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Using a public health registry to conduct medical surveillance: the case of toxic embedded fragments in U.S. military veterans

L'uso di un registro di salute pubblica per condurre la sorveglianza medica: il caso dei frammenti tossici residui nei veterani militari statunitensi

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Summary

Aim: **Beyond inflicting acute traumatic injury, contact with improvised explosive devices, the leading cause of injury for soldiers serving in Iraq and Afghanistan, may result in wound contamination with embedded fragments permitting chronic exposure to toxic materials. Because health effects associated with embedded fragments are not well-delineated, the U.S. Department of Veterans Affairs (VA) is establishing an exposure registry and surveillance center to identify, track and monitor the health of veterans who have embedded fragments.** ***Methods:*** **U.S. Veterans wounded with embedded fragments are identified when making contact for healthcare using a screening process incorporated into the Veterans Administration's national electronic medical record system. A data review results in recommended follow-up which may include fragment analysis, urine biological monitoring, and/or clinical consultation. The registry will link to the individual's electronic medical record and**

Riassunto

Finalità: **Il contatto con ordigni esplosivi improvvisati, la maggiore causa di lesioni per i soldati in servizio in Iraq e Afghanistan, oltre a causare ferite e traumi acuti può dare origine all'infezione delle ferite stesse a causa di frammenti assimilati che danno origine a un'esposizione cronica ai materiali tossici. Poiché gli effetti sulla salute associati a questi frammenti non sono ancora ben delineati, il Dipartimento degli Affari relativi ai Veterani di guerra sta mettendo a punto un registro dell'esposizione e un centro di sorveglianza per identificare, rintracciare e monitorare la salute dei veterani con questo problema.** ***Metodi:*** **I veterani statunitensi feriti da frammenti vengono identificati attraverso un processo di screening incorporato nel sistema di archiviazione elettronico dell'Amministrazione Nazionale dei Veterani, che avviene quando si sottopongono a cure mediche. Una revisione dei dati dà quindi origine a un'azione supplementare che può includere l'analisi dei frammenti, il monitoraggio biologico**

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other data sources to capture injury and exposure data, urine biological monitoring data, health outcomes, and fragment content results, when available. *Results:* Preliminary data suggest that approximately 3% of veterans have embedded fragments and are eligible for inclusion in the registry. Most fragments are metallic; therefore, a suite of 13 metals frequently found in fragments will be included in the biological monitoring protocol. *Conclusions:* Using a public health exposure registry, the surveillance center team will employ population level surveillance to better characterize exposure and identify potential health outcomes associated with retained fragments. The registry also provides an avenue for ongoing contact with exposed veterans as knowledge evolves affecting medical and surgical management guidelines for veterans with embedded fragments. Eur. J. Oncol., 15 (2), 77-89, 2010

Key words: **embedded fragment, medical surveillance, registry, injury, biological monitoring**

delle urine e/o la consultazione medica. Il registro si collegherà al file medico elettronico individuale e ad altre fonti di dati per rilevare informazioni relative alla ferita, all'esposizione, al monitoraggio biologico delle urine, alle ripercussioni sulla salute e ai risultati rispetto al contenuto dei frammenti, quando disponibili. *Risultati:* I dati preliminari suggeriscono che il 3% circa dei veterani ha dei frammenti residui nel corpo ed è pertanto idoneo ad essere incluso nel registro. La maggior parte dei frammenti è di origine metallica; di conseguenza una serie di 13 metalli riscontrati frequentemente nei frammenti verranno inclusi nel protocollo di monitoraggio biologico. *Conclusioni:* Attraverso l'uso di un registro di salute pubblica relativo all'esposizione, il personale del centro di sorveglianza utilizzerà il controllo del livello della popolazione per meglio caratterizzare l'esposizione ed identificare potenziali rischi per la salute associati a questi frammenti. Il registro fornisce inoltre un mezzo per mantenere il contatto con i veterani esposti, mentre la conoscenza delle linee guida mediche e chirurgiche relative ai veterani con frammenti sarà in continua evoluzione. Eur. J. Oncol., 15 (2), 77-89, 2010

Parole chiave: **frammento integrato, sorveglianza medica, registro, ferita, monitoraggio biologico**

Introduction

Public health registries have long been an invaluable mechanism for monitoring the health status of high-risk populations and for conducting epidemiological surveillance. Registries provide an organized system for collecting and analyzing data on individuals with shared characteristics from which population inferences can be derived (1). When first developed for public health use, registries often focused on individuals with a specific disease or health condition. Data captured in disease registries were used to identify and estimate the magnitude of specific health problems, determine the incidence and prevalence of disease, and examine longitudinal disease patterns and trends (1). More recently, public health registries have been established to follow individuals who share or likely share common exposures (2). These exposure-based registries are often established when the health outcomes associated with an exposure are not well-known. They can help identify at-risk populations, lead to a better understanding of exposure-disease associations, and allow for follow-up of exposed individuals as more knowledge is gained about potential health consequences (2). Registries have evolved from databases that are useful for determining the incidence or prevalence of a disease into robust applications allowing for evaluation of clinical programs and promoting efficient delivery of individual patient care (3).

The Department of Veterans Affairs (VA), the largest integrated health care system in the U.S. (4),

has developed numerous registries aimed at optimizing care provided to U.S. veterans. While many of these registries follow the traditional registry model of identifying and tracking veterans with a specific health condition, such as diabetes or amyotrophic lateral sclerosis (5, 6), others focus on cohorts presumed exposed to a hazardous material, such as Agent Orange or Depleted Uranium (4). By collecting both demographic and health information on cohorts of veterans, the VA can quickly offer health information and care recommendations to affected individuals as new information becomes available and contribute epidemiologic observations about specific populations at risk.

In addition to offering care to 5.6 million individuals at over 1,400 medical centers and clinics nationwide (7), a unique advantage that the VA has over other U.S. health networks in developing registries is that the VA has incorporated the use of a comprehensive electronic medical record into inpatient and outpatient practices. This electronic medical record includes medical documentation, physician orders, pharmacy records, imaging results, laboratory data, and other information for all veterans receiving care within the VA system (8). Because a wealth of information is captured, the VA's electronic medical record can be a valuable tool for identifying cohorts of veterans at the national level and for populating registry databases. This paper discusses how a newly developed registry will exploit the electronic medical record system and other data sources to: 1) identify affected veterans, 2) conduct medical surveillance, and 3) determine potential health effects associated with a chronic exposure in a unique population of veterans who have wound contamination with retained embedded fragments.

Background

Traumatic injuries from blasts or explosions, resulting from contact with improvised explosive devices (IEDs), have become the 'signature wound' for soldiers serving in the current Iraq and Afghanistan conflicts. According to Department of Defense (DoD) estimates, more than 44,000 U.S. soldiers have incurred these types of injuries which commonly involve wound contamination with foreign material, such as metal fragments, plastic components, or organic matter (9). Surgical guidelines often recommend removing fragments only if they are in a joint space, near a vital organ, or can be easily removed (10). Often fragments are not removed because of the increased risk of surgical morbidity due to their number or location. For this reason, in addition to acute effects associated with traumatic injury, other health effects may result from chronic exposure to toxic material found in embedded fragments retained in the body. Although the nature and degree of potential health risks associated with embedded fragments are likely a function of fragment content, size and location, evidence suggests that embedded materials, such as metals, can cause harm both locally to the area immediately surrounding the fragment and/or systemically to body systems as the chemical components of the fragment are absorbed and circulated by the bloodstream.

Local effects

Foreign bodies implanted in tissue have been well documented to elicit an inflammatory response triggered by cellular mediators resulting in local tissue damage (11). As well, inflammation can play an important role in the carcinogenic process (12). Encapsulation of a foreign body with fibrous tissue is the primary immune mechanism utilized to protect the body from an embedded material. Animal models have revealed an association between this foreign-body-induced inflammation and carcinogenesis (13). Other work in animal models has shown that reactive oxygen and nitrogen species from inflammatory cells are involved not only with initiation of carcinogenesis but with progression to the malignant phenotype (13). Because of the complexity of the carcinogenic process and the dependence of foreign body carcinogenesis on the physical properties of the fragment (13, 14) not all embedded fragments result in tumor formation.

In animal studies, evidence shows that metals implanted into soft tissue can cause carcinogenic changes in surrounding tissue (15). Regarding metals used for armor and munitions, Hahn and colleagues (16) demonstrated that Depleted Uranium, a metal alloy previously used in tank

munitions, when implanted into the soft tissue of rats resulted in sarcoma formation. In addition, rats with a tungsten alloy (which was proposed to replace lead and depleted uranium in munitions) implanted rapidly developed high-grade pleomorphic rhabdomyosarcomas in soft tissues surrounding the implant which metastasized to the lung (17). While these effects may be related to foreign body carcinogenesis, the metal may also be acting as a chemical carcinogen. As discussed below metal ions are released from the fragments and can be found in the systemic circulation; therefore, free metal ions are available locally as well.

Mechanisms of metal carcinogenesis include inhibition of zinc finger-containing DNA repair enzymes (for example arsenic, cadmium and chromium), formation of DNA adducts and other cross-links as is seen with chromium, and epigenetic mechanisms such as DNA hypomethylation as a result of the methylation of arsenic prior to excretion of the metal (18). Metals can also lead to the formation of free radicals resulting in DNA damage (18). Although a link between cancer and embedded fragments resulting from military operations has not been established in humans, the evidence of foreign body carcinogenesis from other embedded materials establishes the biologic plausibility for such an outcome (13, 14) and suggests vigilance in surveillance of affected populations for early effects.

Systemic effects

Historic studies with retained lead bullet fragments have demonstrated modest elevation of blood lead levels presumably due to systemic absorption of lead (19, 20). More recently, studies show that metals, such as cobalt, chromium and nickel, are released into the circulation of patients after implantation of orthopaedic medical devices (21-23). This is supported by evidence of elevated metal concentrations in the urine of patients who receive orthopaedic devices (24). Similarly, researchers have found elevated urinary uranium concentrations in individuals with embedded fragments who were exposed to depleted uranium munitions (25-28).

Due to these observations and limited knowledge of the long-term potential for health risks associated with embedded fragments, the U.S. Veterans Health Administration (VHA) has established a national registry and medical surveillance program for veterans with embedded fragments. This registry has been established within a comprehensive surveillance program which offers urine biological monitoring and fragment analyses services to assess exposure and conducts studies to identify early evidence of potential long-term health outcomes associated with embedded fragments. Data are also being used to develop medical and surgical management guidelines for veterans with embedded fragments. We describe the construction of this surveillance center and registry and discuss preliminary data collection results here.

Methods

Informing the surveillance center design – initial steps

In developing the Toxic Embedded Fragment Surveillance Center, a team of physicians, nurses, toxicologists and other researchers conducted an analysis of existing data sources to establish a framework upon which to build this new endeavor. These key data sources included available fragment composition data from patients who had previous surgical removal of fragments, as well as an extensive literature review of the pathology and natural history of embedded fragments. Because many of the embedded fragments were composed of metal, reviews focused on patients with retained bullets and other metal related traumatic injuries. Analogies between metal fragments and orthopedic implants led the team to extensively review that literature including recent studies raising concerns about certain health risks from these implants. The team then convened an expert advisory panel meeting.

The purpose of the meeting was to review current knowledge in the scientific disciplines that could best inform decisions regarding the potential for health effects from retained fragments. Experts in the fields of metal toxicology, animal pathology and medical device implants were convened. The group shared ideas on how best to determine the risk of systemic toxicity and/or cancer related to embedded fragments. The meeting also focused on identifying

the methods available for monitoring veterans for early indications of adverse effects that can range from the development of cancers in the vicinity of the fragments to target organ toxicities from systemic release of chemical components of the fragments. Biological monitoring techniques and other components of a medical surveillance program such as radiological imaging were discussed.

These initial steps helped refine the specific objectives of the surveillance center and identify services and functions required to operate a center. These functions include fragment content characterization, biological monitoring and medical surveillance of affected veterans, and establishment of a registry of this population (fig. 1).

Registry case identification

One of the preliminary steps in developing a registry or any surveillance program is to develop a case definition for the population to be included in the registry. For this purpose, the surveillance team defines a case as any veteran who served in Afghanistan or Iraq who has or likely has a retained fragment as the result of an injury received while serving in the area of conflict. Cases are stratified based on their probability of having an embedded fragment which is determined using a two step process incorporated into the VA's electronic medical record system. In Phase 1, VA medical care providers are instructed to ask veterans "Do you have or suspect you have a retained fragment as the result of an injury received while serving in the area of conflict?" If the veteran responds affirmatively, VA caregivers are then electronically prompted to ask additional questions to gather more information about the source of the injury and the presence of embedded fragments. Table 1 lists the questions used to identify cases. Responses are entered directly into the electronic medical record and are electronically transmitted to the surveillance center. Surveillance center staff then review the information to identify veterans for inclusion in the registry and recommend appropriate follow-up, which may include fragment analysis if the fragment has been removed, urine biological monitoring, and/or clinical consultation.

Determining data elements for registry inclusion

The collection of accurate, standardized and validated data is essential when developing a health

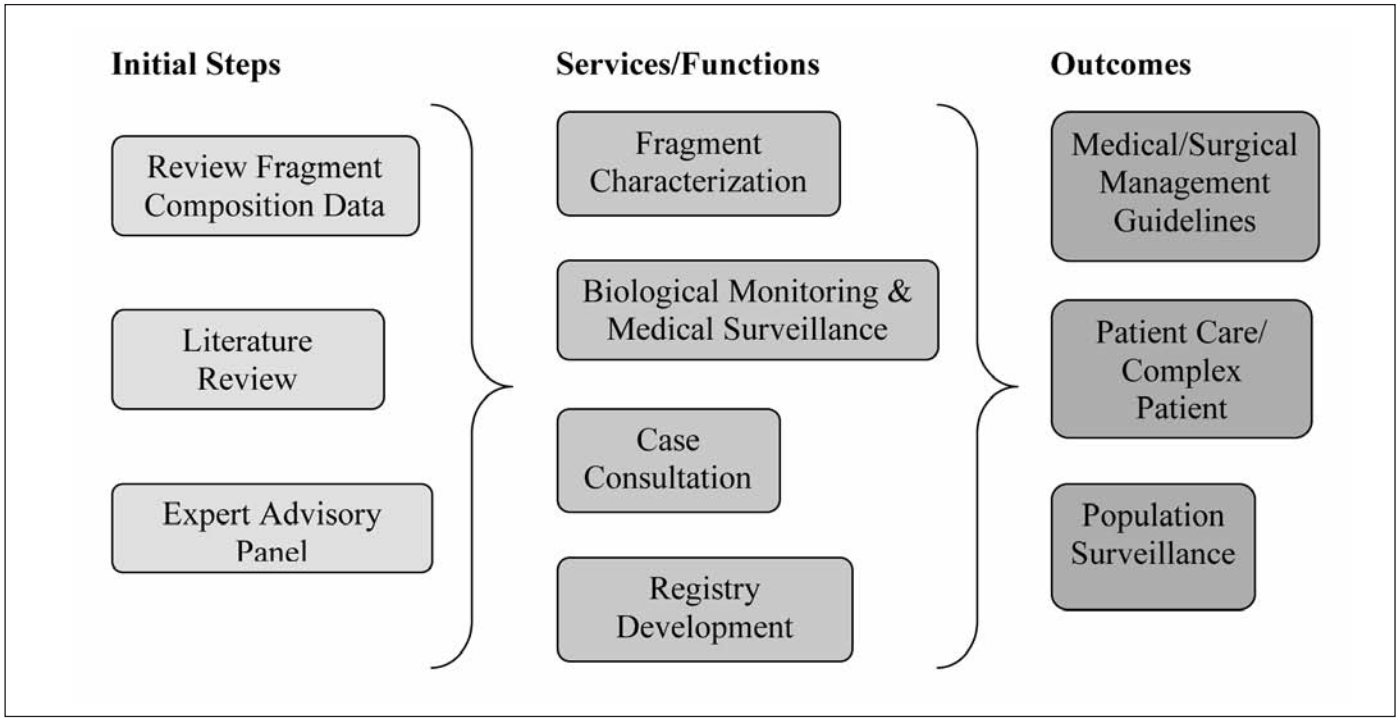

Fig. 1. Development of the Toxic Embedded Fragment Surveillance Center and Registry

Table 1 - Method for determining probability that veteran has an embedded fragment

Phase 1:

Do you have or suspect you have a retained fragment as the result of an injury received while serving in the area of conflict?

If the veteran responds 'yes', Step 2 must be completed. If the veteran responds 'no', the veteran is not eligible for inclusion in the registry and no further action is needed.

Phase 2:

- Were you injured by a bullet?
- Were you injured as a result of a blast or explosion?
  - Were you in or on a vehicle at the time of the blast or explosion?
  - Was the blast or explosion caused by:
    * Improvised Explosive Device (IED)?
    * Rocket Propelled Grenade (RPG)?
    * Land mine?
    * Grenade?
    * Enemy fire?
    * Friendly fire?
    * Don't know?
    * Other? Please describe: _____
- Did you have shrapnel, fragments or bullets removed during surgery?
  - If yes, were they sent to the lab for analysis?
- Do you have retained shrapnel, fragments or bullets in your body?
  - If yes, have they been documented by radiograph?

registry (29). The embedded fragment registry will include data elements related to case identification, demographics, fragment composition if known, urine biological monitoring, injury and exposure circumstances, and health outcomes. In order to enhance the data collection process and to avoid duplication of efforts, the registry will link with existing data sources whenever possible to collect data elements of interest (Table 2). The VA's robust electronic medical record is viewed as the authoritative data source for a number of items captured in the registry, including laboratory results and health outcomes. Other data sources, particularly the medical record which was created during the affected veteran's active duty military experience, will also be an important source of medical information for the new registry.

Fragment composition and analysis of surrounding tissue

Identification of fragment composition, when available, provides important information for assessing internal exposure and identifying potential health outcomes of interest. Laboratory collaborations have been established to allow determination of fragment composition for fragments that are removed during surgery or work their way out of the body. Each fragment will be analyzed to determine gross radioactivity, surface characterization, and whole fragment composition. In addition, histological analysis, including histochemical staining for proliferative cells, will be conducted on any tissue submitted with the fragment (Table 3). Fragment results will be entered into the registry by a surveillance center staff member. If a veteran had a fragment removed and analyzed previously by the DoD during their active duty military service, the registry will automatically capture these results from electronic DoD records.

Urine biological monitoring

Fragment composition data will help inform the biological monitoring process. Once case identification data are reviewed, surveillance center staff will contact local VA healthcare providers who will work with veterans included in the registry to obtain a 24-

Table 2 - Registry data sources

Data type	Examples of specific data elements captured in registry	Data sources
Screening data	Answers to screening questions	VA electronic files and electronic medical record system
Demographic information	Age Race/ethnicity Address	
Healthcare information	Name and contact information for veteran's VA healthcare provider Name of VA facility where veteran receives care	
Health outcome data	ICD-9 codes of interest Specific laboratory test results (i.e., blood lead tests)	
Biological monitoring data	Analytes measured Analyses methods Concentrations Creatinine adjusted values Reference ranges	Baltimore VA Laboratory database
Fragment data	Description of fragment Fragment mass Results of radioactivity testing Analytical method used to determine composition Analytes found in fragment Results associated with surrounding tissue analysis	Electronic medical record files provided by the Department of Defense from veteran's military duty history
Injury and additional exposure data	Date of injury Body part(s) that were injured Specific location(s) of fragments Treatment facility Presence of other foreign materials in the body (i.e., pacemaker or orthopaedic implant)	Standardized exposure questionnaire

hour urine specimen. The urine specimen will be mailed to the Baltimore VA laboratory for analysis. Surveillance center staff already possesses significant expertise in conducting 'distance' urine biological monitoring via mailed samples and is acquainted with the methodologic elements of both the collection and analysis of parts per trillion concentrations of metals as well as the need for clearly communicating collection and handling instructions for patients (26, 30, 31).

Creatinine adjusted concentrations of various metals frequently found in fragments will be determined using inductively coupled plasma mass spectrometry (ICP-MS). Urine metal determinations will be used to help characterize an internal exposure dose and provide insight into the composition and possible bioavailability of fragments that remain in the body. Urine biological monitoring results will be electronically transferred directly from the Baltimore VA laboratory's database into the registry.

Injury and exposure questionnaire data

Veterans submitting a 24-hour urine specimen will also complete an injury and exposure questionnaire. Examples of data elements captured from this standardized questionnaire, included in Table 2, are

Table 3 - Fragment analysis and urine biological monitoring protocol

Fragment analysis	Chemical analysis of removed fragments		
	Surface chemistry		
	Total fragment composition		
	Analysis of tissue surrounding fragments		
	Chemical analysis of tissue		
	Characterization of tissue morphology		
	- Histology: proliferative cells, neoplastic cells		
Urine biological monitoring	Toxicants of interest		
	Aluminum	Copper	Uranium
	Arsenic	Iron	Tungsten
	Cadmium	Manganese	Zinc
	Chromium	Nickel	
	Cobalt	Lead	
	Frequency of testing		
	Perform baseline urinalysis		
	Perform periodic follow-up based on baseline results		

related to injury and exposure circumstances. Although options that would allow questionnaire data to be automatically captured in the registry are being investigated, currently surveillance center staff will enter the data.

Results

Identification of cases

The first phase of the case identification process was implemented throughout the U.S. Veteran's Affairs health system in October 2008. Of 173,000 Iraq and Afghanistan veterans who were asked "Do you have or suspect you have a retained fragment as the result of an injury sustained while serving in the area of conflict?", initial data indicate that approximately 3.2% or about 5,600 of these veterans answered in the affirmative, thus meeting the case definition for registry inclusion. The second phase of the case identification process, which gathers additional information about the injury and presence of embedded fragments, was implemented in November 2009. While fully aggregated data from the second phase of the case identification process are not yet available, pilot data suggests that the majority of injuries, which triggered the affirmative response to the first screening question regarding the veteran possibly having a fragment, are related to blast or explosion injuries caused by improvised explosive devices.

Health outcomes

During registry development, the surveillance center team reviewed the toxicological properties of the chemical contents frequently found in embedded fragments. They also reviewed available animal and human data to identify potential health effects associated with exposure to these chemical agents. Although health outcomes specifically associated with embedded fragments are not well-defined, based on this toxicological review of the common metal contents of these fragments, the team identified key target organ systems including the renal, hematopoietic, immune, and reproductive systems as important targets of surveillance of affected veterans. These target organ systems were then mapped to potential health outcomes also to be included in the surveillance battery. From the information already stored in the VA's electronic medical record system, the team identified specific ICD-9 codes and clinical laboratory tests associated with the health outcomes of interest to capture in the registry.

Fragment composition data

In 2007, the DoD established a policy that required all fragments from injured soldiers removed during surgery to be analyzed for chemical composition (32). As a result of this policy, hundreds of fragments have been analyzed to date. Data from the Armed Forces Institute of Pathology indicate that the majority of fragments are metal alloys containing iron, copper, aluminum, nickel, lead, zinc and trace amounts of other elements (fig. 2). In addition, several nonmetal fragments, consisting of stones, plastics, or other organic matter, have been analyzed. This information helped to identify the suite of analytes to include in the biological monitoring protocol. Moving forward, fragment composition data will continue to be used to inform the biological monitoring process and will assist in identifying biomarkers of early effect for individuals.

Urine biological monitoring data

Informed by fragment analysis, a suite of metals has been identified as a basic battery for embedded fragment patients. Laboratory collaborations have been established to allow urine samples to be analyzed for the 13 metals included in Table 3. The surveillance center team chose these metals based on available fragment composition data and the potential toxicity/carcinogenicity of each element. Urine biological monitoring results combined with available health data will help identify how frequently biological monitoring should occur.

Because urinary measurements of the metals selected are not routinely performed in clinical practice and therefore laboratory norms are not well established, creatinine adjusted concentrations of the various metals will be compared to National Health and Nutrition Examination Survey (NHANES) data when available. The NHANES dataset derives from a nationally representative sample of the U.S. population and is conducted by the U.S. Centers for Disease Control and Prevention (CDC) (33). In instances where NHANES data are not available, the surveillance center team reviewed the literature to identify reference ranges for unexposed populations. Table 4 shows available reference data that will be used initially for comparisons of patient results.

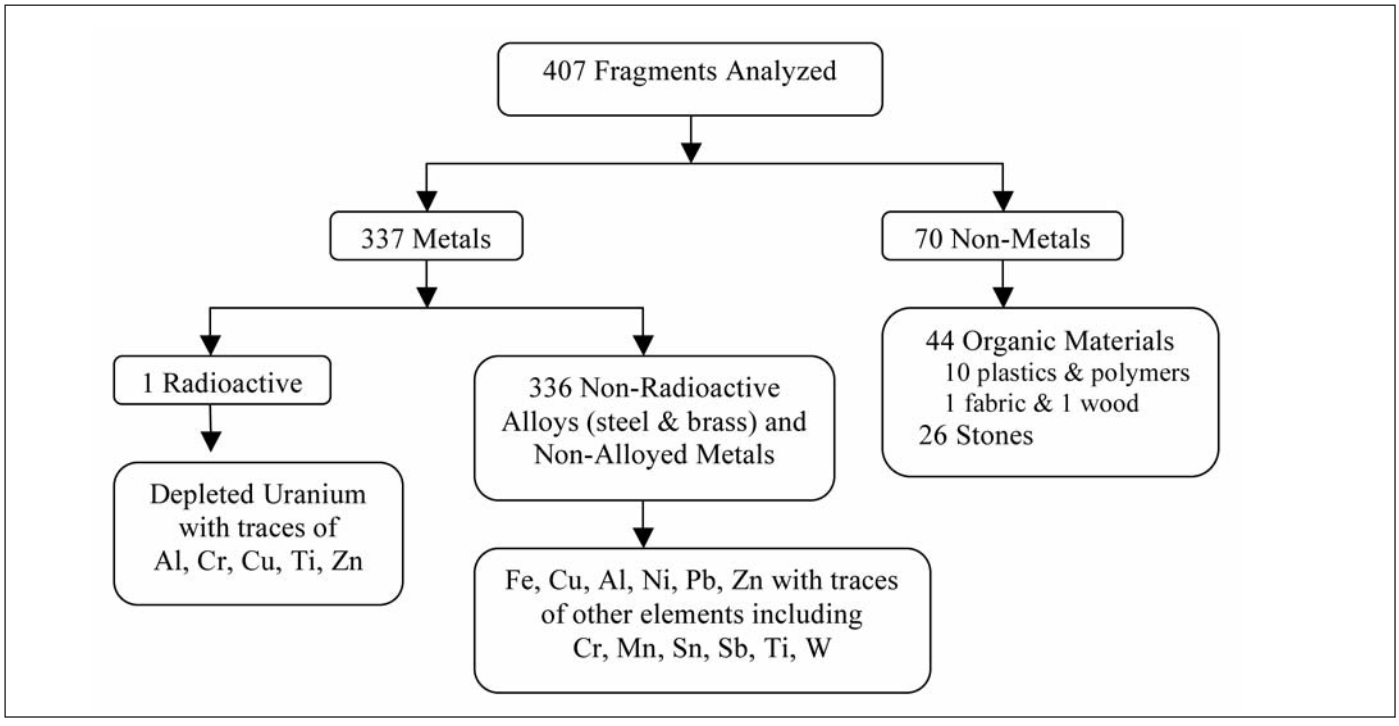

Fig. 2. Fragment composition data for selected fragments removed from military personnel: 2006-2008
Data from the Armed Forces Institute of Pathology (J. Centeno, personal communication, 2008)

Table 4 - Comparison urine metal concentrations

	NHANES Geometric Mean[a]	NHANES 95th Percentile[a]	Upper Range of Clinical Labs Data[b]
Analyte	μg/g cre	μg/g cre	μg/g cre
Arsenic	8.64	53.90	-
Aluminum	-	-	10.0
Cadmium	0.27	1.02	-
Chromium	-	-	2.0
Cobalt	0.29	0.98	-
Copper	-	-	50.0
Iron	-	-	300.0
Lead	0.64	1.94	-
Manganese	-	-	2.0
Nickel	-	-	10.0
Tungsten	0.06	0.28	-
Uranium	Not calculated	0.03	-
Zinc	-	-	1300.0

[a] 2003-2004 NHANES Data for Adults 20 years of age or older (33)
[b] Converted from μg/24-hour to μg/g cre using 1.00 g cre/24-hour (34-36)

Preliminary injury and exposure questionnaire data

To date, 35 veterans included in the registry have submitted a 24-hour urine sample for urine biological monitoring. Although urinary metal concentrations have not yet been determined, descriptive statistics have been used to summarize data from completed injury and exposure questionnaires received with the 35 urine samples. As shown in Table 5, the majority of these veterans (91.4%) reported injuries related to a blast or explosion. In many cases (59.4%) the blast or explosion was caused by an improvised explosive device and occurred while the individual was in or on a vehicle (61.5%). In addition, less than half of the veterans (42.4%) reported that a fragment was removed during surgery, the majority (78.6%) were unsure if the removed fragment was analyzed, and two-thirds (66.7%) indicated that they had retained fragments in more than one body part area. These data, which describe the characteristics of injury, will continue to be used to inform the urine biological monitoring and overall surveillance process.

Discussion

The Embedded Fragment Registry provides a comprehensive, systematic method for collecting data on veterans who have embedded fragments and its linkages with the VA electronic medical record offers several advantages. Principally, the registry links with the VA's robust national electronic medical record system which permits capture of health information on all veterans who receive care at a VA facility. This medical record system also offers a uniform mechanism for actively identifying veterans with embedded fragments nationwide. By linking with the medical record, the registry database can extract case identification information and access already collected laboratory and health outcome data for each veteran in an efficient manner. It also ensures that data collected are consistent across data sources.

Another strength of the registry is the ability to include information about exposure from a variety of sources. Exposure data are often limited or unknown in population surveillance; however, the registry will capture self-reported exposure data from questionnaires and integrate it with other exposure metrics, including urine biological monitoring results and information from fragment analysis. This information can then be used to better characterize and correlate the various types of exposure metrics.

Data collected from the injury and exposure questionnaire can be used to describe injury trends and identify other potential materials for inclusion in the urine biological monitoring protocol. For instance,

Table 5 - Characteristics of injury in veterans requesting biological monitoring

Survey Question and Response	Number of veterans (%)
Injured by:	
Bullet	3 (8.6)
Bullet and blast or explosion	3 (8.6)
Blast or explosion	29 (82.9)
Total number of respondents[a]	*35*
In or on a vehicle at the time of the blast or explosion	
Yes	16 (61.5)
No	10 (38.5)
Total number of respondents	*26*
Blast or explosion caused by an improvised explosive device	
Yes	19 (59.4)
No	13 (40.6)
Total number of respondents	*32*
Retained fragments in body	
Yes	30 (85.7)
No	1 (2.9)
Unknown	4 (11.4)
Total number of respondents	*35*
Identified more than one body part area where retained fragments are located	
Yes	20 (66.7)
No	10 (33.3)
Total number of respondents	*30*
Shrapnel, fragments or bullets were removed during surgery	
Yes	14 (42.4)
No	19 (57.6)
Total number of respondents	*33*
Fragments removed during surgery were sent for analysis	
Yes	1 (7.1)
No	2 (14.3)
Unknown	11 (78.6)
Total number of respondents	*14*

[a] Total number of respondents submitting sample for biological monitoring = 35. Some questions were not answered by some veterans.

knowing that a large percentage of veterans are injured by a blast or explosion while in a vehicle suggests that fragments retained in the body may be composed of material from the vehicle. Therefore, the urine biological monitoring protocol may need to be expanded to include these types of materials.

Comparing urine biological monitoring results to available fragment data can help increase our understanding of exposure, metal absorption in the body, distribution in human tissue, and excretion. Additionally, this information, along with current literature reviews and knowledge of toxicants, will assist in refining the list of potential health outcomes of interest.

Overall, registries and surveillance programs need to do more than just store data. When designed appropriately, these programs allow the captured information to be analyzed and interpreted. Epidemiological analysis of the data will ultimately help estimate the prevalence of embedded fragments for Iraq and Afghanistan veterans who receive care within the VA, describe the population at risk, identify

potential health effects, inform medical management guidelines for providing care to veterans who have embedded fragments, and assist the VA in planning health services.

Conclusion

According to DoD estimates, more than 44,000 U.S. soldiers of the Iraq and Afghanistan conflicts have been victims of blast injuries potentially resulting in retained embedded fragments (9). Due to limited toxicological data on the human health effects associated with embedded fragments, the Department of VA has established the Toxic Embedded Fragment Surveillance Center and Registry. The registry will capture data needed to characterize exposure and identify trends in disease patterns. Importantly, as patients with embedded fragments are experiencing 'on-going' exposure to the toxic contents of their embedded fragments, surveillance data may provide 'real time' feedback to clinicians which may affect a patient's individual medical management and inform population management guidelines.

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