



Graham Lloyd-Jones tells **Caroline Holland** how in 2021 he identified the potential role of the mouth as a critical disease pathway for SARS-CoV-2.

he wisest step anyone in the general population can take to boost their health is to maintain good oral hygiene. So says Dr Graham Lloyd-Jones, a consultant radiologist from Salisbury, UK. Who in dentistry would disagree? You might question, however, why a doctor should give out this advice, and with such authority.

Dr Lloyd-Jones has recently become an evangelical oral health campaigner, and you are likely to hear or see his name frequently in the coming year. He has been working with the World Dental Federation (FDI) in collaboration with Iain Chapple, Professor of Periodontology and Consultant in Restorative Dentistry, to educate on the oral systemic link. He and Professor Chapple are also studying long COVID with research teams in Cardiff and Birmingham, while Dr Lloyd-Jones is at the early stages of writing a book on the links between oral health and development of systemic diseases.

Dr Lloyd-Jones says: 'It's a simple concept – in those with poor oral health the mouth is like an open wound. The absorption pathway for pathogens passing across damaged oral mucosa is the same as for the skin – pathogens can pass into the blood but do not pass through the liver, as is the case for absorption via the gut. Oral pathogens have direct access to the systemic

circulation, which explains why they end up all over the body and are directly implicated in the development of multiple important systemic diseases.

For someone who only two years ago had to look up the word *periodontology*, his conversion to the impact of oral health on systemic health has been spectacular!

A consultant radiologist at Salisbury
Hospital, Dr Lloyd-Jones' interest in oral
health resulted from researching COVID-19.
He describes how, when the pandemic began
in early 2020, he was head of the Radiology
Department, charged with preparing to receive
affected patients. At that time, COVID-19 was
labelled as a pneumonia, a condition with which
he was very familiar.

As soon as he began to study the chest X-rays and CT scans of affected patients, however, he questioned whether this was indeed a disease of the airways, as would be expected for a viral pneumonia like influenza. He would have expected bronchial wall thickening and inflammation of the airways. Instead, he saw a pattern of lung damage which would be expected in the context of clots forming in the small blood vessels at the edges of the lungs. He says the term *pulmonary vasculopathy* (disease of the lung blood vessels) is a better description than *respiratory pneumonia*.

If SARS-CoV-2 were entering the lungs via the bloodstream, he pondered, how could this

be happening? Applying his detailed knowledge of the human anatomy, he went on a mission to identify the mechanism, reading autopsy reports and speaking to other specialists, such as haematologists and respiratory physicians. 'It was like going back to medical school. Why was this lung disease happening like this?'

His zeal for finding answers led to an invitation to join a Southampton-based academic research group studying inpatients with COVID-19 – their study will soon be published. Continuing to research he came across a link between gum disease and COVID-19. He learned that the risk factors for periodontitis are the same as for severe COVID-19 and speculated that gum disease could be a converging risk factor, even the main risk factor, for severe COVID-19.

He rang up two of his friends, one a dentist and the other an oral surgeon, asking whether damaged mucosa of the gums could be the anatomical pathway to the lungs via the blood. They both confirmed his ideas made sense, explaining that the gingival epithelium is easily breached by bacteria in plaque biofilm, so why not a virus? The missing link between the blood and the lungs, they agreed, could well be gum disease. Dr Lloyd-Jones set to work, developing a scientific hypothesis, first published on his own educational website in February 2021.

One of his dental friends put him in contact with Professor Chapple, the UK's foremost

authority on the oral-systemic link. They had a long discussion on the phone one Sunday afternoon in February 2021, and then teamed up to publish a formal hypothesis in the *Journal of Oral Medicine and Dental Research*.<sup>2</sup> 'Iain had given me so much that I needed, I invited him to co-write the paper. It was one of the best decisions of my professional life. Collaboration across our different medical specialties has been fruitful in terms of building understanding both of COVID-19 and how the mouth might be involved in the development of other diseases of the body'.

The hypothesis Dr Lloyd-Jones proposed and developed with Professor Chapple is that the virus enters the body via the upper respiratory tract and then replicates dominantly in the mouth, a *factory* and *reservoir* of SARS-CoV-2, before passing into the blood via damaged gums. A single teaspoon of saliva, says Dr Lloyd-Jones, can contain 500 million copies of the virus. This route of infection is already familiar in dentistry, infective endocarditis being a prime example (patients with certain heart problems who require dental treatment are given antibiotic prophylaxis to protect them from bacterial infection of the heart valves).

The hypothesis would explain the findings of a 2020 study of patients with periodontitis and COVID-19 performed in Qatar by Marouf and colleagues. The team found that periodontitis was associated with a much higher risk of admission to ICU and death.<sup>3</sup>

Salisbury Hospital has been praised for its initiative by Sara Hurley, Chief Dental Officer, England, who said: 'Every patient care pathway, in every hospital, should include routine daily mouth care.'6

Frustratingly for Dr Lloyd-Jones, the pioneering mouthcare regime designed to help patients and staff remains largely limited to Salisbury. 'It's abundantly clear that paying attention to mouthcare is massively important for all sorts of inpatients. Add oral health education into the hospital setting and patients go home quicker and die less, so why are we not doing it everywhere?'

In addition to pushing the oral health agenda, he wants to promote the inclusion of dentists in medical collaborations. 'The thing about medicine is we are siloed, and academic medicine is particularly bad with everyone focusing only on their own narrow field. A concerted, collaborative approach to learning about COVID-19 will mean we learn about other diseases too. I think the thing that has been missing all along is a focus on understanding the disease itself rather than the pandemic. We have had Government advisers giving us statistics - the numbers of people going into hospital, the numbers dying, the numbers being vaccinated - but none of this tells us why some get the severe disease and others do not.'

He and Professor Chapple speak regularly and, having learned about periodontitis, Dr

load in the context of acute COVID-19, and a radiology paper on the vascular nature of the acute lung disease.

Meanwhile, in response to his new-found evangelism, everyone he can possibly influence is becoming far more attentive to their mouths. 'Many of my friends are now more motivated to see their dentist and, perhaps more importantly, the dental hygienist who are key to good oral health'

It is small wonder he is building a name for himself, but he is quick to dismiss his growing reputation: 'I am not interested in being known, I am interested in what I have to say being known. It is time for the world of medicine to take oral health seriously'.

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Having proposed that good oral hygiene might have a protective effect, Lloyd-Jones found that a team in Cardiff had identified that mouthwash products containing cetylpyridinium chloride (CPC) and ethyl lauroyl arginate (ELA/LAE) showed an antiviral effect in saliva. Their study is now published in the *Journal of Lipid Research*.<sup>4</sup>

Inspired by Dr Lloyd-Jones, Salisbury Hospital introduced mouthcare guidance for patients with COVID-19.<sup>5</sup> Dr Lloyd-Jones is also leading a quality improve programme in the hospital with the acronym of SMILE:

Salisbury

Mouthcare

Initiative

Linking oral health to general health Excellent care for every patient. Lloyd-Jones has broadened his interest to understand oral dysbiosis. 'Existing research shows us a clear association between poor oral health and diseases of the body on an epidemiological level. What we need to do now is to pin down the pathological mechanism for each disease.'

The role of Dr Lloyd-Jones as an anatomist and an educator is highly valued by Professor Chapple. There are many more questions to answer about the oral health systemic link than he has time for, but undeterred, he chips away at this 'untapped seam' of medical research.

He continues to work with multiple research teams, including initiation of a pilot study into long COVID which kicked off at the start of January, a systematic review of the efficacy of specific mouthwash products to lower the viral

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