RAJIV GANDHI INSTITUTE OF MEDICAL SCIENCES :: ONGOLE
PRAKASAM DISTRICT

The C.M.E. Programme is conducted in RIMS., Ongole on 15.09.2013 between 9.00 A.M. to 4.00 P.M.

Speaker: **Dr.C. Surya Kumari, MD.,**
Professor and H.O.D., Dept. of Microbiology.

Chairman: **Dr.Mallikarjuna, MD.,**
Professor and H.O.D., Dept. of General Medicine

Co-Chairman: **Dr.K. Prakash, MD.,**
Associate Professor of Microbiology.

Topic:

The term enteric fever includes typhoid fever caused by salmonella typhi and para typhoid fever caused by salmonella paratyphi A,B & C.

Regarding S. Typhi & S. Paratyphi:

Most important member of salmonellae of emus is S.typhi.

Morphology:

- **Gram negative rods**
- **Size – 3x0.5µm**
- **Motile with peritrichate flagella**
- **Non-sporing**
- **Non-capsulated**

Culture:

- **Aerobic**
- **Grows on simple media**
- **Temperature – 37^0c**
- **pH – 6.8**
- **colonies**

On Mac Corkey & DCA

Colour less colony due to non-lactose fermentation.

On Wilson & Blair bismuth sulphate:

- **Jet black colonies due to H_2S production.**
- **S. Paratyphi-A does not form H_2S**

Enrichment Media:

- **Selenite F-broth**

Biochemical reactions:

- **They ferment glucose, mannitol and maltose forming acid and gas.**
- **Indole – Positive**
- **Methyl Red – Positive**
- **Voges-Proskauer – Negative**
- **Citrate – Positive**
- **Urease is not hydrolyzed**
- **H_2S produced by all, except s. Paratyphi-A**

Resistance:

- **Killed at 55^0c within one hour**
- **Killed at 60^0c within 15 minutes**
- **We can destroy by:**
  - **Boiling**
  - **Chlorination**
  - **Pasteurization**
- **They live in polluted water and soil for weeks.**
- **They survive in 'ICE' for months**

Antigonic structure:

1. **H – Antigen (Flagellar)**
2. **O – Antigen (Somatic)**
3. **Vi – Antigen (Surface)**

Antigenic variations:

- **The antigens of salmonellae undergoes phenotypic and genotypic variations.**
- **Variations are:**
  1. **H-O variation**
  2. **Phase variation**
  3. **V-W variation**
  4. **S-R variation**
  5. **Variation in "O" antigen.**

Classification:

1. **Based on "Biochemical properties".**
2. **Kauffman's white scheme (Antigenic characterization).**

- **This scheme depends on the identification by agglutination of the structural formulae of the "O" antigen and "H" antigen of the strain.**

3. **Classification into serological groups based on the presence of distinctive "O" antigen factor, which are designated as 1,2,3 etc.,**
4. **The species were named to the:**
   i. **Disease caused (S. Typhi)**
   ii. **The animal source (S.gallinasium)**
   iii. **The discoverer (S.Schoff mulleri)**
   iv. **The name of the patient (strain S.Thompson)**
   v. **The place of isolation (S.poona, isolated first)**

5. **Biochemical reactions "Kauffmann proposed".**
   Classified into four groups: I, II, III & IV groups.
6. **Ewing, prepared only three species genus salmonella.**
   - **S. Choleraesuis**
   - **S. Typhi**
   - **S. Enteritidis**

Pathogenicity:

- **Salmonellae are strictly parasitic of human beings and animals.**
- **S. Typhi, S. Paratyphi A, B are confirmed to human beings**
- **Salmonellae causes the following clinical syndromes in human beings.**
  1. **Enteric fever**
  2. **Septicemia**
  3. **Gastroenteritis OR Food poisoning**

Enteric Fever:

- **The term enteric fever includes typhoid fever caused by S.typhi and para typhoid fever caused by S.paratyphi A,B&C.**
- **History:**
  - **Bactonneau (1826): He studied study of the disease was made from intestinal lesions.**
  - **Louis(1820): The name typhoid was given by him, which distinguished from typhus fever.**
  - **BUDD(1856): He discovered that diseases come through excreta of human patients.**
  - **Eberth(1880): Described typhoid bacilli.**
  - **Gaffley (1884): He isolated the bacilli from pure culture.**

Pathogenicity:

Ingestion of bacilli, reach the gut and attach to the microvilli of the ileal mucosa and penetrate the lamina propria and submucosa.

- **Some bacilli phagocytosed and some are resist to Phagocytosis bacilli which resist, they multiply in intracellularly.**

- **They enter the mesenteric lymph nodes further multiplication occurred and entered the blood stream through thoracic duct – Bacteremia follows.**
- **Bacteria invasion occurred in the liver, gall bladder, spleen, bone marrow, lymph nodes, lungs & kidney. Here further, multiplication occurs, then clinical disease starts.**
- **As bile is a good culture medium for bacilli, which multiply abundantly in the gall bladder.**
- **Involves the Preyer's patches and lymphoid follicles of ileum.**
- **Typhoid ulcers formed, ulcerated bowel leads to 1.Intestinal perforation and 2.Hemorrhage.**

Clinical signs & symptoms:

(a) Gradual onset:
- **Headache – malaise**
- **Anorexia – coated tongue**
- **Abdominal discomfort**
- **Constipation**
- **Diarrhea**

(b) Typical features:
- **Step-ladder pyrexia**
- **With brady cardia and toxemia**
- **Splenomegaly**
- **Hepatomegaly**
- **Rose spots on the skin**

(c) Complications:
- **Intestinal perforation**
- **Hemorrhage**
- **Circulatory collapse**
- **Bronch pneumonia**
- **Meningitis**
- **Cholecystitis**
- **Arthritis**
- **Nephritis**
- **Hemolytic anaemia**
- **Venus thrombosis**
- **Peripheral neuritis**

- **S.Paratyphi A&B:**
  - **Causes paratyphoid fever, which resembles typhoid fever.**
- **S.Paratyphi – C:**
  - **It also causes paratyphoid fever which leads to "frank septicemia"**

Epidemiology:

- **Typhoid fever eliminated in developed countries, by improving "protected water supply, sanitation.**
- **It present in developing countries, S.Paratyphi "A" present in India.**

- **It is endemic in all parts of India.**
  Incidence in 1990:
  980 patients per 1,00,000 population.
- **It is worldwide: Annually 16 million cases, 6,00,000 deaths.**
- **Age groups: 05-20 years people will get.**
- **Source: (a) patient, (b) carriers.**

Carriers: (a) Temporary, (b) Chronic

- **In temporary carriers, the bacilli present – 3 months to 1 year.**
- **Chronic carrier:**
- **Bacilli present more than one year.**
- **Known typhoid carrier was "Mary Mallon" (Typhoid Mary) Cook in New York.**

Laboratory diagnosis:

1. **Bacilli isolation from patients.**
2. **Antibodies demonstration, from serum**
3. **Antigen demonstration from blood and urine.**

Note: If blood culture positive at the same time negative in feces and urine. Anal also in acute infection, unable to demonstrate the antibodies.

Culture & Tests:

1. **Blood culture**
2. **Feces culture.**
3. **Urine culture**
4. **Other material**
5. **Serology – widal reaction**

Blood culture: Positive in first week of fever.

- **Sub cultures on Mac Conkey medication**
- **For further diagnosis**
- **Biochemical tests**
- **Motility tests – Motile.**

Biochemical tests:

- **Indole - Negative**
- **Urease – Negative**
- **Glucose**
- **Mannitol** } **These sugars fermented**
- **Maltose**
- **Lactose**
- **Sucrose** } **These sugars not fermented.**

Slide agglutination test:

Typhoid "O" antiserum + bacterial suspension = agglutination may appear.

Castaneda's method (for blood culture)

Uses: 1. For proving the contamination
2. For economy reason
3. For safety purpose.

- **It is a double medium: 1. Bile broth, 2. Agar slant.**

2. Clot culture:

- **It is alternative for blood culture.**
- **It yields a higher rate of isolation.**

3. Feces culture:

- **Salmonellae are shed in feces throughout the course of the disease.**
- **Positive fecal culture in carrier and in patients.**

4. Urine culture:

- **It is less important, because salmonellae shed irregularly.**
- **It is positive in 2^{nd} and 3^{rd} week of fever.**

5. Other material for culture:

- **Bone marrow**
- **Bile**
- **Pus from rose spots**
- **CSF**
- **Sputum**

6. Serology: (Widal reaction)

- **The test for the measurement of H&O agglutination for typhoid and para typhoid bacilli in serum.**
- **Two types of tubes used:**
  1. **Dreyer's tube: It is for "H" agglutination. It is marrow tube with a conical bottom.**
  2. **Felix tube: It is for "O" agglutination. It is short and round bottomed tube.**

3. **Controle tubes are also sued.**

This test done by serial dilutions.

H- agglutination: In positive Loose, Large Collon Wooly Clumps at upper side (Fluffy)
O- agglutination: In positive chalky powder sedimentation (disk like pattern) at bottom.

Interpretation of widal reaction:

1. **At first week end – agglutination +ve.**
2. **Titre increases up to 3rd week.**
3. **Two (OR) more serum samples tested for knowing rise of titre.**
4. **Interpretation:**
   a. **Titre for "O" agglutination – 1/100 or more.**
   b. **Titre for "H" agglutination – 1/200 or more.**
5. **Agglutinins (antibodies) already present in previous infections (diseases) and already TAB immunized patients in these patients "Anamnestic Response" present, i.e., antibody titre increased.**

Other serological tests:

1. **Indirect hem agglutination**
2. **CIE**
3. **ELISA**

Demonstration of circulatory antigen:

- **Antigens present in early phase of the fever and in the urine.**
- **Sensitized staphylococcal coagulation test.**
- **Antigens can be demonstrated.**

(Graph) for Laboratory Diagnosis:

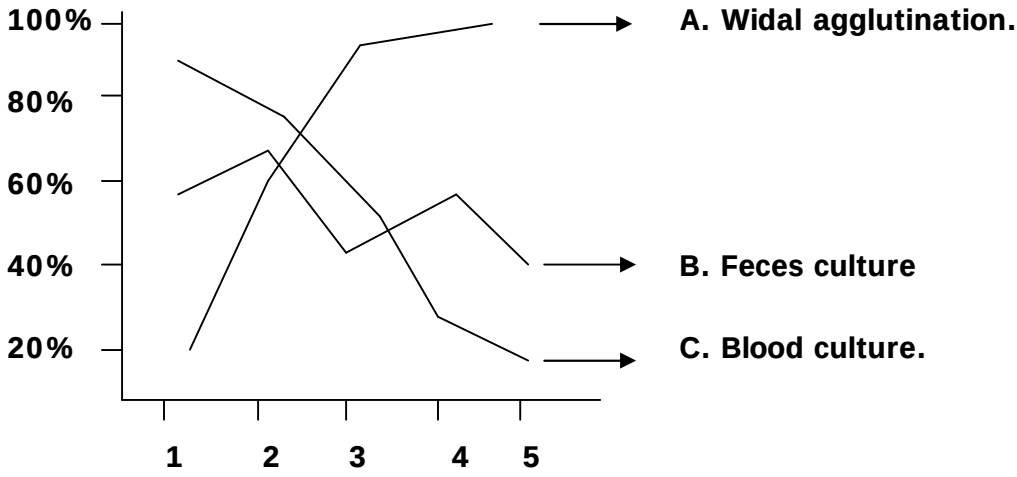

Fig: Laboratory diagnosis of typhoid fever. The approximate percentage of tests for positive during different stages of the disease from 1st week to 5th week.

Diagnosis of carrier:

- **It is important for epidemiological and public health purpose.**
- **Screening of food harless and cooks**
  1. **Identification of foecal carriers**
  2. **Detection of urinary carriers**
  3. **Tracing carriers in cities by:**
     a. **Sewer swab technique**
     b. **Filtration through Millipore membrane**

Prophylaxis:

1. **Sanitation improvement**
2. **Provision of supply of protected water supply**
3. **Vaccination**
   a. **TAB vaccine**
   b. **Polyvalent TAB vaccine.**
4. **Two new typhoid vaccines**
   a. **Oral vaccine (typhoral)**
   b. **Injectable vaccine (typhin-VI)**

Treatment:

- **From 1948, Chloramphenicol was used.**
- **From 1970, Resistance to chloramphenicol developed.**

Other drugs used:

a. **Streptomycin - in vitro**
b. **Tetracycline - in vitro**
c. **Ampicillin**
d. **Amoxicillin**
e. **Furazolidone**
f. **Cotrimoxazole**

Treatment of carrier:

Antibacterial therapy + vaccination

Elimination of carriers:

By a. **Cholecystectomy**
b. **Pyelolithotomy**
c. **Nephrectomy**