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SCIENTIFIC ARTICLES

Endodontic Flare-ups: Bacteriological and Immunological Mechanisms*

Agudizaciones en Endodoncia: Mecanismos Inmunologicos y Bacteriologicos

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You have treated a typical asymptomatic granuloma and the same night the patient calls you and asks "What did you do to me?" The patient's face is swollen. Have you all had that experience? If anyone has not had it, he either does not do root canal therapy or he is a liar.

We assume that everything was done properly, i.e. nothing was pushed out through the foramen and the canal was treated in a sterile manner. You are in the stage now where you open up the lingual or occlusal surface of the tooth and the pus just runs out. Did you have that? Before, the canal was practically dry. And within 10 to 12 h you suddenly have a mass of pus and bacteria. Isn't that strange? One of the prices you pay for practicing endodontics is encountering the flare-up. How many of you have cleaned and filled a tooth in one visit? How many of you have cleaned and filled a tooth in several visits? Raise your hands, who does it in one visit; come on, it's all right, or several visits? How many of you do not have flare-ups? (Someone in the audience raised his hand and the following was Dr. Naidorf's response: "You do not have flare-ups?" "Stay here, I want to take a couple of lessons from you after the lecture!" Someone else in the audience said: "I do not have flare-ups because I use formocreosol." Dr. Naidorf said, "You think that formocreosol prevents flare-ups? That is all I use in my office and I get flare-ups! I was one of the first to use formocreosol and I still get flare-ups.")

Let me give you the biological principles that would explain how flare-ups could happen. You can understand how a flare-up happens if you force material from the canal into the apical tissues. You can understand how a flare-up happens if you put an irritant into the apical area; all the things, including formocreosol. I would like to point something out to you. That is, that bacteria in the canal and elsewhere can grow in different ways. There are aerobic bacteria or obligatory anerobic bacteria and there are so called AC/DC's; those that can live either way. To understand this a little better, let's take a quick look at glucose metabolism. In the Krebs cycle, 1-g molecular weight of glucose plus oxygen will yield the following:

$$C_2H_{12}O_6 + 60_2 \rightleftharpoons 6CO_2 + 6H_2O + \text{energy}$$

You get carbon dioxide, water, and energy. The energy, by the way, is about 54 ATP's. This is an aerobic process and is called cellular respiration, of which the result is an energy yield.

Let us take the same 1-g molecular weight of glucose during the anerobic break down and you will get two lactic acids;

$$C_2H_{12}O_6 \rightleftharpoons 2 \text{ lactic acids} + \text{energy}$$

The energy in this case is about 2 ATP's. This anerobic process is called fermentation or glycolysis. So we have

* This article is a transcription of the last lecture given by the late Dr. Irving J. Naidorf to the First Dental District in New York City in early September 1984, just 3 months before his death. The lecture was transcribed and edited by Syngcuk Kim, DDS, PhD, of Columbia University. The editor has made an effort to maintain the style and flavor of the lecture as originally given.

Este artículo es una transcripción de la última conferencia realizada por el recientemente fallecido Dr. Irving J. Naidorf en el Primer Distrito Dental en New York a principios de Septiembre de 1984, justo tres meses antes de su muerte. La conferencia fue transcripta y editada por Syngcuk Kim, DDS, PhD de la Universidad de Columbia. El director ha realizado el esfuerzo de mantener el estilo y la esencia originales de la conferencia.

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AC/DC organisms, which can go either way, with or without oxygen. The first one who discovered this was Pasteur and it is called the Pasteur effect. Organisms that grow anerobically will grow much faster in the presence of oxygen.

In order to initiate an infection anywhere in the body, a certain minimal amount of inoculum is needed. Organisms are there, but they are sealed in an anerobic environment. But as soon as you open it up and let oxygen get in, the growth pattern changes from anerobic to aerobic in a very short time. Remember that the formation of protein, DNA, and new enzymes, and so forth, are all endothermic reactions. They all require energy and the more energy that is available, the better these organisms grow. So, this theory, as far as I am concerned, has such elegant simplicity that even if it is wrong, I like it. In fact, there is no other way that we have of explaining this extremely rapid changeover. Remember my friends, the generation time of a bacterium is only about 20 min. If you start off with an inoculum which is relatively large, in a few hours the bacteria multiply to astronomical numbers. The question is what to do about it? What would *you* do after a flare-up? You do not send the patients away! You clean out the tooth! By the way, how many of you give local anesthetic for cleaning out the canals? Do you give antibiotics? How many of you have encountered the yo-yo syndrome? You open the tooth and clean it, the patient comes back and you reopen it and reclean it and close it and the patient comes back again. If this happens what would you do? (One student asked, "Is there any way to prevent the flare-up from happening or of predicting that it will happen?" Dr. Naidorf answered, "a part of the price of doing endodontics is flare-ups no matter how carefully you do endodontics."

Let me give you a couple of points. Number one, if you are connected with a hospital, then take a culture, send it to the laboratory and find out what organisms are present in the canal. This is number one and something positive you can do. Number two, some of the people, once they experience a flare-up, they are so frightened that they are afraid even to face the night alone. You will find that many patients will come to see you on Friday, before a weekend, dreading a flare-up. I take care of this situation in the following way: I see the patient in the morning and ask the patient to come back in the afternoon. In this way I am checking not only the possible drainage from the canal, but I also show a particular interest in the patient's concerns. Before a weekend, I tell the patient that I know, that everything is all right but that *I* would feel better if he or she came in Friday afternoon; it'll just take 10 min to open it up and to check that everything is o.k. In other words, they get the feeling that you are not just ignoring it, but have genuine concern for them. And I think that is about the sum and total of the way to handle it.

I want to tell you now about a kind of case that has given me an infinite amount of trouble. Everytime I had to extract a tooth, because of the yo-yo syndrome, and these are generally lower molars, I usually found a web of tissues *between* the mesio- and distobuccal canals, where it is impossible to clean. Do you get the point?

Another thing is pain. Never argue with patients about their pain. If they tell you that the pain reliever that helps them most is Darvon, do not tell them that what you are going to give them is better than Darvon. They have already made up their minds that it is Darvon!! What I do tell them is that I am prescribing it at a greater strength. This adds to the potency of the drug by psychological reinforcement and usually works better than a more potent but unwanted drug.

Let me now go on to the second type of flare-up: How many of you have had this happen? Mrs. X comes in with pain and swelling 10 to 12 h after starting endodontic treatment. She walks into your office and you say to yourself you have to relieve it, drain it! You open up the tooth and nothing comes out. So you take a barbed broach or a file and you push it about 1 mm past the foramen, figuring that maybe the foramen is closed and this will allow the exudate to get out. And what do you get? Nothing, but you *know* that there has to be pus up there because you see that it is all swollen. So you take some ethyl chloride and a lance, give it a spray, and what do you get? Again, nothing that you would expect. But this is an inflammatory response. It is triggered by an immune mechanism. I, and others, have shown the presence of immunoglobulins in the periapical areas. I have also shown that some of the immunoglobulins are related to the antigens in the canal. We can understand that if the canal had antigens and the granuloma has the antibodies, and you push materials through, you always get the antigens combining with antibodies. That is known as complexing. When antigens complex with antibodies, there is a whole series of things that happen, even in inflammatory ways, that you don't want to happen. So let me go through that in a simplified way now. If any of you are interested in more detail, I will be glad to talk to you after the lecture.

What you have been taught in school is that an antigen will meet up with its antibody like a toxin will meet up with an antitoxin and the antitoxin will neutralize it. That's not the whole story. There are a whole series of things that happen, that you don't want to happen. The complexing that occurs will do several things: it will trigger a complement cascade and it will go through a whole series of events of which I will give you a few highlights.

The complement cascade will run from C1 to C9. At C3 histamine will be released. C5 is chemotactic for granulocytes. C6 will cause bone resorption and at C9 it's cell lysis. Lets go back and look at this and see what it means to you as a practitioner. When the patient

gets swelling, where does the swelling come from? Histamine will increase capillary permeability and the increasing capillary permeability will cause edema. That is where you get the swelling and that is what you are dealing with clinically. Knowing that, what is the most commonly used drug that can be used to decrease swelling? Antihistamine. There are many, but I would recommend using the antihistamine which has the least side effects and which has to be taken least often.

Another thing that the antigen-antibody complexing will cause is damage to the cell membrane. When the cell membrane is damaged it will produce prostaglandins (PG's). PG's are very interesting substances; they cause bone resorption and amplification of the kinin system. For instance, kinin gives you pain and in the presence of PG it will give you more pain. PG's are also pyrogens; they cause fever as well as several other things. Aspirin and motrin are used mainly because they are antagonistic to or they prevent the synthesis of the PG's. In doing this, they are useful in preventing bone resorption, fever, and activation of the kinin system.

When Factor XII, the Hageman factor, is activated, let's see what it does. It causes platlet aggregation and it also forms plasmin, which triggers the complement cascade. Once the cascade starts, it does not stop by itself. Another thing it will do is activate an enzyme called free kallikrein which forms the active enzyme kallikrein. Kallikrein converts the precursor of bradykinin, bradykininogen, into bradykinin. Bradykinin does everything histamine does, but it also causes pain. It is one of the most severe pain-producing substances. In the presence of PG's, bradykinin is much more effective. It is as if you had $2x + 2x = 10x$. Let us carry this a step further! The Good Lord in all his wisdom has seen fit to put free kallikrein into saliva. It does not need the breakdown of bradykininogen, which is a long peptide, into bradykinin, which is a 9-aminoacid peptide. Kallikrein is there—it will form. Usually, this type of pain is over with in a hurry. The reason is you've got blood kininases and with one circulation through the lung bradykinin is finished. So you would think you need an area where there is continuing injury and irritation. Not so—because of the presence of free form kallikrein. There are two places where this happens: canker sores and dry sockets. Why? You have got a capillary bed that is open and saliva gets into it. And as soon as that happens, it converts serum bradykininogen into bradykinin. And that hurts a lot and is there all the time. When I went to dental school you know how we treated it? Tincture of benezoin or cavity punch. Anything that will cover that little ulcer is satisfactory to keep the saliva off it. In the case of dry sockets' I hazarded a guess that dry socket pain is caused by the presence of bradykinin in the socket because of the access to saliva. (Someone in the audience came up after the lecture and said that I was right about my guess. He had read an article published 2 years ago by a Scandinavian investigator, who demonstrated the presence of abnormal amounts of bradykinin in these areas.)

There is another funny thing that happens; phagocytic cells love to eat immune complexes. As a matter of fact, under anaerobic conditions, you can show that chemotaxis of phagocytic cells is impaired but not to immune complexes. They eat them up and then spit them out, but something happens. When they regurgitate the immune complexes, not only the immune complexes come out but all of the enzymes, the lysosymes come out, so what you have is damage to innocent bystander cells. So there is much greater damage than you would think. I have simplified this process purposely so as not to make it too cumbersome for you. I left out the discussion of leukotrienes, the discussion of some solid factors, the prostaglandins, what to do about them and so forth and so on. I have also ignored some of the cyclical events involved in the side effects of some of the processes.

Again, the point I want to make is that, once the process starts, much of it is self-perpetuating. That is why you see, in your office, that the clinical symptoms outlast the clinical events greatly. Patients have got pain and swelling lasting much longer then you would expect. And the reasons for this are these cyclical events. As a clinician you cannot do anything to cut down on the effects of bradykinin and the ingestion and regurgitation parts of the cycle. Bradykinin deals with itself. Where you will run into trouble as clinicians is with aphthous stomatitis and dry socket. What you can't do very much about is the kind of pain during injury, but remember that I told you that that pain takes care of itself. The reason that it takes care of itself is that some kininases destroy bradykinin and also because passage through the lungs destroys it, so it's not going to last very long. You are apt to get a spurt of pain but it is not going to stay there and bother you.