

Vaccine Safety and the Military Vaccine Program

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Vaccine Safety and the Military Vaccine Program Objectives



- ★ To describe the Vaccine Healthcare Centers Network - Here to help you and your patients
- ★ To discuss potential risks associated with vaccines
 - Prescription drugs with potential risks of administration
 - Deployment-related vaccines are no exception

Vaccine Safety and the Military Vaccine Program Objectives (cont.)



- ★ To explain reporting and management of vaccine adverse events (VAERS)
 - Safe and effective but rare serious VAERS occur
- ★ To identify tools available to assist with vaccine administration & adverse events management: www.VHCinfo.org/AskVHC

World Health Organization Weekly Epidemiological Record



15 October 1999 (www.who.int/wer) Vaccine Safety Advisory Committee

"However, it is also recognized that there is no vaccine completely safe or protective in all vaccinated individuals. Differences in the way individual immune systems react to a vaccine account for rare occasions when people are not protected following immunization or experience side effects."

Immunization Health Care Standards of Care Reducing Practice Variance



- **★** Congressional concerns
 - How service members are screened for vaccine administration - barriers to medical exemptions when indicated?
 - How service members are treated in the setting of an adverse event beyond a side effect?
 - Adequacy of evaluation, treatment and follow-up, outcomes
 - Adequacy of reporting: VAERS
- ★ Vaccine Healthcare Centers (VHC) Network
 - New DoD Executive Agency collaborating with CDC
 - Support to health care workers, vaccinees, stakeholders

Vaccine Adverse Events

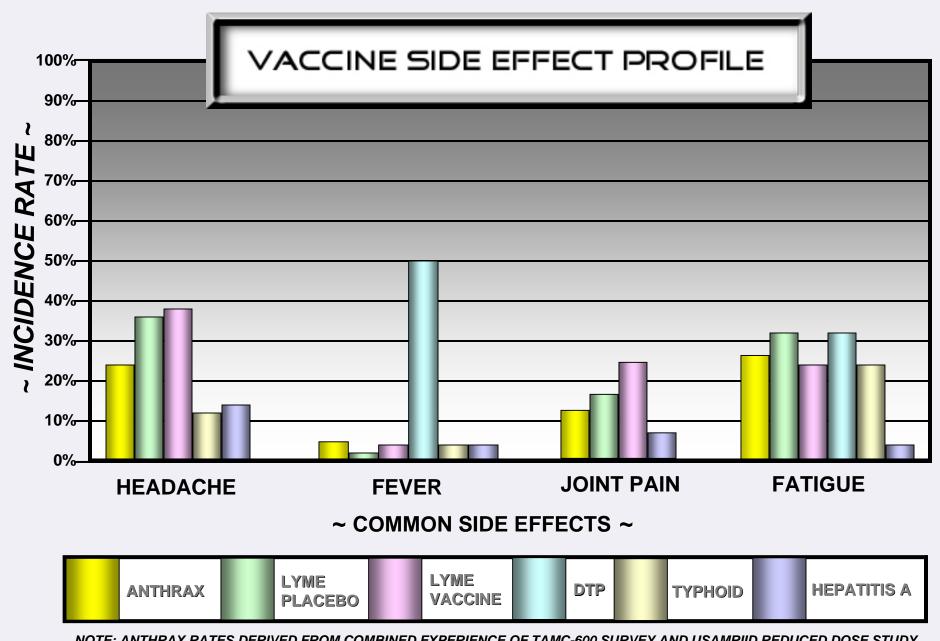


- ★ Rare, previously unrecognized vaccine associated adverse events may occur with a prolonged negative impact on patient quality of life in the absence of hospitalization
- **★ Some of these AEs are unexpected**: e.g. intussusceptions with rotavirus vaccine
- ★ Understanding of rare but serious AEs is needed to enhance public trust in vaccine safety & address future disability claims issues
- **★ NEED**: validate strategies for vaccine adverse events management & rechallenge benefit-risk

From Side Effects to Rare Serious Adverse Events



- ★ Temporal association versus causality
- ★ Clinical management principles for adverse drug reactions
 - Should they apply to vaccines?
- **★ VAER**
 - No barriers, low threshold to file



NOTE: ANTHRAX RATES DERIVED FROM COMBINED EXPERIENCE OF TAMC-600 SURVEY AND USAMRIID REDUCED DOSE STUDY

Vaccine Safety & Adult Immunizations Surveillance, Trust DoD Challenges



- ★ Vaccine Safety Concerns Based on Rare Cases
 - Influenza: pericarditis, myocarditis syndrome
 - Yellow fever: deaths reported in South America
 - Anthrax vaccine: questions of risk raised
 - Pregnancy & birth defects
 - Optic neuritis
 - Rashes: some serious Erythema multiforme
 - Tinnitus
 - Neurological symptoms: ulnar neuropathy, sequellae to large local inflammatory reactions validated by AVEC
 - Chronic fatigue-like syndromes

Clinical Guidelines



- **★** Local reactions
 - Mild: 30-50 mm
 - Subcutaneous nodules
 - Moderate 50-120 mm above elbow
 - Large Local above elbow . 120
 - Large Local extending below elbow
- **★** Other local reactions
 - Parasthesias, localized

Clinical Guidelines (cont.)



- **★** Long term complications
 - Rare but seen
 - Bilateral ulnar neuropathy from severe local reactions to anthrax vaccine – note change in location of administration and route if needed
 - Persistent (months-years) nodules that are painful

www.VHCinfo.org VHC Network

A Clinical Support Resource

Education

Consultation

Case Management

Registry Support

www.vaccines.mil
MilVax Agency

A Policy & Procedure Support Resource

MANAGING ADVERSE EVENTS AFTER VACCINATION

Service Member Receives Vaccine

*If in yellow or red zone, avoid simultaneous administration with other vaccines.

(proof copy, 13 Dec 00)

NO REACTION

MILD LOCAL REACTION: Redness < 50 mm diameter, pain, swelling, itching; lump / nodule (LR1, LR2, LR3) MODERATE
LOCAL REACTION:
Redness 50-120mm
diameter, pain,
swelling, itching;
lump / nodule;
numbness, tingling
(LR4, LR7)*

(More often in women than men)

> LARGE LOCAL REACTION, ± COMPLICATIONS: Redness > 120 mm, pain, swelling to or below elbow; local rash (LR5, LR6, LR8)*

Document.

Educate.

Document.

Educate.

Offer topical corticosteroids, antihistamines, analgesics. 1,2 Document. Educate. Treat within first 24 h with topical

corticosteroids, antihistamines, +/- NSAIDs for pain. Avoid strenuous exercise. Document.
Educate. Take photo.
Consider consultation
with next level of care.
Treat symptoms:
Steroids, antihistamines,
+/- NSAIDs for pain.
Encourage VAERS report.

Avoid strenuous

exercise.

Continue to screen for exclusion criteria (e.g., steroid therapy, pregnancy). Continue series as scheduled. Continue series as scheduled. Avoid strenuous exercise for 24 to 48 h after next dose to avoid aggravating local reaction.

For moderate reaction, continue series. For next dose, consider pretreatment, ^{12,3,7} IM route, or extended interval.

If reactions to later doses decrease, continue. If reactions recur, persist, or worsen:

Reevaluate, consider temporary exemption, pending consultation.

Clinical guidelines for managing adverse events after vaccination: Version 1 January 2001. This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.osd.mil. The probability of events on this chart is not uniform; some are quite common and some are rare. See cover sheet for details.

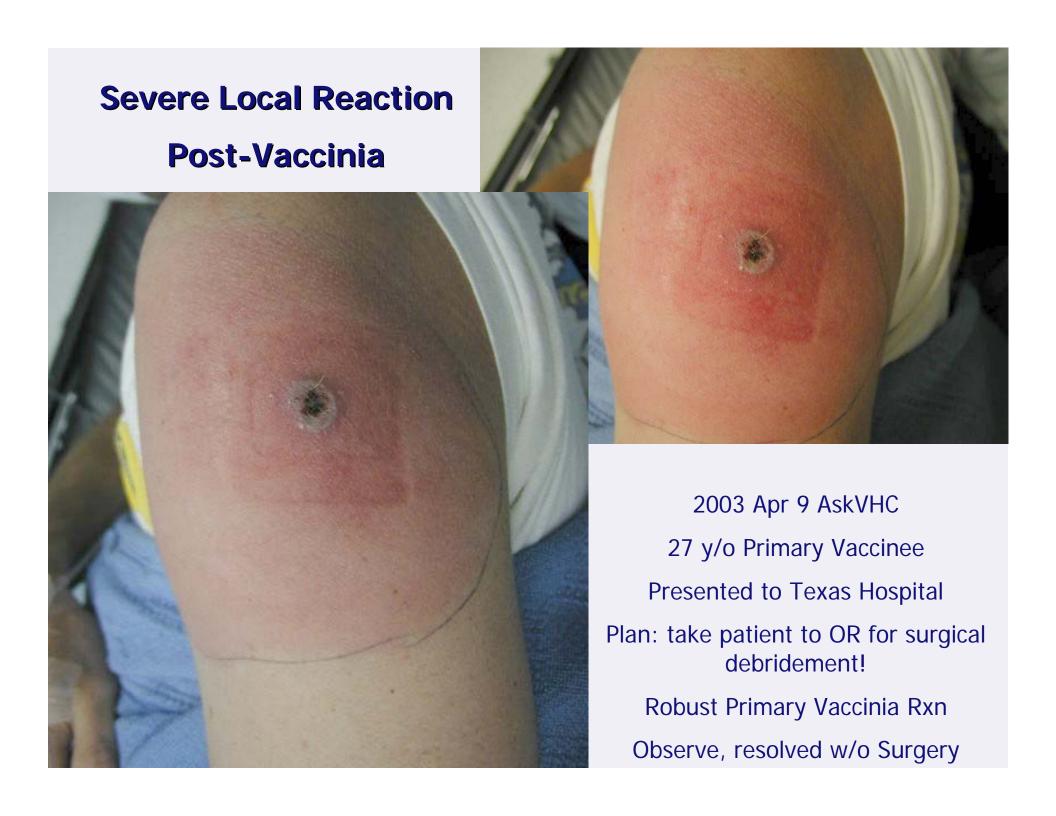
Submit Form VAERS-1 as warranted. Must be submitted for hospitalization, loss of duty ≥ 24 h, or suspected vial contamination. Other events may also be reported. Forms available at www.anthrax.osd.mil/værs/værs.htm.



Large Local Reaction

>12cm

Confusion with
Cellulitis
Actually
Immune Inflammation



Adverse Events & Vaccines Side Effects



- **★** Duration and impact
 - Short term, no impact on function or quality of life (QOL)
 - Prolonged or severe, impact on QOL
 - Long term with disability implications

Adverse Events & Vaccines Side Effects (cont.)



- ★ Possible mechanisms of symptoms, injury
 - IgE immediate hypersensitivity reaction
 - Direct mast cell activator
 - Traumatic or mechanical injury
 - Delayed local reactions
 - Arthus-like, immune complex mediated
 - Delayed type hypersensitivity reaction
 - Secondary complication: hematoma, cellulitis

Systemic Adverse Reactions



- ★ "Flu-Like" systemic reactions
- ★ Anaphylaxis
- **★** Serum sickness
- ★ Neurologic disease
- ★ Generalized skin reaction
- ★ Other systemic disease
- ★ The unexpected and ill-defined...

Vaccine safety as a new clinical specialty Growing complexity with new challenges

Systemic Adverse Events

MANAGING ADVERSE EVENTS AFTER VACCINATION

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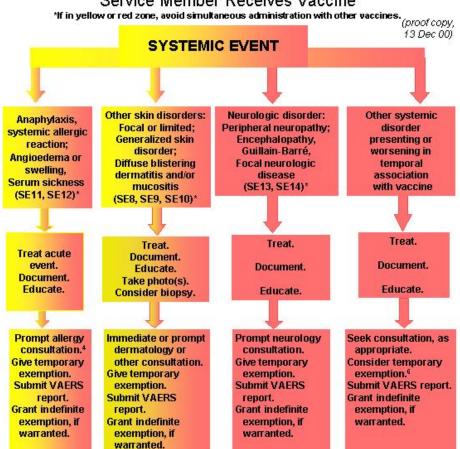
13 Dec 00) SYSTEMIC EVENT "Flu"- or Viral-Like Symptom Groups: Myalgias. Viral-Like Respiratory Gastrointestinal arthralgias. < 96 h: 3 of these: Cough, Nausa, vomiting; Other events: arthritis: Temp 100.5-104°F, coryza or diarrhea. Fatigue > 60 days; headaches: anorexia/nausea. abdom, pain, rhinorrhea. Tinnitus / vertigo: syncope or myalgia/arthralgia, congestion, diosyncratic events near syncope; malaise/fatique. sore throat. indigestion. after live vaccines anxiety light-headedness, (SE7, SE15, SE19)* response. headache (SE2a) (SE17) (SE5, SE18) (SE1, SE4, (but not SE17 or 18) SE6, SE16)* Severe / prolonged: > 96 h or T > 104°F (SE3)* Document. Treat acute event. Educate. Consult as needed. Document. Consider pre/post-Treat symptoms.5 Document. treatment NSAID. Educate. Headache: acetaminophen, Educate. ibuprofen, et cetera. 1,2,4 For mild to moderate events, continue, For mild to moderate Prompt consult.4 At next dose, consider pretreatment.3,5,7 events, continue. Give temporary exemption IM route, extended interval. If event recurs or f tolerates next dose, continue series. worsens: Reevaluate; pending f event recurs or worsens: Reevaluate: consider temporary consultation. VAERS report. exemption, pending consider temporary exemption, pending consultation. consultation.

Clinical guidelines for managing adverse events after vaccination: Version 1 January 2001. This document provides general guidance, to adapt to individual clinical cases. Use with companion tables. Patients may present with symptoms corresponding to more than one category. Revisions to this document will be disseminated via medical command channels and posted on AVIP site, www.anthrax.csd.mil. The probability of events on this chart is not uniform: some are quite common and some are rare. See cover sheet for details.

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Adverse Events and Vaccines Systemic Side Effects & Adverse Events



- ★ Clinical guidelines are a work in progress
 - Extrapolated from broad clinical immunology experience; currently only applies to non-live vaccines...a work in progress
- ★ Outcomes data for degrees of severity of side effects and/or duration not well defined
- ★ Many challenges in perceptions
 - "Safe and effective"
 - "No serious reactions"
 - Medical exemptions: measure of Provider concern

Adverse Events & Vaccines Ranking Side Effect Severity



- **★** TAMC 601 Study: J Occup Environ Med. 2003;45:222-233
- **★** Classification of systemic side effects
 - No symptoms
 - Symptoms can be ignored
 - Symptoms affect activity but can still perform
 - Symptoms affect activity, relieved by medication
 - Symptoms not relieved by meds, cannot perform
- ★ 5 VAERS events reported from a total of 3069 immunizations in the 601 vaccinees

Adverse Events & Vaccines Symptoms Not Relieved by Meds, Cannot Perform Duties

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- Fatigue
- Headache
- Joint ache
- Loss of appetite
- Nausea and vomiting
- Fever
- Itching over entire body
- Chills
- Diarrhea
- Shortness of breath

Male-Female

- 2.0% 3.0%
- 1.2% 2.0%
- 1.4% 2.5%
- 1.4% 1.4%
- 0.2% 0.5%
- 0.6% 1.4%
- 1.1% 4.5%
- 0.5% 0.6%
- 0.3% 0.8%
- 0.3% 0.8%
- 0.3% 0.2%

Anthrax Vaccine Safety Surveillance



- ★ >3.5 million doses of anthrax vaccine administered to >960,000 people
- ★ Soreness, redness, itching, swelling at injection site:
 - 30% of men, 60% of women
- ★ Lump at injection site common, lasting a few weeks, goes away on its own

Anthrax Vaccine Safety Surveillance (cont.)



- ★ Symptoms beyond injection site muscle or joint aches, headaches, rashes, chills, lowgrade fever, nausea – 5% to 35%, like other vaccines
- ★ No apparent differences between prerenovation and post-renovation lots
- ★ National Academy of Sciences: Side effects "comparable to those observed with other vaccines regularly administered to adults"

Serious Adverse Events



- ★ Critical elements to assessment and review
 - History: accurate and detailed
 - Details like a medical student evaluation
 - Detective work required time, patient participation, validation process
 - Physical and laboratory data
 - Detail required with precise documentation
 - Consideration of differential diagnosis
 - Plan for further evaluation, treatment
 - Medical exemption or strategy for protection
 - Connect to the available resources & support
 - DoD Vaccine Call Center 24/7 1-866-210-6469
 - AskVHC@amedd.army.mil

DoD Smallpox Vaccination Program as of 17 Dec 03



★Response teams, hospital workers, operational forces

- Screened: 605,000 -Vaccinated: 530,315

- Primary: 71% - Male: 88%

★Exemption rates vary by location and setting:

- Exemption: Personal 4.9-7.8%, Personal+household: 11-34%

★Take: Primary, 3 jabs: 96% Revaccination, 15 jabs: 96%

★Adverse Events: Expected temporary symptoms seen

- Sick leave: Hospital staff: 3% In theater: 0.5%

Avg: 1.5 days

DoD Smallpox Vaccination Program as of 17 Dec 03 (cont.)



- ★ Noteworthy Adverse Events: JAMA 2003;289:3278-82
 - Generalized vaccinia-35
 - Inadvertent infection-Skin: Self-51, Contact-26
 - Inadvertent infection-Eye: Self-11, Contact-2
 - Contact transfer: Family-13, intimate contact-7, friend-8
 - Eczema vaccinatum-0 Progressive vaccinia-0
 - VIG treatments: Burn-1, eye-1 Encephalitis-1
 - Myo-pericarditis: Suspect-0, probable-66, confirmed-3
 - Deaths: Possible-1 (lupus-like illness), Unrelated-4

Vaccine Healthcare Centers Network



- ★ DoD registry for myo/pericarditis cases: suspect, probable and confirmed
 - Detailed history & physical documented
 - Case manager interviews
 - Records review
 - Provider interviews
- ★ DoD guidelines issued, work in progress
- ★ Standardize follow-up & document
 - Objective measures of recovery or persistent symptoms, loss of function

Post Vaccinia
Cardiac Symptoms
Standardizing
Clinical Approach
Supporting
Evaluation

&

Management
VHC Case
Management

Pericarditis-Myocarditis-Cardiac Evaluation Tables. Suitable for Evaluation After Vaccination Vaccine(s) administered DoD Vaccine Healthcare Centers (VHC), Version: 5/30/2003 In Past 30 Days 8:38 AM Clinical symptoms: chest pain, shortness of breath, palpitations, unexplained syncope, dry cough Initial Evaluation History: characterize symptoms 1 Physical examination 3 Detailed vaccination history & dates Chest X-ray: PA/Lateral Electrocardiogram (ECG) 4 -Coat, Serum • especially smallpox or other live vaccines Laboratory 5: Troponin, CK-MB stored blood Past medical history: Cardiac risk factors ² protocol) Echocardiogram C. Progressive symptoms, B. Symptoms + abnormality LVEF < 40-45%, CK > 1,000, A. Symptoms Only of cardiac enzymes, ECG, ventricular dysrhythmias, echocardiogram hemodynamic instability A. Evaluate, treat, consult B. Cardiology evaluation, treat, C. Cardiology evaluation, treat, consult consult Evaluate as soon as possible • Work up & treat for acute Promptly work up & treat for · Document normal ECG, troponin, coronary syndrome⁷ acute coronary syndrome, as CK, CRP, other if indicated • Differential of myo-pericarditis 6 indicated⁷ · Reclassify if any abnormality or Differential of myo-pericarditis ⁶ Contact VHC + Cardiology indicated by expert review Contact VHC + Cardiology • Enter in VHC registry for FU Special studies⁵ monitoring as suspect case if Viral work-up (serology, PCR) · Serial daily enzymes for 5 days or symptoms continue Transfer to Tertiary Care Center: normalization, and at 3 weeks · Consider non-cardiac etiology Viral work-up (serology, PCR) consider limitations of facility · Monitor if continued symptoms · Apply elements outlined in B Establish functional impairment Treat symptomatically¹⁰ Individual case management Therapeutic options: NSAID. Approach to new severe &/or acetaminophen, COX2 inhibitor. Monitor & document recovery persistent complaints other Rx such as steroids? VHC case management with Management & Recovery¹⁰⁻¹² · Evaluate & treat with consultation tracking of 4-6 months and 12 month evaluation by cardiology as needed • Profile (limited duty) for 4-6 · New problem, vaccine temporal weeks with care plan association, serious impact on All probable & confirmed cases: Follow-up at 6 & 12 weeks and 6 quality of life, unremitting: Contact & 12 months with repeat ECG. disability assessments annually X VHC via 866-210-6469 echocardiogram, enzymes, and 2 years or until asymptomatic exercise test, for clearance at home duty station A&B Refer to VHC Network for second level review

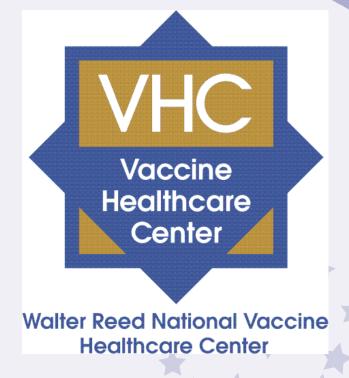
Refer to VHC for individual case management, coordination of second-level evaluation. **Key Centers**: Military medical centers with cardiology services A&B Refer to VHC Network for second level review (CISA/CDC/VHC): Echocardiograms, ECGs, cardiac isoenzyme results, copy of records and patient and provider contact information. Key VHC Consultant Sites: Brooke & Walter Reed AMC

Consultation. Clinicians wishing to consult with Vaccine Healthcare Center and/or military cardiologists regarding optimal care should call the DoD Vaccine Clinical Call Center at 866-210-6469, to request a clinical cardiovascular consult. **NOTE**: Footnotes and additional information described on accompanying sheets.

Vaccine Healthcare Centers Network Vision



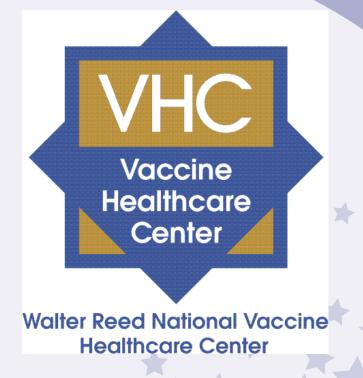
Develop a network of regional VHC's that support continuous quality improvement of immunization healthcare delivery, education, research and case management of complex adverse events for DoD beneficiaries

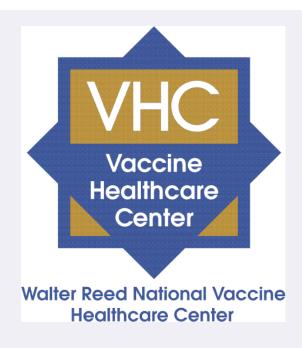


Vaccine Healthcare Centers Network *Mission and Goals*



To provide clinical, educational, research & quality assurance leadership for immune readiness through outreach in support of the goals of enhanced vaccine safety, efficacy, knowledge, trust and services to include diagnosis & management of adverse events





Assuring Quality

Patient Care For Adverse Events "Quality Improvement"

The Right Response

The Right Way

At the Right Time with

The Right Education & VAERS

The Right Access to Care

The Right Exemption

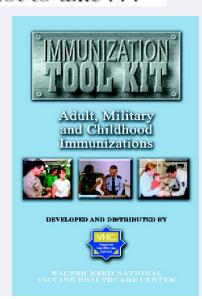
VHC Points of Contact



To take or not to take . . .

Regional VHCs

- Walter Reed
- Fort Bragg
- Portsmouth
- Wilford Hall



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Walter Reed AMC, 6900 Georgia Ave, NW, Wash, DC 20307-5001 Phone: 202-782-8819/0411/9461 Fax: 202-782-7093/4658

Website: www.VHCinfo.org

Distance Learning Tools: Go To Project Immune Readiness
Clinical Consultations, Help, Advocacy Support for Service Members

AskVHC@amedd.army.mil

Questions, Information, Assistance



DoD Deployment Health Clinical Center Walter Reed Army Medical Center Building 2, Room 3G04 6900 Georgia Ave, NW Washington, DC 20307-5001

E-mail: pdhealth@na.amedd.army.mil

Website: www.PDHealth.mil

202-782-6563 DSN:662

Provider Helpline 1-866-559-1627

Patient Helpline 1-800-796-9699