

# A Bad Case of Acne

Problem-Based Learning

Class of 2019

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Case contributed by:

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**Summary:**

This case is about the effect of Accutane (a drug prescribed for cystic acne) in causing birth defects. The case is aimed at reinforcing course material on early development and emphasizes not only what events are taking place during the relevant period but also how body plan is determined, how various substances (in this case, retinoic acid) can act as transcription factors specifically controlling development of certain regions and during certain time periods, and the concepts of critical periods for the development of different organs. A number of epidemiological and ethical issues arise as well such as the right of minors to determine whether or not to have an abortion without parental guidance, sharing of drugs and associated consequences, regulation of drug prescription and risk vs. benefit analysis of prescribing drugs such as Accutane (in this case, especially to adolescent females) that may be highly teratogenic.

**Definitions (Medline Plus dictionary):**

**Teratogenic** – of, relating to, or causing developmental malformations

**Gestational age**- Estimation of the prenatal age of the fetus, typically by reviewing the pregnant woman's menstrual history, making measurements of fundal height, or by making ultrasonic measurements of fetal parts. This information is essential so that appropriately timed obstetrical care can be provided and the pregnancy's progress can be compared with normal standards (Tabor's Cyclopedic Medical Dictionary 21 ed)

**Ultrasound** - the diagnostic or therapeutic use of ultrasound and especially a noninvasive technique involving the formation of a two-dimensional image used for the examination and measurement of internal body structures and the detection of bodily abnormalities

**Planned Parenthood** - used for services and materials promoting the accessibility of effective means of voluntary fertility control

**Apgar score** - an index used to evaluate the condition of a newborn infant based on a rating of 0, 1, or 2 for each of the five characteristics of color, heart rate, response to stimulation of the sole of the foot, muscle tone, and respiration with 10 being a perfect score

**Microcephaly** - a condition of abnormal smallness of the head usually associated with mental retardation

**Micrognathia**- abnormal smallness of one or both jaws

**Microtia**- abnormal smallness of the external ear

**CT**- computed tomography- radiography in which a three-dimensional image of a body structure is constructed by computer from a series of plane cross-sectional images made along an axis

**Cisterna magna** - a large subarachnoid space between the caudal part of the cerebellum and the medulla oblongata

*[Standardized patient interview]*

*The patient, Deena Scott, is a 15 year old female with acne. She received a supply of Accutane (13-cis-retinoic acid) from her boyfriend for whom it had been prescribed and tried it out to see if it would help clear her skin. Starting on January 14, she took 40 mg bid for 4 weeks at which point she ran out of the pills. Her skin has shown marked improvement, and Deena is now visiting the nurse practitioner (NP), Ms. Stendahl, at her pediatrician's office, one week after running out of pills, in an effort to get a proper prescription.*

*The NP is interviewing Deena. She finds out that Deena has been taking Accutane and becomes concerned about whether she might be pregnant since Accutane causes severe malformations in embryos. She asks Deena if she has a boyfriend and tries to ascertain something of their relationship. It takes a lot of reassurance to get her to acknowledge having had sexual relations with her boyfriend. The doctor points out that Deena must take a pregnancy test in order to get a prescription and that the rules for getting the prescription refilled and for guarding against pregnancy are very strict. She asks Deena whether she would be willing to follow this regimen while taking the Accutane and how she would feel about getting an abortion if she became pregnant.*

*Deena says that she would use the recommended form(s) of birth control but that she couldn't get an abortion. Her parents are very religious and she has always been taught that this would be a sin.*

*The interview ends with the doctor explaining that Deena will be able to get the results of the pregnancy test on the following morning and that, assuming the test is negative, she would then write a prescription for the Accutane and explain to Deena about the birth control that she will have to use and about the requirements for obtaining refills.*

## **Interview of Deena Scott by Nurse Practitioner Stendahl who works with Deena's pediatrician.**

Dr: Hi Deena. How are you doing? What brings you to see us today?

Deena: You remember the last time I came in I had acne pretty bad. The lotions you gave me weren't really helping. On my face a little bit, but on my back it wasn't going away at all. So my boyfriend ended up letting me try the Accutane that he had. And that really helped.

Dr: It looks really good. Deena: Thanks! It ran out a week ago so I wanted to get some more for me.

Dr: Anything else? Deena: No, that's it.

Dr: Can you tell me a little bit more about the Accutane, how much you took?

Deena: Yes, I took two pills twice a day.

Dr: Do you know the dosage of the pills? Deena: No.

Dr: And for how long? Deena: Four weeks. A week ago I ran out.

So it definitely helped your face a lot. So you want to get some for yourself. There's a few things that we'll need to talk about if you're going to take Accutane but I want to update your medical history. Have you taken any other medications, supplements, herbs?

Deena: No.

Dr: How's your health been since I saw you last? Deena: Good.

Dr: How was school this year? Deena: Good.

Dr: Are you still doing plays? Deena: Yes.

Dr: What's the latest one? Deena: West Side Story. I'm in the ensemble.

Dr: Last time I saw you, you told me that you weren't smoking, drinking, or any of that. And I also want to remind you that everything we talk about is confidential. I do not need to tell your mom. If there's anything that might be harmful to you in some way that you tell me, I would need to tell you. So smoking?

Deena: No.

Dr: Alcohol? Drugs? Deena: Sometimes alcohol at dinner with my parents.

Dr: Any other recreational drugs? Deena: No.

Dr: When was your last period? Deena: I don't know. I guess I should be getting it soon.

Dr: Any idea? Deena: I don't know. I'm not really that regular so it's hard to keep track.

Dr: How old were you when you started your period? Deena: 13.

Dr: Have they been regular at all? Deena: Sometimes. I don't really keep track.

Dr: I want to make sure that you are healthy and that you aren't taking any medicines that will interfere with it. But also it can be dangerous if you happen to take Accutane while you are pregnant. When we prescribe it, we are given a special thing to fill out that says we will make sure we get pregnancy tests on our patients. Women must be on some sort of birth control. I remember the last time we talked you told me that you weren't sexually active. Has that changed?

Deena: You're not going to tell my mom? ...Yes.

Dr: Do you have a boyfriend right now? Deena: Yes.

Dr: Have you had intercourse with him? Deena: Yes.

Dr: I just need to know so we take care of everything. When you have sex have you used birth control?

Deena: I guess.

Dr: What do you mean you guess? Deena: Sometimes we do.

Dr: What do you use? Deena: Condoms.

Dr: So not every time. Deena: No, I guess there was a couple of times we didn't.

Dr: So you're looking uncomfortable to me. Can you tell me what you're worried about?

Deena: I just wanted to get the Accutane.

Dr: Hopefully you will. There is a procedure we have to go through that has been put in place by the drug companies to protect everybody. If we do go ahead with the Accutane, one requirement is that we do have to do regular pregnancy tests. We have to have you on some sort of birth control to make sure that you're not going to get pregnant. I can explain all of this to your mom. This is part of the rule for taking Accutane. As far as forms of birth control, how do you feel about taking something. Have you thought about that at all?

Deena: I guess not. It's not something my family talks about.

Dr: After we do the tests tomorrow. I can go over some of the possibilities. Generally we want you to be on something pretty effective including birth control pills or the depo provera shots. Do you know about those?

Deena: No.

Dr: It's a shot that you can get every three months and it protects you against getting pregnant. There are also some patches now that you can change once a week that has the same medicine as the pill has but you don't have to remember to the pill every day. Unfortunately with condoms, it's good to keep using them to protect against sexually transmitted disease, but they are not really something you want to 100% rely on for birth control because they can break, come off, as you know you have to remember to use them every time. So that's probably not good enough. Now the other thing you need to think about is that if you take the Accutane and if by some chance you get pregnant anyway or you find out that you are pregnant when we get the results tomorrow, how would you feel about the possibility of having an abortion?

Deena: I couldn't do it.

Dr: For religious reasons? For personal reasons? Deena: My family is very religious.

Dr: I'm hoping we don't have to cross that bridge right now, but we will find out tomorrow. But I would insist on if you are pregnant and have taken the Accutane, I would want you to see a doctor that specializes in problem pregnancies just to make sure you get all the facts that you need to know. But I'm hoping we won't have to do any of that. We do have to draw your blood. Once we find out the results, if you could come back tomorrow, that would be the best so we can talk about it in person. As far as your mom, if we need to explain how the birth control works with the Accutane I'm happy to do that for you. Deena: OK. It would be better if you explain that.

## Part 1

Ms. Stendahl was alarmed when Deena's pregnancy test came back positive the next morning. She quickly placed a call to a colleague who specialized in birth defects, Dr. Yale O'Grott, and asked if he would be willing to see Deena right away. When he agreed, she called Deena to discuss how to proceed. Deena was extremely upset and seemed reluctant to see yet another doctor. She was particularly concerned that her parents would need to give approval. Ms. Stendahl reassured Deena that she would not need her parent's permission although she would need to be able to pay the bill.

After some encouragement, Deena made an appointment to see Dr. O'Grott on February 20. After a few questions about her use of the Accutane and her past medical history, Dr. O'Grott explained his concern about the possible birth defects that might be associated with the use of a teratogenic substance like this. To help determine what the actual risks might be, he asked her to try hard to remember when her last menstrual period (LMP) had been. After thinking awhile, she finally calculated that it had been on December 21. Based upon her LMP, he explained that the period of exposure was day 10 through day 37 after conception, not counting drug elimination time.

## Part 2

Dr. O'Grott explained that the use of Accutane during this period could have very serious consequences on the baby's development since this was a time when many of the baby's structures were being formed. He asked her to think about whether she might want to give birth to the baby given this level of risk or if she would consider having an abortion. Deena mutely shook her head and broke into tears. She admitted that her parents did not like her boyfriend, Justin, and would be horrified if they learned she is pregnant. She said they had always warned her that he would get her into trouble. But, she explained, she was Catholic and didn't think she could ever have an abortion, particularly if it meant she had to tell her parents.

Dr. O'Grott reassured Deena that she had a little time to think about her options and that the best next step would be to see an obstetrician and to use an ultrasound scan to verify whether the baby was conceived when they thought it had been. He wrote out a prescription for an ultrasound and recommended that Deena see an obstetrician at Planned Parenthood in addition to returning for a follow-up visit next week. Seeing her continued level of distress, he offered to make an arrangement for her to talk with a genetics counselor in the office. Deena declined but did make the appointment for the ultrasound and acquired information on Planned Parenthood before leaving the office.

### Part 3

The ultrasound on March 15 revealed a gestational sac that appeared consistent with her date of conception, suggesting that the embryo was 10 weeks old.



Fig. 1: Ultrasound of 10 week fetus with crown-to-rump indicated.

Both the obstetrician and Dr. O'Grott emphasized to Deena that there was a very high probability that this baby would be born with severe birth defects and suggested that she think seriously about terminating the pregnancy. But she had thought about it and realized that she couldn't bear to do that. Also, she had discussed this with Justin, the baby's father, and he said that he wanted her to keep the baby. Dr. O'Grott suggested that, before she made any final decision, they should keep monitoring the baby through regular checkups and ultrasound scans to see if they could detect any anomalies. Deena agreed and said that if anything was seen that suggested a serious problem, she would reconsider her decision.

Ultrasound evaluation at 12 weeks GA (gestational age) showed size consistent with conception date and no detectable anomalies. Fetal heart tones were detected at 17 wks GA, and ultrasound showed a crown size within normal limits.



Fig. 2: Ultrasound 17 Week fetus. Crown diameter indicated.

At 18 weeks GA, maternal serum AFP (alpha fetal protein) was just below the upper limit of the normal range. Another ultrasound at 20 weeks GA revealed no detectable anomalies and normal growth rate.

In the meantime, Deena was encouraged by Dr. O'Grott to tell her parents about her pregnancy and promised to assist her in doing so, if she wished. Feeling braver as the test results suggested things were normal, Deena told her parents. They were extremely angry and upset at first but agreed with her decision to keep the baby.

At week 21, Dr. O'Grott met with both Deena and her parents, emphasizing that many of the types of birth defects that the baby might have wouldn't necessarily show up yet on the ultrasound evaluation. He offered again to arrange for her to talk to with the genetic counselor about her decision, either alone or with her parents, but Deena was adamant. She felt that she had gotten herself into this situation and even if her baby wasn't perfect, she thought that she should take responsibility for raising it. In fact, she asked, *"Is there any danger that I might miscarry? I really want to have this child!"*

## Part 4

Deena had a final ultrasound scan at 34 wks GA on August 30. It showed an unusually short, broad head (brachycephaly) and too much fluid around the fetus (polyhydramnios).



Fig. 3: Ultrasound at 34 weeks.  
Note extra fluid on the right.

Delivery occurred prematurely on September 12, at 36 weeks, because of the polyhydramnios. Baby Bryce was born via spontaneous vaginal delivery. Apgars were 6 and 7, at 1 and 5 minutes, respectively, and birth weight was 2895 grams, length 48.75 cm. with an occipitofrontal circumference of 30.5 cm. Dr. O'Grott examined the baby shortly after birth and noted multiple anomalies: microcephaly, micrognathia, microtia, small genitalia, 13 ribs on chest x-ray, generalized lack of muscle tone with decreased activity and poor responsiveness.

Deena went home with her parents after two days, but the baby had to remain in the hospital for further evaluation. Deena realized that her baby was going to have serious problems, but she didn't really know what they would be like. A cranial CT scan was abnormal on September 5 with a prominent cisterna magna suggesting a Dandy-Walker variant.<sup>1</sup> Deena didn't understand how Bryce could have such severe problems when nothing had shown up in the ultrasound scans, even when the fetus was 20 weeks old.



## Part 5

Dr. O'Grott is due to round with a group of third-year clerkship students on the Pediatric Neonatal Intensive Care Unit. Luckily, you are among these students. Unluckily, the senior resident has warned the students that the attending loves to ask questions so that they need to prepare for rounds. You and your colleagues quickly try to imagine what Dr. O'Grott might ask you and, based on your review of the case and the things you were curious about, you all come up with the following list of questions:

1. Why do micrognathia and microtia (or anotia) almost always go together in Accutane-induced embryopathy?
2. Why did Accutane affect development of the brain but not the limbs?
3. How does Accutane cause teratology? What defects would you expect to observe in Bryce given the period over which his mother ingested Accutane?
4. What factors influence the degree to which Accutane-induced defects are observed?
5. Why weren't the teratogenic effects of Accutane discovered as part of the animal studies done prior to approval of its use in people?
6. How does Accutane prevent acne?