

Chapter 28

Allergy, the Immune System, and Anti-Aging

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ABSTRACT

Morbidity and mortality in the rapidly aging population of the world is increasing worldwide due to allergy and aging. Over the last century, (especially in the last three decades) there has been a marked increase in allergic diseases, particularly allergic rhinitis and asthma. The incidence of these diseases in teenagers has increased from about 1% in 1990 to 40% 1997. Likewise, the incidence of degenerative diseases of aging has also increased significantly.

In this chapter, we will explore the link between allergy, the immune system, and aging. In order to do this we need to understand the natural history of allergy, or “The Allergy March”, the Neuroendocrine Theory as proposed by Walford, and immunopause – the progressive atrophy and breakdown of the immune system.

Keywords: Allergy; Immune System; The Allergy March; Thymus; Immunopause

INTRODUCTION

On my birthday in 1978, I was given a book entitled “Live to be 100 and enjoy it. The secret of a long, healthy life.” It was about a man called Dr Sage who was a physical wreck. After every treatment he tried failed to improve his health, he underwent cellular therapy. The effect cellular therapy had on Dr Sage was dramatic, restoring and rejuvenating both his body and mind, and returning his sexual potency. At the age of 96, he was living proof that the gift of eternal youth was within one’s grasp.

Live Cell Therapy

In 1931, Dr. Paul Niehans of Switzerland followed the practice of Dr. Kuettner who pioneered the concept of live cell therapy in 1912. Live embryonic cells were taken in the first three months of pregnancy from the placenta of bovine, sheep or shark, preserved in saline, and then injected into the muscles of sick or aging patients. It claimed to be the only therapy that

could regenerate cells and tissues, and stimulate the immune system thereby reversing diseases of aging. Consequently, live cell therapy was seen to be the medicine of the future.

THE ROLE OF STEM CELLS

There are three main players in allergy, immune responses and aging; namely cells, molecular signalling, and the neuroendocrine system. Amoeba, zygotes, and stem cells from bone marrow have been extensively studied. It is now evident that these self-renewing pluripotent cells are found not only in the fetal or embryonic tissues and bone marrow, but also in adult tissues of people as old as 75. Stem cells known as CD 34, which can be found in the bone marrow, produce pluripotent cells that are progenitors of various cells found in the hemopoetic system and body. They produce homeostasis with upregulation in responses to allergic and various immune responses. Bone marrow transplants have been carried out for years in immunological as well as other conditions. Now with the discovery of stem cells in the heart, brain, and other organs, we are on the threshold of an exciting era of developing stem cell research and therapy as an anti-aging modality.

The Immune System, Allergy and Aging

At conception, the embryonic stem cells divide and multiply to form an embryo. Immunologically, there are two important phases of the child – the in-utero and post-natal phases. In the uterus, the child is in a safe environment of the amniotic fluid. At about the 18th week, TH (T helper) cells appear in the blood (Figure1). These cells prepare the child’s immune system for postnatal life. When there is a balance of TH1 and TH2 cells, the child produces IL-2 (Interleukin 2) Interferon γ , Tumor Necrosis Factor (TNF), and NK cells. These confer the natural protective effects against viruses, bacteria, and other diseases.

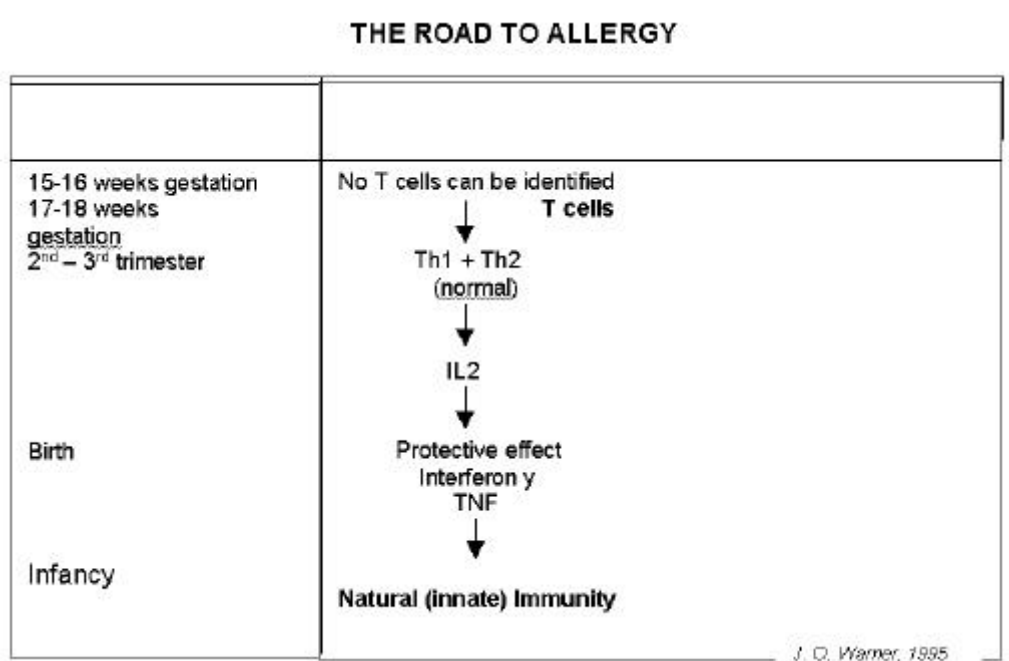
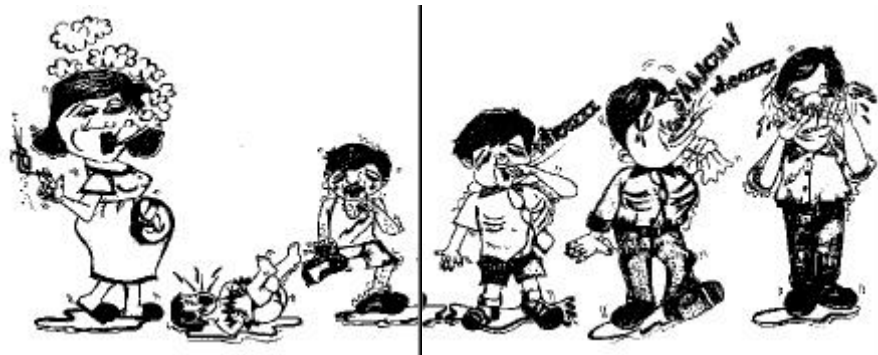


Figure 1. Development of the Immune System

However, the inheritance of certain candidate genes may skew the immune system to produce excessive TH2 cells. When such children are exposed to allergens, they develop allergic diseases. In some individuals, there is hyperactive reactivity of the immune system against its own organs. This results in autoimmune diseases like rheumatoid arthritis, thyroiditis (Hashimoto's Disease) and a whole array of medical conditions. Lastly, the body's defenses may be hypoactive resulting in immunodeficiencies and aging.

HUMAN MODELS OF IMMUNOLOGICAL RESPONSES

The child is born with a defense system, which is mediated by cellular communication throughout the body. Under normal conditions, the child is healthy, but when there is a threat to the body, there is upregulation of the basophil/eosinophil (E0-B) progenitors in the peripheral blood. It is vital to note that the bone marrow actively participates in the production of inflammatory cells that are recruited into the diseased organ. Understanding of the signaling between the affected organ and bone marrow at a molecular level may open new avenues of preventive treatment for allergic diseases and aging. The target organ for expression of allergy tends to change with age.



The natural history of allergy – ‘The Allergy March’ – is very interesting. Several longitudinal studies, e.g. the German MAS study, have shown that the child has four main organs exposed to allergens. The alimentary system is the earliest organ to manifest allergy in the form of infantile colic due to allergens in the food – cow's milk and egg white being the main offenders. As the child walks down the road of allergy, atopic dermatitis manifests within six months – a warning to physicians to be on the alert. Inherited immunity recedes by the 18th month, though the atopic dermatitis tends to persist, unless the child avoids the allergens or undergoes immunotherapy. This is well documented in the WHO (World Health Organization) White Paper on Immunotherapy (1998). If such measures are not implemented, aeroallergen sensitization begins in the first decade. The child suffers from allergic rhinitis and asthma that peaks in the second decade in teenage population. Total IgE – a marker of allergic diseases peaks in the second decade, after which it begins to decrease, indicating a decrease in our immunity (Figure 2).

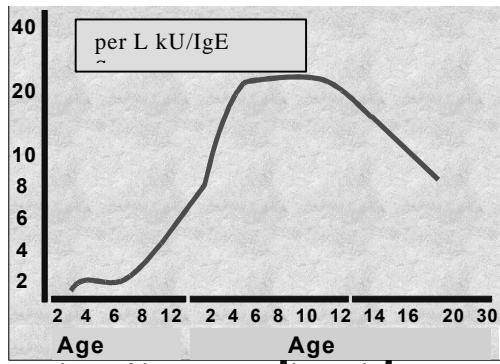


Figure 2. Normal Values of Total Serum IgE (Thymus Dependent)

Over the last century, (especially in the last three decades) there has been a marked increase in allergic diseases, particularly allergic rhinitis, and asthma. The incidence of these diseases in teenagers has increased from about 1% in 1990 to 40% in 1997. Likewise, the incidence of degenerative diseases of aging has also increased significantly.

In 1969, Roy Walford highlighted the Neuroendocrine Theory and its role in the immune system and aging. The thymus had been a very neglected organ. He emphasized the vital role this gland plays in the regulation of body homeostasis. The pituitary was also realized as an important organ of the endocrine system. There are sixty trillion cells in the body, which communicate with each other through cytokine, cellular and neuroendocrine network thereby regulating local and distant organs. There are multiple feedback biological loops with the pituitary acting as the central server. In the immune system of the allergic patient and in aging, the thymus is essential for TH cell maturation, and can be considered the defense academy. The bone marrow is the factory that produces pluripotent cells from the reservoir of the stem cells. Stem cells have now been identified in the brain, heart, and other organs. With biotechnological advances, this will become a potential source of anti-aging therapies.

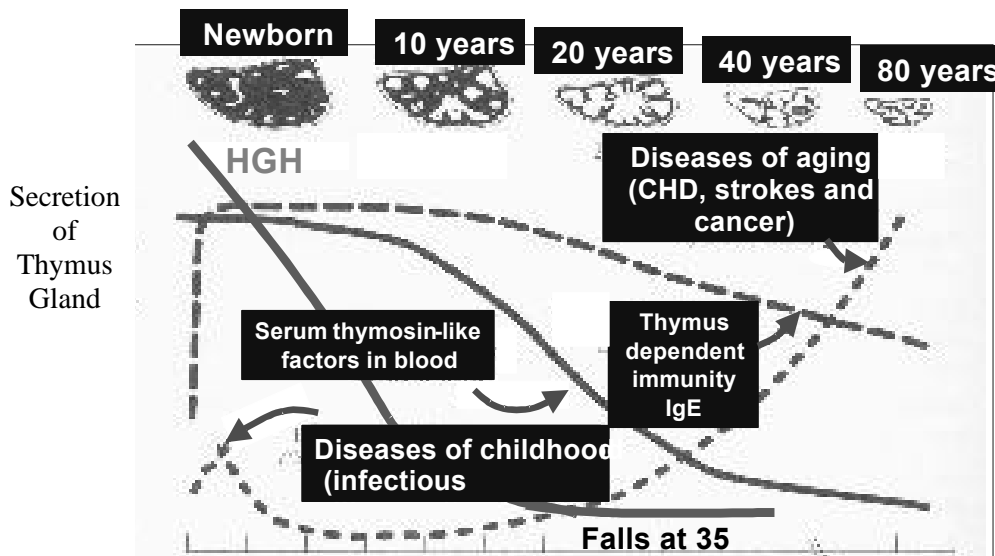


Figure 3. The relationship between the thymus, bone marrow hormones, and Diseases of Aging

By the third decade, the thymus atrophies. It is a locomotive of the immune system, hence responsible force for a healthy body and later, aging. In the fifth decade, the thymus completely disappears – compromising health and the immune system. Aging is caused by the progressive atrophy and breakdown of the immune system – immunopause which along with the twenty pauses in the body is responsible for the increase in diseases of aging – diabetes, atherosclerosis, hypertension, heart attacks and strokes, which begin to rise after the age of forty years:

World Population & Epidemiology of Diseases

Population Markers:

1900 = 1.7 billion;

2000 = 6.2 billion;

2100 = 11.5 billion

Control of infectious diseases with vaccines, antibiotics, better sanitation and medical care

Life expectancy increased >100% in the 20th century

Onset of NEW PROBLEMS:

1. Marked increase in allergic diseases last century
2. Marked increase in global aging population
3. Marked increase in diseases of aging
4. Marked increase in the morbidity and mortality in allergy and aging inspite of medical advances
5. Marked increase in the economic burden on the working population and the nations.

HORMONES AND THE INCIDENCE OF DISEASES OF AGING

Several studies have shown a steep fall in levels of Human Growth Hormone (HGH) in the third decade (Figure 4) due to pituitary dysfunction. This is followed by a decline in thymic peptides and immunoglobulins E (IgE), resulting in a compromised immunity. As a result of the hypofunction of the various organs, there is multiple organ failure with an increase in morbidity and mortality in developed countries where life span has increased.

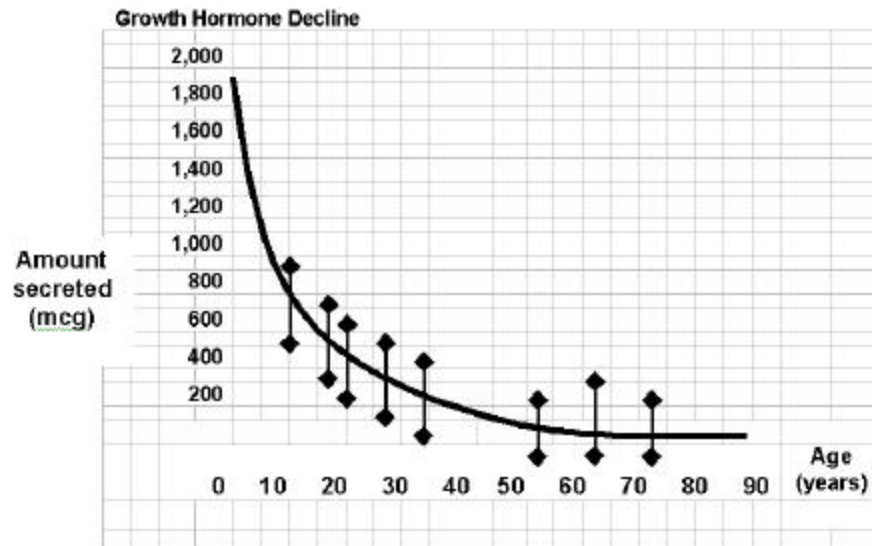


Figure 4. The Age-Related Decline in Growth Hormone: By age 35, geriatric levels are reached.

Before the discovery of vaccination, antibiotics, and improved sanitation, death from infectious diseases was common in childhood. The pattern has now changed from infectious diseases of childhood to degenerative diseases of aging such as coronary heart diseases, strokes, and cancer. Some of the diseases of the twenty-first century may be linked to inflammation and the allergic response.

In allergic and immunological inflammation, various inflammatory cells – leucocytes, lymphocytes, eosinophils, basophils, and mast cells – stick to the endothelium when adhesion molecules like ICAM-1 and VCAM-1 causes diapedesis. These cells then home in on the affected organ and liberate various cytokines, chemokines, and other products that cause inflammation and damage to the organs (see Figure 5).

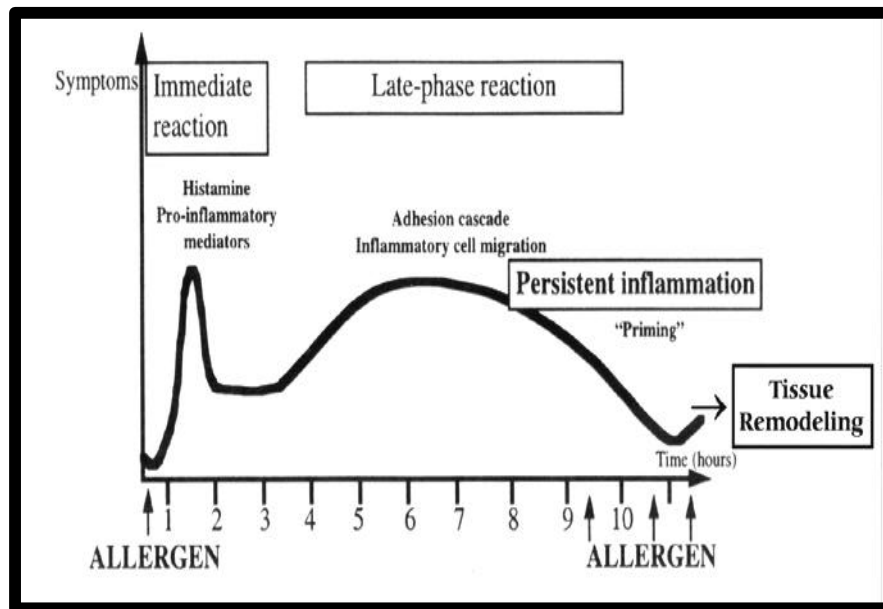


Figure 5. Minimal persistent inflammation and tissue remodelling.

Even in the absence of symptoms, the reaction – minimal persistent inflammation (MPI) continues, ultimately resulting in scarring and permanent damage to the organ known as tissue remodelling. It is vital that anti-aging treatment is started before the organs undergo extensive and irreversible damage. Since somatopause begins by forty, anti-aging therapeutics and hormone replacement therapy should begin between forty and fifty years of age. If left untreated, scarred tissue responds poorly to treatment.

CONCLUSIONS

Morbidity and mortality in the rapidly aging population of the world is increasing worldwide due to allergy and aging. Early treatment of the modifiable risk factors of aging and prevention of diseases of aging is imperative. Conventional treatment by the gerontologist is symptomatic and a late rescue attempt. If modern anti-aging protocols are not implemented, nations around the world will have nursing homes as their leading form of housing, and many governments will go bankrupt due to the high costs of caring for large numbers of invalid aged.

Decreasing levels of immunoglobulins, bone marrow defense cellular progenitors, thymic proteins, and hormones lead to a compromised immune system and aging. Various animal glandular extracts have been used for centuries to boost our immune system. The extracts from placenta, testis, pancreas, and the thymus have been taken orally. Administration of thymic extracts has been shown to increase the NK cell immunity in animal models and humans. Thymic proteins are potent stimulants of the immune system potentiating the TH type of immunity. With rapid advances in biotechnologies and stem cell therapy, we hope thymus replacements along with other anti-aging protocols and hormone replacement therapy will improve our management of the rapidly aging world population to prevent, reverse, and improve the quality of life.

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Dr. Dato Harman is a graduate of the University of Malaysia (now known as the University of Singapore). He has worked as Medical Officer, Registrar, and Senior ENT Consultant for the ENT Department at General Hospital, Kuala Lumpur, Malaysia. Dr Harman is currently a practicing otolaryngologist with a special interest in allergy. He is a founder member of the World Society of Otolaryngic Allergy and the Malaysia Society of Allergy and Immunology.

