Epidemiology of Respiratory Infections – II

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Diphtheria

- The word “diphtheria” originates from Greek “***leather***” which describes the pharyngeal membrane which is ***pathognomonic for diphtheria.***
- The disease results from infection with toxigenic strains of ***Corynebacterium diphtheriae***.
- The diphtheria bacillus was first described by Klebs in 1883 and was first cultured by Loeffler in a culture medium of his own design in 1884.
- It is, therefore, known as the ***“Klebs – Loeffler” bacillus***.

Epidemiology

- In developing countries also, the inclusion of diphtheria vaccination in childhood programmes saw ***a steady decline in the incidence of the disease.***

- Despite widespread immunization, diphtheria remains **endemic in several parts of the developing world** including Africa, India, Bangladesh, Vietnam and Brazil.
- 80 – 90% of the global burden of diphtheria cases still comes from developing countries.
- In India, the number of reported cases has declined from 5,125 in year 2000 to **4,490 in year 2014** with a peak of 10,231 in year 2005.

- *Corynebacterium diphtheriae* are nonmotile, nonsporualting, unencapsulated gram positive bacilli.
- The most important factor determining virulence of *Corynebacterium diphtheriae* is the ***exotoxin***.

- The highest incidence rates for diphtheria are in ***preschool children and school age children.***
- Studies in India have also demonstrated a rise in proportion of cases of diphtheria over five years of age.
- In temperate countries most of the cases occur during the winter.
- In tropical areas, this distinction is blurred with **transmission taking place throughout the year**

- The primary **modes of transmission** are ***airborne respiratory droplets and direct contact*** with respiratory secretions or exudates from skin lesions.
- Transmission can occur through fomites.
- ***Contaminated milk*** has also been implicated in transmission.
- Humans are the ***only known reservoir*** of the disease.
- Infection can spread from both cases and carriers.

- **The incubation period** ---one to five days.

- Period of infectivity ---14-28 days from onset of disease to much longer period.

Clinical features

- **Respiratory tract**
- Anterior nasal / Faucal infection / Laryngeal or tracheobronchial infection
- **Cutaneous diphtheria**

- Death from diphtheria results as a **consequence of**:
- *Severe respiratory disease resulting in airway obstruction or*
- *From systemic complications due to diphtheria toxin*.
  - Diphtheria toxin is toxic to all body tissues but the most important complications result from its effects on the heart and the nervous system.

Diagnosis

- Confirmation can be done ***by culturing smears*** from the membrane on ***Loeffler's or tellurite media***.
- Culture specimens should ideally be taken before administration of antibiotics.
- ***PCR test*** is now available for confirming diphtheria.

Treatment

- **Diphtheria antitoxin** (20,000 – 1,00,000 Units) is the *cornerstone of definitive treatment*.
- Antibiotics including including penicillin, erythromycin, azithromycin, tetracycline and rifampicin.
- ***Management of complications*** including airway obstruction must be done energetically.
- ***Natural infection does not always confer immunity*** against the toxin. Patients must, therefore, be given ***active immunization during convalescence.***

Contacts

- **Household and other close contacts of diphtheria** cases should be investigated with culture from nasal swabs.
- ***Prophylactic antibiotics, either penicillin or erythromycin*** should be given for seven days irrespective of immunization status.
- ***Contacts with positive cultures*** should receive ***active immunization*** against the disease and repeat cultures two weeks after the course of antibiotics.

Prevention & Control

- Active immunization against diphtheria is the mainstay of disease prevention.
- Diphtheria vaccines are based on ***diphtheria toxoid***, which is a modified bacterial toxin that induces *protective antitoxin*.
- The vaccine is available almost always combine with ***Tetanus toxoid (DT) or tetanus toxoid and Pertusis vaccine (DPT).***

Pertusis

- Whooping cough (whoop means loud crowing inspiration)
- '*Hundred day cough*'
- Continues to public health concern ***even in countries with high vaccination coverage.***
- About 2.49 lacs cases were reported globally (2012)
- It is increasingly reported in older children, adolescents and adults.
- In India, cases declined from 1.63 lakh (1987) to 36,661 (2013)

- *Bordetella pertussis*.
- Source of infection is a case of pertussis.
- Mean age of infection : 20-30 months (developing countries) vs. 50 months (developed countries)
- Infants below 6 months has highest mortality.

- Incidence and fatality more among females than males.

- More cases occur during winter and spring months.
- Overcrowding, lower social economic classes.

- It is spread mainly by droplet infection and direct contact.
- Incubation period: 7-14 days.
- Clinical course:
  - Catarrhal stage, Paroxysmal stage, and Convalescent stage.
- Complications: bronchitis, bronchopneumonia and bronchiectasis.

Prevention and Control

- Early diagnosis and treatment with Erythromycin.
- Isolation of cases.
- Disinfection of discharges from nose and throat.
- Active immunization with DPT vaccine.

Influenza (H1N1)

1918: “Spanish flu”

- Associated with Influenza A (**H1N1**).
- An estimated one third of the world’s population was infected.
- The disease was exceptionally severe.
- Case-fatality rates were >2.5%.
- Total deaths were estimated were arguably as high as 100 million.
- Swine influenza was first proposed to be a disease related to human influenza during the 1918 flu pandemic, when pigs became sick at the same time as humans.

1957: “Asian Flu”

- The pandemic occurred due to Influenza A (**H2N2**)
- Caused 1-2 million deaths worldwide.

1968: “Hong Kong Flu”

- This pandemic was associated with Influenza A (**H3N2**)
- 700,000 deaths were reported worldwide.

2004

- Outbreak of **H5N1** was reported in 2003
- Affected poultry in 50 countries
- Caused human infections in 15 countries with 262 Deaths.

2009: “Swine Flu”

- Earlier referred to as “swine flu” because initial testing showed many of the genes in the virus were similar to influenza viruses normally occurring in North American swine.

- But further research has shown that the outbreak is due to a reassortant strain of **H1N1** not previously reported in pigs.

Agent: H1N1 Virus

- An enveloped RNA virus
- Belongs to the family orthomyxoviridae.
- Three types of influenza virus, namely A, B & C based upon nucleoprotein and M capsid protein.
- The virus contains two surface antigens H (hemagluttinin) and N (neuraminidase).
- Presently circulating strains: A (H1N1);
- Circulating seasonal influenza A (H3N2) and Influenza B.

Antigenic Drift:

- It is responsible for new seasonal strains that makes necessary surveillance to detect these strains and to prepare new seasonal influenza vaccine (yearly basis)

Antigenic Shift:

- It may result in a new virus easily transmissible from man to man for which the population has no immunity.
- Results in Pandemics

Person-to-person transmission:

- Influenza virus is present in respiratory secretions of infected persons.
- As a result, influenza virus can be transmitted through droplets by sneezing.
- **Airborne** :Droplets from infected human beings.
- **Contact**: Direct contact / contact with formites

Incubation period:

- 1-2 days

Source of infection:

- Case or sub-clinical case.

Period of communicability:

- 3-5 days from clinical onset in adults;
- Up to 7 days in young children
- Peak viral shedding occurs on day 1 of symptoms

Environmental factors

- **Seasonality:**
  - Temperate zones: epidemics occur in winter
  - Tropics/ Sub tropics: epidemics occur in rainy season
  - Sporadic cases: round the year

- **Overcrowding**

- **Closed populations :**
  - High attack rates may be witnessed in Army Barracks, College hostels, Schools, Residential hostels of schools, etc

Categorization of cases during screening

- Category A
- Category B
- Category C

Category-A

- Patients **with mild fever plus cough / sore throat** with or without body ache, headache, diarrhoea and vomiting.
- They **do not require** Oseltamivir and should be treated for the symptoms mentioned above.
- The patients should be monitored for their progress and reassessed at 24 to 48 hours by the doctor.
- **No testing of the patient for H1N1 is required.**
- Patients should confine themselves at home and avoid mixing up with public and high risk members in the family.

Category-B

(i)* if the patient has **high grade fever and severe sore throat,** may require home isolation and Oseltamivir;

(ii)* individuals having one or more of the **following high risk conditions** shall be treated with Oseltamivir:

- Children <5 years old;
- Pregnant women;
- Persons > 65 years or older;
- Patients with lung diseases, heart disease, liver disease, kidney disease, cancer blood disorders, DM, neurological disorders, and HIV/AIDS;
- Patients on long term cortisone therapy.

*In addition to all the signs and symptoms mentioned under Category-A

- **No tests for H1N1 is required for Category-B (i) and (ii).**

- All patients of Category-B (i) and (ii) should confine themselves at home and avoid mixing with public and high risk family members.

Category-C

In addition to the above signs and symptoms of Category-A and B, if the patient has one or more of the following:

- *Breathlessness, chest pain, drowsiness, fall in blood pressure, sputum mixed with blood, bluish discolouration of nails;*
- Irritability among small children, refusal to accept feed;
- Worsening of underlying chronic conditions.

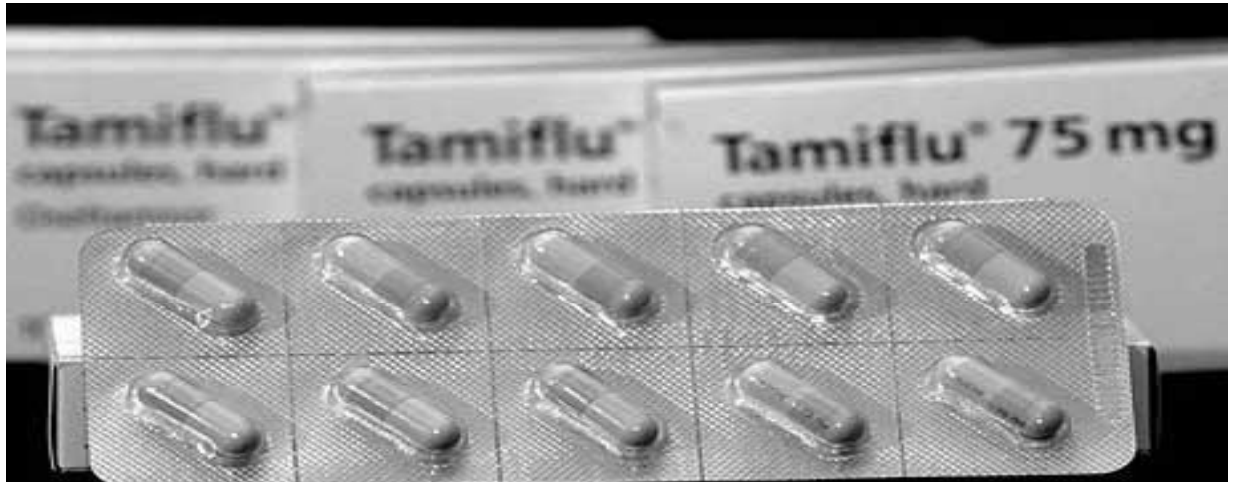
➢All these patients require **testing, immediate hospitalization and treatment.**

How are human infections with swine influenza diagnosed?

- Identification as a swine flu influenza A virus requires sending the specimen to a **specialized laboratory** for testing.

Medicines to treat swine flu

- Oseltamivir (**Tamiflu**) for the treatment and/or prevention of infection.



Advice for Asymptomatic Contacts

- Remain at home **(home quarantine**) for at least 7 days after the last exposure with a case.
- If fever or respiratory symptoms develop (s)he must inform the ***identified Local Health Official/District CMO/DSO by telephone and further management must be done at a designated health facility***.
- Administration of ***antiviral chemoprophylaxis*** should be followed as per policy guidelines.
- ***Active monitoring*** (e.g. daily visits or telephone calls) for 7 days after *the* ***last exposure*** shall be done by the identified Local Health Officials.

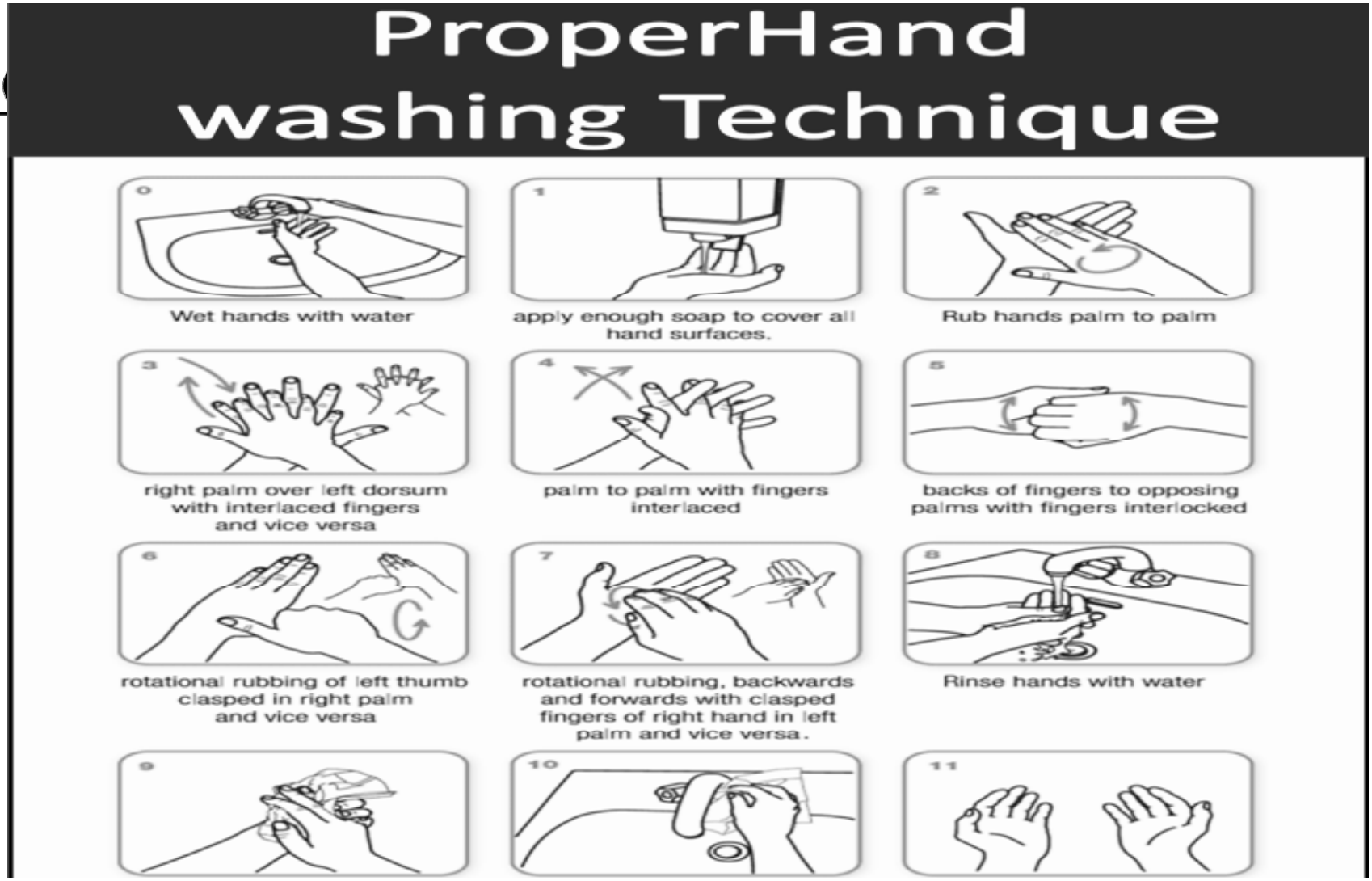
Do's & Don'ts

- Avoid crowded places.
- Stay more *than an arm's length* from persons afflicted with flu.
- Drink plenty of water and eat nutritious food.
- Sleep well.
- Stay at home or in your hotel room if traveling, except to seek medical care.
- Do not travel or go to work or school.
- Do not spit in public.
- *Do not take medicines without physician consultation*.

EVERYONE SHOULD:

- **Cover your mouth and nose with a tissue** when you cough or sneeze
- **Wash your hands** often with soap and water or use an alcohol-based hand gel.
- **Avoid touching your eyes, nose or mouth.**
- **Avoid contact with ill persons.**

Steps


ProperHand washing Technique
0
Wet hands with water
1
apply enough soap to cover all hand surfaces.
2
Rub hands palm to palm
3
right palm over left dorsum with interlaced fingers and vice versa
4
palm to palm with fingers interlaced
5
backs of fingers to opposing palms with fingers interlocked
6
rotational rubbing of left thumb clasped in right palm and vice versa
7
rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa.
8
Rinse hands with water
9
10
11

Respiratory Hygiene/ Cough Etiquette

- Cover the nose/mouth with a handkerchief/ tissue paper when coughing or sneezing;
- Use tissues to contain respiratory secretions and dispose of them in the nearest waste receptacle after use;
- Perform hand hygiene after having contact with respiratory secretions and contaminated objects/materials.

Cover Your Cough

1. Cover your mouth and nose when you cough, sneeze or blow your nose.

2. Put used tissue in the garbage.

3. If you don't have a tissue, cough or sneeze into your sleeve, not in your hands.

4. Wash hands with soap and water or hand sanitizer (minimum 60% alcohol-based).

Vaccination of Health Care Workers

1. Health Care Workers who are working in close proximity to influenza patients :
   - in casualty/ emergency department
   - in ICU and Isolation Wards.
   - identified to work in screening centres that would be set up during Seasonal Influenza outbreak.
   - treating/managing the High Risk Group
2. Laboratory personnel working in virological laboratories testing Influenza samples.
3. Rapid Response Team members identified to investigate outbreaks of Influenza.
4. Drivers and staff of vehicles/ambulances involved in transfer of Influenza patients.

The vaccine should be used every year.

Severe Acute Respiratory Syndrome (SARS)

- A new disease which came into notice when a patient was admitted in Hanoi (Vietnam) on 26th Feb 2003 with respiratory illness.
- Seven health workers who cared for this patient also became ill on 5th March 2003.
- International travel has facilitated its spread rapidly among six continents.
- Later on, it was found that the disease initially emerged in China (Guangdong province) in November 2002 from where it spread to other countries.

- A newly discovered variant of Corona virus (SARS corona virus) is accountable for SARS.
- Most SARS cases have occurred in previously healthy young adults.
- A few suspected cases have been reported among children.
- WHO estimates that case fatality ratio ranges from 0% to 50% depending on the age group affected, with an overall estimate of about 15%

- SARS virus appears to spread most commonly by close person – to – person contact involving exposure to infectious droplets, and possibly by direct contact with infected body fluids.
- The health care workers and family members are at higher risk.

- Incubation period is usually 2 – 7 days but may extend upto 10 days

Prevention and Control

- Isolation of cases.
- Universal precautions taken by the healthcare workers and others who are likely to come in contact with SARS cases.
- WHO recommends that international travellers departing from the places on the affected areas list should be screened for possible SARS at the point of departure.

Meningococcal Meningitis

- Bacterial form of meningitis
  - Several different bacteria
  - *Neisseria meningitidis*
  - Six out of twelve serogroups (A, B, C, W135, X and Y) can cause epidemics.
- It can cause severe brain damage
- Fatal in 50% of cases if untreated.
  - Even when the disease is diagnosed early and adequate treatment is started, 5% to 10% of patients die, typically within 24 to 48 hours after the onset of symptoms.

Epidemiology

- Epidemic rates of meningococcal disease varies:
  - <1 – 3/100,000 in many developed nations
  - 10 – 25/100,000 in some developing countries.

- Occurs in small clusters throughout the world
- Seasonal variation

Outbreak trends

- **The meningitis belt**
- The largest burden of meningococcal disease occurs in an area of sub-Saharan Africa which stretches from Senegal in the west to Ethiopia in the east.
- During the dry season between December to June
- ✓ dust winds, cold nights and upper respiratory tract infections combine to damage the nasopharyngeal mucosa
- ✓ facilitated by overcrowded housing and by large population displacements.

India

- Isolated cases of meningococcal meningitis have been reported from many Indian states
  - including Haryana, Uttar Pradesh, Rajasthan, Sikkim, Gujarat, Jammu & Kashmir, West Bengal, Chandigarh, Kerala and Orissa.
- Serogroup A has been associated with all the repeated outbreaks of meningitis,
- Serogroup B and C have been detected in a few sporadic cases.

Transmission

- Person-to-person
- Droplets of respiratory or throat secretions from carriers.
- Close and prolonged contact with a carrier facilitates the spread of the disease
  - such as kissing, sneezing or coughing on someone, or living in close quarters (such as a dormitory)
- The average incubation period is **four days**
  - can range between two and 10 days.

- *Neisseria meningitidis*
- only infects humans
- no animal reservoir
- The bacteria can be carried in the throat and sometimes, can overwhelm the body's defenses allowing infection to spread through the bloodstream to the brain.

Symptoms

- Most common:
  - stiff neck, high fever, sensitivity to light, confusion, headaches and vomiting.
- Less common but even more severe (often fatal):
  - meningococcal septicaemia, which is characterized by a haemorrhagic rash and rapid circulatory collapse.

- Bacterial meningitis may result in brain damage, hearing loss or a learning disability in 10% to 20% of survivors.

Diagnosis

- History & clinical examination
- Lumbar puncture
  - purulent spinal fluid
  - microscopic examinations of the spinal fluid
- Supported or confirmed by growing the bacteria from specimens of spinal fluid or blood, by agglutination tests or by PCR.

- The identification of the serogroups and susceptibility testing to antibiotics are important to define control measures.

Treatment

- A medical emergency.
- Admission to a health institution is necessary
  - isolation of the patient is not necessary.
- Appropriate antibiotic treatment
  - ideally after the lumbar puncture has been carried out if such a puncture can be performed immediately.
  - if treatment is started prior to the lumbar puncture it may be difficult to grow the bacteria from the spinal fluid and confirm the diagnosis.

- A range of antibiotics
  - Penicillin,
  - Ampicillin,
  - Chloramphenicol,
  - Ceftriaxone.

- Under epidemic conditions in areas with limited health infrastructure and resources, **Chloramphenicol or Ceftriaxone** are the ***drugs of choice*** because a single dose has been shown to be effective in meningococcal meningitis.

Prevention

- Types of vaccines:
- Polysaccharide vaccines
  - bivalent (groups A and C)
  - trivalent (groups A, C and W)
  - tetravalent (groups A, C, Y and W135)

- Group B ???
- Antigenic mimicry
- Outer membrane proteins (OMP) and strain-specific to control specific epidemics
  - particular in Cuba, New Zealand and Norway.
- Additional universal group B protein vaccines are in late stages of development.

- Meningococcal conjugate vaccines:
  - Against group C have been available and widely used since 1999.
  - Tetravalent A, C, Y and W135 conjugate vaccines have been licensed since 2005
    - in Canada, the United States of America, and Europe.
  - In December 2010, a new meningococcal A conjugate vaccine
    - in Burkina Faso, and in selected regions of Mali and Niger.

- The **conjugate vaccine has several advantages** over existing polysaccharide vaccines:
- it induces a **higher and more sustainable immune response** against group A meningococcus;
- it **reduces the carriage** of the bacteria in the throat and thus **its transmission**;
- it is available at a **lower price**;
- it is expected to be particularly effective in protecting **children under two years of age**, who do not respond to conventional polysaccharide vaccines.
- it is expected to confer **long-term protection.**

Global public health response

- With the introduction of the new meningococcal A conjugate vaccine, WHO promotes a strategy comprising:
- **Epidemic preparedness**: surveillance, from case detection to investigation and laboratory confirmation.
- **Prevention**: vaccinating all 1-29 year-olds in the meningitis belt with this vaccine.
- **Epidemic response**: prompt and appropriate case management with oily chloramphenicol or ceftriaxone and reactive mass vaccination of populations not already protected through vaccination.