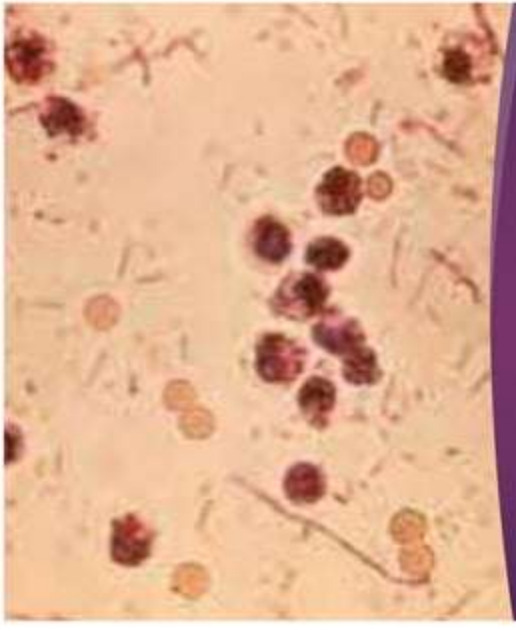

SHIGELLA OUTBREAK
in Kerala 2020

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What is an outbreak?

1. Occurrence of 2 or more epidemiologically linked cases

Or

2. A single case of a new emerging disease / eradicated disease

Endemic → Outbreak → Epidemic

ENDEMIC

- Constant presence of a disease or infectious agent at a usual level, without any importation from outside, within a given population or area

OUTBREAK

- Occurrence of more cases of disease than expected
- ✓ In a given area (**smaller**)
- ✓ Over a particular time
- ✓ Among specific group of population

EPIDEMIC

- Unusual occurrence of disease clearly in excess of normal expectation
- 2 SD from endemic frequency

Trigger	Significance	Levels of response
1	Suspected /limited outbreak	Local response by health worker and medical officer
2	Outbreak	Local and district response by district surveillance officer and rapid response team
3	Confirmed outbreak	Local, district and state
4	Wide spread epidemic Natural disaster	Local, district, state and centre
5	Pandemic	International

History

- **Hippocrates** used the term **dysentery** to indicate a condition characterized by
  the *frequent passage of stool*
  containing *blood and mucus,*
  accompanied by *straining and painful defecation*[1].
- At the end of the 19thcentury, **epidemics of bacillary dysentery** occurred periodically in Japan, when **Kiyoshi Shiga** isolated the bacterium.
- To honour Shiga, this bacterium was christened as *Shigella dysenteriae* type 1, the first organism of the genus *Shigella*[2].

Shigella

- The genus *Shigella* belongs to family *Enterobacteriaceae.*
- Shigella is Gram-negative, facultative anaerobic, non-spore forming, nonmotile, rod-shaped bacteria.
- It comprises four species, based on biochemical differences and variations in their O-antigen.

Group	Species	No: of Serotype	Occurs as	Presentation
Group A	***S. dysenteriae***	17	*epidemic* and outbreak	Moste severe (HUS)
Group B	***S. flexnerii***	14	*endemic* disease in *developing* count ries	Mild to severe
Group C	***S. sonnei***	1	endemic disease in *developed*	Mildest form (watery diarrhea)
Group D	***S. boydii***	20	India and neighbouring countries.	Mild to severe

Shigellosis

- Also called as Bacillary Dysentry
- Invasive diarrhea
- Acute
- Bloody
- Site: colo rectal mucosa
- IP : 1-3 days

Transmission:

- Humans are the only host of *Shigella*.
- Infective dose: 10-100 CFU
- Fecal-oral route is the primary means of human-to-human transmission.
- Even sexual route (esp MSM)

- The five "Fs" of disease transmission are:

1. Food- ingestion (water, food, drinks)
2. Flies
3. Fomites-(taps, toilet seats etc)
4. Fingers
5. Faeces

Pathogenesis:

- *Shigella* species are tolerant to low pH and are able to transit the harsh environment of the stomach.
- SHIGA TOXIN – disrupts protein synthesis
- Pathogenic mechanism of Shigellosis is complex which involves:

1. Enterotoxic/cytotoxic diarrheal prodrome
2. Cytokine-mediated inflammation of the colon
3. Necrosis of the colonic epithelium

SHIGA TOXIN

- Shiga toxin is a heat-labile protein and acts as enterotoxin and neurotoxin.
- It is encoded by a bacteriophage inserted into the chromosome of the bacteria.

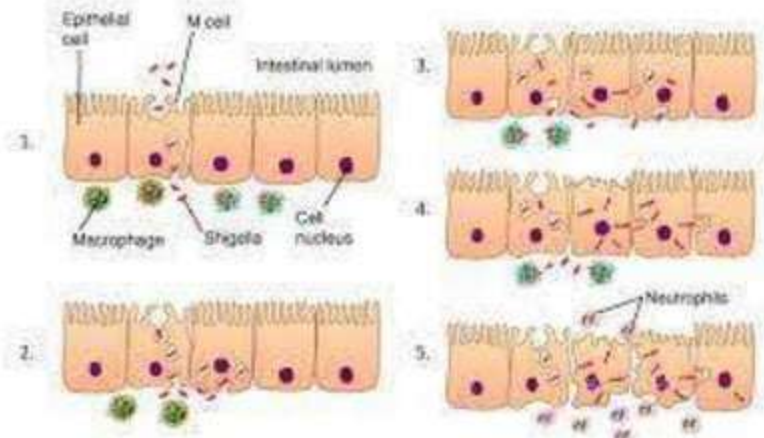
Shiga toxins have one A subunit and five B subunits:

B subunit is to bind toxins to host cell

Subunit A disrupts protein synthesis.

TABLE 33-5 Virulence factors of *Shigella* species

Virulence factors	Biological functions
Endotoxins	Invasion, multiplication, and resistance of *Shigella* to phagocytosis by tissue macrophages
Intestinal adherence factor	Colonization of *Shigella*
Shiga toxin	Disrupts protein synthesis and produces endothelial damage



1. Shigellas are taken up by M cells and transported beneath the epithelium. Macrophage takes up shigellas, die and release the bacteria.
2. The bacteria enter the inferior and lateral aspects of the epithelial cells by inducing endocytosis. The endosomes are quickly lysed leaving shigellas free in the cytoplasm.
3. Actin filaments quickly form a tail pushing the shigellas into next cell.
4. Shigella multiply in the cytoplasm and infection spread to next cell.
5. Infected cells die and slough off, intense response of acute inflammatory cells (neutrophils), bleeding and abscess formation.

Risk Groups

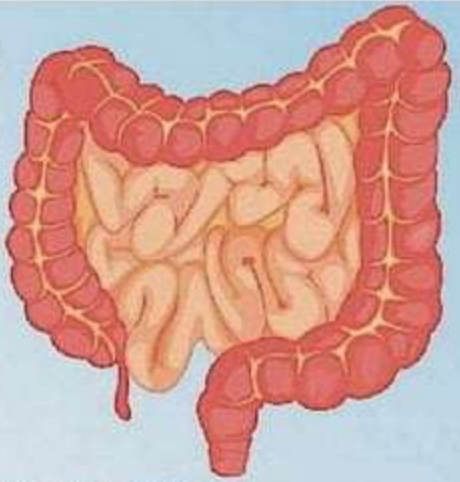
- Children under 5 years of age
- Elderly
- Immunocompromised

Signs and Symptoms

- Acute bloody diarrhea
- Crampy abdominal pain
- Tenesmus
- Passage of mucus
- Fever (1-3 days after exposure)
- Occasionally vomiting (35% prevalence)
- asymptomatic
- Self-limited course (3 days to 1 week and, rarely, lasts as long as 1 month)

Shigella infection

AN INTESTINAL DISEASE CAUSED BY A FAMILY OF BACTERIA KNOWN AS SHIGELLA



SYMPTOMS

- Diarrhoea
- Abdominal pain or cramps
- Fever

COMPLICATIONS

- Dehydration
- Seizures
- Rectal prolapse
- Hemolytic uremic syndrome
- Toxic megacolon
- Reactive arthritis

Diagnosis

- Dx sample: stool sample or rectal swab or mucus flakes
- Isolate and identify the bacteria by culture
- Blood culture fewer positive cases as low chances of bacteraemia
- Serological methods for group typing

Culture:

- MacConkey – NLF colonies
- Transport- Sach's buffered glycerol saline, cary blair
- Enrichment- selenite f broth, gram negative broth
- Selective- DCA XLD SSA HEA

Epidemiology:

- Shigellosis occurs worldwide.
- Majority of cases are children <5 yr of age.
- Low infective dose of 10-100 CFU
- High attack rate of secondary cases in family members of sick children (26-33%)
- Epidemics occurred throughout history
- Follow cyclical pattern.
- Mortality rate in one of the epidemics in Bangladesh was 41%

Epidemics in recent History

- Bangladesh (1972-1978, 2003),
- Sri Lanka (1976),
- Maldives (1982),
- Nepal (1984-1985),
- Bhutan (1984-1985)
- Myanmar (1984-1985)
- Southern India, Vellore (1972-1973, 1997-2001)
- eastern India (1984)
- Andaman and Nicobar islands (1986)
- Chandigarh (2003)

Epidemic trends in India

- In Nothern India
  S. flexneri stood as the most common serogroup from 1994-2002,
  S. dysenteriae type 1 in 2003.
  S. flexneri again emerged as the predominant serogroup since 2004.
- Such cyclical changes have also been reported from National Institute of Cholera and Enteric Disease (NICED), Kolkata, in eastern India where epidemics caused by *S. dysenteriae* periodically occur after a gap of a decade .

Shigella Outbreak in Kerala 2020

- Alert issues on 21st December, 2020
- 26 cases of diarrhea have been reported in the district of Kozikhode over the past few days.
- Admitted to the Kozhikode Medical College
- None critical
- The district administration of Kozhikode has tested the samples of 56 suspected patients. Out of these, only six were diagnosed with Shigella.

"Shigella bacterial infection which spreads through contaminated water had reported in rural parts of Kozhikode last year as well. This year, the infection has been reported in the corporation limit, Mayanad, and Kottamparamba areas. The health department has conducted an awareness campaign and set up medical camps. Wells in the area were chlorinated,"

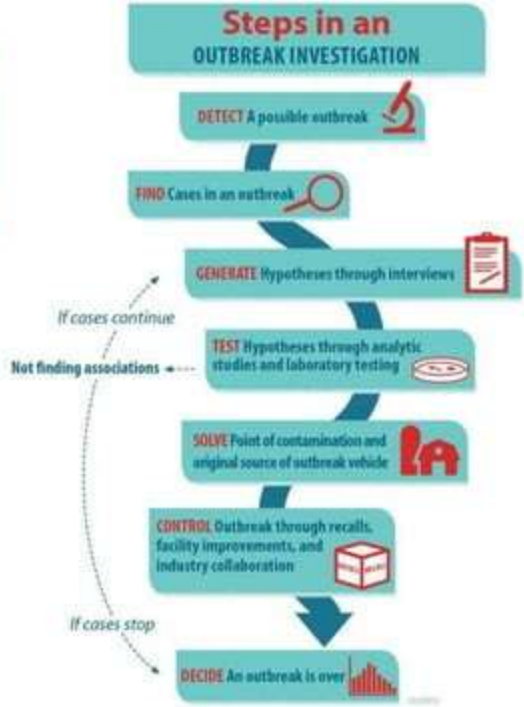
Kerala Health Minister KK Shailaja

“Shigella outbreak in Kerala claims life of 11-year-old, 6 infected, health minister calls for caution”

December 21, 2020

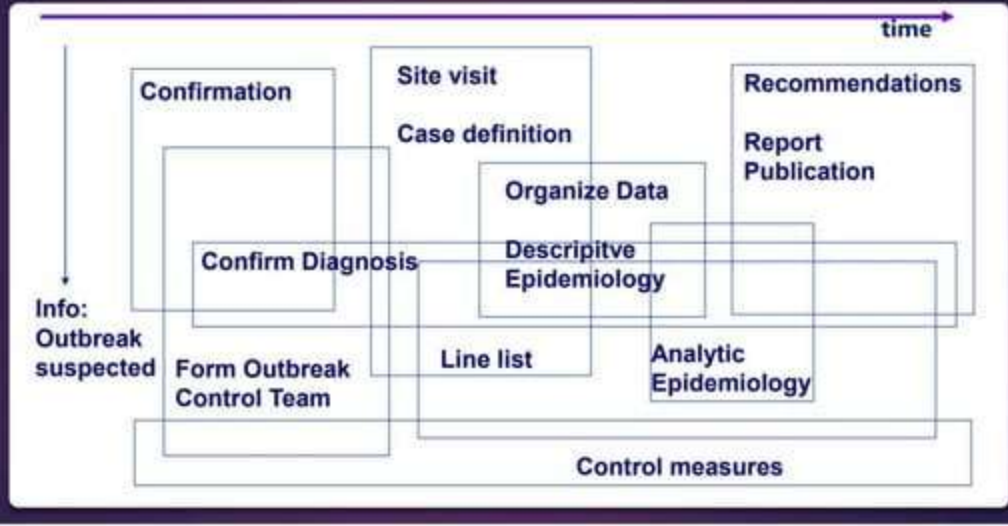
“A 56-year-old woman from Chottanikkara has been diagnosed with the disease on Wednesday. She is being treated at a private hospital in Ernakulam. The patient was admitted to the hospital on December 23 after a fever.”

OUTBREAK INVESRTIGATION



Steps of Outbreak investigation

In a nutshell



First steps for managing an outbreak of acute diarrhoea

THIS LEAFLET AIMS AT GUIDING YOU THROUGH THE VERY FIRST DAYS OF AN OUTBREAK

Two types of emergencies regarding acute diarrhoea exist:

Cholera = acute watery diarrhoea
and
Shigella dysentery = acute bloody diarrhoea

Both are transmitted by contaminated water, unsafe food, dirty hands and vomit or stools of sick people.

Other causes of diarrhoea may produce severe illness for the patient, but will not produce outbreaks which represent an immediate threat to the community.

THE FIRST TWO QUESTIONS ARE:

1. Is this the beginning of an outbreak?
2. Is the patient suffering from cholera or shigella?

1. Is this the beginning of an outbreak?

You might be facing an outbreak very soon if you have seen an unusual number of acute diarrhoeal cases this week and the patients have the following points in common:

- they have similar clinical symptoms (watery or bloody diarrhoea)
- they are living in the same area or location
- they have eaten the same food (at a burial ceremony for example)
- they are sharing the same water source
- there is an outbreak in the neighbouring community

or

You have seen an adult suffering from acute watery diarrhoea with severe dehydration and vomiting.

If you have some statistical information from previous years or weeks verify if the actual increase of cases is unusual over the same period of time.

Be prepared to face a sudden increase in number of cases

2. Is the patient suffering from cholera or shigella?

Acute diarrhoea could be a common symptom. Therefore it is important to differentiate between shigella or cholera in order to improve case management and to estimate needed supplies

- Establish a clinical diagnosis for the patient you have seen (Table1)
- Do the same for the other family members who are suffering from acute diarrhoea
- Try to take stool samples and send them for immediate analysis. If it is not possible to send the samples immediately, collect stool specimens in Cary Blair or TCBS transport medium and refrigerate.

Don't wait for laboratory results to start treatment and to protect the community.
Not all the cases need to be laboratory confirmed.

TABLE 1

Symptoms	Cholera = acute watery diarrhoea	Shigella = acute bloody diarrhoea
Stool	> 3 loose stools per day, watery like rice water	> 3 loose stools per day, with blood or pus
Fever	No	Yes
Abdominal cramps	Yes	
Vomiting	Yes, a lot	
Rectal pain	No	

Treat the patients

Summary of the treatment

A. Rehydrate with ORS or IV solution depending on the severity
B. Maintain hydration and monitor frequently the hydration status
C. Give antibiotics for severe cholera cases and for shigella cases

A. Rehydrate depending on severity

Is the patient dehydrated?

There is NO dehydration: Give Oral Rehydration Salt (Box 1)

If YES, check if the dehydration is very severe

Is the dehydration very severe?

There is some dehydration

There is severe dehydration

80% of the cases can be treated using only Oral Rehydration Salt (ORS)

When there is NO sign of dehydration: give ORS solution (see Box 1) after each stool

Approximate amount of ORS solution to give in the first 4 hours

B. Maintain hydration and monitor the patient

Assess the patient for signs of dehydration regularly during the first six hours

C. Give antibiotics if needed

When is it useful to give antibiotics?

- For cholera cases with severe dehydration only.
- Ideally for all of shigella dysentery cases, but as a priority for the most vulnerable patients: children under five, elderly, malnourished, patients with convulsions.

Treatment

- Rx: maintenance of **hydration** and electrolyte balance (cornerstone)
- Although shigellosis is primarily self-limiting, antibiotics are recommended for reducing illness duration and for preventing transmission especially in high risk individuals

Antimicrobial	Treatment schedule for children	Limitations
1st-line: ciprofloxacin	15 mg/kg orally twice daily for 3 days	Expensive Resistance emerging Drug interactions
2nd-line: pivmecillinam	20 mg/kg orally 4 times daily for 5 days	Cost No paediatric formulation Four times daily dosing Resistance emerging
OR*: ceftriaxone	50–100 mg/kg intramuscular injection for 2–5 days	Requires parenteral administration Generates antimicrobial resistance
OR: (for adults) azithromycin	6–20 mg/kg, orally once daily for 1–5 days	Cost Drug interactions Resistance emerges rapidly, spreads to other bacteria

Antimicrobial	Rationale for not prescribing
Ampicillin	Antimicrobial resistance
Chloramphenicol	Antimicrobial resistance
Co-trimoxazole	Antimicrobial resistance
Tetracyclines	Antimicrobial resistance
Nalidixic acid	Antimicrobial resistance; cross-resistance to ciprofloxacin observed (MIC increased)
Nitrofurans (nitrofurantoin, furazolidone)	Penetrate the intestinal mucosa poorly
Oral aminoglycosides (gentamicin,	Penetrate the intestinal mucosa poorly
1st- and 2nd-generation cephalosporins (cefazolin, cephalotin, cefaclor, cefoxitin)	Penetrate the intestinal mucosa poorly
Amoxicillin	Penetrates the intestinal mucosa poorly

WHAT TO DO IF YOU SUSPECT AN OUTBREAK

- **Inform and ask for help**
- **Protect the community**
- **Treat the patients**

Inform and ask for help

The outbreak can evolve quickly and the rapid increase of cases may prevent you from doing your daily activities

- Inform your supervisor about the situation
- Ask for more supplies if needed (see **Box**)
- Ask for help to control the outbreak among and outside the community

Check the supplies you have and record available quantities

- IV fluids (Ringer Lactate is the best)
- Drips
- Nasogastric tubes
- Oral Rehydration Salt (ORS)
- Antibiotics (see **Table 2**)
- Soap
- Chlorine or bleaching powder
- Rectal swabs and transport medium (Cary Blair or TCBS) for stool samples
- **Safe water is needed to rehydrate patients and to wash clothes and instruments**

Collect data on the patients

Note carefully the following data that will help to investigate the outbreak

N°	Name	Address	Symptoms	Age (<5 or >5 years)	Sex (male M) or (female F)	Date of onset	Outcome

DON'T FORGET ...

PROTECT YOURSELF FROM CONTAMINATION

- Wash your hands with soap before and after taking care of the patient
- Cut your nails

ISOLATE CHOLERA PATIENTS

- Stools, vomit and soiled clothes of patients are highly contagious
- Latrines and patients' buckets need to be washed and disinfected with chlorine
- Cholera patients have to be in a special ward, isolated from other patients

CONTINUOUS PROVISION OF NUTRITIOUS FOOD is important for all patients, especially for those with shigella dysentery

- Provide frequent small meals with familiar foods during the first two days rather than infrequent large meals
- Provide food as soon as the patient is able to take it
- Breastfeeding of infants and young children should continue

World Health Organization

For more information: cholera@who.int
http://www.who.int/cholera

■ Protect the community

HOW TO PROTECT THE COMMUNITY

- Isolate the severe cases
- Provide information
  - on how to avoid cholera through simple messages
  - on the outbreak
- Disinfect water sources with chlorine
- Promote water disinfection at home using chlorine
- Avoid gatherings

Stool and vomit are highly contagious

PRECAUTIONS FOR FUNERALS

- Disinfect corpses with chlorine solution (2%)
- Fill mouth and anus with cotton wool soaked with chlorine solution
- Wash hands with soap after touching the corpse
- Disinfect the clothing and bedding of the deceased by stirring them in boiling water or by drying them thoroughly in the sun

GIVE SIMPLE MESSAGES TO THE COMMUNITY

To avoid cholera and shigella

- Wash your hands with soap
  - after using toilets and latrines
  - before preparing food
  - before eating
- Boil or disinfect the water with chlorine solution
- Only eat freshly cooked food
- Do not defecate near the water sources
- Use latrines and keep them clean

In case of acute diarrhoea

- Start oral rehydration with ORS (see **Boxes 1 and 2**) before going to the health centre
- Go to the health centre as soon as possible

BOX 1. HOW TO PREPARE HOME-MADE ORS SOLUTION

- If ORS sachets are available: dilute one sachet in one litre of safe water
- Otherwise: Add to **one litre** of **safe water**:
  - **Salt** 1/2 small spoon (3.5 grams)
  - **Sugar** 4 big spoons (40 grams)

And try to compensate for loss of potassium (for example, eat bananas or drink green coconut water)

Prevention

- proper washing of hands, especially after defaecation. (Most effective)
- good personal hygiene,
- adequate disposal of faeces
- general measures such as washing, peeling and cooking of all fruits and vegetables,
- proper handling and refrigeration of food,
- encouraging prolonged breastfeeding in infants,
- appropriate case reporting to health authorities

6 Steps Hand Washing

Vaccine:

- Shigellosis is targeted by WHO as one of those enteric infections for which new vaccines are most needed
- the target populations being travellers from developed countries and military service personnel, as well as children living in endemic areas
- Although the need for a *Shigella* vaccine is urgent, not much progress has been done due to :
  the antigenic complexity,
  lack of inter-species
  cross-protective epitopes

- Various live attenuated vaccines such as CVD103, CVD104, CVD107, CVD108, SC602 and WRSS1 have been developed in the past
- however, most were serotype-specific with no cross-protectivity.
- These vaccines progressed into phase 1/2 trials but none could go beyond

“Thank you”

HAPPY NEW YEAR

MAY THIS YEAR BE FROM PANDEMICS AND EPIDEMICS.

AMEN.