Periodontal Disease: Are Plasma Cells and Lymphocytes an Essential Component?[1] (36025)

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Chronic progressive periodontal disease is the primary cause of tooth loss in adults and therefore is a major public health problem in the United States and throughout the world. The disease begins as an inflammatory lesion in the marginal gingiva around the necks of the teeth and progresses into the deeper structures resulting in massive destruction of the connective tissues and bone and eventual exfoliation of the teeth (1–3). While it is now generally agreed that microorganisms of the dental plaque comprise the primary etiologic agent responsible for chronic periodontal disease (4–6), the wide variation in host susceptibility and the observation that the prevalence and extent of the disease increase linearly with increasing age (7) have led to the concept that host tissue factors may play an overriding role in the induction and progress of the disease state. Thus, in this regard periodontal disease may be similar to some other chronic inflammatory diseases such as tuberculosis, in which much of the tissue destruction appears to be a consequence of the immunopathologic response of the host to the presence of the etiologic agent rather than a direct toxic effect of the agent or its products upon the tissues (8).

One consistently observed feature of periodontal disease is the presence within the periodontal tissues of a dense inflammatory infiltrate comprised almost totally of plasma cells and lymphocytes (9, 10). Indeed, in experimental gingivitis in humans, even at the earliest time periods observed, the lesion exhibits this feature (11). These observations have led to the concept that humoral and/or cellular hypersensitivity states resulting from stimulation by antigenic plaque-derived substances may play a major and determinative role in the induction and progress of periodontal disease (12, 13). It is now widely assumed that the presence of lymphocytes and plasma cells at the local site in the periodontal tissues may be an essential component of the disease process and, therefore, a key factor in its pathogenesis. We describe a form of chronic inflammatory periodontal disease in which all of the clinical and histopathologic features of the advanced lesion may be observed, but in which significant numbers of lymphocytes and plasma cells cannot be demonstrated morphologically at the local site.

Methods. Thirty-two marmosets (*Saguinus oedipus*) of various ages and both sexes were obtained from the Tarpon Zoo, Tarpon Springs, FL. The animals had been wild-caught in the vicinity of Barranquilla, Colombia, and had been in captivity for about 3 months. One additional animal of the *Callithrix jacchus* species which had been colony-maintained for several years was kindly provided to us by Dr. Barnet Levy of the Dental Science Institute of the University of Texas, Houston. The wild-caught animals were maintained in our facilities for up to 9 months under conditions of constant temperature and humidity, and were fed a diet consisting of enriched monkey chow pellets, ZuPreem, fruits, and newborn rats.[2] The animals were examined clinically and photometrically for evidence of gingival and periodontal disease, using techniques described elsewhere.[3] An additional

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[2] Vitamin D-enriched monkey chow pellets, Ralston Purina Co., St. Louis, MO. ZuPreem, Riviana Food, Inc., Topeka, KS.

[3] Ammons, W. F., Schetman, L. R., and Page, R. C., unpublished data.

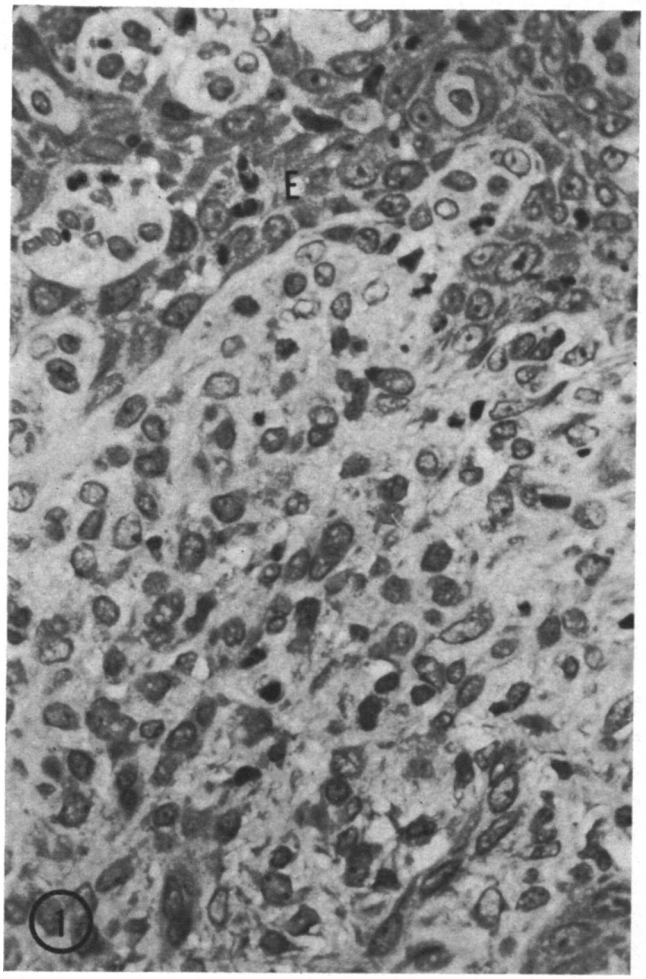

FIG. 1. Crevicular epithelium (E) and underlying connective tissues illustrating the cellular characteristics of the host tissue response in the diseased gingival tissues of the marmoset: Polymorphonuclear leukocytes and large mononuclear cells are apparent but typical plasma cells and lymphocytes are not observed (H and E, original magnification × 640).

125 marmosets were examined clinically and photometrically at the Tarpon Zoo. After 6 months, two of the animals were anesthetized and biopsy specimens of inflamed and non-inflamed gingival tissues were removed and prepared for study by light and electron microscopy. Subsequently, 17 of the animals were killed and the jaws were removed and hemisected. One-half of each jaw was radiographed and defleshed for examination of the bony architecture, and the remaining half was decalcified and prepared for light microscopy. The *Callithrix jacchus* was processed in the same manner.

Results. In the wild-caught animals, small amounts of calculus and bacterial plaque were present universally, and almost all of the animals exhibited a mild gingival inflammatory response of limited extent. However, we did not observe clinical, histopathologic, or radiographic evidence for the presence of chronic periodontal disease in any of the wild-caught animals. In the colony-maintained animal, massive amounts of bacterial plaque and calculus were present and the manifestations of advanced chronic periodontal disease were observed. These manifestations included loss of approximately one-half to two-thirds

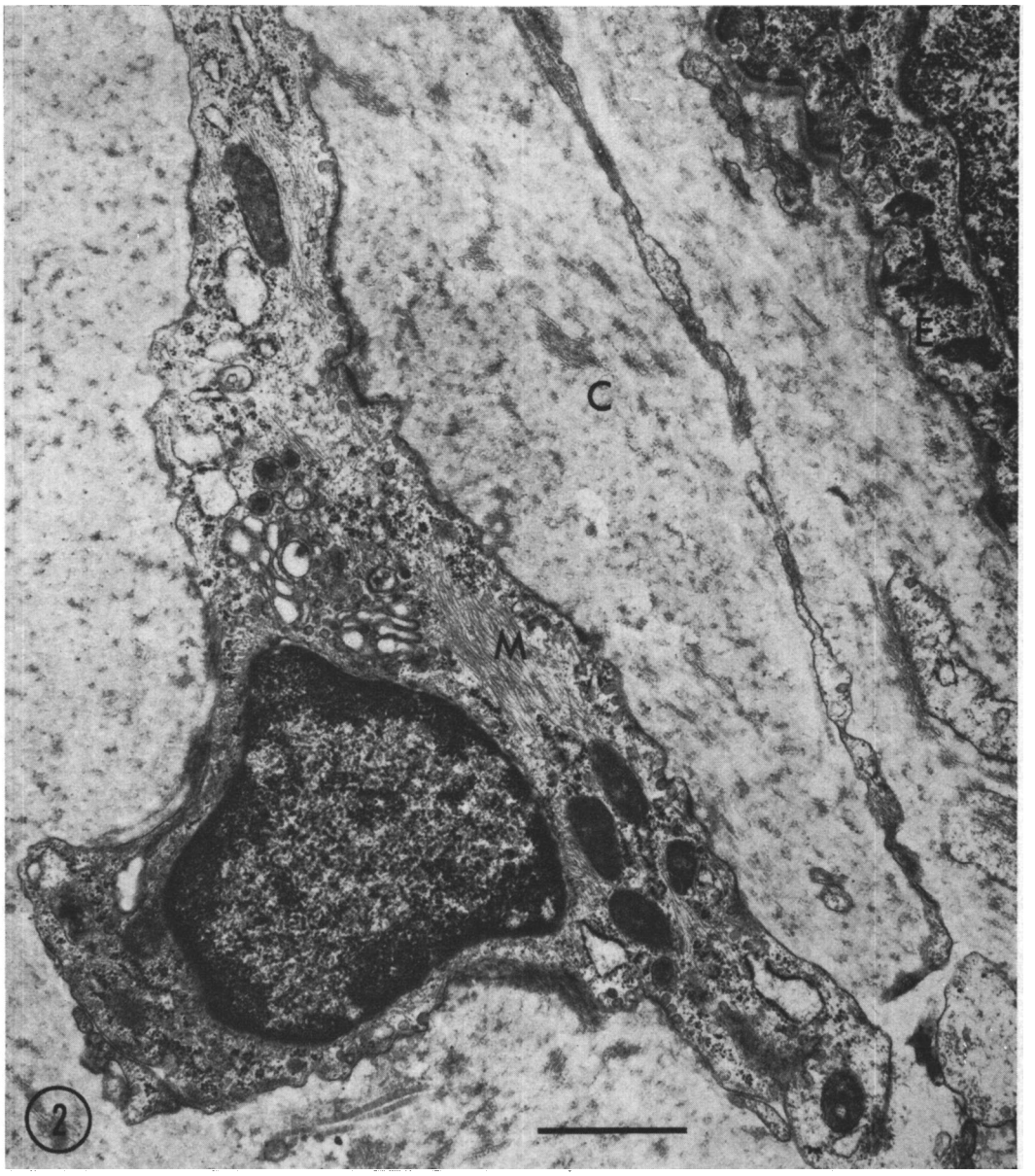

FIG. 2. Electron micrograph of a characteristic mononuclear cell (M) in the inflamed connective tissue adjacent to the gingival crevice: Also observable in this micrograph are a basal cell of the crevicular epithelium (E), the basal lamina at the epithelial–connective tissue junction, and collagen fibers (C). The mononuclear cell exhibits several features characteristic of macrophages. These include an oval nucleus with moderately clumped chromatin, small amounts of rough endoplasmic reticulum with intermittent attachment of ribosomes, several small dense bodies adjacent to a prominent Golgi apparatus, and an extensive array of filaments throughout the cytoplasm. Note also the numerous small vesicles, suggestive of endocytic activity, at the surface of the cell. Scale marker, 1 μ.

of the supporting alveolar bone, loosening and drifting of the teeth, collapse of the occlusal relationship, and acute inflammation of the entire attached gingiva. Thus, while

chronic periodontal disease was not observed in wild-caught animals, a form of the disease with most of the manifestations seen in man apparently can be induced in the marmoset under conditions of colony maintenance. Factors responsible for this induction are not understood currently, but they may relate to diet and to the massive accumulation of calculus and bacterial plaque.

Histopathologic features of advanced chronic periodontal disease in the marmoset, illustrated in Figs. 1 and 2, include epithelial proliferation and apical migration with resultant pocket formation, vascular proliferation, infiltration of large numbers of neutrophilic leukocytes, connective tissue and bone destruction, and the presence of a dense population of mononuclear cells. Essentially the same histopathologic features, but of a more limited extent and not progressing to bone loss, were observed in the mildly inflamed tissues of the wild-caught animals.

Plasma cells and lymphocytes were not a prominent feature of the lesion in either the mildly inflamed tissues or those affected with advanced disease. In spite of intensive efforts using stains specific for nucleic acids which clearly distinguish plasma cells and lymphocytes in the gingiva of humans, chimpanzees, and other animals, we were unable to demonstrate the presence of these cells in the diseased gingiva. The predominant cell present in the connective tissues appeared to be a mononuclear cell with features usually associated with connective tissue macrophages. This conclusion was supported by the electron microscopic observations. A characteristic mononuclear cell is shown in Fig. 2. In addition to these cells, typical fibroblasts and numerous small vessels comprised of endothelial cells and pericytes were seen. Another population of cells exhibiting many features associated with macrophages, but not containing phagocytosed material, was also present. These cells could not be definitely identified and we believe that they may represent a less differentiated cell type. Using electron microscopy, only three typical plasma cells exhibiting classic morphologic features were observed in all of the periodontal tissues examined.

The virtual absence of plasma cells and lymphocytes even in the tissues affected with advanced periodontal disease was an unexpected finding which led us to consider the possibility that these cells in the marmoset may exhibit an unusual morphology. However, this does not appear to be the case, since cells exhibiting classic morphologic features of plasma cells and small lymphocytes were present in the lymph nodes and other tissues of the animals and a few typical plasma cells were observed in the gingiva.

Our observations show that the important features of advanced periodontal disease, including extensive bone loss, connective tissue destruction, and loosening of the teeth, can be induced in the colony-maintained marmoset in the virtual absence of the expected lymphocyte–plasma cell infiltrate. Thus, the presence and activity of these cells at the local site does not appear to be essential for induction and progress of the disease state in this subhuman primate. Alternatively, small numbers of lymphocytes and plasma cells may constitute a "threshold" population which is adequate for development of disease, or cells which participate in antibody production but do not exhibit morphologic features which permit their identification may be present. While we cannot rule out the latter alternatives, they seem to be unlikely.

Summary. Chronic periodontitis is the major cause of tooth loss in human adults. The consistent presence of a dense infiltrate of plasma cells and lymphocytes in the affected tissues is the basis of the widely held hypersensitivity concept of pathogenesis of the disease. The marmoset exhibits an advanced form of the disease, with all of the features of tissue destruction seen in man but in the virtual absence of an infiltrate of plasma cells and lymphocytes.

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