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CORSO DI IGIENE

Scuola
di
Medicina

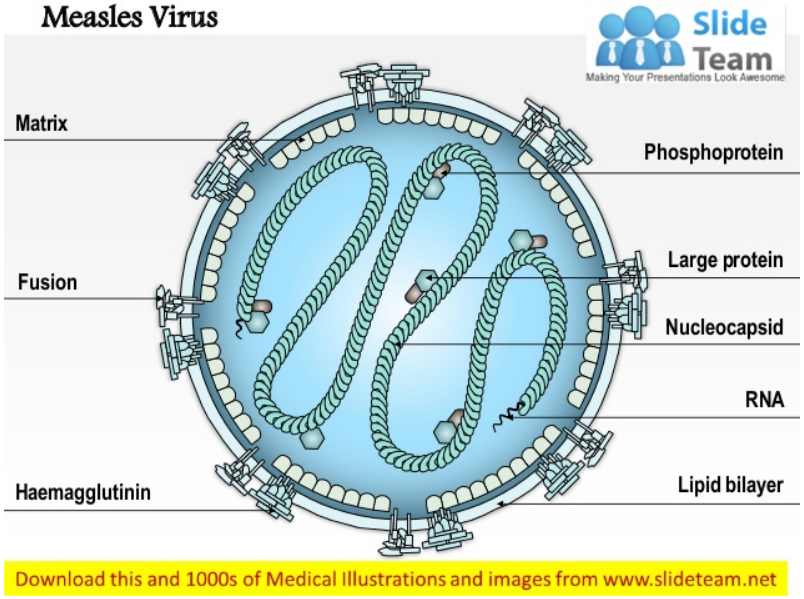
Measles

Measles

- Highly contagious viral illness
- First described in 7th century
- Near universal infection of childhood in prevaccination era
- Common and often fatal in developing countries

Measles Virus

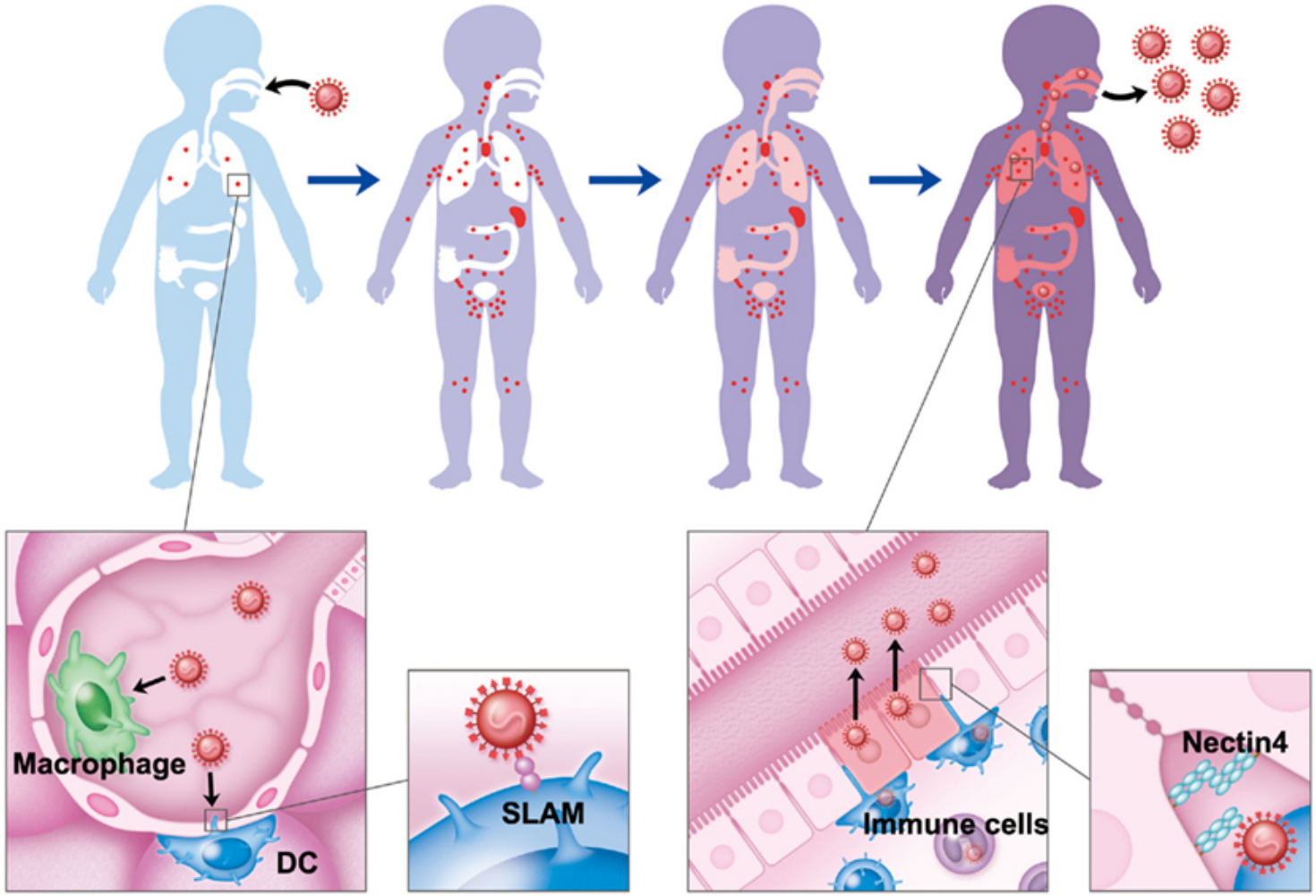
- Paramyxovirus (RNA)
- Hemagglutinin important surface antigen
- One antigenic type
- Rapidly inactivated by heat, sunlight, acidic pH, ether and trypsin



Measles Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymphnodes
- Primary viremia 2-3 days after exposure
- Secondary viremia 5-7 days after exposure with spread to tissues

Measles Pathogenesis



Measles Clinical Features

- Incubation period 10-12 days
- Prodrome 2-4 days
  - stepwise increase in fever to 39°C–41°C
  - cough, coryza, conjunctivitis
  - Koplik spots (rash on mucous membranes)

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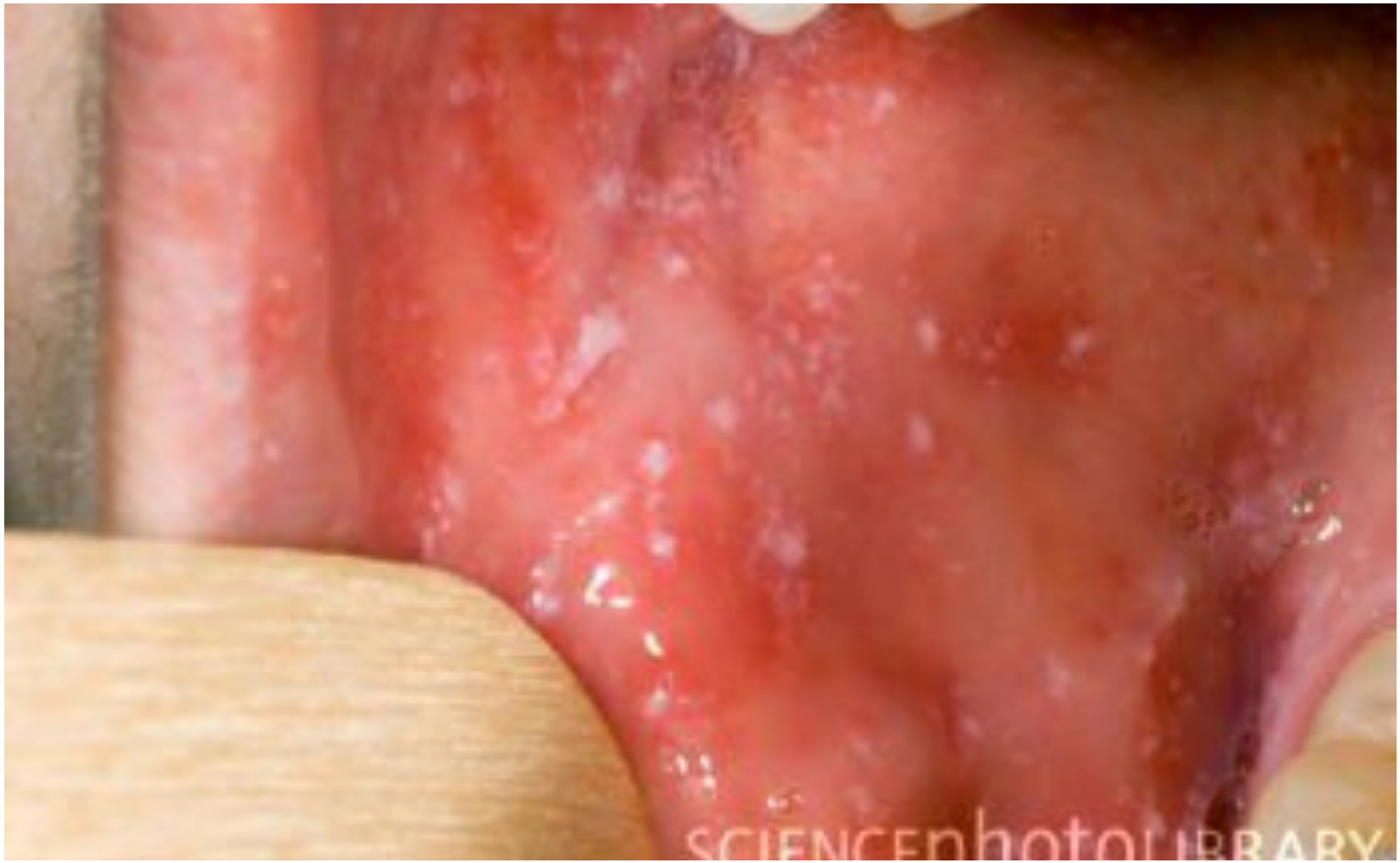
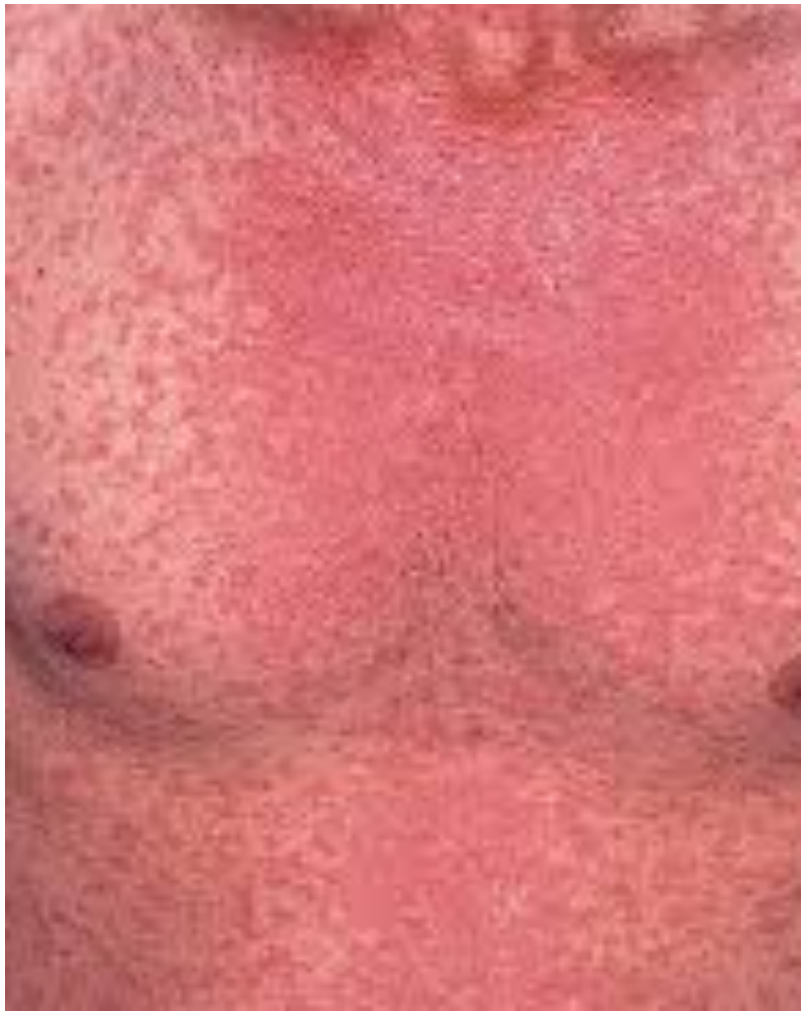
Measles Clinical Features
Koplik spots



Measles Clinical Features

Rash

- 2-4 days after prodrome, 14 days after exposure
- persists 5-6 days
- begins on face and upper neck
- maculopapular, becomes confluent
- fades in order of appearance



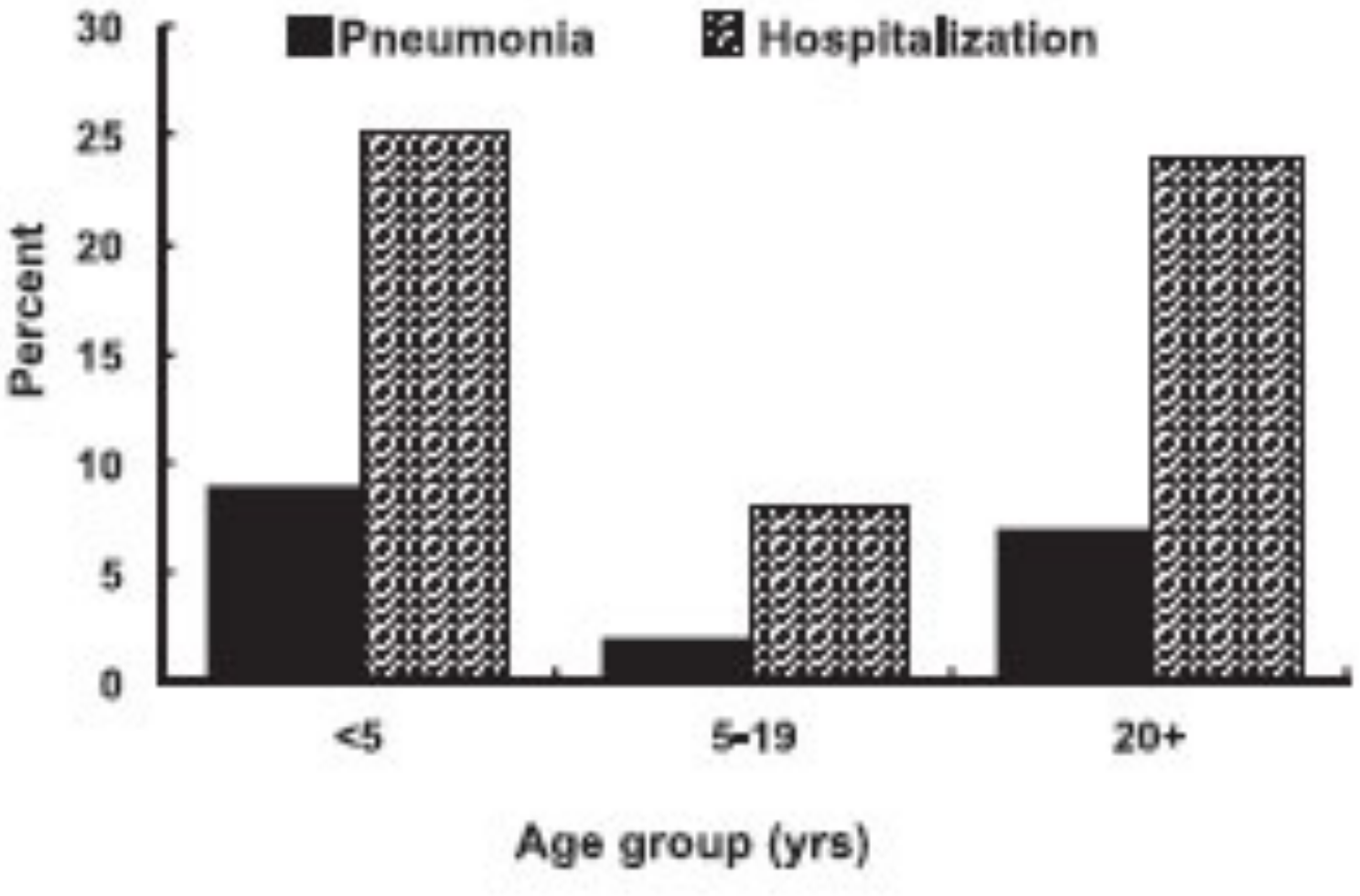
Measles Clinical Features

Measles complications

Complication	Frequency (%)
Diarrhea	8
Otitis media	7
Pneumonia	6
Encephalitis	0.1
Seizures	0.6-0.7
Death	0.2

Based on 1985-1992 surveillance data

Measles Complications by Age Group



Based on 1985-1992 surveillance data

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SSPE

Measles in an immunocompromised person

- reported almost exclusively in persons with T-cell deficiencies (leukemias, lymphomas, AIDS
- Severe with a prolonged course
- may occur without the typical rash
- patient may shed virus for several weeks after the acute illness.

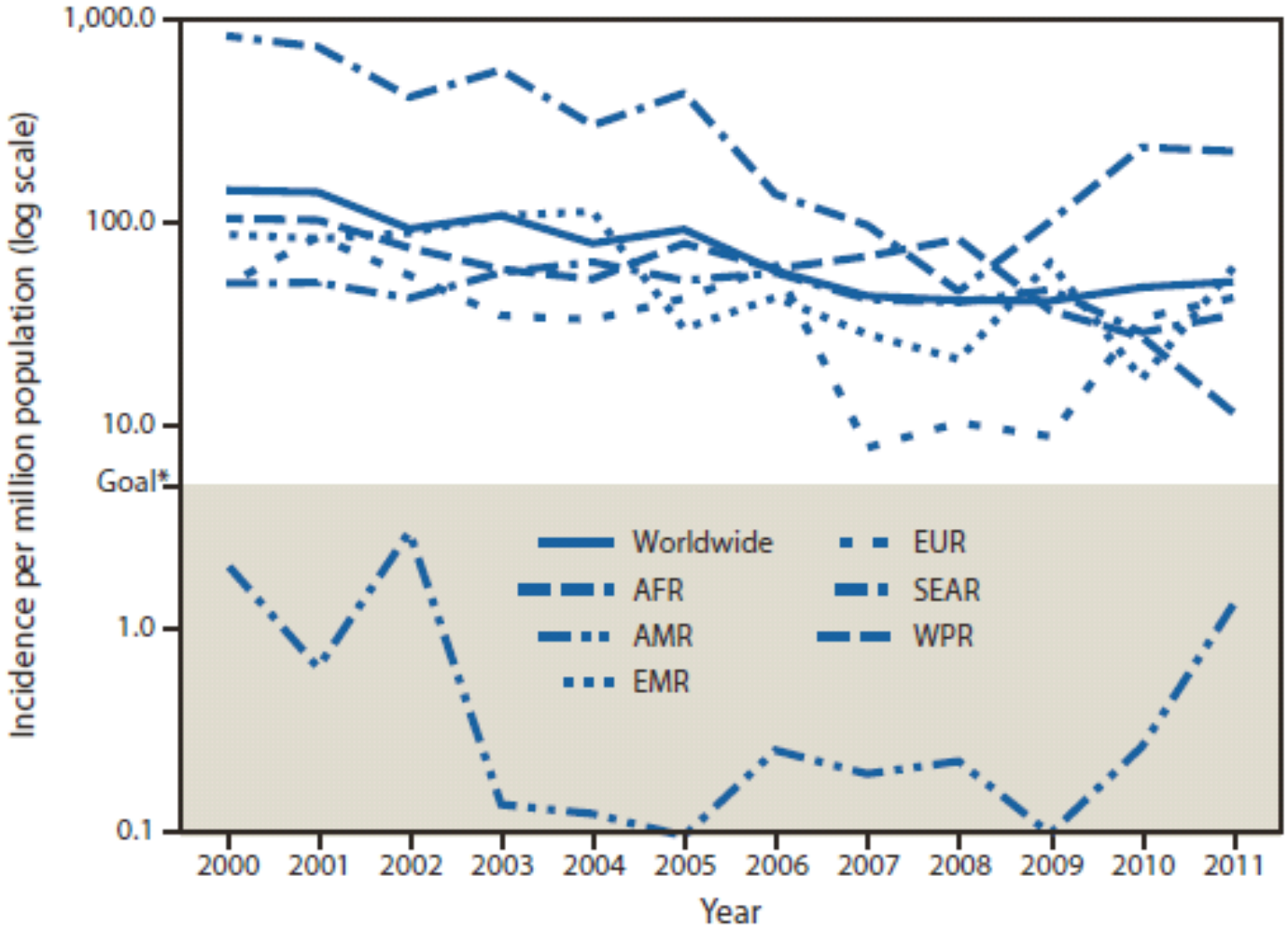
Measles Laboratory Diagnosis

- Isolation of measles virus from urine, nasopharynx, blood, throat
- Significant rise in measles IgG by any standard serologic assay (e.g., EIA, HI)
- Positive serologic test for measles IgM antibody

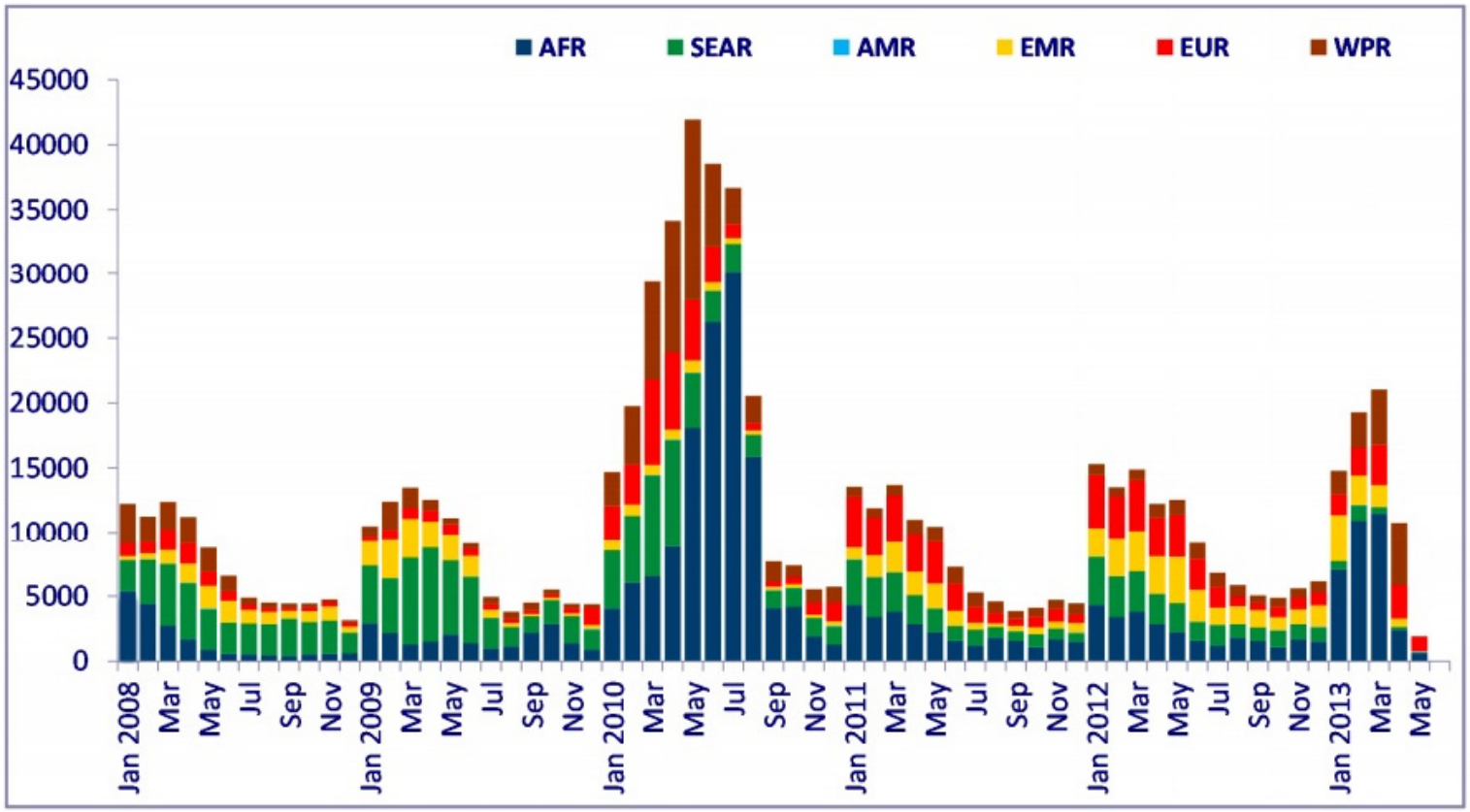
Measles Epidemiology

- **Reservoir**
  - human
- **Transmission**
  - Respiratory Airborne
- **Temporal pattern**
  - Peak in late winter - spring
- **Communicability**
  - 4 days before to 4 days after rash onset

Measles Epidemiology



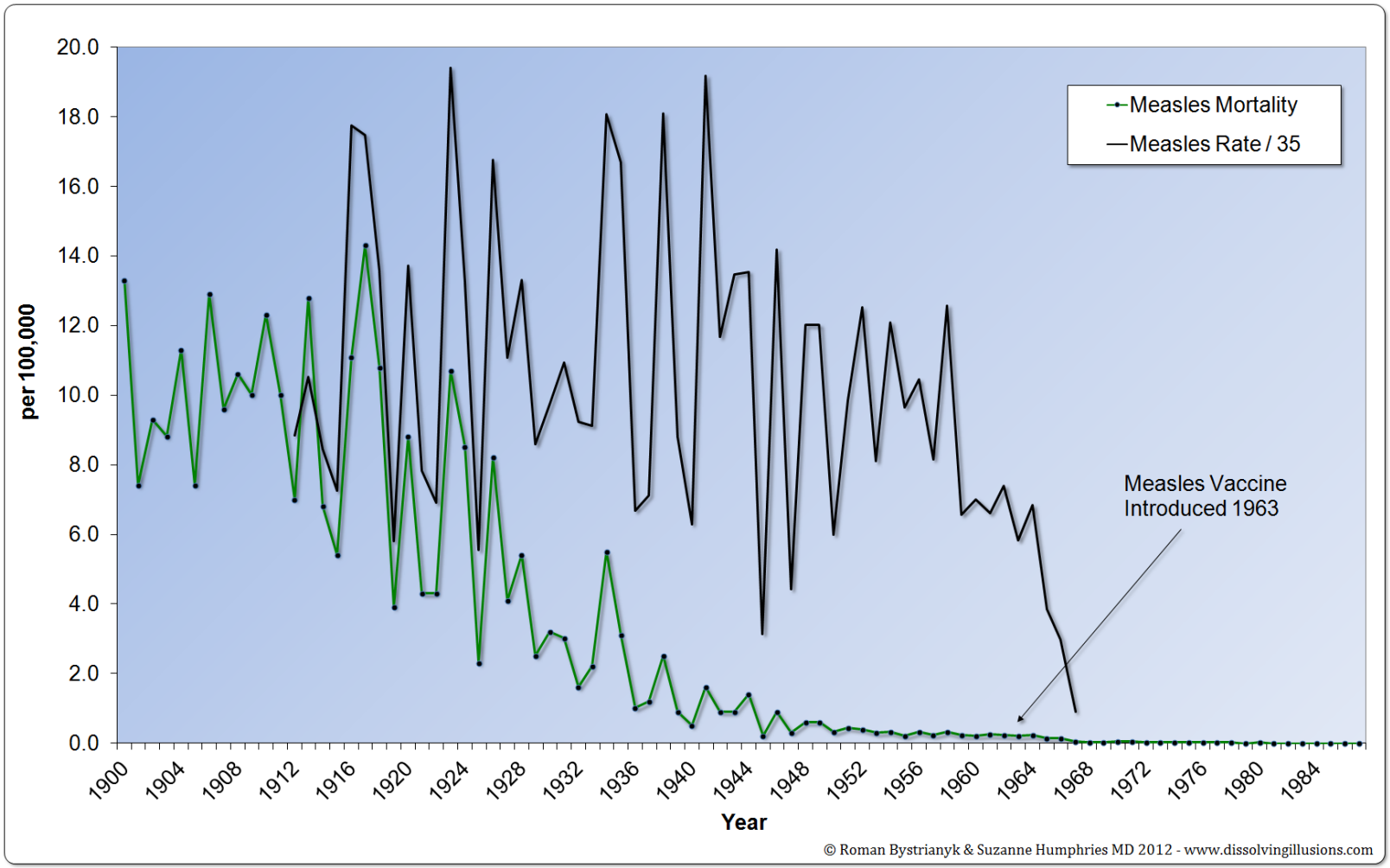
Measles cases distribution by month and WHO Regions, 2008-2013



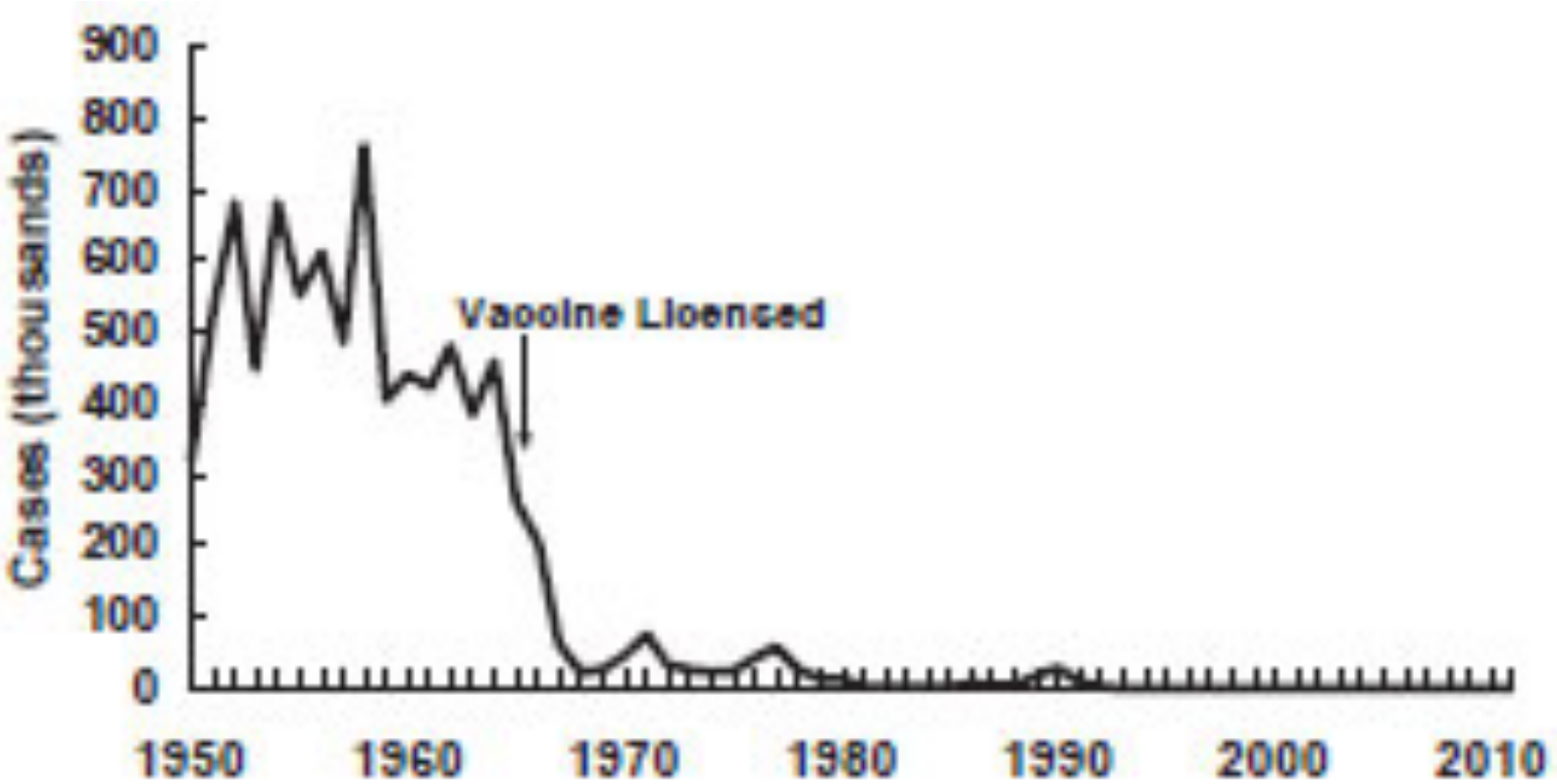
SEAR India is not included in this graph.

NB: This is surveillance data, hence for the previous month(s) the data may be incomplete

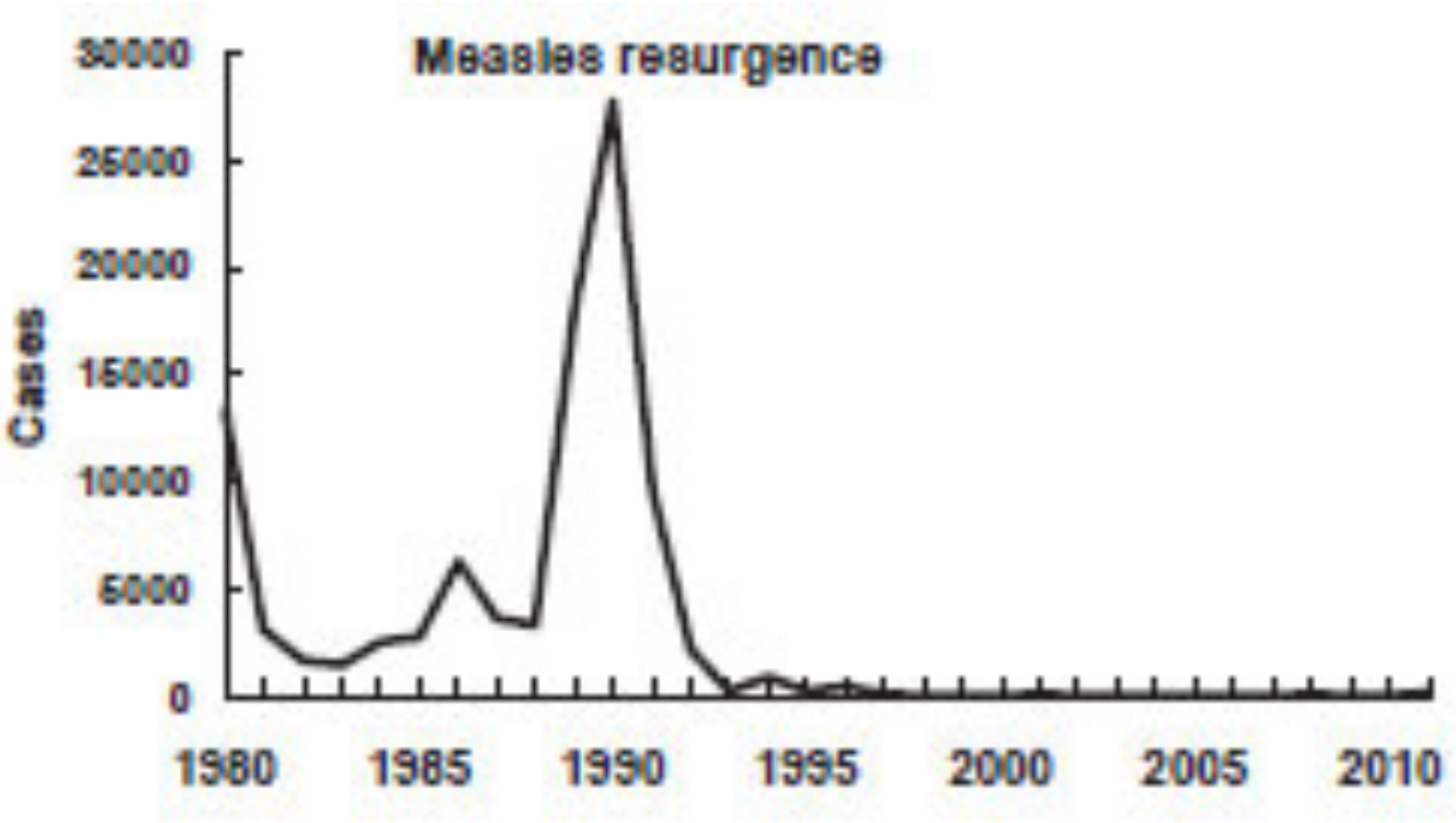
Measles - United States, 1900-1984



Measles - United States, 1950-2011



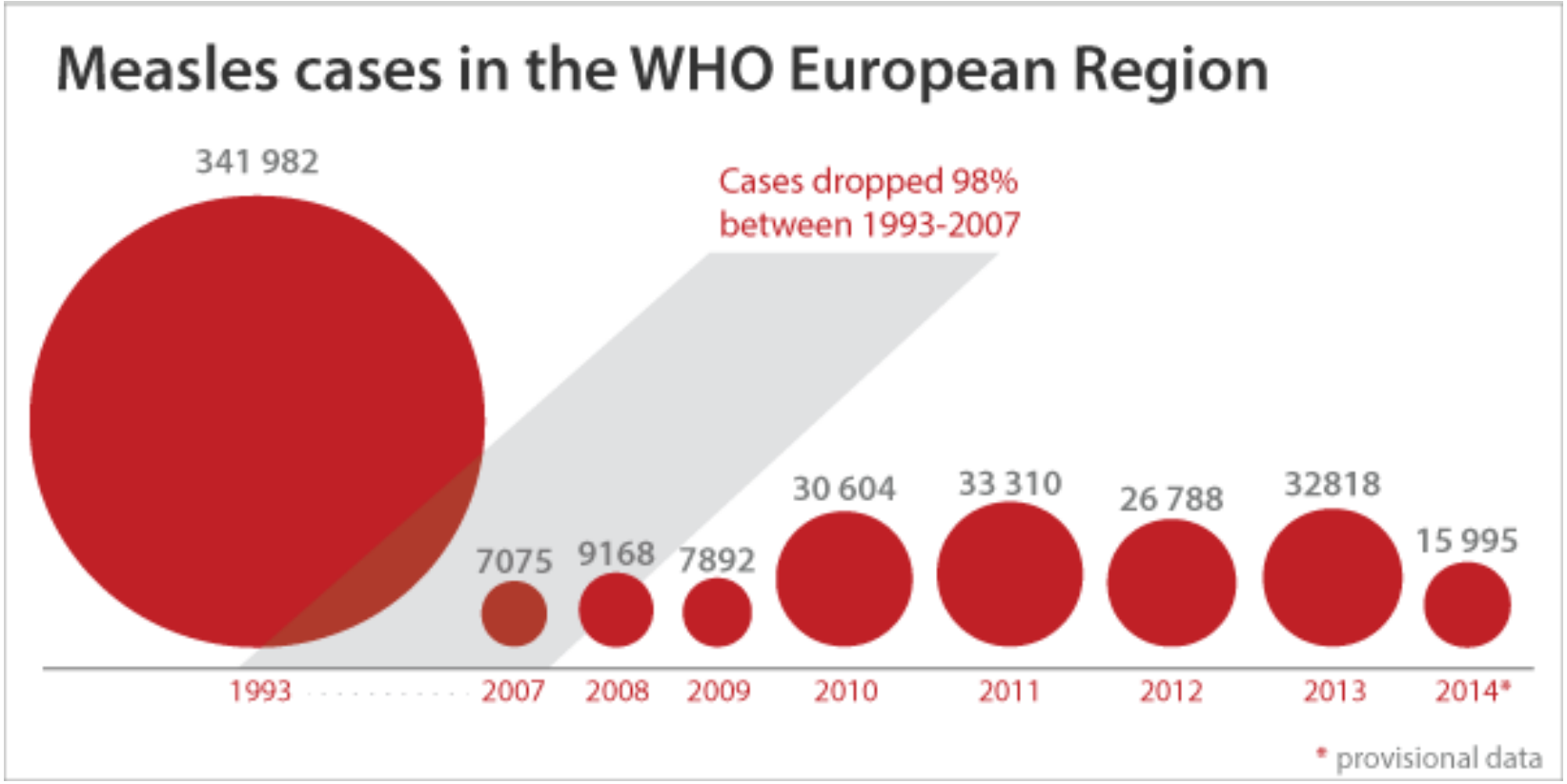
Measles - United States, 1980-2011



Measles 1993-2011

- **Endemic transmission interrupted**
- Record low annual total in 2004 (37 total cases)
- Many cases among adults
- Most cases imported or linked to importation
- Most persons with measles were unvaccinated or unknown vaccination status
- **In 2011, CDC reported 16 outbreaks of measles and 220 measles cases, most of which were imported cases in unvaccinated persons**

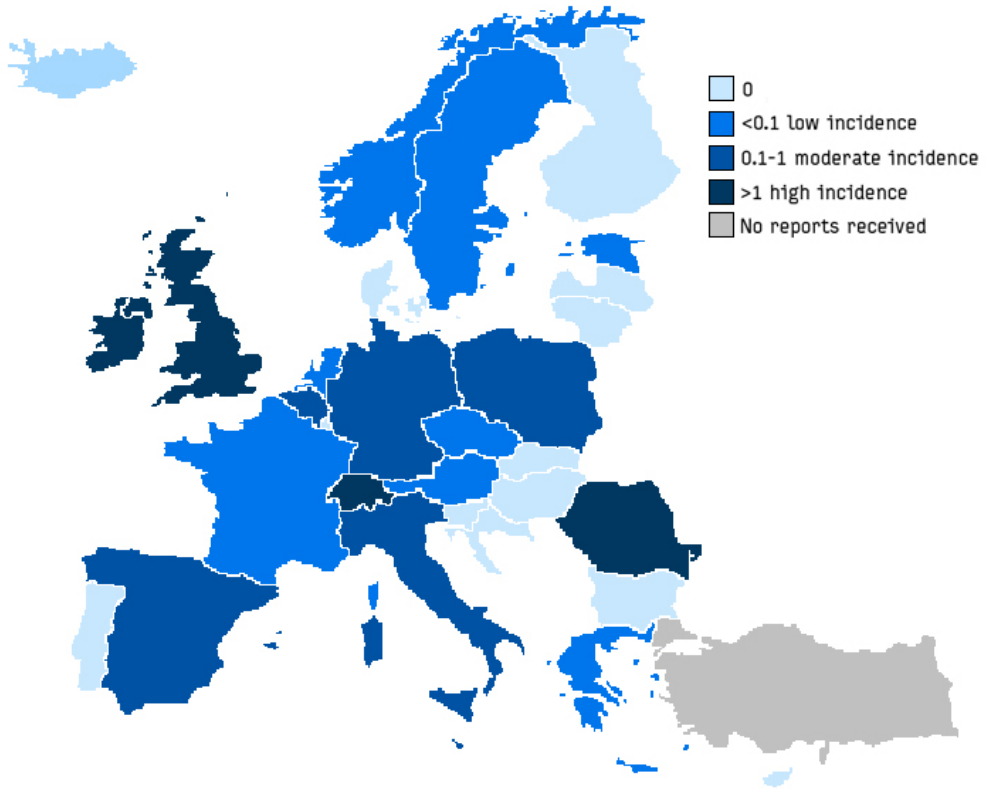
Measles Epidemiology
Europe



Measles Epidemiology Europe

FIGURE

Incidence categories of reported indigenous measles cases per 100,000 inhabitants by country, 2007*



* EUVAC.NET preliminary data. All clinical, laboratory-confirmed or epidemiologically linked cases meeting the requirements for national surveillance were included. The proportion of laboratory-confirmed cases varies in different countries.
Note: For Romania the crude incidence is represented in this figure as data on importation status of cases was not included in the dataset provided. To date, no reports were received from Turkey.

Measles Vaccines

- **1963** - Live attenuated and inactivated “killed” vaccines
- **1965** - Live further attenuated vaccine
- **1967** - Killed vaccine withdrawn
- **1968** - Live further attenuated vaccine (Edmonston-Enders strain)
- **1971** - Licensure of combined measles-mumps-rubella vaccine
- **1989** - Two-dose schedule
- **2005** - Licensure of combined measles-mumps-rubella-varicella vaccine

Measles Vaccines

- **Composition**
  - Live virus
- **Efficacy**
  - 95% at 12 months of age
  - 98% at 15 months of age
- **Duration of Immunity**
  - lifelong
- **Schedule**
  - 2 doses
  - should be administered with mumps and rubella as MMR or with mumps, rubella and varicella as MMRV
  - single-antigen measles vaccine not available in the United States

Measles Mumps Rubella (MMR) Vaccine Failure

Measles, mumps, or rubella disease (or lack of immunity) in a previously vaccinated person

- 2%-5% of recipients **do not respond to the first dose**
- Caused by antibody, damaged vaccine, incorrect records
- **95% of persons with vaccine failure will respond to second dose**

Measles (MMR) Vaccine Indications

- All children 12 months of age and older
- Susceptible adolescents and adults without documented evidence of immunity

Vaccination Schedule and Use

- First dose of MMR at 12-15 months
- 12 months is the minimum age
- Infants of >5 months of age could receive MMR in case of outbreaks
  - Doses given before 12 months should not be counted as a valid dose
  - Revaccinate at 12 months of age or older

Second Dose of Measles Vaccine

- Second dose of MMR at 4-6 years
- Second dose may be given any time at least 4 weeks after the first dose
- Intended to produce measles immunity in persons who failed to respond to the first dose (primary vaccine failure)
- May boost antibody titers in some persons

Adults at Increased Risk of Measles

- College students
- Persons working in medical facilities
- International travelers

All persons who work within medical facilities should have evidence of immunity to measles

Adults at Increased Risk of Measles

Gamblin *et al. BMC Research Notes* 2014, **7**:744
http://www.biomedcentral.com/1756-0500/7/744

BMC Research Notes

CASE REPORT Open Access

Measles cluster at a university in the United Kingdom

Jenny Gamblin[1], Jane Maund[1], Iain Blair[1] and Stuart C Clarke[1,2*]

Abstract

Background: Measles remains an infection of public health importance. We describe a cluster of measles in a university setting between April and May 2007.

Case presentation: The outbreak took place over a period of six weeks and involved nine students, eight of whom lived in halls of residence. Due to the potential for significant spread in an institutional setting, a public health investigation was initiated to identify the source of the outbreak. Follow up of cases was undertaken proactively with the university and local general practitioners. Salivary fluid test kits and questionnaires were sent to suspected cases. Seven salivary test kits were returned, but only one questionnaire was returned. Four cases were confirmed as measles. Although seven students had been previously immunised, immunity was only demonstrated

Adults at Increased Risk of Measles

International Journal of Infectious Diseases 24 (2014) 11–13

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Estimation of secondary measles transmission from a healthcare worker in a hospital setting

Katsushi Tajima [a,b,*], Hidekazu Nishimura [c], Seiji Hongo [d], Masaharu Hazawa [a,b], Al. Saotome-Nakamura [a,b], Kenichi Tomiyama [a,b], Chizuka Obara [a,b], Takeo Kato [a]

[a] Department of Neurology, Hematology, Metabolism, Endocrinology, and Diabetology (DNHMED), Yamagata University Faculty of Medicine, Yamagata, Japan
[b] Department of Radiation Emergency Medicine, National Institute of Radiological Sciences, National Institute of Sciences, 4-9-1, Anagawa, Inage-ku, Chiba-shi, Chiba, 263-8555, Japan
[c] Virus Research Center, Sendai Medical Center, Sendai, Japan
[d] Department of Infectious Diseases, Yamagata University Faculty of Medicine, Yamagata, Japan

ARTICLE INFO

Article history:
Received 31 January 2014
Received in revised form 5 March 2014
Accepted 7 March 2014

SUMMARY

Measles among healthcare workers (HCWs) is associated with a significant risk of nosocomial transmission to susceptible patients. When a measles case occurs in the healthcare setting, most guidelines recommend exhaustive measures. To evaluate the effects of measures against measles transmission in the healthcare setting precisely, it is essential to determine whether secondary

Measles Vaccine Indications for Revaccination

- Vaccinated before the first birthday
- Vaccinated with killed measles vaccine (KMV)
- Vaccinated from 1963 through 1967 with an unknown type of vaccine
- Vaccinated with IG in addition to a further attenuated strain or vaccine of unknown type

Postexposure Prophylaxis

- **Live measles vaccine** provides permanent protection and may prevent disease if given within 72 hours of exposure
- **IG** may prevent or modify disease and provide temporary protection if given within 6 days of exposure

MMR Vaccine Contraindication and Precautions

- History of anaphylactic reactions to neomycin
- History of severe allergic reaction to any component of the vaccine
- Pregnancy
- Immunosuppression
- Moderate or severe acute illness
- Recent blood product

Measles and Mumps Vaccines and Egg Allergy

- Measles and mumps viruses grown in chick embryo fibroblast culture
- Studies have demonstrated safety of MMR in egg-allergic children
- Vaccinate without testing
- Precautions must be adopted for patients who reported an history of anaphylaxis after egg eating

Measles Vaccine and HIV Infection

- MMR recommended for persons who do not have evidence of current severe immunosuppression
- Prevaccination HIV testing not recommended
- MMRV not for use in persons with HIV infection

Tuberculin Skin Testing (TST)* and Measles Vaccine

- Apply TST at same visit as MMR
- Delay TST at least 4 weeks if MMR given first
- Apply TST first and administer MMR when skin test read (least favored option because receipt of MMR is delayed)

MMR Adverse Events

- Arthralgias (susceptible women)
  - 25%
- Rash, pruritis, purpura
  - not common

MMR Adverse Reactions

- Fever
  - 5%-15%
- Rash
  - 5%
- Thrombocytopenia
  - 1/30,000-40,000 doses
- Lymphadenopathy
  - rare
- Allergic reactions
  - rare

Wakefield: the link between MMR and autism is a fake

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VAXXED: an international shame

The right causes of autism

Environ Res. 2016 Aug 25. pii: S0013-9351(16)30317-6. doi: 10.1016/j.envres.2016.07.030. [Epub ahead of print]

Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: A review and meta-analysis.

Flores-Pajot MC[1], Ofner M[2], Do MT[2], Lavigne E[3], Villeneuve PJ[4].

⊕ **Author information**

Abstract

BACKGROUND AND OBJECTIVE: Genetic and environmental factors have been recognized to play an important role in autism. The possibility that exposure to outdoor air pollution increases the risk of autism spectrum disorder (ASD) has been an emerging area of research. Herein, we present a systematic review, and meta-analysis of published epidemiological studies that have investigated these associations.

METHODS: We undertook a comprehensive search strategy to identify studies that investigated outdoor air pollution and autism in children. Overall, seven cohorts and five case-control studies met our inclusion criteria for the meta-analysis. We summarized the associations between exposure to air pollution and ASD based on the following critical exposure windows: (i) first, second and third trimester of pregnancy, (ii) entire pregnancy, and (iii) postnatal period. Random effects meta-analysis modeling was undertaken to derive pooled risk estimates for these exposures across the studies.

RESULTS: The meta-estimates for the change in ASD associated with a 10μg/m^3 increase in exposure in $PM_{2.5}$ and 10 ppb increase in NO_2 during pregnancy were 1.34 (95% CI:0.83, 2.17) and 1.05 (95% CI:0.99, 1.11), respectively. Stronger associations were observed for exposures received after birth, but these estimates were unstable as they were based on only two studies. O_3 exposure was weakly associated with ASD during the third trimester of pregnancy and during the entire pregnancy, however, these estimates were also based on only two studies.

CONCLUSION: Our meta-analysis support the hypothesis that exposure to ambient air pollution is associated with an increased risk of autism. Our findings should be interpreted cautiously due to relatively small number of studies, and several studies were unable to control for other key risk factors.

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The right causes of autism

Format: Abstract Send to

Prenat Diagn. 2016 Sep 16. doi: 10.1002/pd.4926. [Epub ahead of print]

Prenatal diagnosis of 17q12 deletion syndrome: from fetal hyperechogenic kidneys to high risk for autism.

Gilboa Y[1], Perlman S[2], Pode-Shakked N[3,4,5], Pode-Shakked B[5,6], Shrim A[7], Azaria-Lahav E[8], Dekel B[3,8], Yonath H[6], Berkenstadt M[6], Achiron R[2].

Author information

Abstract

OBJECTIVE: The linkage between 17q12 microdeletions, renal anomalies and higher risk for neuro-developmental disorders is well described in the literature. The current study presents prenatal diagnosis of normal-sized hyperechogenic fetal kidneys leading to the diagnosis of 17q12 deletion syndrome and autistic spectrum disorder.

METHODS: Over a period of nine years in a single referral center, seven fetuses were diagnosed with hyperechogenic renal parenchyma and followed prospectively. Amniocentesis for molecular diagnosis was performed in all cases, and subsequently five fetuses were found to harbor a 17q12 deletion by chromosomal microarray analysis. Postnatal evaluation was carried out by a developmental neurologist.

RESULTS: Five of the seven fetuses had molecular diagnosis of 17q12 deletion. One patient elected termination of pregnancy. On long term follow up all of the four children showed symptoms consistent with neurodevelopmental disorders. The two fetuses with no deletion have a normal follow up with regression of the renal hyper-echogenicity.

CONCLUSIONS: We report a strikingly high correlation between prenatal hyperechogenic kidneys, 17q12 micro deletion and autistic spectrum disorder with the advantage of optimal prenatal counseling as well as early diagnosis and intervention.

The right causes of autism

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Reprod Toxicol. 2016 Sep 22;66:31-43. doi: 10.1016/j.reprotox.2016.09.013. [Epub ahead of print]

Prenatal selective serotonin reuptake inhibitor use and the risk of autism spectrum disorder in children: A systematic review and meta-analysis.

Kaplan YC[1], Keskin-Arslan E[2], Acar S[2], Sozmen K[3].

Author information

Abstract

OBJECTIVE: To determine whether an up-to-date systematic review and meta-analysis of observational studies would support the previously suggested associations regarding prenatal selective serotonin reuptake inhibitor (SSRI) use and the risk for autism spectrum disorders (ASD) in children.

METHODS: PubMed/MEDLINE, Cochrane Central Register of Controlled Trials and Reprotox databases were searched; observational studies with an exposed and unexposed group were included.

RESULTS: The meta-analysis of case-control studies demonstrated a significantly increased risk of ASD in the children whose mothers were prenatally exposed to SSRIs during different exposure time windows (except third trimester). The qualitative review of the cohort studies suggested inconsistent findings.

CONCLUSIONS: The significant association between preconception-only SSRI exposure and ASD in the children and negative/inconsistent findings among cohort studies weaken the significant associations detected in this meta-analysis. We suggest that confounding by indication still cannot be ruled out regarding prenatal SSRI exposure and ASD in children.

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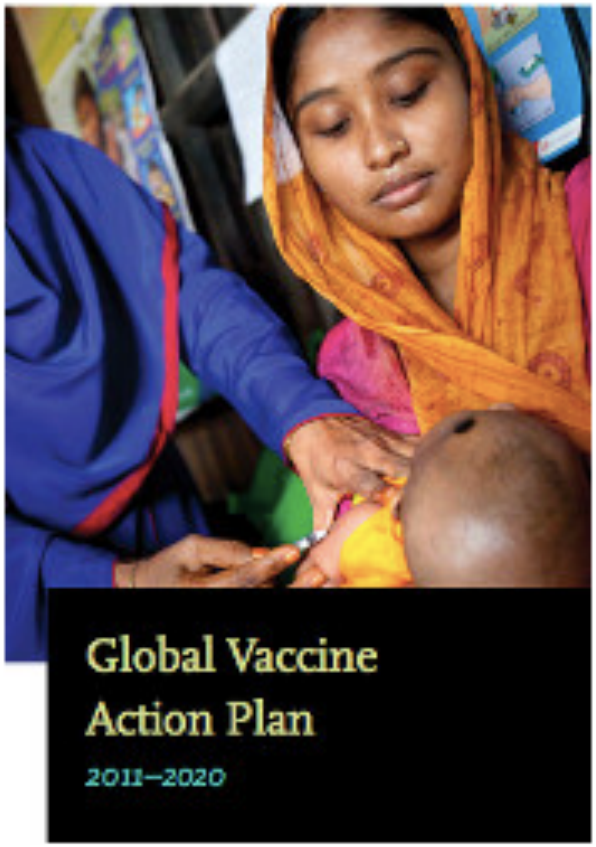
Eradicate measles: an world challenge

Global Vaccine Action Plan 2011–2020



The Global Vaccine Action Plan (GVAP) — endorsed by the 194 Member States of the World Health Assembly in May 2012 — is a framework to prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all communities.

GVAP aims to strengthen routine immunization to meet vaccination coverage targets; accelerate control of vaccine-preventable diseases with polio eradication as the first milestone; introduce new and improved vaccines and spur research and development for the next generation of vaccines and technologies.

Eradicate measles: an world challenge

The global commitment is to eliminate measles in most countries of the world by 2020.

In May 2012, 194 countries at the World Health Assembly committed to the Global Vaccine Action Plan. Within that plan is the commitment to achieve the measles and rubella mortality reduction and elimination goals. Five of the six WHO regions have measles elimination goals, and three of six have rubella elimination or control goals to be achieved before or by 2020.

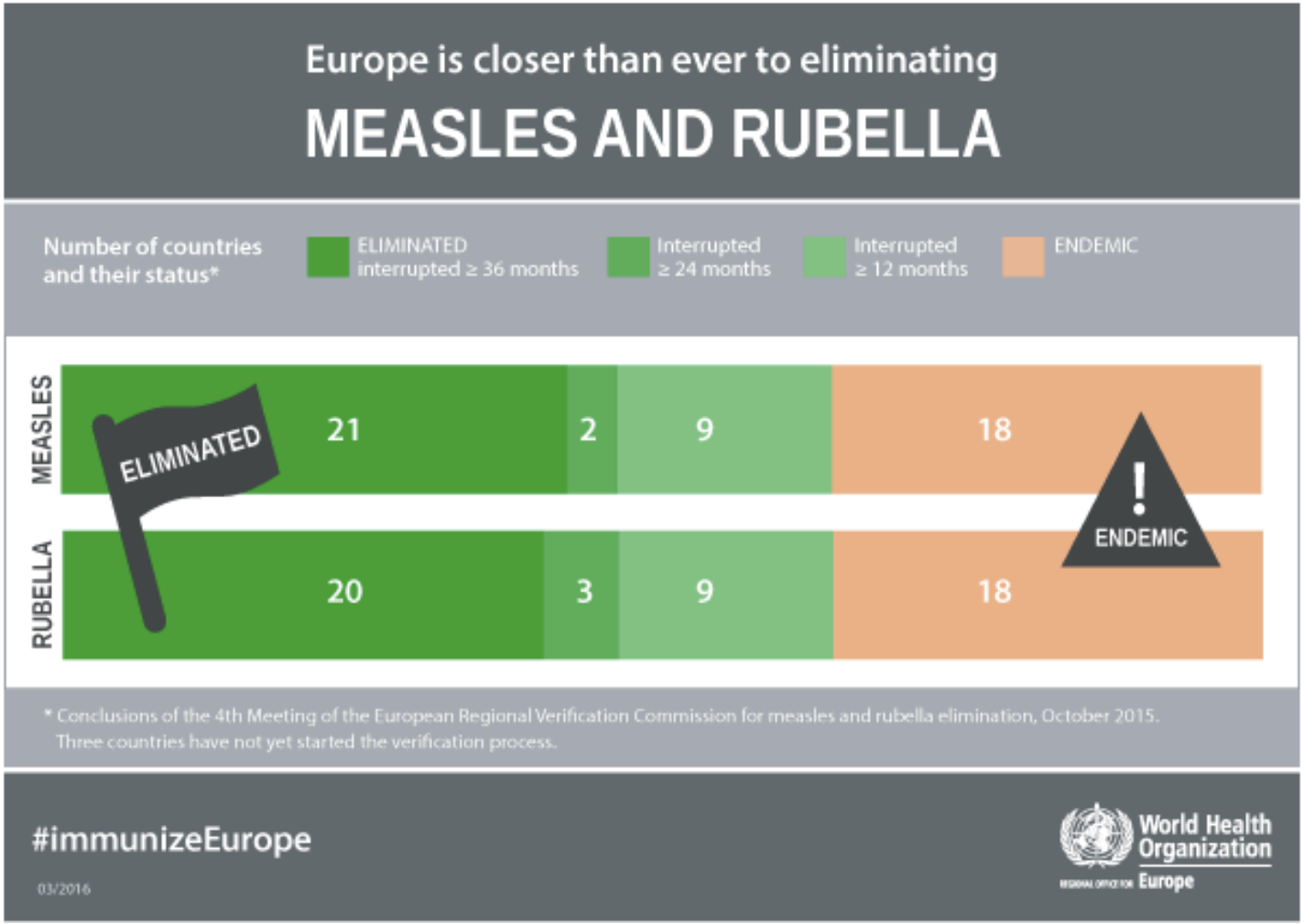
The world has also committed to reduce measles deaths by 95% by 2015.

The strategy

- Achieve and maintain **high levels of population immunity** by providing **high vaccination coverage** with two doses of measles- and rubella-containing vaccines through routine immunization and campaigns.
- **Monitor disease** using effective surveillance and evaluate programmatic efforts to ensure progress.
- Develop and maintain outbreak preparedness, **respond rapidly to outbreaks and manage cases**.
- Communicate and engage to build public confidence and demand for immunization.
- Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.

The objectives

Europe


Europe is closer than ever to eliminating
MEASLES AND RUBELLA
Number of countries and their status*
ELIMINATED interrupted ≥ 36 months
Interrupted ≥ 24 months
Interrupted ≥ 12 months
ENDEMIC
MEASLES
21
2
9
18
ELIMINATED
RUBELLA
20
3
9
18
!
ENDEMIC
* Conclusions of the 4th Meeting of the European Regional Verification Commission for measles and rubella elimination, October 2015.
Three countries have not yet started the verification process.
#immunizeEurope
03/2016
World Health Organization
Europe

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Measles elimination: the state of art in Italy

- MMR vaccine is actively offered in all Italian regions since 2003
  - 1st dose: 12-15 months
  - 2nd dose: 5-6 years
  - Catch-up: adolescents, high risk adults
- The target coverage (>95%) has not been achieved

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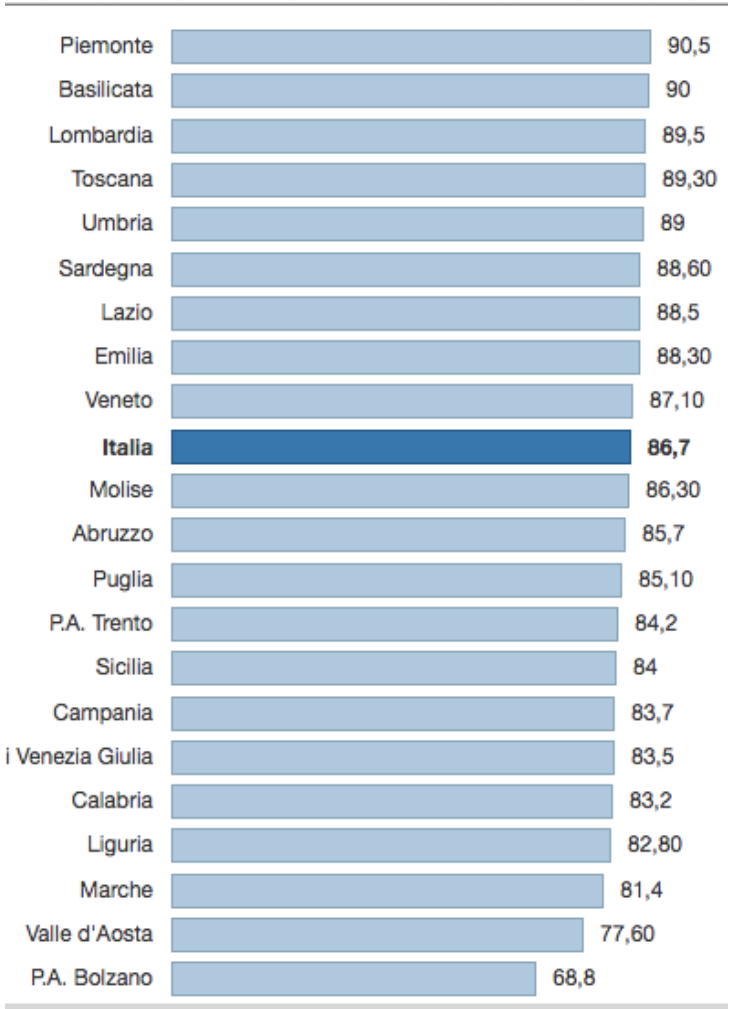
MMR immunization coverage, Italy, 2012 cohort



Epicentro

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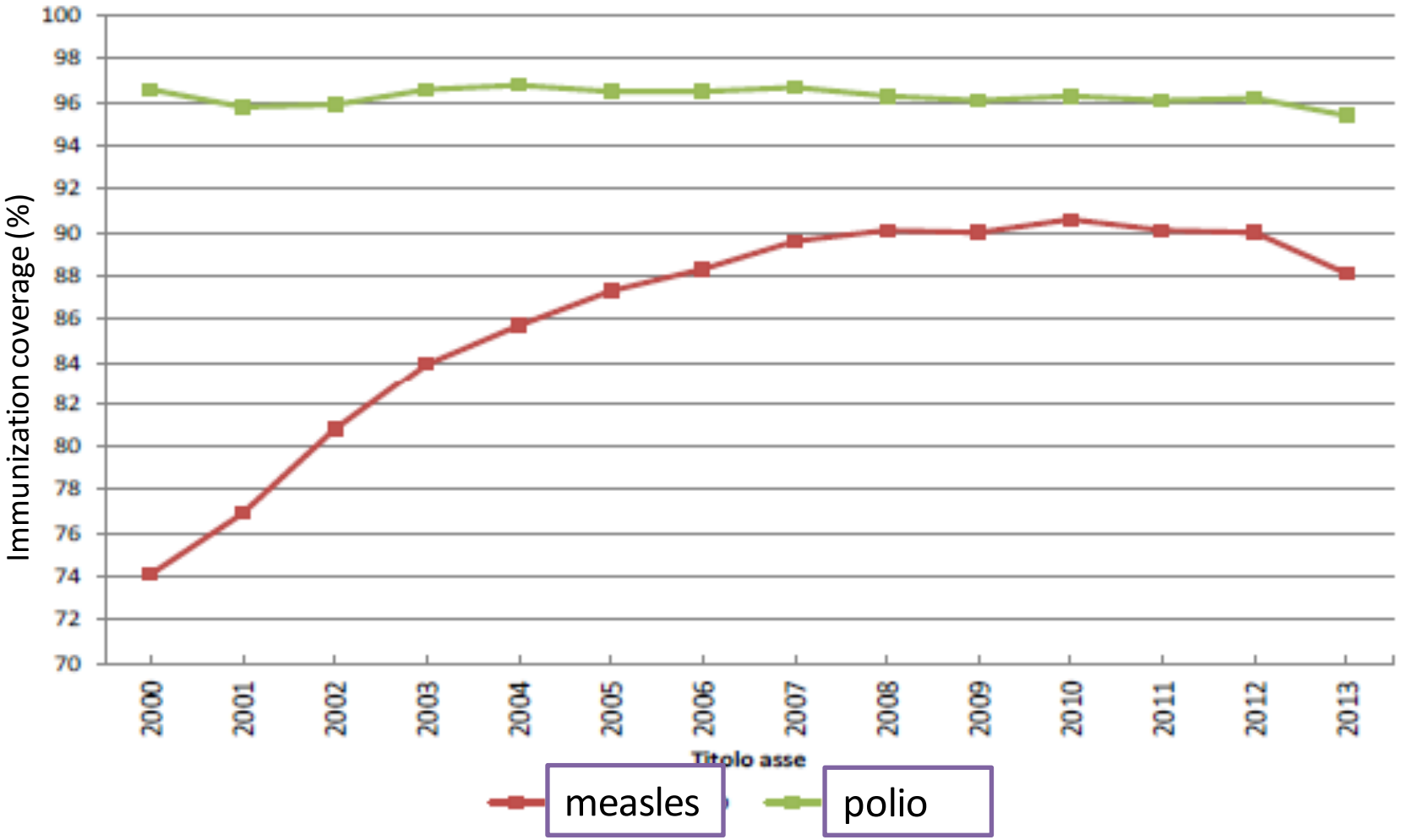
MMR immunization coverage, Italy, 2000-2013 cohorts



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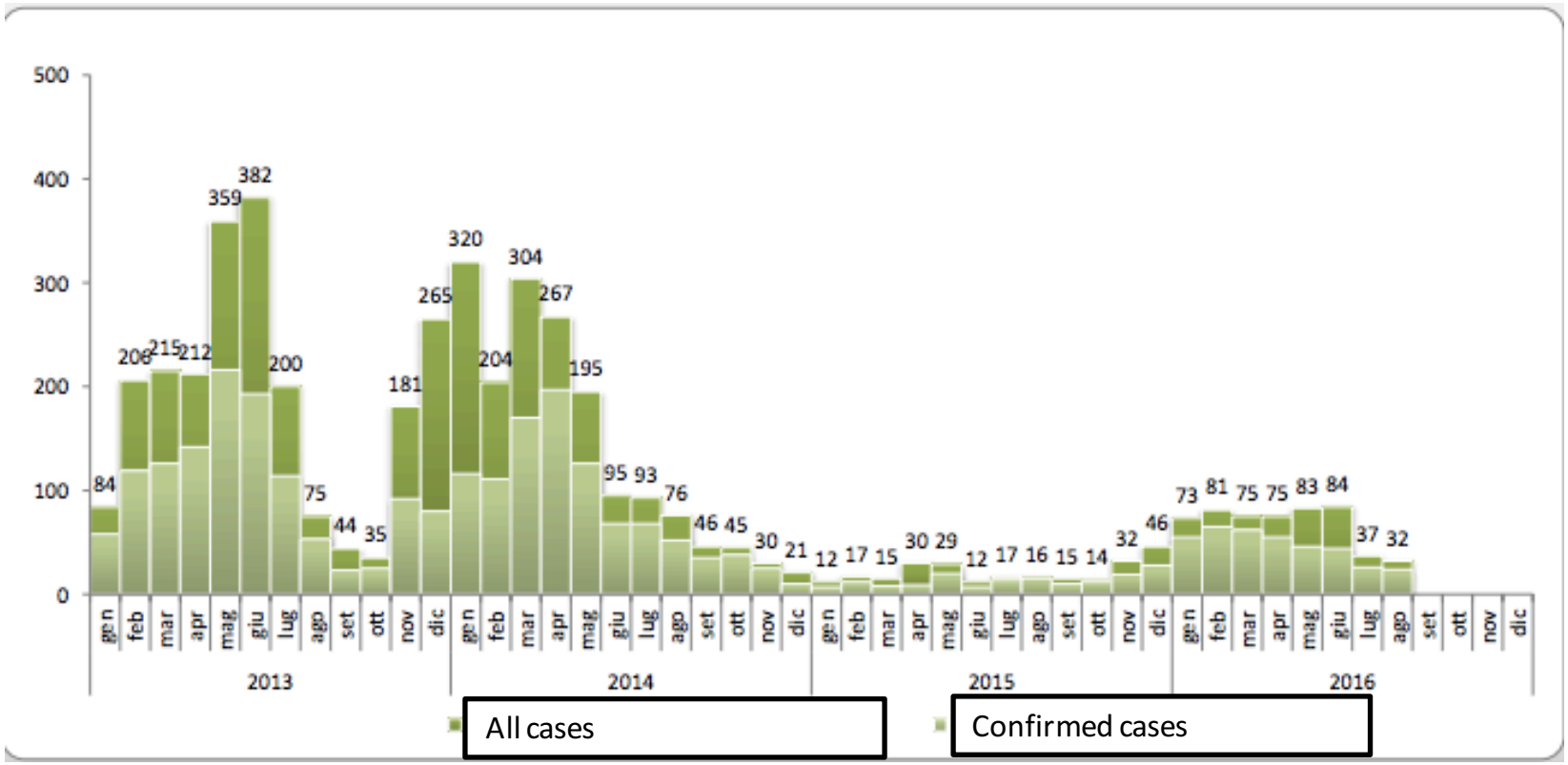
Epidemiology pattern in Italy



Epicentro

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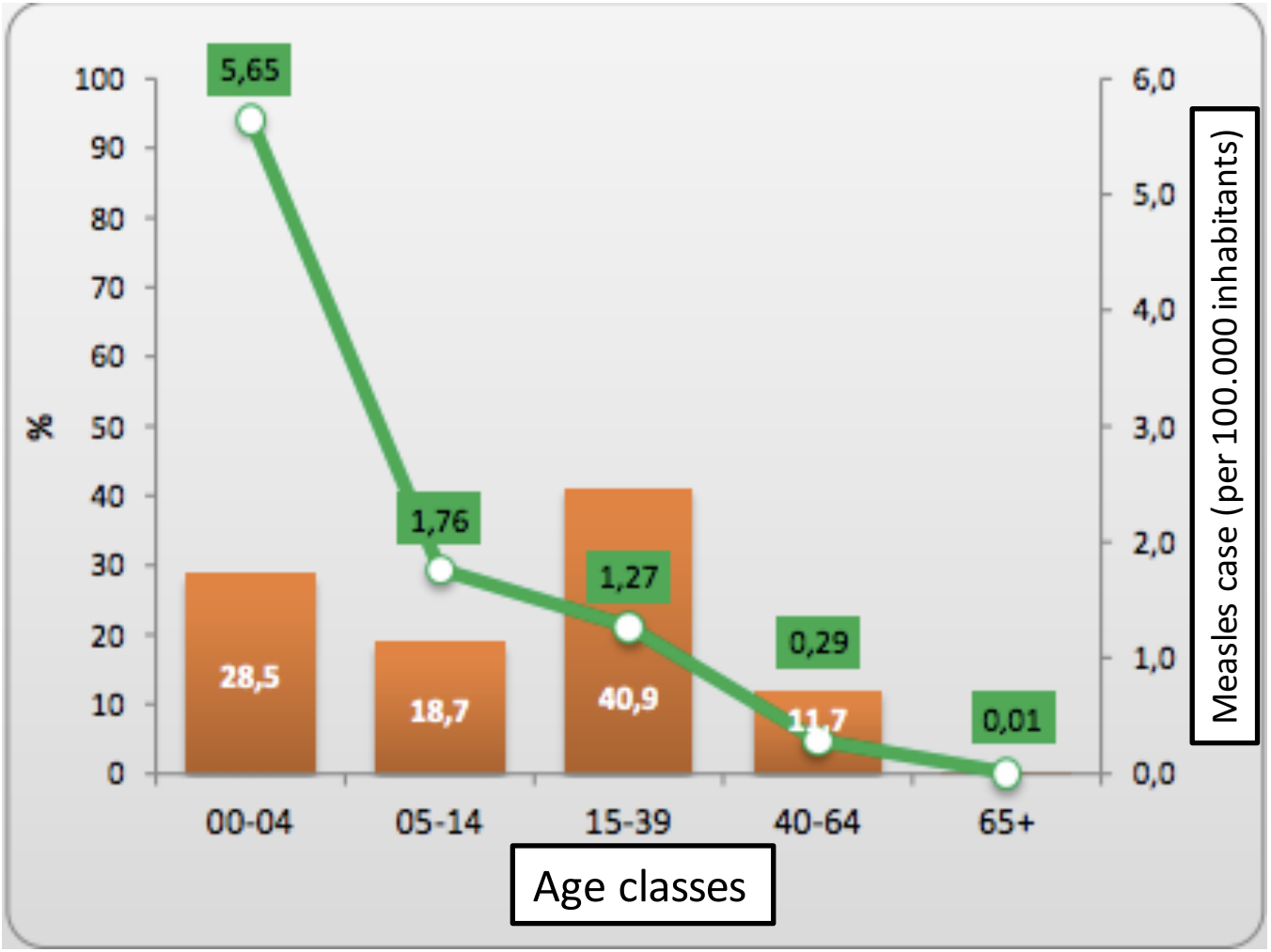
Distribution of 2016 measles cases per age classes



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