94. THE CDC NATIONAL PHARMACEUTICAL STOCKPILE: CONTENTS AND IMPLEMENTATION

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The National Pharmaceutical Stockpile (NPS) consists of drugs and medical/surgical items provided to the U.S. population to reduce morbidity/mortality associated with bioterrorism.

The NPS contains antibiotics, nerve agent antidote, cardiac/respiratory support drugs, and IV fluids. A sufficient quantity of ancillary items to administer and dispense drugs are also provided, (e.g., IV catheters and administration sets, syringes, needles, dispensing bags. Airway management supplies provide portable intubations and ventilator capability for both chemical and biological events. Wound care products are available to care for trauma associated with any type of event. The NPS antibiotic formulary was selected to deter the effects of agents such as inhalational anthrax, plague, and tularemia. Currently, the NPS is stocked with both oral and parenteral versions of a fluoroquinolone, aminoglycoside, and tetracycline derivative. Chemical response consists of an oxime type antidote, anticholinergic, and benzodiazepine symptomatic treatments. Ancillary drugs for cardiac/respiratory support are potentially applicable for any type event. They include vasopressors, corticosteroid, and a beta agonist. Morphine injection is stocked for severe pain management associated with trauma. Lorazepam addresses the need for sedation and patient control during ventilator support.

The philosophy of including sufficient quantities of every ancillary item that may be needed for drug administration and dispensing removes the assumption that the local incident scene will have these items on hand. Under the guise of managed health care, it would be unsafe to assume that sufficient local inventories if med/surg items exist seamlessly throughout the U.S.

The NPS airway management supplies were selected to enable emergency providers to intubate, suction, and ventilate civilian populations. Manual ventilator devices can provide more immediate care, while mechanical equipment provides longer-term needs. The equipment was chosen in various sizes to provide care to infant, pediatric, and adult populations.

Likewise, CDC's NPS Program has attempted to address all ancillary needs to efficiently execute the oral drug dispensing process. Program staff are in the process of evaluating the utility of tablet counting machines for dispensing mass oral prophylaxis. These dispensing aids may act as a sole source or adjunct process to a local incident response plan.

Because the mission of CDC's NPS Program is to provide both treatment and prophylaxis, drugs are available in both oral and parenteral forms. Oral suspensions are included for children and those adults who cannot swallow tablets. The drugs are provided in forms allowing for dosage adjustment based on weight, age, or medical conditions. The chemical response drugs are provided in a military designed spring-loaded injector form, allowing rapid IM administration.

The quantities for each antibiotic were chosen based on the desired number of victims to treat and prophylax for each threat. The numbers of victims, or "N," are derived by technical expert "worst case scenario" threat analysis. The quantities are not static, and will be adjusted up or down as more research and intelligence community information is provided to NPS Program.

Interagency and non-governmental medical expert panels are also routinely convened to determine optimal drug regimens for the identified threats. CDC's preferred treatment for inhalational plague is aminoglycoside monotherapy. Alternatively, a tetracycline derivative is also approved and effective. If patient improvement allows, the treatment course may be completed with a cost-effective oral equivalent.

CDC recommends an oral tetracycline derivative for post-exposure plague prophylaxis. Asymptomatic persons having household, hospital, or otherwise close contact with confirmed untreated plague cases should receive a 7-day course and be monitored for fever and cough. Pediatric doses are adjusted based on age and weight.

Symptomatic inhalational tularemia also responds to aminoglycoside and tetracycline derivates. Additionally, an IV fluoroquinolone can be used. Given the variety of treatment options, the cost factor may come into play when considering treating a large population. In such cases, the aminoglycoside is least expensive, but burdens the health-provider system with a greater degree of therapeutic level and side effect monitoring. Both tetracycline derivative and fluoroquinolone are applicable for post-exposure prophylaxis against tularemia.

In vivo data supports the use of both fluoroquinolone and tetracycline derivative for treatment of inhalational anthrax. In the absence of definitive sensitivity tests, CDC recommends the use of a fluoroquinolone, as tetracycline and penicillin resistant strains of *B anthracis* are known to exist. The tetracycline derivative is, by comparison, much less expensive, emphasizing the need for timely sensitivity results when treating large populations. Because risk of recurrence remains high after IV treatment due to delayed germination of spores, it is recommended that therapy continue with an oral drug equivalent for a total of 60 days.

In the absence of definitive sensitivity tests, it is recommended that anthrax post-exposure oral prophylaxis also be initiated with a fluoroquinolone. The U.S. Food and Drug Administration (U.S. FDA) recently approved a fluoroquinolone as the first anthrax aerosol post-exposure antibiotic regimen. Like treatment, oral penicillin and tetracycline derivatives should be reserved until the strain is proven susceptible. Besides more cost effective, penicillin and its derivatives exhibit a safer side effect profile for children and pregnant women. Thus, conversion to these classes is desirable for these groups considering the long duration of therapy.

Compared to biological response, dosing guidelines for treating nerve agent exposure are based on multiple and sometimes subjective variables. Treatment for inhalational organophosphate is based on the amount of time that has elapsed since initial exposure and presenting symptoms. Minimal exposure (miosis, nausea, vomiting) that occurred more than 5 minutes ago may only require observation. Conversely, moderate exposure that includes dyspnea warrants a first dose of an oxime and anticholinergic agent, with subsequent observation for reversal of symptoms.

Over time, the nerve agent's binding affinity to cholinesterase becomes irreversible. The oxime drug is less effective at reactivating cholinesterase as the enzyme/organophosphate bond matures. Therefore, it is essential to administer the oxime as soon as possible after exposure. This clinical reality has direct implications for emergency response logistics. Where chemical antidotes are stockpiled and how they will be transported

to incident sites must be carefully planned out in advance. Treatment is more aggressive in direct relation to symptom severity. Some patients may require after care with IV maintenance infusions in a facility setting.

Ancillary drugs in the NPS are non-specific to chemical or biological events. They include the vasopressors dopamine and epinephrine and IV fluids for blood pressure maintenance. Corticosteroids and epinephrine are stocked for potential anaphylactic reactions. Bronchodilators have application for dyspnea secondary to both chemical and biological inhalational threats. In the case of an incident that includes an explosion, sever pain management with morphine injection may be necessary.

CDC must take into consideration all special civilian populations when choosing drugs and medical/surgical items for formulary inclusion in the NPS. For example, drug monitoring for renal compromised patients receiving an aminoglycoside should include dosage adjustment based on blood level monitoring. Several of the NPS antibiotics have significant precautions for use in children and pregnant women. Risk versus benefit issues must be taken into consideration.

Currently, one NPS 12-hour Push Package is designed to provide approximately 5-day empiric (pre susceptibility test) anthrax prophylaxis with oral fluoroquinolone to 48,000 persons. Depending on incident specific variables, the 60-day regimen may be completed with the same fluoroquinolone, or cost-effective alternatives. If the decision is made to maintain the same fluoroquinolone for the full regimen, prophylaxis capacity is reduced within a 12-hour Push Package, as the stock of tetracycline derivative will not be used. In such case, the Vendor Managed Inventory (VMI) portion of the NPS will be called upon to provide more of the same fluoroquinolone.

One 12-hour Push Package has the capacity to prophylax 180,00 and 200,000 persons against plague and tularemia. Overall, IV treatment capacity in the NPS is much less than that of oral prophylaxis. It is estimated that the majority of the population after exposure will present as asymptomatic (mostly because they are not infected) and therefore suitable for oral prophylaxis. Especially in the case of anthrax, the majority of victims that become symptomatic will not survive, in spite of initiating IV treatment. Therefore, CDC believes it can have greatest impact of reducing mortality by providing oral prophylaxis to asymptomatic persons at risk of having been exposed.

Because morphine and benzodiazepines have potential for abuse, they are classified as "controlled substance" in the U.S., and therefore subject to strict storage, transfer, and security regulations. This presents a potential burden for drugs that may be needed to respond to an emergency. Therefore, the CDC is working with the U.S. Drug Enforcement Agency (DEA) to determine policies/procedures for efficient handling these items under the guise of a bioterrorism scenario.

The NPS includes written and electronic drug information specific for patients and health care providers. The patient data includes side effect and proper use information available in multiple languages. Issues of patient consent and tracking for efficacy and side effect monitoring have also been addressed.