Dispersion of volatile toxic industrial compounds presents a major threat to nearby residents [1-4]. A scenario of volatile toxic industrial compound dispersion may occur due to an industrial accident (in a plant or during transportation) or from an act of terrorism [1-4]. Central and regional health systems worldwide have therefore developed various response policies to mitigate such an event [1,4-10]. Preparation begins with a thorough understanding of the threat and with development of simple and efficient countermeasures [8]. Important lessons that we have learned from our training sessions and other mass casualty events worldwide have determined the value of the implementation and training of simple response algorithms by first responders as well as appropriate protection of health care providers [11,12].

We have developed a simple yet comprehensive doctrine in order to deal with any toxicological mass casualty event, including chemical terror events. The main issues addressed by the doctrine are outlined in Box 1.

**Box 1. Outline of the proposed management of TMCE**

- **TMCE threat analysis**
  - Strategic level
  - Tactical level

- **Pre-hospital response**
  - Preparedness
  - Recognition / Identification
  - Self-protection & warning
  - Life-saving treatment
  - Rescue & evacuation

- **Hospital response**
  - Preparedness
  - Decontamination
  - Definitive medical care
  - Immediate psychological care

**The threat of TMCE**

On a national strategic level, the main causes of TMCE include accidental events such as industrial malfunction or accidental release either from a factory or during transport, e.g., the Bhopal accident in 1984 [13]. On the other hand, TMCE due to chemical terrorism may result from the acquisition of the classic chemical warfare agents [4], or the manufacture of “home-made” chemical warfare agents in small and primitive laboratories, e.g., the Matsumoto and Tokyo sarin attacks in 1994 and 1995, respectively [14,15]. Another significant threat may be the deliberate attack on a toxic industrial compound reservoir, including tankers, trains, etc. [1]. There is a long list of potential offending chemical agents [16], including the classic chemical warfare agents, pesticides and toxic industrial compounds.

Several tactical characteristics of a chemical terror event raise important considerations at the level of first responders:

- **Type of attack**: Is the attack covert? e.g., dispersing a toxic compound in a shopping mall, or overt, e.g., detonating a bomb containing an agent [4]. The identification of a covert event may be delayed, thus complicating response
and treatment. Moreover, in the covert scenario it is expected that the diagnosis and treatment will be managed by second-line health care providers such as hospitals and community medical facilities and not first responders. It is assumed that an overt event will be immediately determined and treated by first responders in the field.

- Exposure: It is presumed that in both scenarios, inhalational exposure is the most probable threat since most agents are easily absorbed through the respiratory tract and people do not normally carry protective gear. Based on this assumption and the relatively high toxicity of some of the potential offending agents [7], we presume that such an event will result in a massive amount of casualties, especially in the more vulnerable populations, such as children, pregnant women and the elderly. It is important to emphasize that persistent agents such as VX pose huge logistical considerations, including possible massive evacuation for a prolonged time, complex surface decontamination, and safety issues regarding the contaminated area – namely “how clean is safe.” This further highlights the importance of thorough decontamination of casualties before they enter the hospital.

- Warning: In the absence of an early warning, first responders will arrive and function as usual. Only if they become aware of an unusual cluster of signs and symptoms would the involvement of a chemical agent be suspected. At that point, the first responders would put on their protective gear and treat the casualties. Therefore, it is reasonable to presume that the first rescue teams on scene may also be exposed and might even be affected.

Emergency medical teams are expected to enter the contaminated site, treat the casualties and evacuate them as soon as possible. At the same time, it is important to make sure they will be able to work while using appropriate personal protective equipment. By using the industry nomenclature, level A and B protection (self-contained breathing apparatus with fully/partially encapsulating chemical protective suit) is not a good solution even though it provides utmost protection. Working under this protection level is extremely fatiguing and is accompanied by massive sweating and risk of dehydration, thus reducing their ability to perform necessary medical procedures [17]. Our medical teams therefore use Level C protection (full-face air-purifying respirator and chemical-resistant coveralls), which enables responders to work efficiently in the contaminated area.

### Identifying the event: suspicious elements and clinical signs

Most detectors currently available for field use are limited in both the diversity and specificity of detection (they recognize atoms of sulfur and phosphorous). Hence practically, these detectors can be used for confirmation only after the suspicion of a chemical involvement has been raised. There are several crucial suspicious findings that should alert first responders to the possibility of a toxicological event [4]. They include unusual environmental signs, such as atypical smoke or colored residue, atypical smell, ill or dead animals, and a visible active source (such as a container or a pipe). Other findings include fewer trauma injuries than expected, the appearance of similar clusters of signs and symptoms in otherwise healthy people (toxidromes) [18], and the appearance of the same toxidromes among first responders arriving unprotected. Based on the potential offending agents, four major toxidromes, which are applicable to most scenarios, are defined (Table 1).

### Medical management of TMCE in the field

This stressful scenario warrants a quick and efficient reaction. Any mistake in management of the event might end in devastating consequences with additional casualties, some of them EMT personnel. Therefore, once a toxicological event is identified, EMTs must act according to simple and effective guidelines. We have defined an algorithm [19], which is currently practiced by all first responders in Israel for any TMCE scenario [Figure 1]. This algorithm was shown to be efficient in numerous national exercises and drills.

The first and most important step after realizing that a chemical agent is involved is to warn all other relevant emergency teams and their headquarters [7]. These kinds of events will be under the command and coordination of the police forces. At the same time EMTs on site must immediately put on their protective equipment. Physical protection will prevent secondary exposure as a result of handling the casualties. This was highlighted in

#### Table 1. Major anticipated toxidromes in TMCE

<table>
<thead>
<tr>
<th>Toxidrome</th>
<th>Agent</th>
<th>Hallmark</th>
<th>Clinical signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinesterase inhibition</td>
<td>Organophosphates, carbamates</td>
<td>Cholinergic syndrome with miosis, increased exocrine secretions (muscarinic effects), fasciculations &amp; paralysis (nicotinic effects) and central nervous system effects</td>
<td>Miosis, dim vision, eye pain, headache, rhinorrhea, salivation, lacrimation, urination, defecation, sweating, chest tightness, wheezing, fasciculations, paralysis, cognitive impairment, seizures, coma</td>
</tr>
<tr>
<td>Irritants</td>
<td>Chlorine, ammonia, phosgene, CS*</td>
<td>Respiratory tract, skin and ocular irritation</td>
<td>Nose irritation, sore throat, cough, chest tightness, eye irritation, wheezing, stridor, acute lung injury</td>
</tr>
<tr>
<td>Asphyxiants</td>
<td>Cyanide, carbon monoxide</td>
<td>Tissue hypoxia resulting in cardiovascular and CNS depression</td>
<td>Headache, fatigue, dizziness, nausea, anxiety, dyspnea, altered mental status, cardiac ischemia, syncope, coma, seizures</td>
</tr>
<tr>
<td>Vescicants and skin caustics</td>
<td>Sulfur mustard, lewisite, phosphene oxime</td>
<td>Skin burns, respiratory irritation &amp; acute lung injury and ocular injury</td>
<td>Conjunctivitis, erythema, sore throat, cough, corneal damage, vesicles &amp; bullae, nausea, wheezing, stridor, laryngeal edema, acute lung injury</td>
</tr>
</tbody>
</table>

EMT = emergency medical team

* CS is a riot control agent
the Tokyo sarin attack in 1995, where 10% of the first responders and hospital personnel suffered from mild signs of poisoning following secondary exposure to sarin [14].

After understanding that an ongoing incident is a toxicological event, the next step in the algorithm is to decide whether the toxic agent is an organophosphate or not [19]. It is of utmost importance to distinguish organophosphates from other toxic substances, since the former are highly toxic agents for which there are effective and available antidotes that should be implemented immediately at the site of the incident [20,21] as any delay in administration entails grave consequences [22]. Organophosphate poisoning is characterized by a violent cholinergic crisis, with a rather unique combination of clinical signs and symptoms as detailed in Table 1 [23] which could be easily diagnosed following proper training [20,21]. Although cyanide is also a highly toxic agent, for which specific antidotes exist and are available, cyanide intoxication is not characterized by a specific toxidrome, which makes it difficult to identify on-scene without prior knowledge. A false positive clinical diagnosis of OP poisoning, e.g., as a result of opiate intoxication which is manifested by miosis, dyspnea, and altered mental state, is a strategic weak point with possible serious consequences on a national scale. Such a false alarm may have substantial economic impact, mass psychological effects [7] and may even lead to decisive retaliation actions in case of a terror event. In addition, a false positive clinical diagnosis will result in mistreatment of non-OP casualties, which may be harmful. Reduction of the chances for a false positive diagnosis requires increased specificity. In order to increase the specificity of the clinical diagnosis of OP poisoning we suggest that first responders in a mass casualty event initiate the organophosphate algorithm only when at least three casualties are clinically diagnosed with poisoning, of whom at least one

Figure 1. Algorithm currently used by emergency medical teams in Israel in mass casualty events

Table 2. Casualty classification following OP poisoning, showing the classification method used by Israeli medical teams

<table>
<thead>
<tr>
<th>Classification</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Ambulatory casualty with mild signs of OP intoxication</td>
</tr>
<tr>
<td>Moderate</td>
<td>Non-ambulatory casualty with moderate to severe signs of OP intoxication, without the need for ventilation</td>
</tr>
<tr>
<td>Severe</td>
<td>Non-ambulatory casualty with severe signs of OP intoxication, and in need for ventilation</td>
</tr>
<tr>
<td>Combined</td>
<td>Any casualty with both trauma injuries and signs of OP intoxication</td>
</tr>
</tbody>
</table>

is moderately to severely injured. According to that, the presence of mild casualties solely would not be considered an OP event according to the algorithm due to the high potential for false positive diagnosis and low cost of error. The medical triaging system we have developed assists first responders to evaluate severity of injury, as detailed in Table 2 [24].

Pre-hospital medical countermeasures

After defining the event as an OP event, antidotal treatment should be given as soon as possible, together with supportive care and resuscitation measures as needed. The classical antidotes include atropine and oximes [20] (as combined auto-injectors). In case of seizures or decreased consciousness, benzodiazepines should be administered as anticonvulsants and for their neuroprotective effect [22,25]. We recently demonstrated that a bone injection gun is a simple method for introducing an intravenous line for administration of anticonvulsive drugs that could be applied while wearing a protective suit [26]. Another possibility, which is currently controversial, is the administration of the centrally acting anticholinergic drug scopolamine, which has proven central nervous system protective effects, mainly as pretreatment or shortly after OP intoxication in animal models [20,25,27]. We previously recommended scopolamine as an alternative antimuscarinic drug for OP poisoning in patients with adverse reactions to atropine [28]. We believe scopolamine may have an important role in preventing brain damage and long-term neurological sequelae caused by organophosphates. Due to the extreme importance of early antidotal administration we recommend that any ambulance responding to these calls carry a supply of auto-injectors such as atropine or a combination of atropine and an oxime (intended to be used by all medical staff, including trained volunteers). These recommendations are currently implemented by all Israeli EMTs.

Other toxic industrial compounds provoke primarily a respiratory insult, in which case oxygen supplementation, general resuscitation measures and supportive care are the key components of the emergency medical treatment. Other important components include undressing the casualties and evacuating them as soon as possible. We have come to the conclusion that in Israel there is no place for casualty decontamination “on scene” in a TMCE event, since it is too time consuming and probably would not improve the outcome. Moreover, the current capabilities of an on-scene decontamination set-up are clearly insufficient for the
immediate decontamination of possibly hundreds of people in a matter of minutes, considering that every hospital in Israel has the infrastructure that allows “wet” decontamination before entering the hospital. In case of TMCE, emergency medical teams are instructed to undress casualties inside the ambulance, on route to the hospital, while in full protective gear. The rationale is to ensure that the casualties reach a definitive medical facility as soon as possible (“scoop and run”). On the way, they will receive antidotal and resuscitative treatments as needed. This approach takes advantage of the short evacuation distances in Israel. We do not have a good solution for the contaminated ambulances, which is a significant drawback of this approach especially in case of persistent agents; however, it was decided on a national level that saving lives is a priority. We are now in the process of testing several approaches to resolve this problem.

Rescue and evacuation

Israeli EMTs consist of physicians, paramedics, medics and volunteers. All EMT personnel receive CBRN medical training at least once a year [29], when we stress not only recognition and treatment protocols but also the importance of simultaneous team work. Moreover, we have developed a unique simulation-based training for EMTs to manage CBRN casualties, which allows evaluation of learning and performance over time [30].

As mentioned earlier, EMT personnel wear level C protection*. Other rescue teams, including the Israeli environmental protection agency, the fire fighters and some of the police forces wear level A protection. All rescue teams should help to evacuate casualties in addition to their basic missions. All personnel must wear identification labels indicating their role. An important safety rule is to work in groups and not individually, thus enabling fast identification and resuscitation for casualties, as well as for planning. In case of a large accident, teams of the Israeli Environmental Protection Agency by combining risk assessments and field detection.

Upon reaching the scene, teams of medical personnel set up an organized grid to search for casualties. They try to recognize the offending agent by looking for typical clinical signs and symptoms, and administer antidotes if needed. If an antidote is given, it will be marked with a plastic tag around the neck of the casualty. Marking is performed by ripping the tag in the appropriate places (Figure 2). The plastic tag is decontaminated along with the casualty at the entrance to the hospital, thereby enabling the hospital staff to know exactly what medical treatment has been administered so far. Based on our experience, other measures are not as useful. For example, writing on the casualty will be erased during decontamination, and paper forms are impractical while wearing protection and may get lost or damaged.

The evacuation process begins from the periphery and works towards the center. For rescue members with level C suits, the No-Entry line on scene in an indoor event is defined as the point in which bodies are encountered. This was defined after a risk assessment analysis showed that the level of toxic industrial compound or chemical warfare compound in a closed space that was enough to kill a person could penetrate level C protection.

Evacuation consists of short rounds out of the contaminated area. Undressing casualties will take place inside the evacuation circles once a year [29], when we stress not only recognition and treatment protocols but also the importance of simultaneous team work. Currently, every ambulance in the country is equipped with a mobile computer linked to a GPS (Global Positioning System), and once a chemical incident is suspected, the EMT headquarters delineate this circle on the screens of all ambulances in the area. The exact borders of the isolation area are defined later on, more accurately, by teams of the Israeli Environmental Protection Agency by combining risk assessments with field detection.

* Level A: Maximum protection against vapor and liquids. Environment known to be immediately dangerous to life and health (harm occurs within 30 minutes). Fully encapsulating, chemical-resistant suit, gloves and boots, and a pressure-demand supplied air respirator (air hose) and escape self-contained breathing apparatus (SCBA).

* Level B: Non-encapsulating splash-protective chemical resistant suit (splash suit), chemical-resistant gloves and boots/shoes, and a pressure-demand supplied air respirator (air hose) and escape SCBA.

* Level C: The same level of skin protection as Level B, but a lower level of respiratory protection is needed (i.e., air-purifying respirators).
vehicle in order to prevent any delay. Mildly injured casualties can be guided by foot outside the isolation area, while moderate to severely injured casualties, who are by definition non-ambulatory [Table 2], will be carried on stretchers or in any other way (including ambulances if available) outside the isolation. At the same time, due to an anticipated lack of sufficient evacuation platforms, EMTs should prepare several medical field stations at the margins of the isolation for treatment on-site.

If the nearest hospital is within a short enough distance from the incident (up to 5 km), evacuation would be conducted immediately with now contaminated vehicles. If the nearest hospital is at a greater distance, short evacuation rounds will be conducted using contaminated vehicles or stretchers to the margins of the isolation. From there casualties will be taken by "clean" ambulances. Any re-entry to the contaminated area will be approved only after a quick medical evaluation of the team in order to eliminate the danger of heat stroke or accidental exposure to the offending agent.

Hospital preparedness
Hospitals are notified as soon as possible by both the medical command center of the home front command and the EMT command center, with instructions for recruiting off-duty medical personnel. Information to the hospitals should include an estimation of the casualties' number and status and the offending agent. After receiving the information, the hospital declares a chemical incident situation and as many patients as possible are transferred from the emergency department into other departments. Several physicians and nurses in the emergency department open emergency kits and put on level C protection gear, after which they step outside to receive the casualties, taking with them an antidote kit prepared in advance that contains atropine and oximes in auto-injectors. The non-medical personnel function as the decontamination staff. They wear protection and activate emergency showers situated at the entrance to the emergency department. These showers are present in most hospitals throughout the country. Each casualty is decontaminated upon arrival by two members of the decontamination staff. During and immediately after, antidotal treatment with auto-injectors or any urgent life-saving intervention, including ventilation, is given. Only then will the casualty be taken into the clean zone in the emergency department for full medical treatment, including specific tests for cholinesterase inhibition. In case of severe combined injuries (trauma injuries with signs of poisoning), casualties will be taken without decontamination to a separate section in the emergency department for emergency stabilization [31]. In case of a volatile agent or an unknown agent, the medical staff will use an active protection hood and double latex gloves. Only in cases of identified persistent agents (such as VX) will treatment be given and only after full decontamination.

Immediate psychological care
Several studies have examined stress-related mental health symptoms and coping behaviors following terrorist attacks. For example, studies on the impact of 9/11 found that people who experienced the attack directly showed elevated level of distress, lowered sense of security, and pathological conditions such as post-traumatic stress disorder and depression [32]. Moreover, even people (mainly children) who experienced the event indirectly, such as through the media, demonstrated similar symptoms [33,34]. It is therefore reasonable to assume that following a TMCE, citizens will rapidly overflow the hospitals with symptoms related to stress reaction. The spectrum of stress-related disorders will probably include mainly acute stress reaction, anxiety with or without somatization, and concern for relatives. The number of stress-related casualties may exceed the number of physically injured casualties by a remarkable factor of up to 500 [35]. This would impair or even paralyze the capability of hospitals to provide sufficient medical treatment as well as increase the risk of post-traumatic stress disorder developing among both physically injured and stressed casualties. It is therefore necessary that, concomitant to field rescue teams, mental health professionals arrive at the hospitals. These teams should initiate treatment as soon as possible once the possibility of toxic exposure has been eliminated. This challenge highlights the need for a national central medical command that can orchestrate patient transfer between relevant medical facilities.

Summary
The relative accessibility to various chemical agents places TMCE, including chemical terrorism, among the major threats to homeland security. The complexity of a TMCE stems from the combination of mass casualties, potential further spread of the contaminant, and secondary injuries to the rescue forces as well as a severe psychological impact. This poses a considerable logistic and medical challenge to the authorities.

In the last two decades Israeli authorities have expended collaborative efforts on a strategic theoretical analysis of chemical terrorism as well as on practical management. These collaborative efforts yielded a practical doctrine fully implemented throughout Israel that has been tested in numerous national drills. Emphasis is placed on rapid recognition of the event as a chemical event, notification to the central headquarters, and appropriate self-protection. Medically, it is most important to determine whether an organophosphate is involved or not, as it dictates a different approach and treatment. In order to allow efficient work under stressful conditions, we have designed an algorithm as a simple and practical cognitive framework for first responders on the scene. Moreover, as the diagnosis of TMCE entails serious consequences for the entire population, we have defined criteria to increase the specificity of the diagnosis. Casualties will receive the optimal treatment in medical centers and not in the field. Therefore, we recommend performing only life-saving procedures (e.g., antidotal treatment) on site and a "scoop & run" approach using a pre-organized evacuation plan. This approach takes advantage of the short evacuation distances in Israel. Finally, continuous preparedness of the health system, exemplified by periodic CBRN medical training, antidotal auto-injectors in all ambulances, and CBRN emergency kits in the ED, would considerably improve the response to a TMCE.
References


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Let us enrich ourselves with our mutual differences

Paul Valery (1871-1945), French poet and philosopher