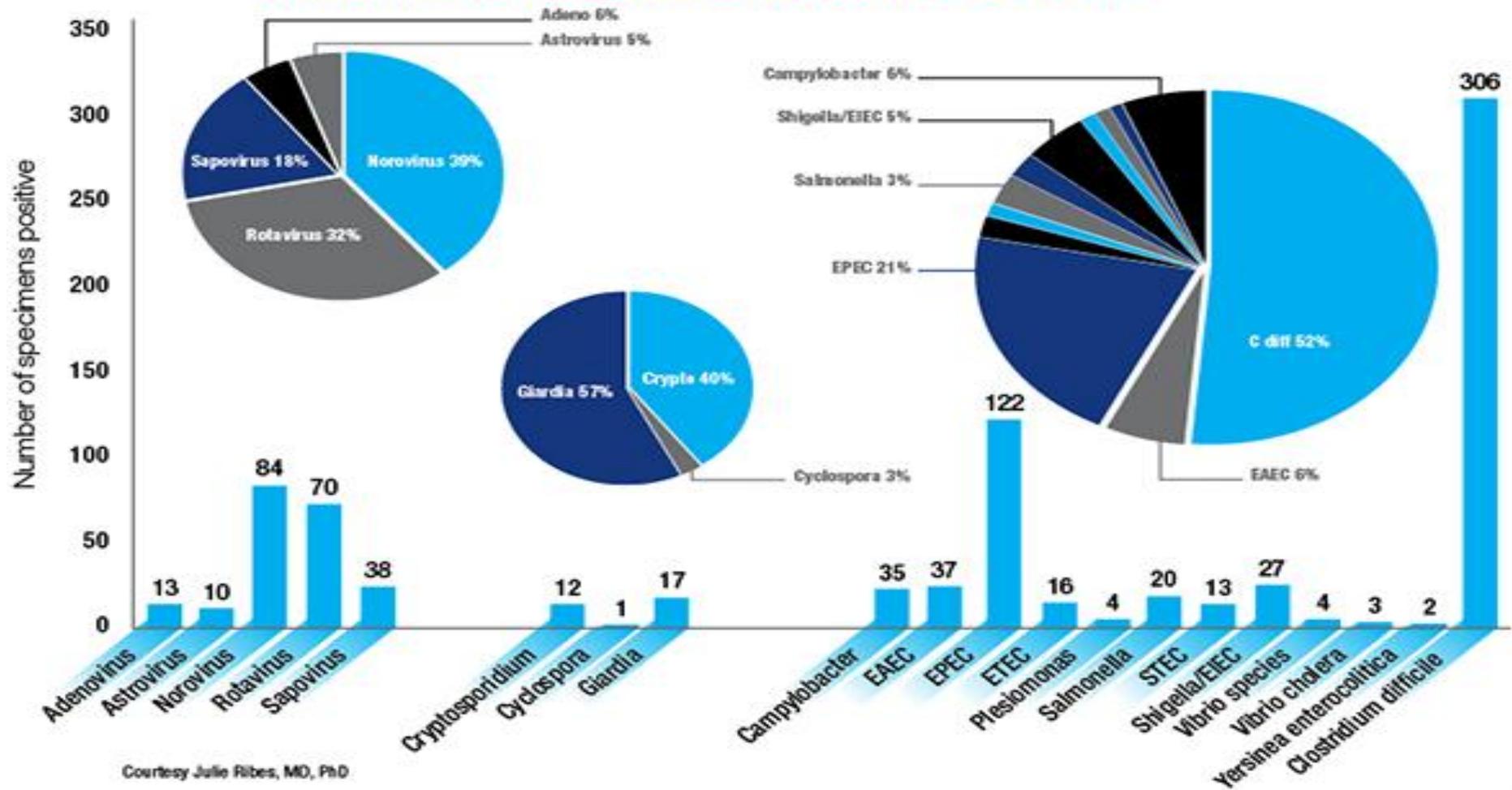
BioFire GI Panel



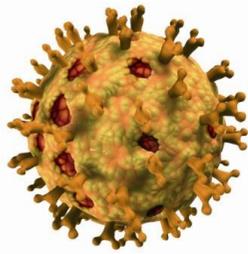


FilmArray GI: Findings from first months of clinical use

Diarrheal agents detected Feb.–Aug. 2015



Courtesy Julie Ribes, MD, PhD



輪狀病毒的經驗分享

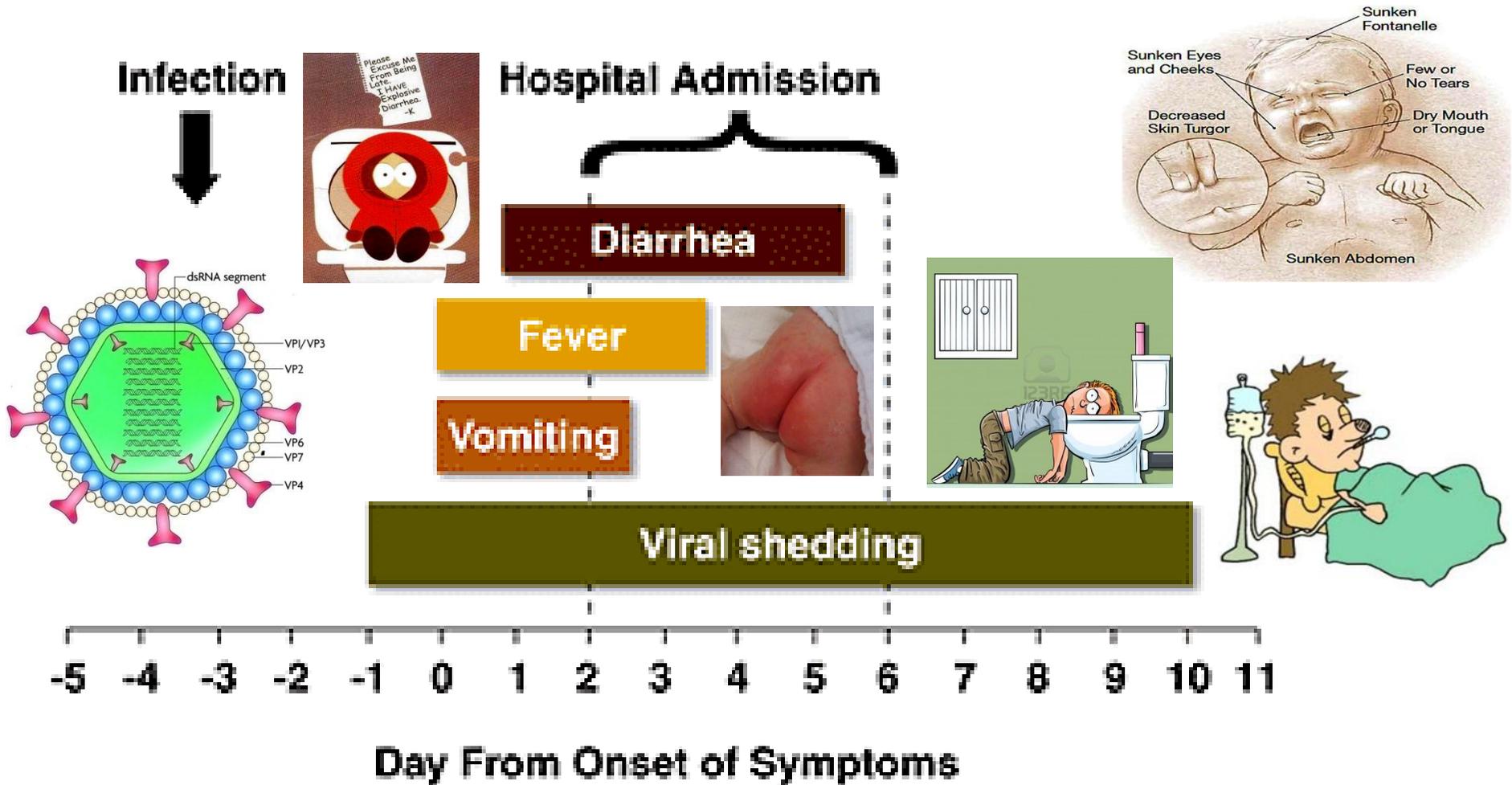


to administer to small children



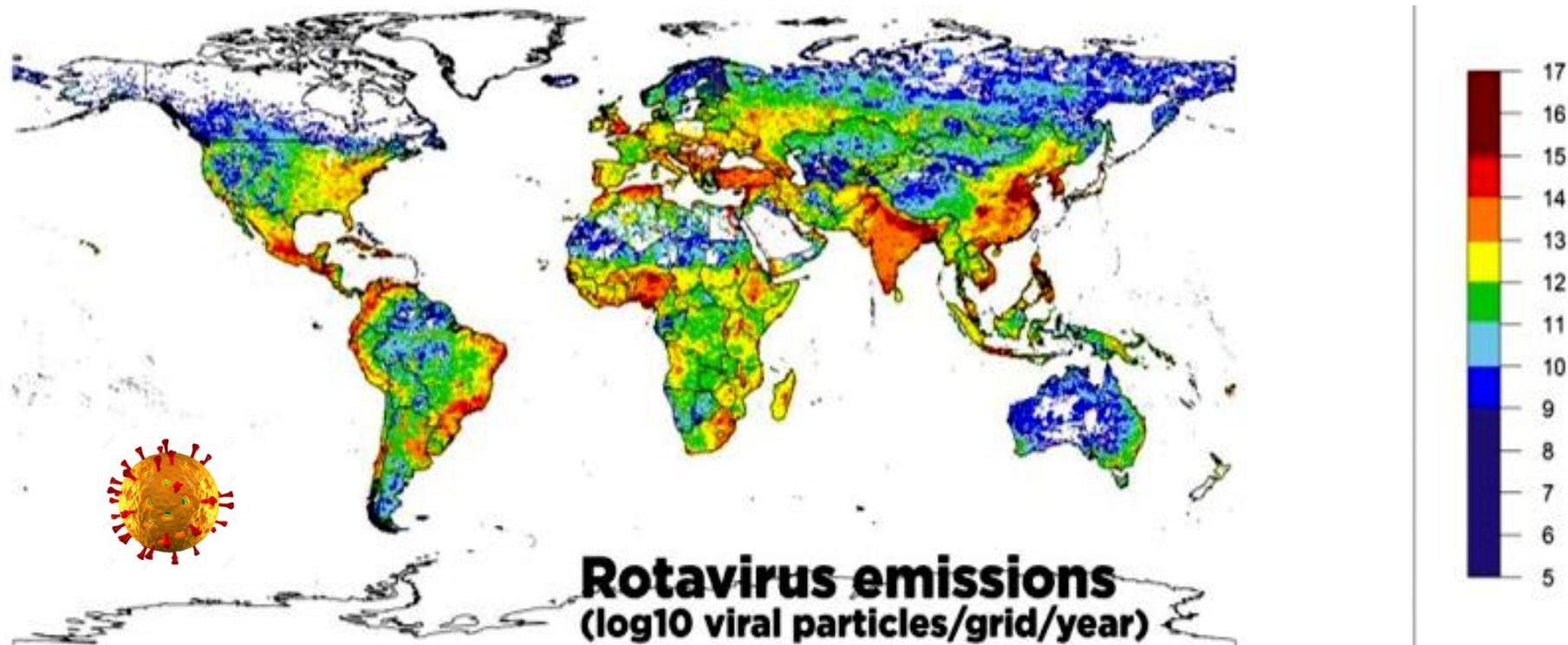
Clinical course of Rotavirus diarrhea

輪狀病毒腸胃炎的病程



全球糞便病毒密度分佈圖

A map of fecal viruses across the globe



Red shades indicate severe concentrations of the deadly rotavirus (based on data from approximately year 2010)

<https://www.sciencedaily.com/releases/2015/06/150616123925.htm>



輪狀病毒在環境中非常常見

Application of a Swab Sampling Method for the Detection of Norovirus and Rotavirus on Artificially Contaminated Food and Environmental Surfaces

Noroviruses and **rotaviruses** are the leading causes of non-bacterial gastroenteritis in humans worldwide. Virus-contaminated food and surfaces represent an important risk to public health. Here, we describe a detailed swabbing protocol combined with real-time RT-PCR for norovirus (NV) and rotavirus (RV) detection on artificially contaminated food and environmental surfaces. Recovery rates **2~78% for NV & 8~42% for RV** were determined for **contaminated food surfaces** of apple, pepper, cooked ham and salami. From contaminated **environmental surfaces** (stainless steel, ceramic plate, polyethylene, wood), recovery rates between **26~52% (NV) and between 10~58% (RV)** were determined. The results demonstrate the suitability of the swab sample method for virus detection on food and environmental surfaces. Compared to other methods, it is easy to perform and significantly time-saving, predestining it for routine testing.

輪狀病毒發病與治療

A zoonological disease

無症狀感染

嚴重脫水

RV persisted on dry inanimate surfaces for 6 – 60 days

BMC Infectious Diseases 2006;6:130



托兒所
幼兒園
幼稚園

~正常成人

~生活中接觸機會頻繁
(但症狀輕微或無症狀)

● 沒有抗病毒藥物可供治療

● 預防與治療脫水: 電解質補充液, 靜脈注射

● 不必嚴格禁食

~嬰幼兒: 4~36 月大
(通常 < 5 歲)

~老年人

~免疫障礙病患



Sick together



Examples of different study designs for assessment of rates of nosocomial rotavirus disease

Location	Citation	Time frame	Age range	Study site	Study design	Nosocomial case definition	Method of RV antigen detection	% of nosocomially acquired RV among total RV cases	*Incidence of nosocomial rotavirus infection
Turin, Italy	⁴ Gianino et al. 2002	12/1999–5/2000	1–18 mo	Pediatrics ward	Prospective, 6 mo of active surveillance	>24 h after admission through <72 h after discharge	EIA	32.6% (61 of 187)	27.7% (61 of 220)
Stanford, California	⁷ Rodriguez-Baez et al. 2002	1998–2000	<5 y	Pediatric general and organ transplant wards	Prospective, 2 y of active and passive surveillance	>72 h after admission	EIA	*14.3% (3 of 21)	†0.97% (3 of 309)
Amsterdam, the Netherlands	²² Widdowson et al. 2002	10/1999–2/2000	Neonates	Neonatal Medium Care Unit	Outbreak	>48 h after admission	RT-PCR	100%	39.8% (47 of 118)
Austria, Germany, Switzerland	⁹ Frühwirth et al. 2001	12/1997–5/1998	≤4 y	Pediatric ward or Pediatric GI clinic	Cohort study	≥48 h after admission	EIA	24.3% (159 of 653)	1.0–2.3 cases per 1000 hospital d
Freiburg, Germany	⁸ Berner et al. 1999	1/1987–12/1996	<15 y	General pediatric ward	Retrospective	>72 h after admission	Chart review	50.8% (453 of 892)	†12.5% (453 of 3618)
Belém, Brazil	³ Gusmão et al. 1999	11/1992–11/1994	<5 y	General pediatric ward	Prospective, 2 y, case-controlled study	>72 h after admission	EIA and PAGE	*30% (18 of 60)	†5.8% (18 of 310)
Poland	¹⁰ Mrukowicz et al. 1999	1994–1996	<60 mo	Pediatric ward	Retrospective	≥72 h after admission	Lab logs	*38.7% (196 of 506)	†14.6% (196 of 1342 GI admissions)
New Delhi, India	²¹ Bhan et al. 1993	11/1986–10/1988	Neonates	Maternity unit	Prospective, 2 y, cohort study	Birth through 4 d after discharge	EIA and PAGE	100%	73% (148 of 204)
Ga-Rankuwa, South Africa	¹² Steele et al. 1993	1/1989–12/1989	>6 mo–<12 y	Pediatrics ward	Prospective, 1 y surveillance of children with diarrhea	>72 h after admissions through < 48 h after discharge	Rotavirus EIA	43% (37 of 86)	†6.1% (37 of 605 GI admissions)



院感性輪狀病毒腸胃炎對住院時間的影響

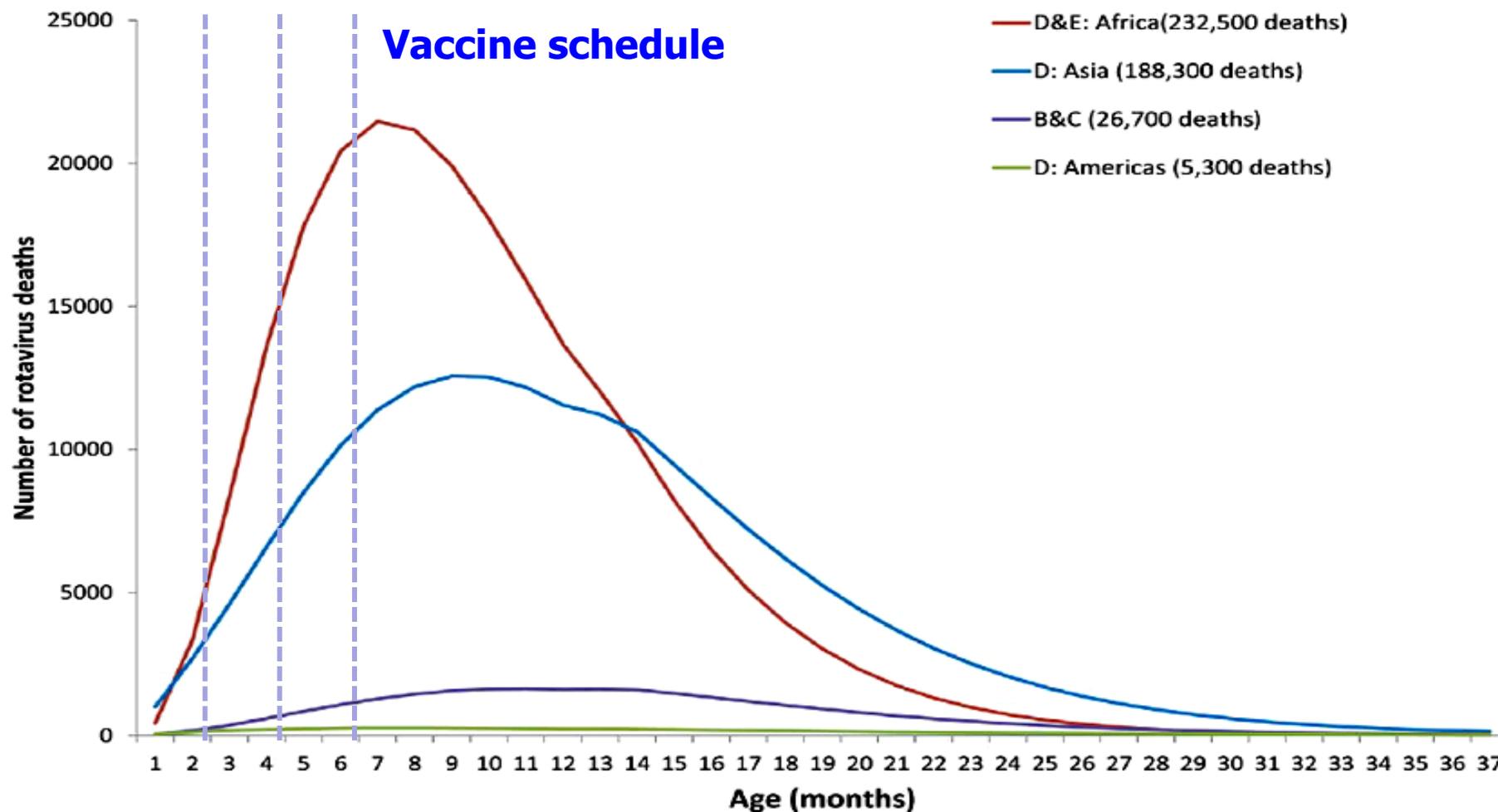
Impact of Nosocomial Rotavirus Infections on Duration of Hospitalization by Country

Country	Duration of Hospital Stay (d)		Extra Length of Stay
	Hospitalizations With RV	Hospitalizations Without RV	
France	N/A	N/A	+3.3
	8.9	4.0	+4.9
	6.3 (4.3–8.3) [†]	3.6 (2.3–5.9)	+2.7
	8.1 (5.5–10.7) [‡]	3.1 (2.2–4.0) [‡]	+5.0 [‡]
	8.3 (4.6–12.0) [§]	3.9 (2.3–5.2) [§]	+4.4 [§]
	7.7	4.1	+3.6
Italy	6.4	4.7	+1.7
Poland	N/A	N/A	+5.9
Spain	8.5 (2.7–14.3)	6.7 (2.1–11.3)	+1.8
United Kingdom	15.0	11.0	+4.0

Gleizes O. *Pediatr Infect Dis J* 2006;25:S12~S21.



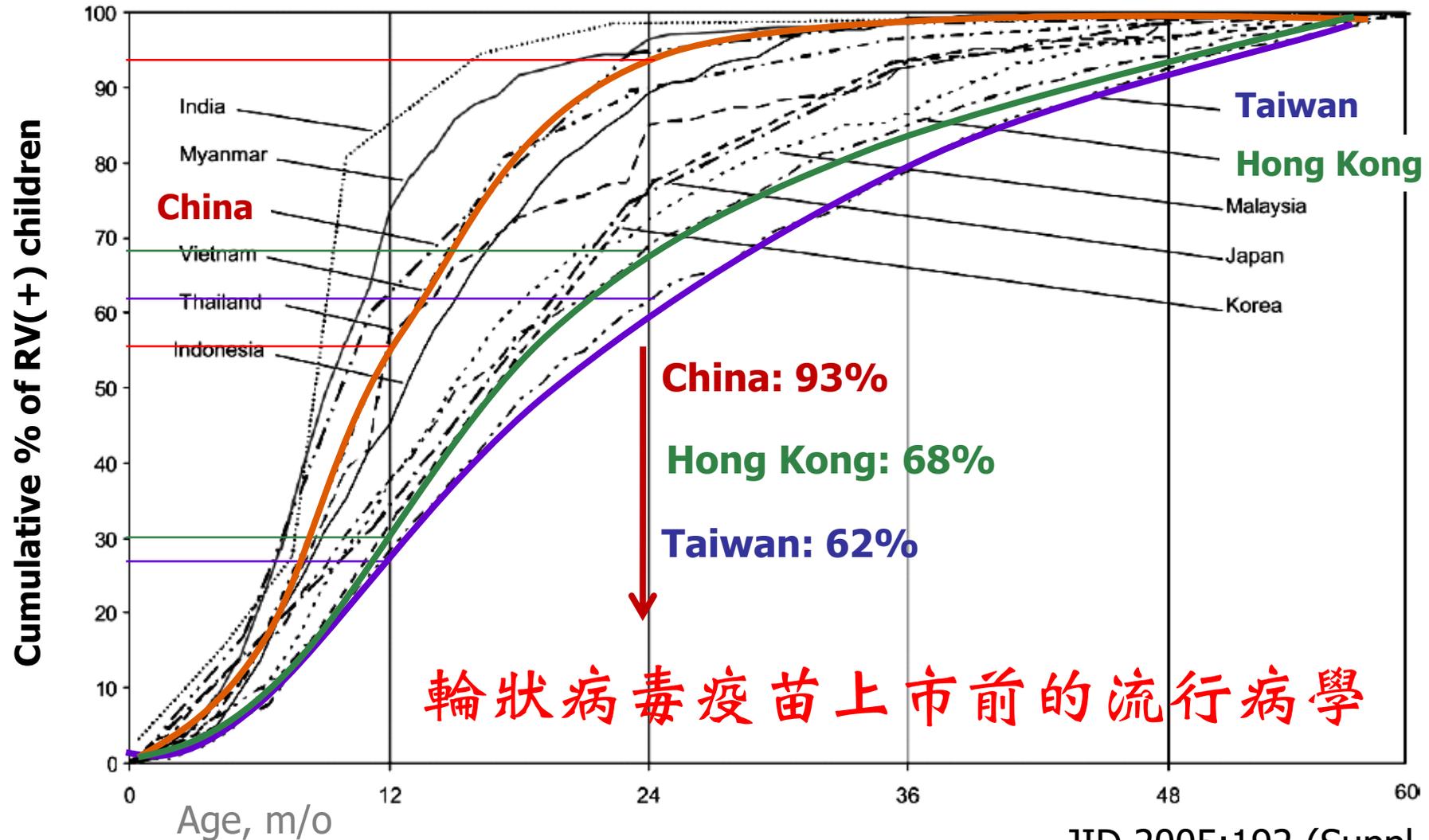
Age distribution of rotavirus deaths among children under 5 y, by WHO mortality group





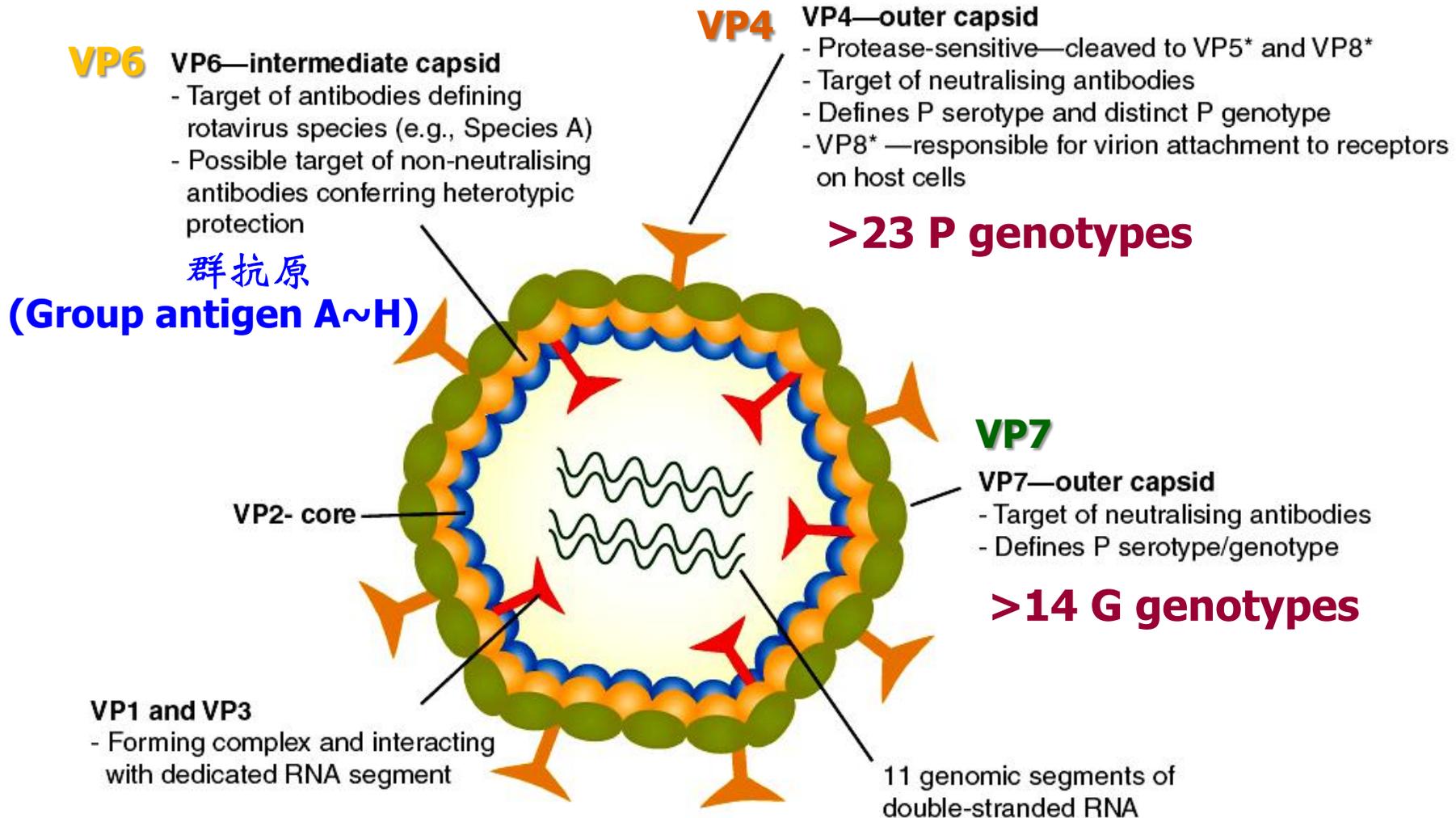
亞洲地區兒童感染輪狀病毒腸胃炎的年齡分布

Cumulative age distribution of hospitalizations related to RV infection among children 0~59 months of age in Asia



輪狀病毒疫苗上市前的流行病學

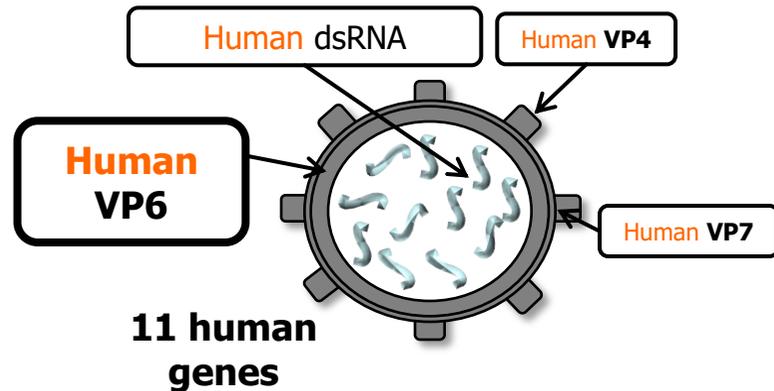
Structure of the RV triple layer particle illustrating the known and potential targets of neutralizing antibodies



兩種輪狀病毒疫苗不同的設計理念

全人類輪狀病毒疫苗

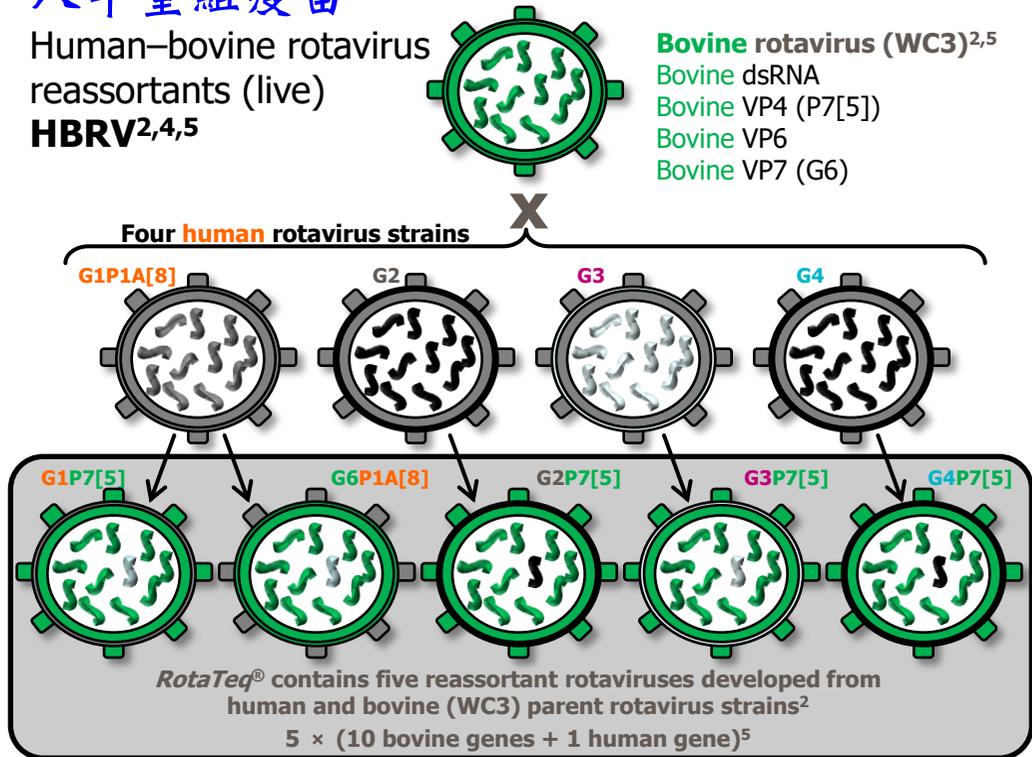
Human rotavirus RIX4414 strain-HRV
(live, attenuated) **G1P[8]**
HRV¹⁻³



The whole vaccine virus is **human rotavirus strain¹**

人牛重組疫苗

Human-bovine rotavirus
reassortants (live)
HBRV^{2,4,5}



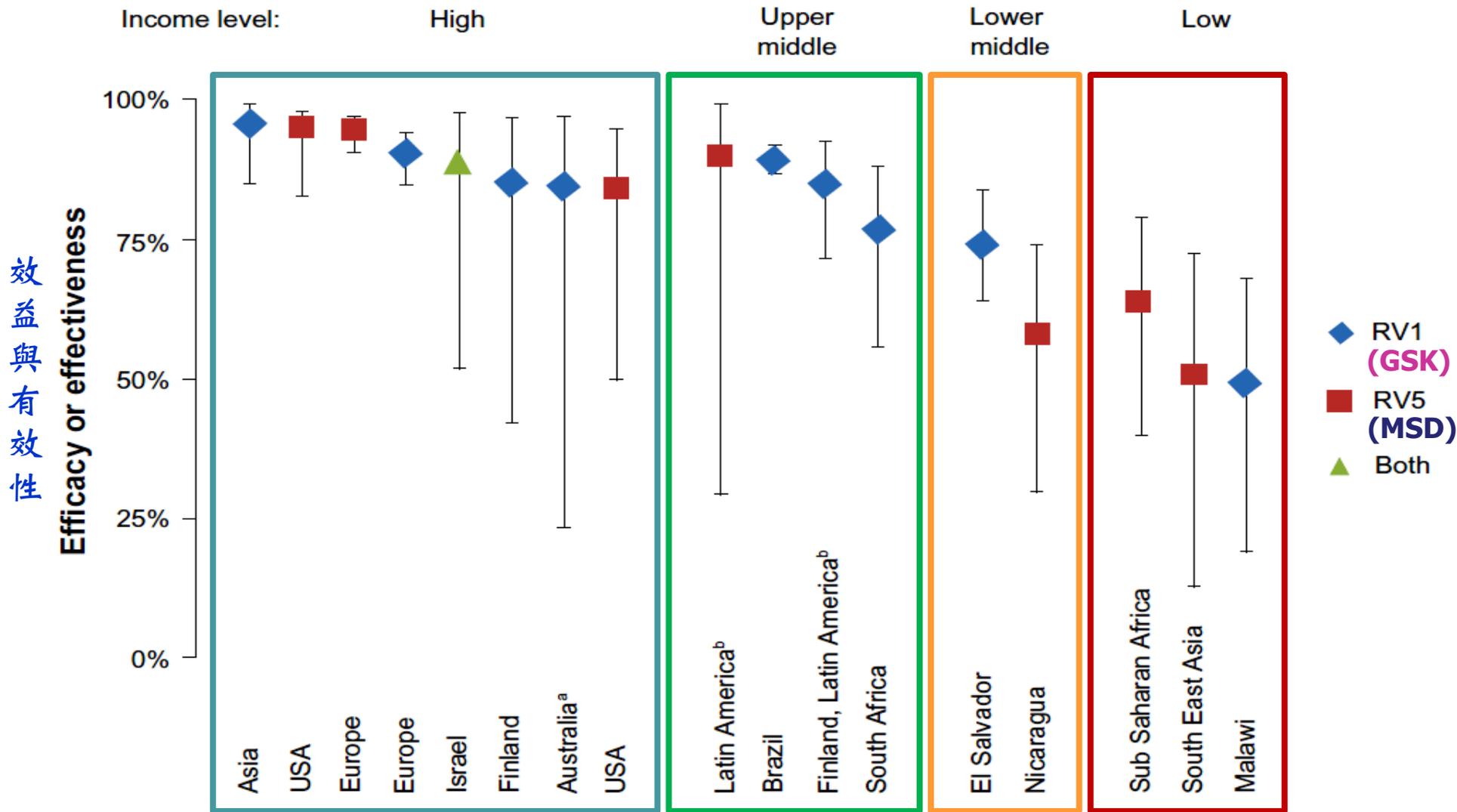
Vaccine virus consists of **human-bovine reassortants⁴**

1. EMA. 2016. *Rotarix™* SmPC 31/03/2016 EMA EPAR update. See notes for web link [accessed Sep 2016];
2. WHO. *Wkly Epidemiol Rec* 2007; **82** (32): 285–96; 3. EMA. *Rotarix™* Scientific Discussion 2006. See notes for web link [accessed Sep 2016];
4. EMA. 2016. *RotaTeq®* SmPC 01/03/2016 EMA EPAR update. See notes for web link [accessed Sep 2016];
5. Offit PA, Clark HF. *Pediatr Ann* 2006; **35**: 29–34

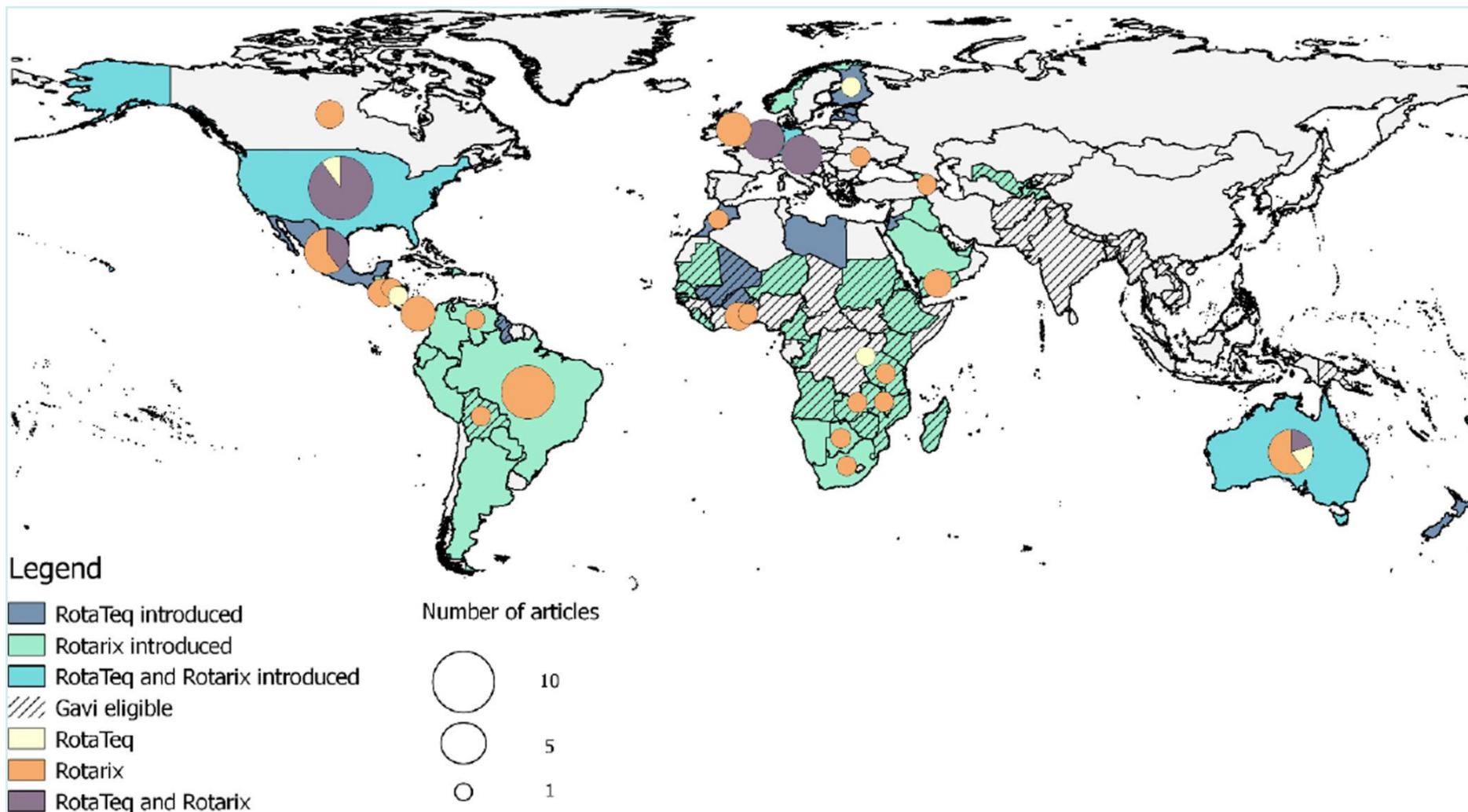


輪狀病毒疫苗在不同生活水平國家的效益與有效性比較

Comparison of vaccine efficacy and effectiveness estimations from clinical trials of RV1 and RV5 against any serotype severe rotavirus gastroenteritis, stratified by country income status

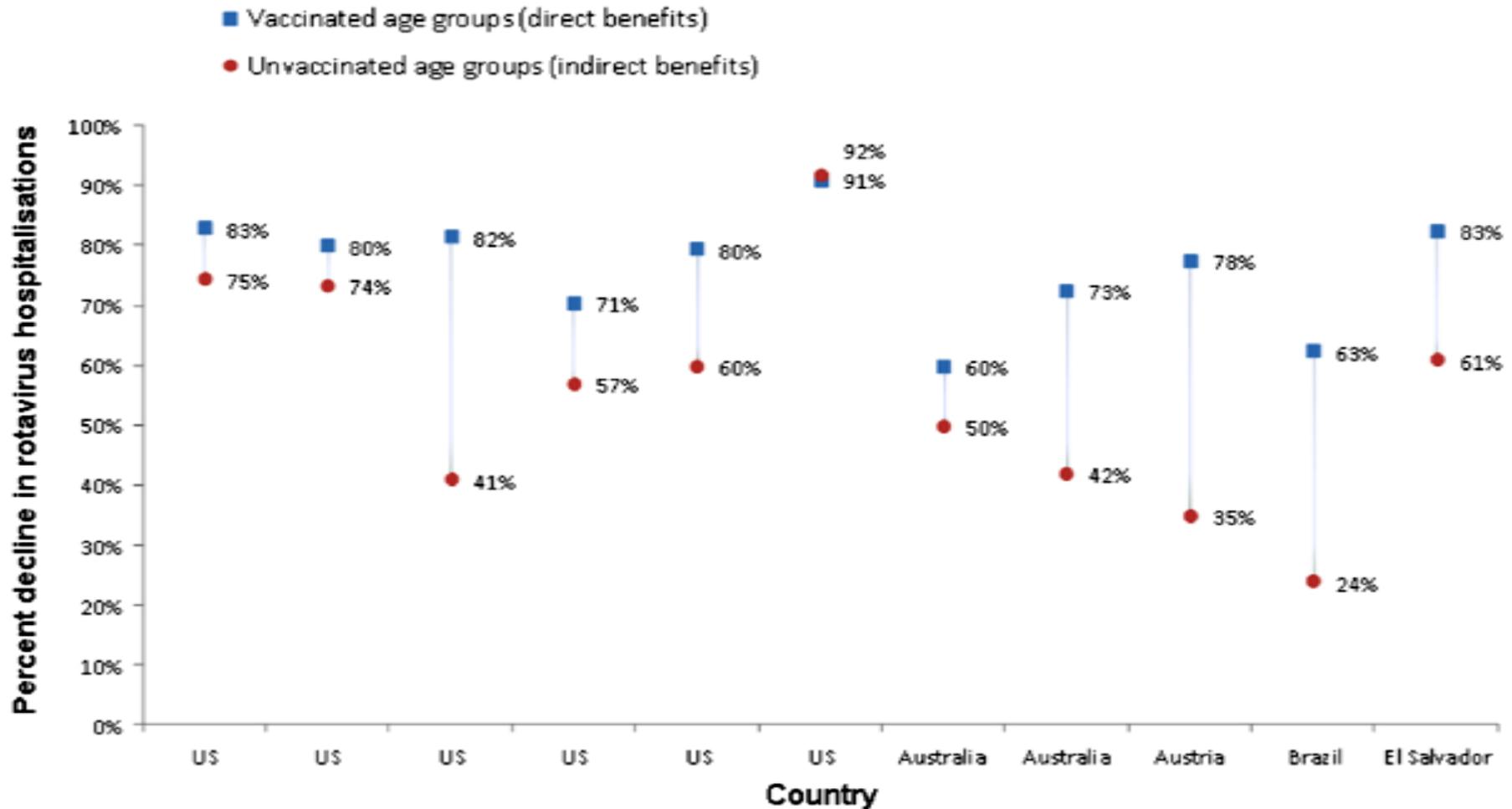


Map of rotavirus vaccine national introductions & estimates of rotavirus vaccine impact by individual countries



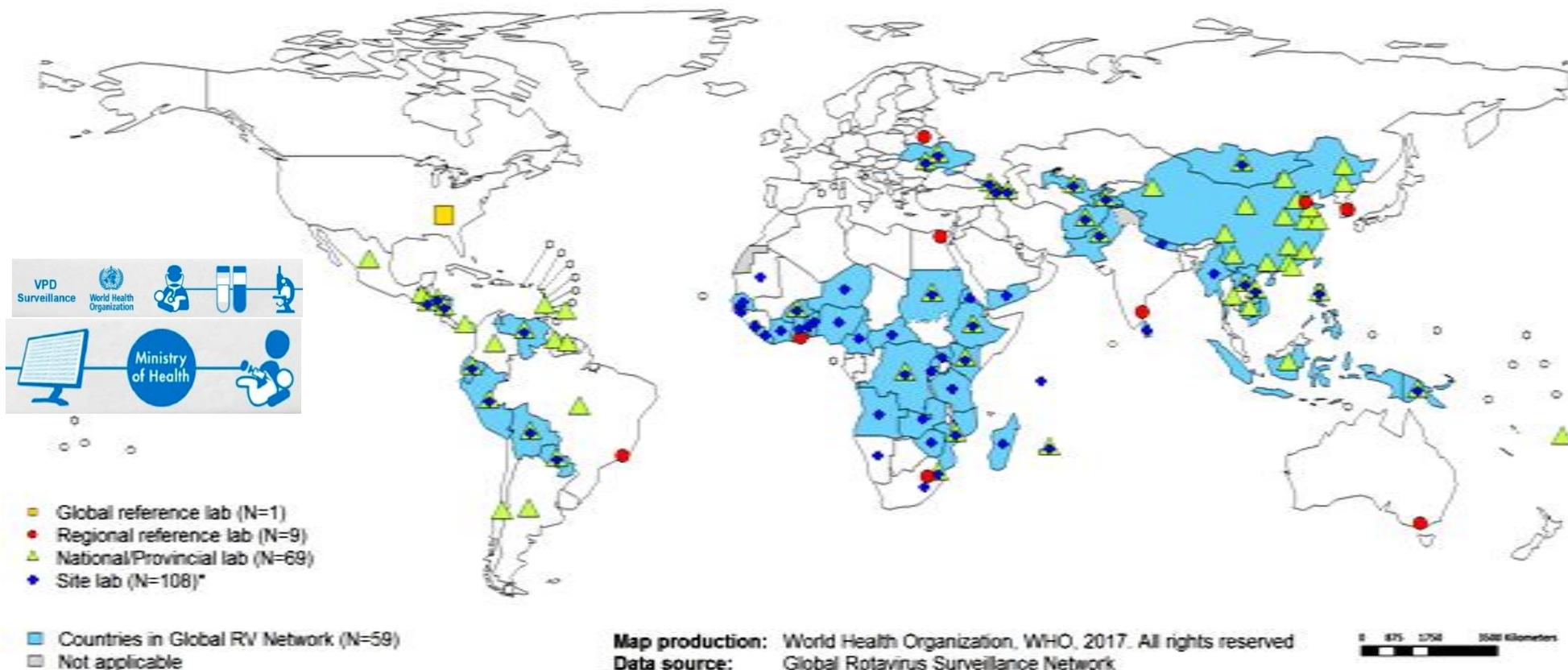


Direct & indirect benefits of vaccine as evidenced by reduction in severe rotavirus diarrhea among vaccinated and unvaccinated children after the introduction of a rotavirus vaccine in various countries





The Global Rotavirus Laboratory Network (GRLN)



Notes:

* Only one sentinel site laboratory plotted by country. Position of labs on the map does not always reflect their exact geographical location.

Disclaimer:

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

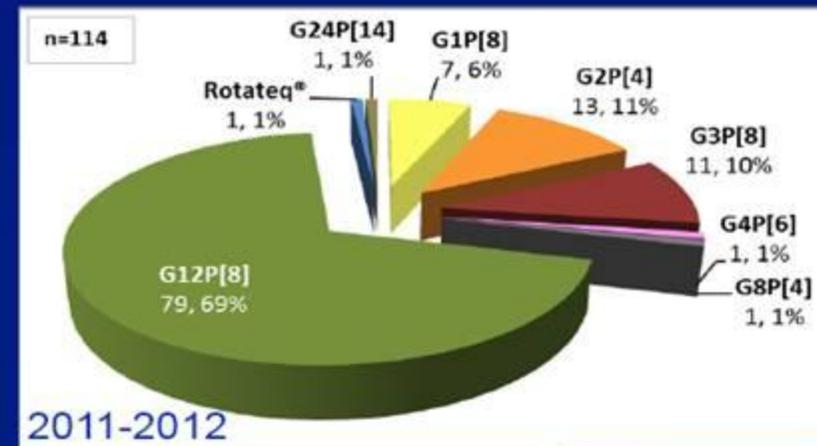
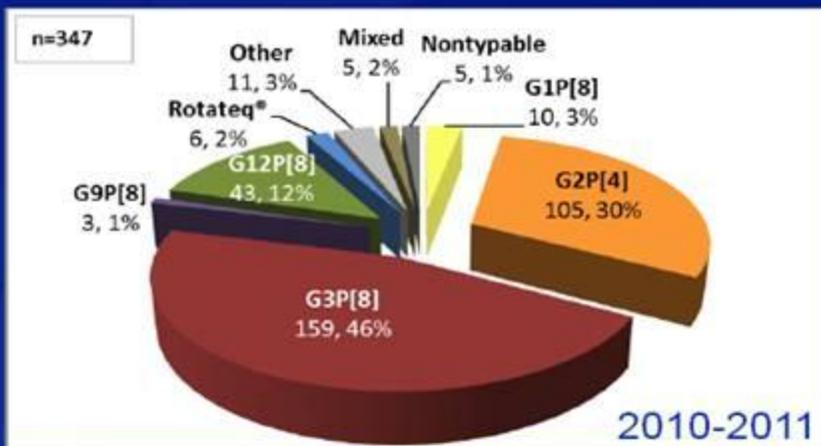
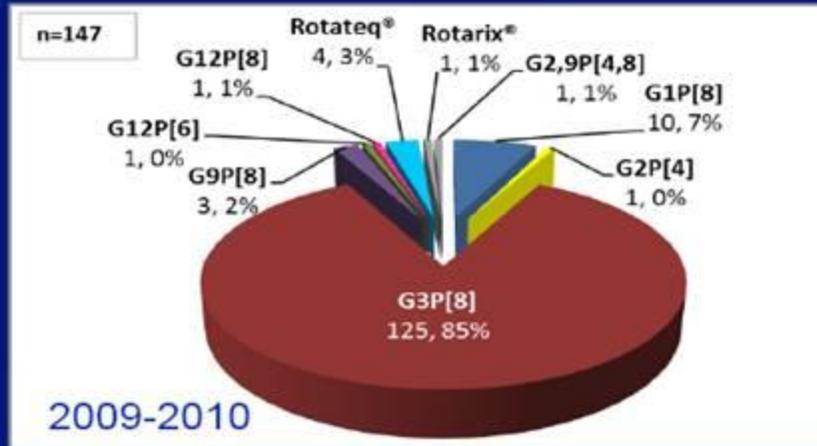
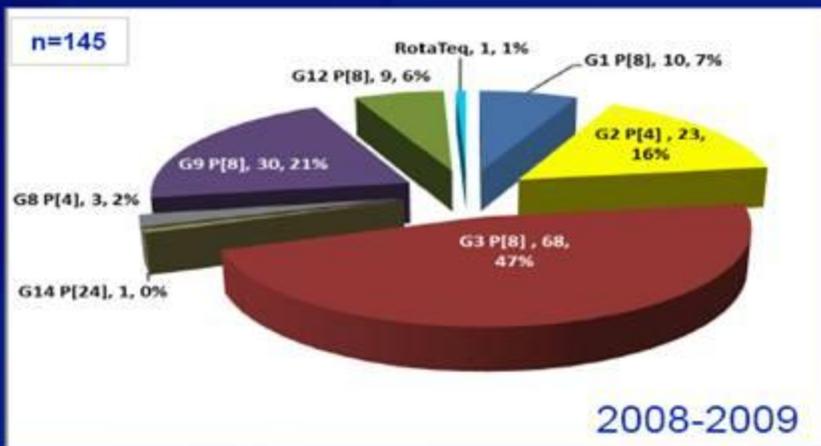
15 December 2017



http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/Rotavirus/en/



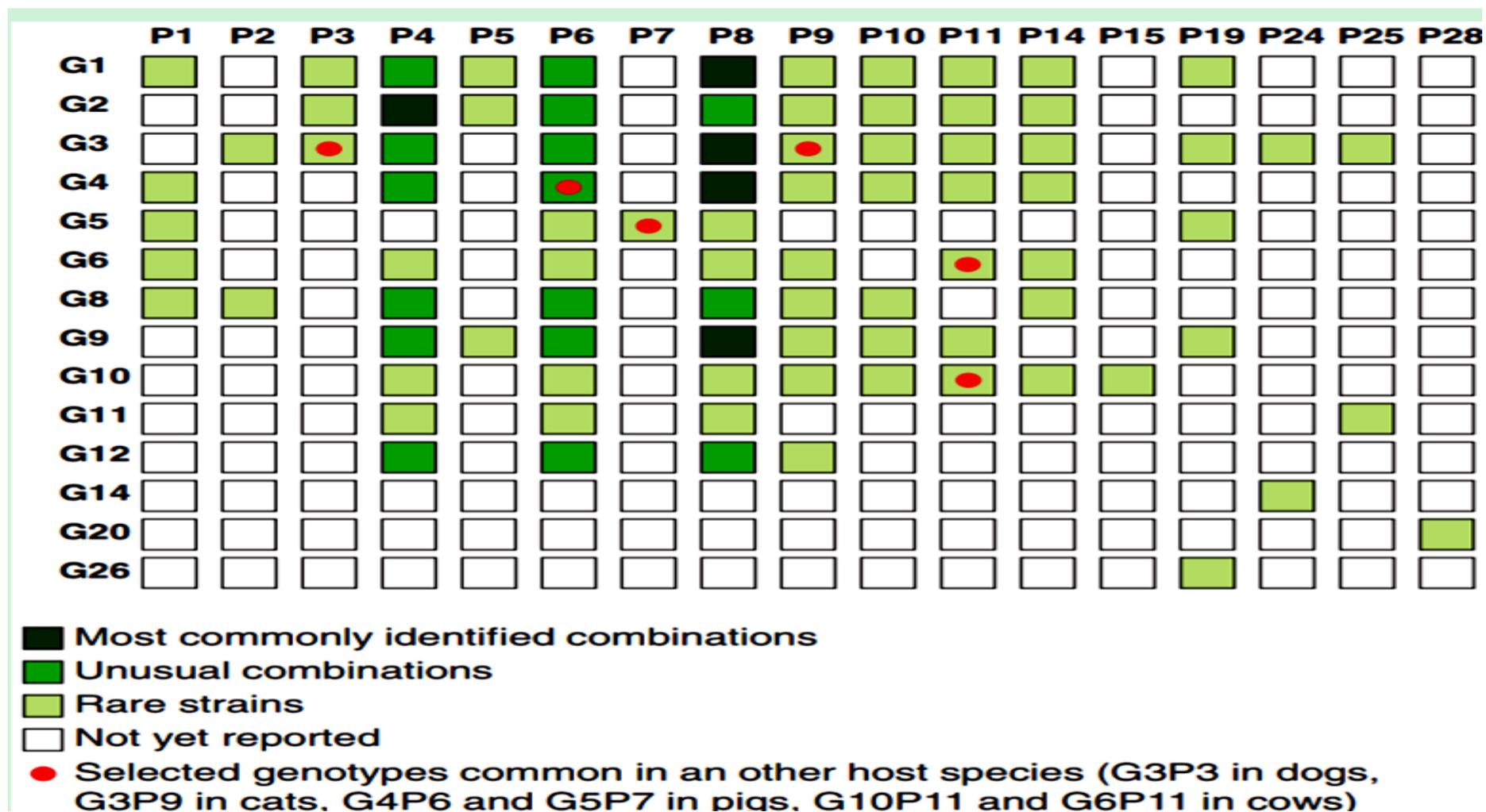
Genotype Prevalence USA, NVSN 2008-2012



Slide courtesy of Dr Mike Bowen

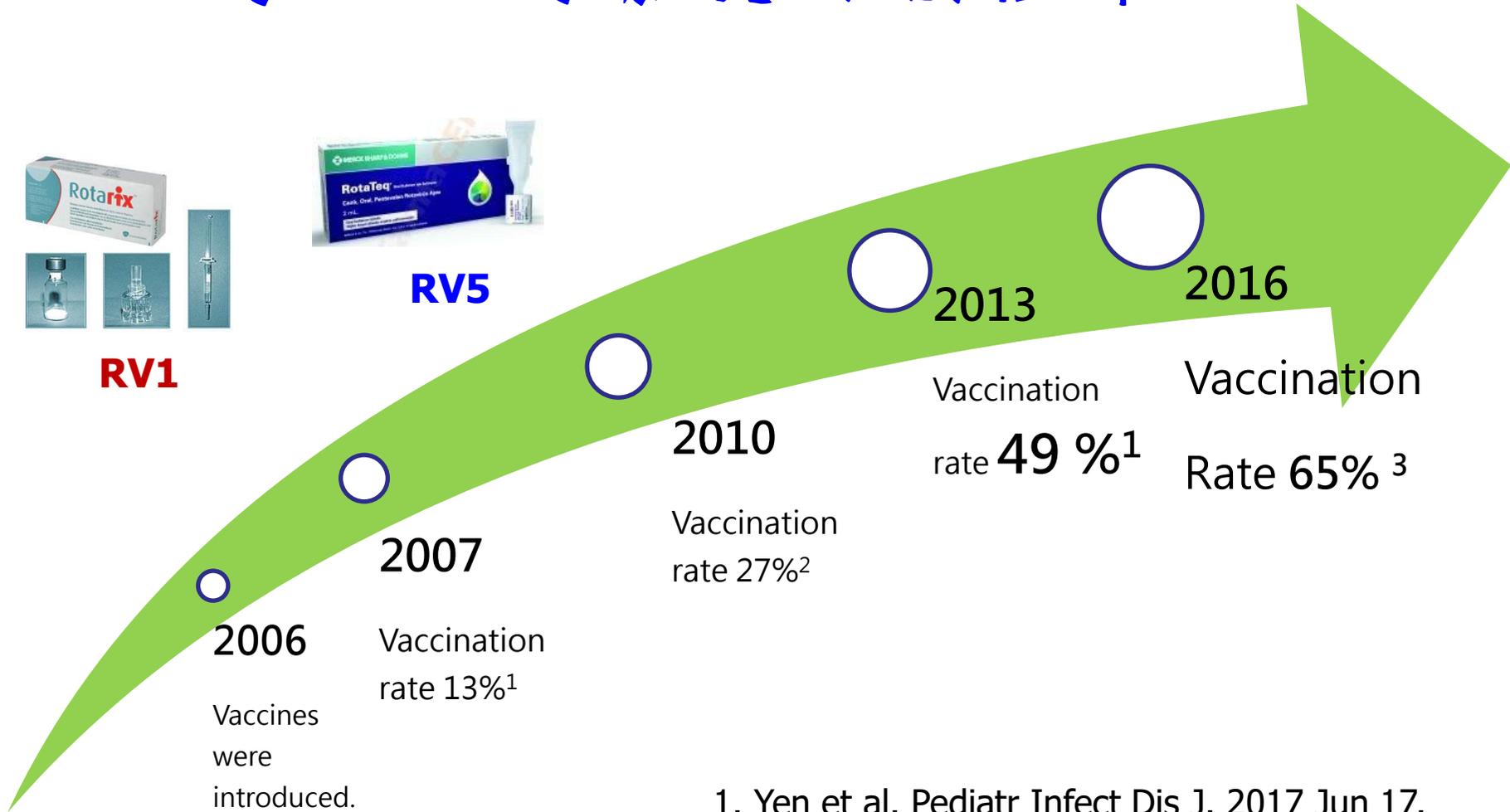


An update of RVA VP7 (G) and VP4 (P) type combinations identified in humans





台灣輪狀病毒疫苗接種率



1. Yen et al. *Pediatr Infect Dis J.* 2017 Jun 17.

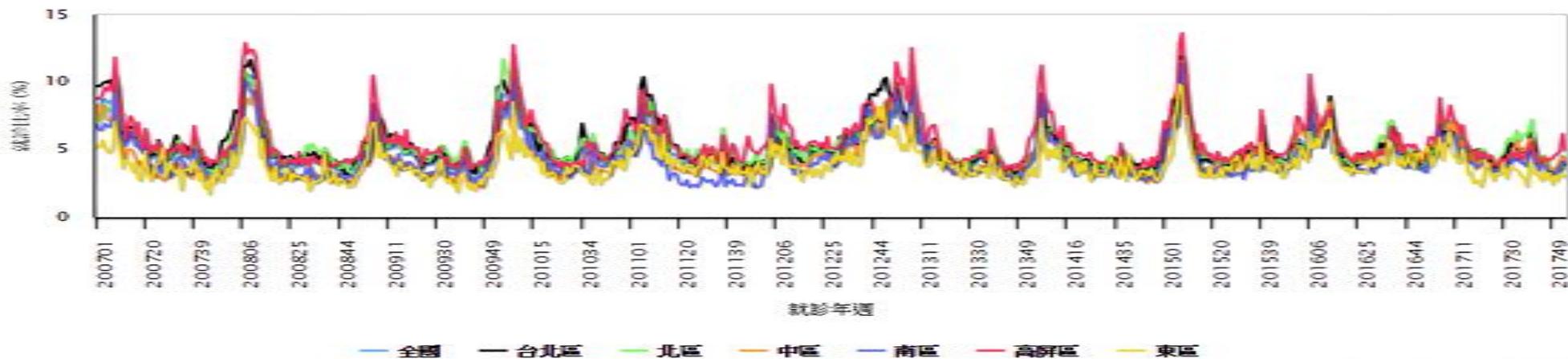
2. Chang et al. *PIDJ* 2014;33:e81-e86

3. Personal communication with Prof. Yhu-Chering Huang

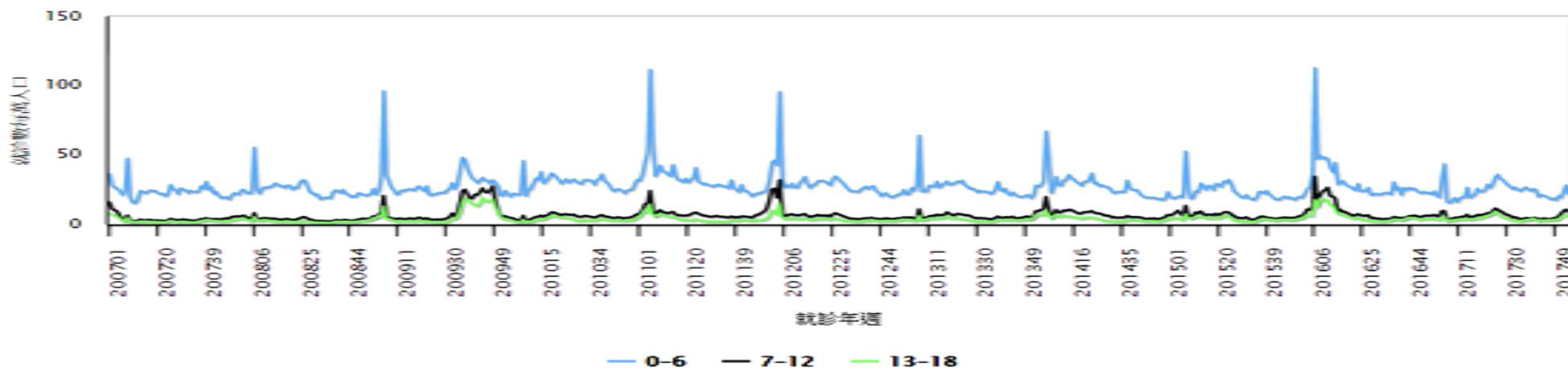


2007~2018 台灣急診急性腹瀉監測

2007年01週-2018年02週急診急性腹瀉地區別每週就診百分比監測趨勢圖



2007年01週-2018年02週急診RODS類流感年齡別每週每萬人口就診率趨勢圖



輪狀病毒疫苗有效嗎？安全嗎？

輪狀病毒疫苗會增加腸套疊 (Intussusception) 風險嗎？根據兩項發表在NEJM的研究結果顯示…

研究	VSD研究	PRISM研究
設計	回溯性觀察性研究、自我對照風險區間 (SCRI) 設計	回溯性觀察性研究，接續式機率比值檢定 (SPRT)
對象	5~36.9週美國新生兒	4~34週美國新生兒
暴露	接種後7天內、21天內	接種疫苗後腸套疊個案
對照	接種後22~42天間	背景值
風險	RV5 7天 1.1件/100,000疫苗 21天 1.5件/100,000疫苗 RV1 未達顯著差異	RV5 RR 1.1 (8/7.11) RV1 RR 8.4 (6/0.72)

資料來源: N Engl J Med 2014; 370:513-519; N Engl J Med 2014; 370:503-512.



台灣輪狀病毒疫苗建議：專家會議結論

- ~建議所有的適齡嬰兒使用輪狀病毒疫苗。
- ~單價與五價的輪狀病毒疫苗皆可以跟例行的注射式疫苗同時使用。
- ~口服輪狀病毒疫苗不建議與口服小兒麻痺疫苗同時使用，兩者之間應間隔至少二星期。
- ~輪狀病毒口服疫苗第一劑應在年齡滿六週到未滿十五週之間使用，最後一劑在八個月零天前使用完畢。兩劑間隔至少四週。如果第一劑超過建議年齡使用，仍可繼續完成後續接種。
- ~不建議兩種口服輪狀病毒疫苗混用。若先前使用疫苗廠牌不明或有缺貨現象，可以接續另一種疫苗，合計用滿三劑。
- ~早產兒依實際出生年齡使用。
- ~嚴重免疫不全的嬰兒不建議使用，但人類免疫不全病毒感染嬰兒可以使用。使用過血液製劑之前後均可使用疫苗。



腸道腺病毒 (Enteric Adenovirus)

- ❖ 裸露的雙鏈DNA病毒，分為六群(A-F)。
- ❖ 腹瀉腺病毒，屬於F群40及41血清型(及部份31型)。
- ❖ 全年性，主要<二歲嬰幼兒；
- ❖ 無症狀感染(約40%)至7-10的上吐下瀉都有
- ❖ 常合併發燒與上呼吸道感染症狀
- ❖ 潛伏期約3至10天。
- ❖ 傳染途徑為糞-口方式(醫護人員與醫療器具可媒介)。
- ❖ 治療主要為針對發燒、水份與腹瀉之症狀療法。

腺病毒種類

Table 1. Infections caused by adenoviruses, by species and types

Species	Infections	Major types	Minor types
A	Gastroenteritis	12, 31	61
B	ARI, PCF, EKC, HC	3, 7, 11, 34, 35	14, 16, 55, 66, 68, 79
C	ARI, PCF	1, 2, 5, 6	57
D	EKC, urethritis	8, 19/64 [*] , 37, 53, 54, 56	81
E	ARI, EKC, PCF	4	-
F	Gastroenteritis	40, 41	-
G	Gastroenteritis	52	-

ARI: acute respiratory infection, PCF: pharyngoconjunctival fever,

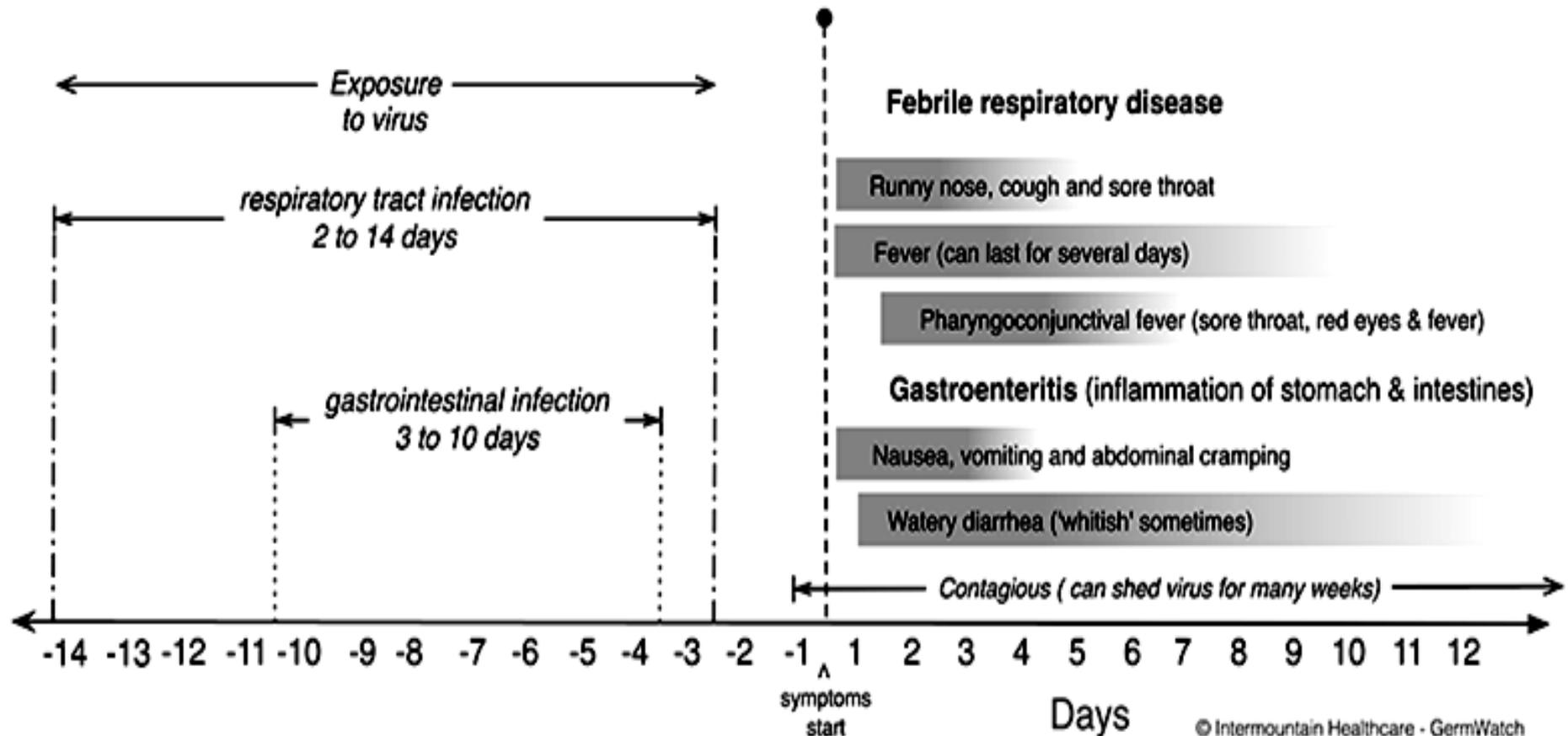
EKC: epidemic keratoconjunctivitis, HC: hemorrhagic cystitis

*19/64 (19a reclassified as 64)



腺病毒 (Adenovirus) 臨床病程

Adenovirus Virus Infection Timeline

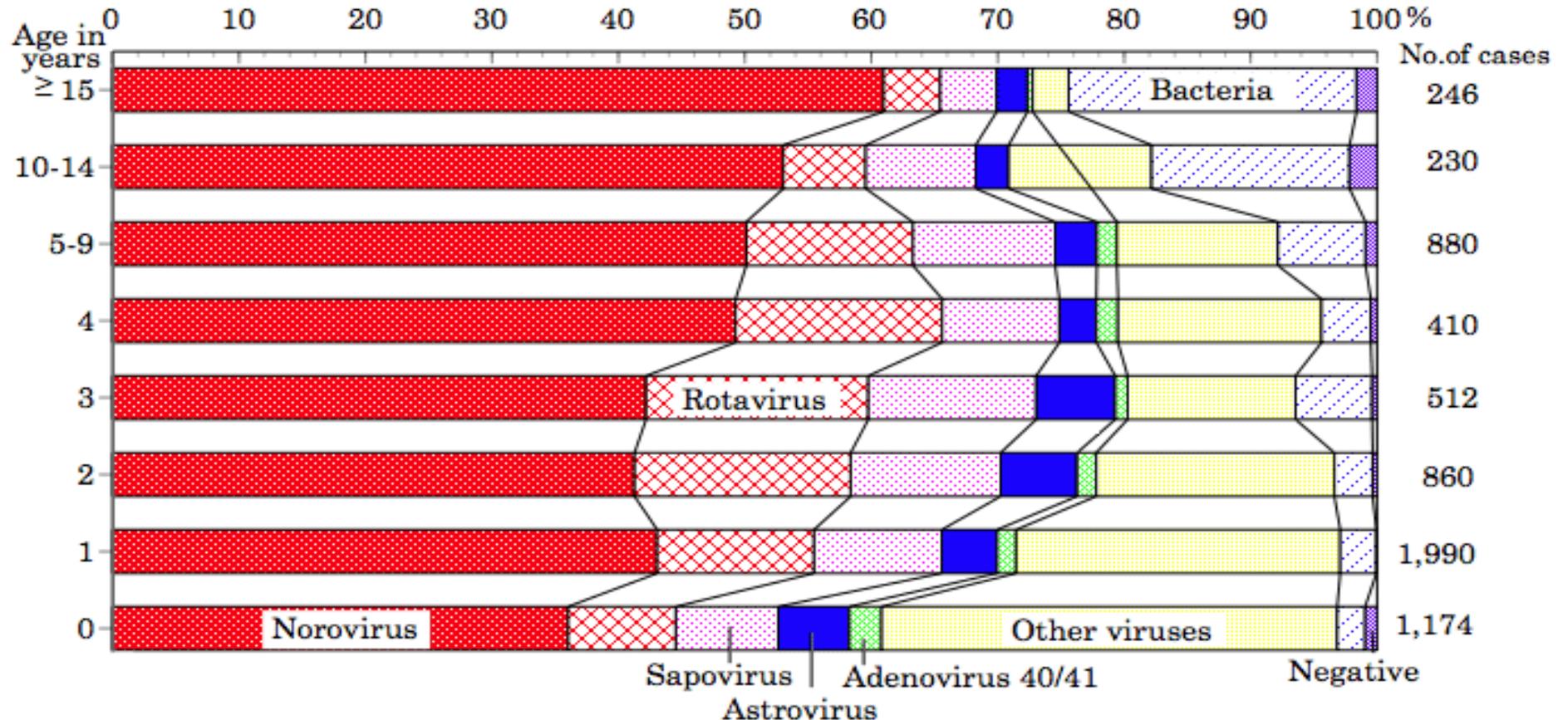


日本腸胃炎病原監測



Distribution of viruses & bacteria detected from sporadic infectious GE by age in Japan

Figure 2. Distribution of viruses and bacteria detected from sporadic infectious gastroenteritis cases, by age, 2014-2016, Japan



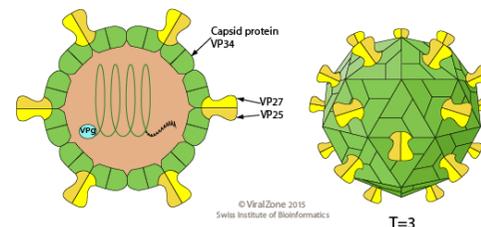
(Infectious Agents Surveillance Report: as of December 26, 2016)



2012年臺灣星狀病毒腹瀉群聚事件流行病學分析

近年來病毒性腹瀉群聚佔通報腹瀉群聚事件約50%，其中以諾羅病毒為主要致病原；引起腹瀉群聚之致病原除常規檢測的細菌、諾羅病毒和輪狀病毒外，針對未知病原之通報腹瀉群聚事件，疾病管制署研究檢驗及疫苗研製中心以研究計畫探討新興腹瀉病毒，如沙波病毒、腺病毒和星狀病毒的感染現況。於2012年間共303起通報腹瀉相關群聚，其中70起為常規未能檢出之未知病原腹瀉群聚，本研究針對此70起腹瀉群聚進行檢測分析與疫情特性探討；其中18 (25.7%) 起為星狀病毒陽性腹瀉群聚，影響年齡層自0~70歲之間皆有感染案例，主要流行季節為春季並只在2012上半年，疫調資料亦顯示，大部分星狀病毒腹瀉群聚傳播途徑藉由食媒性引起。本篇研究為臺灣首次及國際上少數針對未知病原之腹瀉群聚進行星狀病毒之檢驗與流行病學研究。

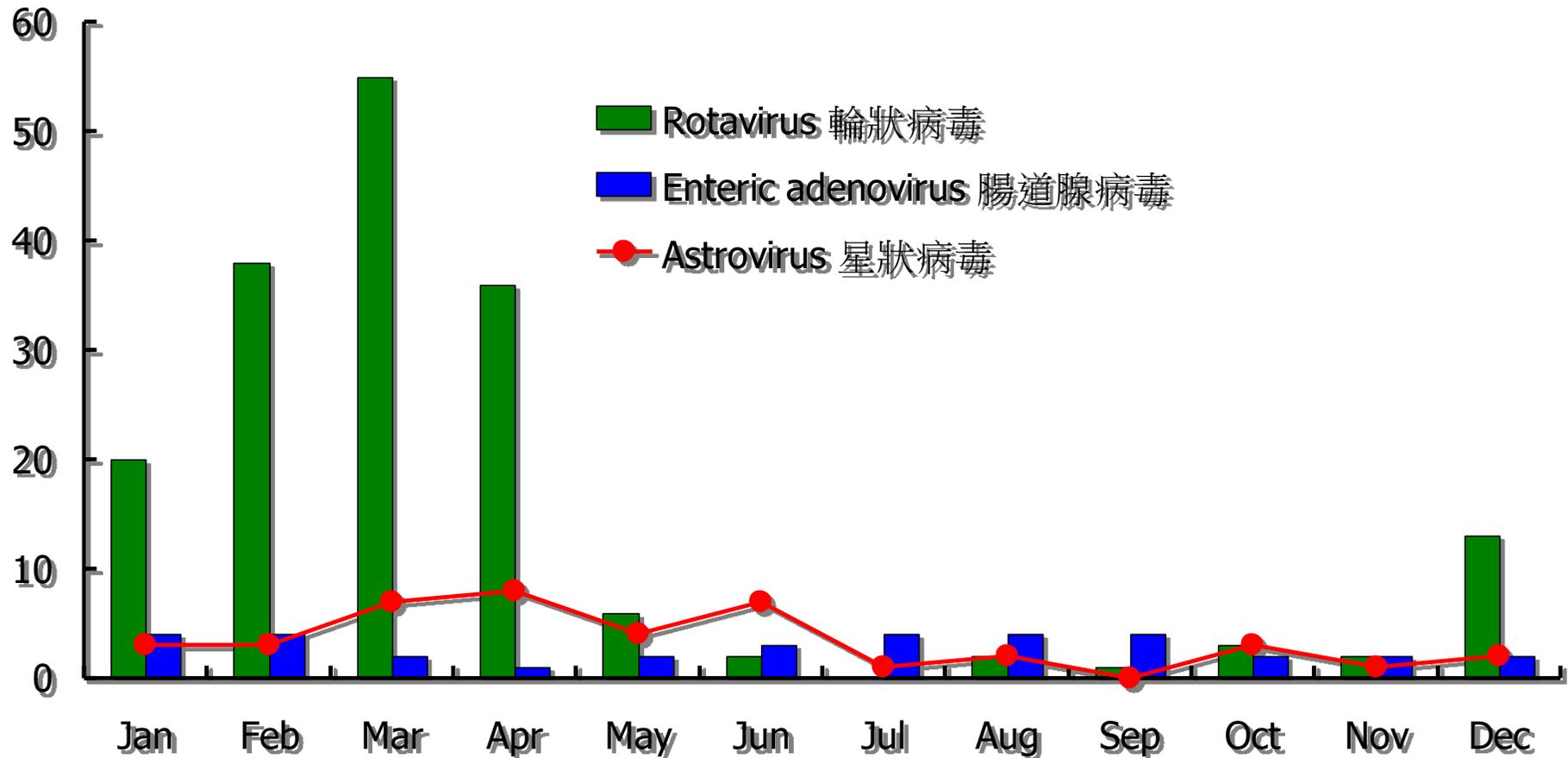
星狀病毒 (Astrovirus)



- > 大小約28-30nm，無套膜正價RNA病毒
- > 基因大小6.8 kb，目前有七種血清型
- > 全球性，佔所有腸胃炎住院病患中的3%至5%。
- > 主要侵擾小於二歲之嬰幼兒，但多為無症狀的感染。
- > 學校、照護中心及兒科病房輕微腹瀉之群突發的病因之一。
- > 潛伏期約24至36小時。
- > 症狀包括有嘔吐、腹瀉、發燒與腹痛。一般為症狀療法。
- > 一般病程約一至四天，與其它病毒性腹瀉無法區別。
- > 傳染途徑主要為肛-口方式，經由人與人間的交互傳染。
- > 院內感染性腸胃炎比率約5%至7%。
- > 電子顯微鏡、ELISA或RT-PCR診斷。



Seasonal distribution of astrovirus in relation to RV / AdV diarrhea during 1988-91 US





兒童星狀病毒腸胃炎的臨床特徵

Clinical characteristics of 15 children with diarrhoea caused by astrovirus alone

Characteristic	No. (%) of children
Age in months	
<6	3 (20.0)
7-12	2 (13.3)
13-24	2 (13.3)
>24	8 (53.3)
No. of diarrhoea stools/24 h	
2-5	6 (40.0)
6-9	8 (53.3)
≥10	1 (6.6)
Type of stool	
Watery	7 (46.6)
Loose	6 (40.0)
Mucoid and/or bloody	2 (13.3)
Duration of diarrhoea in days	
Median	9
<7	8 (53.3)
8-14	4 (26.6)
≥15	3 (20.0)
Abdominal pain	5 (33.3)
Vomiting	5 (33.3)
Fever	4 (26.6)
Nausea	8 (53.3)
Loss of appetite	11 (73.3)
Respiratory symptoms	1 (6.6)

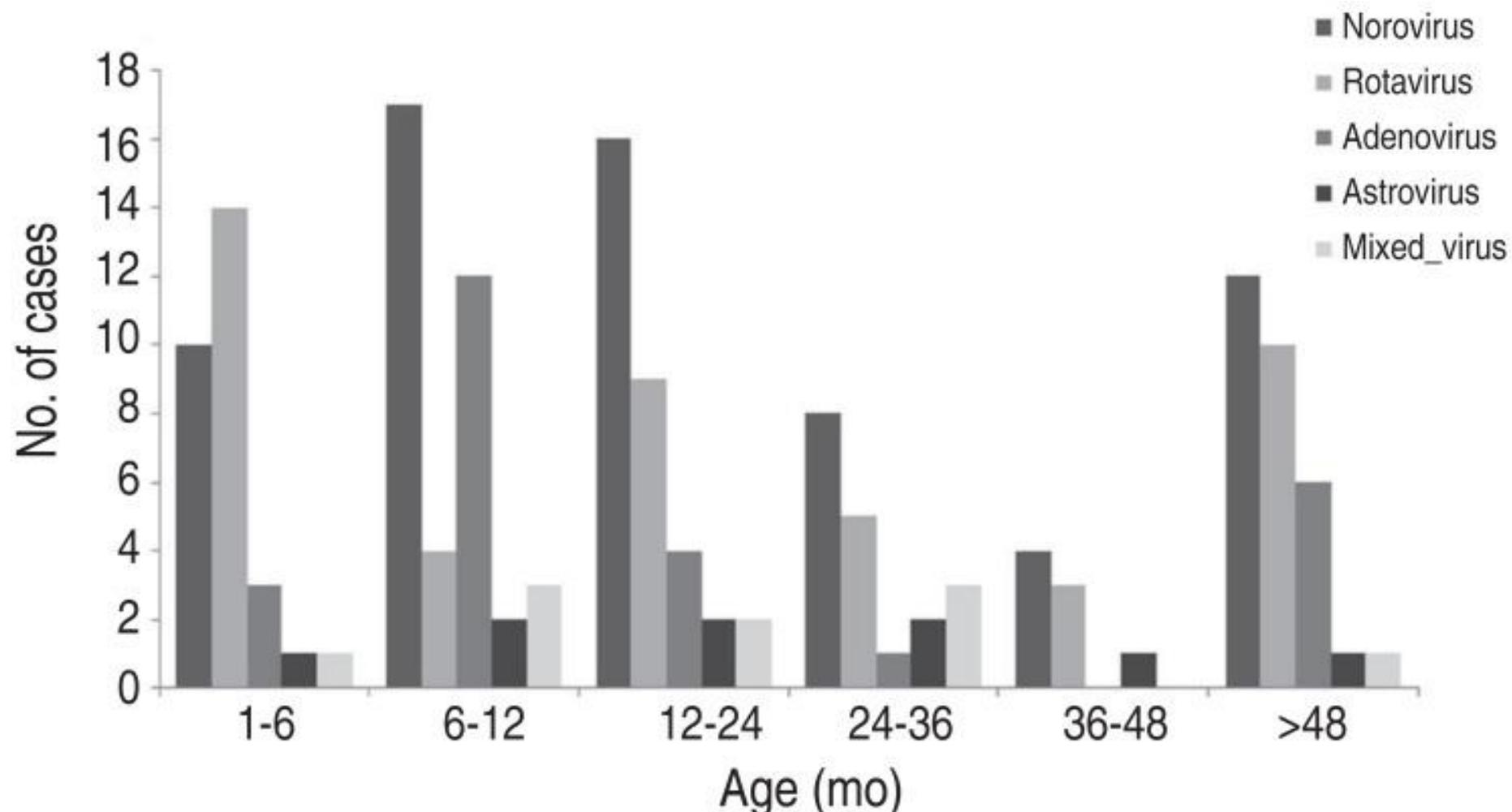


Incidence of causative viruses among children with acute diarrhea, according to results of multiplex reverse transcription polymerase chain reaction

Virus	No. of cases (%)
Virus not detected	188 (54.5)
Virus detected	157 (45.5)
Norovirus	67 (19.4)
Genogroup I + II	3 (0.8)
Genogroup II	64 (18.6)
Rotavirus	45 (13.0)
Astrovirus	9 (2.6)
Adenovirus	26 (7.5)
Mixed viral infection	10 (2.9)



Prevalence of different viral infections according to age





Clinical symptoms of children with viral infections

Symptoms	Norovirus (n=67)	Rotavirus (n=45)	Adenovirus (n=26)	Astrovirus (n=9)	Mixed infection (n=10)	<i>P</i> value
Diarrhea	34 (50.7)	28 (62.2)	21 (80.8)	9 (100)	4 (40.0)	0.172
Vomiting	39 (58.2)	26 (57.8)	17 (65.4)	3 (33.3)	5 (50.0)	0.391
Fever	24 (35.8)	30 (66.7)	9 (34.6)	6 (66.7)	9 (90.0)	0.004
Abdominal pain or irritability	31 (46.3)	13 (28.9)	10 (38.5)	2 (22.2)	4 (40.0)	0.383
Dehydration	8 (11.9)	15 (33.3)	8 (30.8)	2 (22.2)	2 (20.0)	0.044

Rapid identification of rotavirus , adenovirus and norovirus using immunochromatography test among infantile diarrhea , Iraq

TABLE 4: Clinical features of diarrheal infections

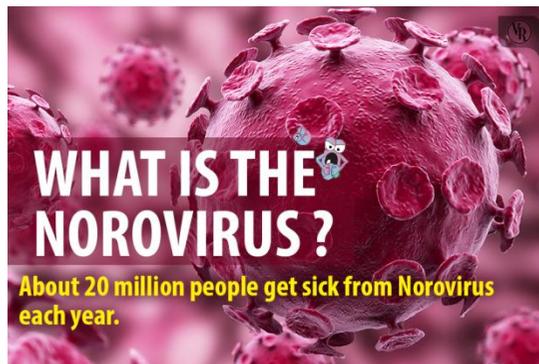
Clinical features	Type of Virus		
	Rotavirus	Norovirus	Adenovirus
Duration of diarrhea more than 7 days	50	22	15
Watery or mucosal stool consistence	42	24	21
Fever > 38°C	44	19	18
Weakness	49	21	18
Abdominal pain	40	26	11
Vomiting	40	16	14



Distribution of the targeted enteric viruses detected by PCR & RT-PCR in stool samples collected from infants with acute gastroenteritis according to the nutritional state

PCR	Gr.	Bottle feeding		Breast feeding		Mixed feeding		Total		p-value
		No.	%	No.	%	No.	%	No.	%	
Rota		13	35.1	5	13.5	19	51.3	37	100	<0.001
Noro		5	35.7	2	14.3	7	50.0	14	100	<0.05
Adeno		2	28.6	1	14.3	4	57.1	7	100	>0.05
Astro		1	33.3	0	0	2	66.7	3	100	>0.05
HBoV		0	0	0	0	2	100	2	100	>0.05

諾羅病毒臨床診療與防治措施



臺中榮民總醫院兒童醫學部兒童感染科
陳伯彥



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EYEWITNESS NEWS

Cruise ship with ill passengers returns to port



Many recent cruise ship passengers have suffered a contagious stomach virus, including those on the Amsterdam.

By The Associated Press

(12/2/02 - Miami) — A Carnival cruise ship returned from a three-day sail Monday carrying more than seven dozen people who had contracted a gastrointestinal virus, health and police officials said.

The Fascination, an 855-foot ship that carries as many as 2,052 passengers and 920 crew members, returned to the Port of Miami waters shortly before 5 a.m. after a voyage to the Bahamas.

It was not immediately clear how many passengers were aboard the cruise, which departed Miami on Friday afternoon.

Florida's Department of Health alerted police officials Sunday that the ship would return to port with numerous sick passengers, although Carnival spokesman Tim Gallagher refused to confirm if anyone aboard was ill.

"We got a call advising us that the Fascination was coming in with 86 people aboard with

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FIGURE 13.7

A Case of Norwalk Virus Gastroenteritis

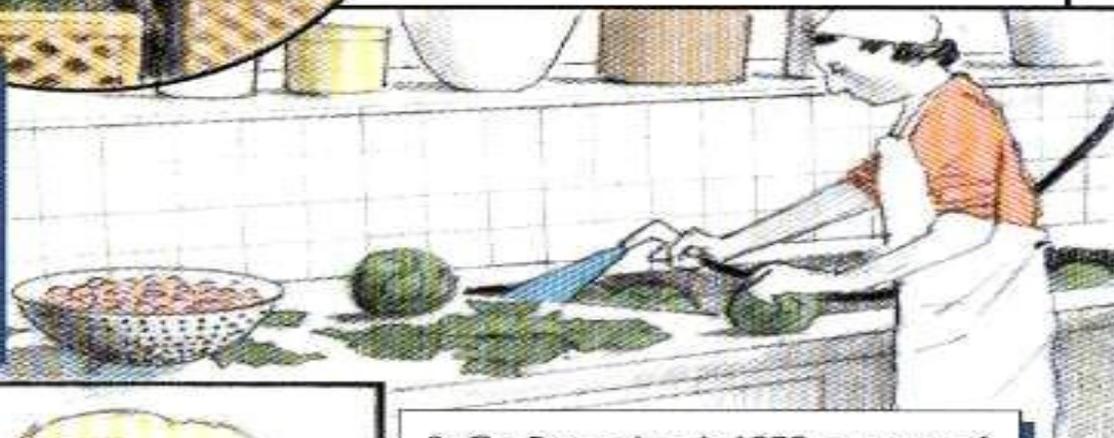
This outbreak occurred in New Jersey during December 1979. It was one of the first reports of Norwalk virus gastroenteritis linked to any food other than shellfish.

諾羅病毒 食物中毒



1. In early December 1979, a New Jersey restaurant and catering facility received a shipment of lettuce from a produce market in Philadelphia.

2. A worker who had just finished washing some shrimp then washed some of the lettuce in the same sink. The shrimp and the lettuce were prepared on the same table.



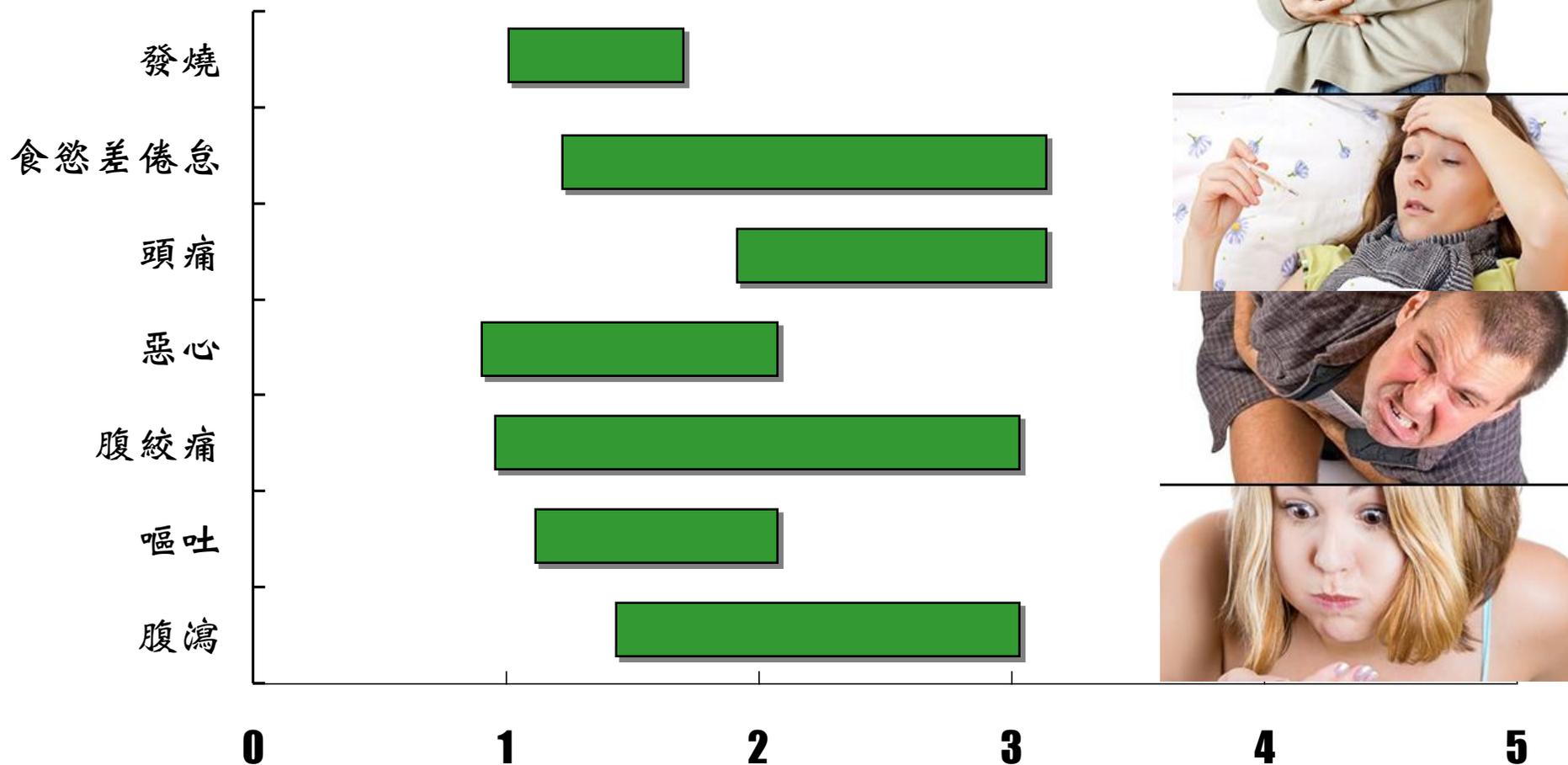
3. On December 6, 1979, a group of businesspeople attended a luncheon banquet at the restaurant. The restaurant served green salad made with the lettuce. A second group of businessmen and women received cole slaw instead of salad.



4. About 30 hours later, 63 of the 87 people who ate green salad developed gastroenteritis. None of those who had cole slaw became ill. Health department microbiologists identified Norwalk virus as the agent and theorized that it had entered the lettuce from contaminated shrimp.



諾羅病毒腸胃炎臨床特徵



近三個月出現數起類諾瓦克病毒感染聚集事件，疾病管制局呼籲 各級人口密集機構加強管控措施，防範類似案例的發



疾病管制局

Center for Disease Control, Taiwan, R.O.C.

▶ SITEMAP

▶ ENGLISH

台灣地區過去三個月內，各級學校、老人之家、呼吸照護病房、精神科病房和身心障礙機構等單位，陸續通報多起學生或住民發生腸胃道集體感染的事件，已有四起18名案例證實是類諾瓦克病毒(Norovirus)的感染，另有三起百餘名疑似冬季急性腸胃炎疫情現正調查中。

美國疾病管制中心報導：2002年間，美國地區類諾瓦病毒的感染流行，估計大約有2,300萬人受到感染，其中5萬人需住院治療，310人死亡(多數為老人、嬰幼兒和免疫功能不全的病患)，造成60%~80%的腸胃道群聚感染事件，包括：學校、餐廳、醫院、安養中心、托兒所、渡假中心等人口密集機構；該報告顯示，只要早期的發現並採取適當管控措施，疫情大多可以在兩週以內獲得控制。近期國際間較嚴重的疫情資料顯示，日本福山地區一間安老院2004年12月下旬傳出病毒性腸胃炎疫情，42名感染的老人中有6人死亡；美國也傳出一艘觀光郵輪120名遊客及員工陸續出現爆發病毒性腸胃炎疫情。

諾羅病毒大爆發，根據疾管署的最新檢驗結果，今年流行的諾羅是GII.17型，並非之前的GII.14或是GII.16型，目前各國對GII.17型的認識有限，包括傳染性、致病力都還無法清楚掌握，而且這傳染力很強，估計一名患者至少可傳染二十人。昨天正好開學，恐怕這波病毒將襲捲校園

3天200人中招 諾羅病毒罩武陵農場

台中市衛生局長徐永年指出，21日接獲宜蘭縣衛生局通報，有41名遊客投宿富野渡假村後，出現上吐下瀉症狀到宜蘭就醫，22日就派員到該飯店進行食物、環境、資材及人員檢體採檢，徐永年說，富野渡假村坦承，過年期間陸續有5名員工出現腸胃炎症狀，目前已勒令其餐廳暫停供餐，並進行環境衛生改善，



蘋果即時

諾羅病毒攻陷阿里山

自17到20日，阿里山森林遊樂區內的高檔飯店「阿里山賓館」陸續傳出員工及遊客10多人上吐下瀉送醫，衛生局採檢體化驗，24日證實3名廚工感染，賓館已展開大規模漂白水消毒，14日一名吳姓廚工因血壓飆高，送往阿里山衛生所再轉診山下醫院，館方請廚工休息2日再上工，不料17日出現噁心、腹瀉等症狀，另名廚工也身體不適，18日又有3名員工因相同症狀前往香林衛生室，前後共10人不適、7人送診。



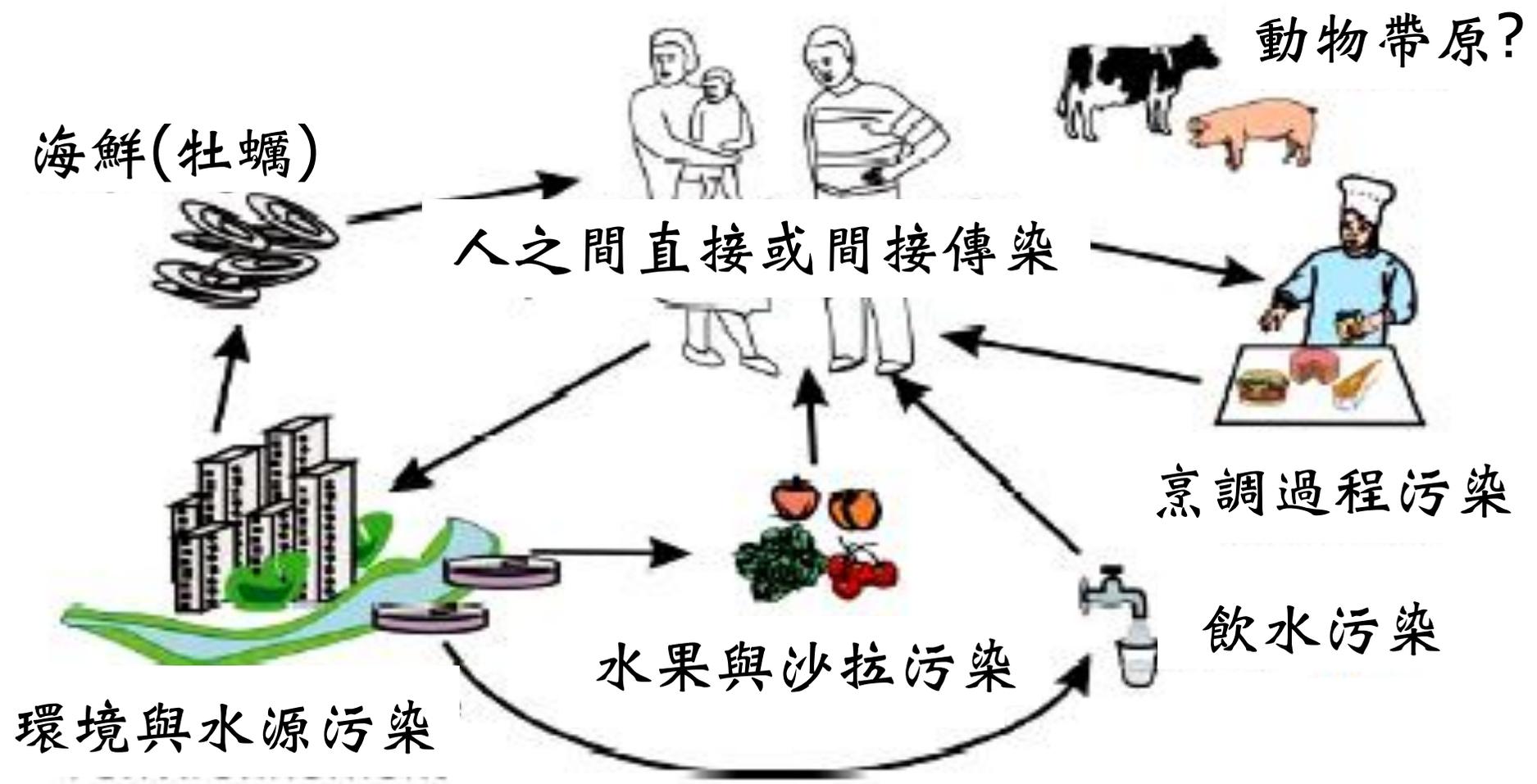
烤海鮮當心烤到「諾羅」

秋天是享受肥蟹、牡蠣、生蠔、貽貝等的最佳季節，在台灣有許多饕客喜歡生食海產，只是受到海洋環境污染影響，近年來國內外吃海鮮吃出問題的案例層出不窮，主要包括諾羅病毒(Norovirus)、腸炎弧菌(*Vibrio parahaemolyticus*)、大腸桿菌(*E. coli*)等感染引發腸胃炎，特別是中秋烤肉將近國人需特別留意以免敗興而歸。

近年來發生諾羅病毒案例爆增，每年引起全球超過2.7億人感染，約20萬人死亡，多數死亡病例發生在開發中國家。在台灣也發生多起病例像今年初台中武陵農場曾爆發大規模諾羅病毒疫情，三月新北市安康高中畢業旅行也發生諾羅病毒感染；七月從韓國進口的生蠔感染諾羅病毒造成綠島遊客食物中毒等事件。

2015/9/28

諾羅病毒(Noroviruses)(諾瓦克)流行病學



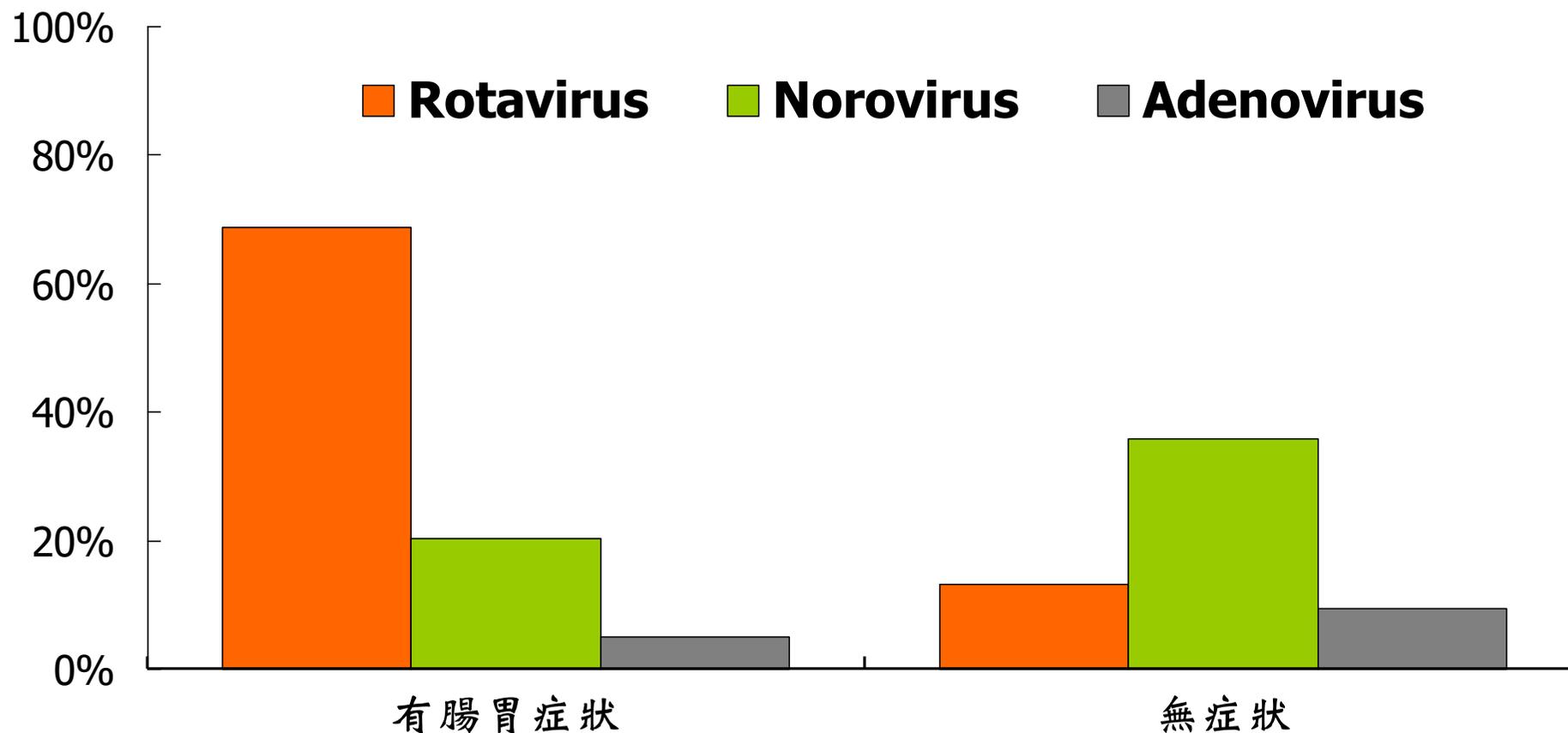


諾羅病毒在公共衛生上的角色~ 常見且難以預防及控制

Feature	Consequence
低病毒致病量 (<100 virus)	Droplet & person-person spread 2 nd spread, food handlers spread
無症狀的病毒排泄期長 (>2 wks)	Increased risk 2 nd spread, problems with control of food handlers
環境穩定性高 (10 ppm chloride ,freezing, heating 60°C)	Hard eliminated from contaminated water; virus in ice, cooked oysters
型別變異大 (many genetic /antigenic types)	Need composite diagnostics; repeat inf. by many diff. Ag types, easy underestimate prevalence
免疫保護效果不佳 (易再感染)	Childhood exposure not protect adult disease; difficult vaccine for lifelong
自然帶原者	Only human - related strain in animal

中國西安兒童腸道病毒檢出率(有症狀或無症狀)

Symptomatic and asymptomatic enteric viral infections among hospitalized children in Xi'an, China



Zhang S. J Med Virol 2011;May 26



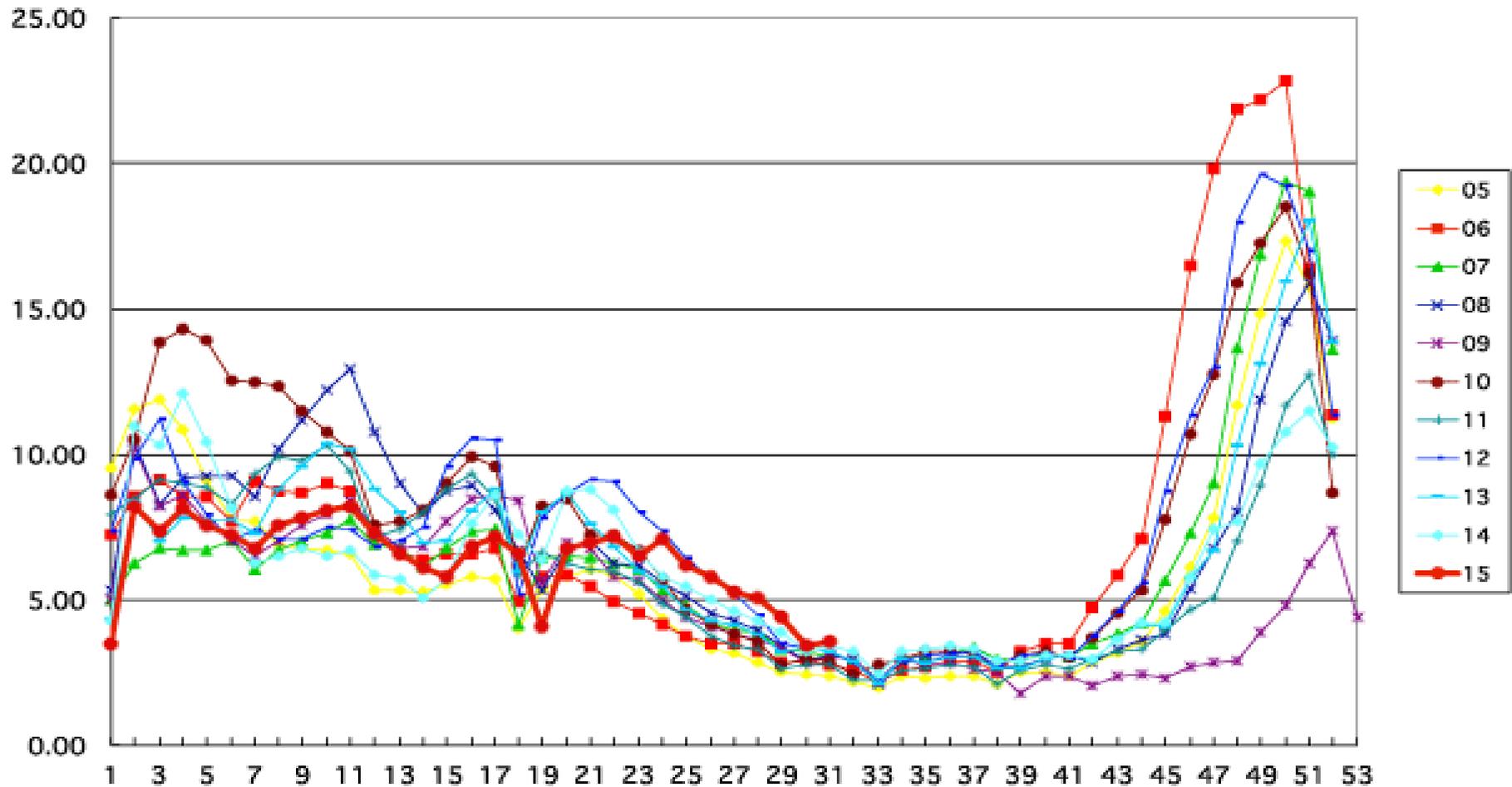
Norvirus 群突發的特徵

	食物中毒	散播性
季節	夏天=冬天	夏天<冬天
感染型態	1~2天內大量病患	1週內逐漸增加病患
傳染模式	食物污染傳染 常有第二波	人傳人或 排泄或嘔吐物污染環境傳染 (廁所,水槽等)
傳染場所	餐廳,學校,渡假中心 遊輪等	精神科病房,呼吸照護中心 老人之家,托兒所等
受感染者	正常人	照護者與行動不便的受照 護者或自我衛生能力不足者
傳染源	食物受污染	醫護人員, 照護者, 清潔工, 家屬



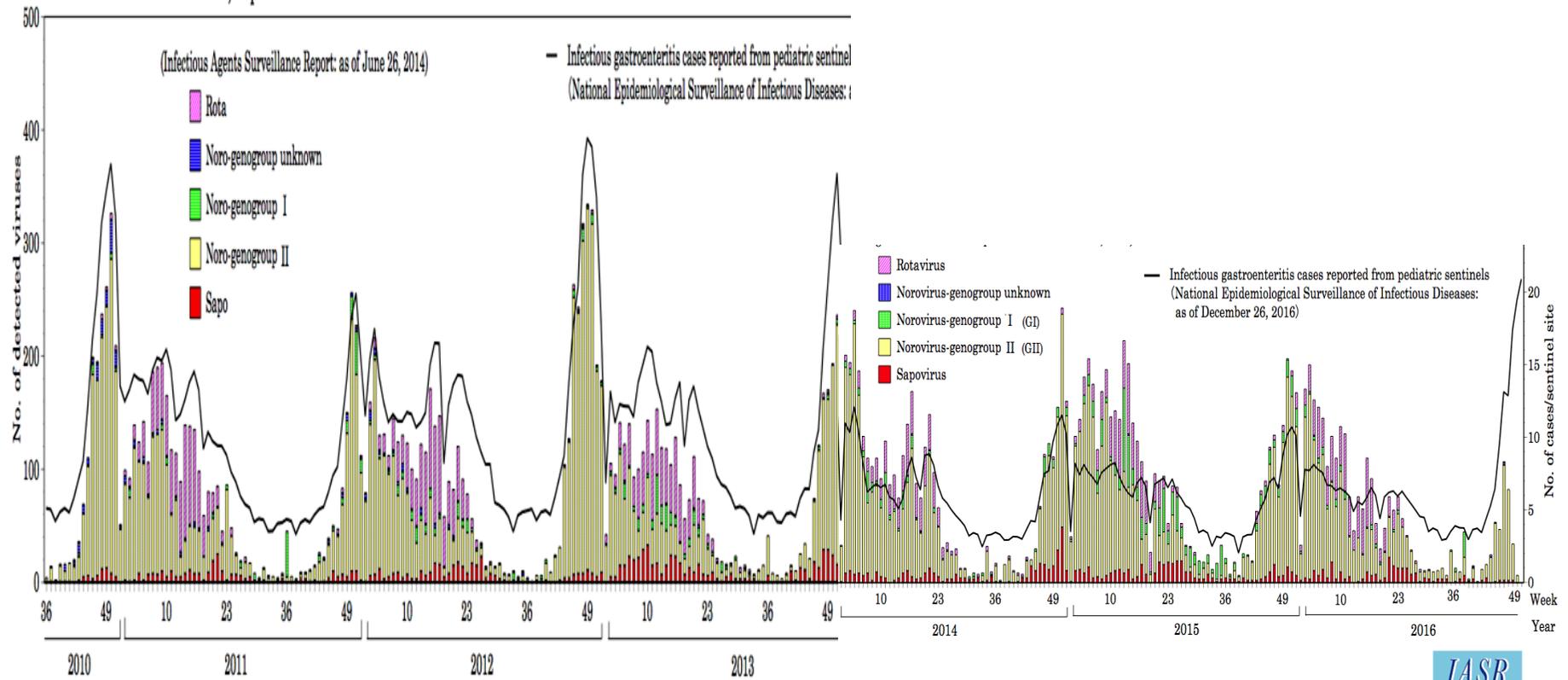
日本傳染性腸胃炎流行病學監測

Infectious gastroenteritis cases reported per sentinel weekly in Japan

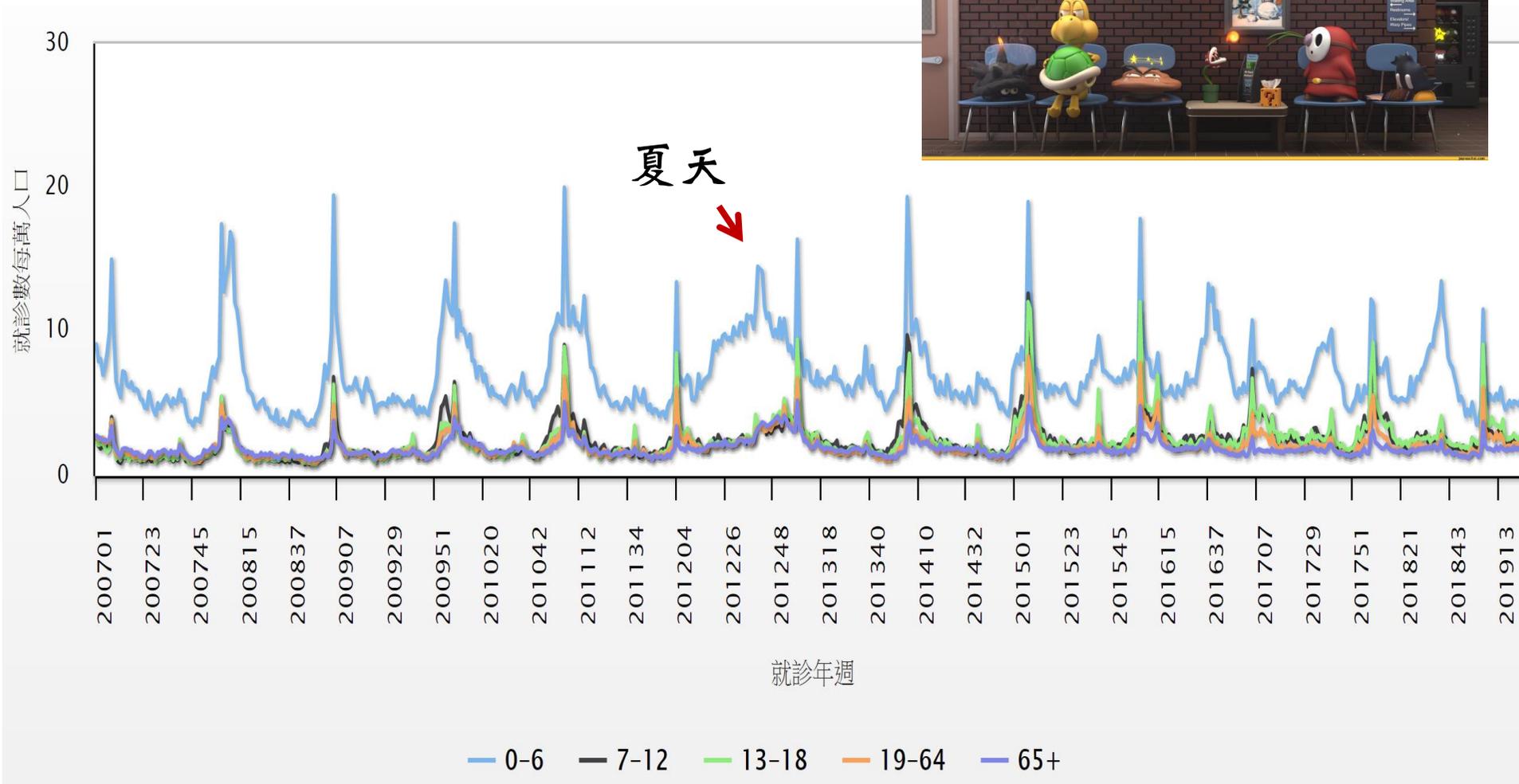


日本病毒性腸胃炎病因監測

Figure 1. Weekly number of reported cases of infectious gastroenteritis per sentinel clinic and detection of norovirus, rotavirus and sapovirus
2010/11-2013/14 seasons, Japan

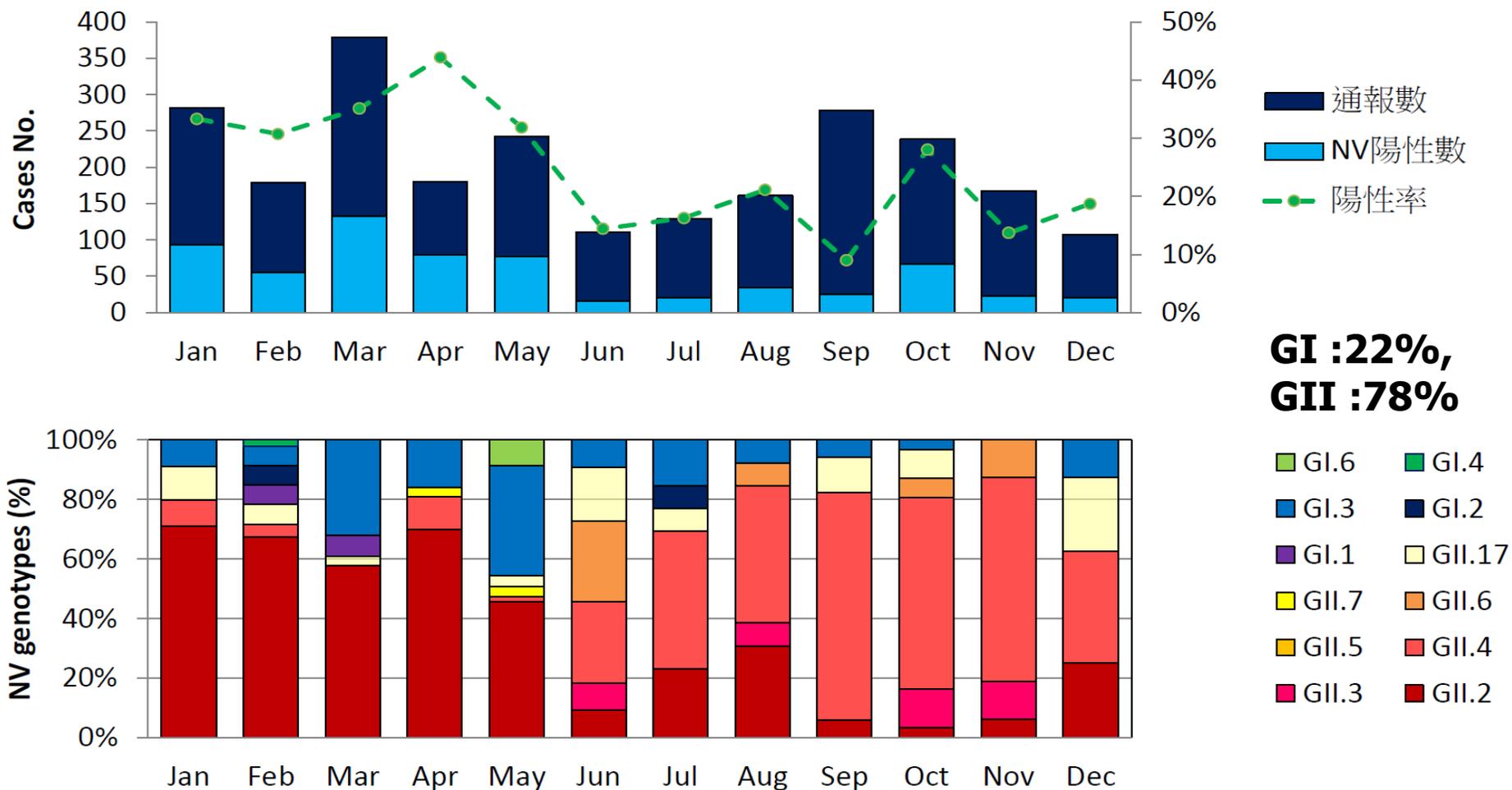


台灣傳染病統計資料查詢系統~急診腹瀉監測



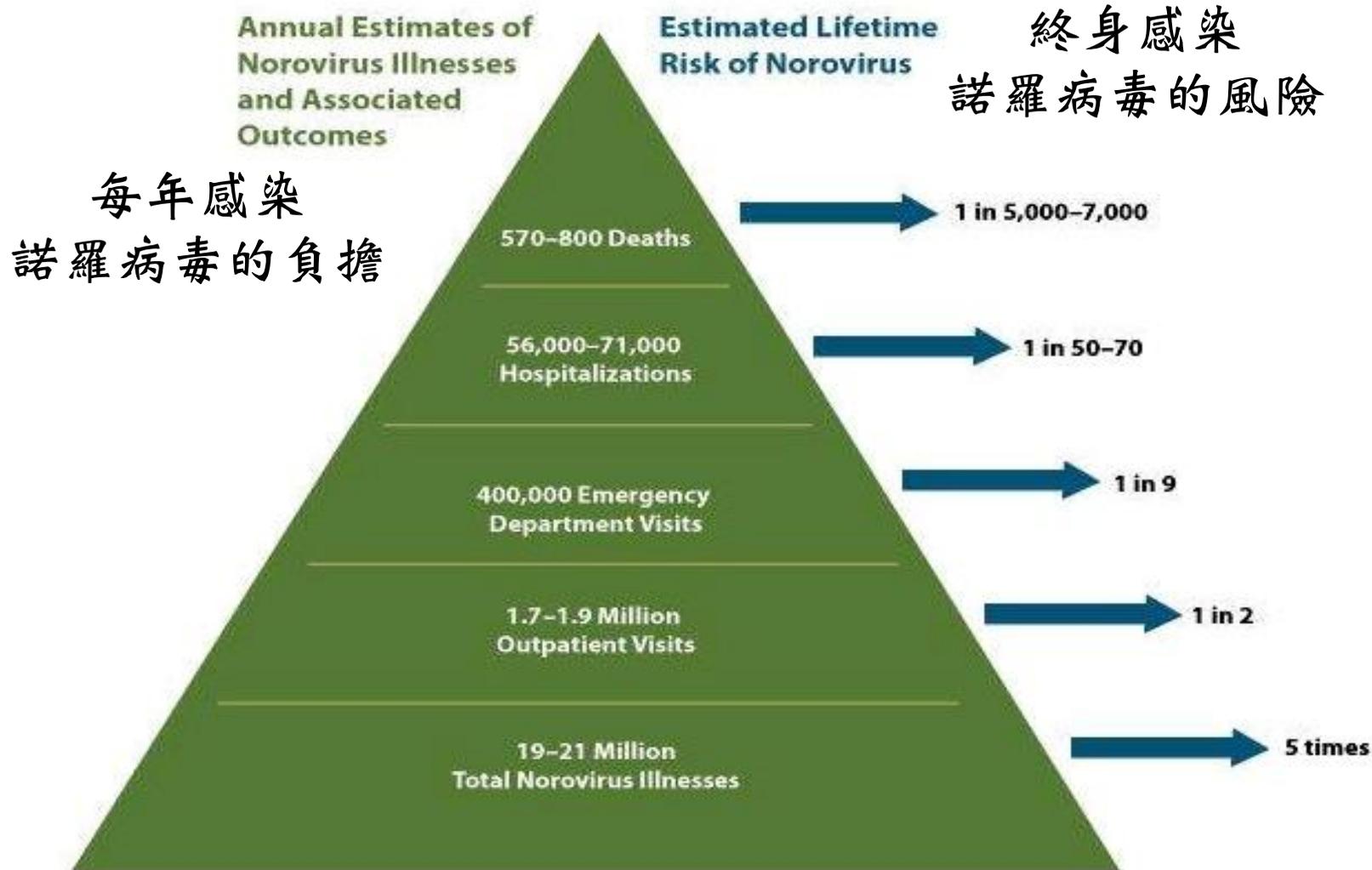


2018年台灣諾羅病毒監測與基因型別分布

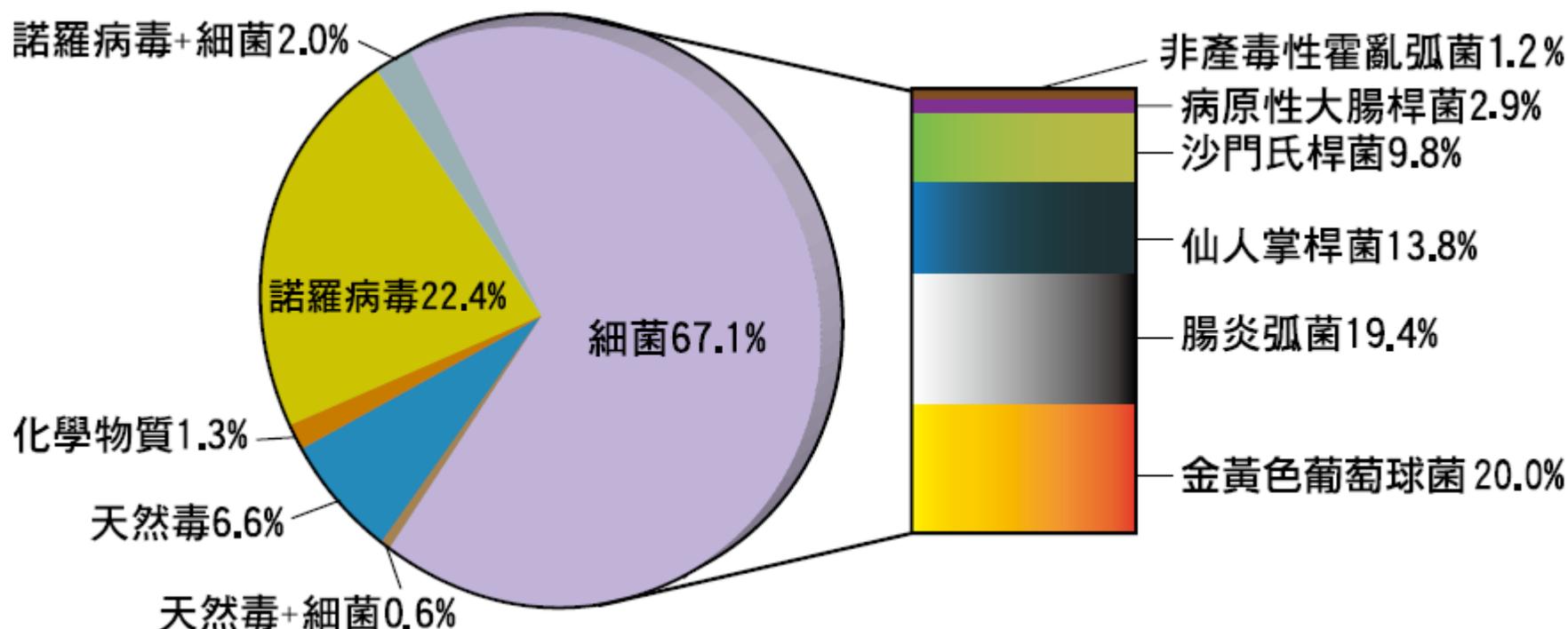




諾羅病毒腸胃炎流行病學與疾病負擔



2012年台灣地區食品中毒 病因物質判明案件數百分比



諾羅病毒流行病學

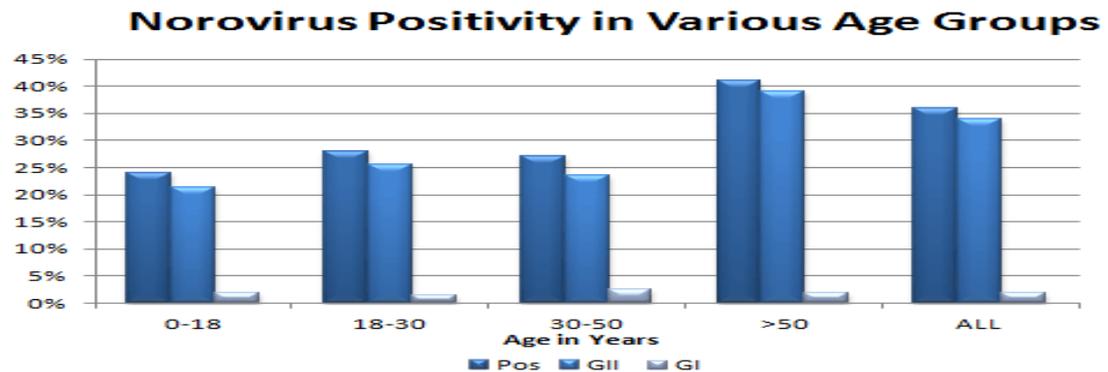
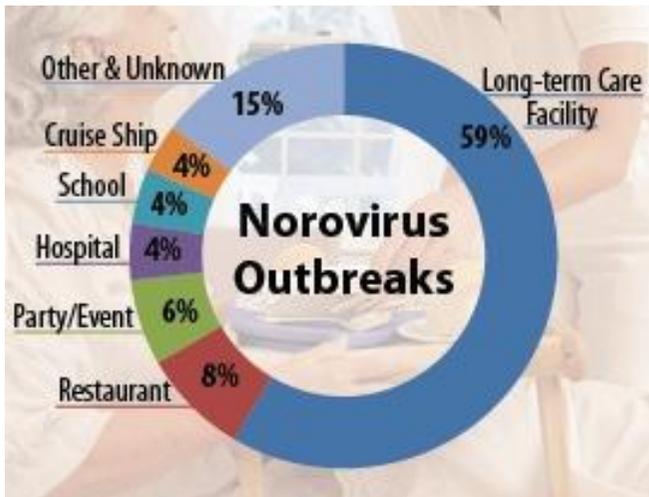
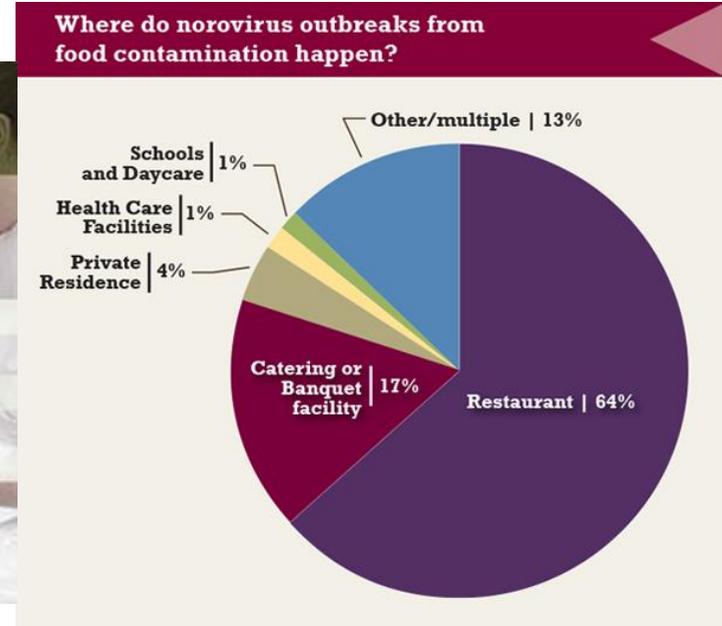
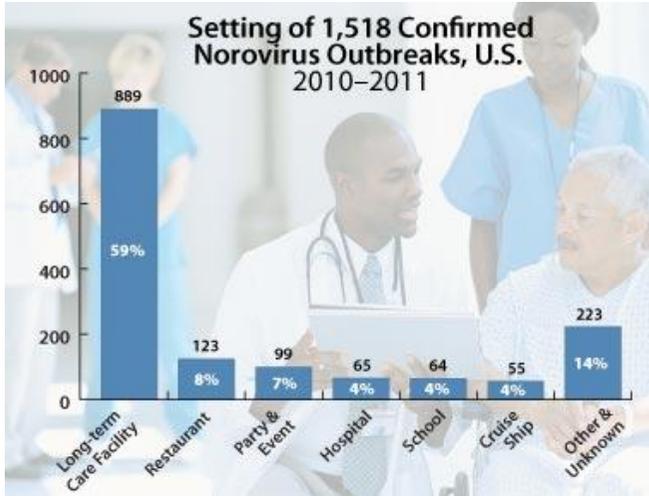
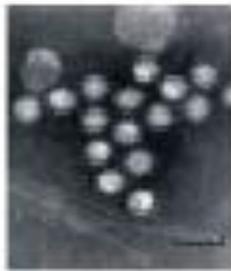


Figure 2. Norovirus positivity rate (%) and genogroup in various age groups.

諾羅病毒的診斷

Norovirus Diagnosis

Microscopie électronique



Particules virales intactes

Isolement par culture sur cellules et Examens sérologiques

non adaptés à ce type de diagnostic



ELISA

ELISA	Rapid antigen test	Real time RT-PCR	No. of specimen (%)
Positive	Positive	Positive	70 (38.0)
Positive	Positive	Negative	9 (4.9)
Positive	Negative	Positive	8 (4.3)
Negative	Positive	Positive	0 (0.0)
Positive	Negative	Negative	8 (4.3)
Negative	Positive	Negative	2 (1.1)
Negative	Negative	Positive	1 (0.5)
Negative	Negative	Negative	86 (46.7)
Total			184 (100)

RT-PCR



Constituants antigénique ou génomique

多重病原基因快速檢驗

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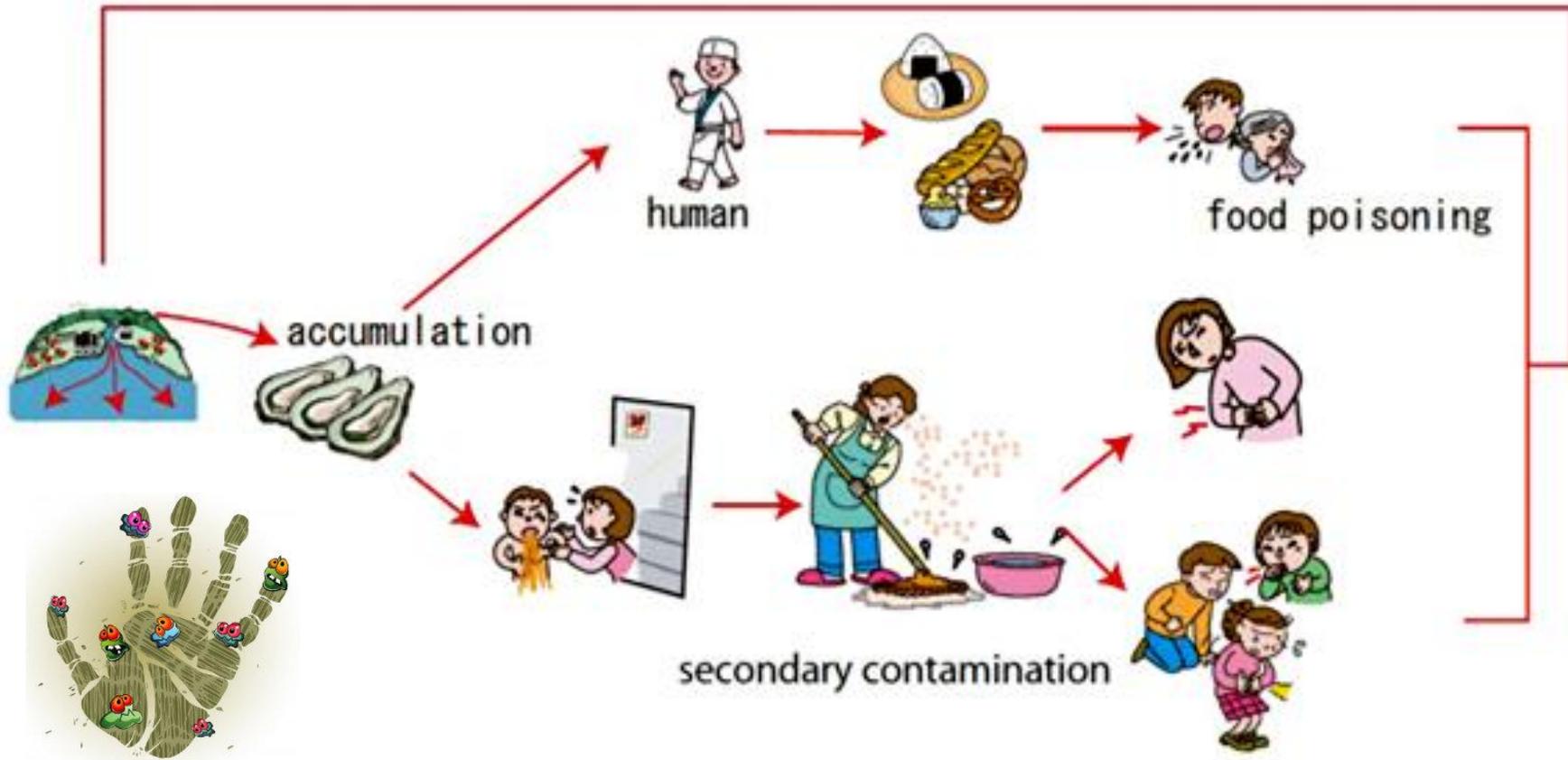
不幸感染諾羅病毒腸胃炎時, 該怎麼辦?

What should I do if I become sick with Norovirus AGE?

- ~多喝水
- ~如廁後多洗手
- ~勿與人共享用食物香菸與杯子
- ~儘可能單獨使用廁所 (否則應增加清潔消毒次數)
- ~腸胃炎期間勿為親人準備飲食
- ~除非健康上的特別考量, 否則不建議須特別請醫師診療;
因為容易散播病毒給他人, 但可電話請教醫師
- ~腸胃炎持續時間過久, 或糞便/嘔吐物帶有血絲-應考慮診療
或住院
- ~只是腸胃炎症狀持續, 不建議返回工作崗位

諾羅病毒的傳染途徑與控制

The study of norovirus stability and inactivation in the environment





諾羅病毒感控指引

諾羅病毒(Norovirus)感染控制措施指引



2013/07/23 訂定

GUIDELINE FOR THE PREVENTION AND CONTROL OF NOROVIRUS GASTROENTERITIS OUTBREAKS IN HEALTHCARE SETTINGS

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NATIONAL GUIDELINES ON
THE MANAGEMENT OF OUTBREAKS OF
NOROVIRUS INFECTION IN HEALTHCARE SETTINGS



Prepared by the
Viral Gastroenteritis Subcommittee of the Scientific Advisory Committee of the
National Disease Surveillance Centre



TECHNICAL REPORT

Prevention of norovirus infection
in schools and childcare facilities



嬰幼兒感染隔離控制的建議

濕洗手 >> 乾洗手

建議之隔離方式

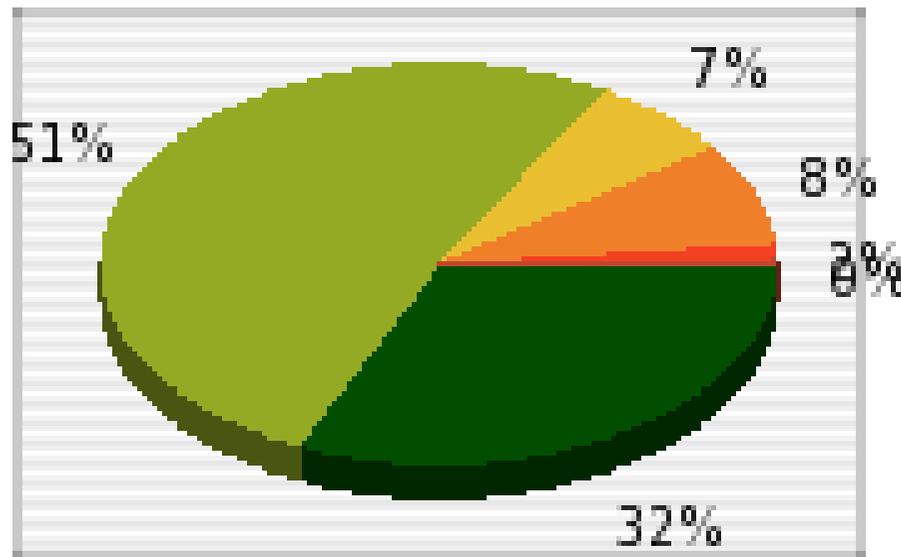
皮膚膿瘍：有包紮	標準隔離
皮膚膿瘍：無包紮	接觸隔離
結膜炎：細菌性, 匹依菌, 淋病, 腸病毒, 腺病毒	標準隔離
巨細胞病毒(CMV)	標準隔離
腸病毒 (Coxsackievirus, echovirus) 	接觸隔離
腹瀉：細菌或病毒(輪狀病毒與諾羅病毒) 	接觸隔離
黴菌：念珠菌, 黃麴菌	標準隔離
A 型肝炎	接觸隔離
皰疹病毒(HSV)：母親或嬰兒	接觸隔離
HIV (AIDS)	標準隔離

民眾對諾羅病毒的觀感

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How do you feel about the norovirus epidemic?



-  Extremely anxious
-  Quite anxious
-  Neither anxious nor not
-  Not really anxious
-  Not anxious at all
-  Don't know about it

腹瀉症候群防治

