

The pathogenesis of human periodontitis: an introduction

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The pathogenesis of human periodontitis was placed on a rational footing for the first time by Page & Schroeder in 1976 (7). Although the details were scanty, the general principles and the overall conclusions reached in that article, which became a citation classic, are still largely acceptable today. An enormous amount has been learned about all aspects of human periodontitis, including its pathogenesis, since 1976. Several reviews of the pathogenesis have been written during that time (1, 3–6, 9–11), but with one possible exception (4), no publication has summarized currently available data and organized it into a relatively complete and rational picture. There are good reasons for this. Whereas the amount of information available in 1976 was limited and all relevant information could be accommodated in a single lengthy article, this is no longer the case. Although much of the detail is still missing, a far more complete and compelling picture of the pathogenesis is now emerging. Indeed, it is possible to approach the pathogenesis not only from the cellular level as was done in 1976 but to extend the story to the molecular level and to some extent to the genetic level.

A staggering amount of information is available about the pathogenesis of human periodontitis. The information derives from a broad range of fields and disciplines, and much of it is highly specialized. We enthusiastically accepted the invitation to lead the effort to create a volume of PERIODONTOLOGY 2000 devoted completely to the pathogenesis of human periodontitis. Such a volume provides sufficient space for an inclusive, highly integrated result and, equally important, it provides the opportunity to include many of the world's experts, whose collective efforts far surpass those that could have been achieved by any one or two individuals. Even with this format, we could not be all-inclusive, and many recognized experts could not be included.

Our goals for this volume are to provide chapters that collectively present the current understanding

of the pathogenesis of periodontitis in a user-friendly manner. Although the individual chapters are intended to be able to stand alone, they are all highly interrelated and integrated and the total is far greater than the sum of the parts. We have chosen the final chapter as a discussion section in which we summarize highlights of all the chapters, emphasize broad concepts, make clinical application where appropriate, speculate based on the data and point out future directions of the field.

Experts agree that human periodontitis is initiated and perpetuated by a small group of predominantly gram-negative, anaerobic or microaerophilic bacteria that colonize the subgingival area. Indeed, at the 1996 World Workshop on Clinical Periodontics, the relevant working group concluded (2) that most human periodontitis is caused by *Porphyromonas gingivalis*, *Bacteroides forsythus* and *Actinobacillus actinomycetemcomitans*. During the 1970s and 1980s, great strides were made in elucidating the infectious nature of human periodontitis; in the 1990s we have come to realize that, although bacteria are essential, they are insufficient for the disease to occur. Host factors such as inheritance, tobacco smoking and various other risk factors may even outweigh the bacteria as determinants of whether the disease occurs and of the severity of clinical outcome. These observations have led to major changes in ideas and concepts about pathogenesis, prevention and treatment.

Over the past 10 to 15 years, substantial new information has been obtained about how these bacteria cause the formation of periodontal pockets, conversion of junctional epithelium to pocket epithelium and destruction of the alveolar bone and connective tissues of the gingiva and periodontal ligament. Bacteria mostly cause the observed tissue destruction indirectly, and they do so by activating various components of the host defense systems in such a manner that destruction ensues. It is enigmatic that the same host systems that provide protection and de-

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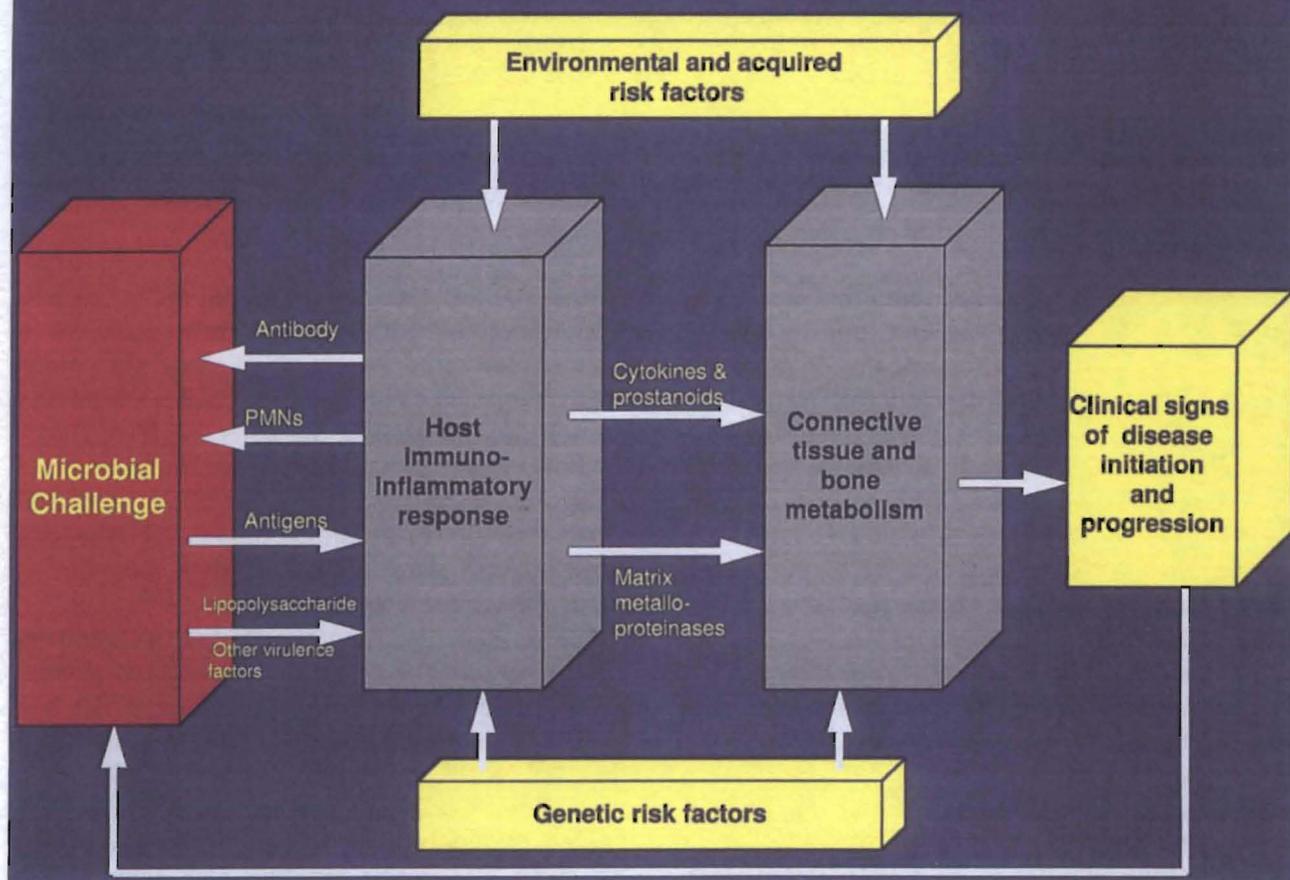


Fig. 1. The pathogenesis of human periodontitis. PMNs: polymorphonuclear lymphocytes

fense are responsible for destruction. Activation of these systems to achieve protection and defense virtually always results in some degree of destruction. The capacity of mammals for healing and regeneration, however, is sufficiently great that the destruction is generally outweighed, and recovery and return to the normal state can occur. Human periodontitis is an example of a condition in which this frequently does not happen, and tissue destruction manifested clinically as continuing or recurrent disease is perpetuated to the point that abscess formation may occur and tooth loss is the end result. The reasons why the progression of periodontitis is not more commonly spontaneously arrested is one of the themes of this volume.

Extensive and diverse research findings in recent years have started to coalesce into a few coherent concepts that appear to explain at least some of the double-edged sword phenomena in periodontitis.

These concepts suggest that the disease may be more destructive if specific aspects of the host defense mechanisms within the local tissue are more exuberant. This appears to occur, at least in part, due to hyperresponsive host factors, both intrinsic (genetic) and induced (such as smoking), or to increased bacterial challenge within the tissues as a result of compromised bacterial control mechanisms at the gingival sulcus. Much of the new perspective that is captured in this volume on the pathogenesis of periodontitis involves the detailed molecular and cellular mechanisms involving regulating 1) the magnitude and balance of the host response within the tissues and 2) the quality of neutrophil and antibody activity that reaches the gingival sulcus.

The major developments since the 1976 article have been elucidation of the pathways through which bacteria activate host cells and systems in a manner that tissue destruction ensues and eluci-

dation of the pathways through which the extracellular matrix components of the gingiva and periodontal ligament are destroyed and alveolar bone is resorbed. Current understanding, although still incomplete, is now sufficient for the development and application of new preventive measures, diagnostics and treatments targeted at blocking or altering these pathways. These applications are highlighted throughout this issue of *PERIODONTOLOGY 2000*, especially in the final chapter.

It is now clear that periodontitis is not a single homogeneous disease but rather consists of a family of closely related diseases each of which may vary somewhat in etiology, natural history and response to therapy (8). Nevertheless, a common underlying chain of events in the pathogenesis is shared by all forms of the disease. This common chain of events is influenced by other factors including genetic and other risk factors that may differ from one form of the disease to another. This volume has been written based on this premise (Fig. 1).

Antigens and various other virulence factors, and in some cases invading bacteria, comprise the microbial challenge, and the host responds with an immediate inflammatory and immune response that can influence the challenge. The host response results in production of cytokines, eicosanoids, other inflammatory mediators such as the kinins, complement activation products and matrix metalloproteinases, which perpetuate the response and mediate connective tissue and bone destruction. All of these events are influenced by disease modifiers, both genetic and environmental or acquired. The clinical picture observed is a result of the sum of these events. The severity and rate of progression of disease feed back to influence the nature and magnitude of the microbial challenge by, for example, influencing the pH and availability of oxygen and various nutrients in the periodontal pocket.

One of the most valuable aspect of earlier pathogenesis discussions (7) was the organization of snapshots of the disease into a coherent sequence of

major cellular events. Page & Schroeder (7) noted that the histological snapshots did not capture the richness of the dynamic interactions, but that the 1976 article provided a practical series of reference points for investigators to enhance understanding of the biological events related to each static picture.

Current information and knowledge of interactions at the basic cellular and molecular levels makes it easier to fill in many of the details that explain the probable mechanisms accounting for the cell patterns in the histological images. This issue of *PERIODONTOLOGY 2000* therefore attempts to capture a dynamic image of periodontal disease that includes the web of communication, cell migration and cell function that truly represents the pathogenesis process.

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