Medical News & Perspectives

Threats to Evidence-Based Care With Teratogenic Medications in States With Abortion Restrictions

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When the US Supreme Court overturned Roe v. Wade this year, treating patients with teratogenic drugs—which can cause congenital malformations—suddenly became more complicated.

Before the court’s decision in Dobbs v. Jackson Women’s Health Organization in late June, patients who unintentionally became pregnant while taking a teratogenic drug usually could choose to have an abortion. As of October 7, though, 13 states had banned all abortions with few exceptions; abortion bans in 10 other states had been blocked while the courts decided whether new or existing bans could take effect.

Teratogenic drugs are widely prescribed—frequently to patients who could become pregnant—for a variety of conditions. They include isotretinoin (first sold as Accutane) for severe recalcitrant nodular acne; valproate for seizures, bipolar disorder, and migraines; and methotrexate for rheumatoid arthritis.

Even thalidomide, notorious for causing a range of congenital abnormalities when used by pregnant individuals for nausea in the 1950s and 1960s, is now on the World Health Organization’s list of essential medications for patients newly diagnosed with multiple myeloma. The US Food and Drug Administration (FDA) also approved the drug in 1998 for treating skin lesions in people with Hansen disease, or leprosy.

Both thalidomide and isotretinoin, which is associated with a 20% to 35% risk for congenital abnormalities among exposed fetuses, have FDA-mandated risk evaluation and mitigation strategy (REMS) programs to prevent pregnancy. The 10 active REMS programs for teratogenic medications emphasize the importance of effective birth control use by patients who could become pregnant while taking the drugs.

However, “any form of birth control can fail,” notes iPledge, the isotretinoin REMS program, which recommends doubling up on contraceptive methods to reduce the chance of pregnancy while using the drug. More than 1 in 16 US pregnancies from 2006 to 2017 were exposed to at least 1 definitely or potentially teratogenic drug, according to a recent study of approximately 3.5 million pregnancies. The authors identified 141 drugs with definite and 65 drugs with potential teratogenic effects.

An Ethical Dilemma

From a physician’s perspective, “the elimination of the availability of an abortion has created an ethical dilemma,” Jane Grant-Kels, MD, a coauthor of the commentary and a past president of the American Academy of Dermatology (AAD), explained in an interview. “Even with the iPledge program, people get pregnant. People get sloppy with birth control.”

A study published in JAMA Dermatology found that 6740 pregnancies among patients taking isotretinoin were reported to the FDA from 1997 to 2017. The reports peaked with 768 pregnancies in 2006, the year iPledge was initiated, before leveling off to a range of 218 to 310 pregnancies annually after 2011.

Grant-Kels, who is vice chair of the University of Connecticut Health Center and School of Medicine Department of Dermatology, practices in a state that not only hasn’t banned or restricted abortion but has passed legislation to protect it. However, she noted, colleagues in other states are wrangling with whether to prescribe teratogenic drugs if abortion isn’t easily accessible. The Ohio Dermatological Association asked her to present grand rounds at its annual meeting this fall about the ethics of prescribing teratogenic drugs in a post-Roe world, Grant-Kels said.

When Ohio dermatologists met September 30 to October 2, abortion through 22 weeks’ gestation was still legal in their state. After Roe was overturned, Ohio had implemented a law banning most abortions after a fetal heartbeat could be detected, or at approximately 6 weeks’ gestation, which is often before people know they’re pregnant. But, after the American Civil Liberties Union (ACLU) of Ohio and the Planned Parenthood Federation of America challenged the law’s constitutionality, a judge twice blocked it for a total of 4 weeks through October 12. On October 7, a judge indefinitely blocked the law while the lawsuit challenging it proceeds, according to a statement from the ACLU of Ohio.

While medical specialists such as dermatologists, rheumatologists, and neurologists don’t perform abortions, they frequently prescribe teratogenic drugs, so state bans on abortions could influence what medications they prescribe, the authors of a recent commentary noted.

“Abortion bans limit patient autonomy by preventing pregnant patients on a teratogenic medication the free and informed decision of terminating their pregnancy,” the authors wrote in the Journal of the American Academy of Dermatology. “Therefore, we may harm our patients and their offspring when prescribing teratogenic medications in states where abortion is restricted because these women will have no alternative option if/when contraception fails.”
When Abortion Is “Absolutely Essential”

University of Cincinnati pediatric rheumatologist Grant Schulert, MD, PhD, is licensed in Ohio and in Kentucky, which has banned all abortions except in cases of rape or incest. On June 25, the day after the Dobbs decision, Schulert tweeted about the impact of abortion bans on his patients and his practice.

“As a rheumatologist I care for teens and young women for whom pregnancy could be life threatening, and whose quality of life is ensured by therapies that are highly teratogenic. Access to safe contraception and abortion is absolutely essential to the practice of rheumatology,” he wrote.

Females are twice as likely as males to be diagnosed with autoimmune disorders, including rheumatological conditions such as rheumatoid arthritis and systemic lupus erythematosus; in an interview, Schulert said three-quarters of his patients are female.

“I’ve certainly had a couple of patients become unintentionally pregnant while on medications that are considered dangerous” to the fetus, he said. One patient had an abortion in Ohio, while another miscarried.

Kristen Young, DO, a rheumatologist at Banner Health in Phoenix, Arizona, told JAMA that she and the other 2 physicians in her practice each typically see 1 patient per year who unintentionally conceives and terminates the pregnancy because carrying it could put their life at risk, they require a teratogenic drug, or both.

On September 23, a judge in her state ruled that a 1973 injunction against a law dating back to 1864—a year after Arizona became a territory and nearly half a century before it became a state—must be lifted. The law bans all abortions except when the mother’s life is in danger. However, on October 7, the Arizona Court of Appeals temporarily blocked the territorial law, although a post-June 25 ban was lifted abortion after 15 weeks remains in effect.

Arizona borders California, New Mexico, and Nevada, none of which have banned abortions, Young noted. In anticipation of the Dobbs decision, a private abortion clinic in Phoenix opened a branch in Las Vegas, but that’s a 4-hour drive from where her practice is located, said Young, a faculty member at the University of Arizona.

Recent news reports also tell of abortion restrictions affecting some rheumatology patients’ access to methotrexate. In much higher doses than are prescribed for rheumatological indications, methotrexate is used to treat unruptured ectopic pregnancies. Some patients who’ve been taking it for years for rheumatoid arthritis have encountered pharmacists in Arizona and elsewhere who refused to fill their prescription for fear of running afool of their state’s abortion ban.

Talking About Sex

Schulert, the Cincinnati pediatric rheumatologist, said the Dobbs decision makes the need greater than ever for “very frank” conversations about sex and contraception with patients who are considering or already taking teratogenic drugs.

These discussions might be out of some physicians’ comfort zone, he acknowledged. “We do a bad job talking about sex with our patients. We’re pediatricians.”

With the overturning of Roe, however, “it’s changed our practice to make us sure to have these conversations early and often with our patients who are already on methotrexate,” Schulert said.

He said physicians in his practice ask adolescent patients whether they’re sexually active, preferably without a parent present. If these patients need a birth control prescription, he and his colleagues can refer them to an obstetrician-gynecologist who specializes in caring for teens.

“For younger children, I lay the groundwork,” Schulert said. Although they might not be sexually active yet, he tells them that methotrexate “is very safe for your body, but it’s very bad for your fetus.”

He noted that the American College of Rheumatology (ACR), which recommends stopping methotrexate 1 to 3 months before conception, has added presentations related to prescribing teratogenic drugs post-Roe to the program for its mid-November annual meeting. “This is a space where I think professional organizations are trying to take the lead,” Schulert added.

One study that will be presented at the meeting found that women aged 18 to 45 years with juvenile idiopathic arthritis had similar, low rates of contraception whether they were taking a teratogenic drug or a pregnancy-compatible medication.

Such low rates might not be the case in every rheumatology practice, though. “I was trained in such a way that we talk about contraception in almost every visit,” Young noted.

Increasing Disparities

Alternatives to known teratogenic drugs could have their own drawbacks. They might not be as effective, and they might have their own safety issues—including some that have not yet been identified.

As a result, observers say, abortion bans could result in health care disparities between patients who can and cannot become pregnant.
“Without isotretinoin in our toolbox, dermatologists are left with fewer and less effective treatment options,” Grant-Kels and her coauthors wrote in their commentary. “Prolonged antibiotic courses may be employed, which have their own downstream effects such as treatment failure, increased risk of antibiotic resistance, and side effects of long-term use of oral antibiotics.”

The same is true for rheumatologists, a recent editorial in The Lancet Rheumatology suggested. “In a post-Roe USA, rheumatologists and patients will likely be faced with the difficult choice between the most effective, guideline-aligned therapies (eg, MMF [mycophenolate mofetil] or cyclophosphamide for lupus nephritis) plus long-acting contraception or—for women with contraindications or intolerance to contraceptives—suboptimal disease control with pregnancy-safe options (eg, azathioprine for lupus nephritis),” the editorialists pointed out.

In an interview, Sara LaHue, MD, an assistant professor of neurology at the University of California, San Francisco, expressed similar concerns for her field.

“Someone who has the capacity of pregnancy will always be seen as someone who is prepregnant,” LaHue said. “I think it’s reasonable to worry about patients not being made aware of the full spectrum of treatments for neurological disorders.”

When pregnancies can’t be timed or prevented, LaHue and her coauthors explained in a recent Viewpoint in JAMA Neurology, “neurologists might possibly restrict use of the effective medications that are standard care for other patient groups because of potential concerns about causing fetal harm.”

What’s more, evidence about teratogenicity is lacking for many medications. Just because a drug isn’t a known teratogen doesn’t necessarily mean it’s not teratogenic, LaHue told JAMA. “So many of the medications we prescribe in neurology have very minimal information when it comes to safety profiles,” she said.

Deciding not to prescribe a teratogenic drug that is the standard of care because a patient could become pregnant and may not be able to access an abortion, Caplan said, “is a very strange way to practice medicine, and, I think, unethical to its core.”

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