Dosing cards for treatment of children exposed to weapons of mass destruction

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uring winter 2003, officers from a U.S. Public Health Service (PHS) Disaster Medical Assistance Team and Office of Force Readiness and Deployment, formerly the Commissioned Corps Readiness Force, were deployed to the Washington, D.C., and New York City metropolitan areas in response to President Bush raising the Homeland Security Advisory System alert level to orange.¹ An orange, or highrisk, condition is declared when there is a high risk of terrorist attacks.^{1,2} PHS officers were deployed to Washington, D.C., and New York City as a precautionary measure to provide ancillary medical support in case the local medical response system was compromised or overwhelmed as a result of a terrorist action. Intelligence reports did not elaborate or provide specific details regarding the type of threats involved.2 Consequently, the PHS officers had to prepare themselves for a variety of medical crises, including those caused by weapons of mass destruction (WMD).

The Centers for Disease Control and Prevention (CDC) emergency preparedness and response Web site provides a list of man-made and natural medical threats.³ The threat list describes many potential bioterrorism, chemical, and radiation emergencies. PHS officers were deployed with ample supplies of antidotes and treatments for the most likely potential WMD events, including formulations appropriate for both adult and pediatric use.

Although WMD pediatric dosing recommendations were readily avail-

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able from CDC and elsewhere, it became evident to pharmacy team members during the orange-alert deployment that the guidelines are inadequate for practical use in a field environment or mass casualty situation in which access to laboratory and other high-level medical approaches would be limited or nonexistent. In general, calculations based on a child's body weight were available, but additional issues must be considered when determining an appropriate pediatric dose (e.g., conversion of pounds to kilograms, calculation of dose based on body weight, calculation of volume to administer based on drug formulation concentration). The need for health care providers to complete a three- or four-step calculation, no matter how simple, during a highstress WMD response significantly increases the potential for errors and inefficiencies.

Development of dosing cards. To improve response time, ensure public safety, and minimize risk, PHS pharmacist officers designed, developed, and produced WMD pediatric dosing cards. These cards provide standardized and simplified instructions to prepare and administer anti-

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The dosing cards described in this article may be downloaded from www.hhs.gov/ pharmacy/ccrf.html.

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dotes, treatments, and prophylactic medications to young victims exposed to WMD. The provision of standardized pediatric dosing cards will improve team readiness by minimizing the opportunity for potential dosing errors, thereby optimizing the care, treatment, and safety of pediatric patients during a WMD attack. Although inspired by a potential WMD crisis, the cards may also be used for industrial accidents or natural disasters.

Each card is a pocket-sized reference that provides a dosing chart for each threat agent based on child weight ranges and commercially available formulations that are potentially available from the CDC's Strategic National Stockpile program and other sources. Cards are color-coded based on the type of WMD agent (e.g., blue for cyanide, yellow for bioterrorism), so providers can quickly identify the correct card for the situation. Adult doses are also included on each card for completeness.

Figure 1. Front and back of dosing card for cyanide poisoning.

Field Administration of Blood Agent (Cyanide*) Antidotes: Pediatric Dosing Procedures *Calcium Cyanide, Hydrogen Cyanide, Cyanogen Chloride, Potassium Cyanide, Sodium Cyanide^{1,2}

1. Ventilate using bag-valve-mask with one ampoule of amyl nitrite (crushed) in bag; after several minutes, add another (crushed) ampoule; keep adding an ampoule every <u>3</u> minutes. This is a temporary measure until IV drugs can be given.

2. Administer 300 mg (10 ml) of **sodium nitrite** IV over at least 5 minutes. Flush line. [*Children's dose: 6-9 mg/kg.* No separate recommendation for infants.] For elderly, use adult dose unless they are small and frail. Be aware: *Nitrites produce orthostatic hypotension, but a patient who can stand does not need them.* If hypotension occurs, slow the rate of infusion.

3. Follow with 12.5 grams (50 ml) of **sodium thiosulfate IV** over 10 to 20 minutes. [*Children's dose: 400 mg/kg.* No separate recommendation for infants.] Adult dose should be used for elderly unless they are small and frail. (Amyl nitrite, sodium nitrite, and sodium thiosulfate are in the Pasadena (formerly Lilly) Cyanide Antidote Kit, the latter two in ampules of 300 mg/10 ml and 12.5 grams/50 ml). Use one-half dose in 30 minutes if no improvement. See instructions on top of Antidote Kit box.

4. If patient continues to remain apneic, intubate and continue oxygen through tube with assisted ventilation. Transfer apneic or unconscious patients to medical facility. Patients often recover rapidly unless CNS hypoxia has occurred.

¹NOTE: Local protocols may supercede the recommended guidelines.

²NOTE: Dosing may also be adjusted based on Hg assessment. If rapid Hg assessment is not available, assume Hg concentration of 12 g/dL (Goldfrank's Toxicologic Emergencies, 7th ed.)

References: Agency for Toxic Substance and Disease Registry Website, Antidotes and Other Treatments: www.atsdr.cdc.gov/HEC/natorg/pehsubrochure.pdf, www.atsdr.cdc.gov/HEC/natorg/pehsu.html, CDC: www.bt.cdc.gov/children/pdf/working/execsumm03.pdf November 1, 2005

	Sodium Nitrit	e 3% Solution (30 mg/mL)			
We	eight				
Pounds (lbs)	Kilograms (kg)	Dose (6-9 mg/kg)	Administer (IV)		
11	5	30-45 mg	1-1.5 mL		
22	10	60-90 mg	2-3 mL		
44	20	120-180 mg	4-6 mL		
66	30	6-9 mL			
=88	=40	Adult Dose (300 mg)	10 mL		
	Sodium Thiosulf	ate 25% Solution (250 mg/m	L)		
We	eight				
Pounds (lbs)	Kilograms (kg)	Dose (400 mg/kg)	Administer (IV)		
11	5	2000 mg (2 gm)	8 mL		
22	10	4000 mg (4 gm)	16 mL		
44	20	8000 mg (8 gm)	32 mL 50 mL		
=66	=30	Adult Dose (12.5 gm)			

Field Administration of Blood Agent (Cyanide*) Antidotes: Pediatric Dosing Procedures^{1,2} *Calcium Cyanide, Hydrogen Cyanide, Cyanogen Chloride, Potassium Cyanide, Sodium Cyanide

¹NOTE: Local protocols may supercede the recommended guidelines. ²This card may be used as a cross-reference to calculate pediatric doses. All pediatric doses should be individualized based on a child's actual weight. Refer to CDC guidelines for complete prescribing information (www.bt.cdc.gov). November 1, 2005

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Providers can swiftly scan the charts available on each card to verify the appropriate dose to administer. Depending on the nature of the event, providers can use the quickreference cards as a crosscheck to verify the accuracy of their calculations or determine an approximate dose to administer without calculations. All doses have been rounded based on the child's weight and the drug concentration. For example, relying solely on the WMD pediatric dosing cards for determining the appropriate dose of ciprofloxacin in postexposure prophylaxis for anthrax, both a 5-kg child and a 9-kg child could receive 75 mg p.o. twice daily. If one were to work through the weight-based calculations (15 mg/kg) and develop a precise dosage for each of these children, the result would be a maximum of 75 mg p.o. twice daily for the 5-kg child and

135 mg p.o. twice daily for the 9-kg child. While this rounding is probably not clinically significant with older or larger children, use of the quick-reference cards without further professional discretion and adjustments can result in wide variability for smaller children in terms of the actual milligram-per-kilogram dosage given. Therefore, we strongly recommend that the cards be used as a guide, supported by a common-

Figure 2. Front and back of dosing card for nerve-agent poisoning.

				SYMPTOMS					SE Autoinjector Produc		E SYMPTOM	3	bination	product (i.e. Atropos
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Atropine O Pralidoxime			en 0.25mg Pralidoxime	n/a			n/a	Atropine 0.5mg Pralidoxime 250mg	1 Atropen 0.5mg (Blue Pralidoxime follow BPF		n	/a		n/a
Atropine Pralidoxime	e 250mg Pra		0.5mg (Blue): e follow BPFG ⁴	n/a			n/a	Atropine 1mg Pralidoxime 500mg	1 Atropen 1mg (Red): Pralidoxime follow BPF	G⁴	n	/a		n/a
s Atropine 9) Pralidoxime s Atropine	e 500mg Pra		n 1mg (Red): e follow BPFG ⁴ n 1mg (Red):	n/a	F	2	n/a	Atropine 2mg Pralidoxime 600mg ² Atropine 2mg ²	1 Atropen 2mg (Green 1 Pralidoxime 600mg / 1 Atropen 2mg (Green	AI R	1 Mar		"⊢	TNAA Combination
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lk Drug F	ormulati	on (Guidelines Mild S	(BDFG) ⁵ symptoms					Severe Sy	ympi	toms			
Weight Ibs (kg)	At	ropine Do	0.4mg/ml	Pralidoxi	ne 333m Jose	ng/ml		ne 0.4mg/ml Dose	Pralidoxime		ıg/ml	D	liazepa D	m 5mg/ml
	Mild 0.05m		Administer IM/IV	Mild 25mg/kg	1000	ister IM/IV	Severe 0.1mg/k		Severe 50mg/kg	~	ninister IM/IV	Severe 0.2		Administer IM/IV
1 lbs (5kg)	0.25mg			125mg			0.5mg	1.2ml	250ma		0.8ml	1ma		0.2ml
			0.6ml			0.4ml								
	0.5mg		1.2ml	250mg		0.8ml	1mg	2.5ml	500mg		1.5ml	2mg		0.4ml
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sense approach, to assist professionals in the field when selecting an appropriate dose for children exposed to WMD. Although designed for empirical treatment in the field or masscasualty setting, the cards have some practical use for limited events in a hospital environment. If access to high-level medical care is readily available, WMD treatments may be based on definitive laboratory moni-

toring (e.g., hemoglobin concentration for cyanide poisoning)⁴ rather than empirically based on weight and signs and symptoms. It must also be emphasized that many states and cities may have local protocols or policies that differ slightly from CDC guidelines. Any local WMD policies and protocols would supersede the guidelines listed on the quick-reference cards. All doses are based on published literature, including CDC guidelines. Each card includes supporting documentation (e.g., WMD agent signs and symptoms, adult dosing, reconstitution and storage instructions) and references.⁵⁻¹⁶ Therefore, each card serves as a minireference for a specific WMD response. Currently, WMD pediatric dosing cards are available for calcium cyanide, hy-

Figure 3. Front a	nd back of dosing	card for radiation	n exposure.

Field Administration of	of Radiation Exposure An	tidotes: Pediatric [Dosing Guidelines ^{1,2,3}		
Antidote Target	Product	Age (or Weight)	Dose		
Americium, Curium, or Plutonium Antidotes	Pentetate Calcium Trisodium: 200	> 12 years	1 g IV STAT		
(chelating agent)	mg/mL injection solution(Ca-DTPA) a	< 12 years	14 mg/kg (not to exceed 1 g) IV STAT		
Americium, Curium, or Plutonium Antidotes	Pentetate Zinc Trisodium: 200 mg/mL	> 12 years	1 g (25 mL) IV QD		
(chelating agent)	injection solution (Zn-DTPA) ^a	< 12 years	14 mg/kg (not to exceed 1 g) IV QD		
Cesium or Thallium Antidote (ion exchange	Ferric Hexacyanoferrate: 0.5 g	> 12 yrs	3 g PO TID (followed by 1-2 g PO TID)		
resin)	capsules (Prussian Blue)	2 - 12 yrs	1 g PO TID ⁵		
	Commercial formulations:	> 150 lbs	130 mg PO QD for 7-10 days		
Radioactive lodine Antidote (antithyroid agent)	Potassium lodide4: 65 or 130 mg	3 to 18 yrs (<150 lbs)	65 mg PO QD for 7-10 days		
for $\geq 5 Gy$ Predicted Thyroid Dose ⁴	tablets or 65 mg/mL solution (KI)	1 month to 3 years	32.5 mg PO QD for 7-10 days		
		Birth < 1 month	16.25 mg PO QD for 7-10 days		
GUIDELINES FOR HOME PREPARATION OF 1. Place one 130mg tablet (or two 65mg tabl) 2. Add 20ml of water to bowl and dissolve th 3. Add 20ml of milk, juice, soda or syrup to fl 4. Resulting solution has a concentration of 5. Unused iodine mixture may be stored in th	lets) into a bowl and grind into a fine po e KI powder. lavor the KI/water mixture 16.26mg/Sml ne refridgerator for up to 7 days.	wder.			
^a Ca-DTPA is preferred initial agent followed by sequenti. DTPA or Zn-DTPA into 100-250 mL D5W, NS or LR; intu ^b Capsules may be opened and mixed with bland food or ¹ NOTE: Local protocols may supercede the recor- pediatric doses should be individualized based or ³ All doses are one time unless repeat dosing is nr References: www.bt.cdc.gov; www.fda.gov/cder/drug Inst. Dec 1999; Drug Information Handbook. Lexicomp.	se over 30 minutes. Length of therapy depen liquid. Administer with food to stimulate excr mmended guidelines. ² This card may n a child's actual weight. Refer to CDC ecommended by public health authoriti g; Ann Intern Med. 2004 Jun 15; 140(12):10;	ds upon patient response and de etion of cesium or thallium. be used as a cross-referenc guidelines for complete pres es. 4Contraindicated in patie	gree of contamination. e to calculate pediatric doses. All scribing information (www.bt.cdc.gov). ents with known allergies to iodine		

Field Administration of Acute Radiation Syndrome Treatments: Pediatric Dosing Guidelines ¹							
Product	Age or Weight	Dose					
Anti-infectives for Radiation Dose Range of 2-10 Gy							
Fluoroquinolone (ciprofloxacin tablet, injection solution, or oral suspension)	1 to 17 years	10-15 mg/kg (up to 500 mg) PO BID 6-10 mg/kg (up to 400 mg) IV Q8					
	> 2 years	20 mg/kg PO QID					
Antiviral ^a (acyclovir capsule, tablet, injection solution, or oral suspension)	> 2 years	250 mg/m ² IV Q8					
	< 1 year	10 mg/kg IV Q8					
Antifungal ^b (fluconazole tablets, injection solution, or oral suspension)	All ages	6-12 mg/kg PO or IV QD					
Antiemetics							
granisetron tablets, injection solution, or oral solution	> 2 years	2 mg PO QD					
granisetron tablets, injection solution, or oral solution	> 2 years	10 mcg/kg IVPB (over 5 minutes) QD					
	> 12 years	8 mg PO Q12					
ondansetron tablets, injection solution, or oral solution	4 to 11 years	4 mg PO Q4					
	0.5 to 18 years	0.15 mg/kg IV (over 30 minutes) Q4					
Colony Stimulating Factor (CSF) for Radiation	Dose Range of	3-10 Gy					
granulocyte CSF (filgrastim) injection solution	Allegee	5 mcg/kg SQ QD					
granulocyte CSF (higrasum) injection solution	All ages	until ANC >1.0 X 10 ⁹ cells/L					
pegylated granulocyte CSF (pegfilgrastim) injection solution	> 45 kg	6 mg SQ STAT					
granulocyte-macrophage CSF (sargramostim) injection solution or powder for reconstitution	Allegee	250 mcg/m ² SQ QD					
granulocyte-macrophage CSP (sargramostim) injection solution of powder for reconstitution	All ages	until ANC >1.0 X 10 ⁹ cells/L					
 ^a Acyclovir is recommended if patient is seropositive for herpes simplex virus or has a ^B Fluconazole is recommended if patient's absolute neutrophil count (ANC) is < 0.500 		he virus.					
¹ NOTE: Local protocols may supercede the recommended guidelines. References: Ann Intern Med. 2004 Jun 15; 140(12):1037-51; Drug Information Handbook. Lexicomp. 2005.		November 1, 2005					

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drogen cyanide, cyanogen chloride, potassium cyanide, and sodium cyanide (Figure 1); the nerve agents sarin, soman, tabun, and O-ethyl S-(2-diisopropylaminoethyl) methylphosphonothiolate (Figure 2); radiation agents (Figure 3); and the biological agents causing anthrax, plague, and tularemia (Figure 4).

All calculations and source information were reviewed and verified by at least two independent PHS pharmacists. In spring 2005, PHS officers reviewed and updated each of the WMD pediatric dosing cards to ensure currency and accuracy. Expansion of the series to other WMD and emergency pediatric medical crises is under consideration (e.g., phosgene, mustard gas, advanced cardiac life support).

Discussion. The dosing cards designed and developed by the PHS pharmacist officers have been field tested in a team training exercise and were received favorably. It was thought that the WMD pediatric dosing cards could improve efficiency and reduce the risk of dosing errors and may maximize the potential to save lives during a WMD crisis. The development of a simplified approach to pediatric dosing can substantially improve our na-

Figure 4. Front and back of dosing card for biological-agent exposure.

eight Kg ¹¹	Dose			ohylaxis ^{3,4}			Pla	gue Prophylaxis D	lose ⁴	
Kg ¹	A	250 mg/	5 mL Susp.	500 mg/5 mL	Susp.	Dose	250 mg/5			5 mL Susp.
	0 mg/kg – 15 mg/kg po BID	Administer	Qty to Dispense for 10-day supply ⁵	Administer	Qty to Dispense for 10-day supply ⁵	20 mg/kg po B	ID Administer	Qty to Dispense for 10-day supply ⁵	Administer	Qty to Dispense for 10-day supply ⁵
	50 mg - 75 mg po BID	1 –1.5 mL po BID	20-30 mL	0.5 mL - 0.75 mL po BID	10 to 15mL	100 mg po BIE	D 2 mL po BID	40 mL	1 mL po BID	20mL
	75 mg - 125 mg po BID	1.5-2.5 mL po BID	30-50 mL	0.75 mL - 1.25 mL po BID	15 to 25mL	150 mg po BI		60 mL	1.5 mL po BID	30mL
	100 mg - 150 mg po BID	2-3 mL po BID	40-60 mL	1 mL – 1.5 mL po BID	20 to 30mL	200 mg po BIE		80 mL	2 mL po BID	40mL
	200 mg – 300 mg po BID 300 mg – 450 mg po BID	4-6 mL po BID 6-9 mL po BID	80-120 mL 120-180 mL	2 mL – 3 mL po BID 3 mL – 4.5 mL po BID	40 to 60mL 60 to 90mL	400 mg po BIE 500 mg po BIE		160 mL 200 mL	4 mL po BID 5 mL po BID	80mL 100mL
	00 mg - 500 mg po BID ⁴	8-10 mL po BID	160-200 mL	4 mL – 5 mL po BID	80 to 100mL	500 mg po BIL 500 mg po BIL		200 mL	5 mL po BID	100mL
	50 mg - 500 mg po BID ⁴	9-10 mL po BID	180-200 mL	4.5 mL – 5 mL po BID	90 to 100mL	500 mg po BIE		200 mL	5 mL po BID	100mL
bs K	g 2.2	2 mg/kg po Bll	D	25 mg/5 mL Susp.	50 mg/5 ml	L Susp.	25 mg/5 mL Susp (60mL/BTL) ⁵	(473 mL	./BTL)	
bs K	.g 2.2	2 mg/kg po Bll	D	25 mg/5 mL Susp.	50 mg/5 m	L Susp.				
1 5	5	11 mg po BID		2.5 mL po BID	1.25 mL p	o BID	1 BTL (50 mL)	25 r	nL	
õ.5 7.	.5 ~	-17 mg po BID		3.5 mL po BID	1.75 mL p	io BID	2 BTL (70 mL)	35 n	nL	
2 10	0 ~	-22 mg po BID		5 mL po BID	2.5 mL p	o BID	2 BTL (100 mL)	50 n	50 mL	
4 20	0 ~	-44 mg po BID		9 mL po BID	4.5 mL p	o BID	3 BTL (180 mL)	90 r	nL	
i6 30	0 ~	-66 mg po BID		13 mL po BID	6.5 mL p	o BID	5 BTL (260 mL)	130	mL	
8 40	0 ~	-88 mg po BID		18 mL po BID	9 mL po	BID	6 BTL (360 mL)	180	mL	
99 >4	45 ~	-99 mg po BID		20 mL po BID	10 mL po	BID	7 BTL (400 mL)	200	mL	
al weight.	All doses have been ro	ounded to nearest ().5ml. Refer to CDC	ay be used as a cross-refer guidelines for complete pre Ciprofloxacin 500mg BID;	scribing information	(www. bt.cdc.g	ov). ³ Renally compron	nised patients require	a dose	November 1,

Tularemia: Doxycycline or Ciprofloxacin

Adult Dosing Guidelines (including pregnant & lactating women; and immuno-compromised individuals) ²
Doxycycline 100mg po BID OR Ciprofloxacin 500mg po BID ³

Available Formulations (Note: italics indicates Strategic National Stockpile Formulation).

- Doxycycline
- <u>25 mg/5 ml suspension (after reconstitution); 60 ml bottle</u>
- <u>100 mg tablet packaged in unit-of-use (20 tablets/bottle)</u>
- 50 mg/ml syrup
- 20 mg, 50 mg, 75 mg tablets
- 20 mg, 50 mg, 75 mg, 100 mg capsules
- Guidelines for Home Preparation of Doxycycline Suspension
- Place one 100-mg Doxycycline tablet into a bowl and grind into a fine powder.
 Add 4 teaspoons (20ml) 50:50 apple juice/table sugar mixture to the Doxycycline powder and stir well until the powder dissolves. The resulting
- suspension has a concentration of 25mg/5ml 3. Unused suspension should be covered and stored in the refrigerator for up to 24 hours.
- FDA recommends that this mixture be prepared daily; unused portions should be discarded.
- ¹NOTE: Local protocols may supercede the recommended guidelines. ²Refer to CDC guidelines for complete prescribing information (www.bt.cdc.gov) ³Renally compromised patients require a dose adjustment for ciprofloxacin when CrCl < 50 ml/min

Ciprofloxacin

500 mg/ml suspension

• 100 mg, 250 mg, 750 mg tablets

<u>250 mg/5 ml suspension (after reconstitution); 100 ml bottle</u>

500 mg tablet packaged in unit-of-use (20 tablets/bottle)

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tion's readiness and ability to respond to a WMD attack in the civilian population.

Conclusion. Pediatric dosing cards for treatment of exposure to WMD were developed to simplify treatment and help prevent medication errors.

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Effect of internal reporting criteria on suspected adverse drug reactions submitted to MedWatch

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dverse drug reactions (ADRs) have been reported in nearly 20% of hospitalized patients and account for approximately 17% of hospital admissions.1 The financial effect of adverse drug events is also considerable. In some analyses, ADRs and medication errors extend hospital stays from two to four days, resulting in an additional treatment cost of \$2500 to \$5500 per patient.²⁻⁴ The Food and Drug Administration (FDA) relies on voluntarily submitted ADR reports to assist in identifying postmarketing drug safety issues.5 MedWatch, FDA's safety in-

formation and adverse-event reporting program, receives 200,000-300,000 reports of suspected ADRs annually. Suspicion of an undesired response to a medication is a requirement for a MedWatch report; causality is not. To facilitate a focus on certain reactions, FDA has specifically sought the reporting of serious ADRs, defined as those that are fatal or life-threatening, result in permanent or significant disability, require or prolong hospitalization, contribute to a congenital anomaly, or require intervention to prevent permanent impairment or damage.6

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