SUMMARY & CONCLUSION
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Atopic dermatitis (AD) remains a puzzling disorder in which a variety of factors are involved in the initiation and evolution of the disease. These factors are the consequence of specific multiple abnormalities which could all together account for the etiopathogenesis of AD.

The term AD is now commonly accepted after a variety of synonyms. Although it opens to criticism it appears to be the best name of the disease. Recently, Rajka, 1983 proposed his own definition: "Atopic dermatitis is a specific dermatitis in the abnormality reacting skin of atopic individual, resulting in itch with its sequelae, as well as in eczematous inflammation".

The true incidence of AD could not be determined. Some new data reflected a raised incidence in infants and in cold and dry geographical areas. On the other hand, the occurrence of the disease in hot and humid areas is also well known. Seen from a global aspect the real prevalence of AD has changed because more people than formerly now have access to medical
care. In addition, some environmental influences may also contribute to the increased occurrence of AD. Discussing the different theories postulated for the etiopathogenesis of AD through analysis of the different data and correlation between these theories, could clarify the most supportive etiological theory.

The genetic theory was supported by the positive familial history being encountered in nearly all cases of AD and the association of AD cases with asthma, rhinitis and hay fever. The association of AD with other congenital defects with dermatological or systemic is one of the proofs given for this theory. The specific mode of inheritance in AD has not yet been defined. This was explained by the fact that what is inherited is not a skin disease but a tendency to pruritus which become evident on exposure of the skin to stressful internal or external environment.

The physiologic theory is generally governed by the dry skin of the atopic patients. Several factors were considered in explanation of such dryness: for example decreased sweating, decreased TWL, decreased sebum, decreased cohesion between corneocytes,
epidermal vasculature changes and excessive scaling. Remissions and exacerbations of the disease with seasonal variations is a good support of the physiologic theory in atopic patients. Sweating provoking stimuli as physical exercise shows the importance of sweat training therapy in AD, both are correlated positively with the physiologic theory. The evidence of different surface lipids composition, as well as the isolation of staphylococcus aureus in higher incidence could be attributed to the physiologic theory.

The autonomic imbalance theory with beta adrenergic blokade (Szentivanyis theory 1968) results in inhibition of beta adrenergic receptors, activation of alpha adrenergic and cholinergic receptors. The beta adrenergic inhibition will result in increased neurons excitability, decreased threshold of cutaneous itching and increased intracellular cAMP with abnormal cell proliferation and inhibition of epidermal mitosis. This will be manifested clinically by lichenification and pruritus. The increased activity of the alpha adrenergic receptors will activate the vascular reaction and pilomotor smooth muscle reaction. This is manifested clinically by different grades of pallor, white dermographism (vascular theory) together with
follicular keratosis of the skin. The activation of cholinergic receptors will directly affect the sweat glands with clinical presentation of oligo/an idroses with subsequent dry skin (physiologic theory). Accordingly, lymphocytes, polymorphonuclear leukocytes and even mast cells could be affected with the changes in different enzymes and histamine. The level was proved to be highly increased (Immunologic theory). The most accepted explanation of this theory is that the fundamental abnormality could be an inherited (genetic theory) or acquired defect in adenyl cyclase enzyme being that identified to the beta adrenergic receptors. This could be happened with reduced synthesis, partial blockage and defective enzyme molecule.

The immunologic theory expanded several immunological abnormalities in AD patients. Such abnormalities are not only due to defects in the humoral or cellular immunity or defects in autonomic balance but also they are more likely to be factors associated with disease activity and severity.

The immunological mechanism necessitates the presence of an allergen. Several allergens were
identified in atopic patients. Sun exposure, foods inhalents, danders lipid solvents, irritants and all factors leading to dry skin. The allergenically active material finds its way to the target cell where in the first stage it causes atopic sensitization to be followed by atopic reaction. By atopic sensitization, the allergen enters through natural portal to react with reagin forming cell. Reagin produced "fixes" to reacting cell (example mast cell) containing inactive or bound mediator, for example, histamine. By atopic reaction, the antigen again enters by natural portal and contacts reagin fixed to reacting cell. Antigen reagin reaction causes release of mediator for example, histamine contained in mast cell granules. Mediator exerts pharmacologic effect on shock organ to cause symptoms. Although IgE is the most common high immunoglobulin detected in AD, but there is no doubt that IgE antibodies and atopic anaphylactic susceptibility are a concomitant phenomenon of AD and not the fundamental disorder. IgE directly or indirectly through abnormal immune regulation is considered to be responsible for a rapid start of itching, its continuity and/or persistence. Also it shares in the production of the inflammatory reactions of the skin with all its clinical manifestations known as late cutaneous reaction (late
phase of the immediate type) of immunological reaction.

This phenomenon is based on the release of mediators from surface of mast cells or basophils during an IgE - anti-IgE reaction. Different authors discuss the role of IgE in AD with several arguments against and several arguments with, but no body could deny or neglect the role of IgE in AD. Reports on changes in other immunoglobulins are fewer but stating the marked increase of IgG, moderate increase of IgM, normal value of IgA and decreased IgD levels.

The delayed hypersensitivity or cell mediated immune response (CMI) in AD was long discussed. Suppression of T cell function is the main factor with all its results. Clinically it enhances the inflammatory process responding to exogenous allergens for example, viral, fungal and bacterial. Also (CMI) through T cell population versus IgE level with resultant high proportion of lymphocytes having IgE bound to their membranes. Suppression of T cell function also results in increased sensitivity of T cell to cAMP and histamine with all its clinical replications.
The vascular theory is positively argumented with the abnormal vascular responses to variety of stimuli rising from physiological, environmental, genetic or immunological factors, these reactions include skin pallor, changes in skin temperature, vasconstriction tendency in areal circulation and white dermographism. Some altered pharmacologic reactions could be contributed to these vascular manifestations. Acetyl choline with an altered pharmacologic reaction result in the delayed blanch phenomenon which occurs frequently in patients with AD. Other altered pharmacological reaction in AD patients is recorded as with histamine prostaglandin, brady kinin, serotonin, kalikenin and catecholamine.

The psychological theory plays some part in the initiation, aggravation or perpetuation of the disease. The personality trait in AD was regarded in the past as a fixed and irrevocable feature. In fact, the personality deviation observed in AD is considered as a result not a cause. The role of maternal rejection in AD is not clear but it is of great importance in contribution to the severity of the disease. The psychological aspects
of AD were considered by some authors in the contexts of immunology, where emotional effects has proved to have a great incidence in the immune system and manifested in skin diseases.

Correlations between different lines of treatment followed in AD and the etiopathogenesis of the disease revealed a very positive correlation supporting the multifactorial opinion in etiology of the disease.

In conclusion, the etiology of AD could not be attributed to only one theory, but a group of theories correlated and interacting with each other can be considered the ideal etiopathogenesis of the disease. These include the genetic, the physiological, the autonomic, the immunological, the vascular, the altered pharmacologic and the psychological. These theories act and/or interact with resulting imbalance in the autonomic system presenting the main features of the disease. This comes into conclusion that the primary and predisposing is the genetic theory. The most mastering theory is the autonomic theory. The clinical manifestations of the disease are the direct expression of the autonomic disturbances. The ideal treating regime should include drug, supportive and immunologic therapy.
CHART (11)

CORRELATION BETWEEN DIFFERENT ETIOLOGICAL THEORIES IN ATOPIC DERMATITIS