INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Zoonotic Infections***
-August 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a review of zoonotic infections and their management, which included avian influenza, plague, and rabies. This marks in the initial review of this topic for the NPTC. Currently, oseltamivir is recommended in the treatment of avian influenza and is available on the IHS National Core Formulary (NCF). Plague is a vector-borne illness managed most frequently with a combination of a fluoroquinolone antibiotic and gentamicin. The NPTC named ciprofloxacin to the NCF in 2022. Rabies post-exposure prophylaxis is commonly provided across the IHS and, as such, the NPTC voted to **ADD (1) Rabies vaccine (any product)** and **(2) Human Rabies Immune Globulin (any product)** to the NCF.

Discussion:

Avian influenza maintains a moderate risk to become pandemic. It is currently responsible for substantial impact on poultry and dairy herds. The most significant avian influenza virus is the H5N1, a subtype of the influenza A virus, but other avian influenza viruses exist in circulation world-wide.[1] The vast majority of human cases in the United States (U.S.) are mild, characterized by conjunctivitis and occur in farm workers. Surveillance for pandemic avian influenza is ongoing and pandemic preparedness includes the stockpiling of pre-pandemic immunization and planning for pandemic immunization production when/if necessary. Oseltamivir is currently recommended by the U.S. Centers for Disease Control and Prevention (CDC) as treatment for H5N1 and other novel influenza viruses. Its use is outlined in the Emergency Use Instructions (EUI) for Oseltamivir.[2]

Plague is a serious bacterial disease caused by *Yersinia pestis*, a gram-negative bacterium. It has impacted human history significantly on multiple occasions, including through use by weaponization.[8] Bubonic plague is the most common syndrome with “bubo” being the typical lesion consisting of severely swollen and painful lymph nodes. Prompt treatment is critical. *Y. pestis* maintains a reservoir in rodents with fleas serving as vectors between individuals. Once a disease associated with urban rat infestation, plague currently maintains a reservoir in rural rodents such as prairie dogs, with the majority of U.S. cases in Arizona and New Mexico.[3] Fleas carry the infection from rodents to humans, however humans are incidental. Other modes of transmission include handling infected animal tissues, secondary vectors such as dogs or cats which have been infected by fleas, and droplet transmission is possible as well.

Clinical syndromes of plague include bubonic plague, pneumonic plague, and septicemic plague. Bubonic plague is most common and follows a short incubation period with rapid onset and progression of flu-like symptoms followed by buboes at or near the site of the exposure. Pneumonic and septicemic plague are complications of advanced bubonic plague but can occur without buboes.[4] Pneumonic plague occurs most likely following weaponized plague exposure.[7] Severe illness and mortality are likely without prompt identification and initiation of treatment. Treatment is considered adequate with a fluoroquinolone antibiotic (such as ciprofloxacin) and dual therapy with ciprofloxacin and gentamicin is recommended for severe illness.[4] Doxycycline is also considered to be an effective treatment.[5] The organism is easily cultured on common media, however automated identification systems do not readily identify *Y. pestis* and an elevated index of suspicion and communication with microbiology professionals is necessary for early identification. Early initiation of treatment is cited as the most important aspect of successful treatment of plague. Antibiotic resistance is uncommon in naturally acquired plague, however should exposure to weaponized plague occur, resistance testing and dual antibiotic coverage are critical in management.[7]

Rabies is caused by the Lyssa virus, which is transmitted through a bite from an infected animal. The incubation period can last from weeks to months. Once rabies becomes symptomatic, it is near-universally fatal. Post-exposure prophylaxis is administered after a suspected or confirmed exposure, thus preventing infection. The most common reservoir for rabies infection acquired in the U.S. are bats.[8] Rabies is also found regionally in foxes, racoons, and skunks. Dogs are the most common source for exposure in many parts of the world. An animal bite from suspected or confirmed-rabid animal is initially managed with wound cleansing.[9] Post-exposure prophylaxis (PEP) is then administered by infiltration of the wound with human rabies immune globulin (HRIG). Rabies immunization series is then initiated. Source animal testing is recommended when possible. If the source animal is available, quarantine and observation or testing for illness is recommended. Treatment can be stopped if the source animal remains well through quarantine or tests negative. Current CDC guidelines detail Pre-exposure prophylaxis (PrEP) with human rabies immunization for people at high risk for rabies exposure.[10] Despite PrEP, rabies PEP remains necessary following a bite by a rabid animal for those who receive PrEP.[9]

Findings:

Avian influenza illness from H5N1 is typically conjunctivitis. The EUI from the CDC recommends use of oseltamivir at a dose of 75 mg BID for 5 to 10 days for most cases. The same dose is used for PEP from an H5N1 exposure.[2]

Plague is caused by *Y.pestis* and is characterized by syndromes of bubonic, pneumonic and septicemic plague. Early identification and treatment of illness is crucial. Ciprofloxacin 400 mg intravenously (IV) every 12 hours or 500 mg orally every 12 hours is the CDC-recommended treatment for plague with dual therapy including gentamicin 5 mg/kg IV every day or 2 mg/kg IV loading dose followed by 1.7 mg/kg every 8 hours in severe illness.[4] Ciprofloxacin alone was recently shown to be non-inferior to combination ciprofloxacin and gentamicin.[6] Doxycycline is also effective for treatment of plague.[5] Ciprofloxacin and doxycycline are currently listed on the NCF. Gentamicin is not named on the NCF but is readily available in the hospital setting. As droplet transmission of plague is possible, isolation is critical when treating confirmed or suspected plague.

Rabies disease, once symptomatic, is not treatable and nearly always fatal. Human infection must be prevented by PEP after a bite from a rabid animal. Thorough wound scrubbing with soap and water is the first step. HRIG and immunization are subsequent treatments.[9] After the bite wound(s) is/are properly irrigated, HRIG is then infiltrated into the wound(s). Any remaining HRIG is then given intramuscularly. The recommended dosing of HRIG is 20 units/kg in a single dose. Rabies immunization is then carried out, typically with 4 doses. Rabies PrEP is recommended by the CDC for a select few individuals at risk for contracting rabies.[10] Ultimately, the NPTC added HRIG and human rabies immunization to the NCF.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

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