Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

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DEPARTMENT CIRCULAR
No. 2020-0364

TO: **ALL UNDERSECRETARIES AND ASSISTANT SECRETARIES; DIRECTORS OF BUREAUS, SERVICES AND CENTERS FOR HEALTH DEVELOPMENT: MINISTER OF HEALTH — BANGSAMORO AUTONOMOUS REGION IN MUSLIM MINDANAO; EXECUTIVE DIRECTORS OF SPECIALTY HOSPITALS; CHIEFS OF MEDICAL CENTERS, HOSPITALS, SANITARIA AND INSTITUTES; PRESIDENT OF THE PHILIPPINE HEALTH INSURANCE CORPORATION; AND ALL OTHERS CONCERNED**

SUBJECT: **Adoption of the Philippines Society for Microbiology and Infectious Diseases (PSMID) 2017 Clinical Practice Guidelines (CPG) for Typhoid Fever in Adults by the National Food and Waterborne Disease Prevention and Control Program**

The 2017 Clinical Practice Guidelines (CPG) for Typhoid Fever in Adults developed by the Philippine Society for Microbiology and Infectious Diseases (PSMID) is hereby adopted by the National Food and Waterborne Disease (FWBD) Prevention and Control Program to be utilized by program managers and coordinators, health workers, training officers and medical practitioners and other stakeholders to harmonized management and strengthened prevention and control of typhoid fever. (Refer to Annex A)

The CPG for typhoid fever in adults shall be posted at the DOH website www.doh.gov.ph.

Dissemination of the information is requested.

By Authority of the Secretary of Health

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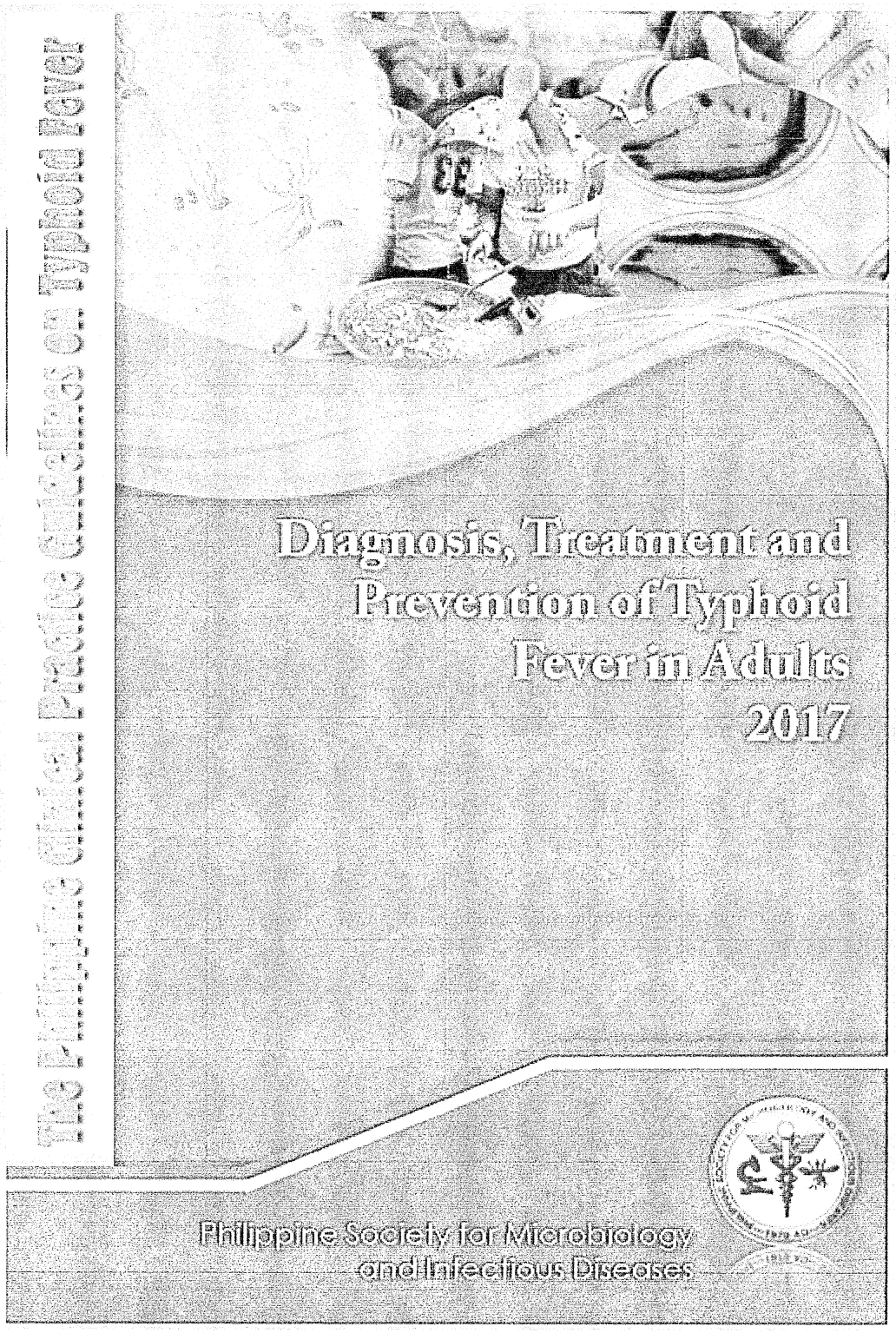
ANNEX A.
DIAGNOSIS, TREATMENT AND PREVENTION OF TYPHOID FEVER IN ADULTS 2017



The Philippine Clinical Practice Guidelines on the Diagnosis, Treatment and Prevention of Typhoid Fever in Adults 2017

INTRODUCTION

Typhoid fever is still a major problem with a reported global burden estimate of 26.9 million cases in 2010 with a case fatality rate of 1%. The Philippines had 2,025 cases of typhoid and paratyphoid fever in 2010, a marked decrease from the 2003 figure of 16,444 cases. Morbidity is 30.5/100,000 population and mortality is 1.7/100,000 population.

To help clinicians in the diagnosis and management typhoid fever, the Philippine Society for Microbiology and Infectious Diseases (PSMID) formulated this CPG to:

- provide diagnostic updates
- provide antibiotic recommendations that would help practitioners in implementing antimicrobial stewardship to reduce and prevent emergence of multidrug-resistant *Salmonella typhi.*
- provide guidelines on the management of complicated cases and special populations (pregnant, carriers)
- provide strategies in the prevention and control of this infection

CLINICAL MANIFESTATIONS OF TYPHOID FEVER

Any individual who lives in or who has history of travel from tropical and subtropical areas; who presents with fever of $\geq$ 5 days of fever; fever documented at > 38°C **WITH** any of the following symptoms: headache, diarrhea, body malaise/ weakness, abdominal distention/pain, gastrointestinal bleeding and changes in orientation/ confusion should be considered a suspected typhoid fever case (strong recommendation,high quality of evidence)

CANDIDATES FOR HOSPITAL ADMISSION

1. Complicated Typhoid Fever
   Patients who are unable to take oral fluids due to persistent vomiting and those who are at risk to develop the severe form of typhoid fever with unstable vital signs, severe dehydration, spontaneous bleeding, persistent abdominal pain, difficulty in breathing, neurologic manifestations and patients showing signs of complications (myocarditis, DIC, hemolytic uremic syndrome, severe pneumonia, etc.) (strong recommendation, high quality of evidence)

2. Typhoid fever in pregnancy (strong recommendation, low quality of evidence)

3. Social circumstances
   Unavailability of a caregiver to give medicines; long distance travel and unavailability of medicines in the locality are social circumstances unique to the patient that may warrant admission in the hospital

LABORATORY TESTS THAT CAN BE USED TO CONFIRM THE DIAGNOSIS OF TYPHOID FEVER

- Direct Detection Method
  Culture and Isolation(strong recommendation, high quality of evidence)
  Polymerase chain reaction (conditional recommendation, moderate quality of evidence)
- Indirect Method
  Antibody detection (conditional recommendation, high quality of evidence)
  - Tubex
  - Typhidot
  - TyphiRapid

The Widal test is NO LONGER RECOMMENDED FOR DIAGNOSIS OF TYPHOID FEVER (Strong recommendation, high quality of evidence)

TREATMENT

Table 1. Summary of Recommended Antibiotics for Uncomplicated Typhoid Fever
(Strong recommendation, High quality of evidence)

Antibiotics	Duration of treatment	Remarks
Amoxicillin 500mg/cap 2 caps q6h	14 days	Compliance issues due to pill burden
Chloramphenicol 500mg 2caps q6h	14 days	Compliance issues due to pill burden Risk for bone marrow suppression
TMP-SMX 800/160 mg 1 tab q12h	14 days	Increased drug pressure and risk for Stevens-Johnson's Syndrome
Cefixime 200 mg 1 tab q12h	7 days	Higher cost Inaccessibility
Azithromycin 500 mg 1-2 tab q24h	7 days	Higher cost Increased drug pressure Risk of QT prolongation
Ciprofloxacin 500mg q12h	7 days	Collateral damage to tuberculosis and MRSA Risk of QT prolongation
Ofloxacin 400 mg 1 tab q12h	7 days	Collateral damage to tuberculosis and MRSA Risk of QT prolongation

Table 2. Summary of Recommended Antibiotics for Complicated Typhoid Fever
(Strong recommendation, Low quality of evidence)

First-line treatment	Step down antibiotics*	Duration of treatment
Ceftriaxone 2-3 g IV q24h	Cefixime 200 mg 1 tab q12h	14 days
Azithromycin 1 g IV q24h	Azithromycin 500 mg 1 tab q24h	7 days
Ciprofloxacin 400 mg IV q12h	Ciprofloxacin 500-750 mg q12h	14 days
Ofloxacin 400 mg IV q12h	Ofloxacin 400 mg 1 tab q12h	14 days

*De-escalation to oral antibiotics should be based on results of culture and sensitivity if available
Stepping down to an oral antibiotic may be done if patient is afebrile for 48hrs and is able to tolerate oral medications.

If intestinal perforation is suspected, surgical evaluation and coverage for anaerobes must be considered

Table 3. Summary of Recommended Antibiotics for Typhoid Fever in Pregnant Patients
(Strong recommendation, Low quality of evidence)

First-line treatment	Step down antibiotics*	Duration of treatment
Ampicillin 1-2 g IV q6h	Amoxicillin 1 g q6h	10-14 days
Ceftriaxone 2-3 g IV q24h	Cefixime 200 mg 1 tab q12h	7 days

*De-escalation to oral antibiotics should be based on results of culture and sensitivity if available

Multi-drug resistant typhoid fever (MDRTF)

Defined as typhoid fever caused by *Salmonella typhi* strains which are resistant to the first-line recommended drugs for treatment namely chloramphenicol, ampicillin and TMP-SMX.

MDRTF should be suspected in the following situations: failure to respond after 5 to 7 days treatment with a first-line antibiotic, household contact with a documented case or during an epidemic of MDRTF, and clinical deterioration or development of complications during conventional antibiotic treatment using first-line drugs.

Table 4. Empiric treatment for suspected MDRTF
(Strong recommendation, Moderate quality of evidence)

Antibiotic*	Duration of treatment
Cefixime 200mg/tab 1 tab q12h	7 days
Ciprofloxacin 500mg/tab 1 tab q12h	7 days
Ofloxacin 400mg/tab 1 tab q12h	7 days
Azithromycin 500mg/tab 1-2 tab q24h	7 days

*For culture proven MDRTF, antibiotic of choice is based on the susceptibility result

Chronic Carrier

An asymptomatic patient who continues to have positive stool or rectal swab cultures for *S. typhi* a year following recovery from acute illness

Table 5. Treatment for Chronic Carriers
(Strong recommendation, Moderate quality of evidence)

Antibiotic	Duration of treatment
TMP-SMX 800/160 1 tab q12h	6-12 weeks
Amoxicillin 100mg/kg/day	6-12 weeks
Ampicillin 100mg/kg/day	6-12 weeks
Norfloxacin 400mg 1 tab q12h	4 weeks
Ciprofloxacin 750 1 tab q12h	4 weeks

TYPHOID VACCINES

Typhoid vaccine is indicated among the following:

- travelers to endemic areas such as Sub-Saharan Africa, Central Asia,Indian Subcontinent,Latin America, Middle East, South and Southeast Asia,
- persons with intimate exposure to a documented typhoid fever carrier and
- for laboratory workers routinely exposed to cultures of *Salmonella* serotype Typhi or specimens containing this organism

(Strong recommendation, High quality of evidence)

Table 6. Schedule for Typhoid fever vaccine

Vaccination	Age (yrs)	Dose/ mode of	No. of doses	Dosing schedule	Boosting interval
Vi capsular polysaccharide vaccine					
Primary series	≥2	0.50 mL*	1	1 dose	--
Booster	≥2	0.50 mL*	1	1 dose	Every 2 yrs
Oral live-attenuated Ty21a vaccine					
Primary series	≥6	1 capsule	4	Days 0,2,4,6	--
Booster	≥6	1 capsule	4	Days 0,2,4,6	Every 5 yrs

*Intramuscularly

Table 7. Strength of Recommendation and Quality of Evidence

Category	**Definition**
Strength of Recommendation	
Strong	Desirable effects (benefits) clearly outweigh the undesirable effects (risks)
Conditional	Desirable effects probably outweigh the undesirable effects but the recommendation is applicable only to a specific group, population, or setting; or the benefits may not warrant the cost or resource requirements in all settings
Weak	Desirable and undesirable effects closely balanced; or uncertain, new evidence may change the balance of risk to benefit
No recommendation	Further research is required before any recommendation can be made
Quality of Evidence	
High	Consistent evidence from well-performed (RCTs) or strong evidence from unbiased observational studies; further research is very unlikely to change confidence in the estimate of the effect
Moderate	Evidence from RCTs with important limitations or moderately strong evidence from unbiased observational studies; further research is likely to have an important impact on confidence in the estimate of the effect
Low	Evidence for ≥ one critical outcome from observational studies, from RCTs with serious flaws from indirect evidence; further research is very likely to have an important impact in the estimate of effect and is likely to change the estimate
Very Low	Evidence for ≥ one critical outcome from unsystematic clinical observations or very indirect evidence; any evidence of effect is very uncertain

Sources:

1. Task Force on The Philippine Clinical Practice Guidelines on the Diagnosis, Treatment and Prevention of Typhoid Fever in Adults 2017

2. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008; 336:924-6.

3. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. BMJ 2008; 336:1049-51.

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