

## Dr. Mark Donaldson - Can Chlorhexidine (CHX) Provoke an Allergic Reaction?

Chiraz: Hello and welcome to CDA Oasis, my name is Chiraz Guessaier. We are back again with our esteemed expert and contributor to Oasis, Dr. Mark Donaldson, and today we are talking about a rare but existing allergy to a product that is too frequently used in the dental practice: chlorhexidine. However, before we delve into our topic of conversation, I'd like our viewers to know that Dr. Mark Donaldson is the recipient of the 2019 Special Friend of Canadian Dentistry Award. The award is conferred on an individual working outside the dental profession in appreciation for exemplary support and service to Canadian dentistry and to the profession as a whole. So, Dr. Donaldson, congratulations on the award and it's great to see you again on Oasis.

Dr. Donaldson: Oh, you too, Chiraz. Always my pleasure. And wow, that award, I'm still so humbled to be recognized by my dental colleagues. So, I'm very, very excited. It's been a tremendous week.

Chiraz: So, before we talk about the chlorhexidine reactions, can you briefly tell our audience what is the history of chlorhexidine and when was it introduced in dentistry?

Dr. Donaldson: Sure. So actually, the history is, I don't know if you'd consider long, but it was back in the 1940s that imperial chemical was the first company to actually synthesize and start to recognize a use for chlorhexidine. First available as a commercial product in 1954 in the United Kingdom. And then, ultimately, it became more of a household word, if you will, in 1969 when a company called Løe introduced it as a mouth rinse. And so, at 0.2% chlorhexidine gluconate solution, if you were to rinse with this mouth rinse twice a day, they found that it actually reduced plaque formation and development of gingivitis. In order to bring the drug to market, obviously they did clinical trials, and they actually found no clinical trial, uh, sorry, no side effects within the clinical trial.

Dr. Donaldson: So, that was pretty exciting. It did take a few years for kind of this product to come over the pond, if you will. And Procter & Gamble, you're probably familiar with them, back in 1986 put forward a new product called Peridex. So, I think Peridex is very familiar to our listeners today and something that we've been using for decades now, but rather than 0.2% it was available here as 0.12%. So, kind of an additional safety factor. Essentially what Procter & Gamble found was that at the slightly lower concentration you still got very good mitigation of brown tooth staining without any potential side effects. And um, this was actually one of the very first products that was approved by the American Dental Association Council on Dental Therapeutics, receiving their seal of acceptance for control of plaque and gingivitis. So, it's been a tremendous product. It's obviously widely used and in fact, looking at all of the safety data to date, the World Health Organization's model list of essential medications lists

chlorhexidine gluconate mouth wash as being essential to overall health. So, I think it's got a very interesting history. It seems to be a very, very ~safe product. But as you and I started to talk about, they're have been some challenges around it, potentially due to overuse. And then we'll talk more about that, I'm sure.

Chiraz: Well, it was indeed because I didn't know how prevalent the product was until I read your article and it was, it seems to be everywhere. So, you mentioned some of the uses of the product, what else is it used for in dentistry?

Dr. Donaldson: Yeah, so, in dentistry it has kind of a long, long list, if you will, for both primary and secondary prevention of gingivitis. Periodontal disease and carries, obviously use in that. Surgical endodontic irrigation, they use it for the management of postoperative sensitivity, cavity disinfection. So, a lot of additional indications above and beyond just being simply mouth rinse. The nice part is in 1994, it became generic, so much less expensive today, but it is found in a number of products from gels, sprays, toothpaste, periodontal discs, chips, varnishes, sugar free chewing gum, hand sanitizers. I mean, it really is kind of everywhere. And I know we focused on the dental realm, but in medicine we use this as a topical antiseptic in many cases, even as a surgical scrub prior to general surgery. So, very, very commonplace.

Chiraz: So, it's safe, it's prevalent, it's used. However, there are rare instances where chlorhexidine provokes actually allergic reaction. How is it allergic? What are some of the reactions that you found when you were doing the literature search and could it be lethal?

Dr. Donaldson: Yeah. So, short answer to all of those questions is going to be yes. But let's start at the beginning. We started to use this primarily because it's a very strong, not only an antiseptic, but also an antimicrobial. In fact, it has broad spectrum antimicrobial activity, meaning that it can actually kill a gram-positives, gram-negatives, anaerobes, fungi, and in fact certain viruses. So, it would seem to be, you know, a very useful product in preparing people again for either oral surgery or helping with oral health care or for general surgery in medicine. It has a very unique property known as substantivity. Now substantivity is basically how the molecule is able to attach to certain tissues. And from an oral health care perspective, it can adhere to both oral hard and soft tissues by binding to mucin.

Dr. Donaldson: So those are the proteins are responsible for salivary film over the teeth and mucosa. So, what this property allows for is basically the substantivity or the ability for chlorhexidine to last in the mouth far beyond just the initial application. In fact, we've got studies that show antimicrobial and antiplaque effects last, you know, 8 to 12 hours after a single application in the mouth. Topically, in medicine, we can see that when it's applied as an antiseptic on the

skin, you actually do get, um, prophylaxis, if you will, for up to 48 hours. So, it has been shown to be very, very effective given this sort of substantivity. Now, we talked a little bit about the history already, so I'll dive back into the history to talk about some of the allergic type reactions.

Dr. Donaldson: The first one actually was reported back in in 1965. So, the drug had been available for a while, and this was in a single case, and while there was sort of a temporal relationship, in other words cause and effect, I don't think it other than being a published case in literature really sort of garnered a lot of notice. This was a 72-year-old lady whose skin was swabbed with chlorhexidine prior to venipuncture and she developed sort of a urticaria hives and itching and swelling in that area. But that was the first one in '64. Now, now you jump forward to 1984 and suddenly we're seeing one or two other cases pop up. Again, typically topical type reactions, again in medicine. And, you know, the allergenicity of this started to gain some notice. By 1986, more than 30 cases had been reported in the medical literature.

Dr. Donaldson: And this was a range from, again, these sort of type IV hypersensitivity. In other words, sort of topical-type reactions all the way up to immediate anaphylactoid reactions resulting in hypotension and in some patients actually death. So, it um, it certainly garnered a lot of attention and you can see that's almost a geometric increase, which, which probably makes sense because the drug has certainly been used much more widespread. And so, with the additional exposures you're starting to see additional negative reactions. Chlorhexidine is often an adjunct in many different products. And so, you know, you see allergic-type reactions, but I don't think the connection has always been clearly made to chlorhexidine alone. So, the first reaction that we saw in oral health care providers, so the very first time we started to specifically see allergic-type reactions in dentists was actually published in 2018.

Dr. Donaldson: And so, this was a very interesting one because a dentist experienced this rapid onset of acute and diffuse urticaria, actually loss of consciousness. And this had happened a couple of other times. Upon sort of, um, investigation, what they found was that the doctor was exposed to aerosolized version of chlorhexidine, which was used for cleaning and disinfecting hard surfaces within the dental office. So just basically environmental exposure. Quickly following that, again, just last year, it was a case series of 14 patients and, not so much patients as healthcare workers and these were nurses, nursing students, midwives and actually an endoscopy technician as well. So, we've seen the use in medicine and the results into effect of allergies in patients. We've seen the use in dentistry and the allergic effect in dental patients. And now we've kind of gone full circle seeing exposure to healthcare workers and reactions from, again, topical non-life threatening urticaria type IV all the way up to type 1 IgE mediated anaphylactoid reactions resulting in death in some patients and workers.

- Chiraz: It is, like you have been talking about, it is very prevalent, and we don't want to scare our oral health professionals, but what are some of the steps that they can take? What can they do?
- Dr. Donaldson: Well, obviously knowledge is power, and I think the most important thing is, you know, read our article, be aware that this is something that is ubiquitous, but may not necessarily be as safe as we have always thought. And again, I would sort of insinuate that as we continue to use and in fact over use this product exposing more and more individuals to it, obviously that that can set up an antibody reaction so that future exposures can lead to these allergic-type reactions. So, awareness is the most important thing. I think second, the early, you want to have a high index of suspicion. In other words, if you are interviewing patients, uh, you know, most patients nowadays have been exposed at some point to chlorhexidine in many of the different products we talked about or prior to surgery.
- Dr. Donaldson: So, find out what historical reactions have been. If anybody ever reports that, yeah, I remember being prepped for surgery and, and you know, I had difficulty breathing due to something that they applied to my skin or if you had a dental patient that said, you know, I've used certain dental products and I've had challenges with swelling or itching or hives. Um, I think one of the biggest challenges too, from a dental perspective, is to recognize that the allergic-type symptoms are not always found in the mouth and so we don't always make that cause and effect that we apply chlorhexidine in the mouth with any one of the products that you and I spoke about and the patient's allergic-type response is actually topical or outside of the mouth. And we don't always make that association.
- Dr. Donaldson: Any patient that does report urticaria or dermatitis anywhere in the body, obviously should be referred to a dermatologist or allergist for testing. But really, without trying to scare everybody, the fact of matter is the incidents of allergic type-reactions is low. But you know, if you happen to be that one patient, you're that health care worker, they can be significant. So, I think it's just important to remember that. It does all almost remind me of our history around latex. So, we use latex in many different things in medicine and probably prior to 1980, we really in our general consciousness, didn't ever sort of suspect or hear about latex allergies. Well, here in 2019, we have a lot of people listing latex-allergic, probably because of our overuse of latex in so many different products. And where are we today? Well, no latex products are allowed in most hospitals because we just can't tolerate that type of reaction anymore.
- Chiraz: And one final question. Did the product ever change between the time it was introduced and today? Could that be a reason, or?

- Dr. Donaldson: Yeah. I do think that through good manufacturing processes, certainly the product today is much more purified than it was in the past. So, a lot of contaminants have been sort of taken out of the system. As I said, when it first came to market 0.2% was the topical amount being used. We're now down to 0.12%. So, I think that that is probably a safer amount. But overall exposure to the patient is probably the greatest thing. Sort of, if we're telling patients to rinse with Peridex twice a day, um, sometimes patients think, well, more is better, bigger is best and so if I do it four times a day, five times a day. You know, these drugs are all very, very effective in that the characteristics that I mentioned around substantivity, the fact of matter is this drug does not need to be applied more frequently and patients should really be counseled on the potential hazards of overexposure. Certainly, in regard to allergic-type reactions.
- Chiraz: Well, surely an eye opener. I personally use chlorhexidine and I never thought about it. I haven't had an allergic reaction up until now, so hopefully it doesn't happen, but, it's great information. And the article is great. We'll have it as part of the post also. Thank you so much, Dr. Donaldson. It's always a pleasure to speak with you and to learn from you.
- Dr. Donaldson: Thank you, Chiraz. So good to see you. Appreciate it very much.