

# ALLERGEN Focus



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## Focus On: Acrylics

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In 1997 the Food and Drug Administration gave indication to the Thin-layer Rapid-Use Epicutaneous (T.R.U.E.) test for use as a valuable, first-line screening tool in the diagnosis of allergic contact dermatitis (ACD). Many dermatologists and allergists use this standard tool in their practices and refer to contact dermatitis referral centers when the T.R.U.E. test fails to identify a relevant allergen. Specifically, the T.R.U.E. test screens for 46 distinct allergens in addition to the balsam of Peru mixture, and this test is thought to adequately identify an allergen in approximately 24.5% of patients.<sup>1</sup>

This being said, many relevant allergens are not detected by use of this screening tool alone and, for this reason, "Allergen Focus" has been expanded to cover the notorious allergens of the year and other top relevant allergens identified by the North American Contact Dermatitis Group (NACDG). **This month, the column focuses on the NACDG standard allergen acrylics. These agents are commonly used in artificial nails, and in dental cements, bonding agents and composite resins.**

### CONTACT DERMATIDES

The contact dermatides include allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), and contact urticaria (CU). The most common form, ICD accounts for approximately 80% of environmental/occupational-based dermatoses. Contact urticaria (wheal and flare reaction) represents an IgE and mast-cell-mediated, immediate-type, hypersensitivity reaction that can lead to anaphylaxis. The foremost example of this would be latex protein hypersensitivity. While this is beyond the scope of this section, we acknowledge this form of hypersensitivity due to the severity of the potential reactions and direct the reader to key resources.<sup>2,3</sup>

Allergic contact dermatitis is a T-cell dependent, delayed-type (Type IV) hypersensitivity reaction that has a high impact both in terms of patient morbidity and economics. This type of hypersensitivity reaction is primarily instigated by small lipophilic chemicals (haptens) with a molecular weight less than 500 Daltons. These chemical allergens trigger a complex immunologic cascade in the skin, which leads to the clinical picture of ACD.

### CASE ILLUSTRATION

A patient presented with pulpitis of the fingertips. She had previously suffered with the same condition, which cleared when she discontinued wearing artificial nails. Of note, she also frequently painted her nails.

### DISCOVERING ACROLEIN

Despite the fact that the famed Swedish chemist, Jons Jakob Berzelius failed almost every subject course he attended, this student of Dalton went on to discover the chemical elements silicon, selenium, thorium and cerium (and mentor the students who discovered lithium and vanadium).<sup>4</sup> His experiments became so complex that in 1828 he decidedly developed a system of chemi-

cal notation that earned him a title as one of the fathers of modern chemistry. His system was to give elements Latin-derived notations, for example Fe for iron and O for oxygen. He derived this naming system to aid in the clarity of his experiments, and it proved so practical that it is still in use today.

In his later career, while experimenting with the thermal decomposition of vegetable oils, Berzelius discovered a pungent substance produced during this process. He named this substance acrolein.<sup>5</sup>

Unexpectedly, it is now known that this same compound (acrolein) is one of the 4,000 constituents of cigarette smoke and that it causes DNA damage in the tumor-suppressor p53 gene.

In fact, the pattern of DNA mutations induced by acrolein has been likened to that which is often found in human lung cancer samples. Moon-shong Tang, a Professor of Environmental Medicine, Pathology and Medicine at New York University, once stated, "If cigarette smoke is the weapon that causes lung cancer, then these mutations are fingerprints on the knife."<sup>6</sup>

Interestingly, in April of 1914 Thomas Edison wrote to Henry Ford, *The injurious agent in cigarettes comes principally from the burning paper wrapper. The substance thereby formed is called Acrolein.* He went on to write, *It has a violent action on the nerve centers, producing degeneration of the cells of the brain, which is quite rapid among boys.* For these reasons, concluded Edison, *I employ no person who smokes cigarettes.*

Ford took this advice and thus, the Ford Motor Car Company "did not suffer from the modern astronomical anti-competitive cost factor caused by smoking-caused health care costs."<sup>2</sup> In fact, Henry Ford is said to have personally paid to circulate tens of thousands of copies of Edison's letter to Michigan schoolchildren and used it as an introductory page to his book, *The Case Against the Little White Slaver.*

Edison was not alone in pioneering efforts to educate people on the detrimental effects of the habitual use of toxic chemicals. In 1898 during the Spanish American War, the U.S. Army would not enlist smokers! The military knew of smokers' notoriously diseased condition!<sup>12</sup>

## A SOCIAL EXPLOIT

But like so many other chemicals that are hazardous to humans, acrolein has maintained an intimate relationship with human health because it provided a social exploit and, ironically, a dramatic impact on all of our lives.

Fifty five years before the hazards of acrolein were proclaimed, chemist Josef Redtenbacher demonstrated that acrolein was in fact formed by the dehydration of glycerol (circa 1843).<sup>5</sup> He further realized that this substance could readily be oxidized to an acid substance, which he named acrylic

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acid.<sup>7</sup> This important discovery would become the impetus for the greatest revolution in the plastics industry.

## PLEXIGLAS REVOLUTION

More than half a century later, a chemistry graduate student by the name of Otto Rohm published the results of his thesis "On the Polymerization Products of Acrylic Acid," describing how the polymer of acrylic acid simultaneously possessed properties of a tough, flexible glass and a rigid plastic.<sup>8</sup>

But this was not Rohm's only discovery; he was also the first person to isolate porcine pancreatic enzymes extracted and use them to soften leather during the tanning process (c.1907).<sup>9</sup> The applicability of this discovery was noted by businessman Otto Haas, and together they started the company Rohm and Haas to mass-produce the new leather tanning solution, which they called Oropon. Of note, Oropon was awarded the gold medal at the International Hygiene Exhibition in Dresden **[[GERMANY?]]** in 1911.<sup>10</sup>

Working on the success of their more than 30-year partnership, Rohm and Haas

revisited new applications for Rohm's original thesis discovery on acrylic acid. As they witnessed the explosion of the plastics industry led mainly by cellophane and Nylon,<sup>11</sup> Rohm and Haas were determined to contribute if not lead this "plastics craze." They debuted their big breakthrough in 1933 with the manufacturing of a transparent composite safety glass composed of polymethylmethacrylate (PMMA), known as Plexiglas.<sup>10</sup>

Plexiglas was first used in bubble-top cockpit windows of WWII fighter planes<sup>12</sup> but quickly gained widespread use in civilian applications such as instrument covers, watch glasses and cutlery.<sup>13</sup> To this day, the Plexiglas windows in those airplanes are still clear and free of yellowing, owing to its ability to resist weathering.<sup>14</sup>

## FROM DENTAL FILLERS TO FINGERNAILS

The broad utility and applicability of Plexiglas was soon realized in the field of dentistry, more specifically as a dental filler.<sup>15</sup>

And, as the popularity of acrylics (which include acrylates) in dental work grew, some resourceful Hollywood beauticians discovered that they could use those same materials to improve the appearance of actresses' nails. (*Personal communication, Doug Schoon, former VP of Science and Research at Creative Nail Designs.*)

Because initially dental acrylates were used as the nail enhancing materials, the products were commonly referred to as "dental acrylics" or "porcelain nails." As the popularity of the nails grew, so did the realization that untoward side effects paralleled their use. By the end of the 1970s, the FDA had received a horde of complaints ranging from allergic reactions to permanent loss of the nail plate to loss of fingertip sensation.<sup>17</sup>

While no formal bans were ever put into place, investigations into the source determined that it was the monomeric methyl methacrylate (MMA) that was the culprit. The FDA issued a warning that stated that the monomeric MMA was considered "to be a poisonous and deleterious substance and [the FDA] may take regulatory action against any products containing methyl methacrylate monomer and may take legal action against those involved."<sup>18</sup> Fortunately, a solution to circumvent the MMA problem came to

fruition through an interaction between a dentist and his manicurist patient.

In the 1970s, dentist Dr. Stuart Nordstrom was mixing a liquid and powder to create a temporary tooth for his patient, who was a manicurist, when she recognized the likeness of the filler material's odor to the materials used to sculpt "porcelain nails" [which happened to be the MMA material in both products]. Because of this episode, Dr. Nordstrom had the idea to improve the current nail technology to reduce its toxicity. Working alongside fellow nail technology pioneer Fred Slack, he formulated the first-ever cross-linked polymer formulation of ethyl methacrylate (EMA) for nail enhancements.<sup>19</sup>

Dr. Nordstrom soon began supplying the material through his patient's place of employment. However, the product received such rave reviews at local cosmetology schools that in 1978, along with his children Jim and Jan Nordstrom, he formed the Creative Nail Designs Company to keep up with the demand.<sup>20</sup> His company is still an innovative leader in today's estimated \$6.84 billion nail industry, and EMA is now the standard in the nail industry.<sup>21,22</sup> **It is important to note** that ethyl methacrylate is very similar to MMA (differing only by an extra carbon and a few hydrogen atoms) and can also cause allergic reaction in the monomeric form, but not so when in large, polymer chains.

Unfortunately, industrialization and the demand for consumer products is not without consequence. The company that started it all, Rohm and Haas, which grew to be a Fortune 500 company, is one of five defendants in a class-action lawsuit filed by residents of McCullom Lake, IL. The lawsuit alleges that contamination of groundwater by the company has been directly responsible for 21 of 1,000 residents experiencing some type of brain or pituitary cancer.<sup>23</sup> Whether acrolein is involved remains to be determined.

## THE HISTORY OF THE MANICURE

Nail modification dates back to India as much as 5,000 years ago when henna was added to nails in a primitive form of manicure.<sup>24</sup> As early as 3,000 B.C., the Chinese used flower petals, bees' wax, egg whites, silver, and gold to tint their nails.<sup>25</sup> In Egypt colored nails were an indicator of social

status for both males and females.<sup>25</sup> Members of the royal classes had nails that were distinguished by their dark tones, as opposed to the paler tones used by the working class.

The art of manicuring, however, didn't make its fashion debut in the United States until the height of 1920s, when coincidentally, Ford began to paint his automobiles.<sup>26</sup> In fact, it was in the midst of the Great Depression that brothers Charles and Joseph Reinson, along with chemist Charles Lachman, founded the Revlon company. (The "L" comes from Lachman). They began marketing a single product, a novel type of nail enamel. In doing so, these three men revolutionized the cosmetic manufacturing process. By using pigments instead of dyes, they could create a more colorful spectrum of opaque nail enamels than was previously considered possible. In 1937 the company began selling the nail products to department stores, and within 6 years Revlon became a multimillion-dollar corporation.<sup>25</sup>

In the 1940s, actress Rita Haywood popularized the look of long, red nails, a look still very popular today. As these sleek nails grew more popular, those who couldn't grow them went to desperate measures to enhance their nails. For example, it became popular for manicurists to perform the expensive extension technique of gluing cutoff natural fingernails onto the clients' nails to lengthen them.<sup>27</sup> Notably, this practice ended in 1970 when Dr. Nordstrom introduced the acrylic nail and brought artificial nail enhancement to the masses.<sup>25</sup>

## ON THE USE OF ACRYLICS

Acrylic resins and their derivatives are widely used as alternatives to glass and can be found in many everyday items. For instance, PMMA is used in the lenses of exterior automobile lights, acrylic paints and even hard contact lenses.<sup>28</sup> Even the Pope traveled in a mobile transport vehicle enclosed by a thick, bulletproof acrylic casing.<sup>12</sup> And generally, the resin poses little risk for initiating allergic reactions. The dental fillings and artificial nails that do cause reactions, however, do so because they are thought to still contain the sensitizing monomer MMA.<sup>29</sup> While acrylic allergies are most commonly seen in nails and dental work, reactions have been reported in chemical workers,<sup>30</sup> in rela-

tion to exposure to paints,<sup>31</sup> and even exposure to incontinency pads.<sup>32</sup>

## TESTING FOR ACRYLIC SENSITIVITY

The standard NACDG screening tray contains 65 allergen components selected for study; 3 of these are acrylic chemicals: ethyl acrylate, methyl methacrylate and 2-Hydroxyethyl methacrylate (HEMA).

**Methyl methacrylate** is the main allergenic monomer in most sources of acrylates such as artificial nails, dental cements, composite dental resin.

**Ethyl acrylate** was chosen as it has also been identified as one of the best acrylate screeners. (*Personal Communication, Melanie Pratt, M.D., NACDG member.*)

**Hydroxyl ethyl methacrylate** has been recently studied by the NACDG because it is one of the main dental monomers and commonest listed acrylics on most dental MSDS for cements, bonding agents and composite resin.

**Of note, there are no acrylic formulations on FDA-indicated commercially available patch tests (TRUE or Hermal).**

## THE VALUE OF THIS PATIENT CASE

The importance of appropriate patch testing with subsequent patient education cannot be overstated. This patient was sensitized to acrylics through the use of artificial nails. Furthermore, she perpetuated her pulpitis with continued use of acrylics in her nail polish and hair spray. A review of her products post patch testing revealed the use of acrylic anti-chip nail polish, and when she discontinued this product (**avoidance**), her pulpitis cleared.

This case highlights the importance of product reviews subsequent to patch testing and the ability to find clues in a detailed patient history. [n](#)

**Dedication: To Dr. James Taylor of the Cleveland Clinic Foundation for his continued guidance and mentorship.**

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## BRIEF SUMMARY

### Rx ONLY

**INDICATIONS AND USAGE:** Naftin<sup>®</sup> Cream, 1% is indicated for the topical treatment of tinea pedis, tinea axillaris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*. Naftin<sup>®</sup> Gel, 1% is indicated for the topical treatment of tinea pedis, tinea axillaris, and tinea corporis caused by the organisms *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*<sup>†</sup>, *Epidermophyton floccosum*<sup>†</sup>. \*Efficacy for this organism in this organ system was studied in fewer than 10 infections.

**CONTRAINDICATIONS:** Naftin<sup>®</sup> Cream and Gel, 1% are contraindicated in individuals who have shown hypersensitivity to any of their components.

**WARNINGS:** Naftin<sup>®</sup> Cream and Gel, 1% are for topical use only and not for ophthalmic use.

**PRECAUTIONS:** General: Naftin<sup>®</sup> Cream and Gel, 1%, are for external use only. If irritation or sensitivity develops with the use of Naftin<sup>®</sup> Cream or Gel, 1%, treatment should be discontinued and appropriate therapy instituted. Diagnosis of the disease should be confirmed either by direct microscopic examination of a mounting of infected tissue in a solution of potassium hydroxide or by culture on an appropriate medium. Information for patients: The patient should be told to:

1. Avoid the use of occlusive dressings or wrappings unless otherwise directed by the physician.
2. Keep Naftin<sup>®</sup> Cream and Gel, 1% away from the eyes, nose, mouth and other mucous membranes.

**Carcinogenesis, mutagenesis, impairment of fertility:** Long-term studies to evaluate the carcinogenic potential of Naftin<sup>®</sup> Cream and Gel, 1% have not been performed. *In vivo* and animal studies have not demonstrated any mutagenic effect or effect on fertility.

**Pregnancy, Teratogenic Effects, Pregnancy Category B:** Reproduction studies have been performed in rats and rabbits (via oral administration) at doses 150 times or more than the topical human dose and have revealed no evidence of impaired fertility or harm to the fetus due to naftifine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Naftin<sup>®</sup> Cream or Gel, 1% are administered to a nursing woman.

**Pediatric use:** Safety and effectiveness in pediatric patients have not been established.

**ADVERSE REACTIONS:** During clinical trials with Naftin<sup>®</sup> Cream, 1%, the incidence of adverse reactions was as follows: burning/tingling (6%), dryness (3%), erythema (2%), itching (2%), local irritation (2%). During clinical trials with Naftin<sup>®</sup> Gel, 1%, the incidence of adverse reactions was as follows: burning/tingling (5.0%), itching (1.0%), erythema (0.5%), rash (0.5%), skin tenderness (0.5%).

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