Chapter 9

MILITARY ENERGETIC MATERIALS: EXPLOSIVES AND PROPELLANTS

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INTRODUCTION

The United States military is a major producer and consumer of explosives and propellants. Although we have recognized the toxic effects of some of these compounds for many years, most of the data on their effects on human health were published during World War I and World War II, and many voids remain in our knowledge of their human and ecological toxicity. The database on the effects on health (especially human) is uneven and we must remain alert for newly discovered or described effects, especially those that concern carcinogenic and reproductive effects. The lack of adequate data on exposure in human occupational epidemiology studies, and the lack of route-specific toxicity data (especially inhalation and dermal absorption) in animal studies, precludes our making dose-response estimates for most explosives. Therefore, it is our responsibility to err on the side of safety in making judgments about human exposures to these chemicals, and we must include data on structurally similar chemicals in our overall assessment of the probable health hazards of the explosives.

The production of most of these explosives parallels the military activity of the United States. Peacetime production is usually sufficient only for research and training needs. During wartime, the manufacture of these compounds increases; the workforce increases (thereby increasing the number of inexperienced workers who are unfamiliar with these compounds), and physicians who are inexperienced with the unique hazards posed by these chemicals are suddenly charged with the care of explosives workers. The rapid increase in production during wartime has tended to result in far higher exposures, with correspondingly more numerous and more severe adverse effects, than the few mild adverse reactions that occur during peacetime production.[1–3]

Furthermore, the evolving regulatory environment surrounds these and other industrial exposures to hazardous substances. For example, the Occupational Safety and Health Administration (OSHA) has revised the air-contaminant regulations for over 400 chemicals, including nitroglycerin. Whether these new standards can be enforced is still undecided; some questions have been raised regarding whether the proposed standards are feasible from an engineering perspective.

This chapter focuses exclusively on military explosives and propellants, and is structured according to the chemical family of the compounds: (*a*) aliphatic nitrate esters, (*b*) nitroaromatics, (*c*) nitramines, (*d*) initiating explosives, (*e*) composite propellants, and (*f*) liquid propellants. Most munitions, however, are mixtures of chemicals. Medical professionals new to propellants and explosives will need to break through the engineering and technical jargon and nomenclature to identify specific chemical exposures before they can deal with them. Occupational health personnel need to expect, in addition to exposures among plant workers, sporadic exposures among ammunition quality-assurance specialists, explosive ordnance-disposal specialists, and personnel who test or use explosives in enclosed spaces.

HISTORY

The Chinese are generally credited with inventing explosives—in the form of fireworks—before AD 1000. Black powder was not introduced to the western world until approximately 1225. Roger Bacon, an English monk, conducted and described some of the first scientific experiments with this explosive mixture of saltpeter, charcoal, and sulfur in 1249. The age of gunpowder began nearly simultaneously in Europe and China with the invention of cannons early in the 14th century, but until 1800, the development of explosives was limited mainly to improvements in the manufacture and application of black powder. Modern explosive technology was developed during the 19th century with increased research and development of propellants, high explosives, and weapons technology.[4]

Because of their ready natural availability, inorganic nitrate-based explosives were the first to gain importance. (Today, the most important inorganic nitrate explosive is ammonium nitrate, which is used in demolition and construction.) Inorganic nitrates formed the basis of black powder, which was the predominant explosive used in the United States before 1900.[5] Its last major military use was during the Spanish-American War of 1898. Black powder is an easily produced physical mixture of sulfur, charcoal, and potassium nitrate, but it is not well suited for most modern military uses: it produces excessive smoke and flash (which could alert the enemy to the position of the gun) and has a dangerous tendency to cake and misfire. However, it is still used in primers, safety

fuzes, flares, grenades, practice munitions, blanks, fireworks, signals, and specialized quarry work.

During the opening years of the 20th century, faster, cheaper, and higher-volume methods for producing explosives were developed. Numerous compounds were synthesized and used as detonators, boosters, and flash suppressors; dynamite almost completely supplanted black powder in commercial use, and trinitrotoluene (TNT) became the most commonly used military explosive.

With these various developments, attention focused on organic nitrate explosives. The aliphatic nitrates were the first group to achieve importance because cellulose, glycerol, sugars, and coal-tar derivatives were readily available for use as raw materials. Later, as cost-effective bulk synthesis of ammonia and formaldehyde became possible, the aromatic nitrates became important militarily. The most recent group to achieve prominence is the nitramines.

Throughout the early years of World War II, the low production capacity for most explosives and propellants plagued the United States, and numerous changes tempts to increase production. Adaptation to the shortages of raw materials, in addition to the unique requirements of each type of weapon, led to the increasing complexity of munitions design. This adaptive solution to inadequate resources was most prevalent in the search for rocket propellants. For example, the addition of nitroguanidine to nitrocellulose- and nitroglycerin-based propellants was found to both increase production capability and meet the unique and exacting requirements for newly developed weapons systems.

Additional weapons research after World War II has further expanded the uses of these compounds. The plethora of explosives and propellants currently in use and under development has resulted from continued research into the properties, cost, safety, stability, and predictable performance of explosives.

The British were the first to respond to the threat that the manufacture of explosive materials posed. In 1875, they passed the *Explosives Act* after an industrial explosion killed 53 people.[4] This law established "inspectors of explosives," who were authorized to inspect all magazines and factories to ensure that operations were accomplished safely.

At the beginning of World War I, TNT was generally believed to be nontoxic in all its stages of production, but this belief changed. During the course of the war, the major powers used approximately 5 billion pounds of high explosives, primarily TNT, resulting in an estimated 10 million battlefield casualties.[4] In the United States, at least 17,000 cases of TNT poisoning occurred during the war, resulting in more than 475 deaths.[6,7] Efforts to reduce the burden of disease included job rotation, medical examinations, and workplace ventilation and hygiene. These efforts were only marginally effective. Successful control of worker exposure was finally achieved through the automation of many operations during shell loading, and the application of strict standards of workplace hygiene.[8]

The World War I experience demonstrated that ammunition-loading plants were among the most dangerous industrial operations, due to the open handling of dusty and fuming compounds. Beginning in 1938, the Ordnance Department and the United States Public Health Service coordinated an intensive effort to forge an integrated health and hygiene program in ordnance plants to reduce this burden of death and disability of the workers.[3] This effort was

> the first large-scale demonstration of what can be accomplished in a large industry offering many serious health hazards by a vigorous medical and engineering program.[2(p558)]

Consequently, the successes of, and lessons learned from, this effort led to the establishment of the field of occupational medicine in the army, where it monitors the health of over 100,000 civilian employees at depots, arsenals, and ammunition plants.

ENERGETIC MATERIALS

An energetic material is a compound that can undergo rapid, self-sustaining, exothermic, reduction-oxidation reactions. Energetic materials may be categorized according to their intended uses: (*a*) explosives, (*b*) propellants, and (*c*) pyrotechnics. Explosives and propellants evolve large volumes of hot gas when burned; they differ primarily in their rates of reaction. *Pyrotechnics* (ie, a powder or ammunition used for igniting a rocket or producing an explosion; the term is also used in the military to designate flares and signals) evolve large amounts of heat but much less gas than explosives or propellants. Energetic materials may also be grouped according to their rate of reaction. Both propellants and pyrotechnics are considered to be *low explosives,* and the velocity at which the combustion proceeds through these materials is usually 400 m/sec or slower (Figure 9-1). In comparison, *high explosives* are *detonated*, a process in which the very rapid rate of the combustion reaction itself produces a shock wave, capable of shattering objects, in the surrounding me-

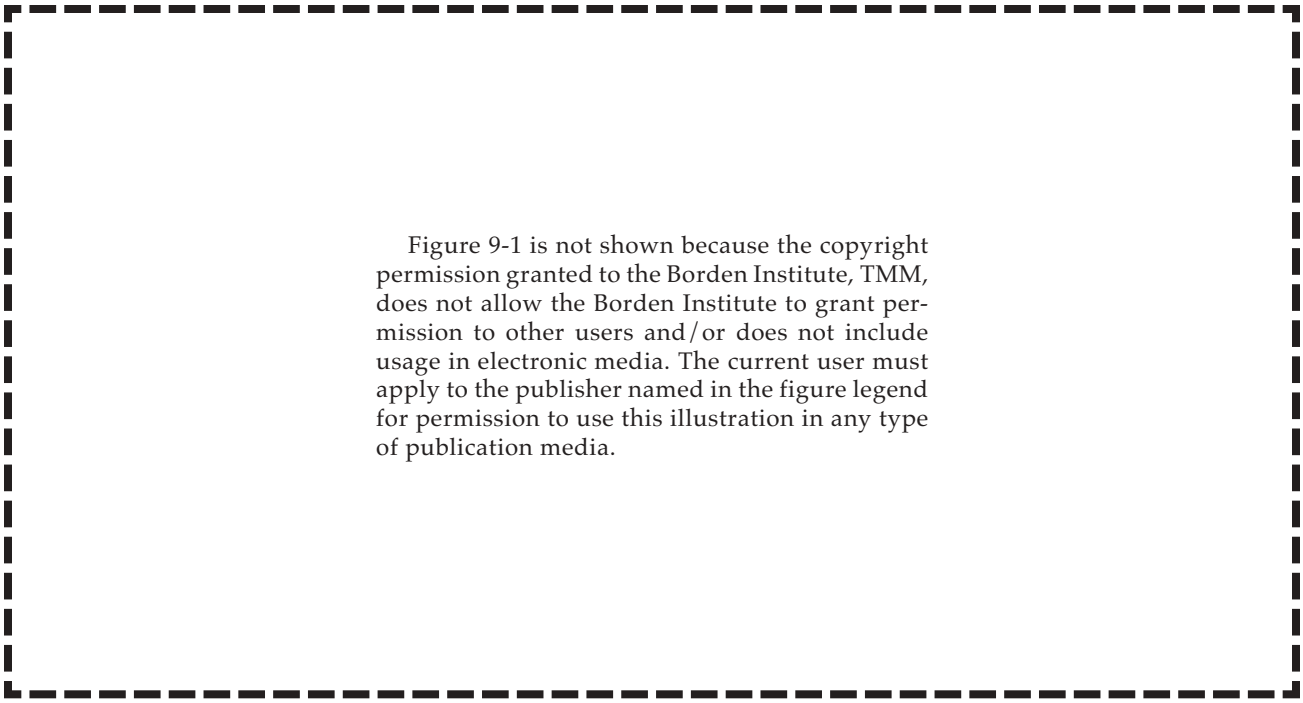


Fig. 9-1. Approximate detonation rates of common military and industrial explosives. Infinite variations on these rates are possible by mixing and by using additives. Both explosive and propellant formulations have taken advantage of these high detonation rates. Adapted with permission from Meidl JH. *Explosive and Toxic Hazardous Materials.* New York: Macmillan Publishing; 1970: 24.

dium. The shock wave moving through the explosive material causes further explosive decomposition of that material, and the reaction rate is determined by the speed of the shock wave. The range of velocities of the shock wave is 1,000 to 9,000 m/sec. In addition to being used as explosive charges, many high explosives are also used in propellant formulations. For purposes of this discussion, the term *explosive* is used generically to indicate any energetic material.

Explosives

Modern explosive devices employ an *explosive train* that takes advantage of the specific explosive properties of its components: the initiator, the detonator, the booster charge, and the main charge (Figure 9-2). The initiator, or primary explosive, consists of a small quantity of material that is very sensitive to heat, spark, impact, or friction. Primary explosives may intensify the energy up to 10 million times that of the initiating stimulus. Geometric arrangement of the explosive device directs either the flame or the detonation wave of the initiator toward the detonator charge. The detonator, a larger amount of less sensitive but more powerful explosive material, then detonates either the booster charge or the main charge. The booster charge is an optional component that further magnifies the explosive impulse. The main explosive (or bursting) charge contains the largest amount of an insensitive, but powerful, explosive. Explosives used as booster and main charges are usually not capable of being initiated by impact, friction, or the brief application of heat, and are known as secondary explosives. Some common primary and secondary explosives are listed in Exhibit 9-1.

The secondary explosives used currently in most military explosive devices are physical mixtures of one or more high explosives with various additives (Figure 9-3). (The use of mixtures, rather than single compounds, provides for greater flexibility in explosive design, and additives extend the range of performance even further [Table 9-1]). *Melt-loading*, commonly used with TNT mixtures, is a process in which a molten explosive mixture is introduced into an empty shell casing and allowed to cool and harden. Secondary explosive mixtures are used to facilitate the melt-loading process to optimize (*a*) the oxygen balance of the explosive, (*b*) explosive characteristics such as blast and fragmentation, and (*c*) engineering criteria such as malleability and strength.

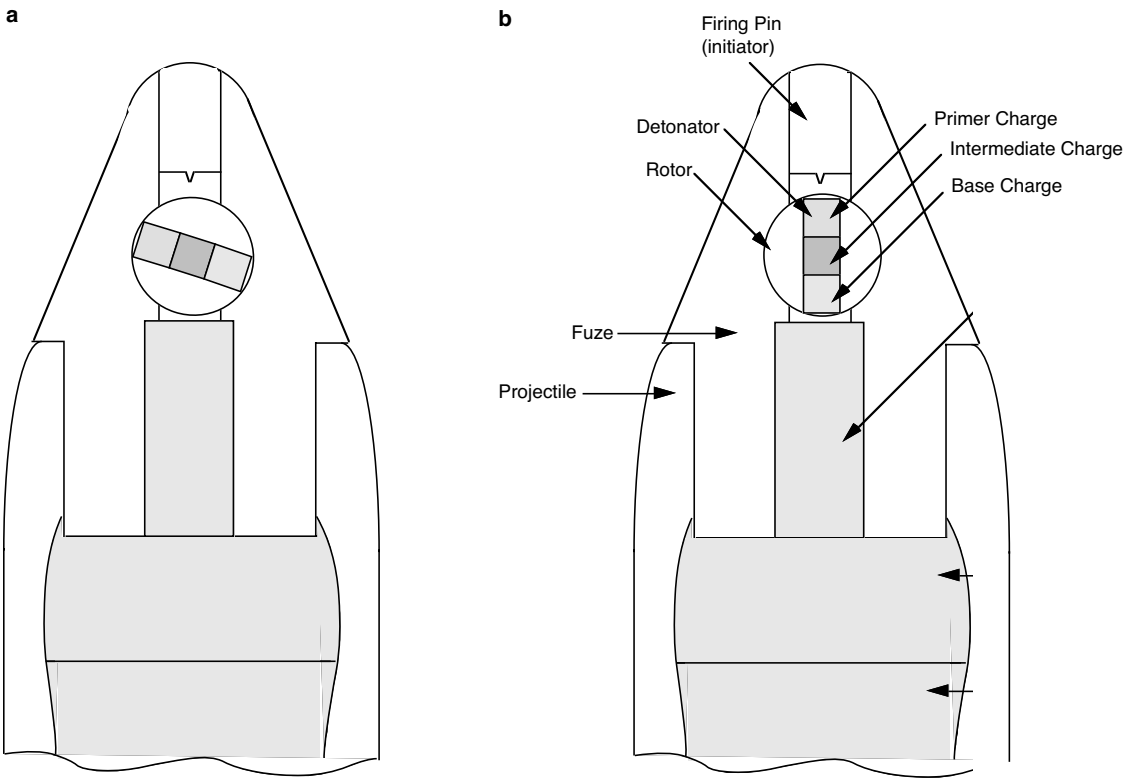


Fig. 9-2. These are diagrams of a typical high-explosive train. In (**a**) above, the rotor is turned in a safe position, interrupting the train. In (**b**), the unsafe, armed position, the rotor is turned, allowing geometric alignment of the various charges. On detonation, the stab firing pin strikes the input end of the detonator (initiation), piercing the thin metal disk and pushing it into the primer charge, which in turn initiates the intermediate charge. This initiation causes a reaction within the intermediate charge that is accelerated and converted to a small detonation. This small detonation is boosted within the booster charge and the train continues into the main explosive charge. Here the reaction is accelerated and converted to a detonation, which is successively transmitted through the remainder of the chain (boosting) to the main explosive charge. Reprinted from US Army Materiel Command. *Explosive Trains*. Washington, DC: USAMC; 1974: 1–3. AMC Pamphlet 706-179.

EXHIBIT 9-1

COMMON PRIMARY AND SECONDARY EXPLOSIVES

Primary Explosives		**Secondary Explosives**	
Lead azide	Diazodinitrophenol	Aliphatic nitrate esters	Ternary mixtures
Mercury fulminate	Potassium dinitrobenzofuroxane	Nitramines	Quaternary mixtures
Lead styphnate	Lead mononitroresorcinate	Nitroaromatics	Plastic-bonded explosives
Tetracene	Primary compositions	Binary mixtures	Industrial explosives

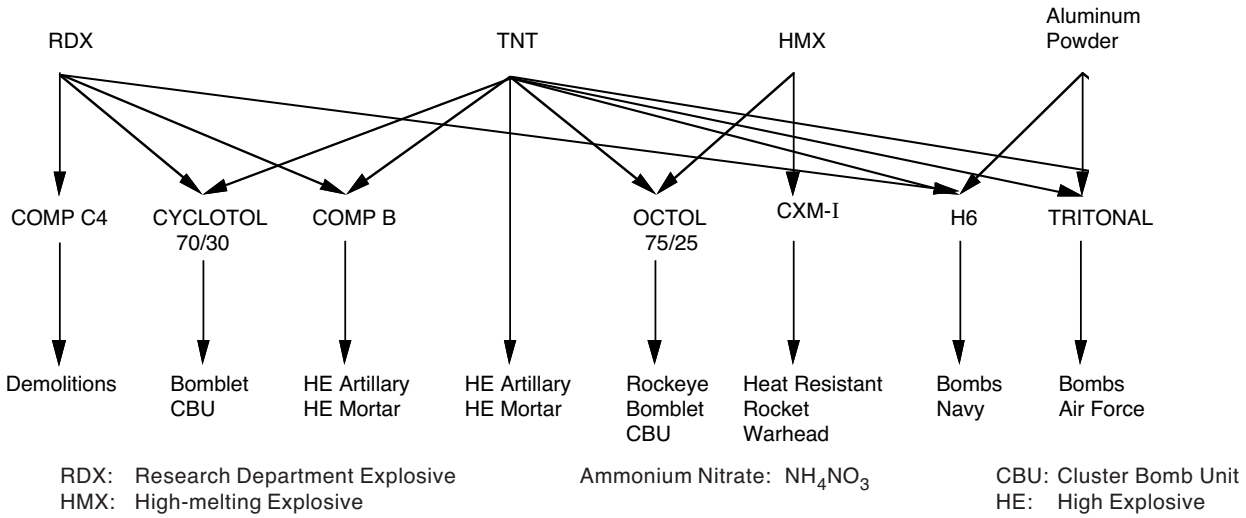


Fig. 9-3. Explosives family tree. Most explosives in military use are based on RDX, TNT, or both, in combination with other explosives. The occupational health practitioner needs to know the common names of the explosives being used at the installation to be able to ascertain the appropriate medical surveillance examinations. Adapted from US Army Environmental Hygiene Agency. *Water Pollution Aspects of Explosive Manufacturing*. Aberdeen Proving Ground, Md: USAEHA; 1985: 4. USAEHA Technical Guide 4.

Explosives and explosive-actuated devices are used widely in both industry and the military. Explosives are used in construction, mining, quarrying, demolition, metal forming, welding, and cladding. Explosive-actuated devices are used to drive turbines, move pistons, operate rocket vanes, start aircraft engines, eject pilots, and to provide heat. Between 1960 and 1975, domestic industrial explosive consumption increased from 500 million metric tons to over 1.4 billion metric tons. During this time, the use shifted from black powder, liquid oxygen, and dynamite to safer ammonium nitrate–based explosives. Today, over 100 million blasting caps are used annually in the United States.[4] Although the specific military uses of explosives are almost too numerous to count, they include the production of fragments, air blasts, and underwater shocks; the penetration of armor; demolition; the ejection of personnel from aircraft; and components of nuclear weapons.

Propellants

Propellants are explosive materials formulated and engineered to react at carefully controlled rates, producing a sustained pressure effect over a longer period of time than high explosives. In contrast to the detonation of high explosives, the process of propellant burning is referred to as *deflagration*, wherein the rate of heat transfer determines the rate of the reaction, which proceeds at subsonic speeds.

Like explosives, propellants utilize a series of materials in an ignition train (Figure 9-4). An electrical or mechanical impulse impinges on the sensitive primer material. This ignites the igniter, a pyrotechnic, which in turn ignites the main propellant grain.

Propellants may be formulated either as solids or as liquids. Solid propellants are used more frequently in guns, cannons, and smaller rockets, while liquid propellants are used in high-performance missile systems and other selected applications.

TABLE 9-1

TYPICAL EXPLOSIVE ADDITIVES

Additive	Purpose	Munitions or Other Use
Aluminum Pyropowder	Increase blast effect	Depth charges Cluster bombs Concrete fragmentation bombs
Wax Stearic Acid	Desensitize to explosion	Composition A Numerous others
Mononitrotoluene Dinitrotoluene	Explosive and plasticizer	Composition C
Polyisobutylene	Plasticizer	Composition CH6

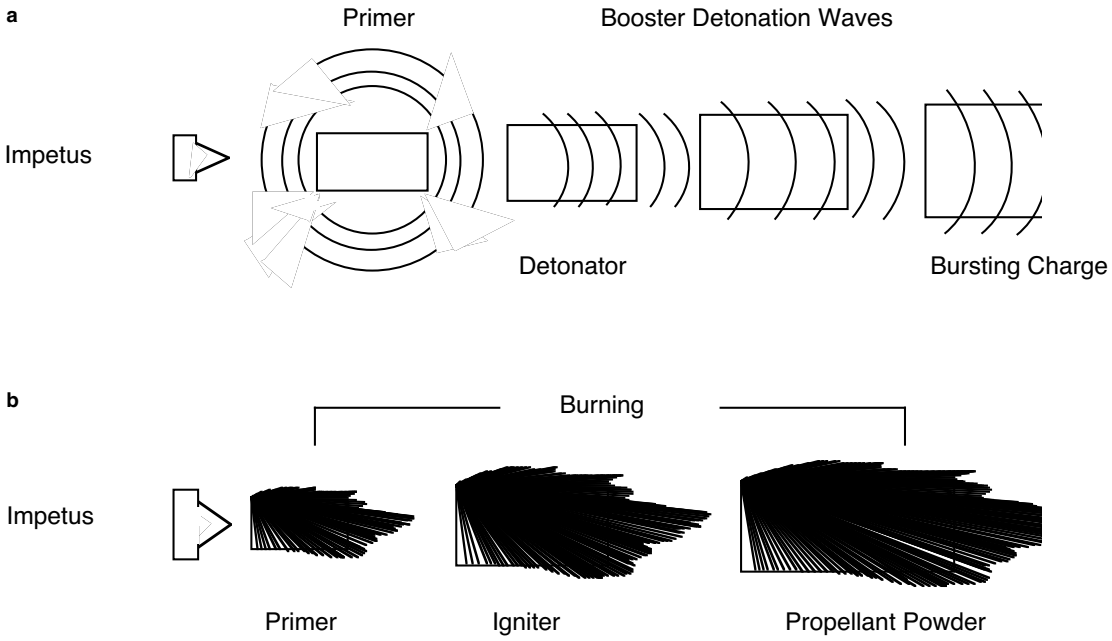


Fig. 9-4. Comparison of explosive train with ignition train. Although significant engineering differences exist between explosive trains (**a**) and ignition trains (**b**), in concept they are very similar. In both, a small electrical or mechanical stimulating impetus is magnified via a succession of intermediate charges to achieve optimum initiation of the main charge or propellant grain. The major difference between the two types of chains is in the component charges' rates of reaction. Adapted from US Department of the Army. *Military Explosives*. Washington, DC: DA; 1985. Technical Manual 9-1300-214, September 1984 with change 1 of 30 November 85.

Solid propellants may be classified by their chemical composition. Each class has unique properties that render it useful in certain applications. All solid propellants may contain additives similar to those used in explosive mixtures. The additives can be more toxic than the principal components of the propellant and must be considered in occupational-hazard analysis. Regardless of the composition class, the chief advantages of solid propellants include their compactness, safety, ease of storage, tolerance of temperature extremes, and ease of handling. In comparison, liquid propellant systems permit greater thrust control and deliver higher specific impulses. Liquid propellants have been limited to use in high-performance missile systems until recently, when research has focused on using liquid gun propellants for howitzers. Several candidate liquid gun propellants will be discussed later in this chapter.

Pyrotechnics

Pyrotechnic materials are relatively slow-burning, nonexplosive powders such as metals, alloys, and hydrocarbon mixtures. The only pyrotechnic compounds discussed in this chapter are those used in initiating compositions and propellants. However, pyrotechnics are also widely used in the military as flares, signals, relays, delays, and fuzes.

EXPOSURE

Ammunition plants, operated by the U.S. Army for the Department of Defense (DoD), are the primary sites of occupational exposure to military explosives. The types of ammunition plants include (*a*) propellant- and explosive-manufacturing plants, (*b*) metal-parts plants, (*c*) small-arms plants, and (*d*) shell loading, assembly, and packing (LAP) plants. Private companies have operated most of these ammunition plants under government contracts since the late 1940s.

In addition to those at ammunition plants, significant actions occur at other types of military facilities: munitions are manufactured (in limited quantities), tested, and stored at *arsenals*; tested at *proving grounds*; and maintained, stored, and demilitarized at *depots*.

Unique operations, with potentially hazardous exposures, are done at each type of facility. Workers at these facilities may perform duties that can potentially expose them not only to toxic hazards but also to other hazards of which occupational medicine physicians must always be cognizant.

Even though propellant and explosives manufacturing plants produce a limited number of specialized products, their workers can still be exposed to *feedstock*, *process chemicals*, and the finished explosives (Figure 9-5). Feedstock is a generic term for the raw materials that are used in chemical manufacturing. It can include chemicals such as toluene and nitric acid in the synthesis of TNT, and raw cellulose such as cotton or paper pulp for the synthesis of nitrocellulose. Process chemicals include all others in addition to the feedstock used in the synthesis (eg, salts or acids may be used in separations.) Exposures are usually controlled at the manufacturing plants by enclosing the *process streams*, which are flows (literal or figurative) of the partially processed feedstock through the additional chemical processes and reactions necessary to complete the synthesis.

LAP plants present the greatest exposure potential for employees, due to their use of a wide variety of explosive compounds and the labor-intensive nature of most loading operations. Comparatively few employees are exposed to explosives at small-arms plants, arsenals, or depots. Because ammunition is *proof-fired* there (ie, a batch of explosive is ignited to "prove" that it works and to assess its particular performance characteristics), small numbers of employees at proving grounds may be exposed to many and varied explosives and combustion products. Workers at all these facilities, especially *metal-parts plants*, can be exposed to common industrial chemicals such as carbon monoxide, lead, nitrogen oxides, solvents, paints, and cutting oils.[2] Metal-parts plants manufacture the hardware in which the explosives are loaded and used, such as rocket tubes, shell casings, bomb casings, and trigger assemblies. Cutting oils (usually mineral oil) are used to lubricate and cool the saws and machining tools that are used to shape the metal parts. During the past decade, cutting oils have been found to be contaminated with nitrosamines, a class of potent carcinogens. Machinists exposed to these oils via the dermal and inhalational routes may be at high risk for cancer.

Exposure Controls

Several types of workplace standards have been established to regulate employee exposure. U.S. Army

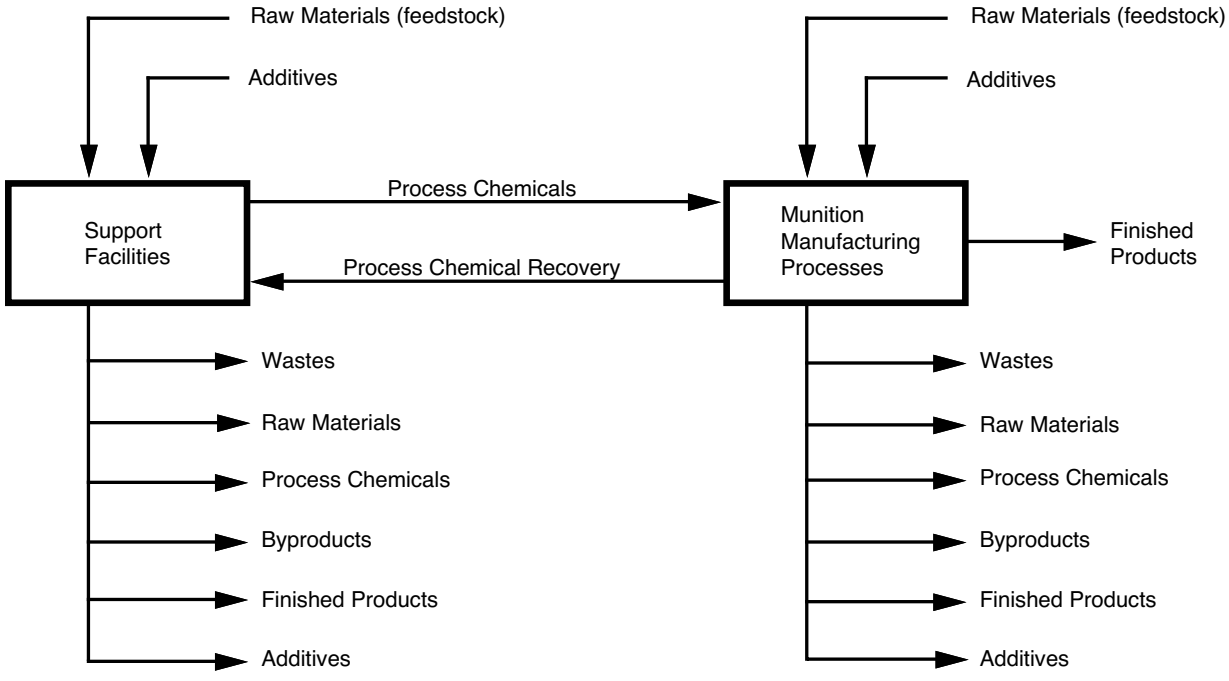


Fig. 9-5. Simplified flow for munition manufacturing processes. Adapted from US Army Environmental Hygiene Agency. *Water Pollution Aspects of Explosive Manufacturing*. Aberdeen Proving Ground, Md: USAEHA; 1985: 5. USAEHA Technical Guide 140.

policy follows the most stringent limit elaborated by OSHA, the permissible exposure limit (PEL); or the American Conference of Governmental Industrial Hygienists (ACGIH), the Threshold Limit Value (TLV). In addition, because dermal absorption is a significant route of exposure for many explosives, OSHA has given a skin designation to those chemicals, to aid in their identification. Therefore, skin exposure to chemicals with significant dermal absorption should be reduced to a minimum. However, where published limits from OSHA and the ACGIH[9] are either unavailable or inadequate to meet army requirements, the U.S. Army Medical Department establishes army-unique exposure limits. Table 9-2 shows the published limits for the more common explosive materials.

General Safety Practices

Safety is of paramount importance when personnel handle explosives and propellants. The accidental detonation or deflagration of these materials poses serious hazards to employees, other people nearby, and property, including blast overpressure, fragmentation, and burns. Creating a safe workplace around explosives demands that the cardinal principles of safety be followed:

- Separate each handling operation to prevent fires, blasts, or fragmentation.
- Use the minimum number of personnel for each operation.

TABLE 9-2

EXPOSURE LIMITS

Chemical Name	CAS Registry No.	Skin Designation	TWA (8 h)	STEL (15 min)
Nitroglycerin[1]	55-63-0	+	—	0.1 mg/m^3
Nitrocellulose[1]	9004-70-0	–	15 mg/m^3* 5 mg/m^3†	—
PETN[2]	78-11-5	+	—	0.1 mg/m^3
PGDN[1]	6423-43-4	–	0.3 mg/m^3	—
TNT[1]	118-96-7	+	0.5 mg/m^3	—
DNT (2,4-DNT)[1] (2,6-DNT)[1]	121-14-2 606-20-2	+	1.5 mg/m^3	—
Ammonium Picrate[2]	131-74-8	+	0.1 mg/m^3	0.3 mg/m^3
Picric Acid[1]	88-89-1	+	0.1 mg/m^3	—
RDX[1]	121-82-4	+	1.5 mg/m^3	—
HMX[1]	2691-41-0	+	1.5 mg/m^3	—
Nitroguanidine[3]	556-88-7	–	4 mg/m^3*	—
Tetryl[1]	479-45-8	+	1.5 mg/m^3	—
Lead Azide[1]	13424-46-9	–	50 μg/m^3‡	—
Lead Styphnate[1]	63918-97-8	–	50 μg/m^3‡	—
Mercury Fulminate[1]	628-86-4	+	—	0.1 mg/m^3 (as mercury)

[1]OSHA, 29 CFR 1910.1000; [2]US Army Environmental Hygiene Agency. *Medical Information Module of the Occupational Health Management Information System.* Aberdeen Proving Ground, Md: OHMIS, USAEHA; 1988; [3]Unpublished data. Aberdeen Proving Ground, Md: USAEHA.

*Total dust; †Respirable dust; ‡Measured as lead

CAS: Chemical Abstract Society; STEL: **s**hort-**t**erm **e**xposure **l**imit, defined as a 15-minute exposure level; TWA: the 8-hour **t**ime-**w**eighted **a**verage exposure level; RDX: ***r***esearch ***d***epartment ***ex***plosive, hexahydro-1,3,5-trinitro-1,3,5-triazine; HMX: ***h***igh-***m***elting ***ex***plosive, octa-hydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

Fig. 9-6. This photograph was made at New River Ordnance Plant, Dublin, Virginia, on 30 September 1941. The first step in the manufacture of powder bags is to lay the material on the table, mark for the size of the bag, and then cut with an electric knife. Numbers are then printed on the cloth to designate the charge that is to be put into the bag. The pieces of cloth are then sewn together to make the bag. The last step, shown here, is to weigh the charge of smokeless powder, fill the bag, and then seal it. The numbers on the bags are very large to prevent any error. Note the administrative safety control measures in place in this pre–World War II army public relations photograph: the number of personnel allowed in the area (8 operators, 2 transients) and the limits on the amount of explosives allowed to be used in the operation (140 lb of smokeless powder, 25 explosive charges in the chute). Photograph: Courtesy of the US Army Bureau of Public Relations.

- Stockpile only the minimum amount of explosive or hazardous material necessary for efficient operation.

The DoD has established uniform safety standards applicable to ammunition and explosives,[10] which the army implemented in Army Regulation 385-64.[11] Most of these are safety standards, which address factors including the sensitivity of explosive materials to accidental initiation; the quantity of material available to be detonated or deflagrated; the heat that would be generated; the rate of burning; the potential sources of accidental ignition and initiation; and the protection capabilities of shields, clothing, and fire-protection systems (Figure 9-6). Other health-focused standards address the potential toxicity of the explosive materials and the control measures that must be in place to ensure that worker exposure is within acceptable limits.

Industrial Hygiene Principles

Applying industrial hygiene principles such as (*a*) engineering controls, (*b*) administrative controls, and (*c*) personal protective equipment (PPE) in the workplace will further limit the potential for workers being exposed.

Engineering Controls

The ideal control of an industrial hazard is achieved through design changes such as substituting a safer or less-toxic process or material. Any such modification of the workplace should be closely coordinated between qualified industrial hygiene and safety personnel. But substitution is a long-term solution, and may not always be possible. For example, the U.S. Army Armament Research, Development, and Engineering

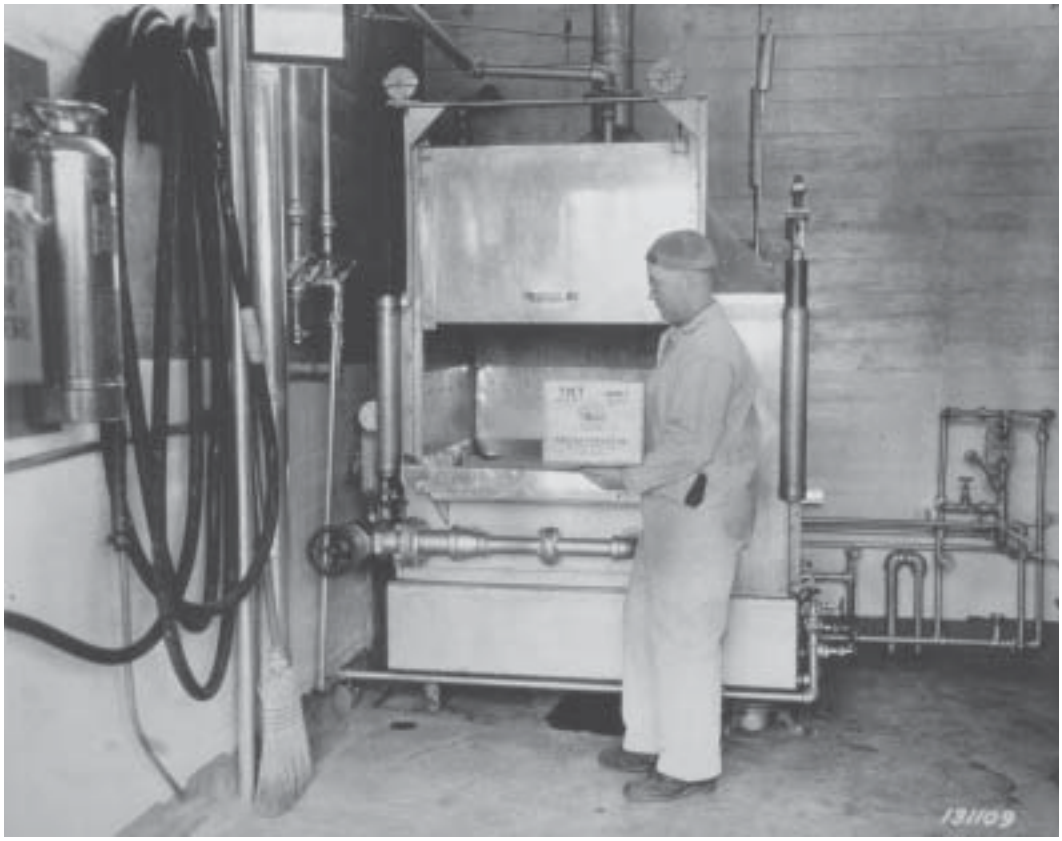


Fig. 9-7. This photograph is dated April 1942. A worker is preparing to dump a box of bulk TNT into the melt unit, through which steam is passed. The liquified TNT will then be poured into shells and bombs. The worker wears special nonsparking safety shoes made without nails. Photograph: Courtesy of the Ordnance Department, Signal Corps College; Ordnance Center, Picatinny Arsenal, New Jersey.

Fig. 9-8. This photograph was made at Wolf Creek Ordnance Plant, Milan, Tennessee, in June 1942. The ordnance worker is shown washing her hands after exposure to TNT, to prevent dermatosis**.** Photograph: Courtesy of the World War II Signal Corps College, *War Production 7:* 12.

Center at Picatinny Arsenal, New Jersey, is currently endeavoring to find a substitute for dinitrotoluene (DNT), which is both toxic to humans and mutagenic in animal systems. It has been classified as a suspect carcinogen.[12] Finding an appropriate substitute is expected to take about 5 years.

Some controls proved their worth during World War II and have endured the test of time. Some of those methods, still in use today, include

- enclosure of processes—the melt unit used in TNT melt-loading operations (Figure 9-7);
- general exhaust ventilation—the type used in rooms where poured TNT munitions are cooling;
- local exhaust ventilation—the type used in dusty operations such as sieving (known as *screening* in the chemical industry) flaked DNT or TNT;
- temperature control to reduce vapor generation—the type used in rolling operations with propellants containing nitroglycerin; and
- remote-controlled operations—the modern continuous-flow nitrators used to produce nitroglycerin.[13]

Administrative Controls

Since World War I, administrative controls have consistently emphasized work and sanitation practices (Figure 9-8). Today's administrative controls encompass more than just rotating employees in and out of areas with high exposure potentials; they include such essential measures as (*a*) educating workers about the toxic and safety hazards of the materials with which they work; (*b*) enforcing strict work-practice guidelines to minimize the generation of dusts and vapors, and to prevent dermal contact; (*c*) initiating appropriate sanitation practices, including paying strict attention to the waste-explosive contamination of workers' bodies and clothing; and (*d*) providing the workers' changing and shower rooms with separate locker facilities, to segregate their street from their work clothing. In addition, contaminated clothing should be removed immediately and placed in closed containers for storage, until it can be laundered or discarded properly. Contaminated skin should be washed promptly with soap and water. Furthermore, a worker who handles these toxic compounds should wash his or her face, hands, and forearms thoroughly with soap and water before eating, drinking, smoking, or using toilet facilities.[14] In keeping with these concepts, the following should also be prohibited in the work area: storing, preparing, dispensing, or consuming food or beverages; storing or applying cosmetics; storing or smoking tobacco products; and storing or using products for chewing, such as gum.

Personal Protective Equipment

PPE to control exposure should be used only when engineering and administrative controls are inadequate. During the world wars, the use of change houses and the wearing of coveralls became widespread. In addition, a great deal of attention was directed to the use of barrier creams to protect against the dermatitis and systemic toxicity associated with explosives such as trinitrophenylmethylnitramine (tetryl) and TNT. These creams have subsequently fallen into disfavor; their efficacy is limited and, increasingly, the emphasis is on exposure controls.

Appropriate respiratory PPE and gloves must be used where indicated; the National Institute for Occupational Safety and Health (NIOSH) has published guidance on the types needed.[12,15] The need for close coordination between safety and health personnel is emphasized by OSHA's position that the respiratory equipment supplied may itself create safety hazards in explosives manufacturing operations.[9] For example, some respirators, especially those with air supplied (by a tank, or a compressor and hose) can create sparks and therefore pose an unacceptable risk of igniting an explosion. In this instance, protecting the worker from a health hazard would compromise overall safety from explosion.

GENERAL MEDICAL CONSIDERATIONS

The greatest challenge facing any physician beginning to work in an industrial environment is to understand the hazards faced by employees in that industry. Military ammunition plants are no exception: each type of projectile and munition contains a unique combination of explosives. A carefully elicited occupational history might reveal, for example, that a worker is exposed to amatol or composition B. The physician must be able to interpret this information in terms of specific chemical exposures, just as he or she would interpret chemical trade names in the civilian sector. Those who work with composition C4 should be assessed for RDX (***r***esearch ***d***epartment ***ex***plosive, hexahydro-1,3,5-trinitro-1,3,5-triazine) toxicity, or given medical surveillance for RDX; cyclotol workers should be assessed for both TNT and RDX toxicity; amatol workers should be assessed for both TNT and ammonium nitrate toxicity; and double-base propellant workers should be assessed for both nitroglycerin and nitrocellulose toxicity. Sources of information include Material Safety Data Sheets, military specifications, and the model designations of specific ammunition items. Often the best information is available from the safety officer, industrial hygienist, or plant commander.

Preplacement Considerations

Preplacement examinations have been used by some industries as a measure to control costs rather than as a tool for maintaining worker health. As a consequence, professional organizations including the American Medical Association and the American College of Occupational and Environmental Medicine have made numerous, well-publicized comments on the appropriate, ethical use of these examinations. The Americans with Disability Act of 1990[16] precludes preemployment examinations from being applied as

discriminatory tools and requires that they be used only to assess critical aspects of job performance.

Despite this controversy, preplacement medical examinations remain part of the foundation of a medical surveillance program for workers exposed to hazardous agents. Medical surveillance should be performed primarily for the benefit of the individual employee and his or her immediate coworkers and should not be used for hiring and firing purposes.

Preplacement examinations are done to (*a*) identify preexisting conditions, (*b*) identify hypersusceptible individuals, and (*c*) establish preexposure baseline values. Preplacement examinations must identify preexisting conditions to ensure the worker's safe performance of critical job tasks. For example, blindness would preclude a worker's being assigned as a forklift operator. Similarly, certain neurobehavioral conditions such as epilepsy and severe psychiatric disorders may not be appropriate among explosives workers.[17] In addition, hypersusceptible individuals must be identified because they may be at higher risk for developing diseases related to specific occupational exposure. For example, individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency may have a hemolytic crisis when they are exposed to methemoglobin-inducing agents.

Preplacement examinations also establish preexposure baseline values for screening programs. For example, erythrocyte counts and liver-function tests may be appropriate for workers who are exposed to agents that are capable of inducing anemia or hepatotoxicity.

Acute Exposure Decontamination

The first-aid measures and treatment procedures for individuals who have been exposed to explosives and propellants are similar to those for exposure to other toxic substances. The rescue procedures follow those dictated for most emergencies, but the rescuers should try to prevent additional casualties among would-be rescuers. The main goals of initial treatment are to prevent further absorption and enhance excretion, which may be achieved by first removing the victim from exposure and then removing the contaminated clothing. Rescuers should thoroughly cleanse the skin with soap and copious quantities of water, paying attention to the hair and nails. Eyewash fountains should also be placed throughout the workplace to provide copious irrigation of the eyes in the event of a splash. Contaminated clothing should be either laundered carefully or discarded. The treatment of mild, asymptomatic cases may require nothing more than removal from exposure and decontamination.

COMMON MANIFESTATIONS OF EXPOSURE

Commonly, organic nitrates share these major toxic effects: dermal sensitization, methemoglobinemia, vasodilation, and carcinogenesis. Nitrates used in explosives are no exception. Each of these effects can occur separately or in combination; however, not every organic nitrate causes all four effects, at least according to current information. The prevalence of each of these effects varies with the specific chemical. For example, tetryl causes dermal sensitization almost exclusively, nitroglycerin causes vasodilation, and DNT is a mutagen and probable carcinogen. Many organic nitrates are potent vasodilators, and a few have found therapeutic uses in clinical medicine.

Dermatitis

Dermal sensitization refers to the induction of an allergic reaction via cutaneous exposure to a chemical. It manifests as allergic contact dermatitis. The other major occupational dermatitis is irritant contact dermatitis, which is a nonallergic reaction of skin exposed to a chemical. The immune system is not involved in irritant contact dermatitis, but is involved in the allergic form. Dermatitides caused by exposure to organonitrates have no pathognomonic characteristics to distinguish them from other irritant or allergic reactions.

Since World War I, both allergic and irritant contact dermatitides have been the most common toxic effects seen in explosives workers.[18] The agents most responsible are tetryl, TNT, amatol, ammonium picrate, picric acid, and mercury fulminate. However, the role of other ingredients and exposures must not be overlooked: industrial exposures to solvents, cutting oils, and degreasers all occur in the munitions industry and can also induce dermatitis.

Occupationally induced dermatitis (from all occupational exposures collectively) is considered to be the most prevalent occupational disease but it rarely causes any mortality. During World War I and World War II, however, morbidity from tetryl and TNT dermatitides was a major cause of time lost from work. Fortunately, these effects resolve after the worker has been removed from exposure, and they generally do not sensitize the individual to other chemicals.

Methemoglobinemia

Methemoglobinemia has been recognized as an adverse occupational effect since the 1800s, when coal-tar derivatives were introduced into the explosives and dye industries. Many drugs and chemicals exert an oxidant stress on hemoglobin, which oxidizes the iron in the heme portion of the molecule from the ferrous to the ferric form, thus rendering the hemoglobin molecule incapable of binding oxygen. The body spontaneously produces small amounts of methemoglobin, but enzymatic reducing systems within the erythrocyte normally maintain that concentration below 1% of the total hemoglobin. Clinical effects of methemoglobinemia may develop when more than 10% to 15% of the total hemoglobin is converted to methemoglobin. The acute signs and symptoms of methemoglobinemia include persistent, slate-gray cyanosis (the most readily apparent sign); fatigability; malaise; headache; and reddish-brown discoloration of the peripheral blood, which does not become bright red when exposed to oxygen. Massive exposure may cause 60% to 70% of the hemoglobin to convert to methemoglobin, which can produce collapse, coma, and death.

Chemicals that induce methemoglobinemia also tend to cause chronic anemia, which may develop insidiously even in the absence of cyanosis.[17] This anemia usually occurs when erythrocytes that contain methemoglobin hemolyze.

As they do with many toxic exposures, individuals have a wide range of sensitivity to methemoglobin-inducing chemicals. For example, individuals with G6PD deficiency and other hemoglobinopathies are uniquely sensitive to the hemolytic effects of exposure to these agents. Preemployment screening should identify individuals with G6PD deficiency and sickle-cell trait. Aggressive medical surveillance of workers at high risk has effectively reduced such exposures and health effects. Methemoglobin can be measured directly, but this must occur within just a few hours of sample collection because methemoglobin in erythrocytes reduces rapidly to hemoglobin. All cases of cyanosis and abnormal blood findings should trigger exposure-control action.[17]

Mild-to-moderate cases of methemoglobinemia will recover spontaneously within 2 to 3 days. In more severe symptomatic cases, methylene blue (administered intravenously as a 1% solution in saline at 1–2 mg/kg over 10 min) is an effective therapy. A second dose may be administered after 1 hour, if necessary.[19,20] Although hyperbaric oxygen has been advocated as a therapy, other authorities have not found it to be efficacious.[21,22]

Vasodilation and Carcinogenesis

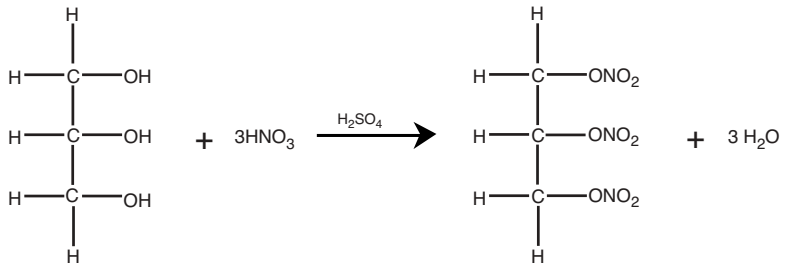
Although organic nitrates as a class cause both dermatological and hematological effects, specific explosives such as nitroglycerin and DNT are vasodilatory and mutagenic, respectively. These substance-unique effects are discussed in their specific chemistry sections, which follow.

THE ALIPHATIC NITRATE ESTERS

The aliphatic nitrate ester class of compounds includes many members with explosive properties, some of which are militarily significant (Figure 9-9). With the exception of nitrocellulose, members of this class are manufactured similarly and are similarly toxic. The physical properties and uses of the individual compounds vary, as does the amount of toxicological data available.

Nitroglycerin

Nitroglycerin was the first organic nitrate to be used



Glycerin Nitroglycerin (NG)

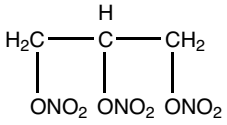
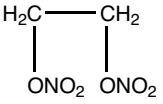
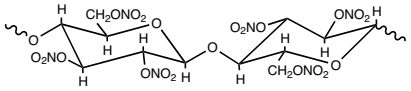
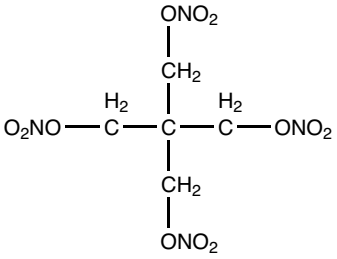
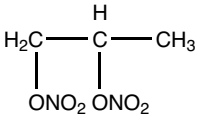
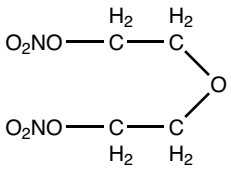
Common Name	CAS Registry Number	Synonyms	Formula	Structure
Nitroglycerin	55-63-0	1,2,3-Propanetriol trinitrate Glyceryl trinitrate Trinitroglycerin NG	$C_3H_5N_3O_9$	
Ethylene Glycol Dinitrate	628-96-6	Nitroglycol Glycol dinitrate EGDN	$C_2H_4N_2O_6$	
Nitrocellulose	9004-70-0	Cellulose nitrate Guncotton Collodion NC	$C_{12}H_{14}(ONO_2)_6O_4$	
Pentathritol Tetranitrate	78-11-5	2,2-Bis[(nitroxy)-methyl]-1, 3-propanediol dinitrate Penthrite Nitropenta TEN PETN	$C_5H_8N_4O_{12}$	
Propylene Glycol Dinitrate	6423-43-4	1,2-Propylene glycol dinitrate 1,2-Propanediol dinitrate Propylene glycol 1,2-dinitrate PGDN	$C_3H_6N_2O_6$	
Diethyleneglycol Dinitrate	693-21-0	2,2'-Oxy-bis-ethanol dinitrate Dinitrodiglycol DEGDN DEGN	$C_4H_8N_2O_7$	

Fig. 9-9. The aliphatic nitrate explosives, together with their common names, Chemical Abstract Society numbers, synonyms, formulae, and structures. The reader can compare the similarities and subtle differences in formulae and structures among the compounds in this group. Nitrocellulose is a variable-length chain consisting of repeated $C_6H_7(ONO_2)_3O_2$ units.

as an explosive. Although Ascanio Sobrero, an Italian chemist, first synthesized nitroglycerin in 1847, it was not widely appreciated until 1863, when Alfred Nobel began to use it as a blasting compound.[8] To make nitroglycerin safer to work with, Nobel began using solid materials to adsorb liquid nitroglycerin, from which *dynamites* were formed. (There are many formulations for dynamite, using different liquid or gelatinous explosives on a matrix of various solid materials.)

In 1888, Nobel demonstrated that, by using nitroglycerin to gelatinize nitrocellulose, the explosive properties of nitroglycerin could be converted to propellant uses; as a result, he developed not only the earliest of the smokeless powders but also the double-base propellants. Until then, all propellants had nitrocellulose alone as their explosive component—now called single-base propellants. Double-base propellants are those with nitroglycerin in addition to nitrocellulose. Triple-base propellants have nitroguanidine included as the third explosive component.[23] Military use of

TABLE 9-3

MILITARY USES OF SOLID PROPELLANTS

Class	Ingredients	Uses
Single Base (Primary)	Nitrocellulose	Howitzers Small arms Grenades
Double Base (Secondary)	Nitrocellulose Liquid nitrate ester	Howitzers Small arms Mortars Rockets Jet-propulsion units
Triple Base (Ternary)	Nitroguanidine Nitrocellulose Liquid nitrate ester	Howitzers
Composites	Physical mixture of fuel, binder and inorganic oxidizer	Rocket assemblies Jet-propulsion units

nitroglycerin is almost exclusively in combination with nitrocellulose as double- and triple-base propellants (Table 9-3).

The freezing point of nitroglycerin (13°C) caused a major safety problem with the early dynamites.[24] Explosions were not uncommon when munitions or dynamite were accidentally frozen during winter. Nitroglycerin in the solid state is much less sensitive than in the liquid. But while thawing, nitroglycerin is much more sensitive to detonation than while either a solid or a liquid. Decomposed nitroglycerin is especially dangerous. Not only is it more sensitive to accidental detonation than when pure, but the formation of nitrogen oxides may also constitute a separate toxicity hazard.[5] However, because the military use of nitroglycerin is limited almost exclusively to the double- and triple-base propellants, which are stable colloidal mixtures with lower freezing points, the instability of nitroglycerin at its freezing point is not a problem.

Other aliphatic nitrate esters have limited, specialized uses. In 1905, ethylene glycol dinitrate (EGDN, freezing point -8°F) was introduced as an additive to lower the freezing point of nitroglycerin, and since 1920, EGDN has been a major component of most civilian dynamite formulations.[24] EGDN has little current military use. However, another of the aliphatic nitrate esters, propylene glycol dinitrate (PGDN), is used as a torpedo propellant.[4]

Manufacture and Exposure Hazards

Nitroglycerin is manufactured by one of three *closed, continuous-flow* processes known as the Biazzi, Schmid-Meissner, and the Nobel-Nitrator processes, in which glycerin is mixed with concentrated nitric acid (Figure 9-10).[4] A closed process is one in which liquid chemicals are piped from one closed container to another—from the beginning of the process where feedstock is introduced to the end where finished product is packed for shipping or storage. A continuous-flow process is one in which the reactions occur constantly, not in batches. The product is subjected to a series of purifying washes and then transported by gravity flow to storage tanks. The nitration and purification processes—controlled remotely via closed-circuit television—are conducted in small, heavily revetted buildings. The other liquid aliphatic nitrates may be prepared by similar methods using other aliphatic polyols instead of glycerin.

Liquid nitroglycerin, together with nitrocellulose and other ingredients, is manufactured into double- and triple-base propellants by two methods.[4] In general, the *solvent process* is used for propellants that contain less than 40% nitroglycerin, while the *solventless process* is used for compositions that contain more than 40% nitroglycerin.

The solvent process begins with the addition of a solvent such as ether or acetone to water-wet nitrocellulose in a dough-type mixer (Figure 9-11). Nitroglycerin and other ingredients are added and mixed until a dry colloid forms. The mixture is then subjected to a series of presses to remove the solvent and complete the colloiding process. The first type of press is a hydraulic *blocking* press, which simply squeezes the liquid from the nitrocellulose mixture; next is the *macaroni* press, which improves the colloiding of the nitrocellulose with the nitroglycerin. Finally, the mixture is extruded through a die, cut to length, and dried in an oven to form the finished propellant.

The solventless process begins with mixing a slurry of nitrocellulose and nitroglycerin in a tank of water (Figure 9-12). Other ingredients are added, and the excess water is removed by centrifugation. The resulting paste is dried further, and any remaining ingredients are added. Repeated rolling between heated rollers removes the remainder of the water and completes the mixture's colloiding. The process is completed by extruding the dried colloid through a die and drying in an oven.

Occupational exposure to nitroglycerin can occur during any of these operations. In the solventless process, dermal exposure is especially significant

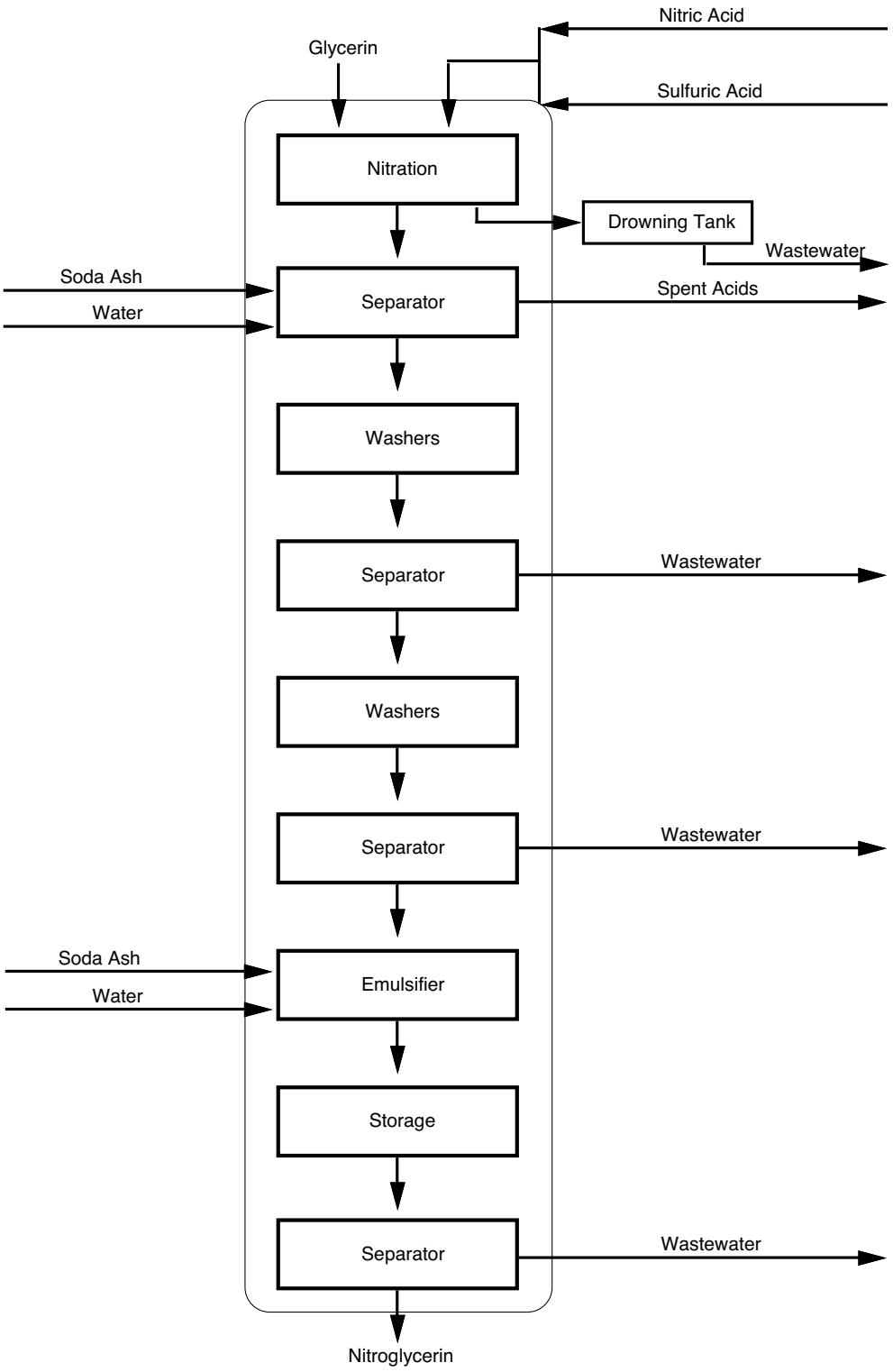


Fig. 9-10. In the Biazzi (continuous-flow) method of manufacturing nitroglycerin, all processes except the drowning tank are completely enclosed within stainless steel reaction vessels, which are connected by stainless steel pipes. Remote control is accomplished via gauges and closed-circuit television. Even the raw materials, wastewater, and nitroglycerin are piped into and out of the process, further limiting potential exposures of the workers. Adapted from US Army Environmental Hygiene Agency. *Water Pollution Aspects of Explosive Manufacturing*. Aberdeen Proving Ground, Md: USAEHA; 1985: 42. USAEHA Technical Guide 140.

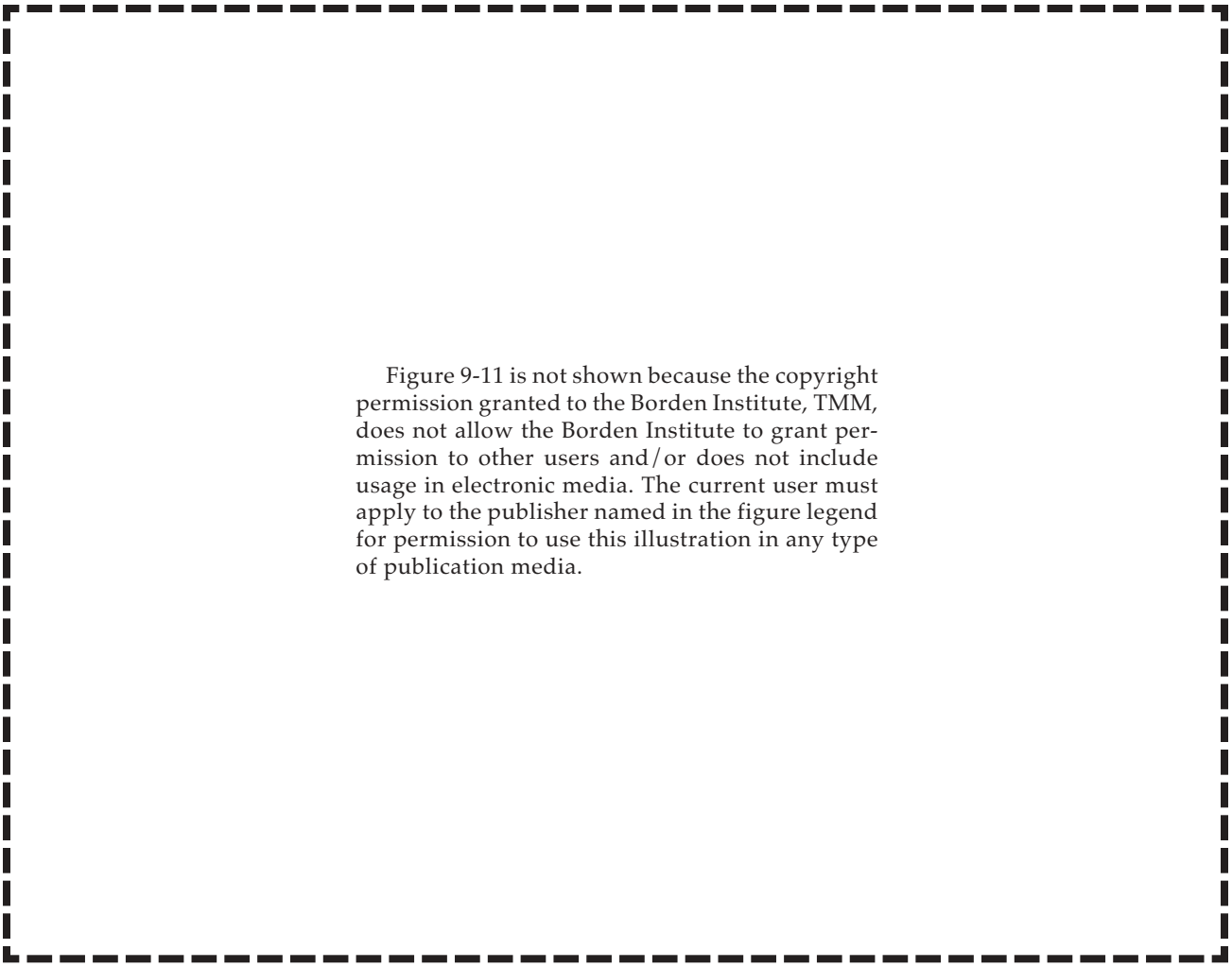


Fig. 9-11. In the solvent-based process of propellant production, the initial mixing is conducted in an alcohol-ether solution, which is then removed via the series of presses. Most production plants prepare these propellants in batches, and utilize manual labor at each step. Reprinted with permission from Chemical Propulsion Information Agency. Gun propellant process operations. In: *Hazards of Chemical Rockets and Propellants*. Vol 2, *Solid Propellants and Ingredients.* Laurel, Md: CPIA; 1985: 3-15. CPIA Publication 394.

among roller-press operators, and can be demonstrated: simultaneously collected samples will have higher concentrations of nitroglycerin in blood drawn from the cubital than the femoral veins. Due to the widespread use of engineering controls, exposure to vapors is minor during nitration, but inhalational exposure can be significant for press operators and drying-room attendants. During World War II, nitroglycerin toxicity caused at least 78 reported cases of lost time among propellant workers, several of whom required transfers to different work sites.[2] Almost certainly, other cases of nitrogly-cerin toxicity (including Monday morning angina, which is discussed below) occurred during World War II, but they either went unreported, were unrecognized, or did not result in time lost from work.

Human Exposure and Health Effects

The effects on human health from exposure to nitroglycerin have been observed since its discovery. Because of its vasodilating properties, nitroglycerin has been a mainstay of antianginal therapy since it was introduced to medicine in 1879. Reports of the effects that appeared in nitroglycerin workers and their families were described in the literature as early as 1890; yet consensus still has not been reached on all of the effects.[25–28] Contention still surrounds the chronic effects such as withdrawal syndrome and sudden death. Little epidemiological study has been done on these effects in humans, and consequently little proof exists of the chronic effects. The acute effects are so

Fig. 9-12. In contrast to the solvent-based process, the solventless process uses no extraneous solvents during mixing. Nitroglycerin (or, less often, another liquid aliphatic nitrate such as EGDN or DEGN) is used to form a colloid with the nitrocellulose. Dissolution does not occur, but rather, the mixing and milling achieve a uniform colloid of the explosives and additives. Milling and extrusion are usually done at warm temperatures, and there is significant exposure potential for inhalation and dermal absorption of nitroglycerin. Reprinted with permission from Chemical Propulsion Information Agency. Gun propellant process operations. In: *Hazards of Chemical Rockets and Propellants*. Vol 2, *Solid Propellants and Ingredients.* Laurel, Md: CPIA; 1985: 3-16–3-17. CPIA Publication 394.

dramatic that our attention is frequently focused on the short term, to the neglect of the long.

Toxicokinetics. The toxicokinetics of nitroglycerin have been studied and reviewed intensively.[29-33] Nitroglycerin is readily absorbed through intact skin, as well as via the respiratory and gastrointestinal tracts. Vascular-tissue uptake and local metabolism are extensive, thus explaining the rapid systemic clearance of nitroglycerin. Once nitroglycerin is absorbed, it is rapidly metabolized by hydrolysis and glutathione-dependent organic nitrate ester reductase.

Because of their rapid hydrolyses, nitroglycerin and the other aliphatic nitrates have shorter biological half-lives than other classes of explosives.[24,33] The variations among individuals in their sensitivity, plasma levels, time of onset of symptoms, and duration of effects are extremely wide. Metabolites may alter the toxicokinetics of the parent compound during chronic dosing.[34]

Acute Effects. Acute or intermittent exposure to nitroglycerin may cause a constellation of symptoms in sensitive individuals. Vasodilatory effects can occur with inhalation of airborne concentrations as low as 0.1 mg/m^3. Most of these symptoms are due to direct vasodilation of the meningeal, cutaneous, and systemic blood vessels. Symptoms due to vasodilation include headache, dizziness, nausea, palpitations, hypotension, flushing, and abdominal pain. Other effects of acute exposure appear to be mediated by other mechanisms and include methemoglobinemia, reflex tachycardia, and increased respiratory rate. Hyperthyroidism has been reported to potentiate the acute toxicity of the organic nitrates.[27]

Inhalation exposure at levels as low as 14 mg/m^3 have led to more severe effects such as electrocardiogram (ECG) changes, chest pain, and palpitation. Massive acute exposure may cause cyanosis, coma, and death.

Other acute effects have been described, but they are less well documented. Central nervous system (CNS) symptoms such as confusion and hallucinations and psychotic episodes such as homicidal violence have been reported in patients after they have handled nitroglycerin. Peripheral nervous system effects such as paresthesias have also been reported.

Ingestion of nitroglycerin is not an industrial problem. It could theoretically occur via contamination of food or smoking materials in the workplace, but this has never posed a practical problem in manufacturing settings. Of course, the use of sublingual nitrates is a common form of therapy for coronary artery disease, taking advantage of the transdermal and transmucosal absorption and the vasodilatory effect of some nitrates.

Chronic Effects. Most workers become tolerant to the vasodilatory effects of nitroglycerin within 1 week after their exposure has begun and develop compensatory vasoconstriction. This effect has also been described in patients who receive therapeutic nitroglycerin.[34] The tolerance persists for approximately 1 week after the worker is removed from the exposure.

Workers who have become tolerant to the vasodilatory effects of nitroglycerin may experience a withdrawal syndrome if their exposure is terminated abruptly. This withdrawal may precipitate angina pectoris, myocardial infarction, and sudden death. The condition has been called Monday morning angina because the symptoms appear after a 48- to 72-hour absence from work. Anecdotal reports of these effects have appeared since the early 1900s, but the first medical case series was reported in 1952.[35]

The mechanism associated with angina and sudden death appears to be a series of events starting with habituation to the hypotensive effects of chronic nitrate exposure. When removed from exposure, the employee develops rebound hypertension, which may be followed by coronary insufficiency.[17] Coronary insufficiency is, therefore, a secondary effect due to rebound coronary vasoconstriction, making the heart less able to compensate for the additional strain caused by systemic hypertension. Studies done with animals have shown that nitroglycerin-tolerant subjects become more sensitive to vasoconstrictors after they are withdrawn from nitroglycerin. Some have shown electrocardiographic ST segment changes and ventricular arrhythmias suggestive of coronary artery spasm.[28] Evidence is accumulating that withdrawal from nitroglycerin increases the sensitivity of alpha 1 adrenergic receptors in the coronary arteries to endogenous and exogenous vasoconstrictive agents.[28]

The chronic cardiac effects of nitroglycerin withdrawal appear to be latent for 6 to 10 years before the onset of symptoms.[35] Several studies of Swedish dynamite workers have demonstrated excess mortality from cardiovascular and cerebrovascular disease. This excess mortality was only significant for workers with long-term employment and had a latency of 20 years.[32] A more recent, retrospective, cohort-mortality study of workers at a U.S. Army ammunition plant showed an excess of mortality from ischemic heart disease among workers younger than 35 years of age.[28] Pathological examinations of nitroglycerin workers who have experienced cardiac events have failed to reveal coronary artery disease, strengthening the conclusion that rebound vasospasm is responsible.[28,36]

A 1965 review of earlier case reports revealed complaints of digestive troubles, tremors, neuralgia, and, in rare cases, skin sensitization among nitroglycerin

workers.[37] Decreased alcohol tolerance is common and may be caused by nitroglycerin's interference with liver alcohol dehydrogenase. Simultaneous exposure to ethanol and nitroglycerin can cause manic behavior.[38]

Numerous other chronic effects of nitroglycerin exposure have been reported, but are poorly documented. Research has been conducted on other chronic effects in mammals, but the results have not been substantiated in humans. Chronic oral administration of nitroglycerin in rats has produced cancer of the liver. Other research with mammals has indicated the possibility of male reproductive, fetotoxic, and teratogenic effects.[29,39] It was previously believed that nitroglycerin could increase intraocular pressure and precipitate glaucoma, but further evidence has disproved this.[31]

Medical Surveillance

Early identification of cardiovascular disease is the primary goal of medical surveillance of nitroglycerin workers. A preplacement examination must be administered to all new employees, and should consist of both medical and occupational histories, a physical examination, and indicated laboratory tests (Table 9-4). When their employment begins, nitroglycerin workers should maintain a daily record of their pulse rates. Periodic examinations should be conducted semiannually, with the same focus as the preplacement examination. During the periodic examination, the physician should be aware that headaches that occur during workshifts can indicate skin absorption of nitroglycerin, even if air concentrations of nitroglycerin are below the PEL. Examinations with similar content are necessary when exposure to nitroglycerin has been terminated, although surveillance should perhaps extend beyond employment, due to the latency of the withdrawal effects.[14]

In addition to performing the medical surveillance examinations, the plant should follow this procedure to safeguard the health of its workers:

- First, the plant physician should alert the worker's private physician to the effects of exposure to and withdrawal from nitroglycerin.
- Second, workers who leave the plant due to any kind of illness should be cleared through the medical department.
- And third, workers should also be examined before they return to work after lengthy absences.

This procedure, common in all types of industries, is a management tool used as an administrative control measure. When workers leave the plant with any illness, a medical examination can help determine if that illness is due to an acute overexposure to nitroglycerin (or any other toxic agent). By early detection of a sentinel event, the plant management can intervene at the worksite and thus protect other workers in the area, as well as the ill individual on his or her return to work. An examination is necessary whenever a nitroglycerin worker returns from an illness to assure that the worker's health status has not changed in such a way that he or she will be placed at risk. Specifically, the occupational physician should look for changes in cardiovascular status, such as a recent myocardial infarction or new-onset hypertension.

A biological marker of exposure would be a useful aid to the occupational health physician (as is true for any chemical exposure). Blood methemoglobin levels increase after high exposures, but these are not sufficiently sensitive to monitor exposure to nitroglycerin.[40,41] Nitroglycerin can be detected in blood, but, because cubital venous blood samples reflect almost

TABLE 9-4

PREPLACEMENT EXAMINATION FOR NITROGLYCERIN WORKERS*

Component	Emphasis
Medical History	Alcohol use Tobacco use Hypertension Cardiovascular system Dermatitis Anemia Neurobehavioral disorders Medications Reproductive system
Occupational History	Prior respirator use Prior nitrate exposure Weekend/vacation chest pain
Physical Examination	Cardiovascular system Skin Nervous system Mental status Blood pressure
Tests	CBC Resting ECG Lipid profile Urinalysis

*Medical surveillance also applies to workers exposed to other aliphatic nitrate explosives.

exclusively the locally absorbed compound from the distal part of the arm, they are unreliable indicators of systemic exposure.[40–42]

Primary Prevention

The most efficacious method to control occupational nitroglycerin toxicity is to prevent exposure using engineering controls and hygienic work practices. This is especially true because adverse effects occur at exposure levels below the odor and eye-irritation thresholds that could warn workers of potentially hazardous environments.[26,43]

Several types of engineering controls have proven to be effective in reducing inhalational exposure, including automation, closed-circuit television, and ample work-area ventilation. Volatilization of the aliphatic nitrates can be minimized by processing at the lowest practicable temperatures. Operations that require heating should be controlled remotely.[17] Maintaining a water seal over liquid nitroglycerin will prevent its evaporation and reduce its concentration in air.

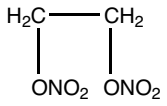
When necessary, PPE should be worn to prevent dermal contact and to reduce airborne levels to an acceptable range. Particular attention must be devoted to the type of gloves worn. Polyethylene gloves may be the best choice, because nitroglycerin easily penetrates neoprene, leather, and rubber. Cotton or canvas gloves, frequently changed, are also preferable to rubber gloves. A face shield or splash-proof safety goggles may also be necessary to protect the eyes. An organic vapor respirator may also be required to prevent headache, especially at concentrations higher than 0.02 ppm.[12]

The selection of a respirator is controversial at present because (*a*) the efficacy of half-mask, air-purifying respirators is unproven and (*b*) the respirators supplied to be used during explosives manufacture have potential safety hazards.[9,12] To date, the only respirators that have been demonstrated to provide a sufficiently high protection factor are the full-face, supplied-air respirators. However, even these are yet to be proven safe in the potentially explosive atmospheres that may exist in nitroglycerin manufacturing operations. Therefore, the only way to assure that workers are protected is to lower the airborne level through engineering controls. However, this is not feasible in all cases. Both the government and industry are aggressively pursuing a resolution to this problem, to comply with the lower OSHA PEL for nitroglycerin that was promulgated in 1989.[9]

Careful attention to personal hygiene is necessary to prevent workers from contaminating their street apparel, and, as a result, possibly poisoning their family members. At a minimum, manufacturing plants should provide change-house facilities that contain an adequate number of coveralls, and shower facilities for employees to use at the end of their shifts. Indicator soaps are available; they turn red in the presence of residual nitroglycerin not removed from the skin. Sodium sulfite in the soap reacts with nitrate groups in nitroglycerin to form sodium sulfonate.[43] (A similar reaction also occurs with asymmetrical TNT isomers and tetryl.)

The treatment for nitroglycerin poisoning consists of removing the patient from the source of exposure, thoroughly cleansing the skin and mucous membranes of nitroglycerin contamination, and providing cardiovascular support. Washing the skin with aqueous sodium thiosulfate will assist in neutralizing any nitroglycerin that remains. The use of oral nitrates and calcium channel–blocking agents has been somewhat efficacious in the treatment of nitroglycerin withdrawal. Both help in nitroglycerin withdrawal (but not in toxicity as such) by reducing reflex vasospasm; the oral nitrates work by drug replacement (analogous to using nicotine gum in tobacco cessation, or methadone in heroin withdrawal, to overcome the physiological effects of withdrawal); the calcium channel blockers work by a different pharmacological mechanism to induce vasodilation.

Ethylene Glycol Dinitrate

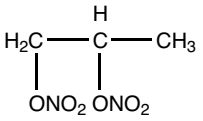


Ethylene glycol dinitrate (EGDN) is frequently used together with nitroglycerin in civilian formulations, but is rarely encountered in military propellants.

Due to its higher vapor pressure, EGDN vapors predominate at all concentrations when present with nitroglycerin. Liquid EGDN appears to be absorbed transdermally more rapidly than nitroglycerin, and EGDN vapors penetrate intact skin. Surgical gloves, used to protect the skin, absorb more of the vapor, but are less permeable to liquid EGDN through direct contact than are cotton gloves.[44]

The symptoms and effects of exposure to EGDN, as well as the medical surveillance and treatment, are the same as those for nitroglycerin. EGDN can be measured in blood and urine, but its concentration in urine is a more reliable indicator of exposure than blood levels. The clinical use of urinary EGDN levels to confirm exposure, however, has not yet been documented.[40,41]

Propylene Glycol Dinitrate



Propylene glycol dinitrate (PGDN) is the principal component (75% by volume) of Otto Fuel II, a torpedo propellant that was introduced in 1966; therefore exposure to PGDN can potentially occur during torpedo maintenance. This liquid has significant vapor pressure under ambient conditions, and is quite soluble in lipids. In the navy during torpedo defueling, refueling, repair, and maintenance, torpedo man's mates have been exposed to PGDN through dermal contact and inhalation. Airborne exposures of up to 0.22 ppm of PGDN can occur during defueling and refueling.

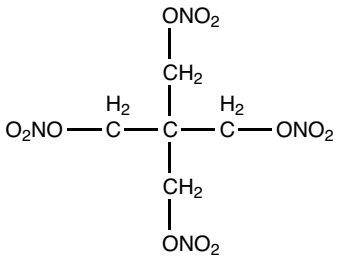
Acute exposure can have several effects similar to those caused by exposure to nitroglycerin, many of which are due to vasodilation. These effects include headaches, nasal congestion, dizziness, impairment of motor coordination and balance, eye irritation, disruption of visual evoked responses, and altered oculomotor function.

In humans, PGDN affects the cardiovascular system and the CNS. At concentrations higher than 0.2 ppm, acute exposure to PGDN produces headaches and CNS depression without evidence of biochemical, hematological, or spirometric changes.[45] Whether PGDN can cause significant cardiovascular effects remains controversial. Exposure to PGDN at levels twice the TLV did not cause cardiovascular or neurological effects in torpedo maintenance workers in one study.[46] Another cohort of torpedo man's mates who were potentially exposed to PGDN at levels up to 0.22 ppm showed an increased risk for myocardial infarction and angina pectoris.[47] The U.S. Navy is evaluating Otto Fuel II for teratogenicity, which is a suspected consequence of maternal methemoglobinemia and related blood dyscrasias.[48]

High doses of PGDN in animals have led to hypotension, methemoglobin formation, and hemosiderin deposits in the liver and kidneys, indicating that erythrocytes, the liver, and the kidneys are also targets for PGDN.[45]

The medical surveillance and exposure controls for PGDN exposure are the same as those for nitroglycerin exposure.[47]

Pentaerythritol Tetranitrate



Pentaerythritol tetranitrate (PETN) is prepared either in batches or by continuously nitrating pentaerythritol (tetramethylolmethane), which is manufactured from formaldehyde and acetaldehyde. PETN is used as a pentolite mixture with TNT in the manufacture of small-caliber projectiles, grenades, and booster charges and is also used alone in the manufacture of detonating fuzes and detonators. Additionally, PETN has been used therapeutically for its vasodilatory effects. Its trade name is Peritrate, manufactured by Parke-Davis.

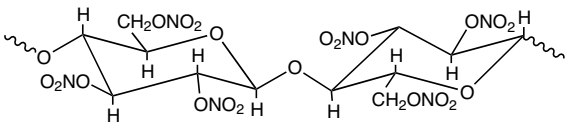
Under ordinary circumstances, PETN has very low potential for exposure. It is nearly insoluble in water, and is usually handled water-wet. PETN is absorbed slowly from the gastrointestinal tract, skin, and lungs. Compared to nitroglycerin, PETN is significantly less toxic and more stable.

The acute effects of exposure to PETN are similar to those of nitroglycerin.[49] Hypotension and increased respiratory rate may both occur, but to a lesser degree than is observed with nitroglycerin. In contrast to nitroglycerin, little reflex tachycardia is observed with PETN. Dyspnea and convulsions have also been reported.

Data on the human effects of chronic exposure to PETN are almost completely lacking. Chronic toxicity of PETN was studied in rats during the early 1940s. Although hemosiderin was found in the spleens of the PETN-treated rats, no pathological changes were observed in their vascular systems. The continued feeding of PETN in doses of 2 mg/kg daily over a period of 1 year did not produce significant effects in the rats.[49]

The medical surveillance for and treatment of exposure to PETN should be the same as that for nitroglycerin.

Nitrocellulose



Nitrocellulose is a nonvolatile, fibrous, white solid consisting of chains of glucoside units in which the hydroxyl groups have reacted to form nitrate esters. The molecular weight depends on the chain length and the degree of polymerization, which in turn depend on the source of the cellulose. Many sources of cellulose may be used, including paper rolls, cotton linters, wood pulp, and waste cotton.

Manufacture and Exposure Hazards

Nitrocellulose was first produced in 1838, but practical difficulties in manufacturing and using the material were not overcome until 1865. Since that time, it has become the basic component of single-base solid propellants. Nitrocellulose is the principal ingredient in gun and mortar propellants, smokeless powder, and ball powder. The military's production of nitrocellulose is second only to its production of TNT. Nitrocellulose is also a component of combustible cartridge cases, and in the civilian sector is used in manufacturing blasting fuzes and mining charges.

In explosive applications, nitrocellulose requires a higher degree of nitration than that produced for its nonexplosive uses such as lacquers, medical collodion, ink bases, or filter membranes. Military-grade nitrocellulose is produced at various U.S. Army ammunition plants in a process wherein cellulose is nitrated with concentrated nitric and sulfuric acids. The only significant byproducts of manufacture are the spent acids, which are concentrated and then reused.

Human Exposure and Health Effects

Insoluble in water and resistant to biological degradation, nitrocellulose per se has a very low potential as a hazard to human health. As an insoluble polymer, nitrocellulose is not absorbed in the gut, and in fact does not appear to be absorbed by any route. The only effects of ingestion are due to the bulk of fiber, which may occlude the intestinal lumen, and are no different than effects of nonnitrated cellulose. Nitrocellulose is not irritating to the skin, and no mutagenic activity has been detected.[50]

Other exposures during the manufacture of nitrocellulose are of greater significance to workers. These include exposures to acids and acid vapors during the initial nitration process, which may lead to dental erosions and chemical burns. Uncontrolled exposure to raw cotton dust from the linters before nitration can cause byssinosis, which is also known as cotton-mill or mill fever. It is a usually allergic, occupational, respiratory disease of cotton, flax, and hemp workers and is characterized by symptoms—especially wheezing—that are most severe at the beginning of each work week (because the lack of exposure over the weekend allows large quantities of the mediators of allergy, such as histamine, to accumulate).

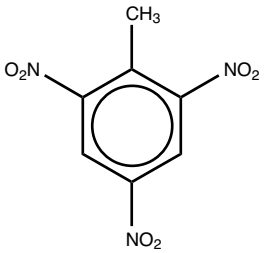
The potential hazards encountered during the manufacturing process necessitate that precautions be taken. Adequate ventilation during both preparation of the linters and nitration is essential. It is recommended that PPE be worn by employees who work near the acids.

No medical surveillance for exposure to nitrocellulose is necessary, and treatment for the sequelae of acid contact is not unique. No exposure limits have been established for nitrocellulose.

THE NITROAROMATICS

The nitroaromatics were the second class of organic nitrates to become important as explosive compounds, and they continue to be represented prominently in the world's arsenals (Figure 9-13). These chemicals are well absorbed by all routes and tend to rapidly penetrate the dermis. The major effects of these chemicals include methemoglobinemia, cancers of the urinary tract, anemia, and skin sensitization.[21,51]

Trinitrotoluene



Not the first to be synthesized but now the best known of the aromatic nitrate explosives, 2,4,6-trinitrotoluene (TNT) was first prepared in Germany in 1863. Although it was not manufactured industrially until 1891, TNT rapidly became the premier high explosive.[24] Major military powers adopted TNT as their major high explosive in 1901, when it replaced picric acid. The first significant military use of TNT was during the Russo-Japanese War of 1905.

Many factors, including its low cost, safety in handling, compatibility with other explosives, low melting point, moderate toxicity, and low sensitivity, have made TNT the most widely used military explosive of the 20th century. Before 1940, its manufacture was limited by the availability of toluene (then a byproduct of the coke industry; see Chapter 1, Occupational Health in the U.S. Army). Advances in petroleum chemistry during World War II permitted the synthesis of large quantities of inexpensive toluene, which greatly enhanced TNT production capacity in the United States.[24]

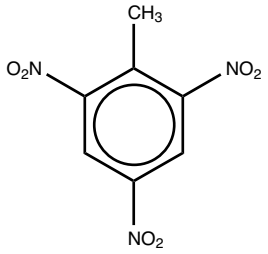
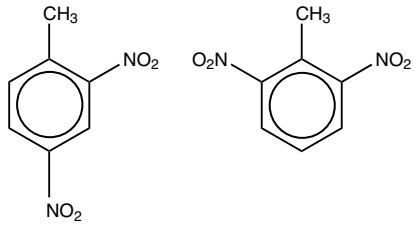
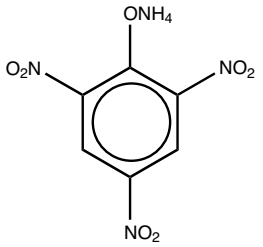
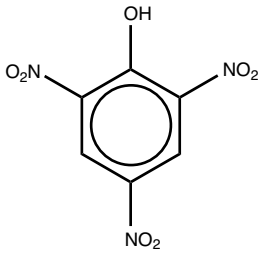
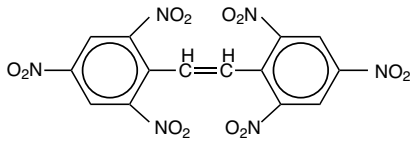
Common Name	CAS Registry Number	Synonyms	Formula	Structure
Trinitrotoluene	118-96-7	2,4,6-Trinitrotoluene 1-Methyl-2,4,6-trinitrobenzene TNT	$C_7H_5N_3O_6$	
Dinitrotoluene	2,4-: 121-14-2 2,6-: 606-20-2	2,4-Dinitrotoluene 2,6-Dinitrotoluene DNT	$C_7H_6N_2O_4$	
Ammonium Picrate	131-74-8	Ammonium 2,4,6-trinitrophenolate Explosive D Dunnite	$C_6H_6N_4O_7$	
Picric Acid	88-89-1	2,4,6-Trinitrophenol Melmite Lyditte Shimose	$C_6H_3N_3O_7$	
HNS	20062-22-0	Hexanitrostilbene	$C_{14}H_6(NO_2)_6$	

Fig. 9-13. The nitroaromatic explosives, together with their common names, Chemical Abstract Society numbers, synonyms, formulae, and structures.

TNT can be found in virtually all military applications and is frequently mixed with aluminum and other high explosives to form binary or ternary explosives. Its easy availability during World War II made TNT a perfect suspension agent for more-powerful explosives such as PETN and RDX, and made melt-loading methods feasible.[21] In 1973, at the end of our mobilization for the Vietnam War, an estimated 200,000 tons of TNT were produced in the United States.[52] By 1986, however, domestic production had been curtailed due to the increasing pressure that had developed regarding the chemical's contamination of the environment. Civilian applications, less common than military, still include using TNT in commercial explosives and propellants, and as an intermediate in the production of dyes and photographic chemicals.[21]

Manufacture and Exposure Hazard

TNT was formerly prepared by batch nitration of toluene, but current manufacturing methods are based on continuous stepwise nitration of toluene, with a mixture of concentrated nitric and sulfuric acids flowing countercurrent to the toluene (Figure 9-14). Soda ash (anhydrous sodium carbonate) and sodium sulfite are used in the washing and crystallization processes to purify the crude TNT solution. The purified TNT is then dried in a steam-jacketed pan before being flaked and packed. Occupational exposure to acids, toluene, and impure TNT are minimal during the continuous-manufacture process, in contrast to the older batch processes.[53]

The most significant risk of exposure to TNT occurs during shell-loading operations. Exposure can occur during several of the steps, most of which involve the melt-loading process. In this process, dry flakes of TNT are poured into a steam-heated melting kettle and heated to approximately 100°C. Other high-melting, nonmetallic additives such as RDX or nitrostilbene are added at this point (usually water-wet to control their flammability). Continued heating drives off the water, and flaked aluminum may be added at this point. The mixture is then cooled until the established pouring consistency is reached. After the mixture is poured, the loaded shells are cooled under controlled conditions before the *risers* (funnellike devices that are fitted into the nose of each shell to facilitate filling the loads to the top) are removed and further processing occurs. Exposure to TNT dust, fume, and vapor can occur during any of these operations.

Exposure to TNT can also occur during numerous circumstances other than shell loading (Table 9-5). During World War II, some of the highest TNT dust levels occurred during screening operations (passing TNT flakes through a sieve), where concentrations up to 75 mg/m^3 were measured in breathing zones.[13] Workers can also be exposed to TNT fumes and vapors during demilitarization (removing TNT from shells), when munitions may be steam cleaned to melt and remove the high-explosive charge.

Humans can also be exposed to TNT that has contaminated the environment. Significant amounts of TNT and its manufacturing byproducts have been released into the environment as huge volumes of liquid wastes from factories and LAP plants. These liquid wastes (the *red* or *pink* water) contain TNT isomers, DNT isomers, and mononitrotoluenes. Due to the difficulty and expense of disposing of this waste, the United States currently relies on imported and stockpiled TNT. Two options may be for paper mills to use the red water as a process chemical in the manufacture of kraft products, or to concentrate and incinerate the effluent to yield crude sodium sulfate.[54]

Human Exposure and Health Effects

TNT's toxicity to humans has been recognized for at least 75 years. Most of our knowledge results directly from work performed during the two world wars. In the United States from 1914 to 1918, approximately 24,000 people were poisoned with TNT, fatally in 580 instances. Similar experiences were described in other combatant nations. In Great Britain from 1916 through 1941, 475 cases of TNT poisoning were reported, of which 125 were fatal.[55] In the United States during World War II, TNT poisoning was a factor at manufacturing and loading plants and arsenals, although the case rates at arsenals and manufacturing plants were less than one-half that at loading plants. Of the 21 deaths that occurred, 18 were at loading plants, 2 at arsenals, and 1 at a TNT-manufacturing facility.[2] Progressively more people were exposed to more chemical as the war continued, yet the morbidity was much lower. Case rates for all locations fell dramatically despite the marked increase in TNT production, thus demonstrating the effectiveness of occupational health interventions.

Researchers analyzed the 21 TNT fatalities of World War II, together with another late death of a former TNT worker. Of this series, 8 died of toxic hepatitis and 13 of aplastic anemia. The late death occurred in a worker who apparently had recovered from hepatitis but later succumbed to aplastic anemia. Only one-third of these fatalities had been exposed to average airborne concentrations higher than the maximum allowable concentration of 1.5 mg/m^3 that prevailed

a

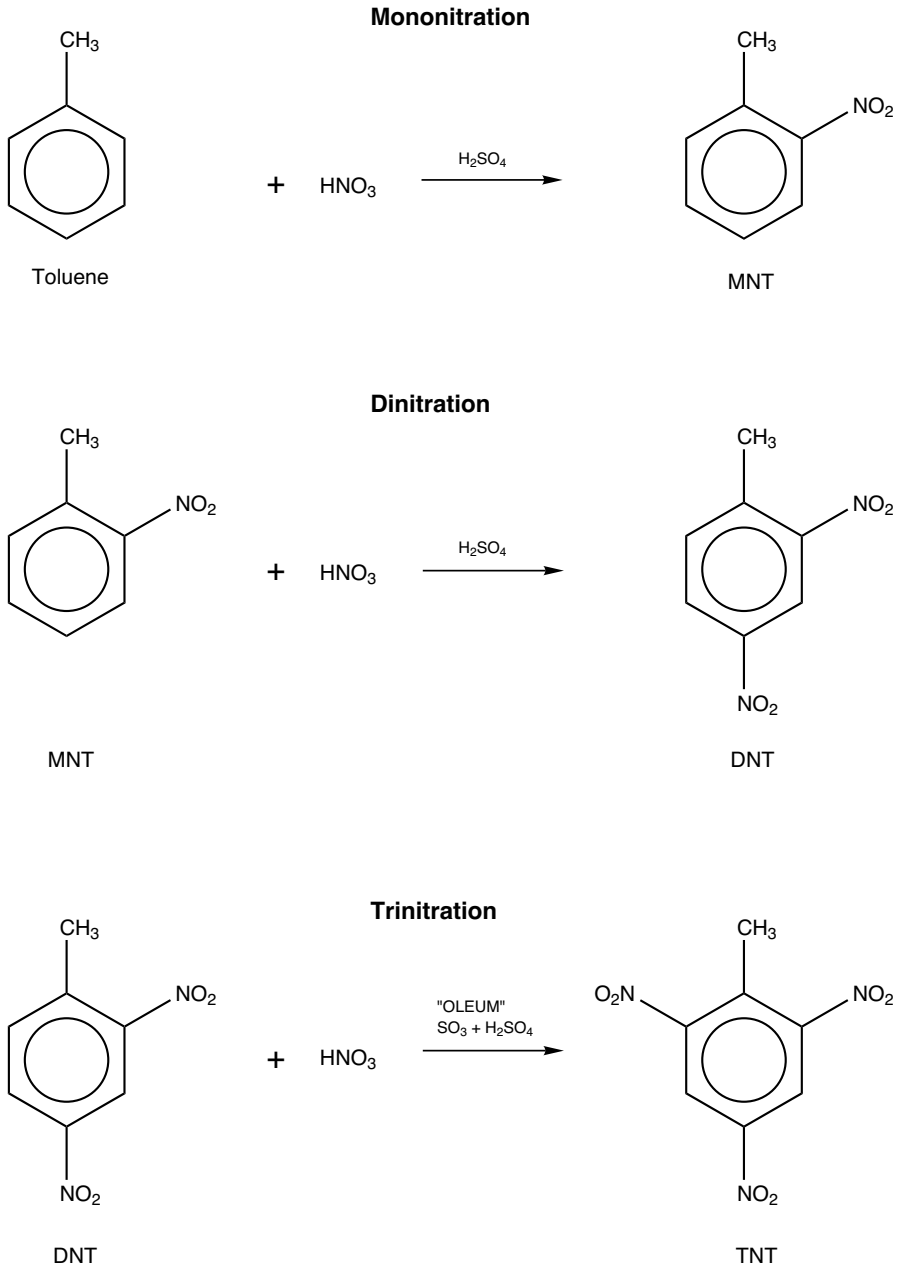
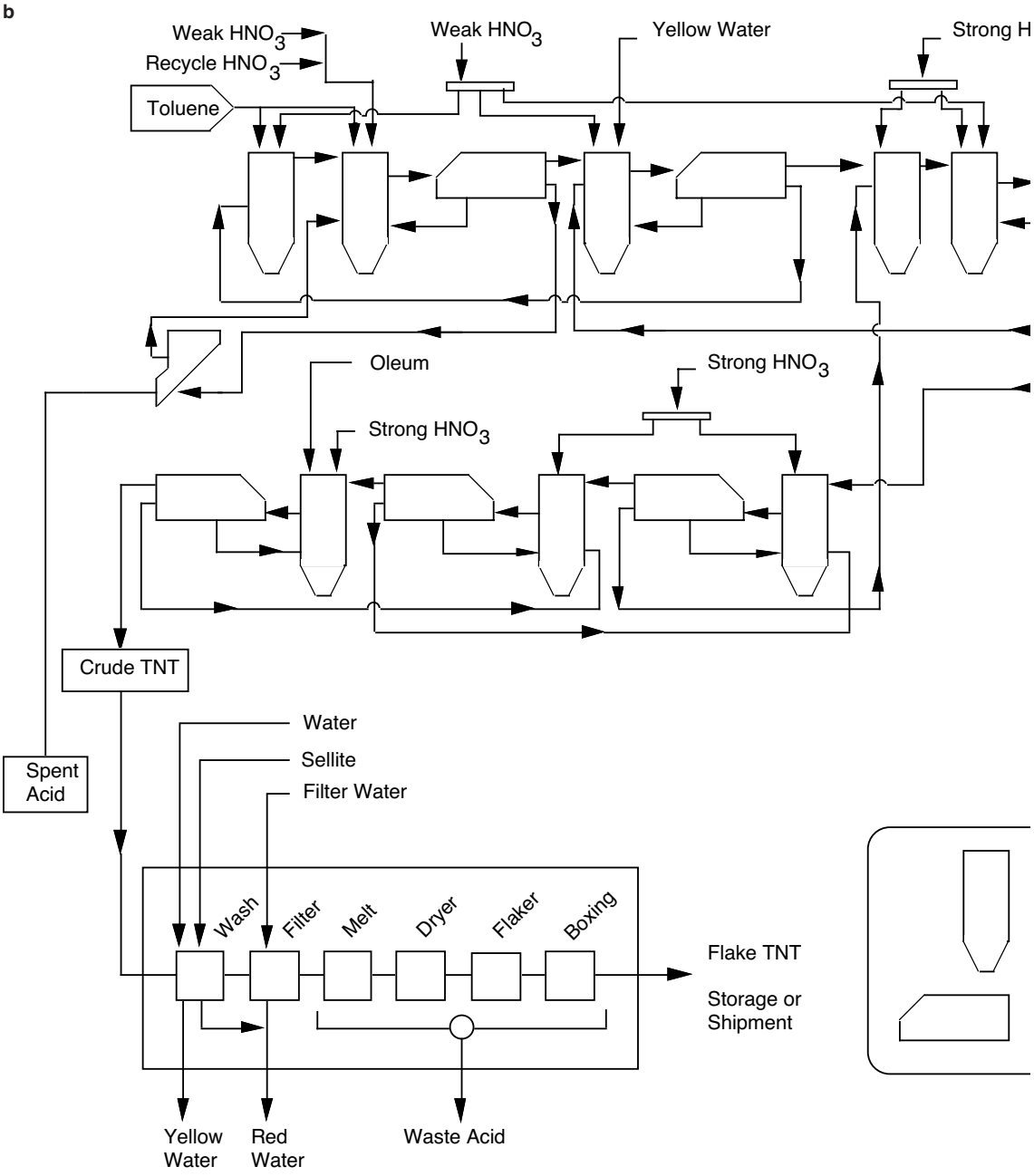


Fig. 9-14. The trinitration of toluene: (**a**) chemical synthesis and (**b**) industrial (enclosed) process stream. In the manufacture of TNT, toluene is first reacted with nitric acid to form mononitrotoluene (MNT), which is then pumped to another area, where it is reacted with nitric acid (under different reaction conditions) to form dinitrotoluene (DNT). The DNT is then pumped to yet another area where it is reacted with oleum (a solution of sulfur trioxide dissolved ——►

b



in anhydrous sulfuric acid) to form crude TNT. The crude TNT then undergoes a series of washes to remove crude unreacted toluene, MNT, and DNT. Reprinted from US Army Environmental Hygiene Agency. *Water Pollution Aspects of Explosive Manufacturing*. Aberdeen Proving Ground, Md: USAEHA; 1985. USAEHA Technical Guide 140; (**a**) p 16, (**b**) pp 28, 30.

TABLE 9-5

HEALTH HAZARDS OF EXPLOSIVE OPERATIONS

Operation	Nature of Exposure	Degree of Exposure	Recommended Control Measures
Screening	TNT dust	Severe	Enclosed operations; local exhaust ventilation
Melting	TNT dust, fume, and vapor	Slight	Local exhaust ventilation
Draw off	TNT fume and vapor	Moderate	Local exhaust and room ventilation
TNT cooling	TNT fume and vapor	Slight to severe	Automated operations; local exhaust and room ventilation
Pouring	TNT dust, fume, and vapor	Slight to moderate	Room ventilation, careful work practices, worker rotation
Bomb filling	TNT fume and vapor	Slight to severe	Local exhaust and room ventilation, careful work practices
Bomb puddling, nose, and tail pouring	TNT dust, fume, and vapor	Slight to severe	Room ventilation, careful work practices, worker rotation
Adding TNT scrap	TNT dust, fume, and vapor	Moderate to severe	Room ventilation, careful work practices, gloves, worker rotation
Booster cavity drilling	TNT dust	Slight to severe	Elimination of deep drilling, local exhaust ventilation
Riser knockoff	TNT dust	Slight to moderate	Well-designed risers, local exhaust ventilation, careful work practices
Riser breakout	TNT dust	Moderate to severe	Enclosed operations, local exhaust ventilation
TNT scrap breakup	TNT dust	Moderate to severe	Enclosed operations, local exhaust ventilation
Flaking and graining	TNT fume and dust	Slight to moderate	Enclosed operations, local exhaust ventilation
Box filling	TNT dust	Slight to severe	Enclosed operations, local exhaust ventilation

Sources: (1) Buck CR, Wilson SE. *Adverse Health Effects of Selected Explosives (TNT, RDX)*. Aberdeen Proving Ground, Md: USAEHA; 1975. Occupational Study 32-049-75/76. (2) Brandt AD. Engineering control of air contamination of the working environment. In: Gafafer WM, ed. *Manual of Industrial Hygiene and Medical Service in War Industries.* Philadelphia: WB Saunders; 1943: 198.

then, which reflects the contribution of dermal absorption. Workers who died of toxic hepatitis were younger than those who died of aplastic anemia (their median ages were 35 and 45 years, respectively). In both conditions, the median period of exposure was quite short: 63 days for hepatitis, and 216 days for anemia.[6]

Other cohort studies of TNT workers have shown that virtually all cases of toxic hepatitis have occurred within the first 3 months of exposure, while cross-sectional studies have not shown significant signs of hepatotoxicity.[56] This may indicate that a sensitive subgroup of individuals is at risk for this effect.

Another World War II–era study evaluated the effects of TNT intoxication in 250 male and 103 female workers in a bomb- and shell-loading facility.[57] No cases of severe TNT intoxication were seen; however, adverse effects of TNT exposure were found in 32 workers (30 of whom were males), of whom 21 had either gastritis or hepatitis; 14 had anemia; and 3 had systemic manifestations of intoxication.[57]

Toxicokinetics. TNT is readily absorbed by all routes of exposure. Approximately 60% to 70% of oral

doses are absorbed; inhaled TNT appears to be not only absorbed faster than oral doses but it also reaches higher concentrations in the blood. Dermal absorption is less efficient, but its significance must not be underestimated. TNT dissolved in water is particularly well absorbed through the dermis. As might be expected, this effect is greater in hot weather due to the combined effects of greater skin exposure and the dissolution of TNT dust in sweat. Workers' coincident exposure to hygroscopic chemicals such as ammonium nitrate further promotes dermal absorption by keeping the skin moist.[8] Consequently, measuring only airborne levels may significantly underestimate the workers' total systemic exposure.[56,58]

TNT is metabolized primarily by a two-step process: the reduction of the nitro group and its conjugation to glucuronide. Some enterohepatic recycling occurs, but urinary clearance of the glucuronides occurs fairly rapidly, preventing bioaccumulation. The urine of humans who have been exposed to (and of most experimental animals that have been given) TNT becomes discolored with a red metabolite.

Dermatitis and systemic effects do not correlate well.[54] Hematological effects appear to occur at lower doses than hepatic effects, but susceptible individuals will develop hepatotoxicity sooner after initiation of exposure.

Acute Effects. Acute exposure to airborne TNT can cause irritation of the upper respiratory tract and skin; symptoms include sneezing, coughing, rhinitis, and erythematous dermatitis. The onset of acute systemic toxicity is frequently heralded by gastrointestinal symptoms such as nausea, anorexia, and epigastric pain.[54] Systemic symptoms may progress to include headache, fatigue, malaise, palpitations, loss of memory, and cyanosis.[55]

Chronic Effects. The most serious chronic manifestations of TNT toxicity are (*a*) anemia and other hematological changes and (*b*) hepatitis; the chronic effects may also include (*c*) dermatitis, (*d*) ocular effects, (*e*) neurological effects, and (*f*) cancer.

Hematological effects result from the action of TNT on both the bone marrow and mature erythrocytes. Although virtually every cell series in the marrow is affected, the most significant hematological effects occur in the erythrocytic series, and may result in anemia with both aplastic and hemolytic components. TNT depresses erythropoiesis and induces aplastic anemia by suppressing two enzymes that catalyze heme synthesis: δ-aminolevulinic acid synthase (ALA synthase; see Chapter 12, Lead) and heme synthase. This suppression has been demonstrated even in the clinical absence of anemia. Some compensation with reticulocytosis may occur, and marrow hyperplasia has been noted as an early effect,[8] but this is followed by marrow hypoplasia and the compensation effect is lost.

Hemolysis in TNT toxicity occurs as a result of methemoglobinemia. This is a dose-related effect, with low-grade anemia and compensatory reticulocytosis noted at airborne TNT concentrations lower than 0.5 mg/m^3. Exposures of 0.2 to 0.5 mg/m^3 appear to have minimal and well-compensated effects on erythrocytes. Poikilocytosis may occur, as well as hepatic and splenic congestion related to hemolysis. Early signs and symptoms of fatal anemia—even in the absence of G6PD deficiency—include weakness, anorexia, weight loss, cough, epistaxis, elevated bilirubin, decreased hemoglobin, and decreased leukocyte counts. Survival in the case reports of fatal anemia varied from 6 to 185 days, but the median was only 40 days.[6] Hemolytic crisis has been seen in G6PD deficiency within the first few days after exposure.

Other hematological effects include both leukocytosis and leukopenia. Transitory leukocytosis and moderate eosinophilia have been described at airborne levels lower than 2.5 mg/m^3. Leukopenia develops late, well after the hemoglobin level and erythrocyte count fall, in contrast to other chemically induced aplastic anemias. Exposure to TNT causes the monocyte count to increase, regardless of the presence of symptoms, and neither the extent of dermal contact nor the length of inhalational exposure influences the intensity of the hematological response.[59]

TNT poisoning can induce both massive hepatic necrosis and cirrhosis. As with most hepatotoxic agents, the hepatitis manifests with increases in the concentrations of serum transaminases and lactate dehydrogenase (LDH). Researchers found no liver function abnormalities at a time-weighted average (TWA) lower than 0.5 mg/m^3, but they found elevated aspartate aminotransferase (AST) and LDH at airborne concentrations of 0.8 mg/m^3, which persisted even at 0.6 mg/m^3.[60] Early symptoms of TNT-induced hepatitis include nausea, vomiting, malaise, and hepatic tenderness. Jaundice, although a late symptom of TNT hepatitis, develops rapidly as the liver atrophies and has a poor prognosis. In a study of TNT-induced hepatitis fatalities from World War II, the average elapsed time from the first definite symptom to death was 34 days, with a range of 12 to 53 days.[6]

Dermatitis is the most common chronic effect of exposure to TNT. Yellow-orange staining of the skin, hair, and nails is a common sign, and irritant contact dermatitis may occur. Dermatitis requires at least 5 days of exposure to develop, and most patients become tolerant to mild cases.[18,61] Palmar lesions with deep vesicles are characteristic. Allergic contact der-

matitis with classic eczematous lesions has been reported, and may rarely appear as an erythema-multiforme-like eruption. The sensitization dermatitis usually affects the upper limb, but the skin at friction points such as the collar line, belt line, and ankles may also be involved.[14] Workers exposed to high levels of TNT dust are especially at risk for dermatitis, although it may occur in workers throughout the manufacturing process.

According to several studies performed in eastern Europe, exposure to TNT has also been associated with cataracts, but at undefined levels of exposure. TNT workers in Finland have developed equatorial cataracts at concentrations of airborne TNT of 0.14 to 0.5 mg/m^3. These characteristic cataracts are insidious in their development and are present only at the lens periphery; consequently, they do not affect vision. They may not be noted on a routine ophthalmological examination, although they are easily observed when the affected eyes are dilated and examined with a slitlamp.[62] Most affected subjects in the eastern-European studies had normal liver-function tests. These subjects' duration of exposure to TNT was 1.2 to 17.0 years, with a mean of nearly 7 years. Older workers were more commonly affected, and the lens changes appear to be irreversible. Cataract for-mation may result from direct action of TNT on the lens via lipid peroxidation and production of superoxide anions.[63]

Research into whether neurological signs develop from TNT exposure has yielded controversial results. European accounts of TNT exposure report neurasthenia and polyneuritis.[4] While some accounts of TNT exposure in the United States support these conditions, at least one investigator has concluded that symptoms of peripheral neuritis among workers were not solely due to TNT exposure.[64] This study found that, when present, symptoms were limited to mild sensory disturbances, with no objective evidence of the disease.

TNT has been implicated in carcinogenesis in studies done with laboratory animals, but this has not been noted in human epidemiological studies. The results of feeding studies performed on rodents have shown increased incidence of bladder papilloma and carcinoma, and statistically insignificant increases in leukemia and lymphoma. TNT might be genotoxic, as it has given positive results in the Ames assay both with and without metabolic activation.[54] (The Ames assay, a basic toxicological tool, is an in vitro test for mutagenicity. It measures the occurrence of reverse mutagenesis in genetically modified *Salmonella typhimurium* strains. See also Chapter 14, Pesticides.)

Numerous other manifestations that have been attributed to exposure to TNT include myalgia, cardiac dysrhythmia, nephritis, increased vascular permeability, cardiotoxicity, pancreatic exocrine abnormalities, increased capillary fragility, menstrual disorders, and testicular atrophy and hyperplasia.[55]

Primary Prevention and Medical Surveillance

Historically, control of exposure to TNT has been accomplished through the general safety and hygiene measures discussed earlier in this chapter, yet additional, specific measures are necessary. The Hazard Communication Program, for example, should instruct workers about the need for strict personal and shop hygiene, and about the hazards of the particular operations that are conducted in that plant. In addition, soap that contains 5% to 10% potassium sulfite will not only help remove TNT dust from the skin, suds that turn red will also indicate any remaining contamination. Further-more, respiratory protective equipment should be selected according to NIOSH guidance, and should be worn during operations that release dust, vapor, or fumes.

Before World War II, research suggested that improving the nutritional status of TNT workers might help improve their resistance to toxic effects. However, in a World War II–era cohort study, multivitamin capsules were not shown to be efficacious in preventing TNT toxicity.[65]

Because TNT interacts with certain medications—including those that cause intrahepatic cholestasis, hepatocellular necrosis, and bone marrow depression—patients taking medications such as isoniazid, halothane, phenylbutazone, phenytoin, and methotrexate, and whose exposures to TNT cannot be precluded, should be closely followed by the occupational physician.

The U.S. Army currently recommends preplacement and periodic (semiannual) examinations of TNT workers. The recommended content of the preplacement examination is found in Table 9-6. The occupational physician should determine on a case-by-case basis which of the elements in Table 9-6 to use in periodic surveillance. However, to identify workers with higher-than-normal sensitivity to TNT toxicity, we recommend specifically that workers undergo monthly hemoglobin, LDH, and AST determinations during the first 3 months of exposure to TNT.[56] One study—which was cited both in the open and in U.S. Army literatures—demonstrated that assaying for AST, LDH, and hemoglobin in combination detected all abnormal cases, whereas if the assays were performed alone

TABLE 9-6

PREPLACEMENT EXAMINATION FOR TNT WORKERS

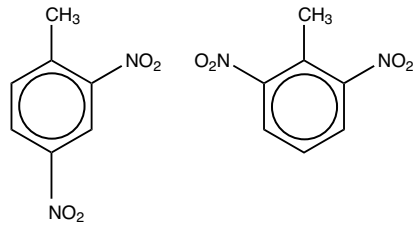
Component	Emphasis
Medical History	Alcohol use
	Tobacco use
	Allergies
	Cardiovascular system
	Skin
	EENT
	Hematologic system
	Liver disease
	Nervous system
	Respiratory system
	Renal System
	Medications
Occupational History	Prior TNT sensitivity
	Prior exposures to hepatotoxins
Physical Examination	Allergies
	Cardiovascular system
	Skin
	EENT, including slitlamp examination of eyes
	Liver
	Nervous system
	Mental status
Tests	CBC with differential and reticulocytes
	Methemoglobin
	Renal function
	Liver function
	Microscopic urinalysis

Adapted with permission from Hogstedt C, Davidsson B. Nitroglycol and nitroglycerine exposure in a dynamite industry 1958–1978. *Am Indust Hyg Assoc J.* 1980;41:373–375.

or in pairs, many cases were missed.[60,66] Periodic examinations provide inadequate warning of impending aplastic anemia.[67] Workers who have abnormal results should be removed from exposure and evaluated further.[66,68]

Bioassay for TNT exposure began during World War II with the use of Webster's test for urinary TNT.[69] This qualitative test was based on the reaction of alcoholic potassium hydroxide with an ether extract of acidified urine, wherein colors are produced when TNT and other metapolynitro compounds are present in urine.[70] (Anthraquinones and indole red may cause interference, however.[69]) In comparison to the qualitative Webster's test, a quantitative test for urinary aminodinitrotoluene (ADNT), a metabolite, can be related to TNT absorption within 24 hours of exposure. The urinary ADNT is measured via gas chromatography with electron-capture detection.[70] Most individuals excrete their highest concentrations of ADNT within a few hours after exposure, but some still excrete significant amounts many hours later. This prolonged excretion time may indicate that TNT or a metabolite has been retained, or may perhaps indicate delayed skin absorption. Prolonged dermal absorption has been indicated in a group of explosives workers whose urinary concentrations of ADNT indicated higher total exposures than were predicted from the concentrations in ambient air.[58,71]

Dinitrotoluene



In 1980, nearly 8% of the total toluene produced in the United States was converted to dinitrotoluene (DNT), which is widely used in military applications and in civilian applications such as dye manufacturing and organic chemical synthesis. Of the DNT produced currently, 99% is used in the synthesis of toluene diamine, an intermediate in the production of toluenediisocyanate. DNT may also comprise up to 10% of commercial dynamite formulations. Military uses of DNT are similarly broad, where it is usually used as an additive to modify the properties of other explosives. For example, DNT may function as a combustion modifier in propellants, as a gelatinizer in explosives, or as a waterproofing agent in explosives.[4]

Manufacture and Exposure Hazard

Due to the serious safety and health hazards inherent in the manufacture of DNT (it is regulated as a carcinogen and is even more hazardous than TNT), current practices for technical-grade DNT use continuous, closed systems that are highly automated and remotely controlled. Technical-grade DNT is a greasy liquid comprised of approximately 80% 2,4-DNT and 20% 2,6-DNT, but military-grade DNT requires highly purified 2,4-DNT flakes. Significant occupational exposure is possible during the purification and flaking

processes, as well as during the later mixing and shell-loading operations. Because DNT is also present in the waste water of TNT manufacturing and shell-loading plants, significant environmental contamination, and thus exposure, can also occur.

Human Exposure and Health Effects

DNT is readily absorbed via all routes of exposure, but absorption through the dermis is probably the most significant. In rats, both the 2,4- and 2,6- isomers are extensively metabolized by the liver and then excreted in bile.[72] Intestinal nitro-reductase-active bacteria further metabolize the product, which is resorbed and remetabolized to an as-yet-unidentified—but genotoxic—product.[73] The excretion of 2,4-DNT metabolites in humans is qualitatively similar to that in rats; however, humans do not excrete the reduced metabolite of 2,6-DNT. This qualitative difference in metabolism makes interspecies extrapolation of the carcinogenic risks difficult.[74,75]

Acute Effects. The most characteristic sign of acute DNT toxicity is methemoglobinemia. Associated symptoms include headache, fatigue, cyanosis, irritability, and nausea. Moderate exposures may cause ataxia, respiratory depression, and arthralgias, while severe exposure may lead to progressive CNS depression and death.[73,74]

Chronic Effects. Anemia and ischemic heart disease are the most commonly recognized chronic effects of exposure to DNT.[73] The anemia occurs when erythrocytes that contain methemoglobin hemolyze, and is typically low-grade and partially compensated.[74] Increased mortality from ischemic heart disease has been seen in munitions workers who were exposed to DNT during the 1940s and 1950s.[76,77] Unfortunately, the lack of adequate exposure data precludes our ability to make dose-response estimates for these effects.

Concerns about the carcinogenicity of DNT have been expressed for several years, and have recently focused on incompletely burned DNT in propellant residue at waste propellant disposal sites. Anyone exposed is at risk for carcinogenesis, including workers at the disposal sites, and all who are environmentally exposed via dust, groundwater, or direct contact with contaminated soil. DNT isomers exhibited only weak mutagenic activity in the Ames assay[74] and no activity in various mammalian cell culture genotoxicity assays. However, feeding studies in rats using both technical-grade DNT and 2,6-DNT showed a high incidence of hepatocellular carcinomas produced by 2,6-DNT, with a lower incidence in females compared to males. Enterohepatic recirculation with hepatic and intestinal microfloral metabolism are necessary for the production of an as-yet-unidentified ultimate carcinogen. Three major mammalian carcinogenicity studies have indicated that 2,6-DNT is both an initiator and a promoter, while 2,4-DNT is only a promoter.[22,74] Evidence of carcinogenicity in humans is lacking, however. Two occupational-cohort studies have been completed on workers exposed to DNT. Neither study showed any excessive incidence of cancer, but both demonstrated elevated cardiovascular and cerebrovascular mortality.[46,76]

Deleterious effects on the reproductive systems have been reported in rats that were given large doses of DNT ($\geq$34.5 mg/kg/d), but such effects were not seen in a NIOSH study of workers at a DNT-toluenediamine (TDA) plant.[78] Testicular atrophy, decreased spermatogenesis, and nonfunctioning ovaries have been seen in rats, mice, and dogs in feeding studies performed to assess chronic exposures. Results of multigenerational reproductive studies in animals have been negative. Only one of three epidemiological studies has shown effects on the human reproductive system, and those were limited to decreased sperm counts, minor morphologic changes in sperm, and a small increase in spontaneous abortions among wives of exposed workers.[73,74] Studies done on animals and humans have failed to identify teratogenic effects.

Other chronic effects noted in studies on animals include neurotoxicity and hepatotoxicity, with histological changes in both organs noted at autopsy. Sensitization dermatitis may also occur, but not as frequently as with exposure to TNT. Friction sites are frequently affected by DNT dermatitis.

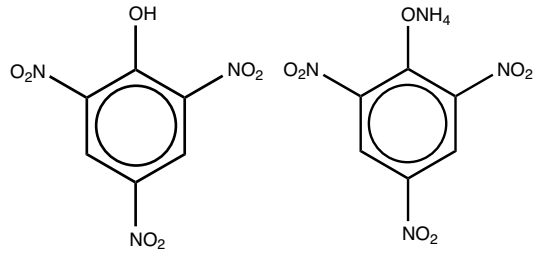
Primary Prevention and Medical Surveillance

As with all potential carcinogens, prevention of exposure is essential with DNT. Workers who could potentially be exposed to DNT should be informed of the deleterious health effects, including the possible reproductive system effects. In addition to the safety and hygiene measures previously mentioned, occupational health personnel should monitor for residual buildup of DNT on clothing, boot linings, and hardhat liners. Respiratory protection is usually unnecessary, because DNT has low vapor pressure.

Medical surveillance should consist of the same protocol as that for TNT, with the addition of a reproductive history, and the measurement of urinary DNT. The preplacement evaluation should include a baseline sperm count and morphology assessment for workers who intend to have children. Semen analysis should

not be necessary during routine periodic medical surveillance of exposed workers.

Picric Acid and Ammonium Picrate



Picric acid was first prepared in 1771 for use as a yellow dye, and in 1885 the French first utilized its explosive characteristics as a bursting charge for shells. However, the introduction of TNT during the 20th century eclipsed picric acid's use as a high explosive. For military purposes, some of picric acid's chemical characteristics are disadvantageous: its high melting point, which makes picric acid more difficult to shape into bombs and projectiles, and its tendency to form sensitive salts with materials such as calcium, lead, zinc, and other metals.[24] Sensitive salts are likely to explode with small shocks or bumps, and the rate and extent of these salts' formation is unpredictable.

The military currently uses picric acid only as a raw ingredient for ammonium picrate, which, due to its insensitivity to impact, is used in some armor-piercing shells. The civilian sector formerly used picric acid in burn ointments[5] and currently uses it in pharmaceutical manufacture,[21] leather tanning, dyes, copper and steel etching, forensic chemistry, and photographic emulsions.

Human Exposure and Health Effects

Systemic effects from inhaling or ingesting picric acid and ammonium picrate are rare; the main health effects that workers experience after exposure have been dermatological. Exposure to dust or fumes may cause skin and eye irritation, allergic dermatitis, and yellow staining of the skin and hair. Picric acid does not appear to penetrate intact skin, and dermal exposure probably contributes little to systemic absorption and toxicity. In contrast, inhaled and ingested picric acid is well absorbed, and in rare cases can cause headache, vertigo, loss of consciousness, myalgias, nausea, vomiting, gastroenteritis, hemorrhagic nephritis, and acute hepatitis. Evaluation of mutagenicity has yielded mixed results in prokaryotic and eukaryotic tests.[79]

Primary Prevention and Medical Surveillance

Preplacement examinations should be conducted according to the information contained in Table 9-7.[68,80] Once again, the contents of the periodic job-related examination should be determined by the occupational physician on a case-by-case basis.

Other Nitroaromatics

Several other nitroaromatics have unique properties that allow them to be used by the military in specialized but limited ways. The powerful explosives 1,3-diamino-2,4,6-trinitrobenzene (known as DATB or DATNB) and 1,3,5-triamino-2,4,6-trinitrobenzene (TATB) are used in plastic explosives.[24] Hexanitrostilbene (HNS) is a derivative of TNT that is very stable at high temperatures. It is used in plastic bonded explosives and detonation fuzes, and is being investigated as a nucleating agent for cast TNT and the TNT-RDX mixture that is known as composition B. As a nucleating agent, it reduces the crystal size in TNT casts and prevents formation of dangerous filling defects when the TNT contracts and cools.[81] HNS is used with 2,2',4,4',6,6'-hexa-nitroazobenzene (HNAB) in detonating fuzes.[4] Data regarding the toxicity of these explosives are virtually nonexistent, although they may be expected to show effects similar to the other nitroaromatic explosives.

TABLE 9-7

PREPLACEMENT EXAMINATION FOR PICRIC ACID AND AMMONIUM PICRATE WORKERS*

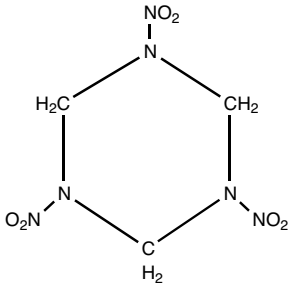
Component	Emphasis
Medical History	Asthma Allergies Sensitization to ammonium picrate and picric acid Sensitization to tetryl
Examination	Kidneys Liver Blood Skin
Laboratory Tests	Chemical and microscopic urinalysis Liver-function tests

*Periodic examinations should be administered annually.
Reprinted from Centers for Disease Control, National Institute for Occupational Safety and Health, Occupational Safety and Health Administration. *Occupational Health Guidelines for Chemical Hazards.* Washington, DC: US DHHS and US DOL; 1981. DHHS (NIOSH) Publication 87-116.

THE NITRAMINES

The nitramines are the most recently introduced class of organic nitrate explosives (Figure 9-15). The most prominent member of this class is RDX (***r***esearch ***d***epartment ***ex***plosive; hexahydro-1,3,5-trinitro-1,3,5-triazine, which is also known as cyclonite); HMX (***h***igh-***m***elting ***ex***plosive; octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine), nitroguanidine, and tetryl are also significant nitramines.

Hexahydro-1,3,5-trinitro-1,3,5-triazine



Although RDX (see Figure 9-15) was first prepared in 1899, its explosive properties were not appreciated until 1920. RDX was used widely during World War II because petroleum was not needed as a raw ingredient.[24] During and since World War II, RDX has become the second-most-widely used high explosive in the military, exceeded only by TNT. As with most military explosives, RDX is rarely used alone; it is widely used as a component of plastic explosives, detonators, high explosives in artillery rounds, Claymore mines, and demolition kits. RDX has limited civilian use as a rat poison.

Manufacture and Exposure Hazard

RDX is manufactured using the continuous Bachman process, in which hexamine is nitrated with ammonium nitrate and nitric acid in a solvent mixture of acetic acid and acetic anhydride. The byproducts of RDX manufacture include nitrogen oxides, sulfur oxides, acid mists, and unreacted ingredients (Figure 9-16). In 1964, during mobilization for the Vietnam War, the Holston Army Ammunition Plant alone produced approximately 750,000 pounds per day of RDX and HMX combined.[82]

Soldiers and other workers have been exposed to RDX during its manufacture, in the field, and through the contamination of the environment. The main occupational exposure to RDX during its manufacture is through the inhalation of fine dust particles. Ingestion may also be a possible route of exposure, but it is poorly absorbed through the dermis.[83]

The greatest potential for occupational exposure to RDX occurs at ammunition plants with LAP operations, where workers involved with melt-loading and maintenance operations have the greatest potential for exposures.[83] During World War II, there were no fatalities and little morbidity at RDX manufacturing plants. Small numbers of Italian and German workers, who handled powdered RDX in the drying, cooling, screening, and packing processes, were reported to have experienced RDX toxicity, but all recovered completely.[84]

In 1962, five cases of convulsions or unconsciousness or both occurred at an RDX manufacturing plant in the United States. In four of these instances, exposure was from inhaled dust during cleanup of a mixing area. The fifth employee screened and blended dried RDX from different batches; gross skin and air contamination occurred because no mechanical ventilation was used and the individual did not follow handwashing and hygiene precautions. All five employees had convulsions during their workshifts or within a few hours after their shifts were over. These patients exhibited little or no prodrome, and the postictal phase lasted up to 24 hours. No abnormal laboratory or physical findings were noted.[84]

Troops have also become intoxicated during field operations from exposure to composition C4 plastic explosive, which contains 91% RDX. These field exposures occurred because C4 was either chewed as an intoxicant or used as a fuel for cooking. Thus, the route of exposure was ingestion or inhalation. At least 40 American soldiers experienced convulsions due to RDX ingestion during the Vietnam War.[85,86]

RDX in the waste water from manufacturing and loading operations has also contaminated the environment. Although contamination has appeared in soil and groundwater near some ammunition plants, RDX's low solubility in water has limited its migration in most cases.

Human Exposure and Health Effects

The mainstay of treatment for RDX exposure is removal from exposure. Patients who are experiencing seizure activity should be given phenobarbital. Phenytoin is ineffective in controlling RDX-induced seizures.[85]

Toxicokinetics. Gastrointestinal absorption of RDX in humans is slow but complete; serum levels peak approximately 12 hours after ingestion. Clearance of RDX from the serum occurs in approximately 15 hours. The highest tissue levels of RDX occur in the kidneys,

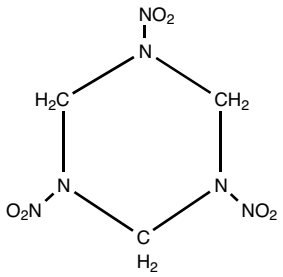
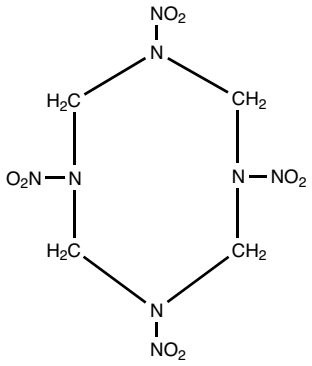
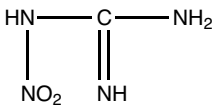
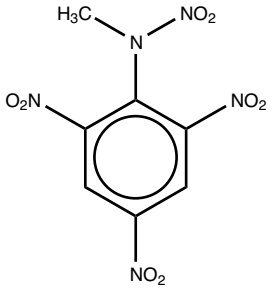
Common Name	CAS Registry Number	Synonyms	Formula	Structure
RDX (Research Dept. Explosive)	121-82-4	Cyclonite Hexahydro-1,3,5-trinitro-1,3,5-triazine	$C_3H_6N_6O_6$	
HMX (High-Melting Explosive)	2691-41-0	Cyclotetra-methylenetetra-nitramine Octahydro-1,3,5,7-tetra-nitro-1,3,5,7-tetrazocine Octogen	$C_4H_8N_8O_8$	
Nitroguanidine	556-88-7	Alpha-nitroguanidine Guanidine-1-nitro N(1)-nitroguanidine NQ	$CH_4N_4O_2$	
Tetryl	479-45-8	2,4,6-Trinitrophenylmethyl-nitramine N-methyl-N-2,4,6-tetranitro-analine N-methyl-N-2,4,6-tetranitro-benzamine N-methyl-N,2,4,6-tetranitro-methylamuline Nitramine	$C_7H_5N_5O_8$	

Fig. 9-15. The nitramine explosives, together with their common names, Chemical Abstract Society numbers, synonyms, formulae, and structures.

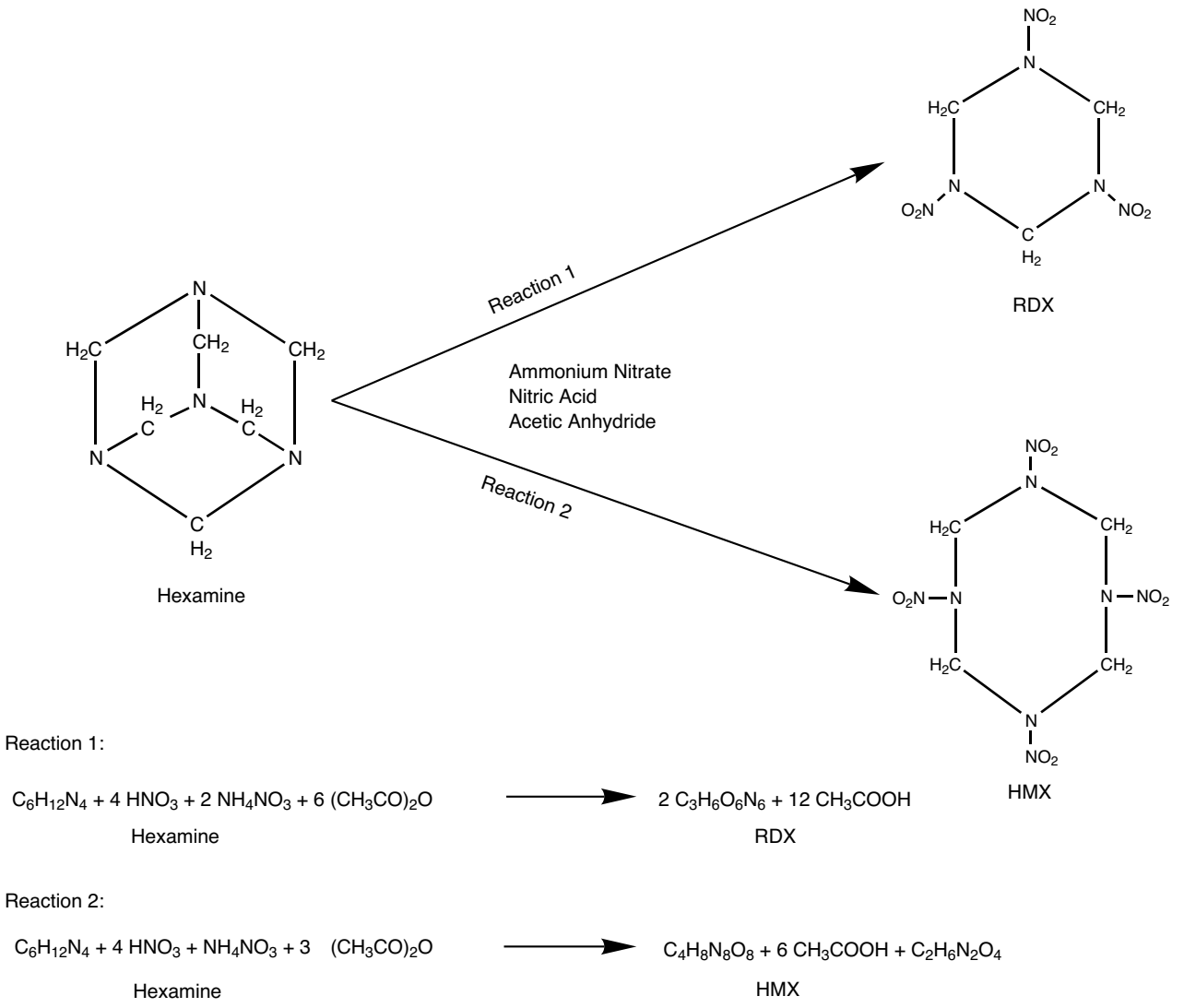


Fig. 9-16. The chemistry of RDX and HMX production. HMX is an unavoidable coproduct of the production of RDX from hexamine. Most RDX preparations contain at least 9% HMX. Reprinted from US Army Environmental Hygiene Agency. *Water Pollution Aspects of Explosive Manufacturing*. Aberdeen Proving Ground, Md: USAEHA; 1985: 21. USAEHA Technical Guide 140.

with slightly lower levels in the liver, brain, and heart. RDX is metabolized by the liver, and the unidentified metabolites are excreted primarily in the urine.[86] Unlike most other nitrated explosives, RDX does not metabolize to form nitrite in the blood.

Acute Effects. RDX has relatively low acute toxicity. After acute exposure by inhalation or ingestion, there is a latent period of a few hours, followed by a general sequence of intoxication that begins with a prodromal period of irritability. Neurological symptoms predominate and include restlessness and hyperirritability; headache; weakness; dizziness; hyperactive reflexes; nausea and vomiting; prolonged and recurrent generalized convulsions; muscle twitching and soreness; and stupor, delirium, and disorientation.[87]

Clinical findings in acute exposures may also include fever, tachycardia, hematuria, proteinuria, azotemia, mild anemia, neutrophilic leukocytosis, elevated AST, and electroencephalogram (EEG) abnormalities.[4] These abnormal effects, transient and unreliable for diagnosic purposes, last at most a few days. In fact, all physical and laboratory tests may remain normal, even in the presence of seizures.[4,84,86] EEGs made at the time of convulsions may show bilateral synchronous spike and wave complexes (2–3/sec) in the frontal areas with diffuse slow wave activity;

normalization occurs within 1 to 3 months.[85]

Patients will recover from acute RDX exposure within days to months, gradually but completely, and they may experience amnesia early in the process.

Several case reports of RDX ingestion have been documented. In one instance, a 3-year-old child ingested plasticized RDX that had adhered to the boots and clothing of its mother, who worked in a munitions plant. The child presented with status epilepticus, but recovered without sequelae. Laboratory tests were essentially normal, and the dose of RDX ingested by the child was estimated to be 84 mg/kg.[88] In the instances of convulsions that occurred among American soldiers in Vietnam, the signs and symptoms usually began 8 to 12 hours after ingestion. Renal toxicity was observed in 3 of 18 patients (16%) in one series.[85] The sequence of symptoms was similar to that which occurred after occupational exposures, proceeding from confusion and hyperirritability to myoclonic contractions, severe prolonged generalized seizures, pro-longed postictal confusion, and amnesia.[4,85,86]

The effects of acute exposure to RDX have also been studied in animals. In rats, the median lethal dose of orally administered RDX was approximately 200 mg/kg. Groups of 20 rats at each dose level were administered 25 mg/kg, 50 mg/kg, or 100 mg/kg; all doses produced hyperirritability, convulsions, and mortality up to 86.6%.[87]

Chronic Effects. Although intensive research with animals has revealed some effects, few effects of chronic human exposure to RDX have been reported. One study reported that occupational exposure to TWAs of 0.28 mg/m^3 to 1.57 mg/m^3 did not cause hematological, hepatic, or renal abnormalities. This study also failed to substantiate a suspected association of RDX exposure with systemic lupus erythematosis. Moderate reductions of the erythrocyte count and hemoglobin occur during the first month of exposure, but these values return to normal by the end of the second month.[86]

Tests done on animals have supplemented the knowledge of the chronic effects of RDX on humans. Dogs fed 50 mg/kg of RDX daily for 90 days developed hyperirritability, convulsions, and weight loss, with no alterations of their blood chemistries or cytology. No histological lesions have been found in animals that have had RDX-induced seizures. In addition to those effects noted in humans, several others have been seen in animal tests: cancer, weight loss, anemia, hepatotoxicity, testicular degeneration, and suppurative inflammation of the prostate.[86]

Investigations into the mutagenicity and carcinogenicity of RDX have yielded conflicting results. RDX does not appear to be a mutagen, based on negative results in the Ames test, the dominant lethal test, and the unscheduled deoxyribonucleic acid synthesis assay. RDX has not been found to be carcinogenic in gavage studies performed on rats, but increased hepatocellular carcinoma and adenoma were noted in females of one strain of mice. Due to this finding, the U.S. Environmental Protection Agency has classified RDX as a possible human carcinogen.[86]

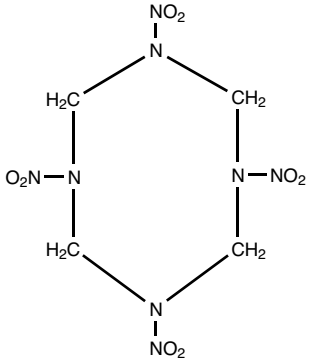
Reproductive effects have been noted in rabbits and rats. A study performed on rabbits showed teratogenic effects at 2 mg/kg/day (10% of the dose that caused maternal toxicity).[86] Similarly, a teratology study performed on pregnant rats exposed to RDX resulted in offspring with lower body weights and shorter body lengths than were found in the control group. These researchers therefore recommended that human females of childbearing age be protected from exposure to RDX.

Primary Prevention and Medical Surveillance

Despite the low toxicity of RDX, exposure should be maintained at the lowest levels possible due to its possible carcinogenicity. Sound industrial hygiene and preventive medicine measures, such as those used in the handling of TNT, should suffice to protect the worker.

General medical surveillance examinations can be conducted, but specific testing for the effects of low-level occupational exposure does not appear to be warranted, given the absence of abnormal results even in those patients with RDX-induced seizures. Surveillance for both males and females should also include a screening questionnaire for reproductive history.

Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine



HMX is the highest-energy solid explosive produced on a large scale in the United States. This explosive is used exclusively for military purposes to implode fissionable material in nuclear devices, as a component of plastic-bonded explosives, as a compo-

nent of rocket propellant, and as a high-explosive burster charge.[4]

Manufacture and Exposure Hazards

Exposure to HMX can occur during the manufacture and filling of munitions or through the environmental contamination of groundwater and soil. HMX, like RDX, is manufactured using the continuous Bachman process (see Figure 9-16). Although its solubility in water is very low, HMX can be present in particulate form in water effluent from manufacturing, LAP, and demilitarization operations.

Human Exposure and Health Effects

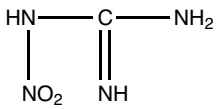
The data on the effects on human health of exposure to HMX are very limited. HMX causes CNS effects similar to those of RDX, but at considerably higher doses.[46] In one study, volunteers submitted to patch testing, which produced skin irritation. Another study of a cohort of 93 workers at an ammunition plant found no hematological, hepatic, autoimmune, or renal diseases. However, the study did not quantify the levels of exposure to HMX.

HMX exposure has been investigated in several studies on animals. Overall, the toxicity appears to be quite low. HMX is poorly absorbed by ingestion. When applied to the dermis, it induces mild skin irritation but not delayed contact sensitization. Various acute and subchronic neurobehavioral effects have been reported in rabbits and rodents, including ataxia, sedation, hyperkinesia, and convulsions. The chronic effects of HMX that have been documented through animal studies include decreased hemoglobin, increased serum alkaline phosphatase, and decreased albumin. Pathological changes were also observed in the animals' livers and kidneys.[89] No data are available concerning the possible reproductive, developmental, or carcinogenic effects of HMX.

Primary Prevention and Medical Surveillance

Both primary prevention and medical surveillance for HMX exposure should be conducted as they would be for exposure to RDX, discussed above.

Nitroguanidine



Nitroguanidine was first prepared in 1877, but was not used as an explosive until World War II. Today, it is a major component of triple-base solid propellants. The properties that give nitroguanidine an advantage over nitrocellulose or nitroglycerin include its cooler burning, greater production of gas, less flash, less smoke, and less corrosion in gun barrels.

Manufacture and Exposure Hazards

Nitroguanidine is produced using the British aqueous fusion process, which is not dependent on either coal or petroleum for raw ingredients. The ingredients and process chemicals used in the production of nitroguanidine include calcium carbide, nitrogen, calcium cyanamide, ammonium nitrate, guanidine nitrate, ammonia, and sulfuric acid.[4]

Workers can be exposed to nitroguanidine during the manufacturing process or during its incorporation into propellants. Nitroguanidine is moderately soluble in water and is rapidly absorbed in the gastrointestinal tract. It is only negligibly metabolized, however, and the body rapidly excretes unaltered nitroguanidine in the urine.

Human Exposure and Health Effects

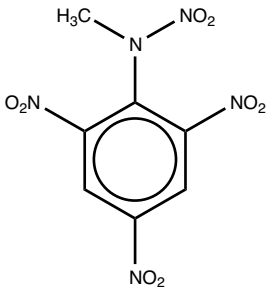
Although studies of the effects of nitroguanidine on humans have not been done, studies performed on animals have indicated generally low toxicity. The oral LD_{50} is 3.9 g/kg in mice and 10.2 g/kg in rats. Direct contact with nitroguanidine may burn the skin and eyes. Single sublethal doses of nitroguanidine in rodents have caused respiratory effects (epistaxis and dyspnea), gastrointestinal effects (diarrhea and hemorrhage), and CNS effects (depression, hyperactivity, ataxia, and tremors). Chronic exposure to nitroguanidine may result in osmotic diuresis and modest hematological and liver-function changes.[90] Results of studies of the reproductive and teratogenic effects of nitroguanidine appear to be negative and results of testing for mutagenicity, despite flaws in the study protocol, appear to be negative.

Primary Prevention and Medical Surveillance

Those who work with nitroguanidine should avoid exposing their skin, eyes, and respiratory tracts, and should wear PPE (safety glasses and respiratory protective equipment) when exposure to airborne nitroguanidine exceeds the exposure limit. Preplacement examinations should focus on the kidneys, the liver, and the blood and include renal and liver-function

tests and complete blood counts. Because the toxic effects are subtle and the long-term implication of alterations in these clinical tests is unclear, the occupational physician should use an interim medical history to determine the contents of periodic examinations on a case-by-case basis. Altered test results may indicate the need for improved exposure control in the workplace and medical follow-up of the abnormal results.

2,4,6-Trinitrophenylmethylnitramine



Tetryl was first prepared in 1877, but was not used as an explosive until World War I, when it was found to be the most efficient booster charge for high explosives. From World War II until recently, tetryl was the booster charge most commonly used by the United States military. The armed forces have also used tetryl in blasting caps, primers, and shell bursters.[4] Although many of our allies continue to produce and use tetryl, production in the United States ceased in 1983 because tetryl tends to corrode steel and is unstable when stored at high temperatures. Thus, our current use of tetryl is limited to the remaining stock. Its only reported civilian use is as a pH indicator.[21]

Manufacture and Exposure Hazards

The manufacture of tetryl involves several steps during which workers can be exposed to nitrogen oxides and acid vapors. Sulfuric acid is first added to dimethylaniline; the acidified dimethylaniline is then nitrated by concentrated nitric acid, forming a granular tetryl precipitate. These grains of tetryl are then dried, screened, coated with graphite, and compressed into pellets for use in munitions.[24]

Occupational exposures to tetryl can occur during the various LAP operations that use tetryl pellets. These operations create tetryl dust, and thus expose the workers through dermal contact, inhalation, and incidental ingestion of the dust. In a retrospective cohort study of systemic toxicity, the chief site of exposure was a powder house in which workers loaded booster bags with tetryl.[91] Virtually all LAP operations with tetryl pellets significantly expose workers to tetryl dust.[13,18,61]

Human Exposure and Health Effects

The primary acute effects of exposure to tetryl are due to its irritation of the upper respiratory tract, the skin, and the eyes. Workers who have been exposed to tetryl dust complain of burning eyes, itching, sneezing, coryza, and epistaxis. These symptoms may begin at any time during the first 3 months of exposure. New workers may also experience nausea and vomiting, but they recover rapidly. Nasal symptoms abate within 48 hours after exposure has ceased, but bronchial symptoms may require up to 10 days to abate. Additionally, a yellow staining of the hands occurs during the first 3 days of exposure. Exposure to the sun deepens these stains to orange, and although they begin to fade soon after the exposure has ceased, some degree of staining persists for several months. Other acute effects include nervousness, headaches, insomnia, oligomenorrhea, weight loss, nausea, vomiting, anorexia, spasmodic coughing, and orthopnea.

Contact dermatitis and skin sensitization are the most common chronic effects of exposure to tetryl. During World War II, tetryl was the most common cause of dermatitis among ammunition workers. The incidence of workers who were sensitized was proportional to their degree of exposure: 2% of pellet workers, but 50% of workers in dusty operations.[92,93] Additionally, the risk for contact dermatitis was highest in those workers who were exposed to significant amounts of tetryl dust. The typical rash initially takes the form of erythema of the malar areas, neck, chest, back, and ventral surfaces of the forearms. Then the affected areas develop papules and desquamate after a few days. Tolerance may develop in workers who continue to be exposed. In severe cases, the dermatitis may develop vesicles and progress to massive generalized edema with airway obstruction and substantial exfoliation from edema of the oropharynx.[18,94] Removing the patient from exposure allows the cutaneous symptoms to resolve within 2 to 4 weeks. These dermal effects result from direct irritation from the tetryl crystals, as well as from the chemical properties of tetryl. Furthermore, because tetryl is metabolized to picric acid, cross-sensitization to picric acid and its derivatives may also occur.[1]

Virtually all workers with significant exposure to dust develop a deep cough that produces a thin, mucoid sputum. The cough appears to be a result of the irritant action of the tetryl particles on the upper airway. The large size (150 μ) of tetryl particles

prevents their entry into the lower respiratory tract; consequently, radiographs of exposed workers' chests have remained normal.[1]

Evidence of systemic toxicity has been overlooked because (*a*) these effects have a long latency, (*b*) exposed workers were scattered across the country after their demobilization, and (*c*) the large turnover of workers limited the number of workers with prolonged significant exposure to tetryl. The draft and other social effects during the war contributed to the very high turnover rate—the average time worked in these factories was only about 1 year. In fact, at least three cases of systemic toxicity have been reported.[91] Systemic symptoms were noted only among workers who did not develop the more common irritative symptoms of dermatitis, conjunctivitis, and nasopharyngeal irritation.

Clinical signs of chronic tetryl exposure include moderate leukocytosis with relative lymphocytosis, anemia, and epigastric tenderness.[91,95] Upper gastrointestinal symptoms (such as gastritis or peptic ulcer disease) were frequently so aggravated that affected workers were forced to leave work. In severe cases, toxic hepatitis can occur with resultant jaundice, edema, and ascites. In several cases, hepatorenal syndrome and death have resulted.[91] Substantiating findings, including irreversible liver necrosis, renal tubular degeneration, bone marrow–depression anemia, pulmonary edema, abdominal pain, insomnia, hyperreflexia, and mental excitation, have been described in exposure studies with dogs.[91] Tetryl is now considered to be a mutagen and probable carcinogen.

In addition, pure and military-grade tetryl were found to be mutagenic in three prokaryotic test systems. Metabolic action on tetryl in salmonella (the Ames assay) reduced the chemical's mutagenicity, suggesting that tetryl is a direct-acting mutagen.[96]

TABLE 9-8

PREPLACEMENT EXAMINATION FOR TETRYL WORKERS

Component	Emphasis
Medical History	Alcohol use Tobacco use Allergies Dermatitis EENT Hematologic system Liver disease Nervous system Respiratory system Renal system Medications
Occupational History	Prior sensitivity to tetryl or picric acid Prior exposure to hepatotoxins
Physical Examination	Allergies Skin EENT Liver Nervous system Respiratory system
Tests	CBC with differential Liver function tests Renal function tests Microscopic urinalysis

Primary Prevention and Medical Surveillance

The most effective exposure control is the isolation or enclosure of dusty operations.[81] Isolating operations that use equipment such as dryers, sieves, and conveyor transfer points minimizes the contamination of other work areas. Manufacturing processes that use granules are less dusty than processes that use crystals. Using sodium sulfite–indicator soap will detect traces of tetryl that remain on the skin. This soap also converts tetryl to a soluble form, which aids in removing it from the skin. However, one control that should be avoided is job rotation, because it may favor sensitization.

Preplacement, periodic, and termination examinations are necessary for workers who could potentially be exposed to tetryl. Table 9-8 shows the content of preplacement examinations. As before, the content of periodic examinations is determined by the occupational physician on a case-by-case basis.

THE INITIATING EXPLOSIVES

The initiating explosives are a heterogeneous group of chemicals, prepared and used in very small quantities, which thus limits their potential for exposure. The most frequently used initiating explosives include lead azide, lead styphnate, and mercury fulminate (Figure 9-17). Other, less common, initiators include

Common Name	CAS Registry Number	Synonyms	Formula
Lead Azide	13424-46-9		$Pb(N_3)_2$
Lead Styphnate	15245-44-01	Lead trinitroresorcinol Lead trinitroresorcinate	$C_6H_3N_3O_8{\cdot}Pb$
Mercury Fulminate	628-86-4		$Hg(ONC)_2$

Fig. 9-17. The initiating explosives, together with their common names, Chemical Abstract Society numbers, synonyms, and formulae.

tetracene, which is used in commercial priming compositions; diazodinitrophenol (DDNP), which is an ingredient in primers and commercial blasting caps; and lead mononitroresorcinate (LMNR), which is used in electric detonators among a variety of applications.

Lead Azide

Lead azide [$Pb(N_3)_2$], first prepared in 1890, is produced when lead nitrate is reacted with sodium azide; sodium nitrate is the byproduct.[24] Because it is quite stable, lead azide is considered to be one of the best initiators for sensitive explosives such as tetryl, PETN, and RDX. Lead azide is usually used in combination with lead styphnate, DDNP, or PETN. In the civilian sector, it is used in cartridge primers, primer cords, and blasting caps.

Lead azide is composed of 70% lead by weight, and it releases poisonous fumes of lead and nitrogen oxides when heated. However, due to safety constraints, there is little opportunity for exposure to lead azide itself. During its manufacture, lead azide is screened in barricaded rooms to avoid continuously exposing the workers. They could be exposed intermittently while entering the screening rooms, but the workers should be wearing their respiratory protective equipment at this time.

Some exposure can occur while primers are loaded, but local exhaust ventilation is helpful. The acute effects of exposure include vasodilation and headache, while the chronic effects are those of lead intoxication. Due to these health effects, silver azide has been investigated as a substitute for lead azide, with some promise. Regulations and medical surveillance associated with exposure to lead azide should be based on the lead content. These specific requirements are dictated by Title 29, Code of Federal Regulations, Part 1910.1025.[97]

Lead Styphnate

Lead styphnate was first prepared in 1914 by von Hertz in Germany, but it was first used as an explosive by Russia early in World War I. Although lead styphnate is ignited easily, it is a relatively poor initiator, and thus is often used in combination with other primary explosives. Lead styphnate, manufactured from 2,4,6-trinitroresorcinol, magnesium oxide, and lead nitrate, may be used as a *covering charge* (ie, the booster) for lead azide, as an ingredient of priming compositions, as a component in blasting caps, and as a component in small-arms primers (eg, the M16 primer uses 4 mg of lead styphnate).

The effects on human health have not been well studied, but acute effects appear to be limited to yellow staining of the hair and skin and dermatitis.[18] Chronic exposure may result in lead toxicity, and it is the lead content of this explosive that should form the basis of monitoring and medical surveillance for exposure.

Mercury Fulminate

Mercury fulminate [$Hg(ONC)_2$], also known as mercury cyanate, was first prepared in the late 17th century, but its explosive properties were not recognized until 1800. Until recently, mercury fulminate was used as a detonator and initiator for less-sensitive explosives such as TNT; however, the military no longer uses mercury fulminate because of its poor stability. Mercury fulminate must be stored water-wet because it is sensitive to accidental detonation when dry; small amounts are dried immediately before being used.

The acute health effects of mercury fulminate include mucosal irritation and the manifestations of mercury poisoning. The most common chronic effect is sensitization dermatitis, due to exposure to dust during the manufacture of detonators. The dermatitis usually affects the face and the anterior surface of the arms.[18]

Exposure limits and medical surveillance for lead styphnate and mercury fulminate are based on their respective metal components and can be found in OSHA 29 CFR 1910.1000[9] and in the ACGIH's *Documentation of Threshold Limit Values,* 1991 edition.[98]

COMPOSITE PROPELLANTS AND EXPLOSIVES

Composite propellants are solid rocket fuels that are being used in an increasing number of applications. As with all explosives and propellants, they consist of an oxygen donor—the oxidizer—and a hydrocarbon fuel. The oxidizer is usually an inorganic salt, while the fuel is a polymeric binder (essentially a plastic). The composites have a wide range of performance characteristics, are tremendously stable, and are inexpensive. However, they are so reactive that they corrode the metal in gun barrels.

The vast number of alternatives available for use as oxidizers and binders preclude discussion of all of them (Exhibit 9-2). Information regarding the toxicity of the inorganic salts is widely available in the toxicology and occupational medicine literature. Therefore, this discussion focuses on ammonium perchlorate, which, due probably to its cost, stability, ease of manufacture, and versatility of use, is the most widely used oxidizer in composite propellants. Ammonium perchlorate is used in the Multiple Launch Rocket System and in rocket-assisted howitzer projectiles. Workers can be contaminated via the dermal and inhalational routes during all stages of propellant production.

Before it can be used in munitions, an oxidizer must be ground and screened by particle size to assure that it will burn uniformly. Both grinding and screening raise significant levels of dust, some of which is respirable and must be controlled. The mixing of the oxidizer with the binder can also be quite dusty.

Numerous polymeric binders are in use currently. After being mixed with the oxidizer, the resultant propellant can be either cast or pressed into a mold. Cast materials are melted, then poured as a liquid into a mold, while pressed materials are kept in their solid state and shaped by simply molding or extruding. A high-temperature curing process then effects polymerization, a process that releases toxic vapors, to which the workers can be exposed. The propellant core is then removed from the mold and machined or trimmed as needed. Workers can be exposed to dust during all of these last three operations.[99]

Plastic bonded explosives are similar in concept to the composite propellants, but are designed to function as high explosives rather than as propellants. Several major groups are the PBX, PBXN, and LX-10 series. They represent a variety of mixtures combining high mechanical strength, excellent stability, and a wide range of explosive properties. They contain a high percentage of basic explosive (RDX, HMX, HNS, or PETN), which is mixed with a polymeric binder (polyester, polyurethane, nylon, polystyrene, rubbers, nitrocellulose, or Teflon), plasticizer (dioctylphthalate or butyldinitrophenylamine), and metallic fuel (powdered aluminum or iron). A major advantage of using plastic bonded explosives is that the final product can be injection (or press) loaded at ambient temperatures, or even loaded in the field. The binders are thermally degradable, so that in de-

EXHIBIT 9-2

TYPICAL COMPONENTS OF COMPOSITE PROPELLANTS

Binders
- Polysulfides
- Polyurethanes
- Polybutadienes
- Carboxy-terminated polybutadienes
- Hydroxy-terminated polybutadienes

Oxidizers
- Ammonium perchlorate
- Ammonium nitrate
- RDX
- HMX

Fuels
- Aluminum
- Metal hydrides

Modifiers
- Metal oxides
- Ferrocene derivatives
- Plasticizers
- Bonding agents

Adapted with permission from Lindner V. Explosives and propellants. In: Grayson M, Kirk RE, Othmer D, eds. *Abridged Version of the Encyclopedia of Chemical Technology.* New York: John Wiley & Sons; 1985: 449.

militarization operations the ingredients can be completely recovered.[4]

Specific medical information regarding composite propellants and explosives is difficult to provide. For all practical purposes, the polymers are medically inert. The other components, which are heterogeneous and from different chemical families, have vastly different effects, many of which are not yet characterized.

LIQUID PROPELLANTS

The two types of liquid propellants are liquid rocket propellants and liquid gun propellants. Both the National Aeronautics and Space Administration and the U.S. Air Force use liquid rocket propellants in high-performance missile systems. The armed services are currently developing liquid gun propellants for use in large-caliber weapons such as the 120-mm main tank cannon, 105-mm howitzer, 155-mm howitzer, and 8-in howitzer.

Rocket Propellants

Many chemicals have been used as components of liquid rocket propellants (Exhibit 9-3). Many are used extensively in industry and are well covered in standard toxicology and occupational medicine texts; most of them have only limited military use and therefore will not be discussed in this chapter. The liquid rocket propellants that do have military applications include (*a*) hydrazine, (*b*) nitrogen tetroxide, and (*c*) the boranes.

Hydrazine is widely used in the chemical industry, where most of the studies of the effects on human health have been conducted. Studies on humans and animals have demonstrated deleterious health effects. The effects on humans have been limited to irritations of the skin and mucosa and hepatic disorders, but the effects found in animal studies have been more serious. Mice have developed hepatomas after being fed hydrazine, rats exposed to hydrazine vapor have developed nasal tumors, and hamsters have developed lung adenomas. Urinary levels of hydrazine have shown some utility in monitoring exposure. At a minimum, medical surveillance should periodically assess erythrocyte indices, hypoglycemia, kidney and liver disease, hemorrhagic diathesis, and allergy to phenylhydrazine and isoniazid.[100]

Nitrogen tetroxide has also been used widely in the space program, but not without harmful health effects. The vapors can cause immediate or delayed swelling and blistering of the adnexa oculi and severely burn the dermis. When nitrogen tetroxide is inhaled, it can react with moisture to form nitric acid and cause delayed pulmonary edema.[5]

EXHIBIT 9-3

TYPICAL COMPONENTS OF LIQUID ROCKET PROPELLANTS

Fuel

- Methyl alcohol
- Ethyl alcohol
- Isopropyl alcohol
- Furfuryl alcohol
- Anhydrous ammonia
- Aniline
- Butyl mercaptan
- Propyl mercaptan
- Amyl mercaptan
- Hydrazine
- Monomethyl hydrazine
- Unsymmetrical dimethyl hydrazine
- Mixed amines
- Nitromethane
- Tetranitromethane
- Aliphatic hydrocarbons

Oxidizer

- Hydrogen peroxide
- Liquid oxygen
- Red and white fuming nitric acid
- Nitrogen tetraoxide
- Liquid fluorine
- Oxygen difluoride
- Ozone difluoride
- Ethylene oxide

Other

- Bromine pentafluoride
- Chloride trifluoride
- Pentaborane
- Triethyl boron

During the past 30 years, the fuel boron hydride and its derivatives—also known as *boranes*—have become widely used within industry and rocketry as rubber vulcanizers, corrosion inhibitors, and in other chemical processes. The reactivity of the boranes has led to a proliferation of uses, but has also contributed to their significant toxicity. Regardless of their use, boranes are toxic to the respiratory system, cardiovascular system, CNS, skin, kidneys, and liver.

Carboranes—boranes that contain carbon in addition to boron and hydrogen—have recently been developed and investigated for use in solid-fuel systems. The carboranes are skin irritants, but they do not sensitize. They appear to have relatively low acute toxicity. Subchronic inhalation exposure in dogs resulted in interstitial pneumonitis and early emphysematous changes, but no developmental effects were noted.[101]

Gun Propellants

Liquid gun propellants have several advantages over conventional solid propellants for use in self-propelled howitzers and naval vessels: they are less expensive to produce and transport, less vulnerable to secondary ignition, easier to store in combat vehicles, and are demilitarized more safely and easily than solid propellants.[102] One disadvantage, however, is that more workers can be exposed to the chemical components during the manufacture, transport, and use of liquid than solid propellants.[103]

The liquid gun propellants of current interest consist of aqueous solutions of hydroxylammonium nitrate (HAN) mixed with either trimethanolammonium nitrate or triethanolammonium nitrate. No studies on the effects on human health have been reported on either of the mixtures or the individual components. However, the aqueous solutions and pure HAN have been evaluated for mammalian toxicity at the U.S. Army Environmental Health Agency (USAEHA) and at the U.S. Army Letterman Army Institute of Research.[103–109] The mixtures were found to be moderately toxic to both rats and rabbits: for male rats, the oral LD_{50} was 822 mg/kg, and for female rats, 520 mg/kg; for male rabbits, the oral LD_{50} was 101 mg/kg.[106] Oral exposure to the mixtures induces cyanosis, respiratory distress, and, at high doses, death.[104] A single intragastric dose of 400 mg/kg produced no ECG changes in dogs. Treatment with methylene blue rapidly reversed the acute toxic effects. The mixtures were also found to be ocular irritants, but were not corrosive to the cornea.[103] However, exposure to mixtures induced hematological changes: methemoglobinemia occurred; oxygen tension decreased; free nitrites, Heinz bodies, and crenated erythrocytes formed; and, at lower doses, serum potassium decreased.[104]

The armed forces have also used rabbits to test the health effects of HAN. When applied to the dermis, it caused chronic and ulcerative dermatitis, and at higher doses, caused hemolytic anemia in addition to the systemic effects described previously for exposure to the mixture; however, no blood chemistry changes were noted.[105] When administered orally to three groups of rabbits (1, 5, and 25 mg/kg/d) for 21 days, HAN induced splenic congestion and hyperplasia of the reticuloendothelial system at all doses.[106] At 25 mg/kg/day, HAN caused anemia and myeloid hyperplasia of the bone marrow.[106] Inhalation of aerosolized HAN has been found to induce Heinz-body formation and upper-respiratory irritation.[107] Several other liquid gun propellants have also been investigated as aerosols, and the effects they elicited were qualitatively similar to those of their principal ingredient, HAN.[108]

The Occupational and Environmental Medicine Division of USAEHA has established preliminary guidelines for medical surveillance and a provisional PEL of 3 mg/m^3 has been proposed for liquid gun propellants.[107,110] Testing for methemoglobinemia or examining the peripheral blood for Heinz bodies may comprise part of the appropriate medical monitoring for exposed employees. Reasonable occupational precautions include: restricting employees from eating, drinking, and smoking in areas where these chemicals are handled or stored; ensuring adequate ventilation; preventing spills and splashes; and using PPE such as splash goggles and gloves.

SUMMARY

In defending the United States, military and civilian personnel must necessarily produce, store, and handle a variety of munitions. In the army, these operations occur around the country at various arsenals, proving grounds, depots, and ammunition plants, which together employ more than 100,000 workers. Despite incomplete laboratory studies and imperfect data, information has been gathered during the last 50 years on the effects of workplace exposures to these chemicals, much of it recorded during wartime while large quantities were being produced.

The chemical families represented among energetic

materials include aliphatic nitrate esters (such as nitroglycerin), nitroaromatics (such as TNT), and nitramines (such as RDX). Considering the properties of the energetic materials—explosives, propellants, and pyrotechnics—it was inevitable that they would be utilized in military weapons. Explosives create a shock wave that progresses rapidly, while propellants release large amounts of hot gas in a more controlled manner. Pyrotechnics burn slowly, emitting tremendous heat or light. Most modern weapons utilize energetic compounds in combination, capitalizing on their individual properties.

As these energetic materials are synthesized and assembled into munitions, workers can be exposed to the raw materials, the finished product, or any number of chemical intermediates along the way. These chemicals are usually absorbed via the dermal, inhalational, and, less importantly, the ingestional routes; as a class they can produce dermatitis, methemoglobinemia, vasodilation, or cancer. The standard industrial hygiene principles of engineering and administrative controls and PPE can minimize these exposures. Obviously, the explosive properties of these chemicals necessitate strict compliance with safety guidelines. Preplacement screening and periodic surveillance must be tailored to the specific hazards in each industrial operation and at each site. Generalized medical guidance regarding these mixtures has little practical significance.

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