Review Article

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Leptospirosis Chemoprophylaxis Following Floods

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Abstract:

Leptospirosis is a globally important zoonotic infection with a high burden in tropical regions, including Thailand, where transmission is strongly associated with rainfall and flooding. In endemic settings, predictable exposure patterns and identifiable high-risk populations have prompted interest in antibiotic chemoprophylaxis as a preventive strategy. This narrative review summarizes the current evidence on antibiotic chemoprophylaxis for leptospirosis, with emphasis on flood-associated exposure and data from Thailand. Doxycycline is the most extensively studied agent. Early randomized trials demonstrated substantial protection against clinical disease, while later studies reported inconsistent findings, particularly regarding prevention of infection. Evidence suggests that doxycycline may reduce the incidence and severity of symptomatic leptospirosis rather than completely preventing infection. Data from southern Thailand provide important real-world evidence supporting post-exposure prophylaxis. A prospective study during flooding showed that a single 200 mg dose of doxycycline reduced the risk of leptospiral infection and clinical disease, with particularly high efficacy among individuals with skin wounds. Systematic reviews, including Cochrane analyses, indicate a modest benefit in preventing clinical illness but highlight limitations related to study heterogeneity and methodological quality. Overall, current evidence supports a targeted approach to chemoprophylaxis in high-risk populations rather than universal use. In endemic regions such as southern Thailand, post-exposure doxycycline may be considered for individuals with significant exposure, particularly in the presence of skin breaches, alongside non-pharmacological preventive measures.

Keywords: chemoprophylaxis, floods, leptospirosis, Thailand

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Introduction

Leptospirosis is a globally important zoonotic infection caused by pathogenic *Leptospira* species, with a disproportionate burden in tropical and subtropical regions. The disease is transmitted through direct or indirect exposure to the urine of infected animals, most commonly via contaminated water entering through abraded skin or mucous membranes. The global burden is substantial, with more than one million cases and approximately 60,000 deaths annually[1]. Southeast Asia is one of the most affected regions, and Thailand remains a well-recognized endemic country. Leptospirosis re-emerged as a major public health concern following large outbreaks in Thailand in the late 1990s. Although national incidence has declined from its peak, the disease remains endemic, with seasonal surges corresponding to rainfall patterns. The southern region of Thailand, characterized by prolonged monsoon seasons and recurrent flooding, continues to experience relatively high incidence rates compared with other regions[2,3]. These epidemiological characteristics have prompted interest in preventive strategies, including antibiotic chemoprophylaxis. Despite decades of investigation, the effectiveness of chemoprophylaxis for leptospirosis remains controversial. This review synthesizes the current evidence on antibiotic prophylaxis, with particular emphasis on data from Thailand and its implications for clinical and public health practice.

Review methodology

This article was designed as a narrative review informed by a structured literature search. PubMed/MEDLINE and Scopus were searched from database inception through April 2026. The search combined controlled vocabulary and free-text terms related to "leptospirosis," "chemoprophylaxis," "flood," and "Thailand". Reference lists of eligible articles and relevant reviews were screened to identify any additional publications.

Eligible sources included randomized and non-randomized controlled studies, cohort studies, systematic reviews, meta-analyses, and official clinical or public health guidance addressing human leptospirosis prophylaxis. Studies were prioritized when they evaluated clinical leptospirosis, laboratory-confirmed infections, and adverse events after a clearly described exposure. Thai studies and guidance were specifically included because of the manuscript's regional focus. Animal studies, in vitro studies without direct clinical relevance, reports focused exclusively on treatment of the established disease, and publications lacking sufficient information on prophylaxis were excluded.

Because the available studies were few and clinically heterogeneous, no new meta-analysis was performed. Findings were synthesized narratively according to exposure setting, prophylactic strategy, outcome definition, safety, and risk of bias. Greater interpretative weight was given to randomized trials, systematic reviews, and official guidance, while observational studies were used to provide context and generate hypotheses.

Epidemiological rationale for targeted prophylaxis

Leptospirosis in Thailand exhibits strong seasonality, with incidence peaking during the rainy season. National surveillance data report annual incidence rates ranging between 5 and 15 cases per 100,000 population, with higher rates during outbreak periods[2]. Heavy rainfall, flooding, and waterlogging create ideal conditions for the survival of *Leptospira* in the environment. Rodents, particularly *Rattus* species, serve as the principal reservoirs, while livestock and domestic animals also contribute to transmission[3]. Occupational exposure remains a key determinant of infection risk, particularly among rice farmers, rubber plantation workers, and individuals involved in flood-related activities.

Several studies from southern Thailand have highlighted critical risk factors for infection. Prolonged exposure to floodwater (typically more than 3–6 hours per day) significantly increases infection risk, while the presence of skin abrasions or lacerations represents one of the strongest predictors of disease[4]. Spatial analyses further demonstrate clustering of cases in low-lying flood-prone areas, underscoring the importance of environmental determinants. These epidemiological features provide a strong rationale for targeted preventive interventions, including chemoprophylaxis in high-risk populations.

Chemoprophylaxis aims to prevent infection or attenuate disease severity following exposure. Given the predictable seasonality and identifiable risk groups in leptospirosis-endemic areas, antibiotic prophylaxis has been explored as a practical preventive strategy, particularly during outbreaks or high-risk exposures. Doxycycline has been the most extensively studied agent due to its in vitro activity against *Leptospira* spp., favorable pharmacokinetic profile, and ease of administration. Proposed strategies include weekly prophylaxis during periods of exposure and post-exposure prophylaxis (PEP) following high-risk contact.

Evidence for leptospirosis chemoprophylaxis

Early randomized controlled trials provided initial support for doxycycline prophylaxis. A landmark study conducted among U.S. military personnel in Panama demonstrated that weekly doxycycline (200 mg) reduced the incidence of clinical leptospirosis by approximately 95% compared with placebo[5]. This study established the foundation for subsequent investigations. However, later RCTs have produced inconsistent results. A trial conducted in the Andaman Islands found that weekly doxycycline did not significantly reduce the incidence of leptospiral infection, as measured by seroconversion, although it was associated with a reduction in clinical illness and severity[6]. These findings suggest that doxycycline may not fully prevent infection but could mitigate symptomatic disease. The discrepancy between studies may reflect differences in exposure intensity, endemicity, and study design, as well as the distinction between infection and clinical disease as outcomes.

Data from Thailand, particularly the southern regions, provide important real-world insights into chemoprophylaxis effectiveness. A prospective non-randomized controlled study conducted during urban flooding in southern Thailand evaluated the use of a single 200 mg dose of doxycycline as post-exposure prophylaxis[4]. The study demonstrated substantial protective effects, with an estimated efficacy of 76.8% against leptospiral infection and 86.3% against clinical leptospirosis. Notably, among individuals with skin wounds, protective efficacy exceeded 90%. These findings highlight the importance of host factors, particularly skin integrity, in determining both risk and prophylaxis effectiveness. In addition, the study identified laceration wounds as the strongest independent risk factor for infection (odds ratio >30), reinforcing the biological plausibility of targeted prophylaxis in individuals with cutaneous exposure.

Systematic reviews, including Cochrane analyses, have attempted to synthesize the available evidence on antibiotic prophylaxis for leptospirosis. Overall, these reviews conclude that while doxycycline may reduce the incidence of the clinical disease, it does not consistently prevent infection[7]. Furthermore, prophylaxis is associated with adverse effects, particularly gastrointestinal intolerance[7,8], which may limit adherence in large-scale implementation. The quality of evidence is also limited by small sample sizes, heterogeneity of study populations, and variability in outcome definitions. More recent reviews have emphasized that the effectiveness of chemoprophylaxis likely depends on several factors, including timing of administration, duration of exposure, and intensity of environmental contamination[9]. These considerations are particularly relevant in endemic

settings such as southern Thailand, where exposure is often prolonged and repeated. A summary of key studies is presented in Table 1. Although doxycycline remains the most widely studied agent, other antibiotics have been evaluated. Azithromycin has shown some efficacy in reducing seroconversion rates in small studies, but evidence for preventing the clinical disease remains limited. Penicillin has not demonstrated sufficient evidence to support its use as a prophylactic agent. At present, doxycycline remains the preferred option for chemoprophylaxis due to the strength of the available evidence and practical considerations.

Drug safety should also be considered when doxycycline is used for chemoprophylaxis. Common adverse effects include gastrointestinal intolerance, particularly in pregnant or breastfeeding women and young children, populations in whom tetracyclines have traditionally been avoided because of concerns regarding fetal or childhood tooth discoloration and effects on bone development. Data specifically evaluating doxycycline for leptospirosis prophylaxis in these populations remain limited. For individuals in whom doxycycline is contraindicated, poorly tolerated, or otherwise unsuitable, there is currently insufficient evidence to recommend a specific alternative antimicrobial regimen for leptospirosis prophylaxis. Accordingly, in patients unable to receive doxycycline, management should focus on intensified non-pharmacological prevention, active symptom surveillance, and rapid initiation of treatment for the suspected disease, which currently represents the most evidence-aligned approach[8].

Current evidence suggests that chemoprophylaxis should not be universally applied to all populations at risk of leptospirosis. Recommendations for leptospirosis chemoprophylaxis remain based on relatively limited and heterogeneous evidence, and routine antibiotic prophylaxis has not been widely adopted in clinical practice. The effect of mass or repeated doxycycline exposure on the human microbiome and antimicrobial resistance has not been adequately studied in leptospirosis prophylaxis campaigns. A targeted approach is more appropriate, particularly in endemic regions[8,10].

In southern Thailand, where environmental exposure is intense and predictable, chemoprophylaxis may be considered in selected high-risk groups, including individuals exposed to floodwater, those with skin wounds, and occupationally exposed populations. Post-exposure prophylaxis with a single dose of doxycycline appears to be a practical and effective strategy in such settings. However, chemoprophylaxis should be integrated with non-pharmacologic interventions, including protective footwear, proper wound care, and avoiding contaminated water when possible. Public health measures, such as rodent control and environmental sanitation, remain essential components of leptospirosis prevention. Leptospirosis continues to pose a significant public health challenge in tropical regions, particularly in southern Thailand. While antibiotic chemoprophylaxis with doxycycline has demonstrated some effectiveness in reducing clinical disease, its role in preventing infection remains inconsistent.

Evidence from Thailand supports the use of targeted post-exposure prophylaxis in high-risk individuals, especially those with skin wounds following flood exposure. Future research should focus on optimizing prophylaxis strategies, identifying high-risk populations, and integrating pharmacologic and non-pharmacologic interventions.

Current guideline and public health recommendations

Major organizations generally prioritize non-pharmacological prevention and reserve chemoprophylaxis for selected high-risk circumstances. Recommendations are summarized in Table 2[10,11].

Future research directions

Future studies should be adequately powered,

Table 1 Summary of studies on antimicrobial prophylaxis for leptospirosis[4–6,8,12–13]

Study	Country/setting	Design	Intervention	Comparator	Outcome	Main finding
Takafuji et al., 1984	Panama; military jungle training	Randomized placebo-controlled trial	Doxycycline 200 mg weekly	Placebo	Clinical leptospirosis	Large reduction in clinical disease; limited generalizability beyond healthy military personnel.
Gonsalez et al., 1998	Brazil; flood water exposure	Small clinical pilot study	Doxycycline 200 mg single dose	No prophylaxis/ placebo	Clinical or laboratory-confirmed leptospirosis	Inconclusive because of small sample size and imprecision.
Sehgal et al., 2000	India; Andaman Islands; endemic exposure	Randomized controlled trial	Doxycycline 200 mg weekly	Placebo	Seroconversion and clinical illness	No clear prevention of infection; possible reduction in symptomatic disease.
Chusri et al., 2014	Southern Thailand; flood water exposure	Prospective non-randomized controlled study	Doxycycline 200 mg single dose	No prophylaxis	Infection and clinical leptospirosis	Reported protection, strongest among participants with skin wounds; susceptible to confounding.
Alikhani et al., 2018	Northern Iran; endemic exposure	Randomized double-blind placebo-controlled trial	Azithromycin or doxycycline regimens	Placebo	Leptospirosis outcomes	Suggestive but insufficient evidence for azithromycin; replication is needed.
Win et al., 2024	Multiple countries/ settings	Cochrane systematic review	Doxycycline, azithromycin, or penicillin prophylaxis	Placebo/no prophylaxis/other antibiotics	Infection, clinical disease, adverse events	Low- or very-low-certainty evidence; no firm basis for routine mass prophylaxis.

Table 2 Current guideline and public health recommendations for leptospirosis prevention

Organization	Population/setting	Chemoprophylaxis position	Key practical points
World Health Organization	People at high risk during defined exposure or outbreaks	Not a substitute for environmental and personal protection; may be considered in selected high-risk settings	Risk-based use; local epidemiology and feasibility should guide decisions.
Centers for Disease Control and Prevention (CDC) Yellow Book 2026	Adults with short-term exposure in a known high-risk area, including adventure travelers, aid workers, and military personnel	Doxycycline 200 mg orally once weekly may be considered	Begin 1–2 days before exposure and continue through the exposure period; evidence is limited.
Thailand Department of Disease Control	Flood-affected or otherwise highly exposed populations under national/local public-health protocols	Targeted doxycycline use may be advised according to exposure risk and national guidance	Combine with boots, wound protection, hygiene, surveillance, and early medical assessment; avoid unsupervised mass use.

multicenter randomized controlled trials conducted in contemporary flood and endemic settings. Core outcomes should include laboratory-confirmed infection, symptomatic leptospirosis, severe disease, hospitalization, mortality, adverse events, adherence, and antimicrobial resistance. Standardized exposure definitions and diagnostic criteria are essential. Future studies should compare pre-exposure with post-exposure strategies and examine whether skin wounds or other risk markers identify the people most likely to benefit. Implementation research should evaluate risk-stratification tools, cost-effectiveness, and the antimicrobial stewardship implications of targeted prophylaxis, as well as integration with protective prevention strategies that combine antibiotic prophylaxis.

Conclusion

Current evidence does not justify universal antibiotic chemoprophylaxis for leptospirosis after floods. Doxycycline has shown benefit in selected trials, particularly for clinical disease during short-term high-risk exposure; however, the effects on infection are inconsistent, and the certainty of evidence is low. A targeted strategy may be reasonable for carefully selected adults with intense, unavoidable exposure, especially when skin integrity is compromised, provided that local guidance, contraindications, adverse effects, and antimicrobial stewardship are considered. Non-pharmacological prevention and prompt evaluation of post-exposure illness remain the foundation of leptospirosis control.

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