

Mixed Dialkyl Thioureas

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A MIXTURE OF TWO THIOUREA chemicals, referred to as mixed dialkyl thioureas (MDTU) has been chosen as the 2009 Allergen of the Year. This is a long-deserved recognition for an allergen mixture that has one of the highest relevancy rates in the North American Contact Dermatitis Group (NACDG) database. MDTU has been a part of the NACDG standard tray since 1991 and is a mixture of diethylthiourea (DETU) and dibutylthiourea (DBTU), tested at 1% in petrolatum.

Thioureas are a class of chemicals used for rubber acceleration and as antioxidants in the manufacture of neoprene. They are also used in the photocopying and photographic industries as antioxidants and fixatives. Thioureas have many other industrial uses and are widely found (Table 1¹⁻⁵).

At room temperature, thiourea is a white crystalline solid. Thioureas are organic compounds composed of hydrogen, oxygen, carbon, and sulfur.⁶ They are manufactured by various means, but one common production method is by passing liquid hydrogen sulfide in an aqueous bath of calcium cyanamide, which results in the formation of thiourea.⁷

MDTU is essential in determining allergic contact dermatitis in patients with a suspected allergy to a rubber-based product (particularly neoprene). DETU and DBTU are the main vulcanization accelerators used in the production of neoprene. These allergens have also been reported to cause photoallergic contact dermatitis in office workers exposed to thiourea in certain photocopy papers.⁸

Many cases of allergic contact dermatitis from these allergens in neoprene have been reported, including cases caused by rubber orthopedic braces, prostheses, splints, and foot supports; athletic shoes; rubber masks; swim goggle; wet suits; a slimming suit; a computer wrist rest; a

sleep apnea mask; neoprene gloves; and rubber-based materials in automobiles (Table 2⁹⁻²⁴). Experiments have shown that large quantities of thioureas are leached from rubber compounds.²⁰ The level of the leached thiourea compounds was found to be sufficient to elicit allergic contact dermatitis. This study may help manufacturers modify their products to decrease the leaching potential of these compounds.²⁵

From 1998 to 2000, the NACDG patched-tested 5,807 patients with MDTU and found a 1.1% positive-reaction rate. Relevance was considered definite in 15.6% of these reactions, probable in 25%, and possible in 42.2%, thus giving this allergen the distinction of being the allergen with the highest relevance rate in the NACDG standard tray.¹ During the same period, members of the Mayo Clinic Contact Dermatitis Group found a 1.2% positive-reaction rate among the 1,321 patients they tested.² The 2001–2002 NACDG results reported a 0.8% positive-reaction rate among 4,897 patients. Of these positive reactions, 18.4% were rated as being of definite relevance; this was good enough for second place in the relevance race, behind epoxy resin's astonishing 27.2% rate.³ These data show that MDTU was responsible for a high number of relevant reactions. Comfere and colleagues published an article on reactions to thioureas that confirmed that these reactions are often relevant, and their recommendation was that patch-testing centers should consider using MDTU in their screening series.⁴ Footwear products were the products most frequently found to cause relevant MDTU reactions; from an occupational standpoint, gloves were the most frequently cited cause of allergic contact dermatitis from dialkyl thioureas.²⁴

It has been estimated that screening with MDTU picks up about 75% of relevant thiourea reactions.⁵ If there is a high suspicion that a thiourea is the cause of a patient's dermatitis, the patient should be tested with a series of thiourea compounds to increase the percentage of relevant reactions. Many other thioureas are available for patch testing, including dimethylthiourea, ethylbutylthiourea, diphenylthiourea, and ethylenethiourea. It appears that they all cross react, with the exception of ethylenethiourea.⁵ The role of these supplemental allergens will likely be

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Table 1. Thiourea Applications and Uses

Adhesive manufacturing
Anticorrosive agents
Paint and glue removers
Pesticides and fungicides
Photocopy paper (diaz copy paper), as an antioxidant
Photography, as an antioxidant
Extraction of precious metals
Rubber accelerator and antioxidant (especially neoprene)
Synthetic resins
Textile and dye industry

Table 2. Neoprene-Based Products Containing Dialkyl Thioureas Causing Allergic Contact Dermatitis

Athletic shoes
Computer wrist rests
Gloves
Prostheses
Rubber-based automobile products
Rubber masks
Rubber orthopedic braces
Sleep apnea masks
Slimming suits
Splints and foot supports
Swim goggles
Wet suits

relegated to expanded patch testing when there is a high suspicion of dermatitis. They should also be included in a rubber patch tray. They are unlikely to be part of a standardized screening tray in the near future.^{24,26–28}

Thus, with the high relevancy of a positive reaction, standard screening series for allergic contact dermatitis would benefit from the addition of MDTU. Testing with this allergen mixture is a definite must for anyone with a suspected rubber allergy, especially from neoprene. Patch-testing with the other thioureas should be done if there is a high index of suspicion that a patient's dermatitis is caused by a product that may contain a thiourea (see Table 1). A resource for allergen alternatives was published recently,²⁹ and some manufacturers can produce orthotics and footwear that are made without thiourea-based accelerators. MDTU is an allergen mixture that frequently elicits positive reactions and an allergen with one of the highest relevance rates. It is certainly here to stay in 2009 and beyond.

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