Measles and rubella: a clinical refresher

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2 April 2025



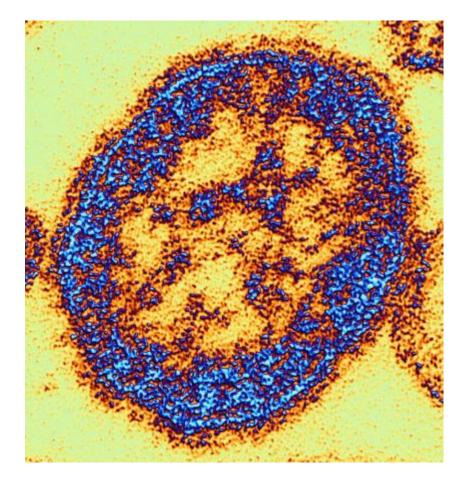
Overview

• Rubella and congenital rubella syndrome

- Clinical presentation
- Notification
- Support and referral for CRS

• Measles

- Some virology
- A case of fever-rash....
 - Thinking with the clinician
- A second case of fever-rash
 - Thinking with the infection-prevention and control practitioner
- A 3rd-4th-5th etc case of measles
 - Thinking with the public health practitioner
- Measles prevention, elimination and eradication



Rubella and CRS – clinical presentation

- Acute rubella
 - A significant proportion of infections (25-50%) are asymptomatic
 - Incubation period 14-21 days
 - Prodromal illness 1-5 days before rash (usually lymphadenopathy)
 - Rash pinpoint macular erythematous sometimes itchy, beginning on face, progressing to trunk, extremities within 24 hours. Lasts for 3 days
 - Self-limiting with spontaneous recovery



- Congenital rubella syndrome
 - Classic triad cataracts, congenital heart defects, sensorineural deafness
 - Ophthalmic abnormalities
 - 40% of cases have some abnormality
 - 25% have cataracts, bilateral in 50%
 - Other abnormalities include pigmentary retinopathy ('salt and pepper'), glaucoma, chorioretinitis, microphythalmia
 - Cardiac defects

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- Patent ductus arteriosis- 20%
- Peripheral pulmonary artery stenosis 12%
- Pulmonary artery hypoplasia, pulmonary or aortic valvular stenosis co-arctation of the
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Rubella and CRS – case definition and notification

- Acute rubella
 - Notify on clinical suspicion (category 1)
 - Use the NMC app
 - Submit a completed 'Measles-rubella' case investigation form with blood for IgM testing.

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MEASLES-RUBELLA CASE INVESTIGATION FORM (health	Notif	able Medical Con	ditions (NMC)	Case Notification Form		Summer.
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	Method of diagnosis			(many or	CONTRACTOR CONVERTING	international and internationa	
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(Croup) Corneal Ulceration Blindness Encephalitis Arthritis Other: If f	 Treatment given for the NMC Date of disprovis 				Date of symptom onset		
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yes, number of doses: 1 2 >2 Date of last measles vaccination:	_//					D!!	

- Congenital rubella syndrome
 - Notify on clinical suspicion (Category 1)
 - Use the CRS Case investigation form
 - Submit blood/urine for serology and PCR to NICD

Page 1 of 3	Patient initials 22 Patient date of birth (dd/mm/yyyy) 22/22/2222
· ·	la Syndrome Case Report form
Part A: Notifyer's details Notifyer's name and surname:	Address of health facility:
	District of health facility:
Facility where form completed:	Province of health facility
	Notifyer's contact details (primary):
Role: Doctor IPC nurse	Notifyer's contact details (alternate):
Other 🗋 state:	
	1
Part B: Patient demographic and cl	inical details (see page 2)
Patient's Name and surname:	Sex: Male 🗧 Female 🗌 Other 🗌
	Date of birth: (dd/mm/yyyy)
Facility where CRS diagnosed:	Age at diagnosis: months: 2 days: 2 year(s): 2
	Race group of infant: Black _ Indian _ Colored _

Rubella and CRS – Clinical care and management

- Acute rubella
 - Complications
 - Arthritis/arthralgia 60-70% of adolescents and adult women 1 week after rash, usually 3-4 days, may persist
 - Rarely (1 in 6,000) post infectious encephalitis may occur
 - Clinical management
 - Symptomatic only.
 - Persistent headache with altered mental status refer for lumbar puncture to rule out
 - Infection prevention and control
 - No need for quarantine or school closure
 - Incubation period is 14-21 days
 - Virus excretion commences 7 days before rash so contacts who are susceptible are likely already infected before the index case is diagnosed.
 - Pregnant women who are in their first trimester and are contacts of a confirmed case
 - SHOULD NOT receive vaccine
 - Should have rubella serology for IgG taken immediately
 - Should be referred for specialist assessment at ANC

- Congenital rubella syndrome
 - Complications
 - A debilitating condition, but many survive
 - Clinical management
 - High index of suspicion for diagnosis with early referral for specialist paediatric care
 - Basic assessment
 - Ophthalmic assessment with early surgery for cataracts
 - Hearing assessment with support for family
 - Cardiology assessment with appropriate and timely surgical intervention
 - Ongoing monitoring
 - Close observation for milestones with early referral for care
 - Psychosocial support for family

To evaluate the natural history of congenital rubella, 50 of the original cohort of patients reported by Gregg were reviewed, 25 years later, at the Children's Medical Research Foundation, Royal Alexandra Hospital for Children.¹¹ These subjects had been born in Australia between 1939 and 1944: 48 were deaf, 26 had cataracts or retinopathy, 14 had cardiac defects, five were mentally handicapped, and one had diabetes mellitus type 2.12 This cohort of patients was followed up again in 1991, when most were 50 years old (seven had died). Forty had a full clinical assessment; five had clinical diabetes mellitus type 2.13

We report here the results of the 60year review in 2000–2001, when the cohort members were 60 years old; 40 were still alive (Box 2).

3: At school in 1948

School class of deal children and their teacher in 1948, with four of the subjects described in this review (used with the kind permission of the owners of the photograph). HISTORY

Gregg's congenital rubella patients 60 years later

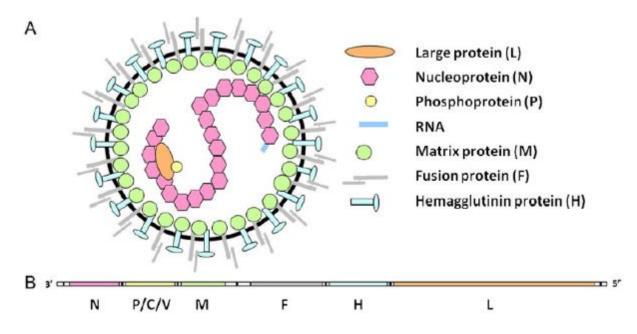
Jill M Forrest, Fiona M Turnbull, Gary F Sholler, Richard E Hawker, Frank J Martin, Trevor T Doran and Margaret A Burgess

AT THE UNIVERSITY OF SYDNEY medical students attend lectures in the Norman Gregg Theatre, but few know it was Gregg who identified the causal relationship between rubella in women during pregnancy and congenital defects in their offspring. (see Box 1).

Background: In 1941, a Sydney ophthalmologist, Norman McAlister Gregg, correctly identified the link between congenital cataracts in infants and maternal rubella early in pregnancy. Fifty of Gregg's subjects with congenital rubella, born in 1939–1944, were reviewed in 1967 and again in 1991. We reviewed this cohort in 2000–2001, 60 years after their intrauterine infection.

Some measles virology

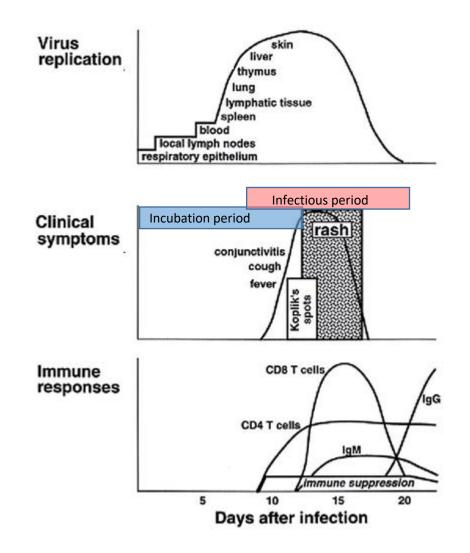
- Measles virus
 - Negative stranded, pleomorphic RNA virus (15,894 nucleotides)
 - Six structural proteins (H, F, M, N, L)
 - 2 non-structural proteins (P gene, transcribed into C and V proteins)
 - One serotype
 - 8 clades (A-H) with 23 recognized genotypes
 - Typing 450 nucleotides of the N protein
 - Genetically stable with very little variation
 - No animal hosts but monkeys can be infected



Bankamp et al. Genetic Characterization of Measles Vaccine Strains. JID 2011; 204:S533-548

Some measles virology

- Measles virus
 - Haemagglutinin molecule attaches to three human proteins
 - CD150 /SLAM Signaling lymphocyte activation molecule (SLAM) on T and B lymphocytes, and all antigen presenting cells
 - CD46 (widely distributed in human tissues)
 - CD147 extracellular matrix metalloproteinase inducer on epithelial cells including in respiratory tract.
- Pathogenesis
 - Enters respiratory tract
 - Multiplies in lymphoid tissues
 - Primary viraemia with dissemination to all tissues including respiratory tract
 - Incubation period 9-14 days
 - Infectious period 4 days before onset of rash, til 2-4 days after rash.
 - Rash signals formation of neutralising antibodies and clinical improvement



Adapted from WHO Immunological basis of Immunity to measles vaccine 2014

A case of fever and rash....

- Infant AM, 14 month infant
 - Presented on 24 November 2021 to the ED of a district hospital in Western Cape Province
 - Recently arrived from DRC (within last 28 days)
 - History
 - Developed fever, conjunctivitis, cough and rash
 - Rash started on 24 November (day of presentation)
 - Measles suspected, and specimens of blood and urine were submitted to NICD for testing



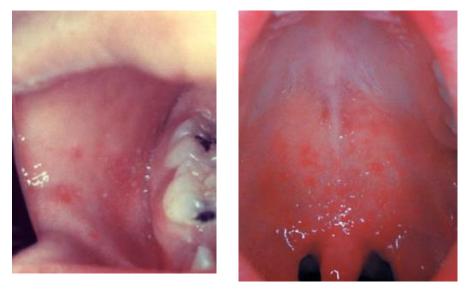
- History and clinical examination
 - Classically begins with malaise, and respiratory symptoms including cough & coryza, together with fever anorexia, conjunctivitis.
 - Rash
 - Erythematous, maculopapular, may become confluent
 - starts on face, progresses to extremities including palms and soles
 - Heals with desquamation (except palms and soles)
 - Worst symptoms on day 1-2 of rash

- Complications
 - Diarrhoea
 - Pneumonia
 - Often clinically inapparent, but when present, may be severe
 - Otitis media
 - Often in younger infants
 - Encephalitis (1 in 1000 cases)
 - Presents with headache, altered LOC, seizures
 - Mortality
 - Rates vary, but up to 20% in malnourished infants <1 year of age.

• Measles rash

Koplik's spots





https://www.cdc.gov/measles/symptoms/photos.html

Tod et al. Dermatological manifestations of measles infection observed in the 2009-2011 Western Cape epidemic. http://www.samj.org.za/index.php/samj/article/view/5342/4126

- Differential diagnosis
 - Rubella,



https://www.nejm.org/doi/full /10.1056/nejmicm1303608



https://www.gponline.com/infectiousdiseases-scarlet-fever/infections-andinfestations/infections-andinfestations/article/1324924

scarlet fever,

ullet



parvovirus B19, cytomegalovirus,



Drago F,. Future Microbiol. 2017 Feb;12:171-193. doi: 10.2217/fmb-2016-0147.

HHV6, HHV7,

https://step2.medbullets.com/pedi atrics/120584/roseola-infantum



meningococcaemia,

https://www.sciencedirect.com/scienc e/article/abs/pii/S0738081X19301476



Find full text for free at https://pubmed.ncbi.nlm.nih.gov/27838923/

• Differential diagnosis should not include Mpox

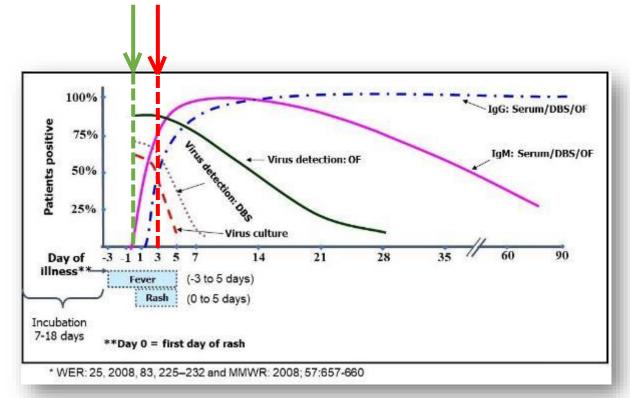
- Mpox Key Characteristics for Identifying Mpox
 - Lesions are well circumscribed, deep seated, and often develop umbilication (resembles a dot on the top of the lesion)
 - Lesions are relatively the same size and same stage of development on a single site of the body (ex: pustules on face or vesicles on legs)
 - Fever before rash
 - Lymphadenopathy common
 - Disseminated rash is centrifugal (more lesions on extremities, face)
 - Lesions on palms, soles
 - Lesions are often described as painful until the healing phase when they become itchy (crusts)

Examples of M'pox Rashes Photo credit: UK Health Security Agency



https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

- Laboratory diagnosis
 - Types of tests
 - Serology (antibodies)
 - PCR (detection of measles RNA)
 - Interpretation of both tests depends on
 - Type of sample and type of test done
 - Timing of collection of the sample relative to rash onset
 - Tests taken before or on day of rash-(green line)
 - PCR likely to be positive
 - IgM may be negative
 - Tests taken after rash onset (red line)
 - PCR likely to be negative
 - IgM usually positive



A case of fever and rash....

- Infant AM, 14 month infant
- Blood results returned 4 days later
 - PCR positive on urine
 - Sequencing
 - B3 genome/lineage,
 - Identical to strains circulating in DRC, Zambia, 2015-2019

	CENTRE FOR VACCINES AND IMMUNOLOGY
	Clotted blood (On ice) NICD:Measles IgM 6, NICD: Rubella IgM 6 & Test referred to another NHLS laboratory
Authorised by	SB Smit on 01/12/2021 at 12:24
Measles IgM	
Measles IgM Results	positive

• Treatment

- Symptomatic
 - Treat fever with paracetamol
 - Manage dehydration
- Supportive
 - Vitamin A to prevent complications
- Prevent complications
 - Treat secondary infections with antibiotics
 - Prophylactic antibiotics not shown to be effective

MEDICINE TREATMENT

All children < 5 years of age with measles should be given an extra dose of vitamin A, unless the last dose was received within a month:

Vitamin A (retinol), oral, as a single dose.

Age range	Dose units	Capsule 100 000 IU	Capsule 200 000 IU
Infants 6–11 months	100 000	1 capsule	-
Children 12 months-5 years	200 000	2 capsules	1 capsule

In children < 5 years of age, give the 1st dose immediately. If the child is sent home, the caregiver should be given a 2nd dose to take home, which should be given the following day.

Administration of a vitamin A capsule

- o Cut the narrow end of the capsule with scissors.
- Open the child's mouth by gently squeezing the cheeks.
- Squeeze the drops from the capsule directly into the back of the child's mouth. If a child spits up most of the vitamin A liquid immediately, give one more dose.

- Whom should you be cautious with and refer?
 - Age: All adults, children < 6 months
 - Measles in immunocompromised host, or TB co-infection
 - Where complications are present including
 - Respiratory distress, pneumonia,
 - Dehydration
 - Neurological complications

What can I do following detection of a suspected measles case?

- Provide appropriate supportive and preventative care
- Be familiar with case definitions for suspected measles and rubella cases
 - (fever, rash + 1 of conjunctivitis, coryza and cough).
- Notify all suspected cases to provincial surveillance officer
- Complete the case investigation forms and submit blood with throat swab or urine to NICD for testing
- Conduct ring vaccination of under-5 and unvaccinated contacts
- Assess vaccination status, explore reasons for non-receipt of vaccine and address uncertainties

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	MATIONAL INSTITUTE FOR COMMUNICABLE DISEASES Developed for Known Practice University Service	COVID-19 • About Us •	Centres 👻 Our Service:	ces • NMC • Media • Contact Us • Disease Index Q		
	PREVENT	>	DETECT & REPORT	RESPOND		
	OVERVIEW		Medical Conditions (NMC) ar	are of public health importance. Surveillance of NMCs involves the use of epidemiologic data to provide scientifically proven and		
	NOTIFICATION PROCESS	accurate in According	formation to detect and act	ct against public health threats rapidly. th Regulations, rapid detection of public health risks, prompt risk		
	NMC COVID-19 DOCUMENTS	NMC patio		quires information from national, regional and local levels to:		
	MONTHLY SURVEILLANCE REPO	Estimati Monitor	ely detect and respond to public health threats in order to prevent disease outbreaks; es bunden of priving viatessas and identify populations at rick - place, person and time trends in priority diseases of public health importance; and ublic health interventions and inform policy decisions.			
	CONTACTS PRIVACY POLICY	FREQ	UENTLY ASKED QUESTIC	nons		
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Any person in whom a suspects measles infect OR any person with fever maculopapular rash (i. vesicular) and one of c	tion and e. non-	Suspected case with a known n case	epi link to	A laboratory-confirmed measles case is any person with clinically compatible measles and a measles-specific IgM result in any specimen or a positive measles PCR test on a throat swab		
(i.e. runny nose) or cor red eyes).				A clinically compatible case according to the WHO is a case that meets the clinical case definition with no blood specimen submitted, or without an epidemiological link to a confirmed case.		

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NMCsurveillancereport@nicd.ac.za NMC hotline 072 621 3805.

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Clinical symptoms relating to	the NMC							
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Patient vital status		300	_	1.0	tabased.		Date of death	2018012
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https://www.nicd.ac.za/assets/files/EPI%20Surveillance%20Manual_15Dec2015.

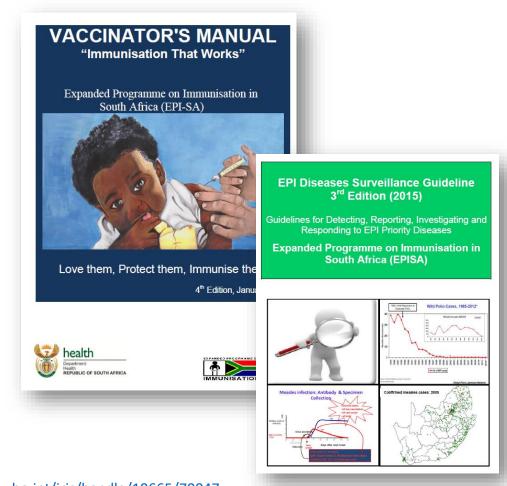
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https://www.nicd.ac.za/diseases-a-z-index/measles/ https://www.nicd.ac.za/wp-content/uploads/2019/04/Final-draft_Updated-Measles-CIF_020817_NVM.pdf

EPID NUMBER: SOA	This is a suspected case of: measles rubella uncertain
PATIENT DETAILS	
Full name:	
Presenting symptoms/signs (Tick all applicable Boxes): Rash: Y N Fever: Occipital/auricular lymphadenopathy: Y N Arthralgia: Y N Coryza/F Presenting complications (Tick where applicable): None Pneumonia Ottit (Croup) Corneal Ulceration Blindness Encephalitis Arthritis Oth	Rhinitis/Runny nose: Y 🗌 N 📄 Other (Specify):
Date of presentation at the health facility:	
MEDICAL AND CONTACT HISTORY History of contact with a fever-rash case in the past 7 to 28 days: Y N History of contact with a confirmed rubella case in the past 7-28 days: Y N History of contact with a confirmed measles case in the past 7-28 days: Y N History of travel: Y N Unknown if yes, travel destination (s): Date of departure: / Date of ret History of visit or admission to a healthcare facility in the past 7 to 28 days: Y	Unknown Unknown Unknown Unknown Unknown Unxnown Uxxnown Uxx
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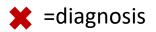
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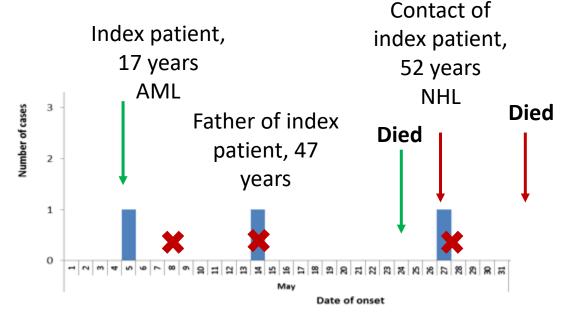
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- Supporting vaccine confidence amongst hesitant parents by adopting a non-judgemental, gentle approach
 - Understand parents context, social struggles
 - Assess parental meaning systems
 - How do people understand the world, and the origin/source of health?
 - Who are the persons/institutions that people trust for health advice?
 - What factors/events would support a person's uptake of vaccination?
 - Accept that forms of rationalizing do not always align with biomedical approaches
 - Understand parental decision-making
 - A desire to protect their child's health
 - A need to be a part of decision making processes
 - Need to belong and feel included among peers
 - To be confident that expert systems have their own interests at heart
 - To have their priorities recognised.
 - A dialogue-based approach with intention of understanding, identifying common ground and developing of alliances

A second case of fever and rash....

- 17 year old female
 - Admitted to a private hospital 13 April for chemotherapy.
 - Commenced with rash 14th April
 - By 5 May condition deteriorated with a pneumonitis.
 - 8th May diagnosis=measles
 - Died on 24 May
- 47 year old male
 - Diagnosed with measles by Gp on 14 May 2015. No known contacts.
- 52 year old male
 - Admitted on 17 May, deteriorated with respiratory symptoms on 31 May. Rash developed on 27 May.
 - Died on 2 June

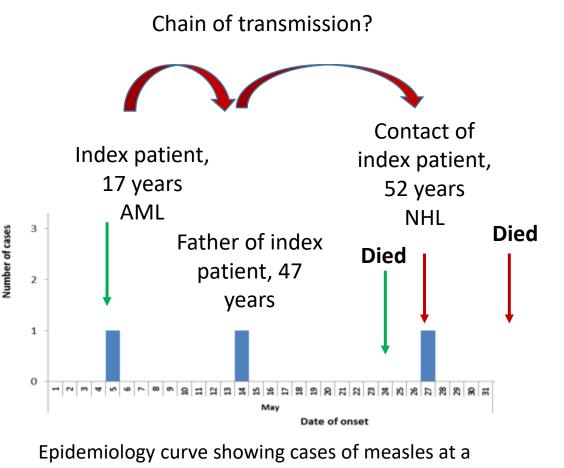




Epidemiology curve showing cases of measles at a private hospital, 2015

A second case of fever and rash....

- Hospital actions taken
 - Isolation of patients (prior to diagnosis, on account of oncology diagnoses)
 - Airborne/droplet precautions
 - Screening of staff vaccination records and offering of measles vaccination
- What was not reported
 - An oncologist (not patient's doctor) had been ill and off work, and his wife had been diagnosed with pneumonitis.
 - The oncologist had become ill after returning from eastern europe
 - Genotyping revealed an eastern European measles strain.



private hospital, 2015

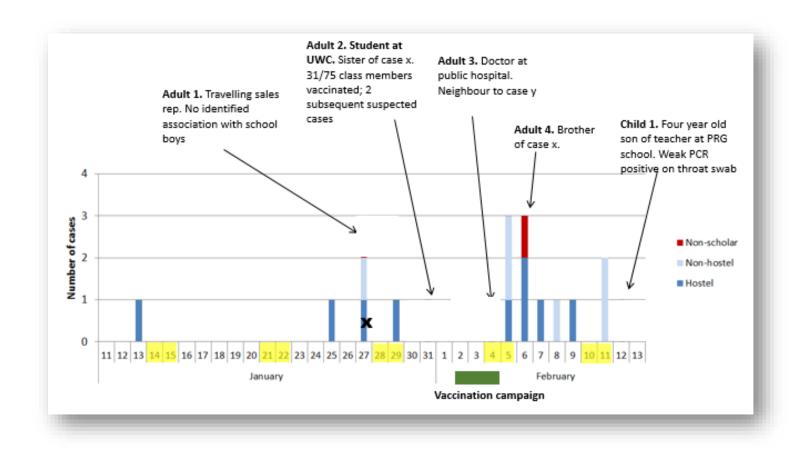
A second case of fever and rash....thinking with the IPC practitioner

- Who is at risk in the emergency department and hospital?
 - All who are not vaccinated even those not directly in contact (airborne transmission)
 - Waning immunity in adulthood does occur.
 - Second infections or measles postvaccination is very rare, but has been documented
- What should be done re IPC?
 - Routine cleaning and disinfection
 - Ensure good ventilation
 - Contact tracing and review of ED patients
 - Review vaccination records of staff
 - Boost or revaccinate (no adverse effects if given multiple times)

- Who needs post-exposure prophylaxis?
 - <u>Vaccine</u> may be given within 3-6 days of exposure to unvaccinated persons
 - Infants under 6 months of age may be vaccinated (but should still receive usual EPI vaccines)
 - <u>Immunoglobulin</u> may be given to all with defective CMI who cannot receive the vaccine
 - Persons with AIDS (even if previously vaccinated)
 - Oncology patients with defective CMI
 - Persons receiving immunosuppressive therapy at doses >20mg/kg
 - Immunoglobulin may be given to pregnant women who cannot receive vaccine

A third...4th 5th 6th case of fever and rash....

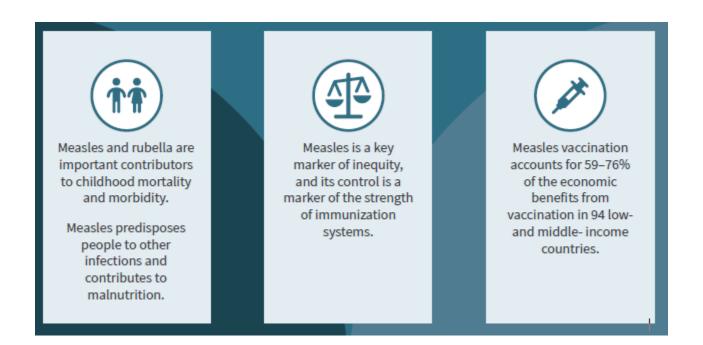
- 17 year old male resident in a boarding house at a school in City of Cape Town
- 10 days later, 4 more cases of measles amongst boarding house members....



A case of fever and rash....thinking with the public health official

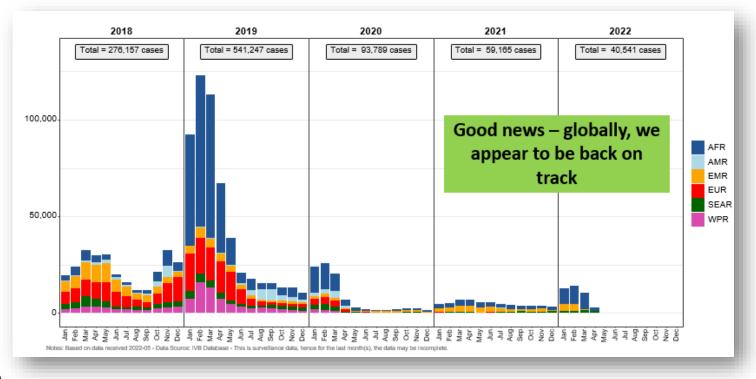
- What is the significance of this suspected case?
 - Measles has a very high effective reproductive number (Rt)
 - R0=11 ie 11 secondary cases in an unvaccinated population
 - Therefore high vaccination coverage (>95%) is required to prevent outbreaks
 - Modelling indicates that when size of unvaccinated population equals birth cohort, outbreaks are inevitable following introduction into community
 - RSA average vaccination coverage c.70-80%
 - It will take 4-5 years before outbreak will occur in RSA (25% of 1million birth cohort)
 - Outbreaks can be averted with early detection, ring vaccination and if necessary, district vaccination

- WHO measles and rubella elimination strategy
 - 'A world free of measles and rubella' by 2030





- WHO measles and rubella elimination strategy
 - 'A world free of measles and rubella'
 - The world was on track declining incidence of measles, increasing vaccination coverage until a resurgence in 2015-7
- What happened?
 - Growing vaccine hesitancy
 - Global transmission through airtravel and trade
 - COVID-19 related disruptions of routine and supplementary immunization campaigns may have impacted elimination efforts
 - Legacy low vaccination coverage in older age groups and re-introduction of the virus



Slide courtesy S. Smit CVI, NICD

• WHO measles risk assessment tool

- To help national programmes to identify areas not meeting measles programmatic targets, and based on the findings, guide and strengthen measles elimination program activities and reduce the risk of outbreaks
- Uses data to categorise risk as very high, high, medium, low
- 4 categories of data
 - Population immunity (40)
 - Surveillance quality (20)
 - Program performance (16)
 - Threat assessment (24)
- Results are scored and maps generated by region

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https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/surveillance/measles-programmatic-risk-assessment-

tool#:~:text=The%20World%20Health%20Organization%20(WHO,reduce%20the%20risk%20of%20outbreaks.

- WHO measles risk assessment tool
 - Required data

Data	Details
Administrative vaccine coverage data (for each district)	 MCV1, for years 1, 2, 3 MCV2 (if introduced), for years 1, 2, 3 DPT1 or Penta1, for year 3
Measles Supplementary Immunization Activity (SIA) campaign data (for each district), if any SIA was conducted in the past 3 years	 Coverage (for each district) Target age group for SIA Year in which SIA was conducted
Measles case-based surveillance data	For years 1, 2, 3
Total population (for each district)	For years 1, 2, 3
Geographic area (in km²)	Year 3, for each district
Shape file of country	For year 3, at the district level

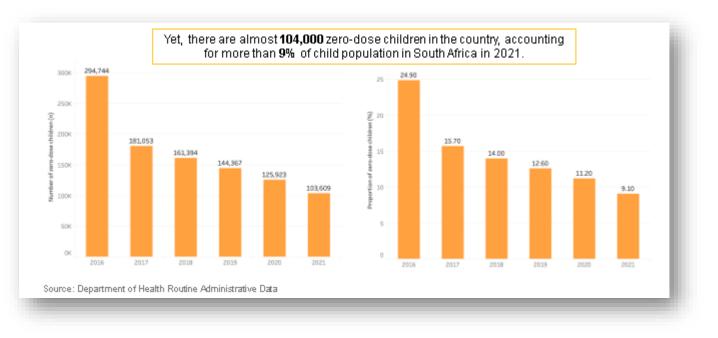
- Vulnerable groups
 - Presence of migrant population / internally displaced population/ slums / tribal communities
 - Resistant to vaccination (ie. religious, cultural issues, etc.)
 - Security and safety concerns
 - Frequented by calamities / disasters
 - Poor access to health services due to terrain / transportation issues
 - Lack of local political support
 - Presence of high-traffic transportation hubs/major roads or bordering large urban areas (within and across countries)
 - Presence of areas with mass gatherings (i.e. trade/commerce, fairs, markets, sporting events, high density of tourists)

https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/surveillance/measles-programmatic-risk-assessment-

tool #: ``: text = The %20 World %20 Health %20 Organization %20 (WHO, reduce %20 the %20 risk %20 of %20 outbreaks.)

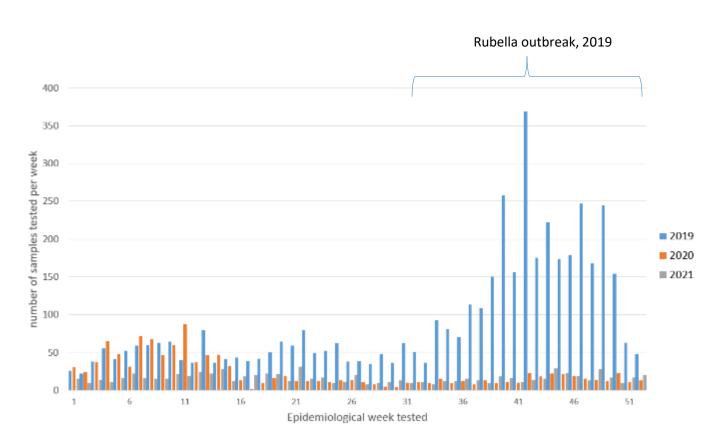
- Zero-dose children
 - Whilst vaccination coverage data indicates the proportions of children who receive vaccines, it is clusters of unvaccinated children that drive outbreaks
 - Identification of clusters of unvaccinated, and particularly zero-dose children is important.
 - These clusters may even occur in districts with high vaccination coverage
 - Identification of 'zero-dose' children is a new focus of GAVI and other vaccine advocacy groups

Zero-dose children in South Africa, 2016-2021



Zero Dose Children from South Africa as identified by UNICEF. Slide courtesy Mercy Kamupira, UNICEF

- South African context:
 - Fever-rash surveillance cases have diminished markedly 2019-2021
 - Nonpharmaceutical measures for COVID also reduced transmission of all respiratory pathogens.



Cases of fever-rash submitted for testing to NICD, 2019-2021

- Mainstay of prevention is vaccination and early detection
- Low vaccination coverage is reason for current outbreak

	MC	W1	MC	W 2
	Dec-20	Dec-21	Dec-20	Dec-21
ECP	75	72,9	68,4	66,8
PSP	78,3	72,4	76,5	68,7
GP	74,2	70,7	66,9	65,5
KZN	88,9	87,9	81,2	79,8
LP	34,9	84,9	77,5	84,8
MP	88,5	101,6	78,1	86,9
NCP	53,4	60,4	54,4	59,8
NWP	66,8	67,4	63,3	63,4
WCP	75,6	65,1	71,4	66,7
RSA	73,7	78,1	72,7	72,8

Vaccination coverage for MCV1 (6 months) and MCV2 (12 months), 2020-2021

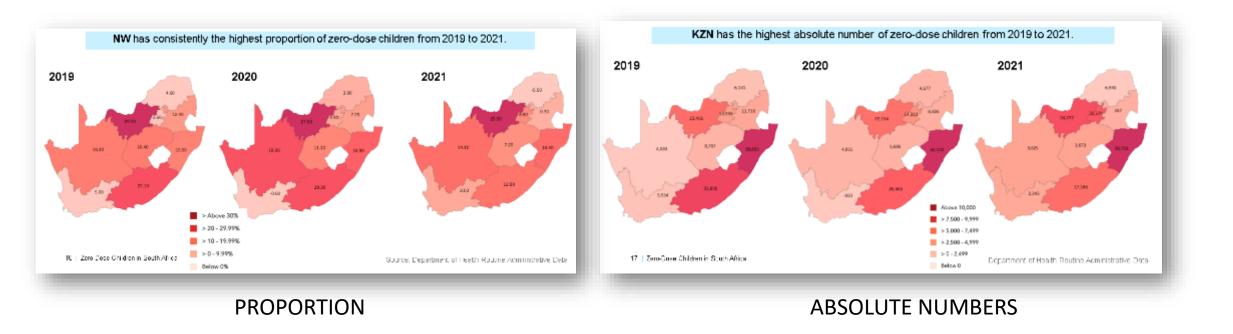
Low vaccination coverage

Table 3 Surveillance adequacy per province during 2015–2020

Province	2020
Eastern Cape	2.0
Free State	2.3
Gauteng	2.0
KwaZulu-Natal	1.4
Limpopo	1.0
Mpumalanga	3.4
North West	2.8
Northern Cape	3.9
Western Cape	2.9
South Africa	2.1

Weak surveillance indicators

• Provincial distribution of zero-dose children in RSA provinces, 2019-2021



Thank you

- Acknowledgements
 - Colleagues and friends at Centre for Vaccines and Immunology
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 - Thulasizwe Buthelezi

