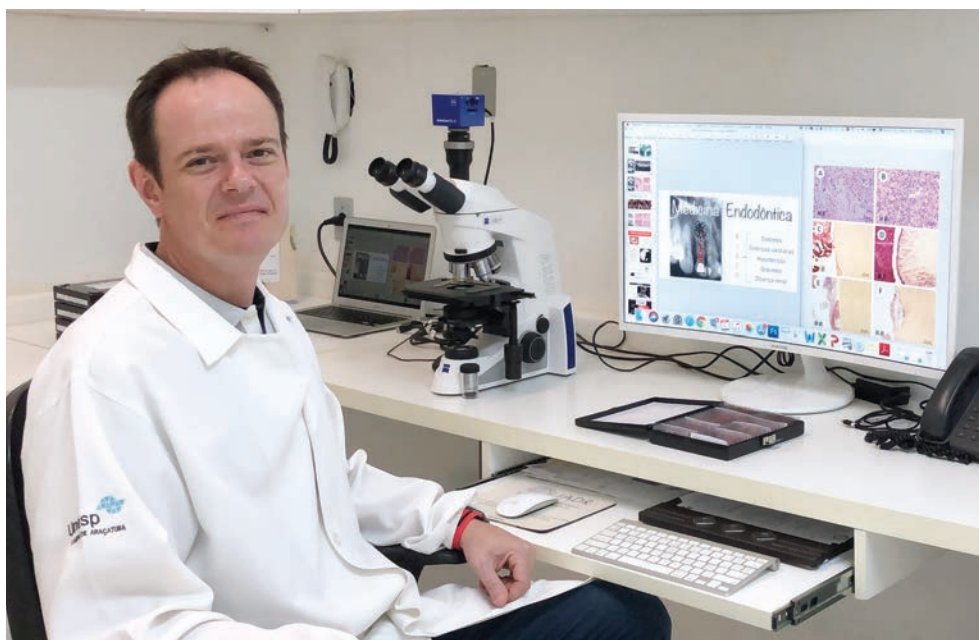


An interview with Luciano Cintra



- » Graduated in Dentistry from Araçatuba School of Dentistry – Unesp (1997-2000).
- » Specialist in Endodontics, Araçatuba School of Dentistry – Unesp (2001-2002).
- » Master in Dentistry, Endodontics, Bauru School of Dentistry – USP (2003-2005).
- » PhD in Dental Clinic, Endodontics, Piracicaba School of Dentistry – Unicamp (2005-2008).
- » Postdoctorate at Maringá State University – UEM (2011).
- » Associate Professor at Araçatuba School of Dentistry – Unesp (2014).
- » Associate Professor of the Endodontics Discipline, Araçatuba School of Dentistry – Unesp, since 2010.
- » Coordinator of the Specialization Course in Endodontics, Araçatuba School of Dentistry – Unesp.
- » Coordinator of the Postgraduate Program in Dental Science, Faculty of Dentistry of Araçatuba – Unesp.

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Interviewer

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I would like to start this interview by asking you to tell us about your general and Endodontic educational background.

I was born in Araçatuba/SP, on September 16, 1978, son of Barcelo Angelo Cintra and Celeste Tavares Angelo Cintra. I studied in public schools and went to high school at Objetivo. In 1996, I passed the college entrance exam and, in 1997, I entered the Dentistry course at Araçatuba School of Dentistry - UNESP. At the end of 2000, I completed my undergraduate degree and was approved to enter the specialization in Endodontics at the same university. I did my specialization in 2001-2002 and, at the end of this year, I was approved to attend the Masters Degree in Endodontics, Faculty of Dentistry of Bauru - USP. At the end of 2004, I was approved to attend the Doctorate, in Dental Clinic, Endodontics area, Piracicaba School of Dentistry - Unicamp. In early 2005, I defended the Master's degree and entered the Doctorate.

All of my specific training has been in the area of Endodontics and my special expression of gratitude for the knowledge acquired goes to my mentors of the Specialization Monographs, Prof. Pedro Felício Estrada Bernabé; Master's Degree Ivaldo Gomes de Moraes; and Ph.D. Caio Cezar Randi Ferraz. Thank you!

What field of research are you in?

My background is all in the biological field, and the masters, doctorate, postdoctoral and free teaching were all in animal models. I had the opportunity to live with Prof. Roberto Holland and his team, and that made all the difference. Currently, I integrate the Araçatuba Endodontics team and work in two research lines:

- » Study of physical and biological properties of materials used in endodontics (<http://dgp.cnpq.br/dgp/espelhogrupo/5672908869738071>).
- » Interrelationship between oral infections and systemic alterations (<http://dgp.cnpq.br/dgp/espelhogrupo/8503565738089034>).

The first study is the trademark of Araçatuba Endodontics - which, since the 1960s, has been producing science and collaborating with the evolution of the specialty. The second study is a line of research that was built along with Prof. João Eduardo Gomes-Filho, from 2010, with my arrival in Araçatuba Endodontics team.

This second line of research you mentioned about the interrelationship of endodontics with systemic health has been highlighted in the scientific literature, and you and your group have been contributing to it. How did this line of research in Araçatuba come about?

We need to go back in time to understand how this happened. Even as a graduate student, I heard about the Theory of Focal Infection, in courses and lectures given by Prof. Pedro Felício Estrada Bernabé, my first great teacher. Accompanying his courses in Brazil and abroad, I witnessed the public reaction - sometimes amazed; in others, discredited or even outraged - so that my appreciation for this controversial theme became more intense.

When I was teaching for the first time in the Ingá School of Dentistry (Maringá/PR), I had the opportunity to relive this subject in the discipline "Prevention and Healing", taught to students of the last year. Again, speculation about the subject arose, and the study of this interrelation was deepened. In partnership with the Biomedicine course of this faculty, we began studies evaluating different systemic parameters in patients with oral infections (TNF- α , IL-4, IL-6, IL-8, free fatty acids, cortisol, C-reactive protein, leukocytes, insulin, endotoxins, nitric oxide, calcium, phosphorus and alkaline phosphatase). Secondly, we treated local infections (periodontal disease and endodontic infection) so that, in a long-term follow-up, the systemic profile of these patients could be evaluated again.

In parallel, in conversations with Prof. Tiago Novaes Pinheiro, pathology professor and a great friend, we discussed the need to perform these studies in animal models, providing better standardization, excluding certain variables, and easy sample acquisition. In this new design, we defined diabetes as the first of the systemic changes to be studied and correlated with oral changes. With the study of diabetes, it was possible to know in depth its manifestations and even the need to study the inverse pathway of the problem, ie the influence that systemic diseases, such as diabetes, could have on the oral cavity tissues, whether the tissues were sick or not.

Thus, we seek to enable the study of diabetes in animal model, with the collaboration of Prof. Zélio

Fedatto Junior, Professor of Biochemistry, who was knowledgeable about the procedure for inducing diabetes by alloxan. In partnership, we conducted three studies inducing diabetes and analyzing changes in healthy pulp tissue or induced endodontic infection, work that gave rise to three studies guidelines: “Study on pulp changes resulting from diabetes induction and progression in rats”; “Evaluation of the influence of diabetes on the development and progression of pulp disease. Radiographic study in rats” and “Evaluation of the influence of diabetes on the development and progression of pulp disease. Histological study in rats”¹.

At the end of 2009, we would continue the clinical study in patients; however, I returned to UNESP as a substitute teacher, and in 2010, after approval as Prof. Assistant Doctor, new challenges appeared. Already at UNESP, in one of the first conversations with Prof. João Eduardo Gomes-Filho, regarding that I would like to continue in Araçatuba, we realized that our goal was common. On that day, Prof. João opened a project that he had written, entitled: “Assessing the Effect of Endodontic Treatment on Type 2 Diabetic Patients.” From that day on, we looked into the topic and numerous researches were published.

What were your biggest challenges and how was it possible to settle this line of research?

The biggest challenge has always been to study a topic that few research groups in the world study. The biggest difficulty is not having parameters in the scientific literature so that we can discuss and compare our findings. On the other hand, the success of this line of research has been achieved through the numerous partnerships we have made, where each researcher, with his or her expertise in a particular area, was critical to success.

The first partnership was with Prof. Doris Hissako Sumida, Professor of Physiology at FOA/UNESP and an expert on diabetes, whose collaboration in the streptozotocin-induced diabetic model was fundamental for the sedimentation of these studies²⁻⁸. Once the experimental model of standardized diabetes was settled, we sought partnership with Prof. Suely Regina Mogami Bomfim, veterinarian and professor of the Veterinary Clinical Laboratory discipline, Faculty of Veterinary Medicine of Araçatuba - UNESP. With Pro-

fessor Suely, we were able to know the hematological parameters and their relationship with the individual's systemic condition, which brought interesting results to science^{9,10}.

Expanding the studies on the hematological profile, we had the opportunity to meet Prof. Paulo Cesar Ciarlini, veterinarian, professor of the Veterinary Clinical Laboratory discipline, Faculty of Veterinary Medicine of Araçatuba - UNESP, who directs and coordinates studies on oxidative stress and tissues antioxidant capacity. Other studies have emerged and contributed to the understanding of the interrelationship between systemic diseases and oral tissue infections and/or alterations^{11,12}.

Considering the need to study inflammatory cytokines and their role in different tissues, we count on the fundamental collaboration of Prof. Valéria Marçal Felix de Lima, Professor of Immunology, Faculty of Veterinary Medicine of Araçatuba - UNESP, whose background in basic immunology allowed the deepening of studies in different tissues and organs, contributing with new scientific information^{5,9}.

Having established the systemic front of the studies, we felt the need to know better the tissue dynamics, and we look for Prof. Edilson Ervolino, Professor of Histology and Embryology at FOA/UNESP and extremely experienced with immunohistochemical techniques. Thus, the study of inflammatory cytokines, which is part of the strategy to study the mechanisms of cellular action in the inflammatory response, could be better explored^{13,14}.

After further studies with the diabetes model, our group expanded the study of systemic changes by standardizing different experimental models, such as atherosclerosis^{15,16}, hypertension^{14,17,18}, osteoporosis¹⁹⁻²¹, menopause²¹, alcoholism²², acute renal failure, liver fibrosis, pregnancy, and others in standardization process, such as Parkinson's disease and cancer.

What were the most important discoveries?

As I mentioned, in this line there are few findings regarding endodontic infection. Thus, most studies bring some new knowledge and, at the same time, indicate the need for further studies^{13,23}. Using a standardized animal model, we found that endodontic infection, when associated with diabetes and periodontal disease, can influence triglyceride levels²,

creatinine³, glycosylated hemoglobin⁶, platelets¹⁰, pro-inflammatory mediators such as IL-17⁵, body and organ weight²⁴, inflammatory markers in organs²⁵, besides altering some blood count parameters, especially the white series⁴.

Isolated endodontic infection was able to alter the insulin signal of the blood and skeletal muscle tissue^{7,8}, in addition to influencing insulin resistance in hematological and muscle tissues^{26,27}. When associated with diabetes, it influenced serum oxidative stress¹¹.

We also found that the presence of four apical periodontitis was able to increase triglyceride levels^{28,29}, inflammatory cells^{12,25} and pro-inflammatory mediators such as IL-17, IL-6, TNF- α , IL-23 and nitric oxide⁹ in hematological tissue. These findings suggest that the impact of endodontic infection on systemic health is proportional to the number of infection foci present^{13,23}.

What are your future expectations and what would be the contribution of these studies to society?

We are now convinced that a serial extraction therapy as an alternative to the treatment of systemic disorders, fostered by the theory of focal infection, is outdated. However, there is a need to improve knowledge about this interrelationship, as the way it is established is not yet fully understood. Perhaps the answer lies in the type of manifestation and local condition that may have some effect on systemic health or in distant regions¹³.

We know that the bacteria present in the oral cavity may participate in the etiopathogenesis of other diseases, by migrating the bacteria to the focus of extraoral infection or by establishing a chronic systemic inflammatory picture from the infection located in the mouth⁴.

Recent scientific evidence suggests that endodontic infection may interfere with systemic health through these two mechanisms, mainly by the continuous release of various chemical mediators and inflammation byproducts. Elevated plasma concentrations of these substances over prolonged periods may influence the onset or progression of other disorders⁶.

Thus, studies that aim to interrelate oral infections with systemic changes, and vice versa, are necessary and of great scientific relevance. Involving the study of the development of local infection and the pathways of dissemination to the organism, as well as the influence of different systemic changes on the development and maintenance of local infection, is a major horizon yet to be explored³⁰.

Our aim is to better understand the mechanism of this interrelationship, so that more effective therapies can be instituted for patients with systemic changes. In this sense, some other aspects of this research line were created to verify the efficacy of different products, such as drugs, supplements and probiotics, as well as clinical protocols, aiming at improving the systemic condition and reducing the impact on endodontic infection development^{31,32}, contributing to the process of tissue repair after endodontic treatment.

Hence, despite several recent discoveries, the interrelationship between endodontic infection and systemic health still needs to be better elucidated in order to determine effective actions to promote population health. This path will certainly lead to an improvement in the quality of life, as the interdisciplinary approach between doctors and dentists in its fullness is unfortunately not yet a reality in Brazil.

Finally, I thank the Great Architect of the Universe for giving me what is necessary to work for the development of science and for the welfare of others. Also, I'd like to thank you for remembering my name for this interview.

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