ALLERGEN Focus

Focus on 2000 Allergen of the Year: Textile Dyes

BY SHARON E. JACOB, M.D., AND CLAUDIA C. RAMIREZ, M.D.

In 1997 the Federal Drug Administration granted an indication for the use of the thin-layer rapid-use epicutaneous (T.R.U.E.) test as a valuable, first-line screening tool in the diagnosis of allergic contact dermatitis (ACD). Many dermatologists and allergists utilize this standard tool in their practice 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. The test is thought to adequately *identify an allergen in approximately 24.5%* of patients with ACD.[1] 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 that have been designated by the American Contact Dermatitis Society (ACDS) as Allergens of the Year.

"Allergen Focus" is a column designed to concentrate on common allergens and is intended to answer some of the most frequent questions relating to their origin and most common uses. Each column also highlights appropriate products that affected patients should avoid, along with tips to avoid cross-reactions and exposures.

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CONTACT DERMATIDES

The contact dermatides include allergic contact dermatitis (ACD), irritant contact dermatitis and contact urticaria.

Irritant contact dermatitis, the most common form, 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 being 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 sources.[2,3]

ACD is an important disease with high impact both in terms of patient morbidity and economics. ACD represents a T-helper cell Type 1 (Th1) dependent delayed-type (Type IV) hypersensitivity reaction. The instigating exogenous antigens are primarily small lipophilic chemicals (haptens) with a molecular weight less than 500 Da. On direct antigen exposure to the skin or mucosa, an immunologic cascade is initiated which includes cytokines, i.e. interleukin 2 (IL-2) and interferon gamma (IFN-γ), T cells and Langerhan cells. This complex interaction leads to the clinical picture of ACD.

CLINICAL ILLUSTRATION

A mechanic presented to the University of Miami Contact Dermatitis Clinic for evaluation of longstanding generalized pruritus, for which he had seen multiple dermatologists and psychiatrists. Of note, numerous prurigo nodules and scars were present on his arms and legs and there were distinct

areas of sparing in the location of his undergarments.

BIRD'S EYE VIEW ON THE HISTORY OF TEXTILE DYES

The earliest written record of the use of natural dyes was found in China, dated 2600 BC.[4] These early records denote the ancient Chinese methods for dyeing silk using various dyes obtained from plants. These plants were selected and harvested by the dyer and boiled in water to form the *dyebath*. Mordants (metal salts such as tin, chrome, iron, copper, alum, etc. used to fix natural dyes to fabric) were also utilized to broaden the range of colors within the same dyebath base.[5]

In early documented European history, the Phoenicians used their renowned dyeing skills and beautifully colored fabrics to enhance trade with other countries.

Colors were also used for sociological classification. For example, in ancient Rome yellow was only used for dyeing bridal garments[5] and Caesar identified his status with the color purple. The Venetians further developed the art of dyeing with imported indigo and Brazil wood from India.[5] Of interest, the Portuguese later used the Brazil-tree to name the newly discovered South American country where many of these trees had also been found.

During the tenth century, the first syndicate of dyers was created in Germany, the Wool Dyer's Guild.[5] The discovery by Pizarro and Cortez of cotton in Central and South America (c. 1519) brought to Spain brightly printed fabrics from the natives.[4]

THE DYEING INDUSTRY BOOMS

The discovery of the Americas gave a great impetus to the art of dyeing, introducing logwood, fustic and cochineal (vegetable coloring matters).

Thereafter, the dyeing industry boomed, guilds formed and regulations and laws were created to protect local industry. For example, the *Law of the Diet* of 1577 prohibited the use of indigo (from India) in Germany, it being described as a "pernicious and corrosive dye".[5]

Kings passed laws to protect commerce and direct taxation. For example, James I of England prohibited the import of logwood dye in 1620 to restrict commerce with Spain, who had been importing it from the Americas,[5] but dyers managed to acquire it under other names.

On the other hand, King James II prohibited exportation of undyed cloth to help reinforce the home industry for English dyers (over Scottish dyers) in 1688.[4]

Furthermore, in 1708, William III signed a law banning the importation of printed silks, but to his chagrin this measure only made silks more popular.

THE VENETIANS FURTHER DEVELOPED THE ART OF DYEING WITH IMPORTED INDIGO AND BRAZIL WOOD FROM INDIA.[5]

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BLEACHING IS DISCOVERED

In 1774 the bleaching properties of chlorine (by destroying vegetable colors) was first employed by Scheele, a Swedish chemist. He had noted the bleaching effect on a cork in a bottle of hydrochloric acid and this discovery was of enormous commercial importance.

The practical application of this new chemical in bleaching cloth soon supplanted the Old Dutch process of "crafting" — that is, extended sun-bleaching by spreading the cloth upon the grass.

This discovery was paramount to textile manufacturers, as the old process of bleaching consumed an entire summer to whiten a single piece of linen. The new process reduced the period to a few hours.[6]

Until this time, the great subject of organic chemistry had remained practically unexplored. Under Scheele's direction, new methods of isolating and studying animal and vegetable dye products were introduced, and a large number of previously unknown acids and other organic compounds were able to be reproducibly prepared.[6]

Prior to Scheele's advances, older green pigments were based on copper carbonate.

With Scheele's new methodologies, he was able to create a new spectrum of green based on the properties of the compound arsenic.

These favored green dyes were used for coloring paper, cotton and linen.[7] Interestingly, the wallpapers containing Scheele's Green were implicated in the arsenic poisoning of Napoleon Bonaparte![8]

THE ERA OF SYNTHETIC DYES IS BORN

In 1856 during Easter vacation from the Royal College of Chemistry, an English chemistry student, William H. Perkin, accidentally synthesized mauve (an aniline basic dye, derived from coal tar).[4]

While attempting to create a possible cure for malaria, he chemically synthesized quinine, which when oxidized yielded a beautiful violet-colored matter with great tinctorial powers (ability to impart color on another object).

This was the beginning of the era of synthetic dyestuffs and an important

AT THE NEW YORK WORLD FAIR PREMIER IN 1939, THE FIRST PAIR OF NYLON STOCKINGS, WHICH WERE THOUGHT TO HAVE BEEN DYED WITH FEDERAL DYESTUFF DISPERSE DYES, WERE FORMALLY INTRODUCED TO THE COMMERCIAL MARKET.[14] WITHIN A YEAR, THE NYLON STOCKING CRAZE WAS IN FULL FORCE, WITH 64 MILLION PAIRS SOLD!

landmark in industrial chemistry. In fact, most of the labor-intensive vegetable pigment processes have now been replaced by the various synthetic coal-tar colors, because they were faster coloring and easier to apply. This allowed for mass production of standardized materials and the boom of the garment industry.

The Post Office Department, the predecessor of the United States Postal Service, was founded in 1775, but official uniforms weren't worn until after 1868, when Congress passed legislation authorizing use of uniforms by letter carriers. These uniforms were cadet blue-gray with black trim.[9] These dark-colored uniforms, especially those made from synthetic or blended fabrics, were and are significant sources of exposure to some of the most allergenic dyes.[10]

As good fortune would have it for the Levi Strauss Company, they selected vat blue 1 (indigo) to color their patented and very popular copper riveted denim pants in 1873.

The vat dyes were very water-insoluble and had to be treated in order to secure binding to the fibers. Once bound, however, they were virtually impossible to remove.[11]

This "fastness" of the dyes rendered the vat dyes one of the least allergenic dye families. As a result, the Levi Strauss Company has enjoyed a long and prosperous history of producing non-sensitizing pants.

In addition, this American-based company is notable for being one the first and few to use American-based dyes and produce their product domestically, which allowed them to maintain production despite changing world events.

In 1914, for example, 90% of the dyestuffs used by North American manufacturers were imported. This specifically became a problem during WWI, as many of the dyes came from Germany.[4] The limited availability of dyes during the War, led Congress to pass a protective duty on homeland dyestuffs to encourage domestic manufacture.

THE AMERICAN DYE INDUSTRY THRIVES

In October 1915, the Federal Dyestuff and Chemical Corporation was incorporated in Delaware.[12] Their strategic acquisition of 200 land acres in Kingsport, TN, bordered by the Holston River and accessible by the Carolina, Clinchfield, and Ohio Railroads served as the optimal supply house for the processing of U.S.-based coal tar dye raw materials: coal, sulfur and salt.

The dye quality produced here was equated to that of the best European dyestuffs, and the American Dye Industry gained a new independence.[12]

Around this time, Harvard chemist, Wallace Hume Carothers at DuPont developed their most notorious innovation, Fiber 66 (a.k.a. Nylon).[13] And, even though it took more than a decade to bring this fiber to the consumer market, its debut was hallmarked. At the New York World Fair premier in 1939, the first pair of nylon stockings, which notably are thought to have been dyed with Federal Dyestuff disperse dyes, were formally introduced to the commercial market.[14] Within a year, the nylon stocking craze was in full force, with 64 million pairs sold!

In 1942, production of nylon stockings ground to a halt, as nylon resources were re-directed to World War II efforts, (e.g. parachutes, aircrafts tires and tent production). People began paying almost 20 times the original price on the black market.[15]

At the end of the war, nylons did become available again, but the supply didn't meet the demand. Thousands of women who learned of the sales of the stockings by word of mouth showed up to stores to purchase the meager supplies, only to find that the stockings were all sold out. In Pittsburgh, for example, 40,000 women waited to buy the available 13,000 pairs of stockings.[16]

Scenarios such as this led to the outbreak of The Nylon Riots Of 1945.[15]

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TABLE 1

AVOIDANCE IN TEXTILE DYE DERMATITIS[10,11,20]

- Use lightly colored garments
- Use 100% natural fibers (cotton, linen, silk, wool)
- Wear loose-fitting clothing
- Avoid dark linens, towels
- Use "safe" undergarments
- Wash clothes before wearing (2 to 3 times)
- Avoid nylon stockings, spandex and lycra exercise clothing
- Avoid or decrease use of hair dyes containing PPD
- Avoid henna tattooing with black henna (natural henna laced with PPD)

TABLE 2

UNEXPECTED EXPOSURE SOURCES OF DISPERSE DYES

- Diapers
- Hosiery
- Shoulder pads
- Synthetic wigs
- Swimsuits
- Underwear

People waiting in lines became so disruptive that police force was needed to disperse the crowds.[15]

Finally, by March of 1946, DuPont was back in full swing with a production of 30 million pairs a month in the U.S.A![15] This is most notable, as to this day, nylon stockings and hosiery represent a significant source of disperse dye exposure (the most allergenic family of dyes).[16]

CLASSIFICATION OF TEXTILE DYES

More than 1,200 dye pigments are used in the textile industry,[17] making it difficult to trace possible sensitizing dyes. Dyes may be classified by their **chemical structure** including azo (subclasses: monoazo, diazo, and triazo), anthraquinone, azine, indigoide, nitro, quinoline and triarylmethane.

Dyes may also be grouped (**within their chemical class**), by their **application**, based on the procedure involved in applying dyes to the fabric, which gives useful information on the optimal fiber composition of the fabric for dyeing and establishes the general conditions (temperature, pH,) under which the fabric accepts the dye. Moreover, the application groups often describe the degree of fastness (quality of being fixed) of the dye.[18] For instance, disperse blue 106 is a disperse dye (application class) and an azo dye (chemical class).

Among chemical structures, **azo** dyes are the most relevant. They comprise around 40% of all the dyes used by the textile industry. Furthermore, they have a 20% cross-reactivity with para-phenylenediamene, an allergen in hair dyes, black henna tattoos, and inks.[19] They are the most common cause of allergic textile dye dermatitis.[11]

A description of the principal application classes follows:

• ***Disperse dyes*** are primarily used to color polyester, acetate fibers and nylon fibers (particularly garments and stockings).

These are the most common dye sensitizers, due to their partial water solubility, resulting in significant leaching out of fabrics in the normal wear, tear and wash life of the garment and ultimately absorption by the skin. Disperse blue 124 and disperse blue 106 are the most frequently positive dye sensitizers. They are related structurally and commonly used together, and thus may present as concomitant positive reactions on patch testing.[10]

In two studies published in 2000, 18%[20] and 40%[21] of the patients suspected of having a textile ACD had positive patch tests to textile dyes (with the most common allergens being disperse blue 124, disperse blue 106 and disperse blue 85). This finding led to the designation of disperse blue dyes as the Contact Allergen of the Year in 2000.[22]

• ***Basic dyes*** represent the second largest group of dye allergens. These have a high affinity for wool, silk and cotton (natural) fibers. And, they have reasonably good wet fastness (ability to stay fixed when exposed to water) for nylon, polyester and acrylics.

• ***Acidic dyes*** work on nylon, wool and silk, particularly well. Interestingly, they are also used to color foods as well.[11]

• ***Direct dyes*** are directly applied to fibers, have poor wet fastness, and thus usually require various "after" treatments (e.g.: copper, chrome, formaldehyde).

• ***Vat dyes*** are named as such because of original storage in wooden vats. Vat dyes are water insoluble, which requires they be reduced in a soluble form and then re-oxided once absorbed into the fiber. They are commonly used on cotton, flax and rayon fibers.[18]

Since vat dyes are the least allergenic dyes, blue jeans colored with a vat blue dye may be used by disperse dye-allergic individuals.

CLINICAL PRESENTATION OF TEXTILE DYE ALLERGY

The textbook presentation of dye dermatitis is in the distribution of contact with the inciting garment. This is generally a good rule of thumb with the areas of increased friction and sweating being more likely to be affected.[20]

When the responsible dye is in a shirt or dress, the neck, upper trunk and the axillary borders are typically involved, whereas the vault is spared. In trousers dermatitis, areas of increased friction are most likely affected, e.g: the anteromedial aspects of the thighs, buttocks and popliteal fossae tend to be affected.[11,23] Furthermore, a pearl to diagnosis is the clinical observation of spared areas, corresponding to skin protected by brassieres or undershirts. In addition, textile dye contact sensitivity may present as hand dermatitis in occupationally exposed individuals.[23]

All this being said, dye allergy may present as a chronic generalized pruritus skin dermatitis, a.k.a Dr. Kligman's invisible dermatosis[24] or as prurigo nodularis.

TESTING FOR TEXTILE DYES SENSITIVITY

Confirming a contact sensitivity to dye is an algorithmic process based on clinical index of suspicion.

First, there are more than a thousand textile dyes to choose from, thus those most encountered by the specific patient should be considered.

Second, one must consider the fact that a specific textile color is often the result of a compilation mixture of several dyes. For example, serisol black 1 1944, used to dye black velvet clothes, contains five dispersed dyes: blue 1, 106, 124, red 1 and yellow 3.[25]

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Last, textile-based chemicals, other than the dyes, could be the culprit allergen and should therefore be considered in the algorithm. A comprehensive evaluation for textile-based allergy should also include patch testing to dyes, textile fibers and resins, rubber additives, glues, cleansers and softeners. As with any diagnosis of ACD, clinical relevance should be assigned.

If there is a high index of suspicion for textile dyes, the dye allergens in petrolatum or aqueous solution may be obtained from chemotechnique, or a swatch extraction test may be performed on a suspect textile. The garment in question may be soaked in solvents such as 4-methoxy-4-methenyl-2-pentanol,[26] and the eluate used for testing along with the solvent as a control.

THE VALUE OF THIS PATIENT CASE

Our patient tested positive for disperse dyes 106 and 124. Notably, these were used in his blue-green mechanic's overall garments. The prurigo nodules corresponded to the areas where the overalls were in direct contact with the patient's skin. With discontinuation of the overalls and substitution with non-dyed 100% cotton overalls, this patient's dermatitis resolved.

This patient underscores the importance of appropriate allergen patch testing and post patch test education. Once the culprit allergen was identified, the patient was counseled on exposure risks and provided with alternative safe products. This is of the utmost importance, as the mainstay of treatment for ACD is **avoidance**. n

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For more information on the educational programs offered by the ACDS, see www.contactderm.org.

DISCLOSURE: *The authors have no conflict of interest with any subject matter discussed in this month's column.*

OUR PATIENT, WHO WAS A MECHANIC, PRESENTED WITH NUMEROUS PRURIGO NODULES AND SCARS ON HIS ARMS AND LEGS. THERE WERE DISTINCT AREAS OF SPARING IN THE LOCATION OF HIS UNDERGARMENTS. HE TESTED POSITIVE FOR DISPERSE DYES 106 AND 124 — WHICH WERE USED IN HIS BLUE-GREEN MECHANIC'S OVERALLS.

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