Allergic contact dermatitis (ACD) affects more than 14.5 million Americans each year, notably defining itself as an important wide-spread disease. Due to overwhelming patient morbidity, loss of school and work time and significant expenditures for healthcare visits and medicaments, ACD presents with a high economic burden. Fortunately, through keen patient interviewing and patch testing, a culprit may be identified. Remission can occur with implementation of an allergen avoidance regimen. Education becomes the critical bridging intervention to ensure treatment adherence and symptom resolution. Patients who are unable to comply with avoidance regimens are at risk for sustained, recurrent, progressive or even systemic dermatitis. T o ensure patients have an appropriate understanding of all the potential outcomes and their central role in disease pathology and treatment, education of the patient may occur even before the diagnostic patch test is placed.

Important aspects of patient counseling include explaining the nature of their disease, for example, the delayed presentation of ACD [aka the importance of a delayed read at 96 hours]; the relationship with the immune system (sensitization to a chemical followed by elicitation of dermatitis with re-exposure) and the indifference to time (a substance the patient has been using regularly, briefly or intermittently can sensitize at any point). In certain cases, irritant contact dermatitis (ICD) and contact urticarial (CU) are also explained. Of note, unlike ACD, history rather than patch testing can often lead one to the correct diagnosis of ICD and CU.

ICD, the most prevalent form of contact dermatitis, can at times precede or be a concomitant diagnosis with ACD. Unlike ACD, ICD may occur on the first exposure to an irritating or abrasive substance. The innate immune system is activated and inflammation ensues. CU (wheal and flare reaction), on the other hand, represents one of the least prevalent forms of ACD. It is an immune-mediated phenomenon governed by a hallmark IgE and mast cell-mediated immediate-type hypersensitivity reaction. We acknowledge this form of hypersensitivity due to its potentially deadly anaphylactic reactions and direct the reader to key sources.

This article focuses on black rubber mix (RBM), the top relevant allergens, regional- and topic-based dermatitis presentations and clinical tips and pearls for diagnosis and treatment.

RUBBER, THE EARLY YEARS

The Aztec and Maya people realized the powers of the *Hevea Brasiliensis* tree long before the industrialized world understood the power of rubber. Recent discoveries have shown that rubber extraction and processing dates back to more than 3,000 years ago within the cultures of Mesoamerica. Rubber was obtained in the form of latex from the aforementioned tree and was called “caoutchouc” in the Maya Indian language, meaning “weeping wood.” These ancient rubber makers not only harvested the white liquid from the naturally found *Hevea* trees, but also discovered the morning glory vines, when mixed with the latex, strengthened and solidified it. The morning glory vines, often found growing nearby the latex trees, are a natural source of sulfur — a substance much later discovered by Charles Goodyear to be a “vulcanizer” of rubber. Maya artifacts at the Harvard University’s Peabody Museum include rubber figures, rubber handles and numerous rubber balls, as well as reports
Natural rubber is a liquid hydrocarbon immersed in a sheath of proteins. Solid rubber may be obtained either by drying off the water, or by precipitation with acid; the latter of which yields a purer rubber because it leaves most of the non-rubber proteins behind. The word rubber, as we know it today, was coined by Joseph Priestley when he discovered that dried latex sap could be used to erase pencil marks — he called this pencil eraser a “rubber,” thus coining the word. The current use of the term rubber is applied to any material having similar mechanical properties to those of natural (or Hevea) rubber — this includes accelerated rubber products.

Interestingly, it was not until the 1880s that there was global demand for rubber wares. At the turn of the 20th century, rubber manufacturing involved mechanically stretching out (pulling), molding and cooling of the wares to achieve the desired structure. The word tire (from French la tire “to pull”) was originally used in reference to the production of toffee candy, which involves the same type of pulling and stretching. Like toffee, the original commercial rubber products remained sticky, gummy and non-durable with changing temperature/humidity conditions.

In 1839, Goodyear serendipitously pioneered vulcanization — the chemical acceleration of natural rubber from a liquid to a solid state, with an accidental sulfur spill on a hot stove. Although already used for thousands of years by the Mayans with the morning glory vine, the addition of the sulfur component to commercial rubber production sped up the manufacturing process leading to the boom of the rubber accelerator industry (using thiurams, carbamates and mercaptans).

With the ability to produce large-scale amounts of rubber came the challenge of protecting the rubber against the destructive forces of oxidation.

**WHAT IS OXIDATION?**

For thousands of years, scientists have been intrigued by the air around us. Was it an empty void without any weight or function, or did it possess unattainable powers not yet discovered? The first elemental theory focusing on air came from a French physician and chemist named Jean Rey. By looking at rusted tin left out in the open air, he theorized that air became incorporated into the metal, accounting for the additional weight of the tin. Rey shocked the world with his groundbreaking theory because it meant that air must have a weight of its own. Despite mass skepticism, his theory on elements eventually gained widespread acceptance and, with time, led to several important inventions, most notably the thermometer and the barometer.

The possibility of more than one “air” was entertained by Priestley, an English minister with a remarkable fascination for gases. While observing the fermenting process at the neighborhood brewery, he witnessed the presence of a gas (separate from the air above the grain) that seemed to “spill” down the sides of the barrel. This gas was later determined to be carbon dioxide. Priestley’s further experiments with carbon dioxide led to soda water, a discovery that earned him the Copley Medal from the Royal Society.

In his later works, Priestley focused on the relationship of fire with gases. Using a vacuum chamber to collect the by-products of combustion, he noted that in the presence of mercuric oxide gas, the burning of a candle intensified, while all of the other gases he experimented with extinguished the flame. Priestley shared these observations with friend, a French tax collector Antoine Lavoisier. Lavoisier, in turn, compulsively experimented with combustion gas chambers, weighing the substrates, reactants and products throughout the condensation reaction. He discovered that water was composed of 2 gases which, when combined and cooled, could reform into water. Furthermore, by observing that 1 of the gases was essential to maintain a flame, Lavoisier correctly deduced that it was necessary to initiate combustion. He also noted that this gas contributed to combustion products having an acidic taste. Lavoisier named this gas oxygen (from the Greek words oxys “sour” and genes “I produce”).

From the discovery of oxygen, came the questions of its effect on the surrounding elements. Oxidation is by far the main cause of age-related deterioration in both organic (skin, internal organs) and inorganic (metals, rubber) systems. Technically, oxidation refers to the loss of at least 1 electron when 2 or more substances interact. At times, oxidation is the necessary step in a formation of a specific material — such as the formation of super-durable anodized aluminum. The production and harnessing of steam derived from the combustion (oxidation) of coal and wood set the stage for a multitude of technological advances, which would be the hallmark of the industrial revolution.

However, oxidation can often be destructive such as the rusting of metal and rotting of fruit. The Statue of Liberty, for example, given to the United States in 1886 by the French, befell to the powers of oxidation in its discolored green coat. When exposed to free air, the pure rubber molecule is susceptible to oxidation, which leads to a deterioration of its physical properties — aging. Unprotected rubber products, such as tires, would quickly demise to the elements around them and crumble under pressure. The Ford Motor Company struggled with this fact as its early models carried white rubber tires, which dried, cracked and quickly showed dirt and age.

**BLACK RUBBER MIX EMERGES**

Antidegradation agents such as anti-oxidants and antiozonants were developed to prevent rubber from drying by preventing oxidation or decreasing the effect of ozone. One of the first utilized antioxidants was hexamethylenetetramine (HMT), a formaldehyde-releasing antioxidant and vulcanizer. While it is still used today, the carcinogenic and allergenic potential of HMT led to its substitution with less toxic chemicals, such as the secondary amines of para-phenylenediamine (PPD). PPD antioxidants are commonly used because they are most effective in rubber. During the antioxidation process, the additives turn the rubber mixture black before damage to the rubber molecules can be done.

PPD is an oxidative substance, which was formulated for hair dye use in 1907 by Eugene Schueller, a young French chemist and founder of L’Oreal. Schueller developed an entire industry based on the principle that, when oxidized, PPD turned hair black. The possibility of capitalizing upon the oxidation
function of PPD led rubber scientists to experiment with PPD derivatives for use in the automotive tire industry. The secondary amine mixture of PPD derivatives were found to offer effective temperature stability, strength and flexibility, and resistance to oxidation over a wide range of physical conditions.36 By 1971, the tire industry had almost unanimously switched to the secondary amines of PPD, which became referred to as BRM. Table 1 summarizes the chemical components of BRM. The name BRM is not all-encompassing because although the chemical ingredients may be found in dark-colored materials, they also cross-react and co-react with many textile and hair dyes (Table 2).26

By 1918, half of all carriages on American roads were sporting a most notable innovation: weather-resistant black rubber tires which withstood the forces of oxidation.22 Currently, BRM can be found in various work and home environments including belts, masks, hoses, cables, aprons, flooring, racquet handles and medical and laboratory equipment (Tables 3 and 4).27

ALLERGIES TO BLACK RUBBER MIX

ACD to the additives used in the rubber industry was noted as early as the 1943 by W. E. Obetz, who coined the dermatitis “rubber itch” or “rubber poisoning.”28 Prosser White, an occupational dermatologist of the time, named HMT as the most active culprit in the dermatitis. White noted that during the summer months, the slight increase in acidity of workers’ perspiration caused the HMT to release formaldehyde. The oxidation of the formaldehyde to formic acid was thought to be the actual perpetrator of the allergic reaction.28 Unfortunately, because the allergy affected only a small occupation-based population, the dangers of these chemicals were not widely known by the general public.

Although natural latex rarely causes delayed-type hypersensitivity reactions (Type IV), it has been linked to several life-threatening anaphylaxis reactions (Type I).29 Several papers have been published on latex allergy.30-33 Manufactured rubber, on the other hand, presents the opposite problem of causing a large number of Type IV reactions. Many of the additives including accelerators, activators, anti-degradants, vulcanizers, retarders, reinforcing agents, fillers and pigments have been named as sensitizers.29 It is important to note that these chemicals may become an occupational hazard, affecting both the skin and airway, especially if they are aerosolized during heating and pressurizing.

From 1985 to 1990, the North American Contact Dermatitis Group determined the incidence of synthetic rubber allergy to be approximately 4%, with more than 55% of the exposures being from occupational sources (85% secondary to glove use).34 Among those who had a positive patch test to a rubber mix, thiuram mix (62%) and BRM (38%) were the most common culprits.35 The contact sensitization prevalence to BRM in the general population is estimated at 2.1% in men and 1.6% in women.26

In the 1990s, recycled tire shreddings were commonly used as fillers for playgrounds. Reports of shredding-associated carcinogens and increasing allergic sensitization to BRM led to playgrounds being recovered with other substances.26 Another source of BRM exposure, albeit novel, is in the handrails on escalators. The BRM antioxidant materials in the handrails remain in their raw form and oftentimes not secondarily sealed before shoppers come into contact with them. Contact dermatitis to handrails has been causally linked to unilateral palmar dermatitis in at least 2 cases.37

PRACTICALS OF PATCH TESTING

Patch testing is often necessary to identify the relevant allergen(s) responsible for the patients’ ACD. Screening patch test trays are available to isolate the most common chemicals and offer the provider clues for potential sources. The American Contact Dermatitis Society (ACDS) North American Standard Series includes allergens from several different categories.38 Supplemental trays (such as hairdressing, dental materials, cosmetics and fragrance/flavors) are also available for purchase.39 Notably, the chance of demonstrating a relevant positive reaction is greater when cross-reactors are added to the test.39

Initially pioneered by Bonnevie in 1939, the use of patch test mixes compared to individual elements widened diagnostic abilities within the ACD.
field.\textsuperscript{40} Specifically, patch test screening for rubber allergy is recommended to be performed with “mixes” of rubber chemicals, in addition to selected single substances.\textsuperscript{26,41} In further refinement of rubber patch test mixtures, the individual component amounts were limited to less than 1% (except for carba mix) in order to reduce ICQ cases.\textsuperscript{26}

**PEARS OF TREATMENT: EVERY DOSE COUNTS**

A person may be exposed to and subsequently sensitized to a particular allergen for days to years before actually developing ACD. Exposures can be additive, eventually causing one’s immune system to become trained to identify a chemical, at which time a cutaneous response would be elicited upon exposure.\textsuperscript{4} The pathophysiologic trick behind ACD that can also be used as its cure is that just as repeated contact over time leads to an immune response, repeated avoidance over time will induce remission. Avoidance creativity, however, may not be necessary by utilizing alternatives and being aware of indirect exposures. For example, patients allergic to BRM commonly have concomitant allergy to PPD.\textsuperscript{42} Both of these dyes are derived from the same para-aminobenzoic acid (PABA) parent compound, and thus, may also cross-react with the other PABA derivatives such as PABA sunscreens, ester anesthetics, hydrochloro-azidine and sulfonylamides.\textsuperscript{43}

There are programs available to aid in the avoidance endeavor. The Contact Allergen Management Program, a service offered through ACDS, and the Contact Allergen Replacement Database, developed by the Mayo Clinic, can assist with identifying allergen-free products.\textsuperscript{44,45} Both programs allow the provider to personalize “shopping lists” of products void of specific dermatitis-inducing chemicals, as well as any cross-reactors.

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