

Neoprene

Denise K. Woo, Giuseppe Militello, and William D. James

Neoprene is a synthetic rubber with many common uses, including use in shoe insoles and adhesives, orthopedic braces, and gloves. Many cases of type IV hypersensitivity from neoprene contact have been reported. Thioureas, the most commonly used vulcanization accelerators in the manufacture of neoprene, are responsible for the majority of these cases. However, thioureas are not included in the TRUE Test whereas the North American Contact Dermatitis Group standard tray contains only mixed dialkyl thioureas. Since most data indicate that many cases will be missed when only mixed dialkyl thioureas are used for screening, a more complete thiourea panel should be used when neoprene hypersensitivity is suspected.

NEOPRENE WAS FIRST DISCOVERED in 1930 and is one of the earliest, as well as most widely used, synthetic rubbers.¹ Its popularity is due to (1) its soft texture; (2) its cushioning properties; (3) its resistance to fire, oil, and ozone; and (4) its resilience to flexion and compression.² It is commonly used in shoe insoles and adhesives, orthopedic braces, gloves, wet suits, swimming goggles, and straps for continuous positive airway pressure (CPAP) masks.

The basic chemical structure of neoprene is a polymer of chloroprene (2-chloro-1,3-butadiene), which is synthesized from butadiene or acetylene.³ The properties of neoprene are created during vulcanization, the process of cross-linking polymer chains, which requires the addition of various compounds. In general-purpose grade neoprene, n-dodecyl mercaptan is used as the chain-transfer agent, and thiourea compounds are the most commonly used vulcanization accelerators since they have been shown to be the most effective, providing the best balance of tensile strength, resilience, compression set, heat aging, and water resistance in the finished product.² One exception is in the manufacture of gloves, in which a variety of other accelerators (such as carbamates) may be used instead to produce the desired physical properties, which include

SECTION EDITOR:

CHRISTEN M. MOWAD, MD

Geisinger Medical Center
Danville, PA 17821

E-mail: emowad@psghs.edu

Neoprene is increasingly found in many products. Multiple cases of allergic contact dermatitis to neoprene have been reported. Patch testing with an expanded panel of thioureas may be necessary to identify the causative allergen. The authors of this Product Allergen Watch thoroughly review common sources of neoprene allergy as well as what allergens are necessary to accurately diagnose allergic contact dermatitis from neoprene.

tactile sensitivity, flexibility, tear resistance, low odor, and comfort. Other additives include aromatic amines such as N-isopropyl-N'-phenyl-para-phenylenediamine (IPPD) and diphenylamine derivatives that may be added to protect the rubber from oxygen and ozone degradation.²

Typically, neoprene products are used without the occurrence of adverse events, but cases of associated allergic reactions have been reported. In rubber allergy, type IV hypersensitivity (with accelerators accounting for the majority of cases) is more common than type I hypersensitivity, which is mainly due to polypeptides found in natural latex.^{4,5} Consistent with this, all reported cases of allergic reactions resulting from neoprene have been type IV delayed hypersensitivity reactions. Thiourea accelerators that include diphenylthiourea (DPTU), dibutylthiourea (DBTU), diethylthiourea (DETU), ethylbutylthiourea (EBTU), and ethylenethiourea (ETU) are by far responsible for the majority of these cases.

Neoprene is used in the cushion insoles of athletic shoes as well as in the adhesive used in the manufacturing process. The adhesive also contains p-tert-butylphenol formaldehyde resin (PTBPF), which is added to provide stability and durability.⁶ Allergic reactions to the various components of the neoprene cushion insole and adhesive have been reported. Roberts and Hanifin documented eight patients with severe diffuse plantar foot dermatitis caused by wearing athletic shoes. The allergen was subsequently revealed to be EBTU found in both the adhesive

From the Department of Dermatology, University of Pennsylvania School of Medicine, Philadelphia, PA.

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and the foam rubber.⁷ Grimalt and Romaguera, in one of the earliest studies reporting allergic contact dermatitis (ACD) from neoprene, performed patch tests on 45 patients with shoe dermatitis and on 123 healthy control subjects; 33% of the patients with shoe dermatitis and 0% of the controls had allergic reactions when patch-tested with n-dodecyl mercaptan, found in the neoprene resin. It should be noted, however, that these patients were selected because they had negative patch-test results from the usual diagnostic series, which includes rubber accelerators and PTBPF. ⁸

In more recent studies of patients with foot dermatitis, the most common shoe allergens were rubber components (accelerators), followed by leather (chromium) and adhesives (PTBPF).^{9,10} This reflects the continued and increased use of rubber components in shoes, as well as the fact that the relatively impermeable nature of athletic shoes increases the probability that perspiration will enhance skin penetration by rubber allergens and hence exposure and sensitization to these materials. In Shackelford and Belsito's series of 70 patients with foot dermatitis, 23 were found to have ACD from shoes.¹⁰ PTBPF and mixed dialkyl thioureas were both among the 10 most common relevant allergens found for these 23 patients as 13% of the patients had relevant reactions to PTBPF and 9% had relevant reactions to mixed dialkyl thioureas.¹¹ Of interest, no reactions to n-dodecyl mercaptan were observed, which suggests that prior results may have been due to the skewed population base and that n-dodecyl mercaptan is, in general, not a major allergen.

ACD due to neoprene splints has been well documented. Neoprene is sold both in the form of commercial splints and as neoprene sheets and strapping materials for custom splinting. It is used as a cushioning and elastic agent in the splint, and the adhesive that binds the neoprene to the lining may also contain neoprene. Numerous cases of ACD due to DETU in knee braces, elbow braces, and ankle supports have been documented.^{12–16} Reactions due to DPTU and DBTU have been reported as well.^{17–20} Other less common allergens include the antioxidant IPPD, which is also found in a variety of other rubber products.^{20,21}

Neoprene can be used as a substitute for natural rubber in protective gloves. Camarasa and colleagues first reported sensitivity to DBTU, DETU, and DPTU in a bricklayer and in a housewife who used rubber gloves.²² Subsequently, more cases of ACD due to DPTU in neoprene gloves (such as DermaPrene protective gloves [Ansell Occupational Healthcare, Coshocton, OH]) have been documented.^{12,23}

Another source of exposure to neoprene is diving gear. Cases of ACD from DPTU, DETU, and EBTU in neoprene wet suits and diving gloves have been reported.^{24–26} Of interest, there has been one reported case of ACD caused by nickel in a neoprene wet suit. The presence of nickel is probably related to dyes or to dyeing procedures, and prolonged contact, friction, and sweating under occlusion enhanced the release of nickel.²⁷

There have also been reports of ACD in patients who use neoprene masks. Scalf and Fowler described a patient with chronic scalp dermatitis from wearing a CPAP mask for sleep apnea. The rubber strap was made of neoprene, and the result of patch-testing with mixed dialkyl thioureas was positive.²⁸ Similar cases caused by DETU and DBTU have been described.^{16,29}

Other reported allergens in neoprene products include DETU in neoprene foam weather strips;³⁰ DBTU, DETU, and EBTU in swimming goggles;^{31,32} DPTU and ETU in knee and elbow heat retainers;³³ and DPTU in a neoprene slimming suit.³⁴ Reactions to neoprene wrist supports used with computer keyboards have also been documented.^{16,35}

Of note, Roberts and Hanifin tested seven of the EBTU-sensitive patients in the previously mentioned athletic-shoe dermatitis study⁷ for cross-sensitivity to other thiourea compounds. All of the patients reacted to DETU and variously

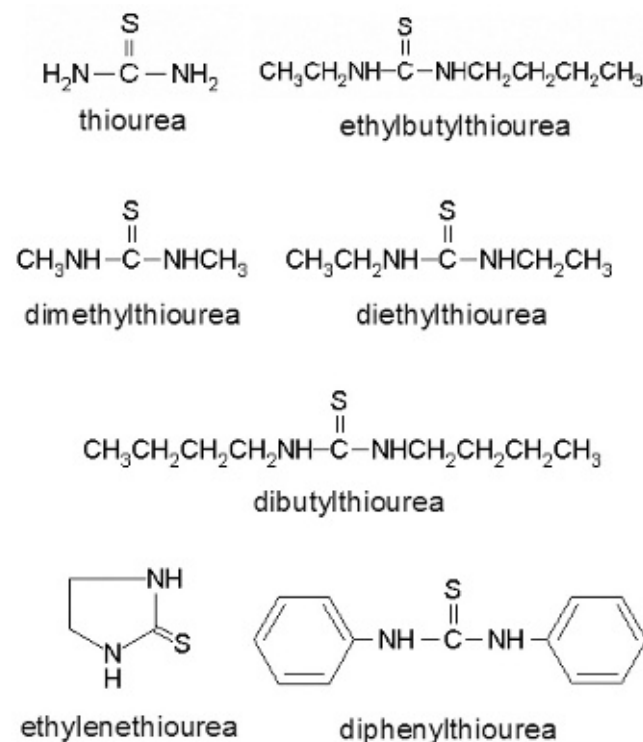


Figure 1. Structures of thiourea compounds.

Table 1. Complete Panel of the Major Thiourea Allergens

Allergen	Supplier
Diethylthiourea, dibutylthiourea, diphenylthiourea	Chemotechnique, Malmö, Sweden, or Dormer Laboratories, Ontario, Canada
Ethylbutylthiourea	(Not readily available)
Ethylenethiourea (prepare at 1% concentration in petrolatum)	Akrochem, Akron, OH

reacted to other alkylated thioureas (DBTU, dimethylthiourea, and trimethylthiourea) and to thiourea itself. Three of the patients were also tested with ETU, and none showed reactivity.³⁶ This is consistent with the observation that of the several cases of multiple sensitivities in a single patient, most have involved alkylated thioureas.^{16,31,32,37} However, the majority of cases do not support cross-reactivity.^{13–15,18–20,24–26,29,30,34} Because of the lack of structural similarity, cross-reactions among DPTU, ETU, and an alkylated thiourea seem unlikely³³ (Figure 1).

Thus, it is important for screening studies to include a complete panel of thiourea allergens (Table 1) and to patch-test with each compound separately. Unfortunately, thiourea is not included in the TRUE Test (Mekos Laboratories A/S, Hillerød, Denmark), and according to one analysis of reported case studies, screening would fail to diagnose 25% of patients if the test were performed with mixed dialkyl thioureas (such as those in the North American Contact Dermatitis Group [NACDG] standard tray, which has only DETU and DBTU).¹⁶ Because of these limitations in testing, the actual incidence of thiourea hypersensitivity remains uncertain. Studies show patch-test reactivity ranging from 0.6 to 1.3%.^{38–42} From

Table 2. Common Neoprene Products

Shoe insoles
Shoe adhesives
Orthopedic braces and splints
Gloves
Wet suits and diving gear
Swimming goggles
CPAP mask straps
Keyboard wrist supports
Car weather strips
Vulkan (Mobilis Healthcare Group, Lancs, UK) heat retainers

CPAP = continuous positive airway pressure.

Table 3. Non-neoprene Products That Contain Thioureas

Diazo papers used in photography and textile patterns
Fungicides
Paint and glue removers
Pesticides
Phone card thermocoating
Polyvinyl chloride adhesive tape
Silver polish dips

1998 to 2000, the NACDG study patch-tested 5,807 patients with mixed dialkyl thioureas, and 1.1% showed positive reactions.⁴²

Given the ubiquity of neoprene products, it is important that physicians be aware of neoprene as a source of ACD. Since there is generally limited or no cross-reaction among the various thioureas, a person hypersensitive to one neoprene item may show no response to another neoprene item that uses a different thiourea compound. The problem is that most manufacturers purchase neoprene from external suppliers and are unlikely to know (or are unwilling to disclose) the chemical composition of the material, so it is difficult to ascertain the chemical present in a specific neoprene product. Thus, physicians should be aware of common neoprene products (Table 2)^{6–8,12–35} as well as other products that contain thioureas (Table 3)^{12,16,37} and should advise patients on avoidance, based on clinical relevance.

It is likely that allergies to neoprene will be seen more regularly as more individuals are exposed to the material through its use in common products. A complete thiourea panel should be used for screening since thiourea is often the source of ACD from neoprene.

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