Chemical, biological, radiological and nuclear terrorism: an introduction for occupational physicians

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Background	Chemical, biological, radiological and nuclear terrorism poses considerable threat throughout the world.
Aim	To provide occupational physicians with an understanding of this threat and its main forms and what action can be taken to counter this threat.
Methods	Presenters at a conference on chemical, biological, radiological and nuclear terrorism were asked to contribute their evidence-based opinions in order to produce a review article.
Results	This paper presents a summary of the different forms of chemical, biological, radiological and nuclear terrorism and the effective counter-measures and also provides a review of current scientific literature.
Conclusion	The threat of chemical, biological, radiological and nuclear terrorism is present throughout the world and is one that occupational physicians should be aware of, as well as the action that can be taken to counter it.
Key words	Bioterrorism; chemical, biological, radiological and nuclear terrorism; terrorism.
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Introduction

Leon Trotsky [1] recognized the power of terrorism when he stated that 'War, like revolution is founded upon intimidation. A victorious war, generally speaking,

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destroys only an insignificant part of the conquered army, intimidating the remainder and breaking their will . . . Terror . . . kills individuals, and intimidates thousands.'

It has been previously argued that 'weapons of mass destruction', now more accurately known as 'weapons of mass effect', would never be used by terrorists because they would have nothing to gain by inflicting casualties on a large scale. Events of recent years have led to widespread re-evaluation of emergency preparedness arrangements by the USA, the North Atlantic Treaty Organization alliance and the European Union. The UK has a history of dealing with the consequences of conventional terrorism and has well-developed systems in place for detecting and dealing with chemical and nuclear accidents and communicable disease outbreaks. This was enhanced by comprehensive guidance and training on planning for major incidents and many individuals and institutions with an international reputation in nuclear biological and chemical defence [2-4].

This article considers examples of chemical, biological, radiological and nuclear terrorism, the agents that may be

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used, the unique psychological impact of chemical, biological, radiological and nuclear weapons and the measures in place for dealing with chemical or nuclear accidents. The specific response generated in one area of business (the UK postal delivery service) is provided as a case example of a response to a potential threat. The work of the Public Health Laboratory Service (PHLS), the Communicable Disease Surveillance Centre (CDSC) and the Centre for Applied Microbiological Research (CAMR) is adequately described elsewhere [5] and is not considered in detail here.

Some previous examples of chemical, biological, radiological and nuclear terrorism

Chemical

The Japanese Aum Shinrikyo sect has twice used sarin against the civilian population, once in Matsumoto in 1994 in which seven people died and 600 were injured [6] and again in the Tokyo Underground in 1995 [7]. Approximately 24 l of chemical agent were reported to have been manufactured approximately 48 h before the second attack. It apparently consisted of a mixture of sarin (GB) and a small amount of tabun (GA), which are two classic military nerve agents and acetonitrile that had been added to 'jump-start' evaporation. The liquid was soaked onto newspaper and contained in plastic bags transported inside umbrellas. Five different subway trains on three separate lines were attacked on 20 March 1995 at 07:55 h by 10 terrorists who punctured holes in the plastic bags.

In total, 5510 people sought medical attention in 278 hospitals and clinics, with 12 dead, 54 critical and 984 moderately poisoned, while 688 victims were transported to hospital by ambulance with over 4000 casualties reaching hospitals on foot or by private transport [8]. The reason why there were not far more casualties in such a confined space as the underground was thought to be that the strong smell of acetonitrile alerted passengers to the danger.

Biological

Bacillus anthracis spores were distributed to senators and media personalities in five envelopes through the US postal service in October 2001. Those responsible are still unknown, but the incident provoked further concern about the threat of chemical, biological, radiological and nuclear terrorism. Five people died from a total of 11 cases of inhalational anthrax, three of them postal workers. The remaining two victims had no direct contact with the anthrax letters and are thought to have contracted the disease as a result of cross-contamination of mail as it passed through the automatic handling and franking machines. There were also 11 cases of cutaneous anthrax [9]. The Brentwood Mail Processing and Distribution Center in Washington, DC, was the source of four early cases including two fatalities after handling spore-containing envelopes addressed to the Hart Senate Office Building. Sampling of surfaces and air samples confirmed widespread contamination of the building [10]. Contamination was also found in a further 11 government offices. In excess of 10 000 individuals were prescribed prophylactic antibiotics, with many more taking them of their own volition. There has been considerable speculation over the source of the particular strain of B. anthracis used and little consensus other than agreement that the production of such refined material was the work of an expert who may even have come from within one of the USA's own biodefence establishments [11].

Radiological and nuclear

In 1995, Chechen terrorists planted a bomb composed of dynamite and a ¹³⁷Cs source in Moscow's picturesque Izmailovo Park [12]. Fortunately for the citizens of Moscow, it was not detonated. More recently, an American citizen has been imprisoned for plotting to explode a 'dirty bomb' in Washington [13].

The hazards: chemical, biological and radiological agents

General considerations

There is a large variety of agents that could be used as terrorist weapons. At one end of the spectrum there are readily available toxic industrial chemicals, naturally occurring diseases and medical or industrial devices containing sources of ionizing radiation, while at the other there are new generation chemical agents, genetically modified organisms and nuclear weapons (Table 1).

Factors influencing agent choice

Effect desired and scale. The number of casualties produced will vary enormously depending on the agent. A large number of casualties or deaths may not be needed if the main aim of the terrorist is economic impact or panic. Consider the effect on the US postal service and the wider economy of three deaths in postal workers. The Hart Building was closed for months whilst it was decontaminated and the government's ability for communicating by post was paralysed.

Targets. People are the obvious target, but the recent experience in the UK with foot and mouth disease

Agent	Naturally occurring or industrial use	Potential weapons	Emerging technology
Biological	Bacteria Rickettsia Viruses	Bacteria Rickettsia Viruses	Genetically modified organisms
Chemical	Chlorine Phosgene Ammonia	Toxins Vesicants Nerve agents Psycho-chemicals	Developments from pharmaceutical and pesticide research
Radiological/nuclear	Medical sources Nuclear power plants	Nuclear Atomic	

Table 1. The spectrum of potential terrorist agents

demonstrates vividly the impact that an attack on livestock would have. Agricultural crops, other parts of the food chain, water supplies and the environment are all potential targets, most of which are very difficult to protect.

Availability of materials. As has already been demonstrated, many of the agents that could be used by a terrorist are readily available from natural or commercial sources. For use on a larger scale, more specialized production capacity would be required, along with the expertise for using it. The difficulty in detecting such facilities is that many can be hidden in or disguised as legitimate plants used in brewing or pharmaceutical manufacture. Smaller facilities can even be mobile. The quality control of the final product is unlikely to be an issue, making production easier in most cases. Alternatively, a terrorist could obtain agents from another source, including material obtained from state programmes.

Delivery means. Depending on their mode of action, agents need to be delivered to the right target at the right time and in the right quantity. Aerial delivery is the method of choice for agents acting through inhalation, hence the brief grounding of all crop-spraying aircraft in the USA in September 2001. Gases and low boiling point chemicals are relatively easy to disperse for producing an inhalation hazard. Materials such as high boiling point chemicals, biological materials and radioactive sources will either have to be pre-prepared into a size range that is buoyant in the atmosphere (below 10 µm) or disseminated by a method that produces the desired size range (e.g. by spray technology or explosive dissemination). Trials on the London Underground have indicated that bacterial spores contained in a powder box thrown from a moving train would contaminate a large part of the system within a matter of 30 min [14]. Explosive devices can be effective in disseminating any agent over a wide

area. Individuals intent on blackmail have targeted food and water supplies, e.g. the poisoning of a salad bar with salmonella, which infected 751 customers [15]. If the target is a single person, the delivery means can be as specific as the ricin-containing pellet shot from an umbrella that killed the Bulgarian journalist Georgi Markov whilst working for the BBC in 1978 [16].

Chemical agents

Nerve agents

The Aum Shinrikyo sect's ability to produce and use sarin demonstrated a level of sophistication that had previously been thought unlikely in a terrorist group. Nerve agents are organophosphorus compounds, which, like the insecticides that they are closely related to, act by inhibiting the enzyme cholinesterase. They interfere widely with the functioning of the nervous system, producing the wide range of symptoms shown in Table 2. The long-term health effects associated with the Tokyo incident are the subject of ongoing and extensive study [17], for example from a recent study comparing occupationally exposed fire and police officers with ageand sex-matched controls [18]. This study suggests that exposure may have resulted in a decline in memory function.

The emergency response to nerve agent poisoning is aimed at preventing further casualties among rescue workers. Of 1364 emergency personnel who were at the incident in Tokyo, 135 (9.9%) showed acute symptoms and received medical treatment [19]. The majority of emergency medical staff showed some symptoms [20]. Casualties should be stripped and decontaminated and their clothes bagged and sealed. Atropine is given to block the effect of high levels of acetylcholine at the muscarinic receptors and mitigates the cholinergic crisis throughout the nervous system both peripherally and centrally (helping to maintain respiration). 2-PAM (pralidoxime) is administered to reactivate the inhibited acetylcholin-

Table 2. Pharmacology of nerve agents

Receptor	Target	Effect
Muscarinic	Glands: sweat, salivary, nasal, bronchial and gastrointestinal	Increased secretion
	Smooth muscle: iris, CB, bronchial, gastrointestinal and bladder	Miosis, bradycardia, constriction, diarrhoea and micturition
Nicotinic	Pre-ganglionic synapses Neuromuscular junction	Hypertension, pallor, weakness, fasciculation and paralysis
Central	Central nervous system	Apprehension, hyperexcitability, convulsions and respiratory failure

esterase and diazepam is administered to prevent or control convulsions. Ventilation may be required for cardiac arrest. The red cell cholinesterase level is assessed in order to monitor the degree of poisoning and progress of treatment.

Blister agents

The other group of chemical agents that is likely to attract the attention of terrorists is the blister agents or vesicants, notably mustard. Sulphur mustard is a liquid with low volatility at room temperature, though it can be mixed with other agents such as lewisite to make it more volatile. Sulphur mustard is an alkylating agent that reacts readily with most biological molecules including proteins and nucleic acids. The effects of mustard are characteristically delayed as shown in Table 3.

There is no specific treatment for mustard lesions. Treatment is aimed at preventing infection, relieving symptoms and promoting healing, in much the same way as any burn [21].

Other

Chemical exposure may also be an incidental side effect of an explosive terrorist incident. Analysis of the dust/ smoke aerosol material that settled east of the World Trade Centre after 11 September 2001 gives cause for toxicological concern, e.g. for cleaning-up operations, particularly inside buildings, where residual contamination could present a risk of long-term inhalation or ingestion [22]. However, another study has suggested that exposure by 11 September rescue workers was well below relevant limits [23]. A recent comprehensive review of chemical warfare agents has been published [24].

Biological agents

Biological weapons are cheap and relatively easy to

 Table 3. The effects of mustard

Time	Symptoms
20–60 min	Nausea, retching, vomiting, eye smarting
1 h	Erythema
2–6 h	Nausea, fatigue, headache, inflammation of eyes with intense pain, rhinorrhoea, erythema, sore throat,
0.101	noarseness, tacnycardia
8–12 h	Erythema and oedema
13–22 h	Inflammation at genitalia, waist, perineum axillae, followed by blister formation, occasionally pendulous with free fluid
42–72 h	Maximum blisters or necrosis, coughing, muco-pus and necrotic slough, skin irritation, increase in skin pigmentation

produce: however, their effects are potentially devastating. Seventeen countries are believed to have programmes for producing bacteriological warfare agents [25]. These could accidentally or deliberately fall into the hands of terrorists. The former Soviet Union alone is believed to have had some 65 000 workers employed in its bacteriological warfare programme in 60 civilian and four military institutes [26].

Diseases such as anthrax, plague and smallpox are of greatest concern as potential terrorist agents, although the range of agents that could be used and the degree of sophistication required is very wide. Attacks involving crude preparations or inadequate methods of delivery would be expected to cause many fewer casualties than for example 'weapons grade' anthrax dispersed as an aerosol.

Anthrax

Four forms of anthrax occur in humans: cutaneous, intestinal, inhalational and anthrax meningitis. Inhalational anthrax is the route of choice for the terrorist, particularly in view of its ease of distribution over a wide area. Early diagnosis is difficult in the absence of other clues, as the clinical manifestations are non-specific. Pyrexia, cough, dyspnoea, headache and abdominal or chest pain form the first stage and may last for a few hours or days. In some cases, there may be a period of apparent recovery before progressing to the second stage with sudden dyspnoea, pyrexia and shock. Haemorrhagic meningitis is common and death may follow in a matter of hours. Naturally occurring strains of B. anthracis are sensitive to penicillin, though ciprofloxacin or doxycline are generally considered the treatments of choice [27]. Treatment at the earliest suggestion of diagnosis is essential and intensive supportive therapy will be required. Because of the possibility of spores persisting in the lungs for an extended period, treatment or post-exposure prophylaxis is normally recommended for 60 days or until a course of vaccine can be administered.

Since anthrax is a spore-borne disease and sporulation does not occur ante-mortem, patient-to-patient transmission does not occur. Effective vaccines are available in the USA and UK, although no vaccine can prevent 'breakthrough' if exposed to sufficiently high levels of challenge.

Plague

Over the centuries, plague pandemics have swept the world many times, leaving millions dead in their wake and small outbreaks continue to occur naturally. Plague is present in many rodent populations and transmitted to humans when bitten by a flea infested with Yersinia pestis. The time course following exposure to an aerosol of Y. pestis used as a weapon would be much shorter than the natural course, presenting as primary pneumonic plague without evidence of buboes. There is currently no effective vaccine against plague. Streptomycin has traditionally been the antibiotic of choice against naturally occurring plague. Evidence for efficacy against an inhaled plague challenge is necessarily lacking, but consensus suggests that ciprofloxacin or doxycline should be used without delay [28]. Patients will also require intensive supportive therapy. Antibiotic prophylaxis would be required for any suspected exposure for 7 days. Pneumonic plague can be spread between individuals through fomites, and respiratory and eye protection is required for all medical staff involved in the clinical care of patients, together with prophylactic antibiotics.

Smallpox

Smallpox (variolla) no longer occurs naturally, having been eradicated in 1977 by a World Health Organization vaccination campaign. In addition, it has no known animal reservoir. The only remaining official stocks of virus are held in Moscow and Atlanta for reference purposes. Orthopox viruses, including smallpox, are stable and could be widely distributed as an aerosol. The virus is also highly contagious and spreads from person to person: a single case might infect 10-20 contacts by droplet spread [29]. Death occurs during the second week of illness due to toxaemia or encephalitis. The case-fatality rate is ~40%. An invariably fatal haemorrhagic form may also occur characterized by petechiae and haemorrhages into the skin and mucus membranes. The different forms of the disease are thought to represent a variation in immune response rather than differing strains of virus. Vaccination is effective, but no specific treatment is available.

Radiological and nuclear agents

Whilst there is no evidence that a nuclear weapon has ever been stolen, there are numerous cases of theft of and/or loss of radioactive materials. International Atomic Energy Agency member states have confirmed the discovery since 1993 of 175 cases of illicit trafficking of nuclear materials, a 'few of which' involved significant quantities and 18 cases involving plutonium or highly enriched uranium [30]. Potential sources of radioactivity are numerous, many having been 'lost' because of poor security or inadequate accounting [31]. The combination of any radioactive source, even nuclear waste, with a conventional explosive produces a so-called 'dirty bomb'. Whilst the extent of loss of life would be determined principally by the explosive component, the presence of radioactive material would cause considerable panic, contaminate property and have major economic consequences.

A small increase in ionizing radiation exposure to a large population would cause a long-term increased incidence of carcinoma due to the dose-dependent stochastic effects of ionizing radiation. The deliberate targeting of a nuclear reactor or its associated spent fuel pools could cause a disaster on the scale of Chernobyl [32].

Dissemination of nuclear material could take place either through the food chain, water supply or by placing a radioactive source in a public place.

The psychological dimension

Terrorists use terror for its psychological effects. By its very definition, terror is a mortal fear or dread and the possibility of the use of chemical, biological, radiological and nuclear agents by terrorists can create uninformed and irrational fears. The experience of military psychiatry is that fear is contagious and therefore both individuals and groups will feel the psychological effects of these agents before, during and after exposure. An acute phase of panic is likely to be followed by prolonged anxiety, individual and societal, due to the uncertainty surrounding the long-term effects of any agent used and fuelled by the media. Terrorist attacks may or may not be predictable: either way they create uncertainty. Information about terrorist threats, whilst generally desirable, is not invariably positive in terms of the effect on the psychological well being of the general public. Information misinterpreted or misunderstood can amplify anxiety and fear as shown by examples of mass socio-genic illness [33] spread locally and in the media by the pernicious effects of gossip and rumour. Trust in the credibility and veracity of information sources is vital if anxiety is to be countered. Given the access to uncorroborated information in the press and on the world wide web, conspiracy theories may flourish: indeed, such organs may be used for actively spreading disinformation.

Ill-informed assessments of vulnerability and threat may lead to inappropriate use of resources in which high-risk, low-probability situations may be targeted for funding [34]. Such systems are open to abuse and/or manipulation by various pressure or lobby groups.

Exacerbation of pre-existing psychiatric disorders is possible, particularly when there is uncertainty over potential chronic health effects of low-level exposure to toxic agents [35].

The UK response

The response to chemical incidents

There are five regional service provider units in the UK providing advice, support and expertise to the National Health Service (NHS) on chemical incident management. The National Focus for Chemical Incidents (NFCI) coordinates these centrally. Regional service provider units provide a 24-h advisory service covering the public health, environmental, scientific, toxicological and epidemiological aspects of chemical incidents. They routinely deal with both acute incidents such as chemical fires and spillages and long-term issues such as contaminated land and epidemiological issues associated with the follow-up of chemically exposed populations. All regional service provider units undertake surveillance within their regions through the collation of systematic information about chemical incidents and these data form part of the national surveillance system operated by the NFCI. Regional service provider units help local NHS bodies develop and maintain emergency plans and conform to Department of Health guidance on major incidents. They also work with other agencies in order to ensure coordinated planning and execution and to participate with neighbouring providers in regional and inter-regional planning for response to major incidents. Regional service provider units notify the NFCI of any major chemical incidents. In England and Wales these units merged on 1 April 2003 to form the Health Protection Agency's (HPA) Division of Chemical Hazards and Poisons.

National arrangements for radiation emergencies

Radiation users in the UK are legally required to produce site contingency plans and to have plans for transport accidents involving their property [36–38] (for example the Radsafe scheme) [39]. These plans are exercised on a regular basis. The National Arrangements for Incidents involving Radioactivity were formed in order to protect the public from hazards arising from radioactive materials in situations where no formal contingency plans exist or are inadequate: a national 'long stop'. They provide quick and widely accessible advice and assistance to the civil police where no radiation expert is otherwise available. They therefore form the basis of the specialist response to a radiation or nuclear terrorist incident. A similar scheme, Radiation Incidents in a Public Place, operates in Northern Ireland.

Assistance is provided in two stages.

- 1. *Stage 1 assistance*. A single radiation expert provides this using simple monitoring equipment. The experts are medical physicists or health physicists drawn from local hospitals, nuclear establishments or government departments. They identify whether a real hazard exists and undertake limited recovery operations. Their primary role is rapid advice to the police, which, if necessary, will include the decision to obtain stage 2 assistance.
- 2. *Stage 2 assistance*. This more sophisticated expertise consists of a team of up to four people capable of coping with relatively large-scale recovery operations and equipped with transport, monitoring and decontamination equipment and protective clothing.

The National Radiological Protection Board (NRPB) maintains and develops the National Arrangements for Incidents involving Radioactivity. It provides training and awareness sessions for responders and users and maintains a 24-h emergency call out number. Police or other users requesting National Arrangements for Incidents involving Radioactivity assistance call the emergency number and the United Kingdom Atomic Energy Authority Constabulary Force Communications Centre (0800 834 153) is responsible for finding a physicist for providing stage 1 assistance. The NRPB also maintains an incidents involving Radioactivity cases are given in Figure 1.

Key issues facing occupational physicians in the National Health Service

The possibility of terrorists using chemical, biological and radiological agents poses new concerns for occupational physicians and health and safety staff. The NHS has a long history in dealing with the consequences of terrorism but NHS major incident planning must now



Figure 1. Types of radiological incident. (Reproduced with permission from the National Radiological Protection Board.)

take account of mass casualties due to terrorist incidents. Consequently, the Department of Health has placed emphasis on the education and training of NHS staff, including scenario-based exercises. This, in turn, requires NHS occupational health and safety services to take account of the needs of NHS staff who are involved in combating chemical, biological, radiological and nuclear terrorism using a risk assessment approach.

The HPA has existed as a special health authority. Regarding chemical, biological, radiological and nuclear matters, it coordinates expert advice and support [41] drawn from the five chemical incident regional service provider units, PHLS, CDSC, NRPB and CAMR.

Department of Health funding has been made available to NHS ambulance services and major accident and emergency units in England for the purchase of personal protective equipment and mobile decontamination units for dealing with chemical incidents.

The NFCI produced a specification for personal protective equipment based on a standard battery of hazardous chemicals likely to be encountered.

NHS guidance on protecting staff who treat patients contaminated with radioactive material, which was developed in 1998 [42], is currently being reviewed.

Regional health emergency planning advisers can advise regarding the personal protective equipment available to the NHS. They work with regional epidemiologists and consultants in communicable disease control. The latter can provide information on other issues, e.g. regarding prevailing chemoprophylaxis or immunization policies and they can be contacted through the local or regional HPA teams.

The experience of one occupational health service: Consignia

The British postal service (Royal Mail Group but previously Consignia plc) has had wide experience of conventional terrorist exposure. The postal system itself has been attacked with incendiary devices and bombs. More often, it has been used as a delivery system with the devices being aimed at others. The passage of biological and other hazardous substances through the postal system is also a normal part of business. The organization has systems for the handling of such materials and therefore had well tried and tested procedures for dealing with terrorist attacks and for handling incidents involving hazardous materials. It was clear from the outset that the US postal service was being used for transporting anthrax spores. The threat of direct targeting of the UK was considered, but of greater concern was the potential for cross-contamination of mail from affected packages originating in the USA.

The occupational health service within Consignia was alerted as soon as it became apparent that anthrax was in the US postal service and the process of educating senior management began. It included explaining the nature of anthrax, its resistance in the spore form to destruction, the difficulties in detection, its infectivity and the means of controlling any infection. The PHLS was a particularly useful source of information. Preventive and protective measures were discussed at considerable length. It was important to ensure that the rationale behind advice about whether to use measures such as personal protective equipment was fully understood.

It was important to determine how cross-contamination might occur during the handling of mail. Mail from overseas arrives at specific locations in the UK and there is therefore a degree of control as to how it may be handled. Anthrax originating in the UK would be more difficult to spot initially, although once identified a considerable degree of backtracking is possible for narrowing down where the package has been and where it entered the system. Once in the UK, machines performing a variety of individual functions largely sort postal system mail. It was important to identify points where spores were more likely to be distributed to other mail or into the atmosphere. Experiments were conducted under the auspices of the Health & Safety Executive using *Bacillus globidii* in a variety of packets. It became apparent that, whatever the nature of the packaging or envelope, almost every stage of the handling process could cause the spores to escape. There was therefore no specific stage of the process that could be engineered out without effectively stopping the distribution of mail.

The major focus in the Consignia plan was clarifying and emphasizing the need for linking in with existing arrangements of the emergency services and the health authorities at all levels. A well-structured plan exists, which has gone through a number of iterations and continues to evolve. The plan has been thoroughly tested, as there have been several hundred incidents within the UK postal system since September 2001. These have ranged from spillages of innocuous powders to clear attempts to produce a major response and at least partially close down the service.

The input to the plan by the Employee Health Services has been significant, but their role in its implementation is relatively small in that the responses are largely those of the emergency and health services. At present, their major role in any real incident would be providing assistance to management on site and any necessary follow-up advice together with a counselling service for those who wish it.

Conclusion

The international view is that the likelihood of the use of chemical, biological, radiological and nuclear terrorism is low, but the impact could be high. Occupational health professionals should have a clear understanding of the hazards and risks to which their staff might be exposed in the event of a terrorist attack. They need to be aware of plans and procedures for minimizing harm to their staff.

Chemical, biological, radiological and nuclear weapons are weapons of terror and their psychological effects are felt at individual, group and societal levels. The UK has prepared for the use of such weapons since before the events of September and October 2001 in the USA and more has been done since to refine the response.

Long-term mental health issues may occur including medically unexplained symptoms, somatization, hypochondriasis and outbreaks of mass socio-genic illness. Information from trusted sources is vital to counter fear and aid personal and societal recovery. Given the 'crisis of trust' within Western (post-modern) society, health professionals may prove to be the best placed to act as 'trusted' sources. However, if we are to avoid causing iatrogenic harm, we must examine the effects of such attacks in their biological, psychological, social and cultural aspects.

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