DES Action® VOICE

Inside

A Focus On Diethylstilbestrol

SUMMER 2016 #149

Transgenderism and DES: Is There a Link?

After researchers first discovered the connection between prenatal DES exposure and clear cell adenocarcinoma, scientists went on to study all the other potential effects and health problems that those exposed to DES in the womb might experience. But as that list grew, one area was almost entirely ignored—the potential impact of the drug on sexual orientation and on gender identity. Recently, that has started to change.

"My gender dysphoria erupted in January 2013," explains Gina Eilers, a 59-year-old retired Lutheran minister who blogs about her male-to-female transition and about DES at eilerspizza.wordpress.com. As she began transitioning, she wanted to understand why she had always felt she was a woman despite being born with male genitalia. That spring, Gina's wife found a link about DES. "I got angry," Eilers says. "I said, you mean somebody did this to me? I sat back and five minutes later, I just started crying. There was finally the possibility that there was a reason for being a freak."

Eilers recognizes that many people do not think of transgenderism as a "problem" with a clear cause, but she considers her gender dysphoria—the feeling that you are a different gender than you were assigned at birth—a birth defect. She never developed an Adam's apple in puberty, did not enter puberty until halfway through her junior year of high school, and did not experience typical body development in several ways.

Gina's mother was pregnant with her in 1956-7, among the peak years when DES was prescribed, and that pregnancy had been preceded by two miscarriages. Although her mother died several decades ago without leaving records to confirm exposure, Gina strongly suspects her mother would have taken DES, and the reading Gina has done has convinced her that DES is almost surely at the heart of her transgender experience.

"Males are supposed to have way more testosterone than estrogen," she says. "If you have a male fetus with a mother taking a drug of estrogen, doesn't it just make sense that the male fetus will be affected?"

What makes sense intuitively still needs research to back it up, however. The problem is that very, very little research exists, and what does exist is very old or of very poor quality. Researchers, even

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Understanding Flap Surgery Options for Post-Mastectomy Reconstruction

An article in the winter issue of the VOICE discussed the risks associated with silicone and saline breast reconstruction implants, but implants aren't the only option for post-mastectomy reconstruction. Several "flap" options exist that use a woman's own tissue (autologous) from the belly, back, thigh or buttocks to reconstruct breasts. (Some flap surgeries can be combined with implants.)

Flap surgeries can be done at the time of a mastectomy or delayed, but they can delay chemotherapy or radiation treatment. The various flap options can be overwhelming, but basic types are below. A comparison chart and other details about flap types is at breastcancer.org.

Flap types are identified by acronyms based on the names of the main artery and blood vessels in the part of the body they come from:

TRAM—"transverse rectus abdomens"—muscle, fat, skin and blood artery tissues from the area between the waist and pubic bone, including the "six-pack"

DIEP—"deep inferior epigastric perforator artery"—same area as TRAM without the muscle

SIEA—"superficial inferior epigastric artery"—same area as TRAM and DIEP with different blood vessels and no muscle

GAP—"gluteal artery perforator"—blood vessels in the

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JOIN THE CONVERSATION

New Member Benefits!

Part of our upgrade to the DES Action USA website includes a new members-only area. As a member, you'll be able to log in to the Members Area for access to:

- **Rate Your Doc**—we've always offered lists of doctors that were recommended by other DES-exposed members. Now you can share your knowledge, and maybe spare some fellow members some pain, about the doctors in your area. Rate your doctor by entering his or her name, location and specialty, then add your comments: Is he or she knowledgeable about DES? Open to discussing options or fears? Tell your fellow members.
- **VOICE Newsletter**—current and historical. The VOICE is the most popular member benefit of DES Action. Now access all 36 years of newsletters and search for any topics or articles you need. The VOICE documents the history, the science and the personal stories of DES and all of us who were exposed.
- **Attorney List**—If you're interested in getting involved in possible future DES-related litigation, we offer a list of knowledgeable attorneys DES Action members have shared with us who might be able to help.
- **Exclusive Content**—an expanding collection of articles and videos accessible only to current DES members.

And more! Update your mailing address, pay your membership dues or make a donation online.

DES Action USA on Facebook

Like DES Action USA on Facebook and follow us on Twitter to stay up to date on medical and environmental health news that affects you, your loved ones and the planet. Share your thoughts with an engaged and active community. There's a ton of information swirling online 24/7 that affects the DES population—don't let it pass you by!

Online Support Group for DES Daughters

Here is a safe place for discussing very personal issues that arise for DES Daughters. We live in the farthest reaches of the country but have developed a sense of community together, via our email listserv.

What we talk about is private—just between us—so we can feel free to raise questions on topics we aren't comfortable bringing up with others. What is amazing is the depth of knowledge in the responses.

It's a terrific resource for information and support from DES Daughters who wrestle with the effects of menopause, family relationships and medical diagnosis issues specific to DES exposure. To join the support group, send an email to: DESactionDaughters-subscribe@yahoogroups.com.

How to Log In

To log into the members area, go to http://members.desaction.org and click on Members in the navigation bar. Enter the email address we have on file and the default password: desUSA2015. Once you are logged in, you can go to Your Account and change your password and update other information.

If you have any problems, email us at members@desaction.org or call us at 800-337-9288.

Find us on Facebook

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MISSION STATEMENT

The mission of DES Action USA is to identify, educate, empower and advocate for DES-exposed individuals.

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New Drug for Uterine Fibroids May Soon Be Available

DES Daughters have an increased risk for uterine fibroids, but there's still a lot we don't know about health risks for DES Granddaughters. Do they also have an increased risk of fibroids? Until more third generation research is done, that will remain an open question. Even without an increased risk, however, fibroids are very common—up to 80% of women experience these benign but painful tumors, and they are the leading cause of hysterectomies in the U.S.

They form from muscle cells and other tissues growing within or near the wall of the uterus and can cause abnormal bleeding, pelvic pain and pelvic pressure. For women still menstruating, fibroids can cause irregular or long and heavy menstrual cycles, infertility and recurrent miscarriages.

Now a new drug that can treat fibroids is getting closer to FDA approval—but it works by mimicking the hormone progesterone. Anyone with knowledge or experience of DES's effects may understandably hesitate to use a drug that works using a hormone-related mechanism, even for a painful condition like fibroids. We have therefore been following the clinical trials for the drug, called ulipristal acetate, very closely. It's an oral treatment that hasn't caused serious side effects in tests so far, but studies are continuing before it goes up for FDA approval, expected in 2017.

The clinical trials involve women ages 18 to 50, since fibroids tend to shrink or decrease during menopause for many women because of their drop in hormone levels. The drug application in 2017 would therefore seek approval for treating fibroids in women ages 18-50. If more research shows the drug to be safe and effective, then DES Granddaughters might benefit from it.

It's not clear if ulipristal acetate would be available for DES Daughters who feel comfortable trying it. It's possible some doctors would prescribe it off-label, but they may also wait until further studies reveal safety in older women. For DES Daughters and other women who continue to experience fibroids after menopause, a hysterectomy would remain the most effective treatment.

Ulipristal acetate is already prescribed in Europe under the name Esmya and in Canada under the name Fibristal. Currently, more than 300,000 women in 50 countries have been treated for fibroids with this new drug. Recent results from a U.S. clinical trial have moved it one step closer to FDA approval.

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In May, the pharmaceutical companies Allergen and Gedeon Richter announced the preliminary results of a phase III study of the ulipristal acetate called Venus I. The findings showed that approximately 60% of the women taking the drug experience a stop in uterine bleeding while less than 2% of those taking the placebo did. The other trial, Venus II, should also have results early in 2017.

Venus I included 157 women with fibroids: 101 women were randomly assigned to take either 5mg or 10mg of the drug while the other 56 women took a placebo. The researchers focused primarily on how many women no longer experienced uterine bleeding and how long it took for their fibroid-related bleeding to stop. Among the women who took 5mg pills, 47% no longer had bleeding while on treatment, and 58% of the women taking 10mg pills stopped having bleeding. Only 2% of the women taking placebo experienced an absence of bleeding.

In addition, 58% of patients taking 10mg and 43% of women taking 5mg had no bleeding from the 11th day of treatment until the end of treatment, showing that the drug works within two weeks. Bleeding did not stop in any of the women taking placebo in that time. The researchers also assessed women's quality of life through questionnaires and found that the women taking ulipristal acetate reported a quality of life score that improved twice as much as women taking placebo.

None of the women stopped taking the drug because of side effects, and no serious side effects occurred. About a dozen women experienced high blood pressure, an increase in the enzyme creatine phosphokinase (CPK) in the blood,

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Understanding DES Lawsuits: An interview with attorney Michael London

Michael London is a New York City-based attorney who has represented hundreds of DES Daughters over his career. Presently London is representing three women with CCA (clear cell adenocarcinoma), two of whom have already died. All of the women were more than 50 years old when diagnosed. DES cases are complex. "Several pieces have to come together in order to have a viable case, and some of those pieces are based on luck," notes London. Since breast cancer was linked to DES exposure in a medical research report in 2006, we asked London: As the numbers of DES daughters and sons with breast cancer rise, why aren't there more lawsuits?

Market Share Precedent

First, the plaintiff has to live in a state that has established a "market share precedent." This addresses the problem that those damaged by DES (mothers, daughters, sons or grandchildren) probably can't prove which pharmaceutical company produced the DES that the pregnant mother was given all these years later. If the case is won in a market share precedent state, all companies that produced DES have to pay a pro-rata piece of the award based on their market share in the 1950s. (The courts have already determined what the market shares were and set the percentages.)

Only about 50% of US states have this precedent, and if you live in a state without it, you will either have to fight to establish it, which is unlikely at this point, or be able to prove which manufacturer made the DES that you or your mother took.

Identify DES as the Primary Cause

"The next challenge is to prove that DES was the only or the primary cause for the cancer," London says. "DES has been positively linked to breast cancer, but it is still difficult as there are so many environmental and genetic possible causes for breast cancer."

In the well-reported Boston sisters case settled in 2013, for example, four out of five sisters were exposed to DES, and all four had breast cancer. The fifth was cancer-free. "That's a rare occurrence and is what made the case so strong," London said.

The CCA cases that London is working on now would seem to be easy to prove—various types of cancers affect the vagina and cervix, but only CCA is associated with prenatal DES exposure. London calls CCA a "signature" marker of DES exposure. However, cases drag on for years.

"Pharmaceutical companies will use many strategies to divert responsibility," London said. "A pharmaceutical company can challenge the science that links DES to CCA, or they can assert that the cancer was misdiagnosed as CCA and is actually another type of cancer, and so on."

Statute of Limitations

A statute of limitations requires plaintiffs to file a claim for damages before a certain period of time elapses. If you trip and fall on a broken sidewalk, for instance, you can't wait 25 years to sue. The statute changes from state to state and is not long. For example, the statute of limitations for New York is three years, for New Jersey two years and for Florida, four years. The clock starts when you discover your injury or diagnosis. If you found you have breast cancer now, you would have to file with the courts within the time period allowed by your state.

The clock starts when you discover your injury or diagnosis. If you found you have breast cancer now, you would have to file with the courts within the time period allowed by your state.

"Before 2006 there wasn't a clear link between DES and breast cancer," London says. "But that year the first research article was published that established the connection. Women who had breast cancer before that time couldn't know (or prove) that the DES injured them, so their statute of limitations clock started in 2006," he said.

Finding a Lawyer

Next you need to find a lawyer willing to take your case. These cases are typically taken on a "contingency" basis by attorneys, which means they and their staff work for free and pay court filing fees in order to earn a rate negotiated with the plaintiff beforehand, typically from 33% to

40% of the award. If the case is lost, the attorneys collect nothing.

Since the defendants are large pharmaceutical companies, few law firms have the resources to commit to a long, expensive fight without a guaranteed payday. Therefore, most attorneys can only afford to take on cases that are highly likely to win. Their ability to take on a case increases greatly if they can gather multiple, similar cases in one state and have the court review them simultaneously, called "aggregating" cases. DES Action keeps a list of attorneys who have told us they are interested in DES cases. Please visit our Attorney List online to start a search for a lawyer. London has worked with DES daughters, sons and mothers for more than 20 years. In 2008, DES Action marked its 30th anniversary by naming a few people, including London, a "Hero of DES Action." He and his firm continue to be supporters of DES Action and champions of the DES-exposed today. DES VOICE

Transgenderism

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those very familiar with the effects of DES exposure, are not typically willing to discuss the topic on the record because the evidence is so scant, so shaky and so inconclusive. Simply not enough evidence exists to definitively connect any dots between DES and transgenderism.

But enough evidence does exist to raise the question, and some people are. The most vocal proponent of DES's link to transgenderism is Dana Beyer, MD, a transgender woman who was exposed to DES in the womb (and was therefore born a DES son). Beyer ran for the Maryland state senate in 2014 and is an active transgender advocate. She is also the medical advisor and web manager of the DES Sons International Network and has conducted research with several other scientists that suggests a link. The study's biggest flaw, however, is something other researchers cannot overlook: The paper does not rely on medical records because they are difficult to get or don't exist.

Anecdotal reports have suggested that a higher than average proportion of DES sons experience gender dysphoria or genital abnormalities, but no formal estimate of transgender women has been determined from among the 2.5 million boys exposed to DES during gestation between 1948 and 1971.

Another obstacle to learning whether a link exists between transgender women and DES is that study findings must be replicated several times by different researchers and published in peer-reviewed medical journals before the results start to be taken seriously in the research community. Only a few studies exist that even tangentially address the topic.

The largest of these was presented in 2005 by Scott Kerlin, PhD, a research associate of Beyer's. Kerlin conducted an online survey of 500 DES Sons during a 5-year time period. Of these, 60% had confirmed DES exposure and the others had strong evidence to suggest exposure. Approximately one in five of the Sons reported that they were male-to-female transgender individuals and/or had a gender identity disorder. (Note: Not all individuals who are transgender are classified as having a disorder. The combining of gender dysphoria and "gender identity disorders" is controversial.)

Before that study, researchers in 1973 studied a group of 6-year-old boys and a group of 16-year-old boys whose mothers had diabetes and took a combination of estrogen and progesterone during pregnancy as treatment, substances that might have similar endocrine system effects as DES. When the researchers compared 20 exposed teenage boys to 20 unexposed teen boys, they found the exposed boys scored about 16% lower than the unexposed boys on scales of masculinity. They also were less assertive and less athletically inclined. Major differences did not show up in comparisons of the 6-year-olds.

Two weaknesses of this research—aside from not involving DES—are that some effects might be explained by other aspects of the mothers' diabetes (only a few of the comparison boys had mothers with diabetes), and the assessments relied on beliefs about gender from the 1960s and 1970s that have changed in academia today. Scientists have learned that many behaviors thought of as "feminine" or "masculine" are actually socialized instead of genetic.

Another study in 1985 investigated sexual orientation among 30 DES Daughters, ages 17 to 30. Although 75% of them were definitely heterosexual, more of the women overall were bisexual, homosexual or leaning toward bisexuality when compared to 30 women of similar demographics at the same clinic. A subsample of 12 Daughters also showed more leanings toward bisexuality or homosexuality when compared to their unexposed sisters.

Leaning toward bisexuality or lesbianism in Daughters and experiencing gender dysphoria as a Son are very different, but some believe a mechanism of DES may partly contribute to both (since most Daughters are heterosexual and most Sons remain men). Right now, the science isn't strong enough to support that belief, but the only way to find out is to conduct more research—though it's not clear if that research will ever be done.

Transgender DES-exposed individuals can find support and resources in the Facebook group DES: Society of Sons and Daughters (So Sad). DES VOICE

Q&A with a DES Action Member: How Does DES Action Help You?

Individuals join DES Action for different reasons, and sometimes a member whose membership has lapsed returns to the organization because of what it offers. We asked Karen Calechman about her journey with DES.

Karen Calechman

Q: Can you describe the experience of first discovering you had been exposed to DES?

My mother called me during my midterm exams at college when I was 19 years old and was hysterically crying. She told me she had taken something terrible when pregnant because she was bleeding and they thought she might miscarry. They told her this would save her baby. Her OB-GYN in Connecticut had been going through his records and just discovered it all these years later after reading an article about DES.

My mom was in France while my dad was in the Army, and it was Army doctors who gave DES to her in the winter/spring of 1956. I was born prematurely at just over 4.5 lbs. in August that year, and I was in an incubator for about a week.

My reaction to the call was panic, of course. I couldn't come home to be checked out as I was in the middle of midterms. I calmed myself enough to try to study. Shortly after that, I went back home for a weekend or break, and was checked out immediately. I was found to be a "classic case" of DES exposure.

My parents told me about DES Action when I was in my early 20s. They were active in a Connecticut chapter with Rosa DeLauro, and I joined upon their suggestion.

Q: In what ways has DES Action helped you?

The biggest help has been providing researched, published information. Emotionally, I find the listserv emails to be upsetting and sometimes informative, but not always definitive. I want facts and information. Sometimes I get too upset in reading about others' medical problems. What they are going through makes me incensed and angry, but it is not always good emotionally to dwell on it. Sometimes the information in emails is erroneous, so I really prefer to have the DES Action newsletters. They have been vetted and checked for accuracy, with research backing the articles up.

Sometimes the information in emails is erroneous, so I really prefer to have the DES Action newsletters. They have been vetted and checked for accuracy, with research backing the articles up.

Q: What would you recommend to improve DES Action?

I'd like to see DES personal stories published.

Q: At one point your membership had lapsed for a short time. Can you discuss that?

I was either in denial that there would be any medical problems in my future, or I got too upset by reading the listserv emails. I may leave the listserve as the emails tend to be long, overwhelming and upsetting, sometimes with erroneous information, or someone is just thanking someone else. I don't have time to sift through them and read them all.

Q: What is your hope for the future based on your experience as a DES Daughter?

I want to see more public awareness, research, information on the third generation, public advocacy, policy changes and FDA oversight. My hope is that every doctor whose patients include a DES Daughter, Mother or Son takes their exposure seriously and looks over their medical conditions with a fine-tooth comb, without calling it a "dead issue" or ignoring their patients' concerns. Personally, I hope that I don't suffer from any more DES-related medical problems and live a long healthy life. But, how will we know what we are up against unless research continues and the word gets out?

Post-Mastectomy Options

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lower butt cheeks, taken with skin and fat but no muscle

PAP—"profunda artery perforator"—blood vessels from the back, upper thigh, taken with skin and fat but no muscle

TUG—"transverse upper gracilis"—the muscle in the upper, inner thigh, which becomes unusable after this surgery, taken with skin, fat and blood vessels

Latissimus dorsi—a broad, flat muscle from the upper back, taken with skin, fat and blood vessels

The choice of flap depends on personal factors of each woman, such as whether she wants to become pregnant later and how much extra fat and muscle she has in different areas. Women can become pregnant after a GAP, PAP, TUG or latissimus dorsi flap surgery but not after TRAM, DIEP or SIEA surgeries. Women without enough extra fat and skin in the abdomen should avoid TRAM, DIEP and SIEA surgeries, but women with extra fat in their thighs may consider a PAP or TUG surgery.

Wherever the tissue comes from, that area will likely have pain or discomfort for several weeks after the surgery, and there's a small risk the discomfort could continue indefinitely. Sitting may be uncomfortable following a GAP flap surgery, for example, and activities using the back or shoulders may be more painful soon after a latissimus dorsi flap surgery.

Another consideration is whether a plastic surgeon has the necessary skills for a specific type of flap surgery. PAP, TUG and GAP flaps are all relatively new and require a surgeon with experience and skills in microsurgery techniques.

Risk of complications during each surgery increases along with the time the surgery takes, as does the amount of anesthesia needed. The PAP (3-5 hours), latissimus dorsi (3-6 hours) and TRAM (3-8 hours) flaps take the least time. The DIEP, SIEA and TUG flaps take 5-8 hours, and GAP flaps require 9-12 hours.

One post-surgical complication that could occur is an infection, a possibility with any type of surgery, typically treated with rest and antibiotics. Any surgery can also cause fluid production around the wound, typically drained with tubes attached to vacuum bottles. Fluid that collects under the wound (a seroma) needs to be manually drained by a doctor or nurse.

Finally, it's always possible for a flap surgery to fail if the tissue that's moved to the breast dies, a less likely risk if it remains connected to its original blood supply, called a pedicled flap. Less than 1% of pedicled back flaps fail and fewer than 1 in 1,000 pedicled TRAM flaps fail. "Free" TRAM and DIEP flaps, though, get connected to a new blood supply, and about 10% of them develop a blood supply problem within two days after surgery that requires immediate surgery. An estimated 3 to 5 of 100 flaps completely fail, requiring surgery to remove the flap and at least 6 to 12 months before attempting another reconstruction. DES VOICE

Uterine Fibroids

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hot flushes or acne, though it's not clear if these are related to taking ulipristal acetate or not. (If fibroids are not causing bleeding or other symptoms, women likely do not need to treat them.)

The drug appears to work by plugging up the receptors for progesterone in the endometrium (the uterine lining), the pituitary gland and the fibroids themselves. Rather than those receptors receiving progesterone, which seems to influence fibroids' growth, ulipristal acetate takes its place instead. It suppresses the bleeding from the endometrium, slows down or stops the formation of new fibroid cells, and causes existing fibroid cells to die.

Ulipristal acetate has already been approved by the FDA as emergency contraception in 2010. (Note: DES was briefly used as emergency contraception in the early 1970s as well.) No studies have been done on pregnant women, and it's highly likely that pregnant women or those trying to conceive would be advised against taking the drug. For now, it's a waiting game to see if the FDA will approve it.

The only medication currently available to treat fibroids is leuprolide acetate, an injection that reduces how much estrogen the body produces. But in doing so, it can induce the symptoms of a temporary menopause, so it's not recommended to take for longer than three months, often leading up to a surgery.

Hysterectomy is the most common treatment for fibroids: remove the uterus, and it's impossible for uterine tumors of any kind to grow or bleed. But a hysterectomy — or even a myomectomy that removes only the tumors — is major surgery requiring up to six weeks' recovery time. It involves all the risks of surgery and can throw pre- or perimenopausal women into menopause. Getting rid of fibroids is the reason for about one third of hysterectomies, approximately 200,000 a year. Hysterectomy will remain an effective treatment option, but for those who still want to have children, such as DES Granddaughters, that surgery is not a viable option. Perhaps ulipristal acetate will be, if used short-term, but that's not known right now. DES VOICE

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What You Need to Know About Oxybenzone and Sunscreen

Oxybenzone has been widely vilified as mimicking progesterone in women's bodies and as a possible cause of sperm function disruption in men. EWG (Environmental Working Group) puts any sunscreen with oxybenzone in it on their "Worst Sunscreens" list. But does the science support these fears?

Sunscreens filter out the ultraviolet rays from the sun that cause burning (UVB) and skin cancer (UVA). They use either mineral filters, such as zinc oxide or titanium dioxide, or chemical filters, such as oxybenzone, found in more than half of sunscreens. Other chemical filters include avobenzone, octisalate, octocrylene, homosalate and octinoxate.

One study has suggested the possibility of a link between oxybenzone and endometriosis, but no other studies have published similar findings. Some studies in rats suggest oxybenzone is a hormone disruptor, but the rats received excessively high amounts of the chemical orally, and the chemical's effects were one-millionth of estrogen's effects. In the only human study finding a possible link with very weak hormone-related effects, participants applied six times the recommended dosage to avoid burning. For humans to have the same effects the rats did, they would have to cover their entire body in one ounce of sunscreen once a day for 69 years.

The Scientific Committee on Consumer Products of the European Commission stated in 2008 that no known health risks result from using products with 1% to 6% of oxybenzone, the range in U.S. sunscreens. Australia, Canada, Japan and the U.S. have also found no risks except possible allergic reactions. Further, no studies in the past 40 years of oxybenzone use have shown any toxic effects in humans.

Some dermatologists recommend that pregnant and nursing women and children under age 2 avoid products with oxybenzone to be extra cautious, and some may just feel more comfortable avoiding oxybenzone regardless. In that case, choose sunscreens with zinc or titanium.

For more information on safe sunscreens, see MedShadow's article "Sunscreens 2016: 3 Do's and 3 Don'ts." DES VOICE

