SUMMARY AND CONCLUSION

Apoptosis is a major mechanism of programmed cell death used by to eliminate superfluous and irreparably damaged cells. It has a crucial role in shaping organs during development and controls homeostasis and integrity of tissues throughout life. Apoptosis can be triggered by a wide variety of stimuli, including developmental cues, severe cellular stress or damage to essential cellular components, caused by heat shock, radiation, cytotoxic drugs, infection and oncogenic transformation.

Apoptosis induction occurs through two distinct pathways: intrinsic and extrinsic. The intrinsic pathway is activated by intracellular events and depends on the release of proapoptotic factors from the mitochondria. The extrinsic pathway receives signals through the binding of extracellular protein ligands to proapoptotic death receptors (DRs), located on the cell surface. Both pathways lead to hierarchical activation of specialized proteases called caspases. Apoptotic signals first activate initiator caspases, including caspase-2, -9 and -10. Once stimulated, initiator caspases proteolytically activate the downstream effector caspases, including caspase-3, which in turn cleave numerous essential cellular proteins, thereby leading to the unique morphological and biochemical features of apoptosis, such as plasma membrane ‘blebbing’, cell shrinkage, chromatin condensation and DNA fragmentation.

Apoptosis is regulated by numerous genes and factors such as Fas, TNF, perforin ⁄ granzyme B, Bcl-2, NF-κB and p53. Aberrant regulation of apoptotic cell death mechanisms is an important pathological factor in variety of major human diseases. Deficiency in apoptosis is one of the key hallmarks of cancer and also contributes to certain autoimmune

diseases and metabolic disorders. In contrast, excessive apoptosis is an important component in neurodegenerative disorders, infertility and inflammatory diseases.

Keratinocyte apoptosis is believed to play an important role in the pathogenesis of spongiotic dermatitis, in particular for the formation of spongiosis. The present study investigates changes in the expression level of the apoptosis regulatory proteins caspase-3, Fas, Bcl-2, NF-κB and p53 in skin samples of patients with spongiotic disorders.

This study was carried out on 2 groups:

(1) Patients group that included 50 patients divided into five subgroups:
   - Group (A): atopic dermatitis
   - Group (B): allergic contact dermatitis
   - Group (C): irritant contact dermatitis
   - Group (D): nummular eczema
   - Group (E): dyshidrotic eczema

(2) Control group that included 10 healthy subjects.

All studied individuals were subjected to history taking and clinical examination; we investigated expression of apoptotic regulatory molecules with variable parameters including duration of cutaneous lesions and age of the patients.

The result of this work showed the following:

1. Caspase-3 cleavage occurs in keratinocytes of the spinous layers of the epidermis in acute spongiotic lesions and that particular high levels are present in spongiotic areas.

2. Positive Fas expression of keratinocytes in acute spongiotic lesions. The ring-like staining pattern suggested that a large proportion of the expressed Fas molecules were located on the surface of these cells.
3. Bcl-2 expression was absent or weak in suprabasal cells in lesional skin. This decrease in epidermal Bcl-2 expression with its antiapoptotic effect may explain the increased sensitivity of keratinocytes to apoptotic stimuli.
4. NF-κB expression was absent or weak in suprabasal cells in lesional skin. This decrease in epidermal NF-κB expression with its antiapoptotic effect may also explain the increased sensitivity of keratinocytes to apoptotic stimuli.
5. P53 expression was absent or weak in suprabasal cells in lesional skin. This indicates that p53 has no role in keratinocytes apoptosis that occurred in spongiotic dermatitis.

Conclusion:

KC apoptosis is the initiating event in the development of the epidermal pathology seen in spongiotic dermatitis (in studied diseases). Most notably, KC apoptosis occurs in suprabasal cells, where spongiosis takes place. Apoptosis of individual KC is the first event leading to disruption of epidermal continuity and vesicle formation. Damage to KCs leads to the loss of intercellular cohesion (acantholysis) and subsequent cleft formation. Fluid influx from the dermis and intercellular edema contributes to spongiosis. The knowledge of this molecular basis is pivotal in understanding the development of pathology in spongiotic disorders, and opens a future for more focused therapeutic applications.