

Background

The National Academy of Sciences (NAS) was asked to advise the Department of Defense (DOD) on a long-term strategy for protecting the health of the nation's military personnel when deployed to unfamiliar environments. As part of the academy's response to this request, the National Research Council's (NRC's) Board on Environmental Studies and Toxicology was asked to develop an analytical framework for assessing health risks to deployed forces.

Dr. Lorenz Rhomberg of Gradient Corporation (formerly of the Harvard University School of Public Health) served as the project's principal investigator. He was assisted by 10 advisers representing a variety of relevant disciplines.

To assist Dr. Rhomberg and the advisers, six papers were commissioned on topics identified as key issues: (1) possible scenarios of future deployments and battle considerations, (2) existing risk-assessment methods and their possible application to deployment situations, (3) approaches for collecting and using personal exposure and biological-marker information, (4) health assessment and risk management integration for biological agents, (5) toxicologic interactions among agents, and (6) possible paradigms for incorporating toxicokinetic information in risk assessment. The six papers were presented at a workshop on January 28-29, 1999 in Washington, DC. Over 60 participants from the military and scientific communities were present. The sessions were moderated by members of the advisory group, and the commissioned authors were asked to consider the comments and suggestions that arose during the workshop in revising their papers. The final papers were also reviewed by two members of the Commission on Life Sciences: Donald Mattison, March of Dimes and John Emmerson, Fishers, Indiana.

The commissioned papers were used as background for the NRC report *A Risk Assessment Framework for Protecting the Health of Deployed Forces*, which is being published concurrently with these proceedings. The findings, conclusions, and recommendations that appear in the workshop papers are solely those of the authors and should not be interpreted as those of the NRC.

Collection and Use of Personal Exposure and Human Biological-Marker Information for Assessing Risks to Deployed U.S. Forces in Hostile Environments

by Morton Lippmann¹

ABSTRACT

Risk management is especially important for military forces deployed in hostile and/or chemically contaminated environments, and on-line or rapid turn-around capabilities for assessing exposures can create viable options for preventing or minimizing incapacitating exposures or latent disease or disability in the years after the deployment. With military support for the development, testing, and validation of state-of-the-art personal and area sensors, telecommunications, and data management resources, the DOD can (1) enhance its capabilities for meeting its novel and challenging tasks; and (2) create technologies that will find widespread civilian uses.

This review assesses currently available options and technologies for productive pre-deployment environmental surveillance, exposure surveillance during deployments, and retrospective exposure surveillance post-deployment, and introduces some opportunities for technological and operational advancements in technology for more effective exposure surveillance and effects management options for force deployments in future years. The issues discussed are (1) information needs for assessing personal exposures and risks for deployed forces; (2) options for pre-deployment baseline determinations, for collection of personal exposure related data during field deployment, and for post-deployment personal exposure assessments; (3) maximizing effective personal exposure data resources during and post-deployment; (4) technical capabilities for personal exposure assessment; and (5) assessing risks.

Advances in information technology have made it possible to envision the collection, maintenance, and utilization of a deployment data resource that would enable theater commanders and medical staff to recognize and evaluate environmental health hazards and to manage deployments so as to avoid or

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minimize those hazards. Such data, together with a deployment sample archive, would also facilitate future epidemiological studies that could identify additional causal relationships between environmental factors and health outcomes.

Applications can include (1) on-line access to remote sensing and continuous monitoring data for tactical planning; (2) data review by medical staff personnel in order to arrange for monitoring military personnel for possible effects of toxicant exposures, provide countermeasures during deployments, and prioritize medical examinations and biomarker sample collections and analyses in the early post-deployment period; (3) additional sampling and/or monitoring, or analysis of archived samples, in order to be able to resolve ambiguities or conflicts concerning levels of exposure or environmental contamination; and (4) review of medical and environmental data by epidemiologists post-deployment in investigations of possible causal factors for delayed illness reports associated with service in a specific deployment.

Each of these applications could consume large amounts of resources, and the allocations should be decided according to pre-established priorities by an appropriate panel of peers, including military users and state-of-the-art research investigators with expertise in the emerging technologies.

INTRODUCTION

Exposure assessment is a key element in risk assessment and risk management, and is especially important for military forces deployed in hostile or uncharacterized environments. Furthermore, on-line or rapid turn-around capabilities for assessing exposures can provide military commanders with viable options for preventing or minimizing exposures that can incapacitate or degrade the on-site capabilities of deployed forces, or that can result in latent disease or disability in the months and years after the deployment. Delayed or latent adverse effects resulting from deployment exposures can degrade force readiness for future deployments as well as cause pain and suffering to force members and/or create compensatory costs needed to care for the force members and their families. Exposure assessments can therefore be valuable and cost-effective tools of primary disease and disability protection. The military could support and mobilize the high-technological resources that will be needed for the development, testing, and validation of state-of-the-art personal and area sensors, telecommunications devices, and data management resources. Such investments would not only help the Department of Defense (DOD) enhance its capabilities for meeting the novel and challenging tasks in deploying forces in the post-cold-war period, but also create technologies that will find productive new uses in other aspects of occupational and environmental health protection in the United States and around the world.

The military services have already established a core unit, the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). It fulfills many of the functions that are outlined in this paper through its Deployment Environmental Exposure Surveillance Program (DESP), which was established in July 1996. The scope of this program could be expanded to include a greater emphasis on personal exposure surveillance and the collection and archiving of environmental and biological samples for later laboratory analyses needed to resolve emerging questions about exposures and their health effects among deployed personnel. The sample archive envisioned here could be viewed as an expansion of the Armed Forces Serum Repository established in August 1997 under DOD Directive 6490.2 for the purpose of joint medical surveillance. The expanded repository would include blood cells for biological-marker (biomarker) analyses, as well as air-sampling filters and cartridges and soil and water samples.

Although this paper focuses on disease and non-battle injuries (DNBI), many of the high-technological capabilities developed for the nuclear, biological, and chemical (NBC) defense programs' spiral

system developments can be envisioned as being applicable to force protection from unintentional exposures to environmental toxicants. This is especially the case for the fully integrated and digitized joint warning, reporting, and analysis architecture that the NBC program expects to implement in the next 3 to 5 years. Plans to acquire very light-weight hazard sensors under the NBC program will also advance measurement technologies that might have eventual applicability to on-site and personal detectors capable of measuring much lower concentrations of agents of concern with respect to DNBI.

This paper introduces and spells out, in a conceptual sense, currently available options and technologies for productive pre-deployment environmental surveillance, exposure surveillance during deployments, and retrospective post-deployment exposure surveillance. It also introduces some opportunities for technological and operational advancements in technology for more effective exposure surveillance and proposes some risk management options for force deployments in future years. The discussions that follow cover

- information needs for assessing personal exposures and risks for deployed forces,
- options for pre-deployment baseline determinations,
- options for collection of personal exposure data during field deployment,
- options for post-deployment personal exposure assessments,
- maximizing effective personal exposure data resource during deployment and post-deployment,
- current technical capabilities for personal exposure assessment, and
- assessing risks.

INFORMATION NEEDS FOR ASSESSING PERSONAL EXPOSURES AND RISKS FOR DEPLOYED FORCES

Environmental Quality Factors at Deployment Sites

The military is obligated to determine identifiable on-site risks whenever possible prior to the deployment of forces. Contaminated sites, such as abandoned gas works, chemical manufacturing sites and waste dumps, with the actual and potential risks of personnel contacting hazardous chemical residues should be avoided whenever mission options permit and less contaminated or noncontaminated alternate sites compatible with operational necessities are available.

Prescreening of potential deployment sites should be done at the candidate sites by appropriately trained environmental specialists or industrial hygienists whenever possible. When on-site surveys are not possible, remote sensors or scanners should be employed to the extent that they are technologically and operationally feasible. (See NRC 1999.)

Survey personnel should prepare guidance and background data on the extent or potential of site contamination to the military (or civilian) engineers assigned to site preparation for large-scale deployments. In turn, the military engineers should take care to prepare the site, to the extent feasible, in ways that prevent or minimize the potential for exposure to preexisting on-site contamination. Both the site survey and site preparation teams should create a record trail on on-site contamination that is accessible to hygienists, medical personnel, and epidemiologists in case subsequent actions or investigations are needed during on-site deployment or for post-deployment follow-up investigations.

During force deployments, the emphasis should shift to the collection of data on personal exposures to on-site contaminants, using personal samplers and monitors, as well as the collection of exposure biomarkers whenever appropriate equipment, sampling opportunities, analytical methods, and proce-

dures are available. Because it will seldom, if ever, be feasible to collect personal exposure data on all members of a deployed force, a sampling strategy will be needed to identify suitable and willing individuals within the force who can serve effectively as representatives of their group for determining exposure. There will also need to be plans and procedures to investigate and ameliorate the sources and extent of detected excessive exposure, as well as procedures for feasible countermeasures for documented excessive exposures.

Exposure-Response Relationships and Exposure Limits for Toxicants

For chemical agents of known toxicity, it is important to have or be able to develop exposure limits or guidelines to serve as benchmarks of excessive exposure for either short or long-term exposures. The recently prepared TG230A Short-Term Chemical Exposure Guidelines for Deployed Military Personnel (USACHPPM 1999a) and the RD230A Reference Document (USACHPPM 1999b) provide guidance for 1-h inhalation exposures for 43 chemicals, for 1-to 14-day exposures for 91 chemicals, and drinking-water concentration limits for 170 chemicals. Guidance for 1-h inhalation exposure limits for other chemicals is available from the American Industrial Hygiene Association (AIHA) in their Emergency Response Planning Guidelines (ERPGs). Currently, the U.S. Environmental Protection Agency (EPA) is supporting a National Research Council (NRC) Committee on Toxicology program to prepare Guidelines for Community Emergency Exposure Levels that will gradually be substituted for ERPGs where appropriate. Based upon the AIHA criteria of protection of “nearly all individuals” against “experiencing or developing irreversible or other serious health effects or symptoms that could impair . . . abilities to take protective action,” the 1-h TG230A criteria are all conservative by factors ranging from 2 to 80. The American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values and biological exposure indices provide guidance for 15-min exposures and longer-term (8-h) exposures.

Descriptors of Deployed Forces

Deployed forces can be expected to vary greatly in age, ethnicity, genetic susceptibilities, and prior histories of exposures to toxicants and disease, as well as in possible allergic or stress reactions to exposures or countermeasures. The information resource that will be used to document known exposures and possible responses to these exposures should contain as much descriptive information on each person in the force as possible to facilitate primary medical management of individuals who develop health problems during deployment or post-deployment. It should also serve as a resource for epidemiologists who might be able to utilize population distributions of exposures and responses to establish criteria and standards that advance the military’s capabilities for optimal force protection. In setting up a computerized data resource to serve such functions, consideration must be given to limiting access of sensitive personal information to those with an approved right-to-know.

The activity patterns of members of the force can be critically important determinants of the extent of the internal doses received as a result of toxicant exposures by dermal contact and inhalation. Dermal exposures can be significant during field exercises and combat situations, and inhalation doses can be greatly affected by the amounts of air inhaled, the frequency of respiration, and the depth of penetration of the air inhaled into the lungs. The selection of force members to serve as exposure sentinels, as noted previously, should be influenced by their known or expected activities and by the exposures they have encountered or are expected to encounter.

Descriptors, Locations, and Access to Data Resources

The emerging technological capabilities of the Information Age create opportunities for the effective collection, storage, and utilization of relevant information on personal exposures, activities, and constitutional risk factors of kinds and magnitudes that are unprecedented. As a result, relationships between exposures and health outcomes that had been impossible to establish for individuals might become apparent when the data from large numbers of exposed individuals are combined. Thus, it might be possible to derive secondary benefits from the results of deployment sampling and dose commitments in terms of new knowledge or insights on latent or chronic effects that can be detected only on a population basis. Consolidation of the diverse data elements needed for such powerful analyses will require a data-management strategy, that includes a system for reporting essential data elements in a uniform and consistent manner across the various commands and services in a given theater of operation.

The full potential of the database envisioned above will require coordination and discipline at all levels. Its ultimate potential will become manifest when theater commanders can readily access on-line area and personal monitor measurements for field-deployment decisions, and medical officers can make timely decisions on the administration of countermeasures to ameliorate the effects of recent exposures to contaminants. Epidemiologists will be able to optimally construct cohorts in appropriate exposure groupings for studies of the overall impacts of the deployments on the health status of active and retired veterans of deployment. Arrangements will need to be made to control access to all of this information to those with a need-to-know to protect the privacy of medical records and the information on deployments for military security reasons.

Framework for Data Analyses

To achieve all of the ambitious potential applications outlined above, there will need to be uniform frameworks for data management. The overall integration of some of the deployment risk-assessment elements is well illustrated in Figure 1, which appeared in the Deployment Toxicology Research and Development Master Plan in September 1997 (GEO CENTERS, Inc.). An approach to combining data resources for developing an overall exposure (and risk) assessment, developed by an ACGIH-AIHA task group (Lippmann et al. 1996) for occupational exposure applications, is illustrated in Figure 2.

OPTIONS FOR PRE-DEPLOYMENT BASELINE DETERMINATIONS

Health Baseline Data

If subtle changes in symptom frequency or physiological functions result from toxicant exposures during deployments, they will be almost impossible to detect without data on pre-deployment baseline levels in the same individuals. This is because of the enormous range of baseline values for such variables, even in the generally healthy young adults in the military services. If conventional batteries of function tests are performed, along with the collection of questionnaire data on signs and symptoms prior to deployment, comparisons of comparable data during deployment and post- deployment on a relatively small cohort of individuals might be sufficient to determine either the short-term effects or the long-term effects, or both.

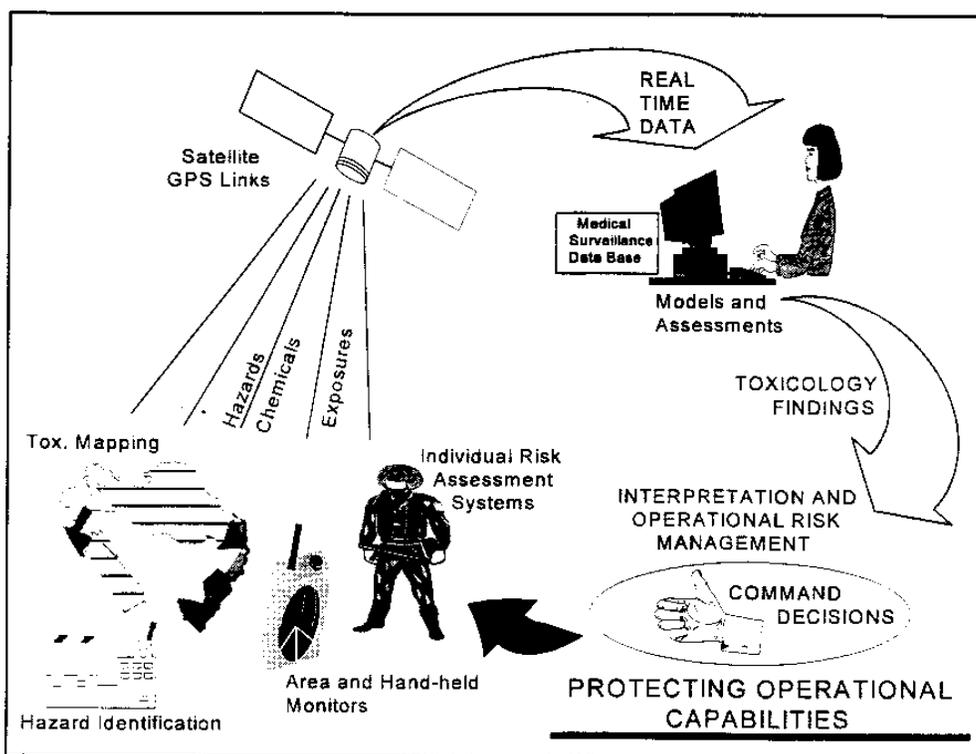


FIGURE 1 Deployment toxicology research and development master plan. (Source: GEO-CENTERS, Inc. 1997)

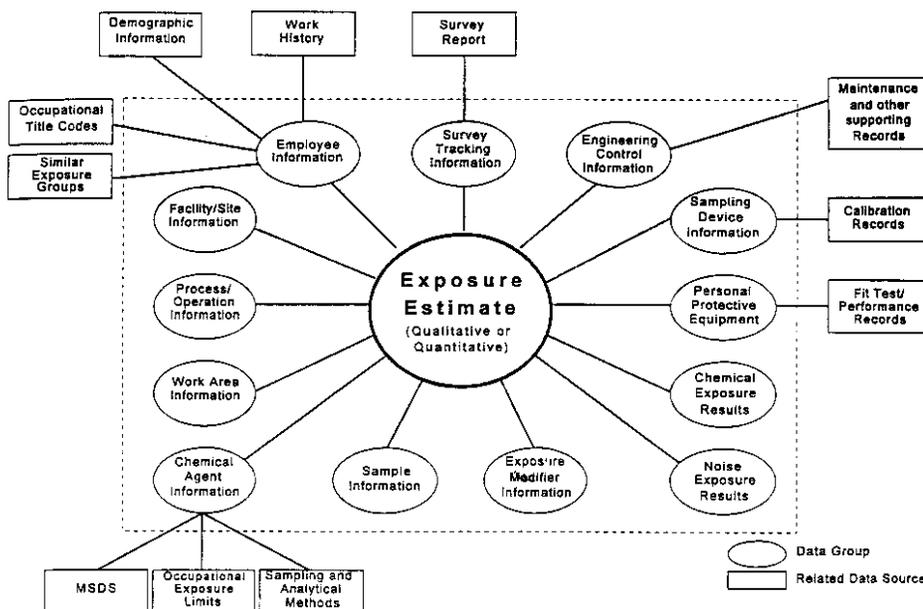


FIGURE 2 Data flowchart. This model illustrates the focus and scope of the recommended data elements for the occupational exposure database. (Source: Lippmann et al. 1996)

Collection of Biological Specimens for Archive and Future Analyses

For exposures to certain gases and aerosols producing acute responses, personal badges and monitors can provide sufficient exposure information. However, for agents that can penetrate the skin after dermal exposure, or for agents that are cumulative toxicants producing delayed effects, valuable information can best be derived from biological monitoring using samples of blood, urine, or hair. The analyses of these biological openings for a specific agent, its metabolites, enzymes induced, or adducts formed in endogenous proteins or DNA can indicate the presence of the agent or its metabolites in the body. For most, if not all of these analytes, there are likely to be broad variations in baseline levels, and the analyses can be quite expensive (Zhitkovich and Costa 1998).

Although analyses might be quite expensive, the collection and storage of the specimens is not, and a prudent precautionary sample collection procedure will permit sensitive determinations of the results of exposures that occurred during deployments. The process begins with the collection, identification, and archiving of samples of the biological materials during the pre-deployment clinical examinations. Comparable samples can be collected and archived during deployment or post-deployment to permit sensitive intercomparisons of assay results for evidence of changes in biomarkers that might have occurred as a result of exposures during the deployment, thus documenting the extent of the exposures or the effects that they produced.

For most purposes, the biomarker analyses will be performed on components of blood or urine. For other analyses, other biological materials that might be easier to collect in the field can also be useful; these include hair, fingernails, and sputum. Under some circumstances, other samples, such as exhaled air, nasal epithelium, and buccal cells might also be useful.

Exposure biomarkers are indicative of delivered toxicant doses and are focused on the early stages of the continuum illustrated in Figure 3, and tend to have higher degrees of agent-specificity (Table 1). An important factor in the practical use of biomarkers is a low and consistent background level of the biomarker response in nonexposed populations. Tight variance in biomarker measurements among unexposed subjects indicates that the biomarker is not strongly affected by unknown factors associated with, for example, diet or lifestyle. Sensitivity and low interindividual variability are the most important parameters influencing the statistical power of a biomarker. Taioli et al. (1994) provide a general strategy and useful examples as to how variability of biomarkers can be estimated, and offer an equation to calculate the minimal sample size. For example, DNA adduct-based assays require relatively small sample sizes, whereas gene expression biomarkers, with very large variability among unexposed individuals, require much larger populations.

Blood biomarkers are a heterogeneous group of biological measurements, including unmodified original chemicals, chemical-specific metabolites, stress hormones, modifications of proteins and DNA, and serum and intracellular components, with half-lives of up to about 10 days. Blood contains large quantities of hemoglobin and albumin, proteins that can be readily isolated in pure form. Carboxyl, amino, and sulfhydryl groups are typical sites of adduction by electrophilic compounds. Many protein adducts are stable under physiological conditions, providing an opportunity to assess cumulative exposure, because the life span of human hemoglobin is approximately 120 days. The biological half-lives of albumin adducts are shorter, due to a faster metabolic turnover of albumin (DeBord et al. 1992). Protein adducts, although not mechanistically involved in the pathway leading to disease, can be useful as long as the relationship between surrogate and mechanistic biomarkers is known.

Peripheral blood lymphocytes are the most frequently used cells to assess biomarkers related to potential genotoxic exposures. Lymphocytes contain DNA and circulate throughout the human body, and therefore they are exposed to any circulating genotoxic agent or its metabolites. These cells can integrate exposure over extended time intervals because they are long-lived (Brasemann et al. 1994)

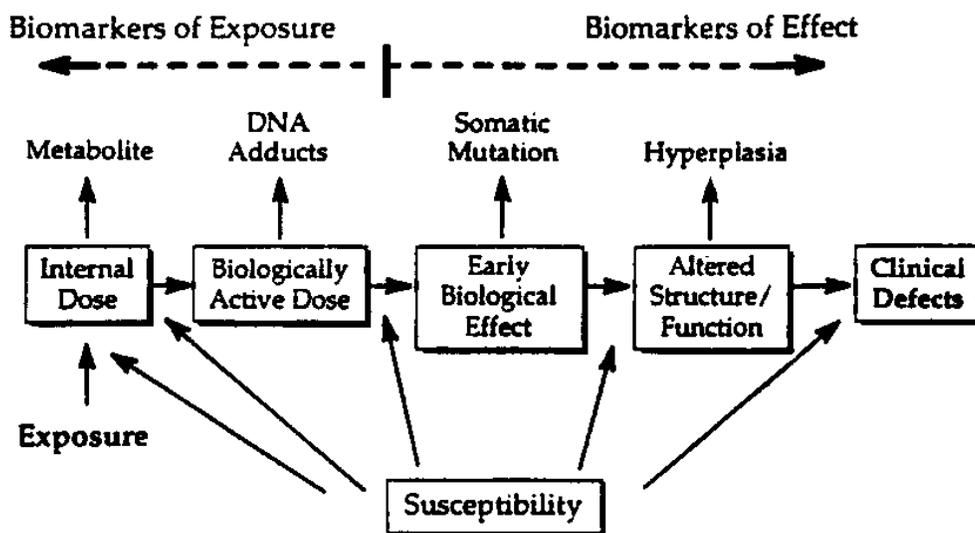


FIGURE 3 Relationship between exposure and disease. (Source: Zhitkovich and Costa 1998)

TABLE 1 Examples of Biomarkers With Different Agent-Specificity

Specificity	Biomarkers	Exposure
Low	Sister chromatid exchanges and chromosomal aberrations in peripheral lymphocytes	Clastogens
	Micronuclei in buccal cells	Clastogens
	β -oxo dG in urine or lymphocytic DNA	Radiation and many chemicals
Intermediate	N-acetyl- β -D-glucosaminidase in urine	Nephrotoxic agents
	Mutagenesis at HPRT locus in lymphocytes or glycophorin A in erythrocytes	Mutagens
	Urinary malonaldehyde	Agents causing lipid peroxidation
	Serum or urinary chromium	Toxic and dietary forms of chromium
High	Urinary nitrosoproline	Nitrosamines
	Immunoassay for PAH-DNA adducts	PAH compounds
	1-hydroxypyrene in urine	
	Cholinergic muscarinic receptors or acetylcholinesterase activity	Organophosphorus insecticides
	Original substance in biologic specimens	For example, cadmium
Substance-specific metabolite	For example, S-phenylmercapturic acid for benzene	
Chemical-specific DNA or protein adducts	For example, styrene-hemoglobin for styrene exposure	
Biologic response characteristic of specific exposure	δ -Aminolevulinic acid in urine (lead exposure) Urinary porphyrins profiles (mercury exposure)	

Source: Zhitkovich and Costa 1998

and do not divide in vivo. Many in vitro studies found that unstimulated lymphocytes have inefficient DNA repair capabilities (Barret et al. 1995; Freeman and Ryan 1988), permitting these cells to accumulate detectable DNA damage from very low exposures. Lymphocytes are also capable of metabolizing many important xenobiotics such as ρ -aminohippuric acids (PAHs) to DNA-reactive species (Gupta et al. 1988).

Measurements of biomarkers in urine samples generally reflect recent exposures, and can be useful for assessing accidental overexposures and psychological or physiological stresses. Analyses of spot urinary samples can be used to estimate exposures in populations, whereas individual exposures are best assessed using 24-h collections. Urinary biomarker measurements are corrected for a dilution factor by normalizing all determinations for a creatinine content. Most analyses of urine samples are based on detection of chemical exposure, and involve measurement of an original substance or its metabolite. A smaller group of urinary bioassays can also estimate a biologically effective dose. Exposure to a majority of carcinogens results in the formation of DNA adducts that later can be excised by cell-repair systems. For some chemicals, excised adducts are then excreted in urine, and determinations of these adducts can provide a measure of biologically effective doses.

Hair samples can provide a temporal history of peak exposures to toxic or trace metals and some organic species or DNA that are incorporated into the growing hair shaft. For personnel who do not get frequent military-style haircuts, hair samples can provide good evidence of previous exposure over periods of many months. In practice, this might apply primarily to female members of the force.

In selecting any biological marker, one should consider the predictive value, specificity, sensitivity, and occurrence of false positives and false negatives. The factors to consider are:

- Does the test measure or evaluate exposure to an agent?
- Does the test provide reproducible results?
- Is analytical error and biological variability small?
- Is the test quantitatively relatable to the relevant range of exposure?
- Have the convenience and risk factors (associated with administering the test) been considered?
- Are the concentrations of the agent measured quantitatively relatable to an adverse health effect or stress that could impair performance of critical tasks?

Actual analyses of samples from the archive would be done on a limited number of individuals' samples when evidence of effects points to the need for such analyses, and would initially be focused on the specific kinds of biomarkers that are likely to be most informative. Depending on the findings of such exploratory analyses, and their potential significance to the future health of the force members, a further expansion of the analysis program might be warranted, looking for other biomarkers and at samples from other individuals in the cohort. Some analyses might be indicated in the near term following deployment, and others might be needed far into the future for evidence of delayed chronic health effects that became apparent from epidemiological follow-ups, or when appropriate and more sensitive assays become available to answer questions that could not be resolved on the basis of the original assay analyses.

Environmental Quality

It might be possible to collect samples of air, soil, and surface waters, and to measure levels of background radiation prior to deployment to determine whether the deployment of forces at a given location would be unsafe or unwise. If such analyses do not indicate risks of contamination, and deployment is subsequently initiated, it would be prudent to store pre-deployment environmental samples

in the deployed forces archive, and to collect and store additional samples during deployment and post-deployment to be able to determine if contamination occurred during deployment, either as a result of hostile actions or as a result of the deployment activities themselves. If evidence of such contamination is found, a determination will need to be made about whether it is sufficient to warrant decontamination or investigations of exposures to deployed forces or indigenous populations.

OPTIONS FOR COLLECTION OF DATA DURING FIELD DEPLOYMENTS

Remote Sensing

Remote sensing of air-contaminant levels and abnormal patterns of ground and vegetation surfaces associated with the presence of soil or water pollution can occur at various levels of spatial resolution using current military intelligence techniques and equipment. Civilian-sector technologies for measuring air concentrations in point- source plumes by LIDAR and by long-path infrared (IR) and ultraviolet (UV) spectroscopy can also be harnessed for air monitoring at deployment sites.

Personal Sampling and Monitoring by Field-Line or Duty Corpsmen

When one wants to know the exposure of an individual to chemical contaminants inhaled in the air, there is no good substitute for sampling or monitoring the air in the breathing zone of that individual. The breathing zone is typically defined as the space within about 1 foot (30 cm) of the nose or mouth, and small sampling heads or passive sampling badges are typically mounted on the lapel to monitor the breathing zone. When comparisons are made between the concentrations in the breathing zone and concentrations in the general area of the individual being monitored, personal exposure is often considerably higher than the concentration in the area, especially when the individual is engaged in activities that release or resuspend the chemicals from soil in the area or from accumulated contamination on the clothing of the individual. For collecting such samples from field personnel there will need to be well-trained field-line corpsmen responsible for issuing, collecting, labeling the sample, storing in short and long-term archives and assuring appropriate means of their delivery to appropriate laboratories for analysis.

Collection of Biological Specimens by Medical Personnel

Biological specimens collected in the field will also need to be collected by well-trained corpsmen, nurses, or other medical corps personnel. It is imperative that the samples are not contaminated by soil on the hands, that low-background sealable containers are used to contain the specimens, and that all samples are carefully and appropriately identified, for example, by unique bar code. For blood and urine samples, it is quite important to record the time of day that the collection took place in relation to recent activities and exposures, and to take appropriate precautions in sample handling and storage to preserve the integrity of the samples for both transit to a laboratory or preservation in a sample archive.

Collection of Samples of Environmental Media

If pre-deployment samples or direct measurements of air, soil, water, and background radiation were collected, and their subsequent analyses indicated potentially serious toxicant exposures, then

comparable samples should be collected at one or more times during force deployment. These should then be analyzed for the toxicants of concern to assess the effect of deployment activities on the nature and extent of toxicant exposures to the troops, and the extent of the dispersion of the on-site toxicants from their initial reservoirs into the environmental media.

If pre-deployment samples did not indicate a serious concern for toxicant exposures during deployment, it still might be prudent to collect comparable samples for an archive to be able to determine whether deployment activities either uncovered previously undetected contamination, or created or released to the environment toxicants that should be cleaned up prior to departure. The samples might also be needed to document the results of intentional releases of toxicants by hostile forces during the deployment.

Performance Measures

Neurobehavioral performance measures can be used as biomarkers of exposure and biomarkers of operationally important responses to exposures. In either case, they can only be properly interpreted as changes in measures from baseline levels, as discussed previously. Exposures to some solvents, pesticides, and metals might alone, or together, or in combination with vaccines and prophylactic drugs, produce altered cognitive functions in the absence of clinical signs or symptoms, and signal the need for confirmatory evidence of exposure through assays of environmental media, air samples, or biological fluids. The effects produced by exposures to neurotoxicants among military personnel might be especially important to the performance of their assigned missions and to their ability to effectively and responsibly manage the weapons at their disposal.

The performance measures that can be quickly self-administered might be the only feasible means for many individuals in the deployed forces. Hand-held computers can be programmed to (1) administer appropriate tests of mental capacity, reaction times, or agility; (2) calculate performance indices; and (3) telemeter the results to a central medical evaluation unit. For further information on the state-of-the-art for assays of neurobehavioral performance in humans, see Anger et al. (1998).

It should also be noted that the U.S. Geological Survey is engaged in the development of physiological and behavioral measures of acute chemical neurotoxicity in aquatic organisms as part of the deployment toxicology research program, and that the indicators that they have developed could be used to assess environmental contamination and associated risks at deployment sites.

Use of Protective Measures

The military has carefully developed specifications for the purchase, supply, distribution, and maintenance of personal protective devices, such as respirators, faceshields and goggles, and protective clothing, which are issued to deployed forces in anticipation of expected exposures. Records of their actual use by individuals in the field should be part of their personnel records to facilitate such retrospective exposure assessments that might be needed in the post-deployment period. On days when there are indications that potentially damaging exposures might have occurred, it should be possible to arrange for the collection and archiving of respirator canisters or samples of protective gear for later laboratory analyses, with appropriate notation of the user's identification, times and locations where the protective device was worn or used, and remarks concerning known contaminant sources or releases relevant to the potential exposure. Analyses of these samples and associated information could prove invaluable to the military for determining (1) actual exposures of deployed individuals to specific agents; (2) indications of likely exposure to other individuals in the same

general operational area who are not being monitored; and (3) the efficacy of the personal protective gear being provided to the forces for reducing or eliminating the uptake of toxicants from the working environment.

Records of Activity Profiles

Environmental exposure is an essential determinant of the amount of the contaminant taken up by an individual in that environment. However, uptake is also dependent on the individual's activities and the effect of any barriers to mass transfer from the environment to systemic uptake by the individual. Uptake of air contaminants is strongly dependent on the volumes inhaled and the lung depths to which it is drawn, which, in turn, is dependent on the activity level of the individual. It is also dependent on the use and effectiveness of any respiratory protective device that is supplied to the individual. It should be recognized that it might not be possible to attain the ultimate protective capacity of a demand-type respirator under the stress and exertion levels encountered by military personnel in the field.

Similarly, dermal exposure represents a potential for uptake that can be strongly modified by contact area, contact times, and the integrity of the skin barrier. Ingestion exposure is governed largely by the amounts consumed, and uptake from any contaminated food and drink that might be consumed by deployed forces is also affected by the amounts and nature of other elements of the diet. Thus, to the extent that it is feasible to collect and retain data on daily activities and meals for the deployed forces, such data might prove to be very useful in determining exposure profiles and estimating toxicant uptake for retrospective health risk evaluations.

OPTIONS FOR POST-DEPLOYMENT EXPOSURE ASSESSMENTS

The late deployment and early post-deployment period can be critically important for the collection of samples and data that can help the military draw the most important lessons about toxicant exposures that might have taken place during the deployment. This period is usually a time when the military emergency or urgent situation justifying a deployment is past and there might be time and resources available during the phase-down for filling data and knowledge gaps that could not be addressed when there were more urgent priorities and when access to deployed personnel for the collection of biological samples and activity logs was infeasible.

Collection of Biological Samples

Evidence for toxicant exposures during deployment will often be possible in the weeks and months after the exposure has taken place for those toxicants that (1) have cumulative effects; (2) accumulate in the body; or (3) produce metabolites or effects that persist in cells that remain in the blood stream, are excreted in the urine, or are fixed in growing hair. The results of post-deployment analyses can be of special significance and value when comparable samples are collected and analyzed or archived before and during the active phases of the deployment, because baseline values might vary greatly from person to person.

In any case, post-deployment biological samples that are collected soon after the deployment is completed could be very useful, even in the absence of pre-deployment reference samples, for analysis of the population distribution of exposures. A special opportunity to collect large numbers of samples can arise when the force is relocated on transport ships. Samples could be collected by unit corpsmen

using the support available from the ship's facility for sample collection, processing, and storage. For troops being relocated by air, there might be opportunities for sample collection at intermediate sites with clinical facilities, or upon arrival at new duty sites.

Collection of Environmental Media Post-Deployment

The collection of samples of environmental media post-deployment can fill several potentially important needs. By comparison of the analyses of comparable samples collected pre-deployment, during deployment, and post-deployment, it might be possible to document the extent of unavoidable or avoidable exposures, due to the presence of background levels of toxicants in the environment. They may also make it possible to document the extent of environmental toxicant burdens created during the deployment, and thereby the need for or extent of remediation of deployment sites or following their return to local control.

Analyses and Comparisons of Pre-Deployment and Post-Deployment Samples

Sensitive and specific analyses of the contents of all of the biological and environmental samples that are archived during the pre-deployment, deployment, and post-deployment periods would be uneconomical and unwarranted. A strategic plan that sets priorities in the selection of samples for analysis will be needed. The priorities will be determined by the information needed to protect the health, welfare, and readiness of the forces that are deployed.

Samples that might warrant a high priority for early analysis include:

- Pre-deployment environmental media samples needed to determine whether there are likely to be exposures that could compromise the health of the forces and could be avoided or minimized.
- Biological and environmental samples collected during and immediately following deployment needed to determine if serious toxicant exposures have taken place, based on evidence such as unusual illness patterns, alarms sounded by areawide chemical or biological agent sensors, and suspicious activities by hostile forces.
- Biological samples collected during deployment and the early post-deployment period needed to investigate any unexplainable health problems that turn up among previously deployed forces, as happened with Gulf War Syndrome.

Depending upon the results obtained in such screening assays, analyses of additional samples from the archive, or analyses of additional analytes in the samples, might be warranted to obtain a fuller picture of the nature, extent, and significance of the exposures that might have occurred during deployment.

In developing a strategic plan for the maintenance and management of a sample archive, consideration must be given to the criteria for the disposal of unneeded samples at appropriate times after the deployment to be able to accommodate the needs for archiving samples in future deployments.

Analyses of Cumulative Exposures

Acute toxicant exposures and their consequences are expected to be obvious to area commanders and their medical support staffs. However, the effects of more slowly acting toxicants might not become evident during the deployment, and the exposure index might be more closely related to cumulative exposure than to peak exposure. Estimates of cumulative exposure can be derived from biomarker analyses. For inhalation exposures, estimates can also be derived or established from cumulative

concentration-time products, with allowance for variable uptake due to activity level and deposition rates. Because continuous records of ambient air-concentrations are not likely to be available at any location, let alone for all individuals in the force, exposure models will need to be employed in making useful estimates of cumulative exposure using air concentration data.

Case-Control Studies

Case-control studies can be powerful forensic tools for elucidating causal relations between outcomes and exposures when reasonable and plausible exposure groupings can be identified. Unfortunately, this proved not to be possible in the investigations of the Gulf War Syndrome because of the lack of any useful data on the agents that might have been responsible or the means of retrospectively determining the exposures to those agents. Should such a mysterious pattern of post-deployment illness occur in the future, and if archived biological and environmental samples are available as outlined above, it should be possible to compare indices of exposure in those with illness with those in matched control populations, without illness, thereby identifying the exposure characteristics most closely associated with the pattern of illness.

MAXIMIZING EFFECTIVE USE OF SAMPLE AND DATA RESOURCES

Information technology developed in both the military and civilian sectors in recent years has made it possible to envision the construction, maintenance, and utilization of a deployment data resource that would enable theater commanders and medical staff to recognize and evaluate environmental health hazards and to manage deployments to avoid or minimize those hazards. Together with a deployment sample archive, it would also facilitate future epidemiological studies that could identify additional causal relationships between environmental factors and health outcomes, and thereby stimulate the development of means of recognizing additional risk factors warranting exposure controls in future deployments.

To take maximal advantage of these new technological capabilities, it is imperative that the biological and environmental samples and data elements that are needed for such applications are collected and maintained in uniform and readily interpretable forms, and that they are accessible to all authorized users. Applications will include:

- on-line access of deployment decision-makers to remote sensing and continuous monitoring data that they could consider in tactical planning;
- data review by medical staff personnel to arrange for monitoring military personnel for possible effects of toxicant exposure; provide countermeasures during deployments; and set priorities for medical examinations and biomarker sample collections and analyses in the early post-deployment period;
- on-line access and data review by industrial hygienists and environmental assessment specialists to arrange for additional sampling and monitoring, or analysis of archived samples, to resolve ambiguities or conflicts concerning levels of exposure or environmental contamination; and
- review of medical and environmental data by epidemiologists in post-deployment investigations of possible causal factors for delayed-illness reports associated with service in a specific deployment.

However, to accommodate all of these needs in a timely and efficient manner, it will be necessary to have a flexible system for sample and data management that can be adopted and applied uniformly by all of the military services. It could be an extension of the Defense Occupational Health Readiness System.

Constructing a Sample Archive

As noted earlier, USACHPPM's DESP is a logical repository for an expanded sample archive, as proposed here. It could incorporate an expanded version of the existing Armed Forces Serum Repository, as well as samples of blood cells, urine, hair, air sampling filters and vapor-collection canisters, soil, and locally available drinking water. Blood cells and urine and hair samples can provide DNA for future molecular-level biological assays, which might be critical in forensic toxicology investigations of possible delayed health effects that might occur among deployed force personnel. The strategic aspects of the design, maintenance, accessibility for sample analyses, minimal analytical efforts justifying use of the archived samples, and reporting data from the analyses should be established by USACHPPM staff with appropriate input from an external scientific advisory committee with expertise in exposure assessment, toxicology, epidemiology, analytical chemistry, molecular biology, and clinical medicine.

Constructing a Data Resource

There are a number of essential features for a data resource that can effectively serve a variety of primary and secondary users. The primary users must first be satisfied with data format, data reduction paradigms, and data access because they will be providing the financial and logistical support for data collection and entry. When the different branches of the military services are engaged in joint deployments, it is also essential that a harmonized array of data elements are adopted, so that the data sets can be merged and the results of data analyses can be uniformly interpreted.

In setting up a data-management system and defining a commonly agreed upon set of well-defined data elements, it is important to also consider the analytical needs of secondary users of the data resource. They might need more descriptive background information on the geography, topography, meteorology, and history of the deployment sites than do the military command or medical units. Some of the considerations involved in setting up comprehensive and harmonized databases for personal exposures that could facilitate primary and secondary data users were described in detail by an ACGIH-AIHA task group (Lippmann et al. 1996) and by a European Community task group (Rajan et al. 1997) for occupational exposure data. In the environmental arena, the EPA (1998) has recently described a major initiative to facilitate increased use of its environmental data resources by secondary users.

In defining its essential data elements and constructing a format and procedure for entering, maintaining, and accessing its own data on exposure and health outcome related factors, the designers of the military databases should consider opportunities for commonalities with the database developments currently under way in the civilian arenas in the occupational health and environmental fields. This examination of recent ongoing activities should, of course, include the efforts already undertaken within each of the military services to broaden, expand, and utilize their own data resources on occupational exposures, and should bring in the perspectives of the services' own professionals who will be secondary users of the data resource.

Engaging Industrial Hygiene Expertise for Cumulative Exposure Assessments

There might need to be a component of the data resource devoted to the assessment of the cumulative exposure of each member of the deployed force to each of the toxicants encountered during the deployment that might account for excess illness observed among the cohort in the post-deployment period. Such assessments will involve the combination of measurement data, exposure models, and

expert judgments. It might also involve the selection of air, biological, or environmental samples from the archive for follow-up analyses to fill in data gaps that limit such assessments. Thus, the creation of files on cumulative exposure assessment might be an iterative process that involves collaboration among hygienists, toxicologists, and epidemiologists.

Engaging Toxicological Expertise for Interpreting Biomarker Data

Currently, there are relatively few biomarkers that are specifically identified with toxic agents or stresses likely to be encountered during military deployments, and therefore few environmental or biological samples collected prior to, or during, a deployment are likely to be analyzed routinely. Most samples will be retained in the archive, to be analyzed when it is necessary to confirm or quantify exposures that are suspected of causing adverse effects. In deciding which samples to analyze and what analyses are appropriate and feasible, there will need to be input by toxicological experts, who will also be needed to interpret the analytical results obtained. They will need access to other parts of the database in forming their judgments about the extent and significance of the exposures indicated from the biomarker analyses, and the lessons they learn from each analysis might be useful in iterative upgrades of the data elements in the overall database and in its management.

Engaging Epidemiological Expertise for Data Analyses

Because the envisioned database is expected to be an unprecedentedly bountiful resource for military epidemiologists, it should be provided with significant input into the selection and format for certain of its data elements by them. This will be especially important for the construction of appropriate summaries of exposures for use in the exploration and definition of exposure-response relationships.

CURRENT TECHNOLOGICAL CAPABILITIES FOR PERSONAL EXPOSURE ASSESSMENT

Personal exposures can be measured continuously on-line for a limited number of gases and vapors, determined from time-integrated samples that are subsequently analyzed for a much broader array of agents in both gaseous and particulate forms, and inferred, albeit with greater uncertainty, from measured exposures to others in the same general area or from exposure models utilizing measured environmental levels and activity patterns within the monitored area. Estimates of personal exposure can also be developed from biomarker measurements when consideration is given to systemic uptake from the environment, knowledge of metabolic fate in relation to times of exposure and sample collection, and other knowledge about retention sites and half-lives in internal organs.

Personal Air Sample Collection

The technology for collecting personal air samples over periods ranging from hours to days is relatively well developed, and reliable devices for such sampling are widely available and relatively inexpensive. The easiest to use and most unobtrusive devices are the passive samplers for gases and vapors that collect the agent penetrating a diffusion barrier onto an adsorption surface at a rate dependent only on concentration and diffusion coefficient. The devices are small and easily worn on a lapel. Recordkeeping requirements for sample collection are limited to the person wearing the device, the times when the cover of the sampler is opened and closed, and the activities of the wearer during the

time it was open for sample collection. In many cases, the samples can be analyzed subsequently in a field laboratory. In others, more sophisticated central laboratory analyses might be required. When the rate of sample collection is too low to determine the concentrations of the agent interest, active samplers that collect samples at higher rates might be needed.

An active sampler requires a battery-powered air mover and a flow meter as well as a sampling substrate, all of which increase the cost and complexity of the sampler and the burden on the wearer by at least a few pounds. However, active samplers sample air at much higher rates (up to ~ 5 L/min), permitting more sensitive assays with a broader range of analytes. Gases and vapors can be collected on adsorptive granules packed within presealed tubes or on chemically pretreated filters, and particles can be collected on a filter disc compatible with the analyses to be performed. Membrane filters are used to collect samples on their surfaces and are scanned by microscopy, x-ray fluorescence, or radioactivity, for viable organisms after incubation in an appropriate growth media. Aerosol samplers can also have an inertial precollector to collect samples restricted to specific aerodynamic particle sizes based on deposition probabilities in functionally distinct regions of the human respiratory tract. In any case, industrial hygiene or other field personnel will be needed to dispense and collect personal samplers and to check out the validity of sample start and end times, flow metering (if active sampling), the temporal and spatial coordinates of the sampling intervals, and the notation of relevant conditions and activities.

Personal Monitors With Electrical Signal Outputs

Opportunities to use personal sensors and transducers to identify gaseous chemical exposures of deployed forces will be increasing in the near future as the inherent capabilities of miniature sensors, circuits, and telecommunications devices mature and are developed in the form of conveniently usable hardware. Recent symposia have highlighted applications of miniaturized electrochemical sensors and interferometers to make sensitive and specific concentration measurements that can be telemetered, along with spatial location coordinates, to central sites, such as military command posts and medical commands, for their surveillance and appropriate responses. Position transducers are already available commercially, whereas the chemical sensors will need further refinement and validation before they are ready for widespread use by military forces.

Biological Sample Collection

The collection of biological samples, such as blood, urine, and hair, is best done under controlled conditions in which scrupulous sanitary and contamination-free control conditions can be exercised. For regularly scheduled collections in noncombatant environments, this might be possible for troops who are accessible to medical personnel. For those in more remote locations, it might be necessary to equip a military ambulance to go to the vicinity of the troops for sample collections and to have the facilities within them for sample identification, processing, and storage. The personnel collecting the samples must also be sensitive to the need to carefully collect the coordinate data on the recent activities and experiences of the individual providing the samples to help interpret the results of any analyses that are performed on the sample.

Temporal Considerations of Analytical Laboratory Capabilities

For each deployment, there will need to be at least one laboratory that collects and processes samples of air, soil, water, and biological fluids for either on-site analyses or transferral to theater-area

labs in mobile army hospitals, modular field medical units, or hospital ships offshore, or to more remote central laboratories. For samples that can be adequately processed in the theater-area, the results can be fed back, within days, to field personnel for guiding further sampling, relocation of personnel or activities, or therapeutic interventions.

For analyses that require more sensitive or sophisticated laboratory facilities or specialized analyses, the turn-around time will be longer, and there will be fewer opportunities for prompt feedback to deployed forces for additional timely sample collection or reduction of ongoing exposures. There will be, however, significant advantages in terms of documenting the full nature and extent of agents that were present at very low concentrations.

Detection Limits of Analytical Laboratory Capabilities

The practical detection limits for a given sample depends on a number of factors whose influences will vary greatly from agent to agent and from one analysis to another. These factors relate to analytical sensitivity and specificity, the interferences produced by co-contaminants in the samples and components of the sampling substrates, the level and constancy of background readings of the sensing elements, the frequency and reliability of periodic recalibrations for span and zero readings, and the care taken to avoid sample and equipment contamination by the analysts. Thus, it is essential that the quality-assurance and quality-control procedures of the laboratory meet the highest standards of good laboratory practice.

Interpretation of Biomarker Changes

Exposure of biomarkers offer so many potential advantages over direct measures of exposure that they must eventually become more routinely used and more readily interpretable. However, it is essential that those relying on biomarker-based exposure estimates are fully aware of their inherent strengths and their fundamental limitations.

One major strength of biomarkers, especially for military deployment applications, is that they are influenced by past exposures, as opposed to direct measures of exposure over a given sampling interval. Thus, biomarker samples that are collected shortly after a suspected exposure has taken place can be used to “look back in time” to establish whether, in fact, the exposure actually occurred for the individual providing the sample and, by implication, for other individuals in the same group or area.

Another, sometimes realized, potential strength of biomarker analyses is the high degree of sensitivity that is possible. This is especially true for biomarkers based on characteristic responses to the exposure rather than the exposure agent itself. Highly sensitive tests for immunological responses and changes in DNA or protein structure are often much more sensitive than chemical analyses, and are longer lasting indicators of past exposures. A further potential advantage of exposure biomarkers is the relative absence of concern about stray contamination of the sample by the original exposure agent during the sample collection in the field. When reaction products are being measured, it is less likely that they will be produced during the sample processing or laboratory analysis. However, they might not be compound-specific.

The major limitations of biomarkers as indices of exposure involve the issues of the interpretability of the measurements that are made. One major potential limitation can be the absence of a benchmark or background level of the index being measured. This need not be a major problem for personnel in military deployments when pre-deployment background biomarker samples are collected, properly stored, and accessible for comparative evaluations.

In the absence of pre-deployment biomarker samples, the utility of biomarker samples collected during post-deployment will depend on the kinds of information that might be needed. If background levels of the biomarker of interest are very low, or if exposures are very high, the absence of a pre-deployment sample will not be important. For the more typical situation in which relatively low levels of exposure to an agent that can produce long-term chronic disease are known or suspected, there are several possibilities. One is to confine the analysis of the exposure to those individuals who have provided pre-deployment samples, and use their biomarker changes as indicative of others believed to be similarly exposed. Another possibility is to compare the distribution of biomarker levels in a large number of members of the deployed force with the distribution of levels in a matched population that has not been engaged in the same deployment. In this case, the level measured in a given member of the deployed force might not provide a personal index of disease risk, but the analyses might still provide valuable information on the average exposure of the deployed population and some indication on its distribution. The population approach might only be feasible, however, for assays that are reasonably inexpensive.

One unavoidable limitation of biomarker samples, however, is the fact that they are inherently “grab” samples collected at specific points in time. This is a relatively manageable problem for interpreting a brief peak exposure that occurred over a known time interval and in which the metabolic and translocation times are known, but it can be a major problem when the temporal pattern and extent of the relevant exposure is unknown. This is because the measured parameter can be highly variable over time and there is only one measurement made of a sample collected at an unknown time after the exposure. Thus, the analysis might be adequate to establish that an exposure took place, but unable to characterize the level of exposure. The problem is most severe for intermittent peak exposures whose timing is otherwise unknown, and least severe for steady-state exposures on which internal biomarker levels reach relatively stable levels.

ASSESSING RISKS FROM PERSONAL EXPOSURES

Within the broad spectrum of risks encountered by deployed U.S. forces on foreign soil, this paper has focused on the risks related to exposures to chemical compounds in environmental media at deployment sites. It has not dealt with chemical warfare agents for which the military services have long had plans for force protection and countermeasures. As a result of this distinction, the risks are generally more likely to be less obvious to the forces on the ground and more likely to produce delayed health effects than promptly observable effects. When delayed effects are seen, they are likely to be nonspecific in origin or causation and the search for causality might require careful sifting through records relating troop activities to areas having environmental contamination and personal exposures and relating those exposures to nonexposed or less-exposed matched control populations. The nature of the risks, and their often unanticipated relationships to exposures on foreign terrains, accounts for the emphasis in this paper on sample and record collection and retention for follow-up investigations to establish causal, dose-related relationships.

Combining Exposure Data with Exposure-Response Relationships

When sample analyses or environmental monitoring data indicate exposures to agents of known toxicity having established exposure limits, the risk analysis is relatively straightforward. If exposures exceed established standards or guidelines for such agents, the medical management of overexposed individuals should also be relatively routine. However, for exposure to agents that produce effects that

have not previously been well characterized and whose long-term prognosis is uncertain, then prudent concern for the future health of the deployed force members warrants careful study and follow-up by military and Veteran's Department medical personnel and epidemiologists. Depending on the nature of the effects and their progression over time, this might require regularly scheduled clinical examination, biomarker sample collections, questionnaire responses, checks on vital status and, for the deceased, cause of death.

Research Needs

This paper envisions a long-term iterative process of exposure and health-status monitoring to identify and characterize health risks to military personnel during noncombat deployments on sites where characteristics of chemical agent exposures are unknown or poorly known. Initially the technological means for pre-deployment environmental or on-line personal exposure assessments are expected to be limited to the detection and characterization of a limited number of chemical toxicants, and quantitative exposure assessments will be delayed by the time it takes for sample collection and laboratory analyses, and by the sensitivity and specificity of the analyses that can be performed.

Table 2, from the Deployment Toxicology Research and Development Master Plan of September 1997 (GEO CENTERS, Inc. 1997), provides a thorough inventory of the technical challenges of exposure assessment for deployed forces and the kinds of advances that could be made through investments in research. Investments in further technological developments in miniature chemical sensors, microprocessors, and telecommunications devices could lead, within a relatively few years, to much greater technological capabilities for long-path area measurements and personal monitoring of a broad range of toxic gases and vapors, which would provide military commanders with options for force deployment that prevent or at least reduce times of exposures to toxic agents.

Investments in biomarker research, development, and validation could provide extraordinarily sensitive means of documenting exposures to toxicants as well as aspects of the biological responses to such exposures. To the extent that measured biomarker responses lie along a pathway leading directly to long-term changes and chronic disease, then it might be possible to prescribe therapeutic interventions that prevent, forestall, or ameliorate such late effects of the exposures.

Investments in the creation, management, and utilization of accessible sample and data archives related to exposures and their health consequences are also needed for various analytical and research purposes. These include (1) use of on-line exposure information for deployment decision-making; (2) use of on-line and sample analyses data for early actions on further sample collection needs and medical interventions for overexposed personnel; (3) identification of military personnel according to exposure category for future clinical or epidemiological follow-up; (4) identification of agents for which new sampling or analytical techniques are most urgently needed for risk-assessment purposes; and (5) identification of archived samples and sample analyses that can resolve issues that might arise from delayed reports of unusual illness patterns following deployments.

Each of these categories of research could consume large amounts of resources, and the allocations should be decided according to preestablished priorities by an appropriate panel of peers, including military users and state-of-the-art research investigators with expertise in the emerging technologies.

TABLE 2 Exposure Assessment Issues and Near- and Far-Term Capabilities

Technical Issues and Challenges	Capabilities (Near-Term)	Long-Term Vision
Personal Samplers and Monitors	Sensor Technologies	Personal monitoring online
Instantaneous	Miniaturization	
Grab	Weight reduction	Personal to population extrapolation
Periodic	Biosensors	
Real-time/Continuous	Artificial nose	Combined risk information systems
Passive	Passive dosimeters	Warning
Area Samplers and Monitors	Ultrasonic Flexural Plate Wave	Summary statements
Real-time results	Devices	Risk avoidance
Remote vs. Local	ELFFS	
Media Sampled (air, water, soil)	Computer Tomography/FTIR	Relationships of exposures to
Statistical considerations	Mini GC/MS	indicators of health effects
Data Transfers		database (extensive)
Relevance to human uptake	Computer Hardware	
Hand-held	Greater capacity and speed	Single biomonitoring device
Biomarkers of Exposure	Miniaturization	integrating measures of
Simple vs. Complex	Portability	exposure and dose
Recent vs. Past vs. Continuous		
Validation—biological relevance	Computer Software	Exposure-Dose models that can
Sample: breath, urine, blood,	Modeling and Simulations	anticipate associated problems
dermal, transcutaneous, hair,	Artificial intelligence	with introduction of new
etc.	Available catalogs/databases	chemical and bio toxins
Contaminant		
Form: gas, vapor, particulate,	Networks & Communications	Personal Status Monitor (PSM):
aerosol, fume, dissolved,	Linking for data collection,	physiological stress indicators
suspended	transfer, and analysis	
Mixtures	Remote/stand off capability	Genetic engineering for sensitive
Stability/Transformation	Ready access to experts and	populations
Relevance of form to toxicity	databases	
Sources of exposure	On call/on demand data	Universal micro-environmental suits
Rates and Distance		
Changing compositions	Molecular Biology	Validated methods for measuring
Exposure vs. Dose	More and better biomarkers of	relevant exposure and total dose
Exposure route contributions	exposure	data directly from biological
Absorption factors and rates		samples taken by non-invasive
Differential uptake or deposition	Exposure models to extrapolate from	techniques
Individual characteristics	limited exposure measurements	Replacement breathing systems
Respiratory rates/Activity	to large study populations and	
Exposure elimination	incorporate short-duration, high	Biologically-based exposure
Countermeasures vs. performance	intensity exposures.	assessment systems
decrements		
Military-unique exposure standards	Improved field methods for	Technological advances that measure
Predeployment screening	characterizing simultaneous	low concentration of chemicals
Retrospective exposure tracking	exposures.	and biomarkers in biological
		specimens linked to internal
		dose concentrations at target
		origins

Source: GEO-CENTERS, Inc. 1997.

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