12 Enemy Agents

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Enemy Agents: Substances that impair physical, mental, or psychological performance or compromise health.

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Key Points

- All tobacco products, including smokeless tobacco, are addictive, and can cause cardiovascular damage and various forms of cancer.
- Alcohol, in excess, can lead to dehydration and compromise performance. Do not mix drugs and alcohol: beware of alcohol-drug interactions.
- Over-the-counter drugs, such as antihistamines, non-steroidal anti-inflammatory drugs, and aspirin should be used in moderation and under a physician's care if being used for long-term therapy.
- NSAIDs should not be used during deployments because they make bleeding difficult to control.
- Steroids and steroid alternatives are illegal and unsafe; they can seriously harm the body and negatively affect performance.

Enemy agents are substances that may pose significant detrimental effects on health, even if some may enhance performance or make one feel better, be it physical, mental, or psychological. If these agents are used, it is important to be aware of their potential harmful effects, on either health or performance. The enemy agents of interest in this chapter will be chewing tobacco, alcohol, antihistamines, steroids, non-steroidal anti-inflammatory medications, other over-the-counter products, and ephedra.

Smokeless Tobacco (ST)

Like 7.3 million persons in the United States, many military personnel have been or are frequent users of smokeless tobacco (ST). The majority of people who use ST are young and middle age adult males. The primary reason ST is considered an enemy agent is because of its adverse effects on health. Persons who use ST have:

- 50-fold higher risk of oral cancer than those who do not use ST.
- Increased risk for gum disease.

National Institute on Alcohol Abuse and Alcoholism.

- Permanent tooth stains.
- Bad breath.
- Sores on the lips and mouth.
- Tooth decay, because of the sugar added to ST.
- Increased blood pressure and heart rate.
- Increased levels of LDL cholesterol, the "bad" cholesterol.

One reason the risk of cancer is so high is because ST products contain at least 28 chemicals that may cause cancer. Despite these issues, many athletes and Warfighters believe that ST improves performance or enhances reaction time by providing a quick "rush" during the event, but this is usually not the case.

Nicotine

Nicotine, the active ingredient in all tobacco products, is very addicting (as addicting as cocaine or heroin), and nicotine addiction is one of the most prevalent addictive behaviors worldwide. Nicotine is a naturally occurring "alkaloid," like caffeine, that exerts potent effects on the human body. It is considered a psychoactive drug, which means it alters the normal functioning of the brain by stimulating the central nervous system. This results in the nicotine "buzz," or "high." When ST is placed in the mouth, the nicotine is readily taken up into the small blood vessels that line the mouth and gums, after which it travels through the bloodstream to the brain where it exerts multiple effects.

Nicotine initially causes a rapid release of adrenaline, the "fight-or-flight" hormone, which increases heart rate, blood pressure, and blood glucose. However, the results of nicotine's effects are short-lived and may last only 40 minutes to a couple of hours. After a period of time the effects of nicotine are lessened, and more and more nicotine is needed to achieve the same degree of stimulation or relaxation.

Although nicotine and tobacco have enough disadvantages to discourage their use, it is important to remember that, in certain situations, they may provide desirable effects. This is why leaders, like George Washington during the Revolutionary War, request "necessary" items like food, munitions, and tobacco for their troops. The reported "benefits" of nicotine include:

- Decreased appetite.
- Control of or reduction in body weight.
- Ability to focus attention.
- Increased energy.
- Decreased pain.

The ability to focus attention or "enhance mental state" is why users claim their reaction time and performance are enhanced. However, no studies have shown differences in reaction times between users and non-users of smokeless tobacco. Remember: there are **no** reaction time improvements with chew.

Nicotine has some very detrimental effects. It:

- Increases blood pressure, heart rate, and rate of respiration.
- Constricts/tightens blood vessels, which is why increases in blood pressure and heart rate are seen. One study of young athletes showed that the amount of blood the heart pumped in one minute decreased while using ST. This would be highly undesirable for Warfighters during strenuous exercise, and could compromise performance particularly in a warm environment.
- Stimulates the nervous system.

Nicotine Withdrawal

Repeated or chronic administration of nicotine usually results in drug dependence. Therefore, cessation of nicotine after dependence develops may result in withdrawal effects (see below). Most of these effects last weeks, but some (body weight gain and nicotine craving) may persist a year after cessation.

The adaptations of nicotine dependence may include increasing or decreasing the number of receptors in the brain and/or increasing or decreasing the release of neurotransmitters that signal the brain. The end result is a disturbance in function. Some of the symptoms of trying to quit nicotine include:

- Irritability.
- Anxiety.
- Depression.
- Moodiness.
- Headaches.
- Trouble sleeping.
- Poor concentration.
- Craving for nicotine.
- Increased body weight.

The military has many programs for individuals trying to quit smoking and chewing, but it is best to never start.

The risks of using ST outweigh the benefits.

Alcohol

Heavy drinking is a major cause of preventable death. It can damage the liver, heart, and skeletal muscles; increase the chance of developing some cancers, contribute to violence, and interfere with relationships. Individual reactions to alcohol differ, depending on many factors. Important factors include:

- Age.
- Gender.
- Race or ethnicity.
- Genetics.
- Weight.
- Fitness level.
- Amount of food eaten before drinking.
- How quickly alcohol was consumed.
- Use of drugs/prescription medicines.
- Family history of alcohol problems.

Regardless of the factors, alcohol has only negative effects on performance. In particular, drinking alcohol leads to a state of dehydration, in the absence of adequate fluid replacement. People have died during road races and regular training after a night of heavy drinking, due to inadequate rehydration prior to, and hydration during, exercise. Although a rare occurrence, it can happen. More frequently, a dehydrated state places an athlete at greater risk for musculoskeletal injuries (cramps, muscle pulls, and muscle strains), which will clearly compromise mission objectives.

Excessive alcohol intake can lead to severe dehydration.

Alcohol consumption also decreases the use of glucose and amino acids by skeletal muscles, which adversely affects energy supply and metabolic processes during exercise. Chronic alcohol consumption may lead to structural changes in skeletal muscle and a decrease in the size of all muscle fiber types, both of which will adversely affect performance. Alcohol also hinders the muscle's ability to replenish energy stores, which may increase recovery time or compromise rehab after an injury. In addition, athletes who use alcohol have twice the injury rate as non-alcohol users.

In addition to performance decrements, using specific drugs with alcohol can have serious medical consequences. The National Institute on Alcohol

Abuse and Alcoholism (NIAAA) has a publication "Harmful Interactions: Mixing Alcohol with Medicines" that details all of the known interactions. Examples include the increased risk of bleeding in the stomach when aspirin and non-steroidal anti-inflammatory medications are combined. Also, taking medications that contain acetaminophen when drinking beer can greatly increase the risk of liver toxicity. Combining beer with antihistamines, barbiturates (Nembutal, Luminal, Seconal), benzodiazepines (Ativan, Valium, Restoril) and tricyclic antidepressants (Elavil, Pamelor), and other agents used as sleeping aids may increase the sedative effect of these drugs and cause other adverse effects.

Click for the NIAAA Publication on Alcohol-Drug Interactions.

Mixing alcohol with drugs can be dangerous!

Antihistamines

Antihistamine use is prevalent among all groups of people because they are common over-the-counter and prescription medications. Many types of antihistamines are used, with the most common "sedating" ones being:

- Diphenhydramine (Benadryl).
- Chlorpheniramine (Chlor-Trimeton).
- Cyproheptadine (Periactin).
- Hydroxyzine (Atarax, Vistaril).

Some detrimental performance and side effects of sedating antihistamines include:

- Decreased ability to concentrate.
- Delayed reaction time.
- Sleepiness.
- More "misses" on target practice.
- Dry mouth.
- Increased heart rate.
- Blurred vision.
- Constipation.

Click here for more information on antihistamines.

Drugs, supplements, and herbal information.

Antihistamines may cause drowsiness and compromise mental performance.

Because of the problem of drowsiness, other "non-sedating" or less sedating types of antihistamines have been developed. The "non" sedating antihistamines include:

- Cetirizine (Zyrtec).
- Fexofenadine (Allegra).
- Loratadine (Claritin).

Allegra (Fexofenadine) is the least sedating, and although Claritin and other Loratadine-containing products are minimally sedating, sedation may occur at higher doses. The antihistamine, Zyrtec (Cetirizine) is considered less sedating than Benadryl, but it can be sedating at the usual dose, so pay attention to individual reactions. No clearly defined effects on physical performance have been reported, but caution should be exercised when taking any type of medication.

The use of anti-histamines, specifically benadryl, has been associated with heat casualties and heat stroke during training. Ranger school has had at least one fatality due to heat stroke in a student who was taking benadryl to treat poison ivy.

NSAID/Vitamin M delays and hampers healing in muscles, ligaments, tendons, and cartilage.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

A number of over-the-counter (OTC) medications, including aspirin and ibuprofen (non-steroidal anti-inflammatory drugs, or NSAIDs), are readily available and widely used by Warfighters, who call these medications "Vitamin M." Vitamin M refers to "Motrin." These drugs are found in most medicine cabinets and in a medic's pack to treat pain, reduce fever, and/or inflammation. However, several dangers are associated with using these medications on a regular basis. They include:

- Potential decrease in the effectiveness of daily aspirin use, if taken at same time as the NSAID.
- Contribute to gastrointestinal problems, including bleeding and ulcers.
- Trigger an asthmatic attack in persons with exercise-induced asthma.
- Mask signs of a more serious medical problem that may require medical intervention.
- Contribute to development of hyponatremia in endurance athletes.
- Cause serious performance and health decrements of some endurance athletes.

- Slow down the healing of muscles, cartilage, ligaments and tendons.

The FDA has requested that package inserts for all NSAIDs include a warning about the potential increased risk of cardiovascular events and, serious, and potentially life-threatening, gastrointestinal bleeding. The clear message is that NSAIDS or Vitamin M should be used on a limited basis. Products with fewer side effects should be used, whenever possible (See Quercitin in Chapter 11). When pain is prolonged or seems to be worsening, medical attention must be sought for a proper evaluation.

With respect to hyponatremia and long distance events, NSAIDs should not be used until after exercise and even then, taken in moderation. A proper warm-up and sound nutritional practices will do more to prevent muscle soreness and inflammation than popping Vitamin M.

Importantly, the mission must be considered before taking NSAIDs as they interfere with clotting. If injured, the use of NSAIDs makes bleeding difficult to control. For general aches and pains, acetaminophen is an alternative. If an NSAID is essential, meloxicam (Mobic) or celecoxib (Celebrex) are alternatives.

Consult with a physician or pharmacist prior to using NSAIDS.

Generic Name	Brand Names
Aspirin	Made by several companies
Ibuprofen	Motrin®, Advil®, Motrin IB®
Naproxen	Naprosyn®, Aleve®
Meloxicam	Mobic®

Steroids (Anabolic-Androgenic)

Anabolic steroids are compounds "designed" to behave like testosterone, the primary androgenic or "masculinizing" hormone that builds muscle and enhances male attributes. These steroids are classified as "Controlled Substances" and regulated by the Drug Enforcement Administration (DEA). They are banned by most athletic associations.

Congress passed the Anabolic Steroid Control Act of 2004 in response to a rise in steroid abuse by athletes, teenagers, and, especially, youngsters. This Act redefined the term "anabolic steroid" to mean "any drug or hormonal substance, chemically and pharmacologically related to testosterone (other than estrogens, progestins, corticosteroids, and dehydroepiandrosterone)." Androstenedione, androstenediol, androstanediol, androstanedione and similar substances (total of 26 androgenic and pre-cursor substances) were banned by the FDA in January 2005. Many of these substances, once sold as dietary supplements, became controlled, which means they are in the same category as cocaine and heroin: they are illegal to purchase or use.

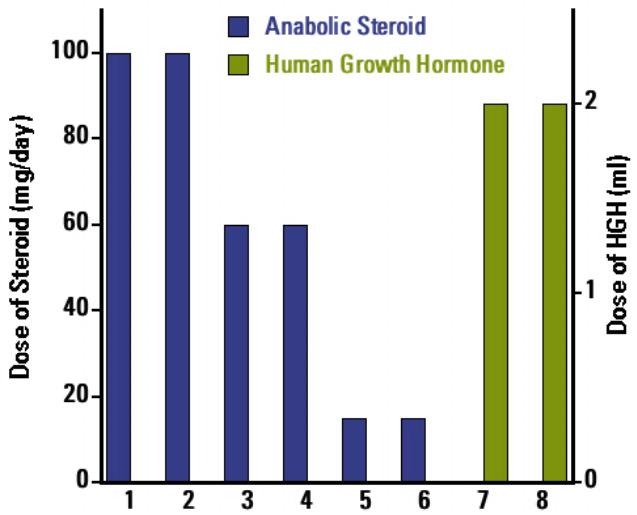
It is important to understand that testosterone itself is not effective when taken orally or by injection because of its rapid degradation by the liver. This is why so many modifications are made to the chemical structure of testosterone with the expectation of finding a substance with actions similar to testosterone. This is the reason why transdermal patches, buccal tablets and nasal sprays are being used as delivery modalities.

Anabolic Steroids and Cycling

Steroids are used illegally by athletes and others to enhance performance and/or improve physical appearance. The use of anabolic-androgenic steroids has been shown to increase body mass, lean body mass, strength, and power, and decrease body fat, which may directly or indirectly enhance performance. Because of these effects, Warfighters may be using them intentionally or unintentionally.

Doses taken by users/abusers may be 10–100 times higher than doses typically used for medical conditions. Anabolic steroids are taken orally or injected, typically in cycles of weeks or months. "Cycling" is when multiple dosages are taken over a period of time and then stopped for a specific period of time before beginning the cycle over again. The primary reason for cycling is to reduce the risk of side effects, which increases with length of time on the drugs.

More information on anabolic steroids.



Steroid use will harm the body, both short term and in the long run.

"Stacking" is a method commonly used by steroid (ab)users. Two or more types of steroids may be taken at the same time, sometimes mixing oral and injection drugs. Some drugs may be obtained "off the economy" of a foreign country, or they may be meant for veterinary use. This is a serious concern, because such drugs may be adulterated with other dangerous substances.

"Pyramiding" is another dangerous method of steroid use/abuse. There are many paradigms, but in one case, the person increases the frequency, dosage, and/or adds various types of steroids, followed by decreasing

dose and frequency until no drugs are taken. The cycle during "pyramiding" is usually 6–12 weeks, with return to a low/no dose at the end of the cycle. The expected or intended benefits of "cycling," "stacking," and "pyramiding" have not been substantiated scientifically. An example of a "Ski Slope Pyramid" is shown below.

Adverse Effects of Steroids

The well-documented short- and long-term negative side effects of anabolic steroids must be understood. It is very clear that the benefits of performance enhancements and increasing physical attributes do not outweigh the risks involved.

The physical side effects of using steroids are shown in Table 1. However, many behavioral changes occur and may include aggression, violence, irritability, anxiety, distractibility, and abrupt shifts in mood: anabolic steroid users are often vulnerable to depression or rage. Of note is the fact that using anabolic steroids disturbs the regular production of testosterone, which may persist for months after discontinuing the drug. An unknown portion of those who use steroids become addicted to them.

Anabolic steroids should be avoided.

Table 12–1. Possible Health Risks/Consequences of Anabolic Steroid Use

Hormonal System	**Cardiovascular System**	**Liver**
Shrinking testicles	Increase in LDL (bad cholesterol)/ Decrease in HDL (good cholesterol)	Cancer (Breast, prostrate, pancreatic)
Develop Breasts	High blood pressure	Tumor(s)
Infertility	Heart attack	
Male-pattern baldness	Enlargement of heart's left ventricle	
Skin	**Infection**	**Psychiatric**
Severe acne	HIV/AIDS	Mania
Fluid retention	Hepatitis	Delusions
Oily scalp		Rage
Jaundice		Aggressive Behavior

Stacking

Of great concern is the use of multiple compounds in combination with steroids to counteract the common adverse effects. Other drugs often used with anabolic steroids include diuretics, anti-estrogens, human chorionic gonadotrophin, human growth hormone, thyroid hormone, insulin, gonadotrophin-releasing hormone, clenbuterol, and clomid. This "polypharmacy" practice is a deadly combination, and has resulted in the death of military members.

Click for additional reliable information about steroids.

Agents Recently Banned

Androstenediol

Claims	Enhances recovery and promotes muscle growth from exercise.
Other Names	4-AD, 4-Androstenediol, 5-AD, 5-Androstenediol, Androdiol.
How It Works	A weak steroid hormone and is a direct precursor of testosterone.
Dose	A dose of 100 mg twice daily has been used.
Adverse Effects	At low doses nothing of note. May increase endogenous testosterone production and increase levels of estrone and estradiol.
Comments	Androstenediol does not appear to increase muscle strength or mass when used during 12 weeks of high-intensity resistance training. The Anabolic Steroid Control Act of 2004 reclassified androstenediol from a dietary supplement to an anabolic steroid, a controlled substance.

Androstenedione

Claims	Enhances recovery and promotes muscle growth from exercise.
Other Names	Andro, Androstene.

Androstenedione

How It Works	A direct precursor of testosterone.
Dose	Doses of 100–300 mg daily have been used without success.
Adverse Effects	May decrease endogenous testosterone production and increase estrogen. Stimulate growth of prostate cancer cells. May increase risk of heart disease in men.
Comments	Taking androstenedione orally in doses of 100-300 mg per day did not result in increased muscle strength or size, or lean body mass when used for 2-3 months during weight training. The Anabolic Steroid Control Act of 2004 reclassified androstenedione from a dietary supplement to an anabolic steroid, a controlled substance.

Multi-Ingredient Steroid Alternatives—The Bottom Line

The increased search for the creation, manufacture, and promotion of new "designer steroids," "pro-steroids," "pro-hormones," and/or "precursor steroids" as over-the-counter anabolic compounds is staggering. Multiple steroid alternative products have surfaced on the market in alarming numbers, but the questions are, do they work, and how well do they work?

Some supplements containing herbs, glandulars, minerals such as chromium and boron, and a number of other compounds (ZMA) are being marketed to build big muscles. They claim to be "alternatives to steroids." The major concerns associated with using such products are:

- Not properly tested and absolutely no basis to substantiate claims.
- Potential for harmful side effects, allergic reactions and toxicities.
- Metabolic pathways and waste products from some compounds are unknown.
- Potential for testing positive for banned substances.
- Expensive and unlikely to replace the benefits of a good diet and sound training program.

Contamination and Adulteration

A large number of "non-hormonal" dietary supplements, like vitamins, minerals, and amino acids, commonly used by athletes and others, are contaminated with and contain prohormones and/or precursor steroids. In 2003 the International Olympic Committee issued a warning of widespread contamination in numerous dietary supplements sold to athletes. These contaminated products included:

- Protein powders and amino acids supplements.
- Creatine.
- Hydroxy-Methyl-Butyrate (HMB).
- Carnitine, ribose, pyruvate.
- Guarana.
- Tribulus Terrestris.
- Vitamins supplements and some mineral supplements containing zinc.
- Numerous herbal extracts.
- Supplements marketed as "pro-hormones" of testosterone.

Approximately one in five dietary supplements (20%) sold for building muscle and improving athletic performance were contaminated with "steroid-like" chemicals.

Ephedra

Ephedra (ma huang), which was discussed in Chapter 11, is an herb containing several substances called ephedra alkaloids (ephedrine and pseudoephedrine). Ephedra was an ingredient in dietary supplements for a number of years until multiple adverse events (heart attack, stroke, and death) were reported. Based on these multiple adverse events, in 2004 the FDA concluded that dietary supplements containing ephedrine alkaloids pose a risk of serious adverse events (heart attack, stroke, and death), and that these risks are unreasonable in light of any benefits that may result from the use of these products. Thus, ephedra became illegal.

FDA has the authority to take action against a dietary supplement when the product (1) presents a significant risk, an unreasonable risk, or an imminent hazard; (2) does not comply with good manufacturing practices, or (3) makes an unsubstantiated structure-function claim. The FDA ruling that banned dietary supplements containing ephedrine alkaloids will remain in effect until further notice. Although it is still available over the internet and some companies are still selling it, this should not be happening. **No product containing ephedra should be purchased or used.**

If a product sounds too good to be true, it is usually not worth trying.