

Professor Iain Chapple PhD, BDS, FDSRCPS, FDSRCS, CCST (Rest Dent)

Professor of Periodontology and Consultant in Restorative Dentistry

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About

Iain Chapple is Professor and Head of Periodontology within the School of Dentistry, College of Medical and Dental Sciences, the University of Birmingham. Iain is also honorary Consultant in Restorative Dentistry with Birmingham Community Health Trust and has honorary consultant contracts with University Hospital Birmingham Foundation Trust and Birmingham Children's Trust. Iain is the Designated Individual for the Human Tissue Authority in Dentistry at Birmingham.

Iain has published over 200 research papers and abstracts in scientific journals, and written and edited 7 textbooks and authored several book chapters in the field of Periodontology, Periodontal Medicine and Surgery, Nutrition and Molecular Methods. Iain has received major grants from the Medical Research Council, European Union and Industry.

Iain is a committed and enthusiastic teacher of undergraduate and postgraduate students within Birmingham and also internationally on various graduate programs across Europe, North America and Asia-Pacific rim.

Iain is former Scientific Editor of the British Dental Journal, current Associate Editor of Journal of Periodontal Research, Editorial Board member of Journal of Clinical Periodontology and Periodontology 2000.

Iain was elected President of the International Association for Dental Research (IADR) Periodontal Research Group (PRG-2006-7), and is currently Treasurer of the European Federation of Periodontology (EFP) and UK Oral and Dental Research Trust. He co-chairs the EFP workshops (research and education).

Iain is clinical lead for a hospital regional specialist periodontal service (referral base >6-million) and a national oral care service for adult Epidermolysis Bullosa patients.

Qualifications

- Honorary fellow of the Royal College of Surgeons of Edinburgh (Dental Surgery) 2004.
- Certificate of completion of specialist training (Rest Dent) – joint Royal Colleges 1996.
- PhD (University of Birmingham) – 1993.
- Fellow of the Royal College of Physicians and Surgeons of Glasgow (Dental Surgery) 1989.
- Bachelor of Dental Surgery (Newcastle) 1986.

Biography

Iain Chapple qualified from Newcastle Dental School in 1986 and became House Surgeon until 1987, when Iain was appointed Senior House Officer in Maxillofacial Surgery at Sunderland's District General Hospital. Here Iain obtained his part-1 FDS of the Royal College of Surgeons and in 1988 Iain became Registrar at Leeds Dental Institute (Restorative Dentistry) and St James Hospital (Oral Surgery). Iain completed his Fellowship of the Royal College of Physicians and Surgeons of Glasgow in 1989 and moved to Birmingham as Clinical Lecturer in Restorative Dentistry in 1990. In 1993, Iain completed his PhD in developing enhanced chemiluminescence assays for biomarkers of periodontal inflammation and in 1996 Iain completed his certificate of Completion of Specialist Training in Restorative Dentistry from the Joint Royal Colleges.

Iain spent a post-doctoral period in 1995 developing chemiluminescence assays for oxidative stress at Harvard's Forsyth Institute, Boston, USA and was appointed to Senior Lecturer and Honorary Consultant at the University of Birmingham in 1996 when Iain also became head of the Periodontal Department. Iain was appointed to his personal chair in 2001 and leads the Periodontal Research Group (PRG), part of Birmingham's MRC Centre for Immune Regulation and the Centre for Ageing Research. Iain was awarded the Charles Tomes medal by the Royal College of Surgeons (2011), the Rizzo Research Award of the IADR PRG (2001). Iain won the British Society of Periodontology (BSP) Sir Wilfred Fish research prize (1993) and former PhD students (Roberts, Brock, Milward) also won this award. In 2010 (Dias) and 2011 (Palmer) post-doctoral fellows of the PRG won the Past Presidents Award of the IADR PRG.

Iain established the clinical trials team at Birmingham's Dental School in 1994, which runs clinical studies on disease pathogenesis as well as diagnosis and therapy to international GCP standards. The trials team allows for the translation of basic research by the group.

Iain has delivered annual keynote lectures/symposia at IADR, EuroPerio, and British Dental Association. The PRGs interests include:

- Innate immunity in the pathobiology of periodontitis.
- Diagnostic biomarkers for periodontitis and associated systemic diseases.
- Periodontal inflammation and systemic inflammatory conditions.
- Periodontitis and immunosenescence.

- Micronutritional modulation of inflammation.
- Clinical trials in periodontal therapy.

Teaching

- BDS
- BSc in Dental Hygiene and Therapy.
- MSc Advanced General Dental Practice.

Postgraduate supervision

- I Garner 1994-1998 - successful.
- H Wight 1998-2002 - successful.
- A Roberts 2000-2006 - successful.
- F Murdoch 1999-2002 - successful.
- G Brock 1999-2003 - successful.
- M Milward 2003-2010 - successful.
- L Palmer 2006-2010 - successful.
- E Allen 2006-2010 - successful.
- M Ling 2009-current.
- 2011-2015 2 MRC College studentships.

Research

RESEARCH THEMES

- Innate immunity, Clinical Trials, saliva/GCF biomarker analysis, microbiology, molecular nutrition.

RESEARCH ACTIVITY

Characterising the saliva and GCF proteome

- As we age our bodies change and leave behind markers of these changes. Powerful profiling techniques such as “proteomics” can determine these changes. Recent studies have already identified changes between young and older women by analysing their saliva. This fluid contains many proteins that are involved in immunological protection as well as serum derived proteins. The group is currently employing highly accurate and sensitive mass spectrometry techniques such as FT-ICR MS/MS with i-TRAQ labelling to profile changes in the saliva proteome in healthy, diseased (gingivitis and periodontitis) and edentulous patients, as well as in gingival crevicular fluid (GCF). As the oral microflora changes with age, as well as with disease, using sensitive meta-proteomic techniques will help us to unravel biomarkers for healthy ageing and non-invasive techniques for disease diagnosis. Higher levels of biomarkers for dental caries (decay) associated proteins (Cystatin S) have already been found to be elevated in elderly patients with caries and many more discoveries are being made. Most recently, new peptides never before described in the periodontal environment have been identified, which provide insights into aspects of periodontal microanatomy and physiology never before contemplated. The development of biomarkers for early diagnosis of periodontitis and associated systemic diseases for near patient testing is a major focus.

Molecular nutrition & oxidative stress

- Micronutrients can drive or resolve oxidative stress through various pathways including regulation of redox-sensitive gene transcription factors. A major interest of the PRG is in understanding how micronutrients control cell signaling pathways and in doing so regulate the inflammation. Clinical trials are also ongoing to evaluate novel therapeutic approaches through micronutrients applied systemically and topically and also to unravel pathogenic mechanisms in periodontitis.

Neutrophil extracellular trap formation

- Recent reports of neutrophil hyper-reactivity in terms of ROS release and the involvement of IFN α in disease pathogenesis, have also, for the first time, raised the spectre of an autoimmune component to the pathogenesis of periodontitis. Moreover, type-1 interferon's and ROS are associated with neutrophil extracellular trap (NET) formation. Whilst normally neutrophils combat periodontal pathogens by intracellular (phagocytosis) and extracellular (degranulation) mechanisms, NET killing has recently been described as an important new paradigm in neutrophil biology. NETs consist of a web of extracellular fibres of DNA plus histones (chromatin) and granular proteins, which bind to Gram-positive and Gram-negative bacteria. These chromatin structures immobilise high concentrations of extracellular antimicrobial peptides, including cathepsins and myeloperoxidase along with histones, leading to physical entrapment and killing of pathogenic bacteria. Lack of NET production (e.g. in Chronic Granulomatous Disease) or presence of bacteria that express DNases which breakdown NETs, results in increased pathogenic activity and potentially catastrophic infections in certain patient subsets. The DNA-histone backbone of NETs acts as a target for endogenous or bacterial peptidylarginine deiminases (PADs), which citrullinate histones as well as other proteins, by deimidating arginine residues, potentially rendering them auto-immunogenic. Further studies are currently ongoing in this area to determine whether this mechanism of generating auto-antigens links periodontitis to other age-related systemic diseases, such as rheumatoid arthritis, and whether decreased efficiency in NET production associates with immune-senescence.

Studying neutrophil behaviour

- Evidence suggests that periodontitis occurs in individuals who have an abnormal neutrophil response to subgingival plaque bacteria and that neutrophil-mediated oxidant injury is an important feature of the disease. Peripheral blood neutrophils from periodontitis patients are hyper-reactive, after Fc γ R and toll-like receptor (TLR) stimulation, as well as being hyperactive in respect of unstimulated, extracellular release of reactive oxygen species (ROS). Although Fc γ R hyper-reactivity is reduced by therapy, baseline, unstimulated-ROS release is not, suggesting that reactive and constitutive mechanisms underlie the “hyper-inflammatory” phenotype. Priming with GM-CSF or the periodontal pathogens *Porphyromonas gingivalis* and *Fusobacterium nucleatum* (1 bacterial cell per neutrophil) reduces the Fc γ R-mediated hyper-reactivity but not hyperactive, baseline unstimulated ROS release.
- Hyper-reactive neutrophils differentially express 25, type I interferon-stimulated genes and IFN α , which can enhance Fc γ R-mediated ROS generation in vitro, and is increased in plasma from periodontitis patients. Recent studies from this group have demonstrated that the ability of periodontitis plasma to prime for f-MLP-mediated ROS generation is, in part, due to the presence of GM-CSF, IL-8 and IFN α , supporting the idea that peripheral neutrophils in periodontitis patients are in a cytokine-primed state. Interestingly, transcripts for GM-CSF and IL-8 are up-regulated in gingival epithelial cells after stimulation with *P. gingivalis* and *F. nucleatum*, (see above), perhaps indicating that local tissue responses to plaque bacteria may contribute to peripheral neutrophil hyper-reactivity. There is currently, no data on the behaviour of PMNLs from older patients with respect to ROS release in response to different priming agents or to periodontal bacteria, and such studies are planned in order to shed light on this potentially important cause of periodontal tissue damage in older patients.

Analysing the oral epithelium

- Epithelium was traditionally perceived as a simple inert physical barrier, whose role was to prevent microbial entry into the connective tissues, thereby protecting the host's vital systems from the external environment. However, contemporary research has revealed that epithelial cells play an active role in the host response to bacterial infections. Gingival (gum) epithelium is intimately related to the bacterial plaque biofilm and research at the Birmingham Dental School has demonstrated that gingival epithelial stimulation by key periodontal pathogens results in activation of cellular transcription factors, which regulate production of pro-inflammatory cytokines. This finding suggests a key role for epithelium in the initiation and propagation of periodontal inflammation. However to date, research investigating how the responses and behaviour of oral epithelial cells change as we age, and thus impacts on these important mechanisms is almost completely lacking, and may help explain the increasing prevalence of periodontitis in older patients.

The Periodontal Research Group (PRG) at Birmingham proposes studies to explore age-related changes in oral epithelium in terms of:

- Changes in efficiency of bacterial recognition (via pattern recognition receptors).
 - Activation of redox sensitive transcription factors (NF-kB, Nrf-2, & AP-1).
 - Gene transcription profiles.
 - Levels of cytokine production.
 - Levels of certain antioxidant micronutrients.
 - Changes in epithelial permeability and barrier function and how these may be manipulated using novel micronutrient approaches.
- The development of novel therapeutic approaches to periodontal therapy is a priority.

Other activities

- Treasurer of European Federation of Periodontology.
- Treasurer of UK Oral and Dental Research Trust.
- Specialist advisor to Department of Health in Periodontology.
- Board member of the European Nutraceutical Association.
- Associate Editor of Journal of Periodontal Research.
- Editorial Board member of Journal of Clinical Periodontology.
- Editorial Board member of Periodontology 2000.
- Executive Committee member of European federation of Periodontology.
- Global Expert Panel – Unilever Oral Care Research.
- Expert advisor for Philips Oral Healthcare.
- Expert advisor for Johnson & Johnson.
- Consultant to PreViser.co.uk – spin out company of The University of Birmingham.
- Executive Board member of European Nutraceutical Association.

Publications

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Grant MM, Creese A, Barr G, Ling M, Matthews JB, Chapple ILC. Proteomic analysis of a non-invasive human model of acute inflammation and its resolution: the 21 day gingivitis model. *J Proteome Res* 2010; 9, 4732-4744.

Matthews JB, Wright HJ, Roberts A, Cooper PR, Chapple ILC. Hyperactivity and reactivity of peripheral blood neutrophils in chronic periodontitis. *Clin Exp Immunol*, 2007; 147; 255-264.

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