

Supplementary Appendix 1: Patients with Plague in the United States, by Antimicrobial Treatment Class and Primary Clinical Form of Plague, 1942-2018

Antimicrobial Class		Number of Patients	Number of Patients with Bubonic Plague (Percent)	Number of Patients who Died (Percent)	Number of Patients with Bubonic Plague who Died (Percent)
Aminoglycosides	Overall	320	253 (79)	31 (10)	18 (7)
	Monotherapy*	73	55 (75)	12 (17)	5 (10)
Tetracyclines	Overall	267	222 (83)	12 (5)	9 (4)
	Monotherapy	51	45 (88)	1 (2)	1(2)
Fluoroquinolones	Overall	48	24 (50)	3 (6)	1(4)
	Monotherapy	12	4 (33)	2 (18)	0 (0)
Chloramphenicol	Overall	84	69 (82)	16 (19)	10 (14)
	Monotherapy	9	7 (78)	2 (22)	1 (15)
Sulfonamides	Overall	36	30 (83)	3(8)	3 (10)
	Monotherapy	11	10 (91)	2 (18)	2 (20)

Additional data derived from: Kugeler KJ, Mead PS, Campbell SB, Nelson CA. Antimicrobial Treatment Patterns and Illness Outcome Among United States Patients with Plague, 1942-2018. Clin Infect Dis. **2020;70 (Suppl 1): S20-S26.**

*Monotherapy was defined as receiving no additional antibiotic considered to be effective for treatment of plague.

Supplementary Appendix 2: Considerations for Treatment and Post-Exposure Prophylaxis of Neonates

Clinical Status of Neonate	Clinical Status of Mother	Action for Neonate
Symptomatic*	Symptomatic, untreated or treated <48 hours prior to delivery	Treat neonate
	Symptomatic, treated ≥48 hours prior to delivery and improving	Treat neonate
	Asymptomatic, exposed to <i>Y. pestis</i> during the last 7 days of pregnancy, not taking antimicrobial prophylaxis	Treat neonate
	Asymptomatic, exposed to <i>Y. pestis</i> during the last 7 days of pregnancy, taking antimicrobial prophylaxis	Treat neonate
Asymptomatic	Symptomatic,	Prophylax neonate

	untreated or treated <48 hours prior to delivery	
	Symptomatic, treated ≥48 hours prior to delivery and improving	Careful observation of neonate
	Asymptomatic, exposed to <i>Y. pestis</i> during the last 7 days of pregnancy, not taking antimicrobial prophylaxis	Careful observation of neonate. If mother develops symptoms of plague, begin prophylaxis of neonate.
	Asymptomatic, exposed to <i>Y. pestis</i> during the last 7 days of pregnancy, taking antimicrobial prophylaxis	Careful observation of neonate

*Neonates might not demonstrate classic signs of plague. Neonates with *Yersinia pestis* infection can present with only nonspecific signs of illness such as fever, difficulty breathing, blood pressure instability, or feeding difficulty.

Supplementary Appendix 3: Safety Considerations for Antimicrobials Recommended for Treatment and Prophylaxis of Plague Among Lactating Mothers

For additional considerations and caveats for lactating mothers, please refer to the references listed below, which were the source for the information in this table.

Acceptable ¹⁻⁵	Limited Human Data but Low Theoretical Risk ¹⁻⁵	Moderate Risk ¹⁻⁵	Not Recommended ¹⁻⁵
Ciprofloxacin*	Levofloxacin*	--	Chloramphenicol*
Amikacin	Moxifloxacin*		Omadacycline [†]
Gentamicin	Trimethoprim/Sulfamethoxazole* [§]		
Streptomycin	Plazomicin		
Tobramycin	Ofloxacin*		
Tetracycline			
Doxycycline			
Minocycline			

* Exercise caution or avoid using for mothers of infants with glucose-6-phosphate-dehydrogenase deficiency.

Source: Drug Induced Hemolytic Anemia in Patients with Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. In: Micromedex IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. <https://www.micromedexsolutions.com/>.

[†] The manufacturer of omadacycline states that breastfeeding is not recommended during treatment and for 4 days after the last dose.

[§] Exercise caution or avoid using for mothers of premature infants or those with hyperbilirubinemia. Short courses of 7-10 days' duration are generally considered safe for lactating mothers.

References:

1. Drugs and Lactation Database (LactMed). Bethesda (MD): National Library of Medicine (US); 2006 [cited 2020 Dec 16]. <https://www.ncbi.nlm.nih.gov/books/NBK501922/>
2. Reprotox (Reproductive Hazard Information Database); 2020 [cited 2020 Oct 8]. <https://reprotox.org/>.

- Briggs GG, Freeman RK, Towers CV, Forinash AB. *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*. 11th ed. Philadelphia (PA): Wolters Kluwer; 2017.
- Association for Promotion of Cultural and Scientific Research into Breastfeeding. *E-lactancia*; 2002 [cited 2021 Feb 2]. <http://e-lactancia.org>.
- Schaefer C, Peters P, Miller RK. *Drugs During Pregnancy and Lactation: Treatment Options and Risk Assessment*. 3rd ed. London: Academic Press; 2015.

Supplementary Appendix 4: Considerations for Dosing of Antimicrobials Recommended for Treatment or Prophylaxis of Plague Among Patients Who Are Obese or Underweight

Antimicrobial Agent or Class	Adults	Children ^{1,2}
Aminoglycosides	Obese: Calculate dose by using adjusted body weight (ABW) ³ Underweight: use total body weight (TBW) ^{3*}	Obese: ABW
Ciprofloxacin	Obese: Use upper end of dosing range ³ Underweight: Usual dose	TBW
Levofloxacin	Usual dose	TBW
Moxifloxacin	Usual dose	TBW
Ofloxacin	No specific recommendations or data available; assume usual dose based on class	TBW
Tetracyclines	Usual dose	TBW
Trimethoprim-sulfamethoxazole	Usual dose ³	TBW
Chloramphenicol	Usual dose; monitor serum levels ⁴	TBW; monitor serum levels ⁴

* TBW = Total body weight; IBW = Ideal body weight; ABW = Adjusted body weight
 $ABW^3 = IBW + ((TBW - IBW) \times 0.4)$

References:

- Kendrick JG, Carr RR, Ensom MHH. Pediatric Obesity: Pharmacokinetics and Implications for Drug Dosing. *Clin Therapeut*. 2015;37:1897-1923.
- Autmizguine J, Melloni C, Hornik CP, et al. Population Pharmacokinetics of Trimethoprim-Sulfamethoxazole in Infants and Children; the Pediatric Trials Network Steering Committee. *Antimicrob Agents Chemother*. 2017;62:e01813-17.
- Meng L, Mui E, Holubar MK, Deresinski SC. Comprehensive Guidance for Antibiotic Dosing in Obese Adults. *Pharmacotherapy*. 2017;37:1415–1431.
- Chloramphenicol Sodium Succinate [package insert]. Bristol, TN: Monarch Pharmaceuticals, LLC; 2004.