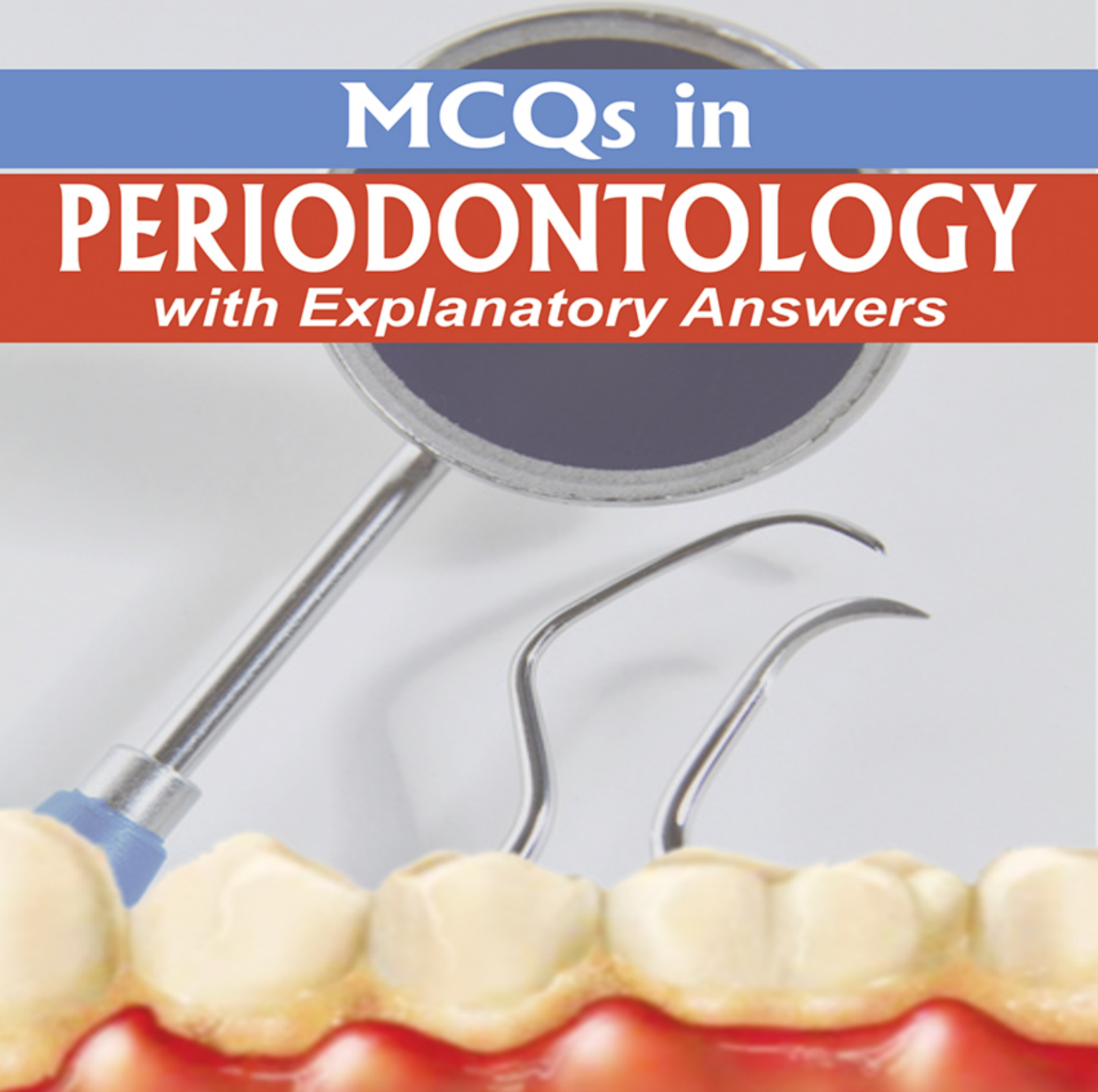
MCQs in PERIODONTOLOGY

with Explanatory Answers



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CHAPTER 6

Immunology in Periodontal Disease

Q. Write in detail about host bacterial interactions.

Host responses play important role in the pathogenesis of many types of periodontal diseases by contributing to the disease process or by modulating the effects of the bacteria. Immune response may be both beneficial (protective) and detrimental (destructive).

The properties of the microorganism that enable it to cause disease are referred to as *virulence factors*. Virulence properties can be broadly categorized into two groups:

1. Factors that enable bacterial species to colonize and invade host tissues, and
2. Factors that enable a bacterial species to cause host tissue damage directly or indirectly.

BACTERIAL COLONIZATION AND SURVIVAL IN THE PERIODONTAL REGION

Bacterial Adherence in the Periodontal Environment

Tooth is coated with salivary pellicle which helps in adhesion of *A.viscosus*, and *P.gingivalis* through fimbriae, it helps to bind to epithelial cells and fibroblasts. This is followed by coaggregation, these factors to get attached to tooth and each other is important in virulence of this microorganism.

Host Tissue Invasion

Bacteria may enter the host tissue through ulcerations in the epithelium of the gingival sulcus or pocket and has been observed in intracellular spaces of gingival tissue. Lab investigations have showed that *AA comitans*, *P. ginigvalis*, *T.denticola* and *F. nucleatum* invade the tissue directly. It is said that 'burst of disease activity' is related to the phase of bacterial invasion of the tissue. An additional possibility is that bacteria in the tissues may enable persistence of

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that species in the periodontal pocket by providing a reservoir for recolonization. Consistent with this hypothesis is that mechanical debridement alone is not sufficient and systemic antibiotics in combination with surgical therapy is required.

Bacterial Evasion of Host Defense Mechanism

To survive in periodontal environment, bacteria must neutralize or evade the host mechanisms involved in bacterial clearance and killing. Bacterial adherence and invasion are representative strategies by which micro-organisms accomplish this goal. Ex. Immunoglobulin function to phagocytose the bacteria by opsinization or may block the adherence. The production of immunoglobulin-degrading proteases by specific microorganisms may counteract these host defenses. Similarly, bacteria produce substance that kills PMN's nad lymphocytes normally involved in host response. *T.forsythia* and *F.nucleatum* have been shown to induce apoptosis, a form of cellular "suicide" in lymphocytes.

Immunity (Fig. 6.1)

- Innate (or natural) immunity: Non-specific defenses or barriers to infection which are (in healthy people) always present.

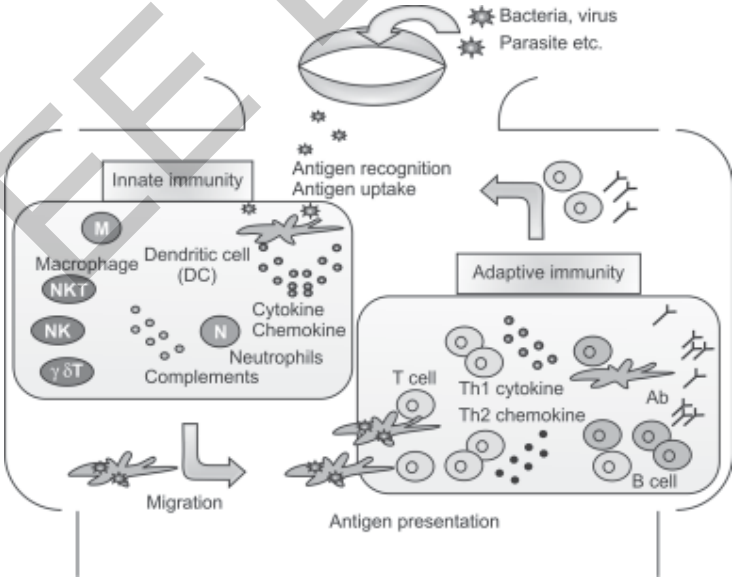

Fig. 6.1: Immune system

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- Adaptive (or acquired) immunity: A response that is directed toward a specific pathogen and develops over time and has "memory" (reactivity changes with repeated exposure).
  Comparison between inmate immunity and adative immunity are given in Table 6.1.

Innate Immunity Components

- Physical:
  - Barriers to infection, e.g. skin
  - Flushing mechanisms, e.g. coughing, urine flow
- Chemical responses, e.g. lysozyme in tears, complement.
- Cellular, e.g. phagocytic cells (able to engulf and ingest material).
- Comparison between innate immunity and adaptive immunity are given in table 6.1

Innate Response-epithelium

- Langerhan's cells in the epithelium
- Dendritic cells are crucial for the initiation and regulation of both types of immune response and also form a bridge between the two.

Specific Immunity Components

- Chemical—the humoral immune response using antibodies.
- Cell mediated—cells that are directed by the immune response to attack an invader.

Table 6.1: A comparison of innate and adaptive immunity

Property	*Innate immune system*	*Adaptive immune system*
Cells involved	Phagocytes (macrophages, Neutrophils, DCs) NK cells	T cells, B cells
Recognition receptors	Fixed in genome Rearrangement not necessary Limited diversity	Encoded in gene segments Rearrangement necessary High diversity
Ligand/antigens	Conserved molecular patterns (components of microorganisms)	Details of molecular structure (peptides, proteins, carbohydrates)
Development	Nonclonal Selected over evolutionary time	Clonal Selected in individual
Response time	Immediate (0-4 h)	Delayed (~72 h)
Site of response	Local, periphery	Secondary lympoid tissues

Contd...

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Property	*Innate immune system*	*Adaptive immune system*
Response	Production of Inflammatory cytokines (IL-I, IL-6, TNF α) and chemokines (IL-8) Induction of co-stimulatory Molecules (CD86, CD40)	Clonal expansion or energy production of effector cytokines (IFN-γ, IL-4)

DC, dendritic cell; IFN-γ, interferon-γ; IL-interleukin; NK-natural killer; TNF-α, tumor necrosis factor-α.

Complement

- A series of molecules present in serum which interact with the bacterial cell membranes and with each other so that, at completion, they punch a hole in the bacterial membrane.
- It is composed of a series of reactions which act as a cascade with the product of one acting on the next in the chain.
- The products amplify the reactions, increase permeability of blood vessels and also act to attract cells to the site of the reaction.
- The products make the target more attractive to phagocytosis by immune cells ("opsonization").

It can be activated by-

- Interaction of one of the initial components with bacterial cell surface substances ("Lectin pathway") , bacterial products ("Alternative pathway") , or
- By antibodies that have bound to antigens ("Classical pathway").
- There is a "recognition unit", made up of some of the initial components.
- The final product is the "membrane attack complex".

Acute Phase Reactants

- Substances that rapidly increase in quantity in the body at the onset of infection. Ex. –
  C- reactive protein.
- These may have antibacterial properties or be involved in sequestration of essential nutrients.

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Interferon (IFN)

- These are substances (IFN α, γ) that are produced by virally infected cells which bind to receptors on other cells and prompt them to produce antiviral proteins.

Phagocytic Cells

- PMN, monocytes, macrophages
- Are a part of the innate system but have a role in activating the specific system and, when activated, become part of the specific system.

Neutrophils

- Polymorphonuclear leukocyte (neutrophil, PMN) are the key protective cell
- First line of defense along with macrophages
- Functions: Chemotaxis, Phagocytosis, Killing — oxidative and non-oxidative mechanism
- Double edge sword – both protective as well as destructive.

Mast Cells

- Cells found in the tissues that contain granules that are rich in histamine and inflammatory mediators.
- These are released on stimulation by complement products and IgE, promoting local inflammation.

Humoral Immunity

Antigens

Molecules which stimulate an immune response.

- Some antigens can only be recognized after having been processed by T cells.
- "Haptens" are substances which are too small by themselves to elicit an immune response but may do so when bound to a larger molecule.
- Antigens may be on the surface of organisms, they may be substances in the serum, including toxins, or viruses

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Antibodies (Immunoglobulins)

Proteins produced by the body that bind to antigens.

- Each molecule is "Y" shaped and has two variable regions that bind to antigens and a "constant" ("Fc") end that binds to the host's receptors.
- An antibody may or may not be able to neutralize the toxin or virus.
- The strength of the binding between an antibody and an antigen is called **the affinity**. It often increases with second or more exposures to an antigen.
- Different types ("classes") are produced that have different properties. These are IgM, IgG, IgA, and the less plentiful IgE and IgD.

IgM

- This is the first antibody produced in response to a first infection.
- It occurs as 5 units that are attached, and so is a big molecule that does not get into tissue from blood or cross the placenta.
- Complement binds to it very well.

IgG

- IgG is the most plentiful immunoglobulin
- It is produced after IgM in infection, a process called class switching, where the IgG antibody produced by a cell has the same specificity for an antigen as the IgM it replaces.
- It is produced predominately when exposure to the agent occurs in a second infection (boosting response).
- Its production is controlled by T cells.
- It binds to complement ("fixes complement") , attracts phagocytes, and opsonizes well. It penetrates tissue and crosses the placenta.

IgA

- Occurs as single or paired molecules.
- Secretory IgA is found in secretions (e.g. tears, saliva, respiratory secretions, colostrum).
- Its production is controlled by T cells.

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IgE

Activities are antiparasitic and involved in hypersensitivity reactions.

IgD

Found as a receptor on B cells surface.

CELLS IN IMMUNITY

Polymorphonuclear Leukocytes (Neutrophils, PMN)

- White blood cells able to phagocytose invaders.
- Most common WBC
- Short lived.
- Circulate in blood and enter the tissues, gathering at the site of infection
- Pus is largely made up of PMN

Eosinophils

- Eosinophils are white blood cells (WBC) that are antiparasitic.
- Contain granules that stain red with the dye eosin.
- Increased in hypersensitivity states (e.g. asthma).

Basophils

- Cells that are involved in hypersensitivity reactions.

Mononuclear Phagocytic System

Monocytes

– WBC that circulate until stimulated to differentiate into macrophages or one of a family of phagocytic cells (dendritic cells) found in various organs throughout the body.

Macrophages

– Macrophages are larger and longer lived than PMN and are found in the tissues. They are able to:
  - Phagocytose invaders.
  - Present the antigens to T-lymphocytes for development of specific immunity.
  - "Call for help" by secreting cytokines.

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Dendritic Cells

- Are phagocytic cells descended from monocytes or the lymphocyte cell lines, which are like little octopuses.
  - Widely distributed in tissues in an immature form.
  - Good at presenting antigen to T lymphocytes.
  - The immature form phagocytoses antigen.
  - Becomes mature, stops its phagocytosis and goes to the lymph node to deliver the antigen to the T cells.

Lymphocytes

B Cells

- Differentiate in bone marrow in mammals.
  - Give rise to plasma cells, which are antibody "factories" or memory cells, which circulate and are primed to produce a specific antibody if they come into contact with the appropriate antigen.
  - During development, B cells are produced that each recognizes a specific antigen. There are so many B cells, that a wide range of antigens can be recognized.
  - When an antigen binds to antibody on the surface of the B cell, it stimulates the cell to divide and to increase in number ("clonal expansion") .
- The antibodies produced vary in their ability to bind and those B cells that produce the antibody that binds best are stimulated to increase.
- This causes the B cells that best recognize an antigen to increase in response to it, and to improve the specificity of the antibody produced.
- With clonal expansion, mutations occur in the genes controlling the antibody region that binds to the antigen.

T Cells

Develop in the thymus; Some develop into memory cells (as do some B lymhocytes).

- Control the immune response by producing cytokines.
- Able to directly kill foreign tissue cells, virally infected cells, or tumor cells.

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- Activate phagocytic cells to destroy the organisms they have ingested
- T cells generally express CD4 or CD8,
- NK (natural killer), specialized for killing cells do not express either.

• Different populations of T cells that perform each of these functions.
  - **CD 4 T** cells, or "**T helper cells**"
  - Activate and control the immune response.

CD4 or T Helper Cells

• Respond to the signals of the antigen presenting cell (APC) differentiate either into

TH1 Cells

• Promote a local response with inflammation and is good at handling intracellular pathogens, e.g. viruses, mycobacteria, fungi.

TH2 Cells

• Promote antibody production and memory cells.
• Is a systemic response that happens later in the infection than the TH1.

CD8 Cells or Suppressor T Cells

- CD 8 cells or "**Suppressor T cells**" patrol, looking for virally infected cells, or tumors.
- On detecting them, they divide and differentiate into cytotoxic T lymphocytes and destroy the target cells.
- Suppress helper T cells function using inhibitory cytokines.

Natural Killer Cells

- Large granular lymphocytes
- Contain granules of cytotoxic material which they use to kill virally infected cells and tumor cells (These are similar but distinct from CD-8 T cells.).

• They have Fc receptors to allow them to detect cells coated with antibody, which they then destroy.

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COMMUNICATION BETWEEN CELLS

Cytokines (most common types are interleukins, also tumor necrosis factors, etc.)

- Substances produced by cells that:
  - Bring about differentiation of cells
  - Cause activation of phagocytic cells and lymphocytes
  - Influence inflammation
  - Influence cell mediated responses and antibody responses
- They are usually produced in combinations.
- They may act on different cells differently.
- T lymphocytes are an important source.

Antigen Presentation

- Antigens must be presented to T cells for them to act upon them.
- important role played by the Major Histocompatibility Complex Class1 and Class II molecules (MHC I, MHC II).

MHC I

- Is found on all cells
- Essential for recognition of "self".
- Used in tissue typing to determine if transplants will be compatible (HLA typing).

MHC II

- Found on monocytes, macrophages, B cells, dendritic cells and phagocytic cells related to macrophages that are found in the tissues.
- Antigen is broken down into peptides by the initial cell prior to presentation.
- The resulting short peptides are presented associated with the MHC molecules.

Antigen is presented with:

- MHC I to CD 8 T cells
- MHC II to CD 4 T cells
- T cells recognize the peptides to be viral or bacterial debris and become activated, producing cytokines to begin activity in other cells.

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