

Erin Welsh

"In 1970 and 1971, I participated in three different types of tests. Two of them, nicknamed the patch tests by inmates, dealt with the experimentation of new products not yet released to the general public. The first patch test was one that tested lotions, creams, skin moisturizers, and suntan products. The procedure for these tests was as follows. A grid made from thick strips of white hospital tape was fixed to the upper portion of an inmate's back shoulders. The grid consisted of about 20 squares. In each of these squares, a dab of lotion was applied and the inmate's back was exposed to different temperatures from a sun lamp.

The exposure to the sun lamp lasted anywhere from 15-30 minutes, after which each square was inspected for degree of blistering or other adverse reactions. The grid was then covered with a large solid piece of tape to prevent tampering by the inmate and the inmate was returned to his cell. This test lasted about 30 days and once a day the inmate was called back over to the lab and exposed to the sun lamp. After about five days of the sun lamp, there were sections of the skin that were burnt a deep brown and the skin started to peel, itch, and blister. If a certain square became too damaged, it was covered over with a permanent piece of tape and the test continued on the grid."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

That sounds awful, Erin.

Erin Welsh

Yeah. It really, really, really is. And so that was from William Robb who was at one point in Holmesburg Prison and participated in these experiments that will make up a big focus of today's episode. And that ultimately was from a book titled 'Acres of Skin' by Allen Hornblum. Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

And today's episode we are covering one half of a big story-

Erin Welsh

Yep.

Erin Allmann Updyke

All about retinoids.

Erin Welsh

Yeah. Sometimes with the topics that we choose, you never know where you're going to end up.

Erin Allmann Updyke

Most of the time.

Erin Welsh

And this story is going to be... Yeah. And this was certainly the case for retinoids. And we decided to do this because we were just like what's the deal with retinoids?

Erin Allmann Updyke

Yeah.

Erin Welsh

And looking into the history of things like Retin-A, I found a darker story than I anticipated. And the story itself, both like the origin of Retin-A and the marketing of retinoids in general, that is one half of this big story. But I also wanted to tell the story of the experiments at Holmesburg Prison from the 1950s to the 1970s because it's not a very commonly told story of a really dark chapter in American medical history.

Erin Allmann Updyke: Also I don't think I realized that this story is going to take place in the 1950s and 1970s. That's like just very depressing, Erin.

Erin Welsh: Like how recent?

Erin Allmann Updyke: How recent.

Erin Welsh: I mean what, Tuskegee was whistleblown in the early 1970s?

Erin Allmann Updyke: I know, I know.

Erin Welsh: Yeah. I know, I know. And then yeah, so that is what this episode is going to focus all on the history. How did Retin-A get to market? Yeah.

Erin Allmann Updyke: And a little bit more about one of the guys who brought it there.

Erin Welsh: Yeah. And then the second episode which will be your focus, Erin-

Erin Allmann Updyke: Yeah.

Erin Welsh: Is do retinoids work?

Erin Allmann Updyke: Right. It's going to be a more lighthearted episode than this one. So next week we'll get into what retinoids are, how they work, do they work? What do we use them for? And a big part, what I'm most excited about in that episode will be what's the difference between an over the counter retinoid and the stuff you get by prescription? And is there one?

Erin Welsh: I'm very excited for that because the amount of claims that I see both on product but also just on the internet and social media and whatnot for the magical powers of retinol, I want to know like are there magical powers?

Erin Allmann Updyke: It is, I mean it's the supplements episode 2.0. Can't wait for it, it's going to be so fun! But first-

Erin Welsh: But first we have quarantini time.

Erin Allmann Updyke: We sure do.

Erin Welsh: What are we drinking this week, Erin?

Erin Allmann Updyke: Erin, this week we could drink only Skin Deep.

Erin Welsh: Skin Deep, yep. And in Skin Deep appropriately is carrot juice because retinoids are derived from vitamin A ultimately, which is found in great quantities in carrots.

Erin Allmann Updyke: Yeah, it's beta carotene which is like it will convert into vitamin A in your body. It's a long story.

Erin Welsh: Technically speaking. And it also has ginger and lemon juice and some simple syrup and some vodka. And it's a tasty little concoction. I might have to play around with the ratios a little bit but...

Erin Allmann Updyke

It's going to be fantastic. You can find the full recipe for that quarantini and the very healthy and non alcoholic placebo on our website thispodcastwillkillyou.com and on all of our social media channels too.

Erin Welsh

On our website thispodcastwillkillyou.com, there's a lot of things that you can find. You can find the sources for each and every one of our episodes. You can find transcripts. You can find links to our bookshop.org affiliate account, links to our Goodreads list, links to music by Bloodmobile, links to merch, links to Patreon. There's a contact us form where you can say like hey, do this episode or hey, come talk at our university. Whatever it is. There's also a submit your firsthand account form.

Erin Allmann Updyke

It's all there. Check it out.

Erin Welsh

Check it out.

Erin Allmann Updyke

And if you haven't already, be sure to check your pod catcher and make sure that you're subscribed to this podcast which really helps us. And if you haven't already left us a review, we would sure love it if you did.

Erin Welsh

Okay. Should we get started?

Erin Allmann Updyke

Yes. Please tell me, Erin, all about how Retin-A came to be.

Erin Welsh

All right, it's a long story so let's take a quick break before we begin.

TPWKY

(transition theme)

Erin Welsh

How many of you out there listening has in their bathroom cabinet a little bottle of serum or a little tube containing retinol or retinoids? Me too.

Erin Allmann Updyke

I have two.

Erin Welsh

I have one.

Erin Allmann Updyke

Two different kinds.

Erin Welsh

And how many of you have been prescribed Retin-A in the past? And it's N of two here, 100% two of two, but I'm guessing that it is a lot of you out there. I haven't used my retinol in a long time because it makes me break out. But I bought it because I had heard on like commercials or on TikToks or like the skincare addiction subreddit that it was great for your skin for preventing fine lines, reducing the signs of aging, like all of those things. But beyond the question of does it actually do those things is a deeper question whose answer reveals the surprisingly dark history behind this ubiquitous skincare component. How did we learn about these effects of retinoids on the skin in the first place?

Erin Allmann Updyke

Yeah.

Erin Welsh

Lurking beneath these claims of anti-aging, pore cleansing, and acne prevention; claims which I know next week you're going to talk about like which is there support for, which isn't their support for? But behind all of those claims is a grim history involving human experimentation on incarcerated individuals. Experiments so profoundly unethical that they were described as a violation of the Nuremberg Code. Like the code that was developed in 1947 in response to Nazi doctor war trials.

Erin Allmann Updyke

Whoa, Erin. That's not...

Erin Welsh

Yeah.

Erin Allmann Updyke

How have we never heard of this?

Erin Welsh

I don't know because it is commonly mentioned alongside Tuskegee syphilis study, alongside the Willowbrook State Schools, alongside the birth control pill experiments in Puerto Rico. Like it's all sort of part of it. I had never heard about this though in medical ethics class. But maybe it was just so long ago that I had forgotten.

Erin Allmann Updyke

Yeah. Or maybe it was just glossed over as like the Holmesburg Prison.

Erin Welsh

Right. Yeah.

Erin Allmann Updyke

And like no detail or something.

Erin Welsh

Right. Still people devaluing human life because of... Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay. I want to learn.

Erin Welsh

Right. Okay. So what were these experiments for? How were they allowed to happen? And who brought them to light? So that's the story that I'm going to tell today. And it's not the history of retinoids that you're likely to find on a skincare company website. And to be fair, retinoids are just one part of the story. But I wanted to focus on it today because I think it's a crucial part of the history of medical ethics and it's one that, yeah, you don't hear about that often. How do highly educated and credentialed individuals get to a point where they feel like they're above the rules, where they lose any self awareness that would allow them to see that they aren't nobly championing science but in fact committing atrocities against humans?

At the heart of this story is Albert Kligman, an American dermatologist who has been credited with transforming the field of dermatology from a little acknowledged subspecialty to a full on giant of industry by the end of the 20th century. As the co-inventor of Retin-A and an advocate for its off label uses, Kligman saw the incredible commercial potential of dermatology in terms of pharmaceuticals and cosmetics, cosmeceuticals. But that is certainly not his only claim to fame. For more than two decades between 1951-1974, Kligman headed a medical research program at Holmesburg Prison in Pennsylvania where he conducted dozens of nontherapeutic experiments on incarcerated individuals, the majority of which were Black. Experiments ranged from assessing the efficacy of certain deodorants to quantifying the impacts of dioxin exposure. Dioxin, if you haven't heard of it before, is a highly carcinogenic substance, like it's sometimes called the most carcinogenic substance known. It's the stuff in Agent Orange that makes it super toxic to humans. So he tested it on humans.

Erin Allmann Updyke

What?

Erin Welsh

And although most experiments didn't specify which race he was looking for, this is a call for white people, this is a call for Black people. The riskiest ones were reserved for Black individuals only. And this is where Retin-A was born, at Holmesburg Prison.

Erin Allmann Updyke

I'm already so mad, Erin.

Erin Welsh

I know. There's so many more pages of being angry, trust me.

Erin Allmann Updyke

I know. My face is going to be like... Talk about permanent wrinkles. I'm going to have one after this.

Erin Welsh

The furrowed brow is going to be too deep for retinoids to penetrate.

Erin Allmann Updyke

This podcast does give me one of those constantly.

Erin Welsh

This podcast will give you a furrowed brow.

Erin Allmann Updyke

Will give you a furrowed brow.

Erin Welsh

Dot com.

Erin Allmann Updyke

Worth it.

Erin Welsh

Yep. But before we get into the backstory of Retin-A, let's first explore how Kligman found Holmesburg, or rather how it found him. Kligman's path to dermatology was not a straight line. He started off by first getting his PhD in botany, studying fungi, at the time mycology was lumped in with botany or like under the botany umbrella. And then he went to medical school with a specialization in dermatology so he could keep pursuing his interest in fungi, like those that cause athlete's foot. A lot of like topical fungal infections.

Erin Allmann Updyke

Skin infections. Yeah.

Erin Welsh

Yeah. A few years after graduating with his MD, Kligman, who was faculty at the University of Pennsylvania, he received a phone call from the pharmacist at Holmesburg Prison. The prison was dealing with a huge athlete's foot problem which is common in large residential facilities. And the pharmacist was at his wit's end trying to find an effective treatment. And in his searches he had stumbled upon a research article written by Kligman about athlete's foot. And so he called the doctor for advice. Kligman was like all right, I'm going to see this for myself. So he went to the prison to scope out the situation. And when he got there, he didn't see an athlete's foot problem or he didn't see that alone. But what he saw instead was limitless potential. Quote: "All I saw before me were acres of skin. It was like a farmer seeing a fertile field for the first time." End quote.

Erin Allmann Updyke

Sorry, you go to a prison, see untold numbers of incarcerated individual human beings, and all you see are acres of skin?

Erin Welsh

Acres of skin.

Erin Allmann Updyke

Cool. Great.

Erin Welsh

So that-

Erin Allmann Updyke

Stand up guy.

Erin Welsh

I think gives you a little bit of a sense for where his sense of morality was when it came to experiments on humans.

Erin Allmann Updyke

Right. I mean it's a lot easier to do stuff if you're just doing it on skin.

Erin Welsh

Right.

Erin Allmann Updyke

It's just skin, it's devoid of humanity.

Erin Welsh

I mean and I think we'll get into this a little bit more later but I think he did see beyond skin. But I think that what he saw was he was a little bit of the savior, right.

Erin Allmann Updyke

Right.

Erin Welsh

Like he was like oh but I am giving them freedom from boredom, I'm giving them money, I'm giving them an opportunity to learn, I'm giving them an opportunity to give back. Like this is a whole... Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so this "Acres of skin" comment is the title of the book that where most of this information that I got for today's episode comes from. It's a great book, it's by Allen Hornblum. It's one of the classic exposes of unethical human experimentation in the US. In Kligman's eyes, Holmesburg Prison represented a near perfect study environment. And that's an opportunity that rarely, if ever, comes along in medicine. In an institutionalized setting, Holmesburg was not Kligman's first foray by the way into institutionalized settings, he also went into schools. But in all of these institutionalized settings, you could control every variable down to how much sleep your test subjects got, what they ate, how much they ate, when they ate, how much sun they got, when they could shower, how often they could shower, all of these things you could have complete control over.

Plus it was cheap. To have someone enroll in the types of trials that he was interested in trying out and testing, you would have to pay someone who was not in prison lots and lots of money to keep them going, to be willing to do these things. So by comparison, Holmesburg was very cheap. And so Kligman wasted no time in setting up shop at the prison. Quote: "I began to go to the prison regularly although I had no authorization. It was years before the authorities knew that I was conducting various studies on prisoner volunteers. Things were simpler then, informed consent was unheard of. No one asked me what I was doing. It was a wonderful time." End quote. I know. I just can't... Like I can believe. It was a wonderful time.

Erin Allmann Updyke

Informed consent didn't exist, it was a wonderful time.

Erin Welsh

Yeah.

Erin Allmann Updyke

Those two sentences cannot go together.

Erin Welsh

Yeah. And I think the other remarkable thing about this is that... So I'm not sure when that quote was pulled from but it was later, like years later, right.

Erin Allmann Updyke

Later. It's obviously him looking back on his time doing this.

Erin Welsh

Exactly. Reminiscent.

Erin Allmann Updyke

Being like it was so great, wasn't it?

Erin Welsh

Yeah.

Erin Allmann Updyke

Cool.

Erin Welsh

Yep. And he wasn't entirely wrong about things being simpler then. It seems that, from my understanding, Kligman didn't do anything technically illegal while conducting experiments at Holmesburg.

Erin Allmann Updyke

Right. Well I was just trying to remember at what point actually IRBs became a thing. Clearly after this.

Erin Welsh

Yeah. I don't remember either. I know that Tuskegee in the early 70s kind of was one of the biggest wake up calls for...

Erin Allmann Updyke

So he just slipped it right in there.

Erin Welsh

We need more regulation. Yeah, yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

But it doesn't mean that Kligman's experiments were ethical, it just means that the laws were simply inadequate. At the time in the mid 20th century, non therapeutic medical experiments on institutionalized populations were normalized. They really were. Especially on individuals in prisons who were seen as expendable and also as needing to quote unquote "give back to society". Prisons were a really popular spot for phase one clinical trials which were intended to test the safety of a drug, not necessarily its efficacy. And so I've talked about several of these infamous unethical experiments on the podcast before and even mentioned them earlier in this episode. There's intentionally infecting children with hepatitis at Willowbrook State School on Staten Island, New York. There's of course, said it a million times, famous Tuskegee syphilis experiment. Just a few episodes ago I talked about how incarcerated quote unquote "volunteers" were given a slurry containing norovirus intended to study the effects of infection.

Erin Allmann Updyke

Yep.

Erin Welsh

And there are so many more examples out there, examples that the Nazi doctors being tried at Nuremberg pointed out in their defense in the late 1940s. Like hey, you guys do this too in the US, you do this all the time. But the American doctors conducting these experiments saw themselves as different, nothing like the Nazis but noble warriors doing what needed to be done in the name of science and giving their test subjects meaning. Quote from Kligman.

Erin Allmann Updyke

Okay.

Erin Welsh

Quote: "Many of the prisoners for the first time in their lives find themselves in the role of important human beings. We say to them you're important, we need you. Once this is established, these guys will knock their brains out to please you. If the experiment does not pan out, they get depressed, they become emotionally involved in the project. The capacity to respond to love is greater than most people realize. I feel almost like a scoundrel, like Machiavelli because of what I can do to them." End quote.

Erin Allmann Updyke

Oh my god, Erin.

Erin Welsh

I know.

Erin Allmann Updyke

This guy is... Okay, I didn't read any history papers but this guy is mentioned in the textbooks and things like that. Not like this.

Erin Welsh

Right. He is hailed as a modern father of dermatology.

Erin Allmann Updyke

Yeah. And they'll be like oh and the experiments that he did had questionable ethics. This is like he is very aware of what he is doing.

Erin Welsh

Right. He is. You know that someone-

Erin Allmann Updyke

You said that to a reporter clearly.

Erin Welsh

You said that out loud, yeah.

Erin Allmann Updyke

Or you wrote that. Like you didn't say that at a dinner party with just your dermatology friends.

Erin Welsh

Right, this isn't a private diary. Dear diary, I feel like Machiavelli. This is like a brag.

Erin Allmann Updyke

It's like basically the equivalent of a tweet back in the day.

Erin Welsh

Exactly.

Erin Allmann Updyke

You can't take it back.

Erin Welsh

No. It's there.

Erin Allmann Updyke

(transition theme)

Erin Welsh

And I think what's... Kligman is one of the individuals that is often put forth as an example. And there were some medical ethicists who at the time spoke out against these experiments. But for the most part, conducting research on institutionalized or vulnerable populations was widely accepted even outside of medicine, right. That sentiment that he expressed, maybe minus the Machiavelli part, but the whole like giving meaning, feeling important, giving back, all these things, that was in the popular narrative about these experiments.

Erin Allmann Updyke

Right. Yeah.

Erin Welsh

So starting in the mid 1950s, for example Life Magazine ran several stories on Kligman and his experiments at Holmesburg with titles like quote "Prisoners Volunteer to Save Lives" and "Prisoners Aid Medical Research: 75% Here Act as Medical Guinea Pigs" or "The Poison Ivy Picker of Pennypack Park". Which that last article detailed Kligman's quest to find a vaccine for poison ivy, not mentioning the not so mild side effects of the alleged vaccine which caused a drop in blood pressure that made many people pass out. And also just like having to have poison ivy oils rubbed all over your skin.

Erin Allmann Updyke

Poison ivy.

Erin Welsh

In a 1966 newspaper article, Kligman did acknowledge to some degree the moral issues inherent in his research. Quote: "We had an ethical problem. How much right do you have to cause risk to a prisoner in medical tests from which he has no direct benefit?" End quote. It seems like a rhetorical question, I don't think he answered it. In that same article, the Superintendent of Holmesburg reassured readers that quote "we will not approve anything which on the face of it would be deleterious to the physical wellbeing of an individual." End quote. And that sounds great, like nice sentiment, but who actually has the power to say whether something is deleterious or not? It was largely up to one man, Albert Kligman.

Let me be clear though, the experiments at Holmesburg Prison are not the work of one mad scientist given too much power. This was a coordinated effort with many major players involved and ample oversight. Pharmaceutical companies like Pfizer, Hoffmann-La Roche, Parke-Davis, Abbott, all hired researchers to conduct experiments at Holmesburg. Others partnered directly with Kligman for years and this was a University of Pennsylvania project. Nor was Holmesburg Prison the only place where medical research was unethically conducted or the University of Pennsylvania the only institution that sponsored it. I'm not defending this experimentation in any capacity, I just want to put it in historical context. Like this is not a one-off.

Erin Allmann Updyke

Which honestly just makes it that much worse.

Erin Welsh

It makes it that much worse.

Erin Allmann Updyke

It was just everyone and everywhere.

Erin Welsh

Right. This is just one that got more attention because there's a full fledged book about it. There are plenty more that are book worthy, I am certain.

Erin Allmann Updyke

Right.

Erin Welsh

And so on that note, let's get more into the medical research program at Holmesburg Prison. What had started out as a small program in 1951-1952 when he first arrived to assess the athlete's foot problem had by the early 1960s become a full fledged research machine with expensive state of the art medical equipment, trailers with monitoring equipment and padded cells, and up to 90% of all individuals who are incarcerated at Holmesburg participating in experiments. So there were times when 90% of all individuals at Holmesburg Prison were involved in one experiment or multiple which was a very common situation.

Erin Allmann Updyke

Oh my god.

Erin Welsh

And also not to mention how being involved in multiple different trials just scientifically is not-

Erin Allmann Updyke

Not great.

Erin Welsh

Not great. Between 1962-1966, only four years, 193 studies were conducted at Holmesburg including 153 experimental drugs. And then more drugs that needed marketing permission and drugs whose new uses were tested. So like some of these were purely experimental. Most of these.

Erin Allmann Updyke

Oh wow.

Erin Welsh

The types of experiments were wide ranging, as were the financial incentives. To test hand creams you could earn a dollar a day, foot powders and deodorants testing could get you \$100 a month. \$150 could be yours if you were willing to have your finger numbed with novocaine and then your fingernail removed to see how it would heal.

Erin Allmann Updyke

Okay.

Erin Welsh

Yep. Other experiments included sticking your arm in a sodium lauryl sulfate solution for one hour each day for 55 days in a row. Testing the relationship between chocolate and acne, walking around with steel cups strapped to your forehead to collect skin cells and perspiration, testing anti-dandruff shampoo that oops, made your hair fall out. Slicing skin on your back to try to induce a keloid, implanting different kinds of gauze or even tissue from a cadaver to just look at healing and like creams to help your skin heal. Applying enormous amounts of fungi to the feet and being forced to keep your boots on continually for a week, even overnight, to see how bad ringworm infection could get. The riskier the test, the higher the potential reward. Like you could get \$1000-\$1500 to test out eye drops or hallucinogenic medications. Pills that were meant to speed up sun tanning but gave people violent GI symptoms, infecting people with pathogens like Staph. aureus, Candida albicans, herpes virus, influenza. Tests that involved liver biopsies and nearly killed seven inmates. I don't know why the liver biopsies were needed.

Erin Allmann Updyke

Why are you doing liver biopsies? What?

Erin Welsh

Yep.

Erin Allmann Updyke

Okay.

Erin Welsh

Don't know. Radioactive isotope testing, exposing people to dioxin and observing the results. Just like what happens? What happens if we do this? At one point the US Army was testing psychoactive or mind control drugs in those padded cells I mentioned. People who used to be at the prison said that you could pick out those who were volunteers from those who weren't from their checkered backs. Like so from the firsthand account how I mentioned the skin test, the patch tests. So many of those tests left physical and emotional scars, extreme sunburns leading to skin discoloration, incisions where the gauze was inserted and never quite fully healed, biopsy marks. And then you have from the mind control or psychoactive drugs, people would experience flashbacks or bad trips years later, personality changes. But what choice did people truly have? Other jobs at Holmesburg Prison, like making shoes, knitting socks and shirts, sewing pants, plumbing. You would get 15 cents a day. It's no contest.

Erin Allmann Updyke

Yep.

Erin Welsh

Put some lotion on your hands, a dollar a day. Sure. Eye drops, if you need to send money back home, yeah, I need to do this. How much choice is there? And those that were involved in the experiments would often get better treatment, better food, and higher social standing in addition to that substantial financial incentive. And a dark side of this that kind of came out later on was that the financial disparity between people who participated in the trials and those who didn't sometimes led to coercion and sexual abuse. The researchers did not mention the health risks involved in any experiment or even what the experiment was testing. None of the people who participated remember ever hearing the words informed consent.

Erin Allmann Updyke

Yeah.

Erin Welsh

Right. I mean even Kligman himself was like it didn't exist.

Erin Allmann Updyke

Right. It didn't exist, we didn't do that.

Erin Welsh

They remembered signing release forms but the forms didn't have any additional information on them. As the author of 'Acres of Skin' Allen Hornblum puts it, quote, "A drowning person does not ask penetrating questions about a life raft." End quote. Even if they had asked questions, would they have gotten honest answers? With the large scale of the research program at Holmesburg, Kligman couldn't have expected to fly entirely under the radar even if he were a careful and detail oriented researcher, which he was not. He ended trials prematurely, there was a lot of evidence of falsified data. He had, like I said earlier, people participating in multiple trials like overlapping that were testing different things. He was just kind of like oh, this looks like it's not where I'm going, we're ending the trial. Oh this looks like it's where I wanted to go, we're ending the trial and saying that this is exactly what I wanted to find.

And so sure enough, red flags were thrown up as early as the 1960s which is when it came to light that Kligman was testing DMSO on humans, which was a solvent banned from human testing by the FDA. Like at that point it had already been banned. And so as a result, Frances Kelsey, who you may remember from our thalidomide episode as the person who was largely responsible for preventing thalidomide from being marketed in the US-

Erin Allmann Updyke

In the US.

Erin Welsh: She led the charge to disqualify Kligman from testing new drugs. It ended up being temporary, his disqualification, much to the relief of the many pharmaceutical companies who loved the Holmesburg Prison as a cheap way to try out medications. And he had a lot of other like eminent dermatologists who wrote in on his behalf like this is unprecedented, he has done nothing but good for the dermatology community, blah, blah, blah.

Erin Allmann Updyke: Wow.

Erin Welsh: This is out of hand. You need to let him do the work that he was put here on this earth to do.

Erin Allmann Updyke: Oh wow.

Erin Welsh: Yeah. That kind of thing. But even though Kligman's disqualification was reversed, the tides had begun to turn, not just for Kligman but for research on institutionalized populations in general. Revelations about the Tuskegee syphilis experiment came to light in 1972 which marked a big shift in attitudes towards medical experiments on vulnerable populations and what informed consent truly means. Can there be such a thing in prisons; in schools? Can there be such a thing? What does voluntary mean? How can you tell if someone is volunteering or if there is coercion? And this is still very much an ongoing discussion in medical ethics. Is it depriving people of an opportunity to earn money?

Erin Allmann Updyke: Right.

Erin Welsh: Is it something that like well then you're not giving them the right to make decisions on their own behalf? But also how are those decisions influenced by the power dynamics?

Erin Allmann Updyke: Right, the power structure.

Erin Welsh: Exactly.

Erin Allmann Updyke: And the dynamics. It's very difficult to overcome.

Erin Welsh: It is. Yeah. And all of these conversations really seemed to ramp up of course in the early 1970s as more and more of these experiments in institutions came to light. Kligman for his part never seemed to acknowledge that what he did was unethical, that he exploited a vulnerable population. He saw the work he did as quote unquote "quite beneficial to all". In his mind, he gave these individuals skills, a reprieve from boredom, money, sure, but also excitement and a purpose. And when the medical experimentation program at Holmesburg was forced to close in 1974, he railed against its closure. Quote: "A very good case of the triumph of the do-gooders. All we did is offer them money for a little piece of their skin." End quote.

Erin Allmann Updyke: All these do-gooders. A do-gooder!

Erin Welsh: All these do-gooders, yeah.

Erin Allmann Updyke: How dare you be a do-gooder?

Erin Welsh: I know.

Erin Allmann Updyke: You're a doctor, man!

Erin Welsh: I know, right? Like where does this fit under your Hippocratic oath? How does this-

Erin Allmann Updyke: Yeah, a doctor is not supposed to be a do-gooder! Who is, man?

Erin Welsh: And that's what's so... The mental gymnastics where he did think he was doing good, right, this is beneficial to all. I don't think that he would ever admit that he violated the Hippocratic oath, right.

Erin Allmann Updyke: Right.

Erin Welsh: Do no harm. Because he did so much good, like the net was good in his eyes.

Erin Allmann Updyke: It's like the train and the one person vs the train and the blah, blah, blah.

Erin Welsh: Yeah.

Erin Allmann Updyke: Get real, dude!

Erin Welsh: Yeah. Get real, dude. The medical experimentation program at Holmesburg did not go quietly into the night.

Erin Allmann Updyke: Wow.

Erin Welsh: There was denial of any wrongdoing, there was bargaining that if they improved things, could they still experiment? There was outrage. Basically all the stages of grief minus perhaps acceptance. Kligman had always seen himself as a maverick. He told his students that rules don't apply to genius, that they just get in the way of creative minds. Yeah. No one could tell him that what he did was wrong and have him actually believe it or acknowledge it, even when the lawsuits came out which were dismissed because of statute of limitations.

Erin Allmann Updyke: Oh god. The statute of limitations.

Erin Welsh: I think there was eventually some settling outside of court although I don't remember the details of it. But even when sweeping changes were made to guidelines for obtaining informed consent in medical research and research on vulnerable populations, he still couldn't admit that what he did was wrong. Even when his research at Holmesburg was deemed to be in violation of the Nuremberg code, he seemed to think that the ends justified the means.

Erin Allmann Updyke: Wow.

Erin Welsh: But what exactly were those ends, right? Was it the advancement of science? Was it relieving people's suffering? Or was it simply making money?

Erin Allmann Updyke: Making a buck. That's my guess, Erin.

Erin Welsh: I can't say for certain because I don't know him in his head. But given his words and actions after Holmesburg, I think that it's pretty clear that money was at least a strong motivating factor. And that brings me finally to the story of Retin-A. Retinoids which include retinol and Retin-A which is the brand name of tretinoin, are all derivatives of vitamin A. And someday we'll probably do an episode just about vitamin A.

Erin Allmann Updyke

For sure because we're focusing on like topical retinoids.

Erin Welsh

Yeah.

Erin Allmann Updyke

Vitamin A is its own. I mean it's the same thing but...

Erin Welsh

There's definitely plenty more to the story of vitamin A.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so the short story that I'll tell right now is that people have used vitamin A for likely thousands of years to treat night blindness. Beginning in the 20th century, people grew interested in the other properties of vitamin A and other vitamins. It was like that vitamin heyday revolution that I've talked about many times. And one of the things that they noticed was that vitamin A seemed like it might be effective in treating acne. In the 1940s, a researcher named Jonathan Straumfjord dosed patients with 100,000 international units of vitamin A every day for a minimum of six months.

Erin Allmann Updyke

Injections, right?

Erin Welsh

I think so, yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

And the results were striking. 79 patients were completely cured and only three showed no improvement. That's like pretty, pretty strong. Later studies conducted in 1962 by Dr. Beer and Dr. Stüttgen used vitamin A acid, which I'm assuming is tretinoin, I'm not sure. I don't know if it went by the name then. This was administered orally and they found similar benefits. All of these researchers noted the extreme skin irritation in the early weeks of treatment. And one researcher was like I don't want to do any more of these studies because I am so alarmed at the strength of this reaction, this can't be good for people. But that didn't bother Albert Kligman. When a UPenn medical resident tried out the vitamin A derivative at Holmesburg after reading Beer and Stüttgen's paper, quote, "Dr. Kligman saw that it irritated the skin and asked if he could work with it." End quote. So he like saw the irritation and was like ooh, green flag.

Erin Allmann Updyke

Right. Like ooh, this means it's doing things.

Erin Welsh

This means it's doing things. By 1963, Kligman had set up human trials at Holmesburg exploring the potential uses of the medication, which he received free of charge from Hoffmann-La Roche who of course saw its commercial potential. At the prison Kligman sought to find the right dose, the right delivery system, like orally or topically, and the right chemical composition of the vitamin on the backs and faces of the individuals at Holmesburg. He's quoted as saying that early on he experimented with quote unquote "very high doses" of vitamin A. Quote: "I near killed people before I could see a real benefit. Every one of them got sick." End quote.

Erin Allmann Updyke

Ah, okay. This guy just keeps getting worse, Erin.

Erin Welsh

He keeps getting... I know you're like surely there's not more to this. Trust me, there is. Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh	He used doses of 1% vitamin A acid, tretinoin, which is 100x stronger than the 0.01% that it became later on.
Erin Allmann Updyke	1%?
Erin Welsh	Yeah.
Erin Allmann Updyke	Oh my.
Erin Welsh	Yeah.
Erin Allmann Updyke	That's way too strong.
Erin Welsh	And unsurprisingly that strong of a dose caused intense irritation to the skin. But that didn't worry Kligman in the slightest. In fact he took it as a good sign, an indication that this drug was working. This trait of his to keep pushing, push past any obstacle, it earned him the admiration of some, like a former student who said that he quote "thought Retin-A would never sell. It caused a severe reaction in patients. Their faces became quite red and irritated. But Kligman has the capacity to push when others won't. He could see the value of Retin-A as possible therapy. Time has shown that it has positive results. It's a fantastic drug. He's a genius." End quote.
Erin Allmann Updyke	Okay.
Erin Welsh	And there's no denying that Retin-A has been incredibly valuable for many people. But I think it's important to remember that it wasn't Kligman dealing with the irritation, he wasn't pushing himself, he was just pushing other people who had no say in the matter. More than dioxin, more than radioactive isotopes, more than the mind control drugs, it was vitamin A acid, tretinoin, that fascinated Kligman the most. And he would be rewarded handsomely for it. After switching allegiance from Hoffmann-La Roche to Johnson & Johnson, Kligman helped bring Retin-A to the market where it first became available in 1971. The timing for Kligman could not have been better. The research program at Holmesburg was winding down, it would fully close in 1974. And Kligman was eager to leave that world behind, to explore the realm of cosmeceuticals. The immediate success of Retin-A gave Kligman the opportunity to think about not just how to study these drugs but how to market them. He believed that Retin-A held promise beyond just treating acne, that it could also reduce signs of aging.
	Kligman, although a lot of literature would have you believe otherwise, didn't come up with this on his own. His patients did. They told him that after a course of Retin-A, their skin looked younger, they had fewer wrinkles, it seemed to be brighter. Kligman didn't believe them initially. Quote: "I have always told students that if you start to believe your patients, you're gonna end up as a quack. I have a doctrine. Don't believe patients. So I was a victim of my doctrine." End quote.
Erin Allmann Updyke	Erin, these quotes cannot be real.
Erin Welsh	I know. I'm like this is a caricature of one of the worst like... Did he ever study hysteria? I can only imagine, right?
Erin Allmann Updyke	I have a doctrine, don't believe patients? Oh my. This guy is so celebrated. I cannot.

Erin Welsh	I know. Don't believe patients. If you believe your patients, you're a quack. He told students, like he trained students, right?
Erin Allmann Updyke	Yeah. I'm not trained in dermatology so I am only knowing what I'm reading on papers. So I don't know how much they like him in dermatology circles but I hope they don't. Because what?
Erin Welsh	Yeah. Yep. So there you go.
Erin Allmann Updyke	Cool, cool, cool. Yep, yep, yep.
Erin Welsh	I don't know what made him decide to eventually believe at least these patients. But in the early 1980s he began running experiments to see whether their claims had any basis. This time he used animal models it seems. But the reported results were remarkable, a complete transformation. Retin-A could be the most powerful anti-aging drug to hit the market according to Kligman. There was just one problem and it was a big one. Retin-A was approved by the FDA to treat acne, not as an anti-aging product. To sell it as an anti-aging product, Ortho, a subsidiary of Johnson & Johnson that made Retin-A, would have to get FDA approval for this new use which meant going through all those steps that would take years and lots of resources with no guarantee of success. And so Kligman proposed a workaround, a propaganda campaign using Ortho sponsored conferences, paid for doctors, ads in medical journals, articles in medical journals, features in fashion magazines, and testimonials on TV programs to promote the anti-aging, anti-wrinkle properties of Retin-A. The campaign was a major success. In 1987, the year before they started spreading the propaganda, 6% of Retin-A sales were for off-label uses. The following year it shot up to 65%.
Erin Allmann Updyke	Okay.
Erin Welsh	Sales grew to around \$1.5 million each day, which is 10 times higher than it had been before the campaign. Kligman for his part was getting paid by Ortho for his work as a consultant and enjoying his share of the royalties. This massive change in revenue stream and in off-label uses of course drew the attention again of the FDA. It was legal for physicians to prescribe off-label usage of Retin-A for their patients, like if someone came in and was like I want to try this out as an anti-wrinkle cream, can you prescribe this for me? Okay, I'm going to use it in this way. But it was illegal for a company to promote such off-label usage. The FDA began an investigation into Ortho for off-label marketing and this caught the attention of the popular media who saw the situation as the latest example of the sneaky doings of the pharmaceutical industry. An article about Retin-A in Money Magazine pointed out the following. It's a hefty list but I like it because it just... Have any of these things changed? Okay. Number one, the pharmaceutical industry's increasing propensity to bypass clinical physicians and promote new prescription drugs directly to consumers through the popular press.
Erin Allmann Updyke	I mean every single ad on my Hulu.
Erin Welsh	Yep. Number two, major corporate publicity of medical researchers who abandon objectivity for corporate dollars on behalf of new products and lavish PR campaigns.
Erin Allmann Updyke	Every single dermatologist and researcher who has their own skincare line now.
Erin Welsh	Yep, yep. Number three, the extremely close relationships between pharmaceutical companies and doctors.

Erin Allmann Updyke Weirdly especially true in dermatology. Like very. I mean there's supposed to be more things in place for that than there are.

Erin Welsh Yeah. Number four, the shallow perusal by the general press of pharmaceutical company press releases in the quest for bold headlines.

Erin Allmann Updyke Hi. Yeah.

Erin Welsh Number five, the FDA's underfunded, understaffed administrative situation in the face of well organized corporate initiatives and sophisticated publicity techniques.

Erin Allmann Updyke Imagine if we funded organizations that are supposed to protect the public!

Erin Welsh What a concept.

Erin Allmann Updyke Sorry, this was written yesterday or...?

Erin Welsh I know, right. 1988 I believe. Yeah. Yeah. So that is just... Have things changed? I don't think so.

Erin Allmann Updyke No.

Erin Welsh But all of this bad press was not ideal for Ortho. And things were only going to get worse because the University of Pennsylvania had caught wind of what was going on and sued Kligman for filing a personal patent for this new anti-aging Retin-A called Renova, effectively cutting out UPenn and keeping all the profits between Kligman and Johnson & Johnson.

Erin Allmann Updyke So sorry, but also because when you said that they sued him, I got really excited like they knew he did something wrong. But no, it's just because they weren't going to make any money off of it.

Erin Welsh They were like you cut us out. I know.

Erin Allmann Updyke Oh goodness me.

Erin Welsh The case was ultimately settled out of court to presumably everyone's satisfaction. But Ortho still had the FDA to contend with and they were panicking. Ortho ordered employees to start shredding documents, destroying videotapes, hiding any evidence at their employees' houses, that they had entirely orchestrated this plan to market Retin-A for off-label uses. It was such a shred fest. I'm not kidding. Isn't this wild?

Erin Allmann Updyke They really thought that was gonna work though?

Erin Welsh I know, I know, right. Every time. I don't know how they thought they weren't going to get caught, it doesn't make sense. And they definitely got caught.

Erin Allmann Updyke Yeah.

Erin Welsh

In 1992 the US government filed criminal charges against Johnson & Johnson. But a lot of the requested documents that were in those charges had been destroyed. So they were also charged with destroying documents. The trial went on for two years and corporate officials were very aware that every day that that trial went on, the release of Retin-A as an anti-wrinkle medication was delayed. And so in January 1995, they pled guilty to unlawfully promoting Retin-A for photo aging and for other unapproved indications. To the question of did Ortho knowingly and corruptly persuade and attempt to persuade the employees to destroy, mutilate, and conceal documents and other objects, they said yes. They also answered yes to did Ortho persuade employees to destroy those documents quote "with the intention to impair the integrity and availability of those documents and objects for use in an official proceeding". End quote. Their guilty plea brought them a hefty fine, a total of \$7.5 million which is one of the largest ever paid for an FDA violation at the time.

Erin Allmann Updyke

Wow. Yeah.

Erin Welsh

But to Ortho, to Johnson & Johnson, it may have well been pocket change.

Erin Allmann Updyke

Right. Especially compared to what they're about to make.

Erin Welsh

Exactly. They had already made millions, untold millions on off-label, well on Retin-A sales in general but off-label uses and they were about to make a whole lot more with Renova. A month after the decision, the FDA approved Renova for sale with a caveat on the label. Quote: "Renova does not eliminate wrinkles, repair sun damaged skin, reverse photo aging, or restore a more youthful or younger dermal histologic pattern." End quote.

Erin Allmann Updyke

Sorry, so it was proved to treat photo aging but they had to say that it doesn't treat photo-

Erin Welsh

Doesn't reverse photo aging. Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

Yeah.

Erin Allmann Updyke

Histologically.

Erin Welsh

Histologically.

Erin Allmann Updyke

Okay.

Erin Welsh

I don't know what the standard for-

Erin Allmann Updyke

We'll get into it.

Erin Welsh

Evidence was I guess. Yep. But it didn't really seem to make a difference in sales, right. Or at least like I don't know if it did, having that caveat on there. Because for every skincare product that promises eternal youthfulness and a wrinkle-free life, you'll find die hard supporters, you'll find clinically supported claims, and you'll find it next to impossible to actually get to the bottom of whether or not a product works as it's supposed to, all because of the vast sums of money to be made obscuring the truth. And I know that that's like a very cynical take and I'm sure that there are products out there that work or that work for some people. Which is why I'm really excited for next week's episode where you'll tell me all about the actual data on tretinoin and retinol and all of the rest of the retinoids.

But before I finally wrap this up for good and tell you my short list of sources, I want to circle back to what I said at the beginning of this history section. How we don't think enough about where our knowledge comes from and who bore the cost. We know about different hepatitis viruses and had an early hepatitis B vaccine in part because of the unethical experiments performed by Saul Krugman at Willowbrook State School on Staten Island. We know how syphilis progresses untreated in part because of the Tuskegee Syphilis Study which continued even though treatment was available. We know how the birth control pill works in part because Gregory Pincus measured its efficacy by testing it out on women in Puerto Rico who were never told the purpose of the pill or any risks involved. We know about tretinoin as a treatment for acne and possibly for wrinkles in part because of the unethical experiments performed by Albert Kligman at Holmesburg Prison. I'm not saying throw out your retinol in protest but just that I think it's so important that we remember how we came about this knowledge and all the knowledge that we have.

Erin Allmann Updyke

I feel like it's also what is so often missing from all of the discussions about the scientific achievements and advancements, like not just current ones but ones that we don't even think that much about. I think for me I know it's one of my favorite parts of this podcast is learning how even though it's usually very depressing and horrific, like I can always never believe that we didn't already know this.

Erin Welsh

Yeah.

Erin Allmann Updyke

That I didn't learn this in all of the training that I've gotten. It's so left out of the story.

Erin Welsh

It is. And I sometimes wonder why that is. Like obviously in a classroom setting, your time is limited and you need to get across this, this, and this. But do people think that it's a distraction?

Erin Allmann Updyke

Yeah.

Erin Welsh

So like for instance how Upton Sinclair's 'The Jungle' highlighted how gross the meat was instead of the worker conditions. Like do people think that it's just going to distract from how retinoids help with acne? I don't know.

Erin Allmann Updyke

I think it's bigger. I think it's in part, and maybe this is just me like hypothesizing too much or whatever, but I think it's also in part like the way that we always learn everything in isolation, right.

Erin Welsh

Yeah.

Erin Allmann Updyke

Like we're so used to well you have to learn your history in a history class. And like well you don't take a history of medicine class in med school, that's not a thing.

Erin Welsh

Right.

Erin Allmann Updyke

So you're never getting that then because you learned what European history or whatever history that you took in college as a general requirement? That has nothing to do with the specific field that you might be in and you never might learn the history of that field because I mean there's just too much to know. The same way there's too much science to know; there's too much history to know too. So yeah.

Erin Welsh

Right. Yeah. But it is that sort of that siloed nature of education.

Erin Allmann Updyke

Yeah.

Erin Welsh

Where if you learn about unethical human experiments, you're going to learn about it in a medical ethics class.

Erin Allmann Updyke

Right, in your ethics class.

Erin Welsh

Right. But you're not going to learn about it in your dermatology class.

Erin Allmann Updyke

No. Also I'm not sure that we even had a specific ethics class in med school.

Erin Welsh

I think I did in my epi master's.

Erin Allmann Updyke

Yeah, I might have had one there. But doesn't that seem problematic?

Erin Welsh

Yes, certainly does.

Erin Allmann Updyke

We all just need to learn, we need to learn it. We need to learn more.

Erin Welsh

We need to learn it. And speaking of learning it, sources.

Erin Allmann Updyke

Sources.

Erin Welsh

So I pretty much just had one for this episode which was 'Acres Of Skin' by Allen Hornblum. I also have a few other papers that I'll post that are by Kligman in case you are interested in reading like firsthand how he wrote about some of these experiments. And it's really funny, one has at the top like this research was sponsored by an unrestricted educational grant from Ortho Pharmaceuticals. Which is least it's like loud and clear.

Erin Allmann Updyke

At least it's easily disclosed and not like in the sub footing or whatever.

Erin Welsh

Right. It's not in the very, very last page after you've read it and you're like are you kidding me?

Erin Allmann Updyke

Right.

Erin Welsh

Like this is now like disclosure here? But yeah. So I will post all of those sources and also, Erin, your sources next week will go on the same page on our website thispodcastwillkillyou.com.

Erin Allmann Updyke

You can find the list of sources from this episode and every single one of our episodes there, check it out.

Erin Welsh

You can. Thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to Lianna Squillace and Tom Breyfogle for the incredible audio mixing.

Erin Welsh

And thank you to everyone at Exactly Right.

Erin Allmann Updyke

And thank you to you, listeners. We hope that you enjoyed this episode and are super stoked for next week's episode where we're going to get into what are these retinoids anyways and what is their evidence?

Erin Welsh

And a big thank you as always to our wonderful, generous patrons. We appreciate your support so, so, so, so very much.

Erin Allmann Updyke

Yeah, we do. Thank you.

Erin Welsh

Well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.