

Typhoid Fever (*Salmonella typhi*) Investigation Guideline

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Revision History:

Date	Replaced	Comments
05/2018	07/2014	Updated Notification sections and Isolation, Work and Daycare Restrictions sections with updated regulations.
07/2014	11/2009	Added notification section and table of contents. Added definition of Chronic Carrier. Edited data management section.

Typhoid Fever

Disease Management and Investigative Guidelines

CASE DEFINITION (CDC 2005)

Clinical Description for Public Health Surveillance:

- An illness caused by *Salmonella typhi* that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of *S. typhi* may be prolonged.

Laboratory Criteria for Case Classification:

- Isolation of *S. typhi* from blood, stool, or other clinical specimen. Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should not be reported as typhoid fever.

Case Classification:

- **Confirmed:** A clinically compatible case that is laboratory confirmed. Serologic evidence alone is not sufficient for confirmation.
- **Probable:** A clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak.

Additional Definitions for Case Management:

- **Chronic carrier:** individual who is asymptomatic and continues to have positive stool cultures for *S. typhi* a year following recovery from acute illness.

LABORATORY ANALYSIS

There is no definitive test for typhoid fever. The initial diagnosis is made clinically; one should suspect typhoid or paratyphoid fever in a patient at a high risk for infection who presents with a gradual onset of fever that increases in severity over several days.

- Testing currently available:
 - Blood culture: positive in only half the cases.
 - Stool or Urine culture: not usually positive during the early acute phase of the disease but is used to determine if a person is a typhoid carrier.
 - Bone-marrow culture: increases the diagnostic yield to about 80%.
 - Culture of bile (collected from a bile-stained duodenal string): used with blood culture resulting in 90% diagnostic yield in children with enteric fever.
 - Widal test, a serology test for antibodies to O and H antigens of *Salmonella*; unreliable but is used in developing countries because of its low cost.
 - Newer serologic assays are more sensitive and specific than the Widal test but are not an adequate substitute for blood, stool, or bone marrow culture.
 - Vi antibody: found to be very high in chronic *S. typhi* carriers; has been used as a screening technique to identify carriers among food handlers, but stool cultures are necessary to remove food handling restrictions.
- Isolates: Submission of *Salmonella* isolates to the Kansas Health and Environmental Laboratories (KHEL) is required by law.

- **Specimens:** Feces for culture.
 - Collection: Use an enteric kit (bottle with a Cary-Blair medium (0.16% agar))
 - Amount: Marble size (3-10 gram sample; preferred over rectal swabs)
- For additional information, call (785) 296-1620.

EPIDEMIOLOGY

Worldwide, approximately 17 million cases and 600,000 deaths occur annually. In the U.S., less than 500 cases occur annually and 70% of these are acquired while traveling abroad; travelers to Asia, Africa and Latin America are at higher risk. Antimicrobial resistant strains are becoming more prevalent. Outbreaks have occurred in the United States from food imported from other countries. Outbreaks do not result from floods or other disasters in countries that are not endemic for typhoid, such as the U.S.

DISEASE OVERVIEW

A. Agent:

Typhoid fever is a bacterial disease caused by *Salmonella typhi*.

B. Clinical Description:

Typhoid fever is a systemic infectious disease, symptoms include: sustained fever, headache, malaise and anorexia. Vomiting and diarrhea are typically absent, but constipation is frequently reported. Bradycardia, enlargement of the spleen and rose spots on trunk, may also occur. Ulceration of Peyer's patches in the ileum in late untreated disease causes bloody diarrhea. Mild and atypical infections are common. Relapses are common. The case-fatality rate is <1% with prompt antibiotic treatment.

C. Reservoirs:

S. typhi only infects humans; chronic carriers are important reservoirs.

D. Mode(s) of Transmission:

Person-to-person, usually via fecal-oral route. Fecally contaminated drinking water is a commonly identified vehicle. *S. typhi* may also be found in urine and vomitus which in some situations could contaminate food or water. Shellfish grown in sewage-contaminated water and vegetables from developing countries are potential vehicles. Flies can mechanically transfer the organism to food, where it then multiplies to achieve an infective dose.

E. Incubation Period:

Incubation period depends on the infective dose. Range 3 days to 1 month; average 8-14 days.

F. Period of Communicability:

The disease is communicable for as long as the infected person excretes *S. typhi* in their excreta, usually after the 1st week of illness through convalescence. Approximately 10% of untreated cases will excrete *S. typhi* for 3 months and between 2-5% of all cases become chronic carriers.

G. Susceptibility and Resistance:

Susceptibility is general. Specific immunity follows recovery from clinical disease and/or active immunization.

H. Treatment:

With resistant strain prevalence, antibiotic sensitivity tests must be obtained. Ciprofloxacin is considered the drug of choice with chloramphenicol, amoxicillin and TMP-SMX having high efficacy if the strain is shown to be sensitive. Relapse is common, retreat as necessary.

I. Vaccine:

Two typhoid vaccines are currently available in the U.S. CDC recommends typhoid vaccine for travelers to areas where there is a recognized increased risk of exposure to *S. Typhi*. Typhoid immunization is not 100% effective, and typhoid fever could still occur. See [Additional Information /Resources](#).

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Suspected cases of Typhoid Fever shall be reported within 24 hours, except if the reporting period ends on a weekend or state-approved holiday, the report shall be made by 5:00 p.m. on the next business day after the 24-hour period:

1. Health care providers and hospitals: report to the local public health jurisdiction or KDHE-BEPHI (see below)
2. Local public health jurisdiction: report to KDHE-BEPHI (see below)
3. Laboratories: report to KDHE-BEPHI (see below)
4. KDHE-BEPHI will contact the local public health jurisdiction by phone within one hour of receiving any suspected typhoid fever report.

**Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)**

Phone: 1-877-427-7317

Fax: 1-877-427-7318

Further responsibilities of state and local health departments to the CDC:

As a nationally notifiable condition, confirmed and probable typhoid fever cases are ROUTINELY NOTIFIABLE to the Center of Disease Control and Prevention (CDC).

- **Local public health jurisdiction** will report information requested on the disease reporting forms as soon as possible, completing the forms within 5 days of receiving a notification of a report.
- KDHE-BEPHI will file an electronic case report the next regularly scheduled electronic transmission.

INVESTIGATOR RESPONSIBILITIES

- 1) Use current [case definition](#), to confirm diagnosis with the medical provider.
 - Collect all information requested in [Step 1](#)) of case investigation.
 - Ensure that case is aware of his/her diagnosis.
 - If an individual is self-identifying as a [chronic carrier](#), but no medical record is available or only a Widal test was done in a developing country, a stool culture to confirm will be necessary.
- 2) Continue a [case investigation](#) to identify potential source of infection.
 - Start the investigation within 3 days of receiving the report.
 - Complete the investigation within 5 days of receiving the report.
- 3) Conduct [contact investigation](#) to identify additional cases.
- 4) Identify whether the source of infection is major public health concern.
- 5) Initiate control and prevention measures to prevent spread of disease.
- 6) Complete and report all information requested in EpiTrax.
- 7) As appropriate, use [Typhoid carrier agreements](#), and the disease [fact sheet](#), as needed.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

A suspected typhoid fever without labs is reported as “suspect”, with the pending lab results noted. **Additional** case investigation is required only after cases are laboratory confirmed or epidemiologically linked to a confirmed case.

- Upon receipt of the confirmatory lab results, the “Date Reported to LHD” is manually entered with the date the positive laboratory report was received under the **[Administrative]** tab and the investigation should be started.

Note: *If no laboratory results are received within 2 weeks of the initial report, the LHD with jurisdiction should follow-up with the physician to determine the results of testing, and any results (negative or positive) should then be forwarded to KDHE.*

Confirmed or probable cases are investigated as follows:

- 1) Contact the medical provider who ordered testing of the case and obtain the following information. (This includes medical records for hospitalized patients.)
 - Identify if the patient was ill with symptoms of typhoid fever.
 - If yes, record onset date of illness.
 - Record symptoms: fever, abdominal pain, headache, or other (specify).
 - Examine the laboratory testing that was done; noting type of specimen that grew *Salmonella typhi* and date it was first isolated.
 - Examine antibiotic sensitivity testing and note any resistance to: ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, or fluoroquinolones.
 - Collect case’s demographic data and contact information (birth date,

- county, sex, race/ethnicity, occupation, address, phone number(s))
 - Record the patients' history of typhoid vaccine within the five years before illness onset; including the type of vaccine and year received.
 - Record hospitalizations: location, admission and discharge dates
 - Record outcomes: recovered or date of death
- 2) Interview the case or proxy to determine source and risk factors; focus on incubation period **30 days prior** to illness onset.
- Travel history:
 - Travel outside of KS; list states visited; dates visited
 - Travel outside of U.S.; list country; date of departure and return to U.S.
 - Record reason for travel: business, tourism, visiting family/friend, immigration, or other (specify)
 - Identify if the case was possibly exposed to a typhoid carrier, and if the carrier was previously known to the health department.
 - Collect information from case for the [Contact Investigation](#). (See below).
 - If the case had no travel outside of the United States and was not exposed to a possible typhoid carrier, collect information on the case's food history focusing on a period of **2 weeks before** illness onset. Focus on the food history section (verify any raw shellfish, fruit or vegetable consumption) and ask about restaurant exposures.
- 3) Investigate epi-links among cases (clusters, household, co-workers, etc).
- Investigate highly suspected sources. Refer to [Environmental Measures](#).
 - For suspected [outbreaks](#) to Managing Special Situations section.

Contact Investigation

- 1) Consider the following contact types during a contact investigation:
- General: Household, close contacts and sexual partners of a case.
 - Daycare: All employee direct caregivers and "room" mates of a case.
 - School: with evidence of transmission in the school setting, the close contacts of a case
 - Travel companions in a commercial travel group
 - Food Service Contacts:
 - Co-workers who work the same shift as the infected food handler.
 - Patrons of the establishment of an infected food handler if (1) the food handler worked while infectious, (2) had poor personal hygiene, and (3) had the opportunity to have bare-hand contact with ready-to-eat food.
- 2) Create a contact roster. Include visitors/contacts within incubation period (to identify source) and during communicable period (to examine transmission)
- Name, address, relationship, occupation, dates of contact.
 - History of typhoid exposure or similar illness; if so, where and when.
 - Identify persons involved in special situations (foodhandler, daycare, etc.).

Isolation, Work and Daycare Restrictions

Most people may return to work or school when their stools become formed as long as they carefully wash their hands after using the toilet. The exceptions are food handlers, caretakers of patients or the elderly and daycare situations.

K.A.R. 28-1-6 for Typhoid Fever

Control of Cases

- Each person with a case shall be excluded from working as a food employee, health care worker, and attending or working in a child care facility until three consecutive negative stool cultures are obtained at least 24 hours apart.
 - The first cultures shall be obtained not sooner than 48 hours following the completion of appropriate antimicrobial therapy and not earlier than one month after onset of illness.
 - If any one of these tests is positive, cultures shall be repeated monthly until three consecutive negative cultures are obtained.

Control of Contacts

- Each susceptible contact shall be excluded from working in an adult care home, correctional facility, or health care facility and attending or working in a school, child care facility, or adult day care until two negative stool cultures are obtained not less than 24 hours apart and 14 days following the last exposure to an infectious case

See [Table 1](#) on page 6 for managing a food handler associated to *S.typhi*.

Acute GI*?	Stool culture positive for <i>S. Typhi</i>?	Illness in last 3 month with <i>S. Typhi</i>	Exposed/ Associated † to <i>S. Typhi</i>	Restriction or Exclusion ‡	Reinstatement of Employee to Full Duties
	Yes			Exclude from all facilities.	With the approval from regulatory authority. §
No		Yes		Exclude from all facilities.	With the approval from regulatory authority. §
No	No	No	Yes	Restrict from facilities that serve highly susceptible populations ™.	14 days after employee was exposed / associated to illness or 14 days after household contact became asymptomatic.

*Acute GI (gastroenteritis illness) is associated to diarrhea, fever, vomiting or jaundice.

† Exposure / association is defined as a food handler consuming or preparing food implicated in a foodborne outbreak of *S. typhi* or that was prepared by a person infected with *S. Typhi*; or a food handler who has a household contact diagnosed with *S. Typhi* or a household contact who attended or worked at a setting where a foodborne outbreak of *S. Typhi* or occurred.

‡ Exclusion is not allowing the employee to work at the food establishment. Restriction is not allowing the employee to work with food; to clean equipment, utensils or linens; or to un-wrap single-use articles in the food establishment.

™ A highly susceptible population is more likely to experience foodborne disease because they are immunocompromised or older adults and in a facility that provides health care or assisted living services, such as a hospital or nursing home; or preschool age children in a facility that provides custodial care, such as a daycare center.

§ Approval by a regulatory authority (i.e. local health officer) requires written documentation of 3 consecutive negative stools taken 48 hours after discontinuance of antibiotics and 24 hours apart. (A case with schistosomiasis must also have three negative urine cultures collected at the same time as the stools.) If any one of the tests is positive, cultures shall be repeated monthly until three consecutive negative cultures are obtained.

Case Management

- 1) Educate case and caregivers on blood/body fluids and enteric precautions to take until clinical recovery.
- 2) Arrange for case to follow-up with the health department until the case has had no fewer than three (3) consecutive negative cultures of stool (and urine in patients with schistosomiasis) taken at least 24 hours apart and at least 48 hours after any antimicrobials.
 - If any are positive, repeat cultures at intervals of one month during the 12 months following onset until at least three (3) consecutive negative cultures are obtained.
 - Case may work in non-sensitive occupations during the follow-up period.
 - For [chronic carriers](#), refer to [Managing Special Situations](#).
- 3) Assure compliance with control measures ([Isolation, Work and Daycare Restrictions](#)) for those who attend school or daycare or are involved in food handling, patient care, and any occupation involving the care of young children and the elderly.
- 4) Report on any changes in patient status (i.e. date recovered or released from hospitalization or date of death).

Contact Management

- 1) Consult [Table 1](#) above if a contact of the *S. Typhi* case is a food-handler.
- 2) Follow-up with all contacts to assure compliance with any [control measures](#) and to determine if any have become infected.
- 3) Routine immunization with typhoid vaccine is of limited value for family, household and medical providers that have been in direct contact with a case, but the use of vaccine is indicated those who will have close contact (i.e. household contact) to a documented [S. typhi carrier](#).

Environmental Measures

If a commercial food service facility, daycare center or public water supply is implicated in transmission. Activities should be coordinated through the proper regulatory agency, including:

- Inspection of the facility.
- Collection of food, drink or water samples and, if necessary, human stool specimens for testing.
- Possible detailed trace-back investigation of any suspect food products.

The agency involved in traceback and inspections will depend on the source of infection.

Education

- 1) As needed, inform of communicability, incubation period and symptoms.
- 2) Provide basic instruction to cases and potentially exposed contacts about:
 - The importance of personal hygiene, emphasize hand washing and the proper cleaning fingernails;
 - The proper disposal of feces, urine, and fomites;
 - The importance of seeking medical care should contacts develop symptoms or if the case's symptoms worsen and/or return.
- 3) Use the [Public Health Fact Sheet on Typhoid Fever](#) to assist with education.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

- A single case is actively pursued to identify any outbreaks with unidentified cases associated to the same source. The situation should be treated as a public health emergency until additional cases and the possibility of an unidentified contaminated source has been ruled out.
 - Foodborne disease outbreak is defined in the following ways:
 - o Two or more individuals (from different households) who experience similar illness after eating a common food or in a common place.
 - o An unexplained, unexpected increase of a similar illness and food is a likely source.
 - Waterborne disease outbreak is defined as an incident in which two or more persons experience a similar illness after consumption or use of water intended for drinking, and epidemiologic evidence implicates the water as the source of the illness.
 - Other outbreaks may be defined as unexplained, unexpected increase in cases that are clustered in person, place, or time.
- Notify KDHE immediately, 1-877-427-7317.
- Active case finding will be an important part of any investigation.

B. Chronic Carriers:

- Review the definition of a [chronic carrier](#).
- Presumptive and confirmed carriers are subject to certain restrictions that are enforced by the local health officer (or local board health). These restrictions are itemized in the [Typhoid Fever Carrier Agreement](#).
- This agreement, which is signed by carrier, provides that the carrier will:
 - Not work as a food handler or provide personal care in daycare or residential care facilities.
 - Notify the health officer at once of any change in address or occupation;
 - Notify the health officer at once of any suggestive illness among household members or other personal contacts.

- Provide specimens for culture as required by the local health officer.
- Chronic carriers should be supervised by the local health department with contact made at intervals of no longer than a year to ensure that all instructions are being followed.
- Chronic carriers may be released from their agreement following three consecutive, negative cultures are obtained, as directed by [K.A.R 28-1-6](#).

C. Case Is a Food Handler or Restaurant Is Implicated:

For one case, proceed with the following activities (coordinating with the local food inspector and regulatory agency, as necessary):

- Conduct an environmental evaluation of the facility, interview the operator and review worker attendance records to identify employees with any illness suggestive of typhoid within the past month.
- Employees with a suspicious history within the past month must submit a single stool specimen for culture; symptomatic employees should obviously be excluded until disease status is ascertained.
- Ask about any complaints of illness from patrons during the past month.
- Review previous facility inspection reports and consider the personal hygiene of infected workers to determine the risk of transmission to patrons.
- The extent of further investigation depends on circumstances. Consult with the on-call epidemiologist at 1-877-427-7317.

D. Case with Association to Childcare

For one case, proceed with the following activities (coordinating with the local inspector and regulatory agency, as necessary):

- 1) Interview the operator and check attendance records to identify suspect cases that may have occurred during the previous month.
- 2) If other potential cases are identified, complete a sanitary inspection.
- 3) Instruct the operator and other staff in proper methods for food handling and hand washing, especially after changing diapers.
- 4) Instruct the operator to notify the health department immediately if new cases of illness similar to typhoid fever occur. (Symptoms of *S. typhi* infection may be mild to severe and can include fever, headache, loss of appetite, constipation or diarrhea, and nonproductive cough.)
- 5) Consult with the on-call epidemiologist at 1-877-427-7317 about the need to collect and test stool specimens from daycare attendees and workers.
- 6) Call or visit once each week for 4 weeks after onset of the last case to verify that surveillance and appropriate hygienic measures are being carried out.

E. Public Gathering Implicated:

- 1) Determine if anyone who prepared food for the gathering had any symptoms suggestive of typhoid at any time during the previous month.
- 2) Find out if any other food preparers or attendees became ill within 4 weeks of the gathering.
- 3) Enforce [Restrictions](#) for attendees or their household contacts who handle food.
- 4) Collect stool specimens for culture from any food handlers with suggestive histories. (Mandatory for workers of a commercial food service facility.)
- 5) The extent of further investigation depends on circumstances. Consult with the on-call epidemiologist at 1-877-427-7317.
- 6) If a food establishment or distributor is implicated as the source of infection, or for any outbreak, KDHE will assist in coordination with outside agencies.

F. Intentional Contamination

S. typhi is considered a Category B bioterrorism agent in that it is a food and water safety threat. If the natural etiology cannot be readily established by a prompt and vigorous investigation, the situation should be considered to be a bioterrorist act until proven otherwise.

If suspected:

- Notify local law enforcement and state public health officials.
- Implement “[Chain of Custody](#)” procedures for all samples collected, as they will be considered evidence in a criminal investigation.
- Work to define population at risk which is essential to guide response activities. Public health authorities will play the lead role in this effort, but must consult with law enforcement, emergency response and other professionals in the process. The definition may have to be re-evaluated and redefined at various steps in the investigation and response.
- Once the mechanism and scope of delivery has been defined, identify symptomatic and asymptomatic individuals among the exposed and recommend treatment and/or chemoprophylaxis.
- Establish and maintain a detailed line listing of cases, suspect cases, exposed, and potentially exposed individuals with accurate identifying and locating information as well as appropriate epidemiological information.

Safety Considerations:

- Food and water are the most likely mechanism of delivery.
- No isolation or quarantine measures are indicated beyond standard enteric precautions.

For [clinical information](#), [incubation period](#), [treatment](#), [vaccine](#) and [laboratory testing](#); refer to the previous sections.

DATA MANAGEMENT AND REPORTING TO THE KDHE

- A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the **[Administrative]** tab.
- B. Organize and collect data.
- Investigators can collect and enter all required information directly into EpiTrax **[Investigation]**, **[Clinical]**, **[Demographics]**, **[Epidemiological]** and **[Contact]** tabs without using the paper forms. Enter all data that collected during the investigation that helps to confirm or classify a case, including:
 - ✓ **Demographic Tab:** All demographic data available or mark 'unknown'
 - ✓ **Clinical Tab:** **Onset date, Diagnosis date, Patient Outcome**
 - ✓ **Contacts Tab:** **Contact name, Disposition, Disposition Date, Contact Type** (make a note of any contacts who are foodhandler)
 - ✓ **Epidemiological Tab:** **Foodhandler?, Occupation, Place of Exposure** (source and/or transmission locations), **Imported from**
 - ✓ **Investigation Tab:** **Symptoms, Typhoid Vaccination History, Exposure Risk Factors**
 - ✓ **Notes Tab:** Progress on investigation, follow-up, and other notes
 - During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.
- C. Report data collected during the course of the investigation via EpiTrax.
- Verify that all data requested in [Step 1](#)) has been recorded on an appropriate EpiTrax **[tab]**, or that actions are completed for a case lost to follow-up as outlined below.
 - Some data that cannot be reported on an EpiTrax **[tab]** may need to be recorded in **[Notes]** or scanned and attached to the record.
 - Paper report forms do not need to be sent to KDHE after the information is recorded in EpiTrax. The forms should be handled as directed by local administrative practices.
- D. If a case is lost to follow-up, after the appropriate attempts:
- Indicate 'lost to follow-up' on the **[Investigation]** tab with the number of attempts to contact the case recorded.
 - Record at least the information that was collected from the medical records.
 - Record a reason for 'lost to follow-up' in **[Notes]**.
- E. After the requirements listed under [Case Investigation](#) have been completed, record the "Date LHD investigation completed" field located on the bottom of the **[Administrative]** tab.
- Record the date even if the local investigator's [Case](#) or [Contact Management](#) for the contact is not "Complete".
- F. Once the investigation included contact management is completed, the LHD investigator will click the "Complete" button. This will trigger an alert to the LHD Administrator so they can review the case before sending to the state.
- The LHD Administrator will then "Approve" or "Reject" the CMR.
 - Once a case is "Approved" by the LHD Administrator, BEPHI staff will review the case to ensure completion before closing the case.

ADDITIONAL INFORMATION / REFERENCES

- A. **Treatment / Differential Diagnosis:** American Academy of Pediatrics. Red Book: Report of the Committee on Infectious Disease, 29th Edition. Illinois, Academy of Pediatrics, 2014.
- B. **Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual, 19th Edition. Washington, DC, American Public Health Association, 2010.
- C. **Case Definitions:** www.cdc.gov/nndss/
- D. **Quarantine and Isolation:** Kansas Community Containment Isolation/ Quarantine Toolbox Section III, Guidelines and Sample Legal Orders www.kdheks.gov/cphp/operating_guides.htm#coc
- E. **Caring for Our Children: National Health and Safety Performance Standards; Guidelines for Early Care and Education Programs:** <http://cfoc.nrckids.org/index.cfm>
- F. **Kansas Regulations/Statutes Related to Infectious Disease:** www.kdheks.gov/epi/regulations.htm
- G. **KDHE Foodborne Illness Resources:** www.kdheks.gov/epi/foodborne.htm
- H. **Additional Information (CDC):** www.cdc.gov/health/default.htm
- I. **CDC's Travelers' Health - Yellow Book (Typhoid-paratyphoid fever):** wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/typhoid-paratyphoid-fever.aspx

ATTACHMENTS

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