

BEAUTY DOES NOT HAVE TO HURT

Ocular surface disease can be exacerbated by chemicals hiding in plain sight in everyday products. This is the first of a three part series.

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The US Food and Drug Administration (FDA) requires that ocular prescription medications scientifically demonstrate a statistically significant improvement in the

signs and symptoms of disease. Without demonstrating efficacy and safety, new pharmaceuticals do not receive FDA approval. Prescription medications that we recommend for our patients with dry eye disease (DED) have proven safety and efficacy documented through rigorous clinical trial studies. Unfortunately, the cosmetics that our patients use in and around their eyes daily are not required to meet such high standards.

The Breast Cancer Fund reported that the average woman in the United States uses 12 cosmetic products daily, and the average man uses six.¹ More than 10,000 chemicals are used to create these products, and less than 20% of these ingredients have been proven to be safe. These chemicals, many of them synthetic and industrial chemicals, when absorbed into the body, can act as carcinogens, endocrine disruptors, neurotoxins, and reproductive toxins.

The FDA regulates makeup, products such as lipstick, blush, foundation, eyeliner, eye shadow, and mascara, as cosmetics under the Federal Food, Drug, and Cosmetic Act. In 1938, this statute was enacted after 100 patients died from using a sulfanilamide medication. In the manufacture of this medication, diethylene glycol, a cousin of poisonous antifreeze, had been used to dissolve it into liquid form.² The FDA defines cosmetics by their intended use: that is, "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body ... for cleansing, beautifying, promoting attractiveness, or altering the appearance."³

Cosmetics labeling laws available on the FDA's website note that "ingredients must be declared in descending order of predominance" and "ingredients present

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at a concentration not exceeding 1% may be listed in any order after the listing of the ingredients present at more than 1% in descending order of predominance.” “The Federal Food, Drug and Cosmetics Act (FFDCA) includes 112 pages of standards for food and drugs, but just a single page for cosmetics. The cosmetics title of the

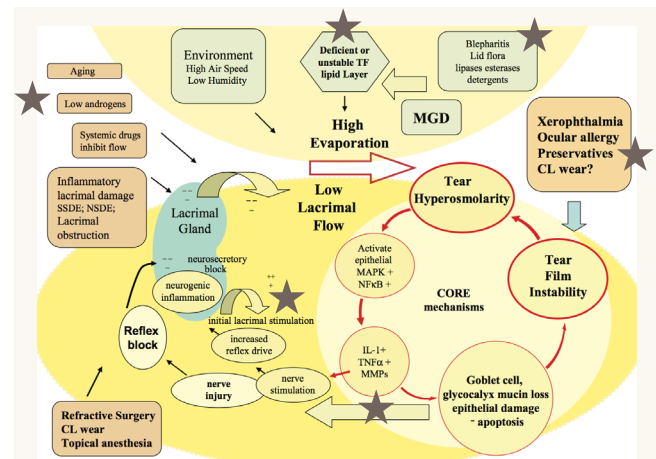


Figure 1. Diagram adapted from the TFOS Dry Eye Workshop 2007 report illustrates the problem of cosmetics ingredients and detergent loads for the DED patient. The stars have been added to highlight the multiple mechanisms by which cosmetics and detergents have the potential to contribute to the mechanisms of DED.

Q3 Do you know the effects of Retinols on the eyes?

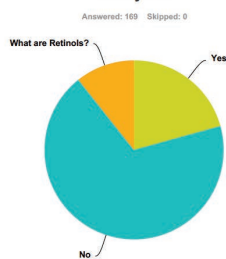


Figure 2. Online survey results: Most respondents are not aware of the potential effects of retinols on the eyes.

Q10 When choosing cosmetics, do you look for "hypoallergenic" in the name?

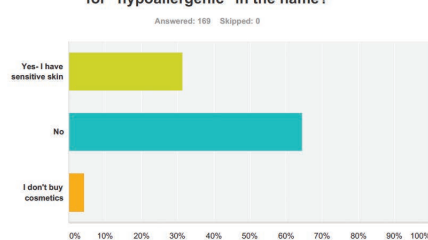


Figure 3. Online survey results: About a third of respondents said they buy products because they are labeled hypoallergenic.

FFDCA ... provides virtually no power to perform even the most rudimentary functions to ensure the safety of an estimated \$71 billion cosmetic industry." This according to the Campaign for Safe Cosmetics, a Project of Breast Cancer Fund. In 2015, Senators Dianne Feinstein (D-CA) and Susan Collins (R-ME) introduced legislation to update the regulations covering cosmetics and personal care products for the first time in 75 years.

In the United States, 11 chemicals are banned from use in cosmetics (see *Chemicals Banned from Use in Cosmetics in the United States*). This is a remarkably low number in comparison with the situations in the European Union (EU), Canada, and Japan. The EU Cosmetic Directive, enacted in 2003 and updated in 2013, bans 1,328 chemicals from cosmetics due to risks of cancer, genetic mutation, reproductive harm, or birth defects. The EU also requires premarket safety assessment and mandatory registration of cosmetics, neither of which are required in the United States.

Figure 1 illustrates the problem of cosmetics ingredients and detergent loads for the DED patient.

HIDING IN PLAIN SIGHT

Remember when you started reading food labels? Your eyes were opened to all of the additives present in processed foods. Similarly, reading cosmetics labels can be overwhelming at first. Once you learn the chemical vocabulary, however, you begin to understand the scope and extent of the problem.

Sodium Laureth Sulfates

A top selling, "dermatologist recommended" facial wash may not be ideal for use around the delicate and specialized skin of eyelids. Many facial washes and cleansers contain

sodium laureth sulfates that over-strip the delicate oils of the eyelids, contributing to the evaporative burden of the ocular surface. Mouse models of desiccating stress showed that the protein-to-lipid ratio of mature meibum suffered under the increased demands of desiccating stress in a controlled adverse environment.⁵ Imagine the desiccating stress of iatrogenically stripping your oil reservoir every day, sometimes twice a day, with facial cleansers. The synthetic skin conditioners of most facial cleansers make the skin feel moisturized, but the oils that nature intended are stripped away. Makeup removers fall into this category of concern for our patients as well. With so many available, it is important to ask patients, especially DED patients, what they use around their eyes.

Preservatives

Preservatives are important to prevent bacterial and fungal contamination in cosmetics and hygiene products. However, they also are problematic for the delicate ocular surface. Common preservatives used in cosmetics include formaldehyde-donating preservatives such as parabens and phenoxyethanol (more later).

Formalin

Formalin, a cousin of formaldehyde, is particularly toxic in cell culture.⁶ Formaldehyde is released from formaldehyde-donating preservatives and is a well-known allergen.⁷ However, you will not see formaldehyde listed in cosmetics. Formaldehyde-donating preservatives in cosmetics hide in plain sight under the cloak of organic-chemistry-nightmare names such as DMDM-hydantoin, quaternium-15, imidazolidinyl urea, diazolidinyl urea, and 2-bromo-2-nitropropane-1,3-diol.

Formaldehyde is a known ocular irritant at levels of

0.05 ppm and 0.5 ppm, producing a sensation of irritation in the eyes with burning, itching, redness, and tearing. An increased rate of blinking and eye closure generally protects the eye from damage at low levels.⁸ These protective mechanisms may be insufficient for the DED patient with compromised aqueous production and/or evaporative protection, allowing formaldehyde to contribute to ocular surface damage.

Parabens

The detrimental effects of estrogen and progesterone hormones on the meibomian glands have been well described.⁹ Parabens have a weak estrogenic effect and have the potential to inhibit the function of human meibomian gland cells. Methylparaben demonstrates significant toxicity similar to that of benzalkonium chloride (BAK) in human conjunctival and corneal cell cultures.¹⁰

Phenoxyethanol

What smells like a rose, in this case, is not a rose, it is phenoxyethanol. Phenoxyethanol is an alternative non-formaldehyde-donating preservative. With it, the amount of parabens needed in a product for adequate contamination control is reduced. The phrase “paraben-free” is used as a marketing tag, and phenoxyethanol is one of the main ways cosmetics companies get around using parabens to cater to the “natural” and “vegan” markets. A strong rose or perfume-like smell is prevalent among mascaras at the drug store, the department store, and the natural foods store. Although a seemingly rose-scented, non-formaldehyde-donating preservative may sound like a good idea, watch out for the thorns. According to Japan’s Standards for Cosmetics, phenoxyethanol is restricted to a level of 1% in cosmetics.¹¹

CHEMICALS BANNED FROM USE IN COSMETICS IN THE UNITED STATES

- Bithionol
- Chlorofluorocarbon propellants
- Chloroform
- Halogenated salicylanilides
- Hexachlorophene
- Mercury compounds
- Methylene chloride
- Prohibited cattle materials
- Sunscreens in cosmetics
- Vinyl chloride
- Zirconium-containing complexes

Other Potential Tear Film-Disrupting Ingredients

Alcohols speed the drying times of cosmetics, but they also dry out the native oils and moisture of the lids and ocular surface. Waxes and pine tar derivatives in eyeliners have the potential to physically obstruct the meibomian gland terminal orifices, thereby limiting meibum delivery to the lid margin lipid reservoirs and subsequent delivery onto the tear film. This effect can increase the inflammation-inducing evaporative load of patients with ocular surface disease (OSD), particularly when eyeliners are used along the eyelid margin covering the meibomian gland orifices in a practice known as “tight-lining” or “waterlining.” Although this should not be confused with waterboarding, we suspect this so-called beauty practice is torture to the meibomian glands and an unrealized hazard among many of our OSD patients. We see

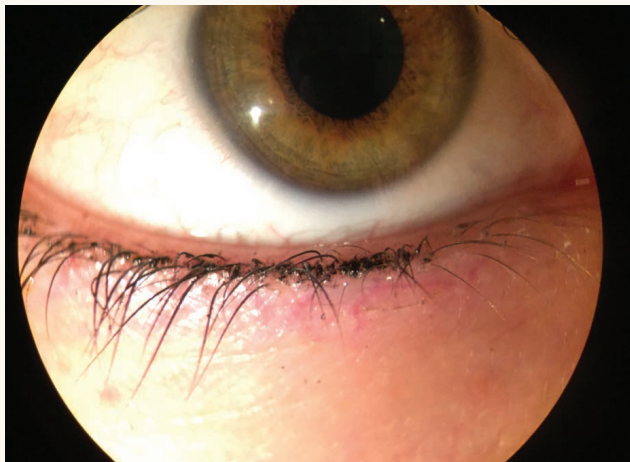


Figure 4. Significant buildup on the lash margin indicates makeup residue despite makeup removal with a commonly used makeup remover.

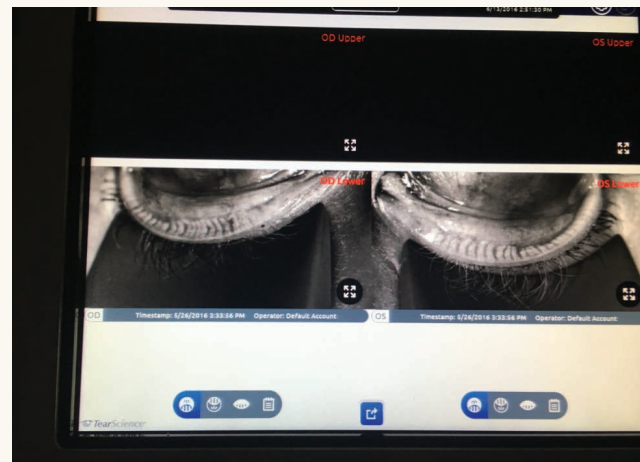


Figure 5. LipiView II images show meibomian gland truncation in both eyes of a 20-year-old-patient.



Figure 6. The patient reported using a waterproof eyeliner and mascara daily and applying her eyeliner to the “waterline.”

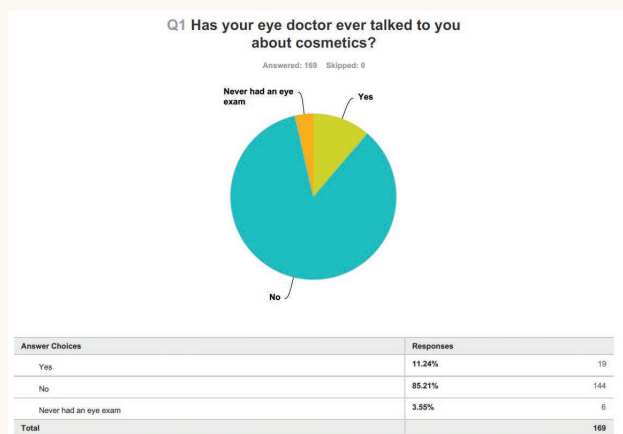


Figure 7. Online survey results: Almost 90% of respondents are not talking to their eye care providers about their cosmetic use.

cosmetics-associated iatrogenic meibomian gland blockage in our OSD patients routinely, as outlined in the case reports below.

Teaching patients to care for their eyelids like their grandmother’s best cast iron frying pan helps drive the point home. Eyelids are delicate, and they need gentle care. Tell patients to lightly soak (with warm compresses), gently scrub, avoid soaps and detergents, and gently condition (eg, with hyaluronic acid–containing moisturizers). Hyaluronic acid moisturizers are excellent humectants for the skin and lashes, but watch out for detrimental co-ingredients such as parabens (weakly estrogenic) and retinols (toxic to the meibocytes), particularly in so-called antiaging formulations. When lid hygiene and over-the-counter product details are optimized for the OSD patient, whether a woman or a man, the patient’s daily desiccating stress load is reduced.

ANTIAGING PRODUCTS AND OSD

Tretinoin (also known as Retin A; available from multiple manufacturers) and its retinoic, retinol, and retinyl cousins are wonderful antiaging products for the face, but their application anywhere near the eyes should be avoided. Skin products are thought to migrate up to 1 cm, so when tretinoin-like products are applied at bedtime to the face they become potential nightly offenders to the health of the meibomian glands.

The keratinizing, apoptotic, interleukin 1 beta–, and matrix metalloproteinase–inducing effects of retinoic acid have been described in human meibomian gland cell culture.¹² This potential for harm to the meibomian glands is a public health issue that eye care providers must address, as, according to an online survey we conducted, most consumers do not understand the potential of retinols to harm the eyes (Figure 2). We must educate

patients to avoid products that claim antiaging effects, as the antiaging ingredient is likely to be one of these substances toxic to the meibomian glands. The best antiaging product is a paraben-free sunscreen.

Botox and “Botox in a Jar”

The neuromuscular blocking agent onabotulinum-toxinA (Botox; Allergan), injected into the crow’s feet area, has a wrinkle-relaxing effect. However, it is also known to correlate with DED.¹³

Acetyl-hexapeptide 3, a peptide that is a fragment of SNAP-25, a substrate of botulinum toxin, is a common antiaging additive to luxury products that is often enthusiastically promoted at the cosmetics counter as “Botox in a Jar.” The problem is that this neurotoxic chemical may weaken the orbicularis muscle, creating the promised wrinkle-smoothing effect but also thereby potentially working counter to our blink exercise counseling efforts. These exercises are important to promote tear wetting and spreading, lid-to-lid contact, and mechanical expression of meibum into the lipid reservoir and precorneal tear film.

Hypoallergenic: Just a Buzzword

As noted previously, the FDA does not require all ingredients to be listed on a product if they are present at a level of 1% or less. This is of particular relevance for patients allergic to certain ingredients in cosmetics, as a potential allergen may not be listed.

We conducted a recent online survey of 169 cosmetic users that uncovered some interesting trends. When looking to purchase cosmetics, about one in three survey respondents said they buy products because they are labeled hypoallergenic (Figure 3). The designation hypoallergenic is not determined by any federal standards or

definitions; it is simply a term companies use to make their products more appealing to these sensitive consumers. Dermatologists agree that the label hypoallergenic has very little value.

Other words used to attract sensitive consumers include herbal, natural, vegan, and organic. These terms have no FDA backing and are simply used as marketing tactics to attract consumers. Consumers and the patients we serve need to understand that there is no guarantee that a cosmetic will not cause an allergic reaction.

REAL-WORLD SCENARIOS

Patient No. 1. (Dr. Periman)

I began to realize the scope of the cosmetics and OSD problem years ago while taking care of a delightful and beautiful 73-year-old woman with severe DED and stage 3+ meibomian gland loss who was referred for severe DED nonresponsive to treatment. She had received appropriate therapies for years and was still miserable from her DED. Her makeup was full and expertly done, and she even had waterproof eyeliner on the lid margins in addition to tattoo eyeliner under the lashes done years before.

At the slit lamp, she had significant debris in the tear film that looked like eye shadow had dropped in. She had pigmented micro-shards imbedded under her inferior palpebral conjunctiva that also looked like eyeshadow pigments. Her history included cosmetic surgical procedures, 10-plus years of injectable neurotoxins (botulinum toxin) to the forehead and crow's feet, as well as daily application of full makeup (including applying eyeliner to the eyelid margin) and nightly removal with makeup removers. Notably, she reported that her DED flare-ups occurred 3 to 4 times a year, within 1 to 2 weeks after her

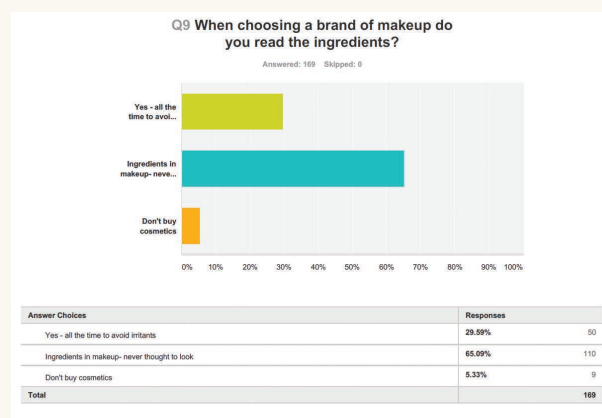


Figure 8. Online survey results: About 70% of respondents said they do not look at ingredients when deciding what cosmetics products to purchase.

HELPFUL WEBSITES



- Think Dirty
www.thinkdirtyapp.com
- EWG's Skin Deep Cosmetics Database
www.ewg.org/skindeep
- GoodGuide
www.goodguide.com
- FDA MedWatch Online Voluntary Reporting Form
www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home

last crow's feet injection of neurotoxin. She was surprised to realize this connection upon history questioning.

Although correlations between DED and eyelid tattoos, lid and facial cosmetic surgeries, and botulinum toxin are known,¹³ her disease was more severe than other patients I had seen with similar risk factors. Upon request, at follow-up she brought her full arsenal of beauty products. Particularly impressive was her luxury brand, expensive, department store eye makeup remover. This incredibly effective eye makeup remover probably also removed more than makeup. It also likely removed the healthy oils of the lipid reservoir, creating a nightly drying and stripping effect.

The actual percentage of BAK in the product was not mentioned on the package or online, but BAK was listed after benzyl alcohol (drying) and quaternium-15 (formaldehyde donor preservative), implying that its level was above 1%. This is significantly more BAK exposure than anyone in eye care would dream of prescribing for use around the eyes. BAK is known to damage goblet cells, thereby decreasing mucin production, compromising tear-film stability, and furthering desiccating stress—a core mechanism of DED as outlined in the 2007 report of the TFOS Dry Eye WorkShop.¹⁴ Her waterproof eyeliners had waxes, pine tar extracts, and alcohols that were likely contributing to terminal ductule obstruction and irritation of the already severely diseased meibomian glands.

Patient No. 2. (Dr. O'Dell)

I transilluminate every patient at the slit lamp, and when it is indicated, I use LipiView II (TearScience) to produce meibography images. Based on my observation, there are a surprising number of patients with meibomian gland truncation, atrophy, and tortuosity. One patient stands out, a 20-year-old white woman, an emmetrope, who came to our office complaining of fluctuating vision.

“Our online survey showed that 89% (150/169) of respondents are not talking to their eye care providers about their cosmetic use.

Significant findings during examination included make-up residue on the lashes, although, when questioned, she said she did not apply fresh makeup on the day of her exam and had removed it the night before (Figure 4). She also had significant meibomian gland changes (Figure 5), with almost 50% truncation of the glands in both eyes. Regarding her daily cosmetic use, the patient reported using a waterproof eyeliner and mascara daily and applying her eyeliner to the “waterline” (Figure 6), thereby covering the meibomian gland orifices with waxes and other offending chemicals. Her removal habits were equally concerning, as her makeup remover contained chemicals found in paint, acetone derivatives, and alcohol, all of which had the potential to strip her oil reservoir and potentially harm her meibomian glands.

The patient’s comfort improved significantly after she was educated as to the ingredients to avoid in her cosmetics, the proper placement of her cosmetics to avoid the waterline, and recommendations for less OSD-offending makeup removers.

CONCLUSIONS

Our online survey showed that 89% (150/169) of respondents are not talking to their eye care providers about their cosmetic use (Figure 7). In addition 70% (119/169) said they do not look at ingredients when deciding what products to purchase (Figure 8). With so many chemicals with the potential to harm the ocular surface hiding in the cosmetics our patients are using daily, we need to start a conversation with our patients. We must educate patients that the delicate eyelids and ocular surface need thoughtful and special care. What is good for the face and skin may be detrimental to the lacrimal functional unit.

The conversation with patients should include information about dry eye and how the cosmetics, soaps, facial cleansers, and make-up removers they use daily can affect their eye health. A few websites that can help are listed in the sidebar, Helpful Websites. Another resource that will be available in 2017, is a report from the TFOS Dry Eye WorkShop II, which will update the seminal report from the first TFOS Dry Eye WorkShop in 2007, sponsored by

the Tear Film & Ocular Surface Society (www.tearfilm.org). A patient version, to be available in multiple languages, will also be published.

If a patient has adverse reaction to eye cosmetics, the FDA encourages us to report it much like we would report adverse events to medications we prescribe. A link to the MedWatch Online Voluntary Reporting Form is shown in an accompanying box.

Beauty does not have to hurt. The more we understand the dangers lurking in plain sight, and the more we can guide our deserving patients in their daily use of products, the more effective our OSD-fighting strategies and therapeutics will become. ■

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