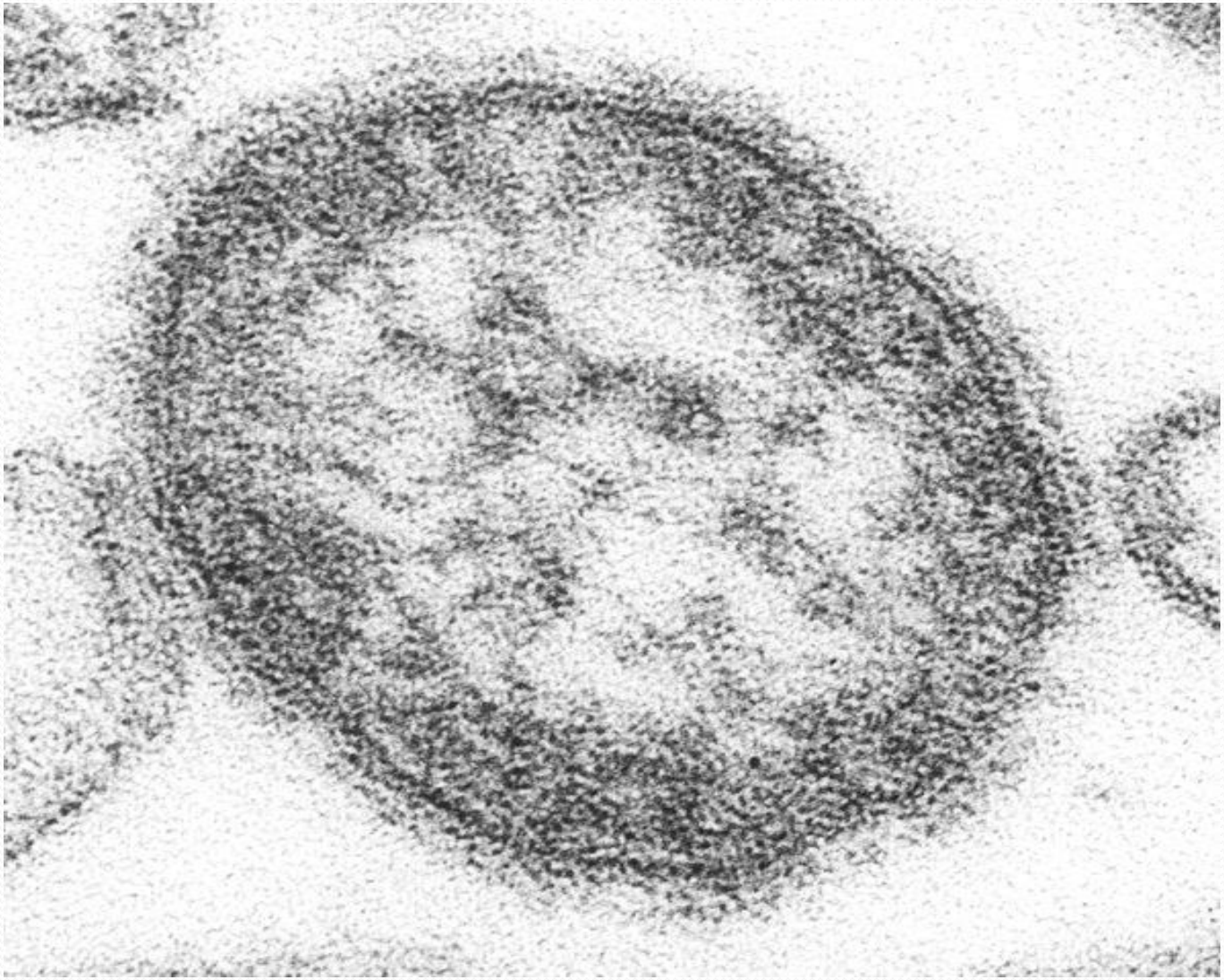
Measles

Dr. Ommar Swe Tin
Virology Section
National Health Laboratory

Measles(Rubeola)Virus
Description of the Agent

- Member of the genus Morbillivirus of the family Paramyxoviridae
- Pleomorphic, generally Sphericle, Enveloped virus
- ss non segmented RNA
- two glycoproteins, embedded in the envelope are hemagglutinins-neuraminidase (HN), Fusion (F)
- Antigenically stable, monotypic virus

Measles Virus



Susceptibility to Physical and chemical agents

- heat labile
- destroy by 56°C x 30 mins, exposure to UV light
- infectivity reduced by 50%, at 37°C x 2hrs
- Ether, alcohol and phenol inactivate virus
- Stable at pH 5-10.5 with an optimum at pH7.0

Transmission of infection

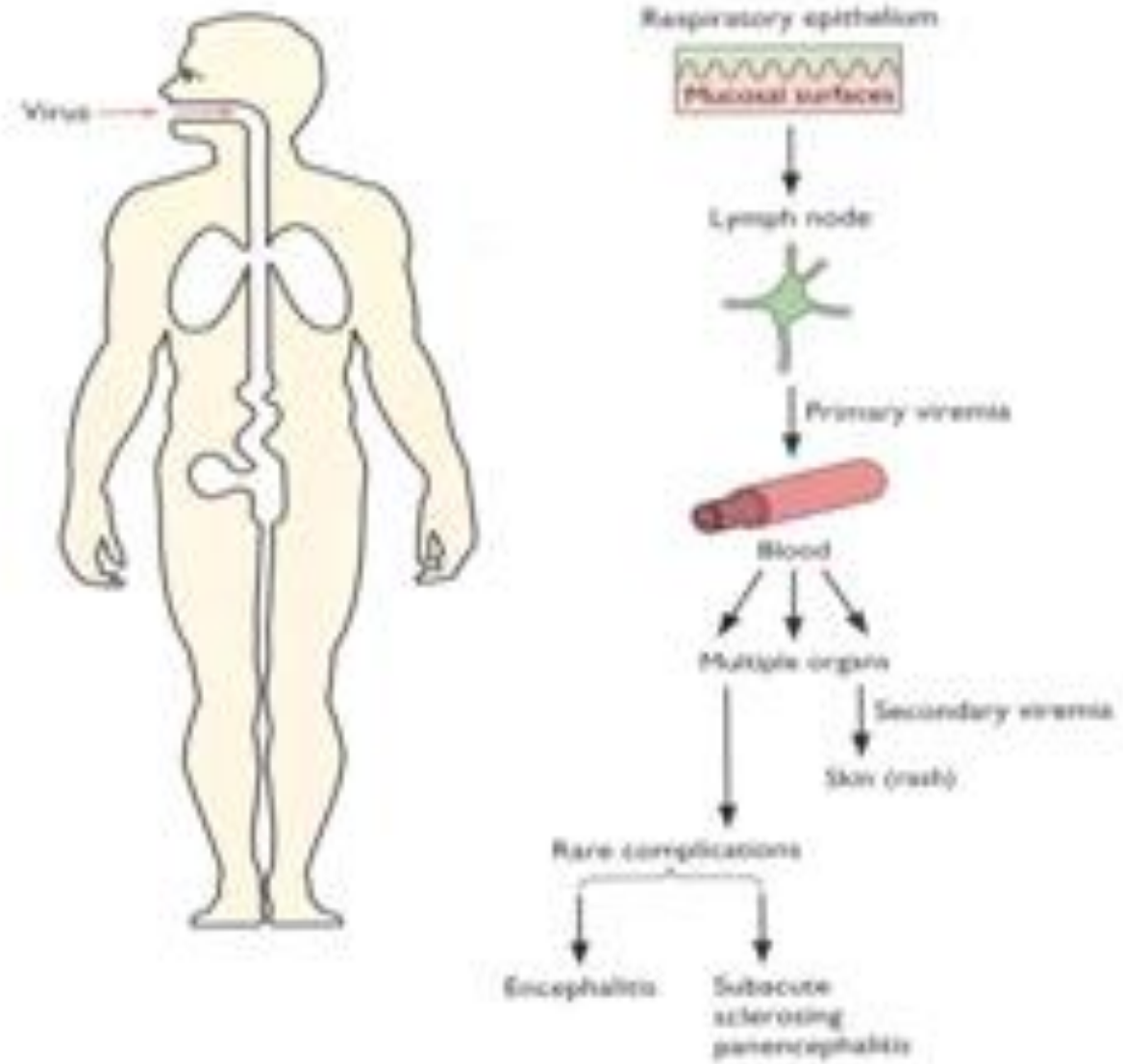
- Through the inhalation of infected aerosols and droplets
- Infected formites are involved less frequently
- Highly communicable (99% chance of acquiring disease in non immune person)
- Infected people can spread measles to others from four days before through four days after the rash appears.

Pathogenesis

- Replication of the viruses in epithelial cells of the resp: mucosa
- viruses spread to monocytes and other cells, to seed the lungs and draining lymph nodes where replication continues and Primary viremia occurs
- Replication of virus at the secondarily infected lymphoreticular sys; lead to formation of Warthin- Finkeldey giant cells

Pathgenesis contd

- Secondary viremia then occurs, lymphocytes and monocytes carry viruses throughout the body
- Another type of giant cell the epithelial giant cell develops during secondary viremia and has been observed in the mucosa of the body



Pathogenesis of Measles Infection

Principles of Virology, Flint et al 2nd Edition,

Clinical Features

- Incubation period approx: 1 week to 10 days
- Clinical features are

fever , cough, coryza conjunctivitis	3-4days
Koplik's spots (50-90%) Rash	4-5days

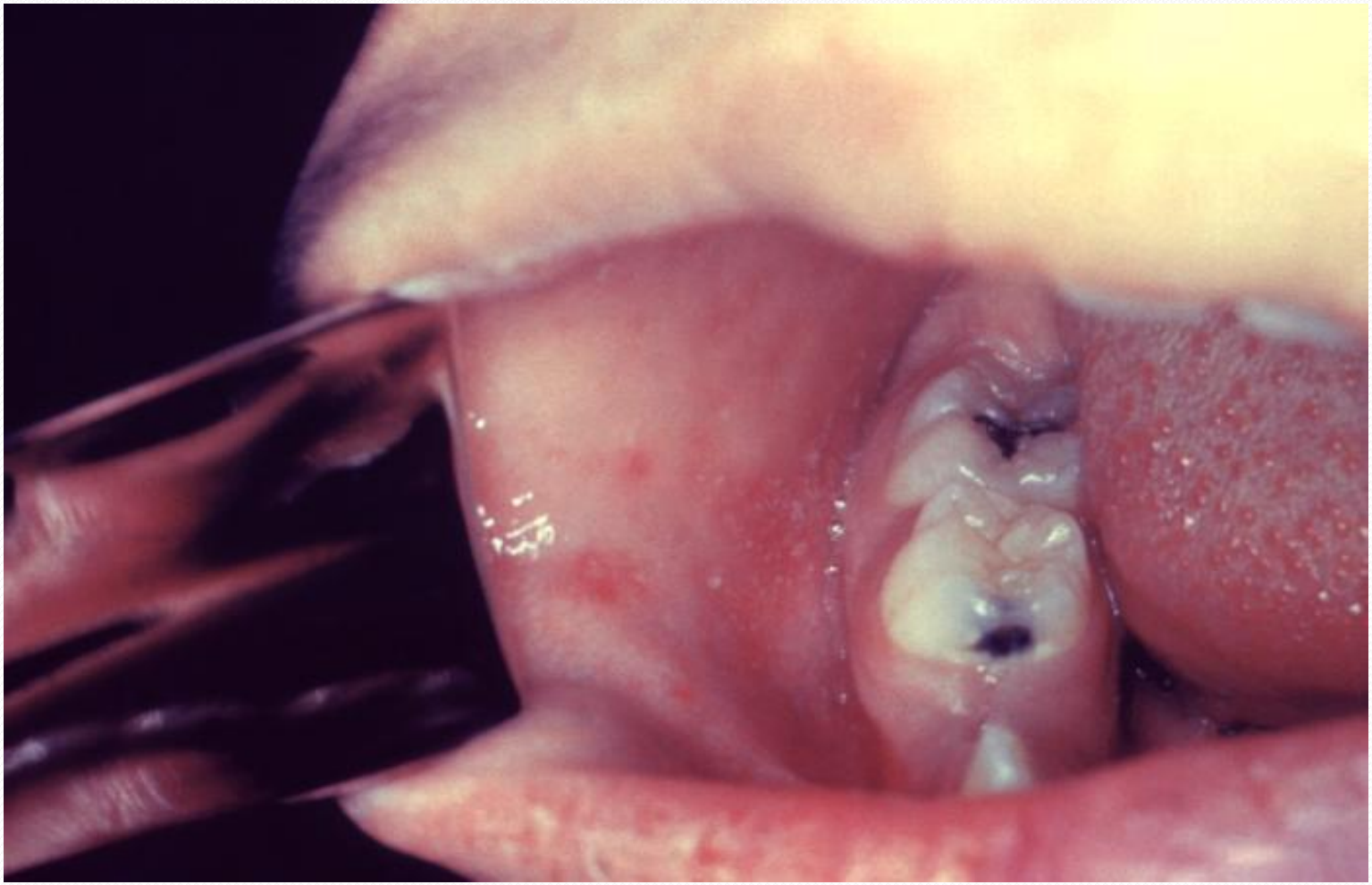
Koplik's spots

- Appear on the buccal mucosa
- Shortly before rash onset
- Small irregular red spots with a bluish white speck in the centre

Koplik's Spots

Koplik's spots

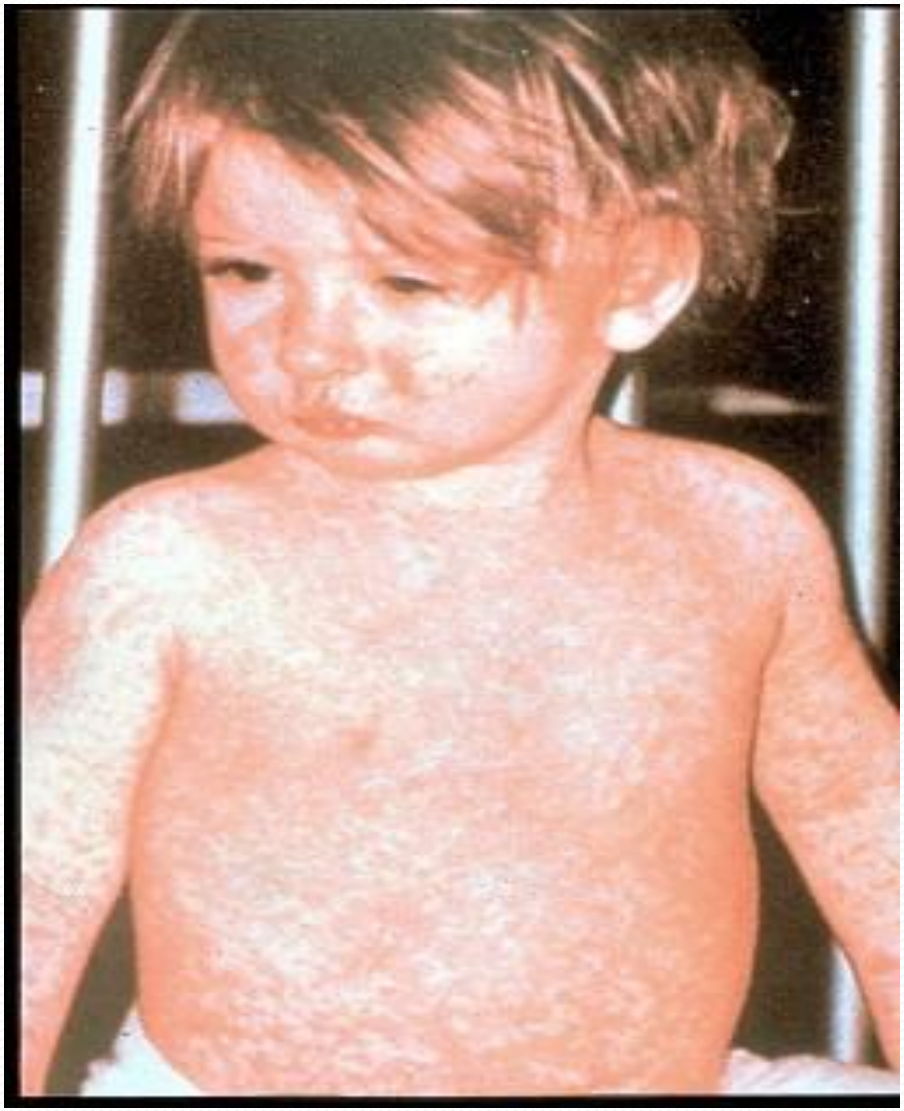
Koplik's spots



Measles Rash

- First appear on the forehead or neck or behind the ears
- Lesions are red macules and become maculopapular
- By the end of second day upper extremities and trunk
- Third day lower extremities are affected

Measles



Measles Rash contd

- Rash resolves in the same order first disappearing from the face and neck
- last about 6 days
- turn brown and persists for 7-10 days
- Followed by fine desquamation

Complications

- Bronchitis, bronchiolitis, pneumonia and otitis media
- Encephalitis
- Diarrhoea
- Blindness
- Death- 1/1000 cases
- Risk of death is greater for infant and adult than children and adolescents

Complications contd

- **Acute post infectious encephalitis**

  -0.1-0.2% of patients, 2to7 days a/f onset of rash

  -presented with confusion and seizures accomp: by recurrence of fever

  - mortality 30%

  -30% of survivors have permanent brain damage and mental retardation

Complications contd

- **Measles Inclusion Body Encephalitis (MIBE)**

  - occur weeks to months a/f acute infection - generally fatal

  - unchecked replication of measles virus in CNS

  - involves immunocompromised patient

Complications contd

- **Sub acute sclerosing panencephalitis**

(SSPE) -due to persistent measles infection

(1/100,000-1/1000,000)

- variably fatal, personality changes, mental deterioration, involuntary movements and muscular rigidity

- begins 4-17 yrs a/f recovery form measles

Complications contd

- Atypical measles

  - occurs in children exposed to wild virus, with measles vaccination 2-4 yrs ago

  - immunopathological responses due to a combination of Arthus reaction and delayed hypersensitivity

Laboratory Diagnosis

- Samples for viral isolation should be collected early in the acute phase when concentration of virus is high

Samples for isolation of virus and detection of viral antigen

-whole blood (leukocytes)

-Throat and nasopharyngeal secretions by swabbing or washings

-Urine, brain and skin biopsies

1.Urine

- 10-20ml of urine collected in a sterile container
- First urine passed in the morning
- **Collect within 3 days after the onset of rash**
- Label the tube with the patient's name, outbreak ID number, specimen number, date of collection and specimen type.

1.Urine

- Before transport, in the hospital laboratory, they should be kept at 4-8°C.
- Urine should be sent to NHL within 24 hours after collection (in cold box) with laboratory request form.

2.Throat Swab

- **Collect within 3 days after the onset of rash**
- Tilt the patient's head back and gently depress the tongue with a tongue depresser.
- The tonsillar areas and the posterior pharyngeal wall should be rubbed with the polyester swab to dislodge the epithelial cells.
- Care should be taken not to touch the tongue and the lateral walls of the buccal cavity to avoid contamination with commensal bacteria

2.Throat Swab

- After collection, break the shaft of the swab and place immediately into a sterile leakproof container containing viral transport medium (VTM).
- Label the tube with the patient's name, outbreak ID number, specimen number, date of collection and specimen type.
- Before transport, in the hospital laboratory, they should be kept at 4-8°C.
- Throat swab should be sent to NHL within 48 hours after collection (in cold box) with laboratory request form.

Laboratory Diagnosis contd

- Direct detection of Viruses and Viral Antigens

  - Cytological Examination

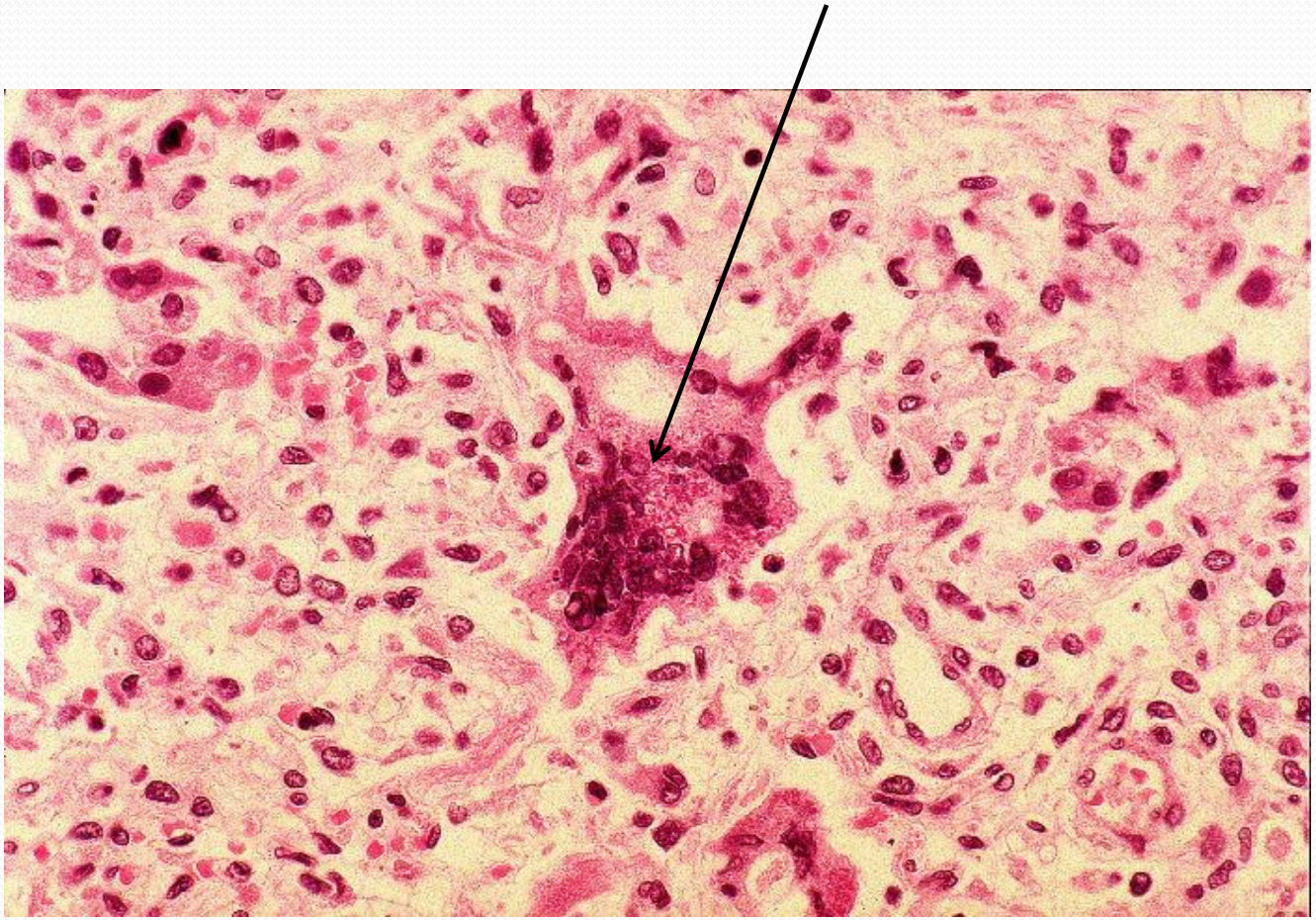
    Examination of intranuclear and intracytoplasmic inclusions and giant cells

    Slides can be stained with Wright and Hematoxylin and Eosin (H+E)

  - Immunofluorescence (IFA)

    sensitive for clinical specimens and infected cell culture

Histopathology of Measles pneumonia-giant cells



Laboratory Diagnosis contd

- Other methods

  -PCR and hybridization assay

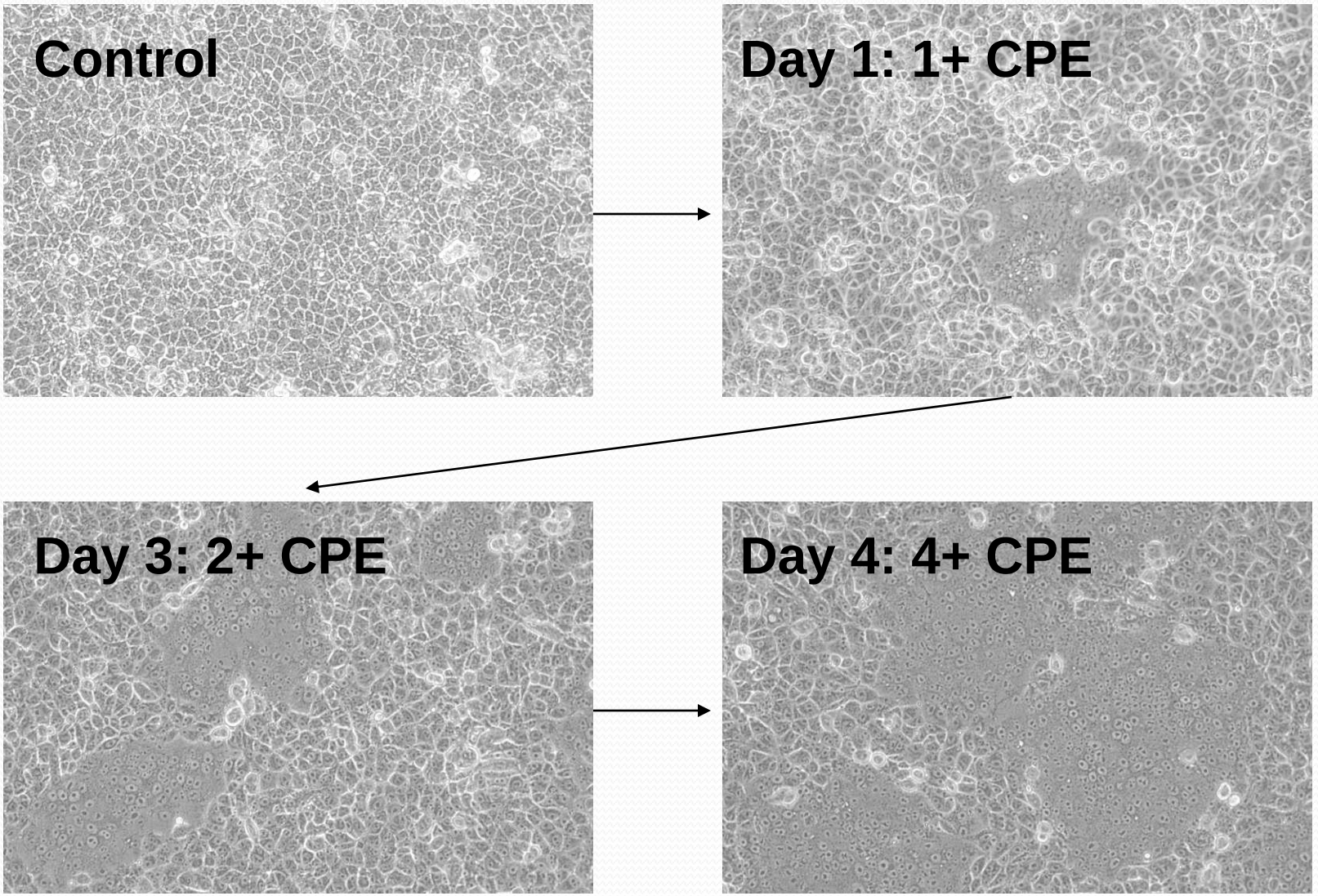
Isolation of virus

- Isolation in VERO h SLAM (VERO human Signaling Lymphocyte Activation Molecule) cell line.
- Positive culture shows syncytia formation

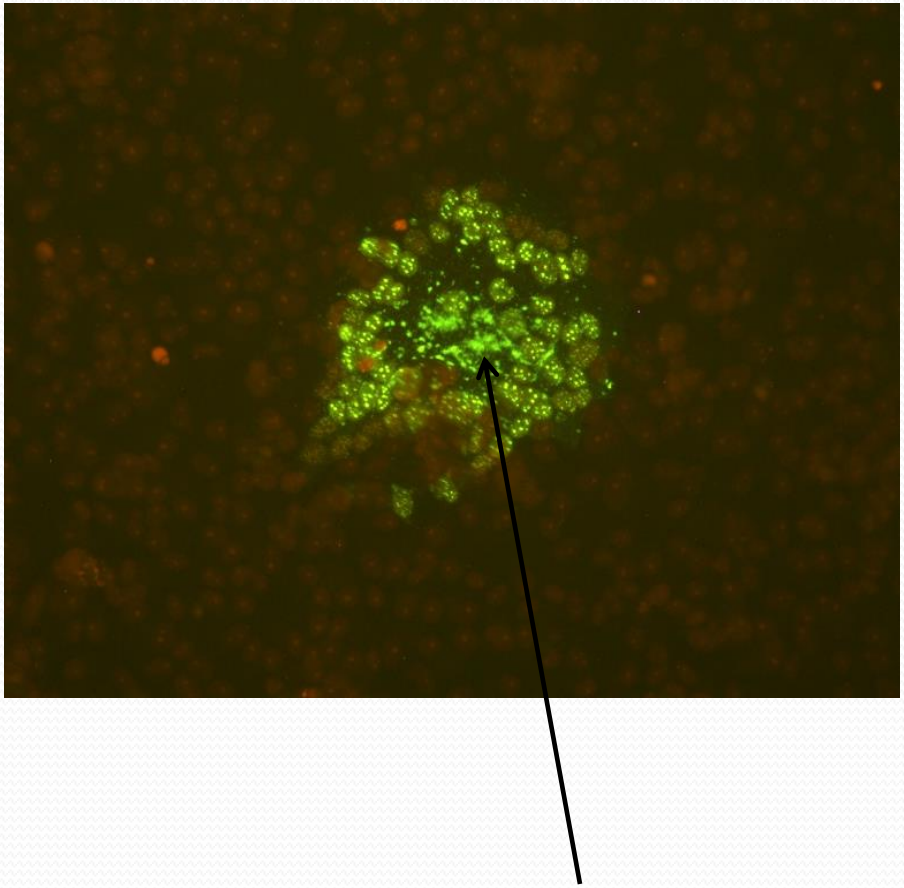
Genotyping

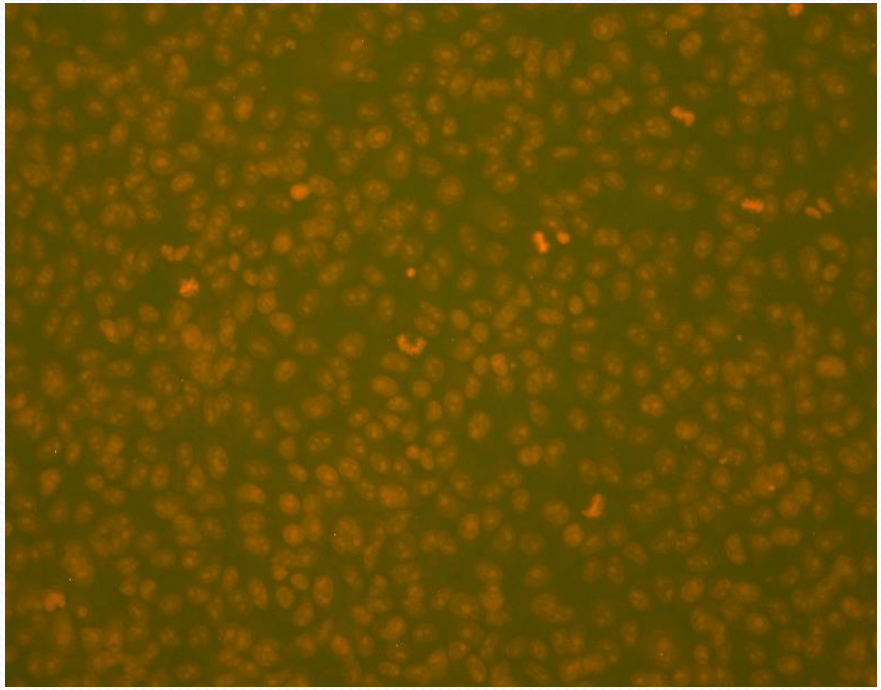
WHO recognizes 20 genotypes

Progression of CPE: Measles Virus in Vero/SLAM



IFA for Measles in Vero/SLAM





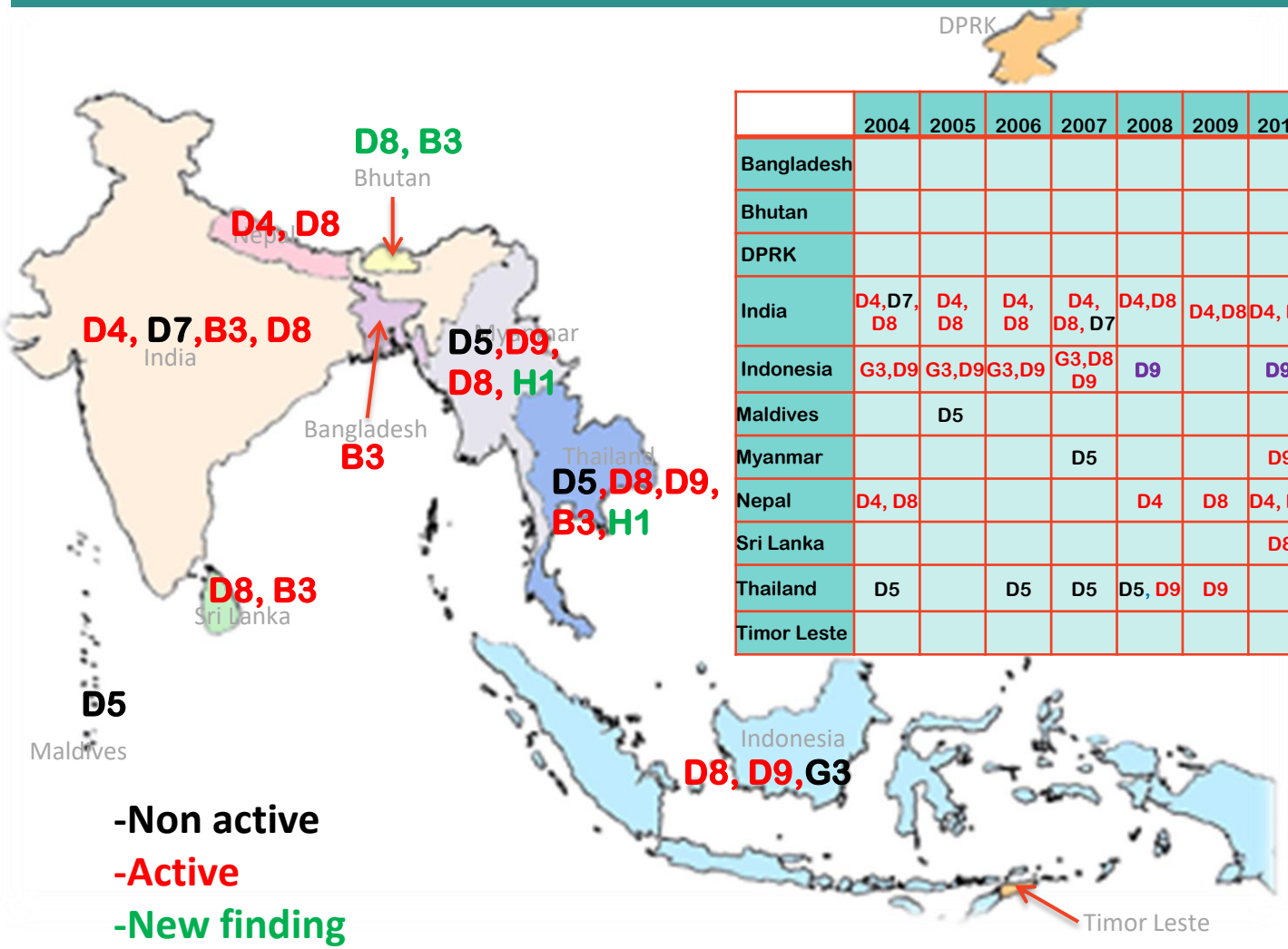
Negative control

Isolation and Identification of MeV

1. Isolation in VERO h SLAM cell line
2. Positive culture shows syncytia formation
3. Isolated MeV or sample by PCR
4. Positive PCR product is sent to RRL for sequencing
5. Sequence analysis for measles genotyping is done in NML and submit the result in MeaNS, which serves as the Global Measles Sequence Database for the WHO LabNet
6. Myanmar MeV
   - 2006 - D5,
   - 2009/2010/2011/2012 - D9
   - 2016 – D8 (Naga Outbreak), H1 (Ygn outbreak)
   - 2017 – H1

MEASLES GENOTYPES

Measles genotypes circulating in SEAR between 2004 and 2016*



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Bangladesh											B3	B3	
Bhutan												D8,B3	D8
DPRK													
India	D4,D7, D8	D4, D8	D4, D8	D4, D8, D7	D4,D8	D4,D8	D4, D8	D4, D8	B3,D4, D8	D4, D8	B3, D4,D8	B3,D4, D8	B3,D4, D8
Indonesia	G3,D9	G3,D9	G3,D9	G3,D8 D9	D9		D9	D9,G3	D8, D9	D8, D9	D8,D9	D8, D9	D8,D9
Maldives		D5											
Myanmar				D5			D9	D9	D9				D8, H1
Nepal	D4, D8				D4	D8	D4, D8	D4, D8	D8			D4,D8	D8
Sri Lanka							D8	D8			B3		B3
Thailand	D5		D5	D5	D5, D9	D9		D8, D9	D8, D9	D8, D9	B3	H1	H1,B3, D8
Timor Leste													

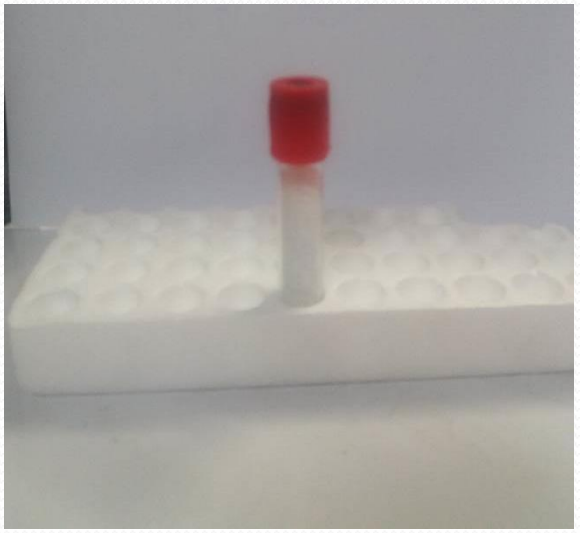
* Data as of 12 Aug 2016

Source: Measles RRL in SEAR, Nation Institute of Health, Thailand, MeaNS, WHO SharePoint and **Intercountry Training on Molecular Technique for the SEAR Measles and Rubella Laboratory Network, Bangkok, Thailand, Feb 2014**

Laboratory Diagnosis contd.

For serology

- **Collect within 4 - 28 days after the onset of rash**
- Collect 5ml of blood in a sterile plain tube
- **one tube** is enough
- Only test for Measles IgM Ab for recent infection. IgG Ab is not done (e.g. SSPE)



Laboratory Diagnosis contd

- Label the tube with the patient's name, age, sex, outbreak ID number, specimen number, date of collection and specimen type

- **Tubes are without label. We cannot do the samples without label**

Laboratory Diagnosis contd

- Transport the whole blood specimen to NHL if it can reach within 24 hours.
- If it cannot reach NHL within 24 hours, do separation of serum
- Separate serum after clotting, and transfer into a new sterile bottle or microvial and send to NHL.
- To prevent insufficiency, collect 5 ml of blood or 2 ml of serum in a sterile bottle
- For outbreak, 5 cases enough.

Laboratory Diagnosis contd

- Before transport, in the hospital laboratory, they should be kept at 4-8°C.

- The specimens should be sent to NHL in cold box with laboratory request form.

Laboratory Diagnosis contd

- The serum/ blood samples should not be haemolysed samples.

(Prevent hemolysis of samples – narrow needle, rapid suction, rapid pushing blood out of syringe, wet container should not be used)

Laboratory Diagnosis contd

Measles Laboratory Requisition Form must include

- Date of collection
- Date of onset of rash
- History of measles vaccination
- Patient's address

Some of the lab forms are not filled completely. Please fill completely. Some samples are without lab request forms.

Serological Tests

- Enzyme Linked Immunosorbent Assay (ELISA)
- Neutralization Test
- Immunofluorescence Test
- Haemagglutination Inhibition test

Measles Serology

- Commercial test kits available - ELISA
- Measles IgM antibody can be detected 4-28 days
- Positive Measles IgM antibody indicates acute Measles virus infection
- SEAR _Algorithm of MeM&RuM.ppt

- Measles IgG antibody appears at 7-10 days after the onset of rash
- Ig G antibody persist for life long after infection
- Presence of IgG antibody indicates immunity (past infection or immunization)

Prevention

- Measles immunization - 1st dose at 9 months of age (MR) and 2nd dose at 1½yrs of age (MR)
- MMR (Measles, Mumps, Rubella) – 1st dose at 1yr of age and 2nd dose at 4yrs of age

Contraindications to the use of live virus vaccine

(a)Patients with immune deficiency diseases

(b)Patients with severe acute illness

(c)Persons with anaphylactic hypersensitivity to a previous dose of measles vaccine

(d)Pregnancy

Thank you for your kind attention