

ALLERGIES IN THE WORKPLACE

CONTACT DERMATITIS WITHIN THE EXPLOSIVES INDUSTRY – A CASE REPORT

Haidee Williams, MB ChB, DOH

Occupational and Environmental Health Research Unit,
School of Public Health and Family Medicine,
University of Cape Town

ABSTRACT

Introduction. Explosives are widely used, within the armed forces as well as civilian society, but the health effects associated with the explosive manufacturing industry are not well described.

Case report. We present the case of a 48-year-old explosive manufacturing factory operator who developed contact dermatitis to trinitrotoluene as the presumed causative agent and paronychia from prolonged wet work.

Discussion. The main health effects of exposure to organic nitrates (including those used in explosives) are dermatitis, methaemoglobinaemia, vasodilation and carcinogenesis.

Conclusion. It is essential for health care workers to take a detailed occupational history in order to determine the possible contribution of work to a patient's health.

Introduction

Explosives are not only used by the armed forces but also extensively in the mining and demolitions industries. A review of the literature on this subject revealed that the spectrum of occupational diseases within the explosive manufacturing industry is not well described. What is known is that during World War I, workers involved in the munitions industry developed severe hepatotoxicity and anaemia.¹ In the USA, 17 000 cases of 2,4,6-trinitrotoluene (TNT) poisoning occurred, resulting in over 475 deaths.² Although more people were exposed to more chemicals during World War II,² fewer cases of morbidity were reported; this demonstrates that the handling conditions had improved, resulting in far lower exposures and less overt poisoning.

In South Africa, the Explosives Act (Act No.15 of 2003) governs the manufacture, distribution, storage and prevention of injuries within the industry, whereas the Hazardous Chemical Substances Regulations promulgated under the Occupational Health and Safety Act (Act No. 85 of 1993) governs the safe use of regulated chemicals. Occupational diseases are compensatable under the Compensation for Occupational Injuries and Diseases Act (Act No.130 of 1993). It is therefore not only important to investigate potential occupational diseases in order to prevent further exposures but also to ensure that the workers have access to the appropriate

personal protective equipment, compensation and care.

I present a case from the explosive manufacturing industry of a chronic relapsing skin disorder as an introduction to the subject.

Case report

A 48-year-old operator of 29 years standing presented with a 4-month history of an itchy, erythematous rash on his hands and forearms. He related the rash to working with TNT as the rash had started after he steam-cleaned a machine that had been used to make a TNT-containing explosive. When he was transferred to another production line where he was not exposed to TNT, the problem disappeared; when transferred back to the TNT production line, the problem re-occurred. Even handling closed bags containing TNT triggered the rash.

The patient also complained of swelling and discolouration of the nail folds and nails of his right hand that had been present for 3 years. He had received antifungal medication with no relief and nail clippings showed no fungal growth. This problem was unrelated to any specific production line.

He had a background history of hypertension, using one Betaretic daily, and had had a work accident in 1997 that led to the amputation of the distal phalanx of his left index and middle fingers. Our patient was married with one child, had four dogs and enjoyed working in his garden.

At the time of examination, he had been removed from TNT exposure and the dermatitis had cleared, but photographs taken while the rash was active showed vesicles on an erythematous base on his forearms and dorsal surface of his hands (Fig. 1). He was also noted to have unrelated swollen and inflamed nail folds, with loss of the nail cuticle and dystrophic discoloured nails involving the right thumb, index, middle and ring fingers. There were no signs of a fungal or bacterial infection. He was otherwise completely well.

Clinically he was assessed as having a resolved contact dermatitis and chronic paronychia.



Fig. 1. Contact dermatitis on the hand and arm.

Correspondence: Dr H Williams, Fine Chemicals Corporation, 15 Hawkins Avenue, Epping 1, 7460.
Tel 021-530-8126, fax 021-531-8376, e-mail haidee@fcc.co.za

A patch test was performed using the standard battery of 43 international allergens. These were applied under occlusion in Finn chambers for 48 hours. The test was read 24 hours after removal of the chambers. A positive reaction was seen to formaldehyde.

Despite a work history that identified some of the chemical exposures and significant water exposure, the patch test was not helpful. Before recommendations could be made regarding further patch testing using his own products, a work visit was undertaken to evaluate exposures and risk.

The manufacturing process to which he ascribes his rash involves the mixing of TNT with other chemicals such as cyclotrimethylenetrinitramine (RDX/cyclonite), hexanitrostilbene (HNS) and beeswax in a steam-heated melting kettle to form a paste. This kettle has point extraction in order to extract the dust and vapours generated by the heating of the TNT and other additives. TNT, when it enters the process, is in flocculate form and is poured into the kettle from sacks, so the generation of dust is possible despite extraction. The molten mixture is then solidified in moulded trays overnight forming solid slabs resembling large chocolate bars. PVC and cotton gloves are prescribed as personal protective equipment in this area. The solidified explosives are then transferred by tractor to a separate facility for further processing. Rubber mallets are used to separate the slabs into the individual moulded pieces. This is done under an extraction hood to minimise dust exposure generated in the pounding process. After passing through a sieve they are manually weighed into specially manufactured bags and packaged in accordance with strict regulations. The packaging is taped with paper taping and the boxes stamped using an inkpad. The workers are therefore also potentially exposed to glue and dyes.

A third process in the manufacture of explosives in which this worker participated, involved the refinement of the explosive cyclonite. Friction and the generation of sparks is a constant concern in the manufacturing of explosives. For this reason the powdered cyclonite is first manually poured into a running stream of tap water directed from a hose held by the worker to form a slurry which is then piped into reactors containing cyclohexanone. The heated mixture is distilled and allowed to cool to produce cyclonite crystals of specific size. Our patient holds the hosepipe with his right hand, which means that his hand is wet for approximately 4-5 hours while this production step is taking place. Personal protective wear is used but does not help as water constantly contaminates the inner surface of the glove and soon saturates the cotton glove appropriately used inside to reduce maceration of occlusion.

Discussion

Clinically the patient had occupational contact dermatitis. The history of flaring when exposed at work and resolution when removed from exposure supports a diagnosis of an occupational disease. He also had chronic paronychia, a well-recognised occupational irritant contact dermatitis caused by wet work. Our patient had been doing similar work for the last 29 years although the demand for explosives, and consequently his workload, had decreased. The reason for the sudden onset of the dermatitis is speculative. His 3-year history of chronic paronychia suggests irritant damage to the skin barrier function, predisposing him to sensitisation.

When exploring the explosive industry and related occupations for occupational diseases, one is struck by

the scarcity of information. There is usually an understandable focus on workplace accidents and injuries as opposed to occupational diseases.

The discussion concentrates on occupational diseases associated with a selection of chemicals involved in making explosives and commonly discussed in this context.

The organic nitrates (including those used in explosives) share four major toxic effects; dermal sensitisation, methaemoglobinaemia, vasodilation, and carcinogenesis. While these effects can occur separately or in combination, not all the nitrates cause all four effects.²

Dermatitis

Allergic and contact dermatitis are the most common occupational diseases seen in explosives workers.² The most common causative agents are tetryl, TNT, amatol, ammonium picrate, picric acid and mercury fulminate.² Other agents known to cause dermatitis, such as solvents, cutting oils and degreasers also occur in the munitions industry and should not be forgotten.

Methaemoglobinaemia

Oxidant stress on haemoglobin oxidises the iron in the molecule from the ferrous to the ferric form resulting in methaemoglobin. This form of haemoglobin is incapable of binding oxygen. Clinical effects such as cyanosis, malaise and headache develop when more than 10-15% of the total haemoglobin is converted to methaemoglobin.² Individuals with glucose-6-phosphate dehydrogenase deficiency and other haemoglobinopathies are particularly vulnerable to haemolytic episodes.^{2,3} Chronic anaemia can develop insidiously even without cyanosis.

Vasodilation and carcinogenesis

As a class, the organic nitrates cause dermatitis and haematological effects but specific agents such as nitroglycerin and dinitrotoluene cause vasodilation and mutagenesis, respectively.² These effects will not be discussed further in this report.

Explosive compounds

The focus is on 3 explosive compounds: 2 nitroaromatics (TNT and hexanitrostilbene (HNS)), and a nitroamine (cyclotrimethylenetrinitramine), as they are the possible causative agents for our patient's dermatitis.

The nitroaromatics

The nitroaromatics are absorbed by all routes (inhalation, ingestion and dermal exposure) and exhibit rapid dermal penetration.

Trinitrotoluene

2,4,6-Trinitrotoluene is the most widely used military explosive.^{2,4} TNT is a yellow, odourless, solid manufactured chemical. Systemic effects can occur after inhalation, dermal absorption and ingestion, and TNT generates a bitter taste in the mouth once absorbed.^{3,4} TNT dissolved in water increases dermal absorption.²

Its use increased sharply during World War I when the effects of anaemia, liver function dyscrasias, respiratory dysfunction and possibly aplastic anaemia were first observed.^{3,4} The combination of methaemoglobin with vasomotor changes contributes to the presentation of classic TNT intoxication.³ Researchers analysed a series of 21 fatalities due to TNT exposure during

World War II: 8 people died of toxic hepatitis and 13 of aplastic anaemia.²

Acute effects

Acute exposure to TNT results in irritation of the upper respiratory tract and skin. Systemic effects include gastrointestinal symptoms such as nausea, anorexia and epigastric pain. These symptoms may progress to include headache, fatigue, loss of memory and cyanosis.²

Chronic effects

Chronic effects include haematological changes, hepatitis, dermatitis, ocular effects and cancer.

TNT toxicity may result in both an aplastic and haemolytic anaemia. An aplastic anaemia occurs when TNT suppresses erythropoiesis and haemolysis develops as a result of methaemoglobin formation.²

TNT toxicity can induce hepatic necrosis and cirrhosis.^{2,3} The initial manifestation of the hepatitis occurs with increases in the serum transaminases and lactate dehydrogenase.²

Dermatitis is the most common chronic effect reported as a result of TNT exposure. Allergic contact dermatitis⁴ and an erythema-multiforme-like eruption⁵ were reported in two munitions workers and have been ascribed to direct TNT exposure. In both cases, the affected workers tested positive to a 5% concentration of the allergen on patch testing. Dermatitis was also observed on the hands of temporary workers in a munitions filling room, where there was environmental TNT exposure.³

Long-term systemic exposure to TNT has been associated with cataract formation.³ These cataracts are present only at the lens periphery and do not affect vision.²

TNT exposure has also been implicated in numerous other health effects such as myalgia, dysrhythmia, nephritis, menstrual disorders, and testicular atrophy and dysplasia.^{1,2} These health effects decreased sharply after World War II because of the availability of increased information and the improvement of working conditions.

Toxicity studies in animals showed a reduced number of red blood cells, reduced haemoglobin and haematocrit, anaemia, testicular damage, bladder papilloma and carcinoma, hepatomegaly and splenomegaly.^{2,4} TNT has shown positive results in the Ames assay^{2,3} (an *in vitro* test for mutagenicity that measures the occurrence of reverse mutagenesis in certain *Salmonella typhimurium* strains).

Hexanitrostilbene

2,2',4,4',6,6'-hexanitrostilbene (HNS) is a derivative of TNT and is a thermally stable explosive used extensively in the military environment, as well as industry.⁶ Toxicity data for HNS is virtually non-existent, but it is expected to show similar effects to other nitroaromatics.²

The nitroamines

The nitroamines are the most recently developed class of nitrate explosive.²

Cyclotrimethylenetrinitramine

Cyclotrimethylenetrinitramine, also known as cyclonite, RDX, hexagon and T4, is a nitroamine widely used as an explosive in mixtures with other explosives and plasticisers or desensitisers. It has also been used as a rodenticide.^{2,7}

Reports of overexposure were widespread in the munitions industry. Excessive RDX exposure within the workplace has resulted in seizures and unconsciousness with lower levels of exposure leading to irritability and insomnia.^{2,8} Troops have also become intoxicated after either chewing a RDX-containing explosive or using it as cooking fuel.² The American College of Governmental Hygienists has given it a 'skin' designation, as skin absorption is a possible route of entry as reported by Kaplan⁷ in a munitions workers' study. RDX does not metabolise to form nitrate in the blood.

Acute effects

Neurological symptoms predominate and include irritability, restlessness, headache, dizziness, generalised convulsions and stupor, delirium and disorientation.^{2,7} Patients completely recover from acute RDX exposure within days or months.

Chronic effects

Few effects of chronic human exposure have been reported.

A 1944 study quoted in the *Agency for Toxic Substances and Disease Registry*⁹ toxicological profile on RDX describes dermatitis in workers exposed to RDX fumes for an unknown length of time.

Acute overexposure to cyclonite in various laboratory animals resulted in CNS effects such as hyperirritability, convulsions and seizures.⁷ Skin absorption was not confirmed in animal studies, as topical cyclonite did not penetrate the clipped backs of rabbits and guinea-pigs, though rabbits developed dermatitis with topical application.¹⁰ Adverse hepatic, prostate and haematopoietic effects have been observed in animals in long-term studies.⁷ Cyclonite was not considered to be carcinogenic in rats and mice.⁷ Reproductive studies have yielded conflicting results. Fetotoxicity and developmental effects were only observed in the face of maternal toxicity.⁷ However, pregnant rats exposed to RDX resulted in pups with slightly lower body weights and shorter body lengths than pups not so exposed.² This difference did not reach statistical significance and showed no dose-response relationship.⁷

Conclusion

Our patient had an occupational skin disease, with TNT being the most likely allergen. This is supported by the fact that the patient had a remission of symptoms when removed from TNT exposure and a recurrence on re-exposure. Dermatitis is a well-described effect of TNT exposure and patch tests are planned for this patient. Understandably, regulations are very strict regarding removal of these products from the workplace so on-site tests will be done by the occupational health care team.

The management of the patient's occupational allergic contact dermatitis consisted of removal from exposure, a claims submission to the Compensation Commissioner, as well as reporting of the occupational disease to the Department of Labour.

The management of his chronic paronychia will be more difficult as water exposure is sentinel to the explosive manufacturing process and cannot be avoided. Advice on how to keep wet work to a minimum, education on personal protective equipment choice, use and maintenance, and the use of topical products to reduce inflammation and prevent maceration and secondary infection will be given.

Precautionary measures such as engineering controls, staff rotation and training and, as a last resort, person-

al protective equipment, are advised to prevent additional cases.

This case can be viewed as a sentinel case sensitising health care workers to the hazards of the explosive industry and the many and varied occupations in which exposure can occur and alerting them to possible substance exposures. It is the duty of the attending health care worker to take an adequate and complete occupational history for all patients and to assess the possible contribution of the work to the patient's problem. Although the industry is strictly regulated and access to manufacturing plants is rightly controlled, it is necessary for knowledge of these exposures and their health effects to be available.

Declaration of conflict of interest

The author declares no conflict of interest.

REFERENCES

1. Stellman JM, Osinsky D, Markkanen P, eds. Nitrocompounds, Aromatic. In: *Encyclopaedia of Occupational Health and Safety*, 4th ed. Geneva: International Labour Office, 1998.
2. Bodeau DP. Military energetic materials: explosives and propellants. In: Zajchuk R, Jenkins DP, Bellamy RF, eds. *Textbook of Military Medicine*. Washington: Office of The Surgeon General, Department of the Army, USA, 1993: 305-357.
3. American Conference of Industrial Hygienists (ACGIH). 2,4,6-Trinitrotoluene. 2001. *TLV Chemical Substances*, 7th ed. 2001 (CD-Rom available from ACGIH Worldwide, Cincinnati, Ohio, USA).
4. Agency for Toxic Substances and Disease. Toxicological Profile for 2,4,6-Trinitrotoluene. *Agency for Toxic Substances and Disease Registry*. Atlanta: US Dept of Health and Human Services, 1995.
5. Goh CL. Erythema multiforme-like eruption from trinitrotoluene allergy. *Int J Dermatol* 1988; **27**: 650-651.
6. Neyer BT, Cox L, Stoutenborough T, Tomaszki R. HNS-IV Explosive Properties and Characterization Tests. 2003; Available at: <http://neyersoftware.com/Papers/AIAA2003-5138--HNS-IVExplosivePrper...> Accessed July 4, 2007.
7. American Conference of Industrial Hygienists (ACGIH). Cyclonite. 2001:6. *TLV Chemical Substances*, 7th ed. 2001 (CD-Rom available from ACGIH Worldwide, Cincinnati, Ohio, USA).
8. Occupational Safety and Health Administration. *Toxicologic Review of Selected Chemicals*; Cyclonite. <http://www.cdc.gov/pel88/108-94.html> (last accessed 1 July 2007).
9. Agency for Toxic Substances and Disease. Toxicological Profile for RDX. *Agency for Toxic Substances and Disease Registry*. Atlanta: US Dept of Health and Human Services, 1995.
10. McNamara BP, Averill HP, Owens EJ, et al. The Toxicology of Cyclotrimethylenetrinitramine (RDX) and Cyclotetramethylenetetranitramine (HMX) Solutions in Dimethylsulfoxide (DMSO), Cyclohexanone, and Acetone. 1974;EB-TR-73040. <http://toxnet.nlm.gov/cgi-bin/sis/search/f?temp/-zlor31:8:BODY> (last accessed 25 June 2007).

PRODUCT NEWS

PIMECROLIMUS CREAM 1% IN ATOPIC DERMATITIS: A 6-MONTH, OPEN-LABEL TRIAL IN PAEDIATRIC PATIENTS

Pimecrolimus, a new, non-steroid, inflammatory-cytokine inhibitor, has been shown to prevent progression to flare in atopic dermatitis (AD) and to improve long-term disease control when applied as a 1% cream. In this 6-month, open-label, multinational study, 177 infants aged 3-23 months and 489 children aged 2-17 years, with mild to severe AD, were included. The study was designed to evaluate the efficacy and safety of pimecrolimus cream 1% used as a first-line treatment. Treatment consisted of an initial bid regimen, for as long as signs and symptoms of disease persisted; this was followed by treatment as required at the first signs and symptoms of AD. Emollients were allowed as per the physician's normal practice, and topical corticosteroids could be used to treat severe flares at the discretion of the physician. Efficacy was assessed by evaluations of pruritus, and total-body and facial Investigators' Global Assessment (IGA). Results from the first return visit (day 7) showed an improvement from baseline of ≥ 1 in total-body and facial IGA for infants (59.1% and 72.8% of patients, respectively) and children (59.3% and 62.2%, respectively). Pruritus was absent or mild in 67.8% and 65.4% of infants and children, respec-

tively. This level of improvement in the patient population was maintained throughout the 6-month study. Adverse events occurred in 75.7% of infants and 71.1% of children. Most adverse events were common childhood illnesses that would be expected in this population (e.g. nasopharyngitis (infants 22.0%, children 12.8%), upper respiratory tract infection (infants 18.6%, children 11.9%) and cough (infants 8.5%, children 10.1%)). Concerning pimecrolimus's local tolerability, application-site burning occurred in 2.3% of infants and 7.0% of children, and local pruritus occurred in 0.6% infants and 1.0% children. Application-site reactions were most frequently reported during the first 6 weeks of treatment and were mild to moderate in intensity. In conclusion, pimecrolimus cream 1% was effective in the treatment of the early signs and symptoms of AD (including pruritus) in infants and children, and demonstrated a good safety profile.

Reference available on request. Contact Thoko Nzama, 011-929-9111

