

Iain Chapple: 'As a clinician, you assume that people know what periodontitis is'

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Iain Chapple talks to the *BDJ* about implant failure, the teaching predicament for UK dental schools and why we must teach the public about the dangers of periodontitis.

Why did you choose dentistry?

I wanted a care-based career but I needed it to be practical as well as theoretical. The truth of the matter is that, at the age of 15, I had a very romantic picture in my mind of having a country practice where I knew all the families and generations. That picture changed within six months of working practice when I realised I couldn't be in the same room, doing the same thing day in, day out. Personally, I needed more variety.

I worked for a year part time in practice and, don't get me wrong I enjoyed it, but I did find it incredibly limiting. It may have been because it was in the early days when it felt like a treadmill. I wasn't able to deliver work at the quality I was capable of for my patients, and when I did try to do it that way I was finishing at eleven o'clock at night. I gave one old lady a lift home having fitted a denture at 10:55 pm! It was not a good place to be in those days. I think it's very different now and there are a lot more opportunities.

Once I left practice one of the reasons I didn't then go on to become an NHS consultant was because I enjoy teaching, research *and* my clinical work. The only way to do all three was to become an academic.

What research projects are you working on at the moment?

Lots! A great deal of what we do is basic science: asking questions about why and



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Iain has published over 200 research papers and abstracts in scientific journals; written and edited seven textbooks; and authored several book chapters in the field of periodontology, periodontal medicine and surgery. He is the former scientific editor of the *British Dental Journal* and a current associate editor of the *Journal of Clinical Periodontology*. He was president of the International Association for Dental Research (IADR) Periodontal Research Group in 2006-2007, and is currently treasurer of both the European Federation of Periodontology (EFP) and UK Oral and Dental Research Trust. He co-chairs the EFP workshops in research and education. Iain was awarded the Charles Tomes Medal of the Royal College of Surgeons of England in 2011.

how a disease develops. Teasing out the mechanisms of diseases allows us find new ways of treating them. So we do a lot of work with epithelial and skin cells, and investigate how these cells respond to the bugs and talk to each other. We work with white blood cells (neutrophils) because they are probably the most destructive cells in terms of periodontal health. We have also started to do a lot of work analysing proteins – asking questions such as what is in crevicular fluid; what is in saliva?

I think it is important to avoid research that doesn't have a clinical question to start off with or it is in danger of becoming a little bit esoteric and almost pointless. We are always thinking about diagnosis or about treatment, for example a lot of the basic research we did has

been on oxidative stress. Oxidative stress underpins an awful lot of chronic diseases. It occurs when oxygen radicals swamp out the body's antioxidant defence systems, then you start to get disease developing. We found that periodontology patients often have antioxidant deficiencies so we started to develop treatments based on natural products that you find in fruits, vegetables, spices, etc. We took these nutritional treatments into the lab and looked at how they affected the cells. We found that they calmed down inflammation in these cells so we started to investigate their efficacy in clinical trials and published the first of these last year. This was one of the first trials really looking at fruit and vegetable extracts in a concentrated form to investigate whether or not they improve

treatment outcomes in periodontal disease. We also work with industry on topical applications, developing natural ways of trying to calm down inflammation as a way of managing periodontal disease.

What about your work on salivary diagnostics?

This is an important area for us. In terms of diagnosis, a lot of what we have discovered comes from analysing saliva. We have discovered new proteins that we didn't know existed before. Some of those appear to discriminate between healthy gums, gingivitis and periodontitis. We are working with a company who have handheld diagnostic technology to try and develop a saliva test that would enable us to work out if a patient appears to have periodontal disease or not. This could be done by a nurse or a receptionist, provided the patient is then referred to the dentist or the periodontist.

Other research I am doing is in collaboration with a young colleague of mine, Owen Addison, looking at mechanisms of implant failure. Owen has done some great work demonstrating that titanium is not inert. It breaks down in the tissues and fires off the immune response. It obviously happens very slowly but we have never really understood why the implant failure rates are starting to increase dramatically, failures starting at around eight to nine years. Some of the figures are as high as 50% failures. If we can understand why they are failing we might be able to do something about it. Implant companies used to define failure as loss of the implant. But now we have some better definitions such as progressive bone loss and pus formation. All of a sudden you can identify that the failure rates are much higher. When implants start to fail, unlike teeth, it's very hard to stop them failing because you don't have a periodontal ligament with stem cells to regenerate, just bone and titanium.

Tell us about your work in general health and systemic disease.

In Birmingham we are very fortunate to have some holistically thinking medical colleagues. Together we created something called the Chronic Disease Resource Centre (CDRC). It's basically a collaboration between the kidney physicians, the

rheumatologists, the lung physicians, the diabetologists and us (the periodontologists). All the pathways that cause these diseases are the same though they may have different triggers.

The first cohort we worked with was chronic kidney failure patients. These are patients whose kidneys are failing at different rates so some of them end up on dialysis, some sadly die and some end up having transplants done. In this ten-year project we have examined well over 600 patients and we find that patients with chronic kidney disease have much higher levels of periodontal disease than the population (85% as opposed to 50%). But what's really interesting is that if you measure how stiff their arteries are and you compare the kidney disease patients who don't have periodontal disease and those that do, the ones with periodontal disease have significantly stiffer arteries. So the two chronic inflammations together seem to have an effect on cardiovascular risk. We are sampling saliva to see if we can identify diagnostic markers for rapid kidney failure. We will be investigating whether intervening to treat the periodontal disease improves kidney failure rate and cardiovascular health. Because we have a whole host of medical measurements in addition to the oral measurements it's an absolute gold mine of information. The idea is to do the same with lung disease, diabetes and arthritis.

The oral-systemic interface is a big one for us. All the studies that have been done on these different conditions show robust associations independent of the common risk factors but there is always the possibility of residual confounding and genetics. For example, if someone is susceptible to inflammation they are going to be susceptible to heart disease and many other inflammatory diseases. So ultimately you have to do intervention studies but they take a long time and are expensive to run.

The public perception of gum disease and its significance for general health looks like it's set to change – do you agree and how quickly do you think this will happen?

On my way to the last European Federation of Periodontology (EFP) Workshop in Spain (more info in

information box below), I got in a taxi to go to the venue and one of the people running the media campaign Javier Garcia jumped into the back of the taxi with me and shut the door. It was like being hemmed in by the Mafia! He said '*right, we have an hour and a half, let's talk*'. He asked a very interesting question: '*If you asked the public in the UK what periodontal disease was, would they know?*', and I had to say that I didn't think they would. He pointed out that this was a starting point, just making people aware what periodontics is.

As a clinician, you assume that people know what it is. However, the reality is that though they might be familiar with the term 'gum disease', they don't know what periodontitis is or how common it is, what the consequences are, or that it is a silent disease until it's too late. I think if they did know those basic facts a lot of people would be a lot more motivated towards getting it checked out. The EFP realised a few years ago that the things we were really good at was the science side of things and the big congresses, but we are terrible at communicating with the public. So we produced a strategic plan and there is now a whole section on communication with the public, and also with general dentists and other general medical workers. We have invested a lot of money to raise people's awareness about perio.

What is your proudest research achievement to date?

It's always the most recent one! About eight years ago there was an amazing paper published in *Science* by a German group; it showed that when neutrophils die they don't go quietly. If pushed hard, due to a lot of bacteria challenging that cell, they literally release all of their DNA in an explosion into the cell. The cell literally vomits its DNA into the tissues. The DNA is sticky and the bacteria get caught on it. All of the enzymes and the various toxic chemicals that neutrophils use to kill bugs are also released. The DNA mixes with these enzymes and antimicrobial proteins, and so the bugs get stuck and die. People are saying it's a brand new, powerful killing method. We didn't know it existed before. Now we understand why some patients suffer from severe infections because they cannot

produce these neutrophil extracellular traps (NETs). However, there are other diseases that are triggered by the DNA itself, conditions like lupus for example, so NETs are a double-edged sword.

The research I'm most proud of actually defined the trigger mechanism that releases the NETs. It was really fundamental stuff and we proved that the trigger identified by the group to first define the NETs was incorrect. There was a flaw in one of their experiments. It took a long time for us to do it but we demonstrated what the trigger actually was. This enabled us to take a group of patients suffering from a horrible disease called acute granulomatous disease (where they can't produce NETs or O₂ radicals) and by supplementing their cells with the trigger they were able to produce NETs. It involved a careful, stepwise series of experiments that ended up with a patient at the end of it to prove that it actually had physiological and clinical relevance.

What advice would you give to someone setting up a clinical trial for the first time?

The regulatory process involved in running clinical trials now is horrendous, almost inhibitory. So my advice would be to allow a hell of a lot more time than you think it's going to require. Don't think you are going to get your ethical approval overnight. If you haven't run a trial before, go to a professional clinical trials design centre (and every university has them now) as it will save you a lot of time. The most important thing is to have a very clear question and really well-defined outcome measures. That's what the success of your trial is going to be judged on.

Also, make sure you have a really good team. I have a fantastic team. Some of the best people for running clinical research trials are dental nurses because of the way they are trained. They are meticulous, incredibly organised and rigorous; nothing slips past them so when it comes to having clear audit trails they are invaluable.

You are the Designated Individual for the Human Tissue Authority in Dentistry at Birmingham – what does this involve?

Like a lot of government organisations now, someone is made personally

responsible to ensure that regulations are implemented. I take that responsibility at Birmingham – this involves consent for biomaterials and their storage for research, which may sound easy but in reality is a minefield. It is about having secure biobanks for tissues etc and making sure that everything is done properly to ensure patients' identities and best interests are protected.

I must say that the Human Tissue Authority (HTA) is a fantastic organisation and they have revolutionised regulation. Their attitude is not one of blame, unlike some other government organisations. They empower you and are pragmatic. Now, if something serious goes wrong they come down on you like a ton of bricks as they should do, but they are actually incredibly helpful to work with. It's a really good way of getting compliance and improving standards. The other agencies need to learn from them, particularly the CQC. The area around human biomaterials is incredibly emotive so it's high risk taking a supportive approach, but the HTA have certainly pulled it off.

Teaching – what are your tips on keeping students (of all ages) engaged?

Teaching is probably the thing that I still get the biggest buzz out of for two reasons. Firstly, if you can really motivate a group of students you get immediate positive feedback. With research it can take a hell of a long time for that to happen.

Secondly, I went through a period of looking at dental students and seeing how they have gone from Cs to Bs and A*s; brilliant kids coming in to university. Then, when I had them on clinic they did not appear to be particularly bright at all; they were not interested and they didn't have searching minds. I reflected on it and realised the reason for that is because of the way we teach dentistry. We teach dentistry didactically; we take these bright kids and we almost de-intellectualise them. That was a big lesson for me which I learnt relatively recently when I presented to a tutorial group, for a laugh, all the complex science we were doing on NETs. It was way beyond them but they were transfixed, asking incredibly intelligent questions. When they left

that tutorial, on what was essentially basic science, they left buzzing because it was relevant and it was coming from Birmingham where they were studying. It made me realise these are really intelligent kids and what we need to do is keep challenging them. So now when I run tutorials I just fire questions at them; the students are active and we have fun. I set very clear standards; they don't cross a certain line and they know that.

It's about motivating students and I don't think we are very good at that in dental schools. At the moment academic dentistry has a massive problem in this country because it is a small, orphan discipline and schools have a paucity of staff. So if you are in the medical school you can be a high-flying researcher and you won't be expected to do teaching as there is a sufficient number of staff. In dentistry there is no chance of this. I make a real effort to keep myself engaged with teaching. What often happens is, because of the pressure on academics to bring grants in, publish papers and run their research groups, the first thing to go is the teaching. Then it becomes the responsibility of part-time staff, which is unfair on them because they don't have the time to prepare or train. I think that's a real problem. It doesn't matter how senior you are, you have a duty to engage in educating these students. If you want to get a message out and make a difference, teaching is the best way to do this.

As a journal editor yourself, what are your views on the future for dental publishing?

Publishing is hugely important and incredibly difficult. It is going down the open access route which raises huge challenges for publishers. The main challenge is assuring the quality of papers in open access journals. Another challenge is that publishing relies massively on the academic community giving up their time free of charge. What you want is someone to spend at least an hour and half reading the paper and writing a valuable report. One-liners and straight accepts are not useful to an editor as no paper is perfect.

One thing that we are suffering from a lot now is that everyone is busy and

it is really hard to get good reviewers. The danger of paying reviewers is that they might do it for the wrong reasons and end up doing lots of reviews to earn money with the risk of little or no real increase in quality. Quite a lot of academics go into academia because they are conscientious people. But busy lives and workloads mean that getting quality reviews is hard today. As an editor, I once had to send a paper to 22 reviewers to get it reviewed!

Three desert island research papers?

1. Brinkmann V, Reichard U, Goosmann C *et al.* Neutrophil extracellular traps kill bacteria. *Science* 2004; 303: 1532–1535. This 2004 paper described NETs for the first time. It is a stunning piece of research and I still enjoy reading it. It was beautifully illustrated; with wonderful microscopy. It is an example of a really top quality contemporary research, with lots of different techniques and methods used to produce a robust outcome.
2. Loe H, Theilade E, Jensen S B. Experimental gingivitis in man. *J Periodontol* 1965; 36: 177–187. This paper reports Harold Loe's classic study on experimental gingivitis. It was simple, really clever and it proved (not quite 100%) that plaque causes gingivitis. He stopped people cleaning their teeth for a period of three weeks and observed that gingival inflammation developed. The clever bit was taking the plaque away and when you did that the inflammation resolved. If things get better when you intervene you have *almost* demonstrated causality. I say *almost*

because of course it didn't quite as in stopping them brushing, it stopped them massaging their gingival tissues with a toothbrush. So it may not have been the plaque build-up but the lack of massaging with the toothbrush. They had to do a follow-up study doing chemical plaque control to eliminate the mechanical effect of the toothbrushing.

3. Brånemark P I, Adell R, Breine U *et al.* Intra-osseous anchorage of dental prostheses. I. Experimental studies. *Scand J Plast Reconstr Surg* 1969; 3: 81–100. This is a basic science study describing Per-Ingvar Brånemark's work on titanium blocks. He was studying healing around titanium plates in rabbits (I don't support animal research at all but there are certain situations when sometimes you have to prove a point). When he went to remove the plates he couldn't get them out because the bone had integrated with them. That was the birth of osseointegration. This may have been a chance finding but it is a landmark paper in dentistry that has had an impact on surgical and medical care in general. Quite often the key research findings are serendipitous.

What luxury would you bring to the island?

Am I allowed to say my two girls and my wife? If I've got to give you something else it would have to be my Bang & Olufsen system. I love technology that is beautifully designed. Though it's obscenely priced, that stuff. The first one I bought was after working for two years and all I could afford was the amplifier and the radio tuner, no

speakers. I sat on the floor of the flat in the dark just watching the lights go up and down with a pair of cheap headphones plugged in. Isn't that sad?

As a child I never had much opportunity to engage with the arts and it's a massive regret. So both my young daughters have had arts fed into them from the day they were born. Arts and science are so integrally linked; a different way of thinking but so important. I couldn't be without music.

To the island the music I would bring is Led Zepplin *Four* or a live Genesis album because it's intelligent music, timeless. Or maybe Pink Floyd 'Wish you were here'!

Interview by Ruth Doherty

'The EFP and Perio Awareness UK'

The European Federation of Periodontology (EFP) is one of the largest dental organisations in Europe, with 28 national periodontal member societies (www.efp.org). The associated member society in the UK is the British Society of Periodontology (BSP) – www.bsperio.org.uk.

In 2013, the EFP, in association with the BSP, launched Perio Awareness UK: a nationwide campaign to raise awareness of the importance of healthy teeth and gums both to the general public, and to GPs and the general medical profession. Find out more on Twitter @HealthyGumsUK and on Facebook by liking their group 'Perio Health Awareness UK'.

In November 2012, the EFP held a PerioWorkshop to bring together researchers in the field of periodontology from all over the world to carry out a comprehensive systemic review of key studies into the links between diseases in the mouth and those affecting other vital areas of the body. You can watch interviews with key attendees and read about the review outcomes by visiting the comprehensive webpage: <http://perioworkshop.efp.org>.

The next EFP conference, Europerio, will take place in London in June, 2015. More information about the meeting can be found at www.efp.org/europerio.