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Historiography of Immunology in Oral Pathology-A Concise Review

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Review Article

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Abstract

The historiography of immunology has become a bustling, pluripotent discipline, and continues to develop in many new and exciting directions that include immunohistochemistry and immunopathology in the field of Oral pathology. Immunology, the science that studies the structure and functioning of the immune system, began long before anyone knew about disease causing microbes or even that individuals had an immune system that protected the body against disease. In the field of Oral pathology, one encounters various immunological diseases in routine day-to-day practice, hence having the complete knowledge on this aspect which many a times is overlooked, is of utmost importance for proper investigations and latest research in this field that in turn comes from the past historical knowledge. The terminology and techniques today have the foundation in the past. The historical considerations of past events give perspective to the present programmes and direction for future development. Hence, the present review is a good starting point for compiling the historiography of immunology in the field of Oral pathology and includes a short compilation of the past historical background about basic immunology, hypersensitivity and autoimmunity. In addition, future consideration of this discipline in Oral pathology should be emphasized and targeted.

Keywords: Historiography; Oral pathology; Immunotherapy; Immuno-histochemistry

Introduction

As rightly said, by Sir Winston Churchill, in 1944, when addressing the Royal College of physician, London "Science, now so largely perverted to destruction must raise its glittering shield not only over the children's but over the mothers, not only over the family, but over the home. The longer you can look back, the longer you look forward: the wider the span, the longer the continuity" [1]. The concept of immunity from disease began long before in the 5th century BC. Historiography is the study of the methods of historians in developing history as an academic discipline and covers topics using particular sources, techniques and theoretical approaches [2]. The historiography of immunology has become a bustling, pluripotent discipline, and continues to develop in many new and exciting directions in the field of Oral pathology [3,4]. Immunology, the science that studies the structure and functioning of the immune system, began long before anyone knew about disease causing microbes or even that individuals had an immune system that protected the body against disease [5]. Immunity refers to the resistance exhibited by the host towards injury caused by micro-organisms and their products [5]. Immune system is the collection of cells and molecules that are responsible for defending us against the countless

pathogenic microbes in our environment [6]. In the field of Oral pathology, autoimmune diseases affect approximately 5 percent of the population and for many years, the central dogma of immunology focused on the clonal deletion of these autoreactive cells, leaving a repertoire of T cells and B cells that recognize specific foreign antigen. Auto antigens help to form the repertoire of mature lymphocytes, and the survival of naïve T cells and B cells in the periphery requires continuous exposure to antigens [7-9]. Hence having the complete knowledge on this aspect which many a times is overlooked, is of utmost importance for proper investigations and latest research in this field that in turn comes from the past historical knowledge. The terminology and techniques today have the foundation in the past. The historical considerations of past events give perspective to the present programmes and direction for future development. Hence, the present review is a good starting point for compiling the historiography of immunology in the field of Oral pathology and includes a short compilation of the past historical background about basic immunology, hypersensitivity and autoimmunity.

The Greek historian of the Peloponnesian War, Thucydides (430 B.C.), recorded that during the plague of Athens only those persons who recovered from the disease could nurse the sick because they did not catch the disease a second time. During the 15th century, the Arabs and the Chinese translated this knowledge into a crude form of clinical practice by infecting individuals with material from the pustules of smallpox patients. The intentional infection usually gave the infected person a mild form of the disease and induced immunity. This practice, called Variolation (L. variola, smallpox) – the term meaning the insertion of variolous matter with the intention of transmitting small pox in a mild from , became popular in England, mainly due to the efforts of Lady Mary Wortley Montague who survived smallpox but who lost a brother to it. Married to Lord Edward Wortley Montague, the ambassador to the sublime Porte of the ottomans in Istanbul observed the practice of variolation. She directed the surgeon of the embassy to learn the technique and, in March 1718, to variolate her five year-old son. After her return to England, she promoted the technique, and had her surgeon variolate her four-year old daughter in the presence of the king's physician. The surgeon, Charles Maitland, was given leave to perform what came to be known as the Royal experiment, in which he variolated six condemned prisoners who later survived. By these and other experiments, the safety of the procedure was established, and two of the king's grandchildren were variolated on april 17, 1722. After this, the practice of variolation spread rapidly throughout England in the 1740s and then to the American colonies [5,10-12].

Edward Jenner, an English physician, in 1798 improved variolation. Based on the observation that milkmaids who contracted cowpox from cows rarely contracted smallpox, he further tested this hypothesis by inoculating an 8-year-old boy named Philip with fluid from a milkmaid's cowpox pustule and later inoculated the boy with smallpox. The experiment results showed that the boy was protected from smallpox. Thus, Jenner was credited with the technique of vaccination, which replaced variolation. Because cowpox and smallpox viruses were structurally similar, the immune system could not differentiate between the two. The similar structures allowed for cross-reactive protection to smallpox with cow pox vaccine [10,11].

In 1870-1880, Louis Pasteur, the founder of bacteriology, formulated the germ theory of disease. This theory suggested that disease was caused by microorganisms rather than by an imbalance of body humors. Pasteur used vaccines i.e. substances which contained components from infectious organisms that stimulate immunity but not disease, which protects against reinfection by those organisms. Pasteur accidentally at first showed that the causative agents of chicken cholera and rabies lost their virulence when maintained in culture for longer period but still could induce immunity. At the same era, the underlying mechanism of acquired immunity was unknown and based on Pasteur's achievements, the new field of immunology began to develop wherein several efforts were made to treat a wide range of diseases by vaccination and to find new ways of preparing these vaccines [5,10,11]. In 1888, Elie Metchnikoff demonstrated that certain blood cells could ingest microbes and called them as phagocytes. In 1894, Jules Bordet discovered complement; in 1897, Robert Kaus discovered precipitans. These discoveries heralded an era marked by an explosion of new discoveries and controversies relating to the mechanism of host defense and recognition of self and non self [11].

In the 19th century, several mediators were recognized and evolution of immunology began. Paul Ehrlich, in 1908, observed one more important characteristic phenomenon called horror autotoxicus (fear of self-poisoning), now currently known as immunologic tolerance [5,11,12]. Richet and Porteir , in 1913, studied the antitoxin immunity of dogs to a poison obtained from sera anemones and found that dogs previously exposed to a poison collapsed and died within a few minutes after

reinoculation with doses of the poison that were nontoxic to unexposed dogs. The paradoxical result is not immunity or a prophylactic state, but a reversed state, which they called as anaphylaxis. Later Prausnitz, injected himself with serum from an individual named Kustner, who was sensitized to fish. Prausnitz then took a fish tissues. E.g. - Red blood cells may differ from person to person; if a wrong blood type is transfused, an immune response called a transfusion reaction occurs. The same holds true for Rh factor during childbirth whose incompatibility results in disease so called hemolytic disease of the newborn [10].

In 1930, Snell and his co workers conducted work on genetics of graft rejection & showed that the problem of transplantation was partly genetic and that inherited tissue markers that could be recognized by the immune system, thus differentiating self from nonself leading to graft rejection. This discovery of tumor-specific immune responses produced an entirely new area of medicine, immunotherapy, and opened a major sub discipline of immunology called Tumor immunology [10,11]. In late 1940s, the recognition of activation, proliferation, and differentiation of lymphocytes that to perform specific biologic functions lead to the discovery of basis of immunology into its classical and current divisions-humoral (antibodies) and cellular (immune cells) immunology [10]. In the late 1950s and early 1960s, Rodney Porter of Great Britain and Gerald Edelman of the United States elucidated the chemical structure of antibodies and structurally studied gamma globulins and myeloma proteins. Edelman treated rabbit Ig G with dithiothreitol (a reducing agent), iodoacetamide (alkalyting agent) and a denaturating agent and generated Ig G, thus concluded that the Ig G consisted of two heavy and two light chains linked by disulphide bonds and noncovalent interactions whereas Porter fragmented rabbit Ig G with the proteolytic enzyme papain in the presence of the reducing agent cysteine and discovered three fragments having similar molecular weights but different charges. In this, two of the three fragments were identical and retained the ability to bind antigen. And called them as Fab fragments. The third fragment produced by papain digestion did not bind with antigen and crystallized during cold storage. Porter called this extract and inoculated in the same site that had received the serum. He observed redness within minutes. The reaction is called Prausnitz-Kustner reaction or passive cutaneous anaphylaxis [5,12-14]. 1930- Karl Landsteiner discovered the three main human blood groups (A, B, and O) and showed that immunologic reactions can affect piece the Fc fragment. Thus the ratio of Fab to Fc is 2:1. Edelman confirmed Porter results by cleaving and electrophoresing human Ig G into two antigentically different fractions equivalent to two fragments from rabbit Ig G. In similar studies, Alfred Nisonoff used pepsin, which hydrolyzes different sites on the IgG molecule than does papain. IgG treated with pepsin yielded one large fragment with a molecular weight (100KD) double that of one Fab fragment, and many small fragments. Nisonoff called the large fragment F (ab'). This fragment also could bind antigen, but unlike the Fab fragment, it led to a visible serologic reaction. It had both of the antigen-binding sites of IgG (the chains remained linked) and could be treated further with reducing agents to yield two Fab-like fragments called Fab'. Collectively, the two enzymes cleave at about the same region of the IgG molecule. Papain splits the molecule on one side and pepsin on the other side of the bond that holds Fab fragments together. Following these studies, Porter showed that either Fab or Fab' fragments compose the entire light chain and part of the heavy chain. These data led to the formulation of the structure of an antibody [5]. Johansson described an Ig E myeloma in 1967. It was then that Ishizaka and coworkers isolated Ig E. Their work led to the understanding of the immunochemical basis of immediate hypersensitivity, which is related to the antibody known as Ig E. Later the importance of mast cells and basophils was shown, followed by the description of antigens that provoke immediate hypersensitivity. This information provided a more complete description of the mechanism of IgE mediated immediate hypersensitivity. In 1987, Susumu Tonegawa was awarded the noble prize for discovery of genetic basis of antibody diversity. In 1990, Joseph Murray and Thomson were also awarded the noble prize for use of immunosuppressive drugs and transplantation of kidney and bone marrow. The following pioneers who won noble prize in the field of immunology is enlisted in Table 1.

Year	Name of the scientist	Contributions
1908	Paul Ehrlich	Theories of immunity
1908	Metchnikoff	Phagyocytosis
1913	Richet	Anaphylaxis
1919	Bordet	Immunity
1930	Land Steiner	Blood group

1960	Bordet & Medawar	Immunological tolerance
1972	Edelman & Porter	Structure of antibody
1980	Snail Dauset	MHC genes and transplantation
1987	Susumu Tonegma	Genetics of antibody production
1990	Murray & Thomas	Use of immunosuppressive drugs in transplantation
1996	Doherty & Zinkernagel	Recognition of viruses by immune system

Table 1: Noble Prize Winners in Field of Immunology.

Conclusion

The terminology and techniques today have the foundation in the past. The historical considerations of past events give perspective to the present programmes and direction for future development. Compiling the historiography of immunology in the field of Oral pathology aspect is many a times is overlooked and is of utmost importance in field of research. This review includes a short compilation of the past historical background about basic immunology, hypersensitivity and autoimmunity.

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