Bob ten Cate: 'Ninety percent of the cells in our body are bacterial cells'

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Bob ten Cate, speaker at the 2013 BDA/BDJ Winter Lecture, describes how we are just scratching the surface of understanding bacteria in biofilms.

Why were you attracted to studying teeth?

I was never trained as a dentist. I was originally trained as a chemist, specifically in the area of polymers and physical chemistry. As part of my master's thesis I wanted to do a medical project so I studied the development of bonding cements for orthodontic brackets. That was back in the early 1970s. Then, during my master's studies, I had the option of going to work for Shell or Dutch State Mines (DSM) but I wanted to continue to work in the medical research field. So I was offered the opportunity to work on a project to investigate the retention of polymers to dental enamel. That was quite successful, and my first publication, in the *American Journal of Orthodontics*, came as a result of that.

From there I just kept going in the dental field. I took up a PhD position in Groningen looking at the fundamentals of enamel remineralisation and the effect of fluoride on it. This was predominantly thermodynamics and physical chemistry. Then, quite early in my career in the mid 1980s, I was offered a professorship in Amsterdam to further develop my own group. That was a difficult time for chemists because it was right after the oil crisis so that professorship provided a good opportunity for me.

I stayed in the dental field throughout my career, working on fluoride, erosion and calculus formation for the majority of the last 40 years or so. Actually I became head of a big clinical department and I think I was the first non-clinician to run a clinical department. Subsequently I was appointed Dean of the Dental School in Amsterdam. Later it became more common for a person without a dental qualification to head up a dental school.

I've always been very much involved in a combination of research and administration, and also served in many international organisations. For example, I was President of the European Organisation for Caries Research and President of the IADR. I always say I have the most wonderful job that I could ever have had because it is an excellent combination of doing research that is meaningful and being able to run a group. I have always enjoyed it and still do. My research is an application of chemistry which I think is very useful and allows us to really make a difference. I always say that I work on the 'chemistry of the mouth'.

Dr J. M. ('Bob') ten Cate is Academy Professor with the Royal Netherlands Academy of Arts and Sciences (KNAW) and Head of the Department of Oral Health Sciences at the Academic Centre for Dentistry Amsterdam (ACTA). His research focuses on caries prevention and oral infectious diseases, specifically the mode of action of fluorides and antimicrobials. In the past he served as Dean of ACTA, President of the European Organisation for Caries Research (ORCA), World President of International Association for Dental Research (IADR) and Editor-in-Chief of *Caries Research*. He has received many awards including the ORCA-Rolex Prize (1986), the Yngve Ericsson Prize for Prevention (2000), the IADR Distinguished Scientist Award in Caries Research (2003), an honorary doctorate University of Oslo (2010) and an Award of Excellence EurFedConsDent (2011).

Was there every a challenge in leading a clinical department as a non-clinician?

Not really, I had a number of dentists around me and of course I was careful to stay away from clinical decisions or decisions that involved patients. I've probably seen as many X-rays in my life as any dentist in research but I know the line that you should not cross as a non-dentist and that has never been a problem.

What were you able to bring from your foundation in chemistry to your work in dentistry?

I think I was able to bring theoretical knowledge. For instance, you could never study enamel remineralisation without an understanding of thermodynamics. In the past, one of the reasons why the impact of dental research was limited was that the research was very pragmatic. People really knew too little about the basics. Though the different countries

do vary in the amount of background scientific information dentists qualify with. For example, in the US you go to a pre-med college for four years before you start dentistry or medicine, whereas in the UK or The Netherlands people start dentistry right after school. So if you do dentistry you have very little additional training in the basic sciences. With a combination of people with basic sciences training and those with experience of dealing with patients you can make a difference. In my group there is a mix of PhD students who are dentists and scientists. You need this mix.

Why is understanding the microbiology of biofilms so important?

I worked on fluoride and the hard tissue side of dental caries for a long time. Around 2000 we realised that we needed to find out more about the bacterial side of dental caries. I felt that we really knew everything about fluoride that needed to be understood from a fundamental point of view. We had all the fluoride products we would need. Dental caries is now really limited to the lower socioeconomic groups in society and is predominantly a behavioural science issue. That's why we gradually moved to studying dental plaque.

The biofilm field really emerged around 2000 and we dove into that. Until then, not much progress had been made in that area. At the same time there were a lot of new techniques being developed, such as microscopic methods and the discovery of bacterial genomes, allowing us to go more in depth in studying the aetiology of caries. I got some really good people in my group with great backgrounds in microbiology and molecular biology so we were able to take off.

Five points about biofilms that dentists should know?

1. We really need biofilms. A healthy biofilm can protect you from invasion by pathogens. It increases your colonisation resistance to other bacteria, just as for antibiotics. If people are using more antibiotics they are more susceptible to other infections.
2. Ninety percent of the cells in our body are actually bacterial cells. So most of our physiology is actually the physiology of the combined bacteria.
3. We should be aware that biofilms are much less sensitive to anti-microbial treatments than isolated bacteria. This is critical because in the past all the agents were developed through studying culture systems with isolated bacteria. One of the things we have done in our group is to develop a model of the biofilm as it occurs in the mouth and then look at the modern agents to see how they affect the bacteria inside the biofilm. The biofilm is resilient. One of the reasons for this is that agents diffuse slowly into it. This also means that the bacteria are initially warned by the anti-microbials and can upregulate all of their defence mechanisms against it.
4. We have begun to understand that biofilms in the mouth have similar properties to biofilms elsewhere in the body. And also elsewhere in nature; for example, they are related to the layer of bacteria on a ship's hull. This is interesting as it means biofilm research is global research, not just restricted to the oral research field. Many people who work on other types of biofilm find that the mouth is really interesting to study because it is so easy to sample. It's easy for you to open your mouth for the researcher to take a sample of the biofilm.
5. Bacteria in biofilms have many subtle mechanisms of interaction between each other and to try to kill them with something as crude as chlorhexidine or similar chemotherapeutics is not an appropriate way to deal with them.

What new approaches do you see in dentistry in ten years' time as a result of biofilm research?

I think we will see a whole new set of agents developing because we know more about the physiology of the biofilm. We know more about how bacteria interact in the biofilm to survive. One of the things we found out five or six years ago is that there are so many different bacteria in the biofilm. Traditionally people were interested in about ten bacteria – those responsible for dental caries, periodontitis and gingivitis. But we discovered, using DNA-based assessment methods, that there are actually a lot more bacteria in the plaque but you cannot culture them in traditional culture media. We are not seeing the full story as we have only been able to culture about 50% of the bacteria in our bodies. Indeed, 95% of the bacteria living in the earth are not culturable by traditional methods. I think this is where things are really changing with the introduction of new DNA-based techniques.

We can better understand what is there and also how the bacteria live together. For example, if bacteria all have different growth rates then why doesn't one out-compete all the others? We now know this is because they have very intricate methods of sensing each other, namely quorum sensing. The quorum sensing molecules notify them to slow down their metabolism if they are above a certain population level. They know that if they keep producing at a maximum rate they will produce waste at a maximum rate, which would result in them killing each other. I always say that they are more clever than humans – if a lot of human people are together in a party they make more noise, if bacteria are together at the party they make less.

Generally dentistry will change because of evidence-based dentistry and all the guidelines etc. In the past dentists were to a large extent working on their own, doing the things they thought were best. Nowadays, with the internet (and databases such as Medline and the Cochrane databases) patients are becoming much more knowledgeable. This also means that they are more critical. That will change clinical dentistry.

What one thing would help reduce global caries levels?

The 'triple A principle': accessibility, affordability and availability. There are many countries around the world where you still cannot get fluoride toothpaste or they are so expensive that people cannot afford it. I think that the appreciation of how important oral health is for general health is significant. In some countries around the world the whole health budget is less than we would need solely in oral care to get people to a proper level. Some people are working

very hard on stem cells and implants etc but I think we really should focus more on prevention. It is much less costly and you can do a lot.

People have shown, in countries such as the Philippines, that with very little money you can really make a difference and also get oral healthcare promotion incorporated into general medical programmes for improving health. Of course we know that in many countries where people's income is improving, teeth are not the first thing they think about. Usually they increase their sugar consumption because they can afford it and it is only much later that they start to worry about their teeth. Like I said the accessibility and affordability of oral care products and the appreciation of how important oral health is is really important on the global level.

What about water fluoridation?

That is the perfect way to provide fluoride. However, it is a political problem. We had that political discussion in the Netherlands before I started in the dental field. Between 1963 and 1973 we had fluoridation of the water and it was stopped for political reasons. However, there are still countries where water fluoridation is starting.

In your career to date, what are you most proud of?

I'm really proud of the way colleagues have appreciated the work that we do; if you get a lot of prizes for research that is something to be proud of. We have developed a number of models that have been used to study dental caries in more detail, and now also models for biofilms. These have started to be used around the world by different groups. Also, students from China, Brazil etc that worked in our group here in Amsterdam took these models home with them. I think that is one thing we are proud of: that people appreciate your work and you see that reflected in other people using your models and citing your work.

What past scientific discovery do you wish you could have been responsible for?

The discovery of fluoride. This is really fundamental in caries prevention. People have been trying to look at different anti-caries agents and have been unable to come up with anything else so far. In the dental field, it is the most important discovery ever.

What do you dream of discovering yourself before you retire?

In our work on biofilms we seem to have some clues that the biofilm composition could give us an indication of the caries risk of a particular individual. So biofilms might perhaps be used for caries prediction in the future. I have to say that with a lot of caution but if we could have that it would be of enormous economic benefit. We spend so much time and resources in healthcare on dental issues and if you could somehow limit that, it would be very important.

Interview by Ruth Doherty

Bob ten Cate will be giving this year's BDA/BDJ Winter Lecture, kindly sponsored by Wrigley Oral Healthcare Programme, at the BDA on Thursday 12 December 2013. His talk, entitled 'Biofilms: a new approach to dental plaque', will subsequently be made available to all BDA members to view online. More information at www.bda.org/winterlecture.