

# Stress — the enemy of human health

Attendees at UCD's Charles Institute Seminar Series heard a presentation from expert in psycho-neuroimmunology **Prof Eva MJ Peters** on how hair has become an easily-accessible surrogate marker for the close connection between psychosocial wellbeing and physical health

The Charles Institute, Ireland's national dermatology research and education centre, played host to a range of guest speakers who covered a variety of topics ranging from skin cancer to psoriasis, among others. The series, which was sponsored by RELIFE (part of the A.Menarini group), was designed to provide expert advice from a range of distinguished national and international experts in their respective fields and was chaired by Prof Desmond Tobin, Full Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology. The seminars were broadcast to attendees with a special interest in dermatology in other locations, who accessed the talks remotely via an audio-visual link.

Attendees at the series took part in an interactive presentation by Prof EMJ Peters, Head of the Psychoneuroimmunology Laboratory, Department of Psychosomatic Medicine and Psychotherapy, Justus-Liebig University, Giessen, Germany. Prof Peters explained how the study of hair is an accessible surrogate material of the close connection between psychosocial and physical health in neuroendocrine-immune research and its relevance to maladaptive stress responses and disease development.

Prof Peters told attendees that the hair follicle microcosmos contains dense innervation and blood vessel supply and its associated epithelial, mesenchymal and functional cell populations produce an abundance of stress mediators and carry corresponding receptors, as do the cells of the immune system surrounding each hair follicle.

The hair follicle microcosmos is also closely linked to systemic stress response systems such as the hypothalamus-pituitary-adrenal axis and the autonomic and sensory nervous system that communicate to the general state of alarm and defence to the skin. This enables evidence-based study of a range of stresses, such as anxiety, depression or significant life events and their corresponding biological effects. She explained that research has already shown that below the skin's surface, neuroendocrine-immune interaction malfunctions as a result of excessive stress and this is being used to study epigenetic stress responses in humans to better understand their role in a number of diseases, ranging from allergy to cancer, for example.

## Change in awareness

Prof Peters told the seminar: "We are experiencing a change in awareness that stress may not only be a 'personal problem', but also an environmental problem in terms of human health," she said. "One of the reasons people are beginning to think like that is because we all feel deep down that if we don't reduce our stress, we may age faster and acquire a number of diseases. However, if I were to ask medical doctors the question in a professional teaching context, 'Do you believe stress contributes to disease?', sometimes the answer is not so clear. Doctors in somatic disciplines such as surgery, internal medicine or infectiology often think that stress is not so important as to take it into account when it comes to treatment, medications, and so on."

Prof Peters described hair and skin as "the tip of the iceberg" in terms of indicat-

ing health dysfunction and told the seminar that when skin is examined, there is an intimate interaction between keratinocytes and nerve fibres, and an intimate interaction between nerve fibres and mast cells. In terms of other immunocytes, there is also a close interaction between nerve fibres and blood vessels and smooth muscles — "virtually every cell in the skin can be reached by neuropeptides, neurotrophins and neurotransmitters, the mediators of the super-systems that conduct the response to stress," Prof Peters told the seminar.

"We have now learned that innervation of peripheral organs is not just there to perceive what's coming from the outside or do simple things, such as sweat secretion or muscle contraction, but it is also there to allow the brain to communicate with the periphery and make it participate in a fight-or-flight response," she explained. "That means we have to have immune regulation, we have to have management of oxidative stress, we have to have energy supply and metabolic functions and we need constant remodeling of the tissue, a constant tissue repair process to be able to adapt to environmental needs."

## Tumours

Prof Peters presented an overview of some laboratory work, one aspect of which showed that mice subjected to prolonged stress developed UV-induced skin carcinomas more quickly and severely than mice not subjected to such stress. Moreover, mice kept under stress-free so called "enriched environment conditions had less and smaller lung metastasis than mice kept under standard laboratory housing conditions, after they were inoculated with malignant melanoma cells. Human hair cortisone is now being used to objectivise biologically effective stress and determine whether this translates into chronic deregulation of inflammatory conditions in patients, she added.

Prof Peters summed up some data on the relationship between stress and socioeconomic circumstances, among other factors, and told the attendees: "If we have homeostasis, we have a situation where there are a lot of psychosocial resources and good coping abilities, promoted for example by good early attachment to our mothers and fathers. On the biological level, we then have an epigenetic situation that allows us to have a flexible immune response, a flexible stress response and a vigilant immune response that is always able to answer new challenges and fulfill homeostatic tasks in the body."

She continued: "In acute stress, this will change into what you could call a 'neuro-immunological fight-or-flight response; we need an innate immunity to quickly and effectively defend ourselves, but if this situation becomes chronic and the stress is not interrupted by phases of relaxation, this results in a deregulated immune response, with continuously heightened proinflammatory activity that can cause permanent damage to peripheral organs."

Prof Peters described the need for "an integrated attitude" to the relationship between stress and illness and told the attendees: "If what we do to the skin to treat it is not enough, then often, we introduce a vicious cycle. People who go to the doctor and get a cream that perhaps doesn't help will start



Pictured L to R: Mr Johnny Murphy, A.Menarini; Prof Eva MJ Peters; Prof Desmond Tobin, UCD

to avoid the doctor and ignore the problem," she said. "They will suffer increased tension because the problem is not going away, they will have increased symptoms and they will start to 'treat' themselves with maladaptive behaviours, trying to 'escape', not sleeping properly, and so on. They will eventually feel helpless and depressed and that will close that vicious cycle, out of which there seems to be no escape for them.

"It is important to learn and observe in each and every patient at what point in this cycle they are — what kind of help does he or she need to reduce and reverse that cycle. In the beginning, stress reduction will be enough and when you get deeper into the problem, behavioural training will be useful and if the problem becomes severe, in my opinion, psychotherapy is required."

Prof Peters concluded by telling the seminar she hopes "in future, we can reverse some very old-fashioned attitudes in psychodermatology and get dermatologists to think about the psyche of their patients as a relevant aspect of every interaction... I will close with a quote from Voltaire, who stated: 'Because it is better for my health, I decided to be happy.'"

## Mast cells

During a lively Q&A session following the presentation, Prof Tobin asked Prof Peters about mast cells and touched on how mast cells are often implicated in a number of stress-related conditions. "There is something unusual about the skin, in that we seem to be capable of making mast cells locally, and bone marrow is not necessarily needed," said Prof Tobin. "Does that potentially set up the skin to be fundamentally much more primed for engagement with neurostimulation by mast cells, and does that have an implication in some aspects of skin disease?"

Prof Peters replied: "It certainly does have an implication. I think what we have to learn is that we are so used to thinking of the body as a 'top-down' organism — the brain is the 'boss' and everything else comes second. In fact, it is more accurate to describe the body as a 'federal state', where a lot of things are going on independently. The mast cells should be seen as independent, organising a local stress response and local tissue homeostasis, while still being hard-wired through the nerve fibres to the overall systemic situation. I think that's an important point to

learn."

It is commonly known that the burden of stress can be relative in its severity, depending on the individual and their ability to process stress. Speaking to the *Medical Independent (MI)* following her presentation, Prof Peters explained that a similar variation had previously been seen in laboratory animals studied for their stress responses. "Other groups have looked into this," said Prof Peters. "For example, in rheumatoid arthritis, there is one study that does a really nice stress paradigm in rats. They let the rats run around a cage so that the researchers can identify the rats that like novelty, for example, and the ones that avoid it.

"They then divided the rats into two groups for their studies — those that liked novelty, and those that didn't," she continued. "The ones who didn't like it had certain problems that were more severe, and the ones that liked novelty developed other problems, such as a higher rate of arthritis. So it seemed the more active and creative they were, the less depressive they were, but also more prone to getting inflammatory disorders."

Prof Peters also believes there should be more emphasis and integration of stress reduction in people with serious illnesses among the medical profession in order to improve their patients' outcomes. "That should be part of medical education in general," she told *MI*. "We tend to think that a person who lies in bed and can't say anything does not perceive much, and that is simply not true. They perceive a lot and often, when they recover and are able to tell us about it, they report that they found it highly traumatic to be ignored and to feel like a piece of flesh in the bed, where the covers were changed but nobody talked to them... doctors will know that if they have an excitable or stressed patient, they will need more anaesthesia, for example, and of course that comes with its own problems."

"To reduce the stress that a patient in the medical context experiences will have a significant impact on the results of the care of the patient."

*RELIFE has had no input into the content of this article or series of seminar*

If you have any suggestions for dermatology topics for future presentations, please send them to [info@mind.ie](mailto:info@mind.ie).