Challenges of the interface of Oral Medicine and Periodontology – some lessons for the future?

Stephen Porter Institute Director and Professor of Oral Medicine

UCL Eastman Dental Institute

256 Grays Inn Road

London WC1X 8LD

Newell W Johnson

Honorary Professor of Dental Research, Griffith University, Queensland, Australia;

Emeritus Professor of Oral Health Sciences, Faculty of Dentistry, Oral and Craniofacial

Sciences, King's College London

Stefano Fedele

Professor of Oral Medicine

UCL Eastman Dental Institute and NIHR UCLH Biomedical Research Centre

256 Grays Inn Road

London WC1X 8LD

All correspondence:

Stephen Porter

Institute Director and Professor of Oral Medicine

UCL Eastman Dental Institute

256 Grays Inn Road

London WC1X 8LD

Tel: +44 (0) 20 3456 1038

Fax: +44 (0) 20 3456 1039

Email: S.porter@ucl.ac.uk

Abstract

This final chapter provides a commentary of what might be learned from this series of articles in relation to the 2017 Classification of Periodontal and Peri-implant Diseases and Conditions and argues that future classifications should expand sections on non-dental plaque-induced disease that will further patient care, education and research in periodontology and allied subjects.

Introduction

The present series has demonstrated the breadth of disorders, unrelated to dental plaque- induced gingival and/or periodontal inflammation, that may impact upon the gingivae and/or periodontium. There are notable challenges ahead for oral health care that require to be considered in light of the changing diversity and epidemiology of disease and the need (and wish) for clinicians to provide safe, effective, long lasting care that demonstrably lessens disease burden and enhances the quality of life of affected individuals.

Across the globe the management of disorders of the periodontal structures or the oral mucosa is usually undertaken by different types of clinicians, each sometimes but not always having followed separate training pathways and thus having different competencies and clinical demands. Unless there is common understanding of the risk factors and clinical presentation of disease, and a working appreciation of how a particular disease should be managed (and who should do so), there is a risk that a patient may not receive the most appropriate care to return them to optimal oral health and systemic wellbeing. This Volume of Periodontology 2000 clearly indicates that practitioners of Periodontics are interested in knowing the possible relevance of such diseases to their practice. This, together with the relatively recent publication of the 2017 classification of the periodontal diseases[1], provides impetus to consider how the fields of Periodontology and Oral Medicine might be harmonised to enhance patient care.

The 2017 Classification of Periodontal and Peri-implant diseases – an Oral Medicine viewpoint

The fact that diseases and disorders of the periodontium have a wide range of causes and mechanisms has long been recognised as has the interdependence of local and systemic causes and responses [2]. The 2017 Classification of Periodontal and Peri-implant diseases recognises this. This new classification represents the agreed conclusions of a workshop comprising representatives of the European Federation of Periodontology and the American Academy of Periodontology, both of which have an international reputation for excellence in aspects of Periodontology and Implantology. The classification provides a summation of opinions as to the clinical presentation of health and disease of the gingival and periodontal structures and, as appropriate, there is emphasis upon plaque-induced disease and the factors that may influence the presentation or risk of such disease. A relatively small section that considers the classification of non-dental plaque-induced gingival and/or periodontal disorders is included. This covers a very large spectrum of disease presentations and pathogenic mechanisms.

The 2017 classification will be undoubtedly of significant help in informing and shaping research, education, clinical care and ultimately positively impacting upon patient wellbeing. However, publication of the present Volume of Periodontology 2000 allows the opportunity for those in Oral Medicine to suggest that future classifications should consider modification of the non-dental plaque related disease section, as it does not entirely reflect the true impact of non-dental plaque-induced disease upon the gingival and periodontal structures.

As the contributions of the present Volume and the 2017 classification indicate, there are a plethora of disorders of the oral mucosa that can also give rise to abnormalities of the gingivae and/or periodontium. The underlying pathological mechanisms are wide ranging, varying from genetically determined defects of collagen structure and function, of DNA processing through to acquired autoimmune disease (e.g. the immunobullous disorders), infections and disease secondary to lifestyle habits (e.g. tobacco) or medical interventions (eg. Graft versus Host Disease, Medication-related osteonecrosis of the jaws, or mucosal immune-related adverse effects of checkpoint blockade cancer

immunotherapy). Yet an even cursory comparison between the 2017 classification and the content of the present Volume reveals that there is a mismatch: a number of disorders known to impact both oral structures are not mentioned. Learned experts of Periodontology and of Oral Medicine are not uniformly reporting the disorders that affect the oral mucosa and gingival/periodontal structures. As an example the 2017 classification only cites one developmental/systemic disorder as having an impact upon non-dental plaque induced gingival/periodontal health and yet, as is clear from the Chapter by Pinna et al[3], there are a wealth of genetically-determined disorders that can give rise to manifestations within these structures. The list of fungal disorders in the 2017 classification does not include paracoccidioidomycosis, yet this is known to give rise to very striking gingival manifestations, that in the appropriate clinical setting may be of notable diagnostic importance[4]. The same may also be true of Chronic Mucocutaneous Candidiasis and related disease[5]. The immunobullous group of the 2017 classification does not include the emerging Paraneoplastic Autoimmune Multi-organ Syndrome (PAMS)[6] nor the IgA immunobullous disorders[7]. It could be argued that the inclusion of uncommon disorders is not justified in a classification system designed for regular use by clinicians, including general dental practitioners: but if so why has the classification included the rare reports of histoplasmosis, aspergillosis, molluscum contagiosum and Hodgkin's disease?

Of concern, there is no inclusion of Kaposi's sarcoma that (as indicated in the chapter by Warnakulasuriya[8]) can affect the gingivae – and cause notable destruction of the underlying periodontium or occasionally mimic pyogenic granuloma[9]. Similarly, malignant melanoma (or possible antecedents) that, while rare, has a propensity to affect the palate and adjacent gingival and periodontal tissues[10], is not mentioned under malignancy nor under pigmented lesions. Discussion of metastatic neoplasms, which commonly affect the mandible and manifest as a gingival swelling, is absent[11]. Inclusion of haematological disorders that impact upon dental plaque-related gingival disease is helpful, and these diseases should have been included in the non-dental plaque related section as their impact may be unrelated to the presence of dental plaque. It is surprising that, in view of its propensity to affect the gingivae, that hypoplasminogenaemia has not been included[12].

While the clinical features of dental-plaque related disease are defined, there is no indication of the predominant clinical characteristics of the non-dental plaque induced disorders – for example localised or generalised enlargement and, as reviewed in the present Volume, ulceration or red or white patches[8]. Of further concern, there is conflict in the terminology used. In the 2017 classification under the heading of premalignancy are mentioned leukoplakia and erythroplakia. As noted in the chapter by Tilakaratne *et al*[13] these are not diseases in their own right, but signs of epithelial disorders that may include hyperkeratosis, oral epithelial dysplasia and oral squamous cell carcinoma[14]. In addition, not cited in the 2017 classification - nor indeed any of the chapters of this Volume - carcinoma cunniculatum may manifest as solitary white patches of the gingivae[15].

Where change might be justified

While the AAP and EFP do acknowledge that for many of the non-dental plaque- induced disorders there will be a need for other health care providers to be involved in diagnosis and treatment, a unification of terminology, agreement on which disorders impact upon the gingival and periodontal tissues, how they may manifest, together with a simple rearrangement of the way clinical signs are listed, are each desirable. This would facilitate diagnosis of, sometimes significant, disease and liaison with the most appropriate health care team to further the management process.

Disease may sometimes manifest with pain, altered or reduced sensation without any clinically visible damage to the gingivae, periodontium or oral mucosa. Examples of this include trigeminal neuralgia and related disorders giving rise to “lancinating” pain, persistent dento-alveolar pain disorder (PDAP) and trigeminal neuropathy secondary to diabetes mellitus[16]. There would seem to be little evidence that these symptoms have been considered in the 2017 classification, possibly reflecting the generally low frequency and level of reported pain that would seem to accompany dental plaque-induced gingival/periodontal inflammation. Nevertheless, a simple additional section in the classification could have provided a further *aide memoire* for diagnosticians – and further promote the importance of Periodontists in the management of oral disease.

Future collaboration

Classification systems are highly important as they provide the bedrock upon which research, epidemiology, education and clinical care are built. It is highly commendable that the EFP and the AAP have refined the classification of 1999 and certainly global Periodontology is more advanced in classification systems that Oral Medicine. For example, one of the most cited classifications in Oral Medicine was the 1993 EC-Clearinghouse classification of the oral manifestations of HIV disease (as detailed in the chapter by Ranganathan and Umadevi[17]. This is now largely redundant as Anti-Retroviral Therapy (ART) is so notably effective, and will hopefully be available to more than 90% of affected individuals in the near future (this being the WHO/UNAIDS target for 2020 in the so-called 90/90/90 initiative)[18]. ART itself, however, can give rise to a plethora of oral signs or symptoms. The 1993 EC-Clearinghouse classification may still have an important role for the diagnosis of oral disease in individuals who have unknown HIV disease, are unfortunately unable to receive ART, predominantly for socioeconomic reasons, or who are unable to tolerate therapy: it is, nevertheless, time that this classification was critically appraised and modified if required. Similarly, the descriptions of oral lichen planus are not uniformly agreed – there are often conflicting views from specialists as to the definitions of erosive and ulcerative oral lichen planus, and indeed if they are one and the same. Herpetiform aphthous stomatitis has been rarely described and yet continues to be considered part of the spectrum of recurrent aphthous stomatitis[19]. Thus Oral Medicine is not without its' own problems in deciding on disease types or descriptors.

The afore-mentioned commentary points towards a need for better engagement by those who deliver education allied to Periodontology or to Oral Medicine: there is a need to enhance the curricula of both specialties. However, a balance has to be struck. Specialty training is already complex and lengthy and any significant additional content (e.g. modules of "Periodontology for Oral Medicine" or vice versa) will further burden training. The practice of Periodontics is principally directed towards dental plaque-induced disease, while Oral Medicine is focused upon non-dental plaque-related disease.

Complex aspects of periodontal care tend to be focused around interventions that require significant surgical skill while management of complex oral mucosal disease (for example) by specialists of Oral Medicine is often centred upon systemic therapies that require medical-type skills. Correct diagnosis underpins both. This plays into the debate regarding what is increasingly referred to as "periodontal medicine". We do not recommend creation of yet another dental speciality: both current specialties have the relevant talents which, with use of a common language, based upon an agreed disease classification that points towards who should principally manage the patient, will ensure that training and patient care is optimal for the public.

Just as a multidisciplinary approach, based upon a commonly agreed classification, is essential to education and clinical care, the same is true for research. Without doubt the 2017 Classification will be informing research of dental plaque-induced disease for the next 10 to 15 years. Thus even with the caveats indicated above the Classification has significance for Oral Medicine research – for example the impact of granulomatous, autoimmune immunobullous disease or lichen planus of the gingivae upon dental plaque-induced disease is largely unknown – yet ever more patients are developing such immune driven disease that remains notably challenging to manage. Similarly, the use of the classification along with the agreed International diagnostic criteria for Sjogren's Syndrome will allow the impact of salivary gland dysfunction upon gingival health to be truly defined. These are but two simple examples of why the 2017 Classification of Periodontal and Peri-implant diseases has value to research allied to Oral Medicine and perhaps a further indication that future classifications must continue to be well informed and relevant to as many patients, clinicians, researchers, educators and trainees as possible.

Conclusion

The numbers of individuals likely to develop complex disease of the gingival and periodontal structures will rise as longevity of life extends, lifestyles change and medical and dental care advance. There will thus be a need to ensure that clinical classification systems reflect such changes. Communication and collaboration between specialists of Periodontics and of Oral Medicine will also remain central to ensure that relevant research and education ultimately lead to advances in clinical outcomes that benefit the oral health and general wellbeing of patients and those at risk of developing relevant disease.

Acknowledgments

SF receives support from the UCLH/UCL NIHR Biomedical Research Centre, London, UK.

References

1. Chapple ILC, Mealey BL, Van Dyke TE, Bartold PM, Dommisch H, Eickholz P, Geisinger ML, Genco RJ, Glogauer M, Goldstein M, Griffin TJ, Holmstrup P, Johnson GK, Kapila Y, Lang NP, Meyle J, Murakami S, Plemons J, Romito GA, Shapira L, Tatakis DN, Teughels W, Trombelli L, Walter C, Wimmer G, Xenoudi P, Yoshie H. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018 Jun;89 Suppl 1:S74-S84.

2. Wilton JM, Griffiths GS, Curtis MA, Maiden MF, Gillett IR, Wilson DT, Sterne JA, Johnson NW. Detection of high-risk groups and individuals for periodontal diseases. Systemic predisposition and markers of general health. J Clin Periodontol. 1988;15(6):339-46.

3. Pinna R, Cocco, Campus G, Conti G, Milia E, Sardella A, Cagetti MG. Genetic and Developmental disorders of the oral mucosa: Epidemiology; molecular mechanisms; diagnostic criteria, management. Periodontology 2000 2019 Newell please add

4. Iatta R, Napoli C, Borghi E, Montagna M T. Rare mycoses of the oral cavity: a literature epidemiologic review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(5):647-55.

5. Porter S R, Scully C. Candidiasis endocrinopathy syndrome. Oral Surg Oral Med Oral Pathol. 1986 Jun;61(6):573-8.

6. Niimi Y, Ohyama B, Di Zenzo G, Calabresi V, Hashimoto T, Kawana S. Paraneoplastic pemphigus presenting as mild cutaneous features of pemphigus foliaceus and lichenoid stomatitis with antidesmoglein 1 antibodies. Dermatol Res Pract. 2010. pii: 931340.

7. Leuci S, Ruoppo E, Adamo D, Elena C, Mignogna MD. Oral autoimmune vesicobullous diseases: Classification; clinical presentations; molecular mechanisms; diagnostic algorhythms; management. Periodontology 2000 2019 Newell please add

8. Warnakulasuriya S. Red, White and Mixed lesions: a clinico-pathological approach to diagnosis. Periodontology 2000 2019 Newell please add

9. Speicher DJ, Wanzala P, D'Lima M, Njiru A, Chindia M, Dimba E, Johnson NW. Diagnostic challenges of oral and cutaneous Kaposi's sarcoma in resource-constrained settings. J Oral Pathol Med. 2015;44(10):842-9

10. Topić B, Mašić T, Radović S, Lincender I, Muhić E. Primary Oral Mucosal Melanomas - Two Case Reports and Comprehensive Literature Review. Acta Clin Croat. 2017;56(2):323-330

11. Rao R S, Patil S, Sanketh D, Amrutha N. Metastatic tumors of the oral cavity. J Contemp Dent Pract. 2014;15(2):263-71.

12. Chi AC, Prichard E, Richardson MS, Rasenberger KP, Weathers DR, Neville BW. Pseudomembranous disease (ligneous inflammation) of the female genital tract, peritoneum, gingiva, and paranasal sinuses associated with plasminogen deficiency. Ann Diagn Pathol. 2009;13(2):132-9.

13. Tilikaratne W, Jayosooriya PR, Jasasuriya N, De Silva RK. Oral epithelial dysplasia: Causes; quantification; prognosis; management challenges. Periodontology 2000 2019 Newell please add

14. Porter S, Gueiros LA, Leão JC, Fedele S. Risk factors and etiopathogenesis of potentially premalignant oral epithelial lesions Oral Surg Oral Med Oral Pathol Oral Radiol. 2018;125(6):603-611

15. Suzuki J, Hashimoto S, Watanabe K, Takahashi K, Usubuchi H, Suzuki H. Carcinoma cuniculatum mimicking leukoplakia of the mandibular gingiva. Auris Nasus Larynx. 2012; 39(3):321-5

16. Porter SR, Mercadante V, Fedele S. Oral manifestations of systemic disease. Br Dent J. 2017 ; 223(9):683-691

17. Ranganathan K, Umadevi KMR. Common opportunistic infections in HIV/AIDS: changing epidemiology; diagnostic criteria and methods; management protocols. Periodontology 2000 2019 Newell please add

18. UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic . Geneva, Switzerland: UNAIDS, 2014. Available at: http://www.unaids.org/en/resources/documents/2017/90-90-90. Accessed 4th April 2019

19. Bilodeau EA, Lalla R. Recurrent oral ulceration: Types and classification; diagnostic algorhythms; management. Periodontology 2000 2019 Newell please add