

EXCISE



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E.O. 12065: RDS-3 06/29/02 (ANDERSON, L. DESAIX)
TAGS: SHUM, PARM, TBID, SREF, LA, VM, CB, UR
SUBJECT: CM TREATMENT PROTOCOL

REF: A) BANGKOK 30864 B) STATE 159129

1. (S) THE FOLLOWING UNCLASSIFIED MATERIAL IS SENT IN
RESPONSE TO REF. A AND CAN BE GIVEN TO SIRIRAJ
HOSPITAL, WORLD VISION, AND OTHER APPROPRIATE MEDICAL
GROUPS. IT WAS COMPILED BY AN INTERAGENCY GROUP OF
PHYSICIANS, TOXICOLOGISTS, AND CONSULTANTS!

DEPARTMENT OF STATE A/CDC/MR
REVIEWED by PMS DATE 11/4/88
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(6/21/75)

2. (U) BEGIN TEXT:

MEDICAL PROTOCOL FOR SCREENING AND TREATMENT OF SUSPECTED CHEMICAL WARFARE VICTIMS.

BACKGROUND:

THE U.S. GOVERNMENT THROUGH THE DEPARTMENT OF STATE HAS RECEIVED A NUMBER OF REQUESTS FOR ADVICE AND BASIC INFORMATION ABOUT TREATING LIKELY CHEMICAL WARFARE INJURIES, THEIR DIFFERENTIAL DIAGNOSIS, AND SPECIFIC TREATMENTS. TO DATE, THE FOCUS OF THE PROBLEM IS FOUND IN REFUGEE CAMPS IN NORTHERN THAILAND WHERE VICTIMS ARE SEEN BY PHYSICIANS FROM THREE TO SIX WEEKS POST-ATTACK. SOME OF THE MORE ACUTELY ILL VICTIMS PRESENT WITH WELL-DEFINED DERMATOLOGICAL AND PULMONARY SIGNS AND SYMPTOMS. OTHERS ARE DIAGNOSED AS PROBABLE OR POSSIBLE CW OR TOXIN EXPOSED CASES BASED ON CLEAR HISTORIES, BUT NONSPECIFIC CENTRAL NERVOUS SYSTEM, PULMONARY, AND/OR GASTROINTESTINAL FINDINGS. THERE SEEMS TO BE A ROUGH CORRELATION OF SEVERITY WITH TIME SINCE OR NUMBER OF EXPOSURES (MANY VICTIMS HAVE BEEN INVOLVED IN MULTIPLE ATTACKS). SO FAR, NO GOOD WAY HAS BEEN FOUND TO TELL WHICH SPECIFIC AGENT WAS USED IN ANY PARTICULAR CASE, ALTHOUGH MYCOTOXIN, ORGANOPHOSPHATE, VESICANT, AND HIGH CONCENTRATIONS OF RIOT-CONTROL

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AGENTS MUST BE INCLUDED IN THE DIFFERENTIAL DIAGNOSIS BASED ON MEDICAL AND INTELLIGENCE DATA. A NUMBER OF MEDICAL SCREENING PROJECTS ARE BEING INITIATED TO DEVELOP ALGORITHMS FOR DETERMINING AGENTS USED BASED ON THESE DATA, REFINED DIFFERENTIAL DIAGNOSTIC SCREENS, TESTS, AND TREATMENT PROTOCOLS ESPECIALLY FOR MYCOTOXIN EXPOSURE.

IN THE MEANTIME, IT IS NECESSARY TO PROVIDE GUIDANCE FOR APPROPRIATE SYMPTOMATIC TREATMENT FOR THE SUB-ACUTE

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(SEVERAL WEEKS POST-ATTACK) AND CHRONIC (MONTHS POST-ATTACK TO YEARS) LESIONS AND ILLNESSES BEING ENCOUNTERED BY PHYSICIANS IN THE PRIMARY ZONES OF THE REFUGEE CAMPS AND IN HOSPITALS WHERE INCREASING NUMBERS OF PATIENTS ARE BEING ADMITTED. THE FOLLOWING OUTLINE WAS PREPARED FOR THESE NEEDS, BUT INCLUDES REFERENCES TO U.S. ARMY MEDICAL MANUALS APPROPRIATE FOR FIELD USE UNDER ACUTE (HOURS) CONDITIONS IF THEY CAN BE PROVIDED TO PERSONS NEAR ATTACK SITES.

DISCUSSION:

I. ACUTE AND SUB-ACUTE TREATMENT OF TRADITIONAL AGENTS

SUCH AS THOSE PRIMARILY AFFECTING CENTRAL NERVOUS SYSTEM, RESPIRATORY SYSTEM, AND RIOT-CONTROL AGENTS.

A. USE ATTACHED ARMY MEDICAL MANUAL P-6, PART III. NOTE: EVEN IF THE AGENT CANNOT BE IDENTIFIED THE SYMPTOMATIC TREATMENT PORTIONS OF THIS DOCUMENT ARE APPROPRIATE.

B. IN HOSPITAL, JUDGEMENT OF ATTENDING PHYSICIANS MUST BE PRIMARY, PARTICULARLY SINCE COMPOUNDS SUCH AS CHLORPROMAZINE, ATROPINE, OTHER ANTI-EMETICS AND ANTI-HISTAMINES MAY BE CONTRA-INDICATED IN THE
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DEBILITATED PATIENT. ALSO, IF IT IS BELIEVED THE PATIENT IS IMMUNOSUPPRESSED USE OF STEROIDS I.V., ORALLY, OR IN CONCENTRATED OINTMENTS ARE CONTRA-INDICATED.

C. SECONDARY FUNGAL INFECTIONS (ALSO SEE BELOW, MYCOTOXIN SEQUELAE) ARE LIKELY, AND BACTERIAL INFECTIONS OF SKIN ARE POSSIBLE. CURRENT EVIDENCE FROM PATIENTS FROM BAN VINAE AND SIRIRAJ HOSPITAL SUPPORTS THIS CONCERN.

II. CHRONIC PROBLEMS EXPECTED:

A. INTERSTITIAL PNEUMONITIS AND ALVEOLITIS (AND ALSO WITH MYCOTOXIN EXPOSURE).

B. SECONDARY CHRONIC DERMATITIS OF FUNGAL AND
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BACTERIOLOGIC ETIOLOGY.

C. CONVENTIONAL MEDICAL TREATMENT FOR ALL CHRONIC CONDITIONS IRRESPECTIVE OF ORIGINAL AGENT KNOWN OR SUSPECTED IS THE RULE.

III. TREATMENT OF TRICHOPECENE AND OTHER MYCOTOXIN POISONING

A. AT PRESENT STANDARD TREATMENT FOR MYCOTOXIN EXPOSURE IS SYMPTOMATIC AND SUPPORTIVE SINCE NO SPECIFIC DRUG THERAPY OR ANTIDOTE HAS YET BEEN DEVELOPED.

B. ACUTE EXPOSURE; POST-ATTACK HOURS TO SEVERAL DAYS: THE MOST IMPORTANT MEASURE IS DECONTAMINATION OF

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EXPOSED SURFACES. THE TRICHOPECENES CAN BE DESTROYED BY EXPOSURE TO A 2.5 PERCENT SLURRY OF CALCIUM HYPOCHLORITE OR SUPERTOPICAL BLEACH FOR 30 MINUTES; HOWEVER, SUCH SOLUTIONS ARE NOT (REPEAT, NOT) SUITABLE

FOR IRRITATED SKIN OR MUCOUS MEMBRANE DECONTAMINATION. IT HAS BEEN SHOWN IN THE LABORATORY THAT COPIOUS WASHING WITH SOAP AND WATER WILL BE EFFECTIVE IN REDUCING BOTH LETHALITY AND SEVERITY OF EFFECTS. SUCH WASHING IS FAIRLY EFFECTIVE FOR UP TO SIX HOURS AFTER EXPOSURE AND IS THE MOST IMPORTANT THERAPEUTIC PROCEDURE AVAILABLE. CONTAMINATED EYES SHOULD BE WASHED WITH ISOTONIC BICARBONATE OR SALINE SOLUTIONS, IF AVAILABLE; OR COPIOUS AMOUNTS OF WATER, IF THESE SOLUTIONS ARE UNAVAILABLE.

C. THE VOMITING INDUCED BY MYCOTOXINS APPEARS TO RESULT FROM EFFECTS ON THE CENTRAL NERVOUS SYSTEM AND CAN BE BLOCKED BY CHLORPROMAZINE, ATROPINE SULFATE (0.5MG) IS ALSO EFFECTIVE IN CONTROL OF SOME OF THE GASTROINTESTINAL EFFECTS (DIARRHEA, NAUSEA, AND VOMITING). HOWEVER, IT SHOULD BE NOTED THAT EXTREME CAUTION IS REQUIRED WHEN CHLORPROMAZINE IS USED IN COMBINATION WITH ATROPINE OR SIMILAR DRUGS. (SEE THE PHYSICIANS' DESK REFERENCE, 36TH EDITION, 1982; PUBLISHER, C. E. BAKER, P. 1815-1818 FOR A DETAILED

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DISCUSSION OF POTENTIAL DRUG INTERACTIONS AND PRECAUTIONS.) CHLORPROMAZINE AND ATROPINE SHOULD NOT BE USED IN A SHOCKED OR DEHYDRATED PATIENT. DUE TO THE SEVERITY OF THE TRICHOHECENE-INDUCED GASTROINTESTINAL EFFECTS AND THE ANOREXIA CAUSED BY THE AGENTS, EVERY EFFORT SHOULD BE MADE TO MAINTAIN AN ADEQUATE NUTRITIONAL STATUS AND TO REPLACE THE LOSS OF FLUID AND ELECTROLYTES BY TRADITIONAL METHODS.

D. SKIN LESIONS RESULTING FROM TRICHOHECENE EXPOSURE

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CAN BE VERY SEVERE AND SUPPORTIVE THEORY SHOULD BE DESIGNED TO DIMINISH THE ITCHING AND PAIN, TREAT INFECTION, AND PROMOTE HEALING. THE SKIN OFTEN RAPIDLY TURNS RED AND ITCHES INTENSELY AFTER TRICHOHECENE EXPOSURE. THIS ITCHING CAN BE DIMINISHED BY LOCAL APPLICATION OF PREPARATIONS SUCH AS CALAMINE LOTION OR LOCAL ANAESTHETICS OR AMYLSALICYLATE. BLISTERS MAY BE TREATED WITH TROPICAL ANTIBIOTICS AND CORTICOSTEROIDS. STRONG ANTISEPTICS SHOULD NOT BE APPLIED. ANTIBIOTICS, ANTIHISTAMINES, CORTICOSTEROIDS, AND SEDATIVES SHOULD BE USED AS INDICATED.

E. THE TERM EFFECTS OF THE TRICHOHECENES ARE VERY SIMILAR TO THOSE CAUSED BY RADIATION. THERE IS A VERY STRONG IMMUNOSUPPRESSIVE EFFECT, THEREFORE, PREVENTION OF SECONDARY INFECTION IS CRUCIAL. EFFECTS ON THE BONE MARROW RESULT IN HEMATOPOIETIC DEPRESSION, AND WHOLE BLOOD OR FRESH PLATELET TRANSFUSIONS MAY BE INDICATED

TO REPLACE CRITICAL CELLULAR ELEMENTS LOST. ADMINISTRATION OF VITAMIN COMPLEXES (PARTICULARLY CONTAINING VITAMIN K MAY BE HELPFUL IN TREATMENT OF BLOOD CLOTTING PROBLEMS. LITTLE IS KNOWN CONCERNING THE MECHANISM OF ACTION OF THE TRICHOHECENES ON THE CLOTTING MECHANISM, HOWEVER; THUS THE USEFULNESS OF SUCH MEASURES IS DIFFICULT TO PREDICT.

IV. OTHER CONCERNS:

A. A TENDENCY TO SEEK A SPECIFIC TREATMENT FOR AN AGENT SHOULD BE AVOIDED SINCE:

1. NO TEST OR MEASURE IS AVAILABLE FOR EITHER FIELD OR
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HOSPITAL USE THAT WILL PROVIDE A DEFINITE IDENTIFICATION FOR ANY TRADITIONAL OR MYCOTOXIN AGENT.

2. NO DEFINITIVE, SPECIFIC, NOR ANTIDOTE METHODOLOGY EXISTS FOR SUB-ACUTE OR CHRONIC EXPOSURE TO ANY AGENT, EVEN IF IT WERE IDENTIFIED.

3. THE MYCOTOXIN EFFECTS ON CELLULAR AND SUBCELLULAR CHEMISTRY, IMMUNOLOGICAL SYSTEM, AND TENDENCY FOR PROLONGED GASTROINTESTINAL, RESPIRATORY, AND CNS PROBLEMS ARE BEST TREATED SYMPTOMOLOGICALLY BY PHYSICIANS IN FIELD AND URBAN HOSPITAL SETTINGS WHO CAN MONITOR CHANGES IN BLOOD CHEMISTRIES, ELECTROLYTES, AND WHO CAN ALSO TREAT THE OTHER NON-CM PROBLEMS IN BALANCE AND PARALLEL.

B.

1. FROM PHOTOGRAPHS, OBSERVATION, AND HISTORY WE BELIEVE MOST OF THE SKIN LESIONS ARE NOT CAUSED BY TRADITIONAL URTICANTS OR VESICANTS (BLISTER AGENTS). THEREFORE, THE SECONDARY AND TERTIARY SKIN LESIONS ARE EVEN MORE LIKELY TO HAVE BEEN INSTIGATED BY FUSARIUM MYCOTOXINS AND SECONDARY FUNGAL INFECTION CAN BE EXPECTED TO BE A COMMON PRESENTING COMPLAINT. TREATMENT SHOULD BE BY ACCEPTED DERMATOLOGICAL PRACTICE, E.G., GRISEOPULVIN. IN ANIMALS, VITAMIN E IN OIL HAS BEEN SUCCESSFUL IN TREATING SKIN EFFECTS OF MYCOTOXINS, AND CONSIDERING ITS LOW HUMAN TOXICITY COULD BE USED AS A TRIAL OF THERAPY IF AVAILABLE. IN THE ABSENCE OF ACTIVE BACTERIAL INFECTIONS, DERMATOLOGIC OR SYSTEMIC, OR LEUKOPENIA, STEROIDS AS DESCRIBED ABOVE AND IN ATTACHED REFERENCE WOULD BE A TREATMENT OF CHOICE.

2. FOR THOSE INJURIES SEEMING TO PRESENT AS BURNS,

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DEBRIDEMENT AND CLASSIC BURN THERAPY WOULD BE MORE

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ESPECIALLY ASEPTIC CONJUNCTIVITIS ARE COMMON. ROUTINE TREATMENT.

2. SIMPLE VISUAL TESTS SHOULD BE DONE AS BASELINE.

THERE IS A POSSIBILITY THAT LATE MACULAR DEGENERATION OCCURS WITH TOXIN EXPOSURE.

MEDICAL EFFECTS OF THE TRICOTHECENES IN HUMANS

THE MOST PROMINENT SYMPTOMS ASSOCIATED WITH TRICOTHECENE POISONING ARE LISTED IN FIGURE 1. STRIKING AMONG THESE IS THE RAPID ONSET OF VOMITING WITH SEVERE ITCHING AND TINGLING OF THE SKIN. HEMORRHAGE OF THE MUCUS MEMBRANES AND BLOODY DIARRHEA FOLLOW.

THE LD50'S (DOSE REQUIRED TO PRODUCE DEATH IN 50 PERCENT OF A TEST POPULATION) OF THE TRICOTHECENES IN LABORATORY ANIMALS RANGE FROM 0.1 MG/KG TO GREATER THAN 1,000 MG/KG, DEPENDING ON THE PARTICULAR TOXIN, SPECIES, AND ROUTE OF EXPOSURE. THE LD50 OF T2 TOXIN IN THE CAT IS 0.5 MG/KG. HOWEVER, THE ED50 (DOSE REQUIRED TO PRODUCE A DESIRED PHYSIOLOGICAL EFFECT IN 50 PERCENT OF A TEST POPULATION) IS MUCH LOWER. THE

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ED50 TO PRODUCE A VOMITING REACTION IS 0.1 MG/KG, AND FOR SKIN IRRITATION IT IS IN THE TENTHS OF MICROGRAM RANGE.

MOST OF THE DATA CONCERNING THE TOXICOLOGICAL EFFECTS OF THE TRICOTHECENES IS DERIVED FROM ANIMAL DATA IN WHICH PURE COMPOUNDS WERE ADMINISTERED BY ORAL, SUBCUTANEOUS, INTRAPERITONEAL OR INTRAVENOUS ROUTES. THERE UNFORTUNATELY ARE NO REPORTS CONCERNING THE EFFECTS OF INHALATION OF MIXTURES OF THE COMPOUNDS. THEREFORE, IT IS DIFFICULT TO SPECULATE CONCERNING THE EFFECTS THAT WOULD BE EXPECTED IN HUMANS WHO WERE EXPOSED TO AEROSOLIZED MIXTURES OF THESE VERY POTENT TOXINS. THE MOST USEFUL DATA CONCERNING EXPOSURE IN HUMANS WAS OBTAINED IN A PHASE 1 CLINICAL EVALUATION OF ANGIUDINE (DIACETOXYSCIRPENOL) AS AN ANTICANCER DRUG. DIACETOXYSCIRPENOL WAS ADMINISTERED BY IV INFUSION. AT

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SENSATION IN THE MOUTH, TONGUE, THROAT, PALATE, ESOPHAGUS AND STOMACH AS A RESULT OF THE TOXIN'S EFFECT ON THE MUCOUS MEMBRANES. THE TONGUE MAY FEEL SWOLLEN AND STIFF AND THE MUCOSA OF THE ORAL CAVITY MAY BE HYPEREMIC. INFLAMMATION OF THE GASTRIC AND INTESTINAL MUCOSA OCCURS AND VOMITING, DIARRHEA, AND ABDOMINAL PAIN. IN MOST CASES, EXCESSIVE SALIVATION, HEADACHE, DIZZINESS, WEAKNESS, FATIGUE, AND TACHYCARDIA ACCOMPANY THE INITIAL STAGE. THERE MAY BE FEVER AND SWEATING, BUT THE BODY TEMPERATURE NORMALLY DOES NOT RISE. THE
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LEUKOCYNE COUNT MAY BEGIN TO DECREASE IN THIS STAGE, AND THERE MAY BE AN INCREASED ERYTHROCYTE SEDIMENTATION RATE. THIS FIRST STAGE MAY LAST FROM THREE TO NINE DAYS.

THE SECOND STAGE IS OFTEN CALLED THE LATENT STAGE OR INCUBATION PERIOD BECAUSE THE PATIENT FEELS WELL AND IS CAPABLE OF NORMAL ACTIVITY. IT IS ALSO CALLED THE LEUKOPENIC STAGE BECAUSE ITS MAIN FEATURES ARE DISTURBANCES IN THE BONE MARROW AND THE HEMATOPOIETIC

SYSTEM, CHARACTERIZED BY A PROGRESSIVE LEUKOPENIA, A GRANULOPENIA, AND A RELATIVE LYMPHOCYTOSIS. IN ADDITION, ANEMIA AND A DECREASE IN ERYTHROCYTES, IN THE PLATELET COUNT, AND HEMOGLOBIN OCCURS. DISTURBANCES IN THE CNS AND AUTONOMIC NERVOUS SYSTEMS MAY OCCUR. WEAKNESS, VERTIGO, FATIGUE, HEADACHE, PALPITATIONS, AND MILD ASTHMATIC CONDITIONS MAY OCCUR. VISIBLE HEMORRHAGIC SPOTS BEING TO APPEAR ON THE SKIN AND THIS MARKS THE TRANSITION TO THE THIRD PHASE. THE SECOND STAGE MAY LAST THREE TO FOUR WEEKS. THE TRANSITION TO THE THIRD STAGE IS SUDDEN AND SYMPTOMS PROGRESS RAPIDLY.

IN THE THIRD STAGE, PETECHIAL HEMORRHAGES OCCUR ON THE SKIN OR THE TRUNK, ARMS, THIGHS, AND FACE AND HEAD. THEY CAN VARY FROM A MILLIMETER TO A FEW CENTIMETERS IN SIZE. CAPILLARIES ARE VERY FRAGILE AND ANY SLIGHT TRAUMA RESULTS IN HEMORRHAGE. HEMORRHAGES OF THE MUCOUS MEMBRANES OF THE MOUTH, TONGUE, SOFT PALATE AND TONSILS OCCUR. NASAL, GASTRIC, AND INTESTINAL HEMORRHAGES CAN BE VERY SEVERE. AREAS OF NECROSIS BEGIN TO APPEAR ON THE LIPS, FINGERS, NOSE, JAWS, EYES.

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AND IN THE MOUTH. LYMPH NODES ARE FREQUENTLY ENLARGED

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AND THE ADJOINING CONNECTIVE TISSUE CAN BECOME SO EDEMATOUS THAT THE PATIENT HAS DIFFICULT OPENING HIS MOUTH. BLOOD ABNORMALITIES PREVIOUSLY DESCRIBED ARE INTENSIFIED. DEATH MAY OCCUR FROM HEMORRHAGE, STRANGULATION (DUE TO SWELLING) OR SECONDARY INFECTION.

THE FOURTH STAGE IS CONVALESCENCE. THREE TO FOUR WEEKS OF TREATMENT ARE REQUIRED FOR DISAPPEARANCE OF NECROTIC LESIONS AND HEMORRHAGE EFFECTS. TWO MONTHS OR MORE MAY ELAPSE BEFORE THE BLOOD FORMING CAPABILITY OF THE BONE MARROW RETURNS TO NORMAL.

TOXICOLOGICAL CHARACTERISTICS OF TRICHOHECENE MYCOTOXINS:

1. VOMITION, EMESIS, TACHYCARDIA, DIARRHEA
 2. HEMORRHAGE OF MUCOSAL EPITHELIA OF STOMACH AND INTESINE
 3. HEMORRHAGE, EDEMA, AND NECROSIS OF SKIN
 4. DESTRUCTION OF HEMATOPIETIC TISSUES
 5. DECREASE OF CIRCULATING WHITE BLOOD CELLS AND PLATELETS
 6. MENINGEAL HEMORRHAGE IN BRAIN
 7. NERVOUS DISORDERS
- END TEXT. STOESSEL

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