

There are 2 main categories of environmental factors involved in autoimmunity: drugs and infectious agents. Many drugs are capable of inducing autoantibodies in large segments of the normal population. These autoantibodies often react against nuclear or erythrocyte antigens. Drug-induced autoimmunity is often asymptomatic and tends to be reversible. Symptoms generally disappear rapidly upon discontinuation of the offending agent, although serologic abnormalities may persist (Talal, 1980, p. 224).

This autoimmune reaction does not seem a mistake, but is elicited by a foreign agent. This would rather indicate a process of protection in balancing the body in case of a problem.

That the idea of an autoimmune disease is too narrow also becomes clear by the fact that there are *many examples of autoimmunity without autoimmune disease* (Talal, 1980, p. 224).

When we presented the melatonin pathway, we showed that the immune system could act against its own tissue. We stipulated before that to have a broader view and stimulate a deeper insight on the immune system it would be better to call those actions of the immune system *autoimmune reactions*.

The body presents an ingenious example of attacking healthy tissue in order to save the whole with an autoimmune reaction in the case of an insult or other CNS injury. From the core of an insult a cell degenerative spread can occur. In order to prevent this, an autoimmune reaction is deployed that kills healthy cells surrounding the insult area, thus stopping the insult area fromspreading, without causing an autoimmune disease (Moalem et al., 1999; Yoles et al., 2001). Moalem and colleagues were the first to speak about protective autoimmunity and Nevo and colleagues call this protective autoimmunity (Nevo et al., 2003). As Nevo and colleagues say: Tolerance to self is thus not a lack of response to self, but the ability to tolerate an active defense response to self without developing an autoimmune disease. They stipulate that when the injury spreads this means that the intensity of the immune response is weaker than required. In 2004 a mathematical model was conceived by Nevo and colleagues (Nevo et al., 2004) where they postulated that there were three conditions in the fight of autoimmunity against malfunctioning of the body (autoimmune situations):

- 1: Autoimmunity operates and wins.
- 2: Autoimmunity cannot compete with the ongoing loss.
- 3: Autoimmunity causes the loss of tissue.

We think there could be a fourth and fifth *autoimmunesituation*:

- 4: Autoimmunity constantly balances the ongoing malfunctioning of the body.
- 5. Autoimmunity has to deliver such a fierce and ongoing fight that the disease elements become the foreground.

In 2004, Schwartz and Kipnis, eleven years before the discovery of the brain being connected to the immune system spoke about the protective capacity of the immune system (Schwartz & Kipnis, 2004; 2005). At an early stage Schwartz and colleagues already spoke about a function of 'protective autoimmunity' to the CNS immunosurveillance by immune cells circulating in the brain. Schwartz has continuously stressed that autoimmunity has a protective role in CNS injuries and pathological conditions and could play a preventive role (Schwartz & Ziv, 2008; Schwartz & Schechter, 2010; Schwartz & Ziv, 2014; Schwartz & Raposo, 2014).

6.3 Paraneoplastic syndromes

Sometimes neoplasms grow that can be benign or can become cancerous tumours. In the case of cancer an autoimmune reaction very often accompanies the cancer, called the *paraneoplastic autoimmune diseases* or *paraneoplastic syndromes, PNS*. They are considered a side effect of the damaging cancer tumour formation in the body. Somewhere there is an association between the cancer and paraneoplastic syndrome. Instead of thinking that the cancer coexists with autoimmune diseases, it would be interesting to find out if these autoimmune reactions could be an attempt of the body to balance the cancer. It would be logical that it has a role in the case of cancer, because it often occurs when cancer is showing itself.

The PNS is a consequence of remote effects of tumours on different organ systems, sometimes even years before the tumour is apparent (Zaborowski et al., 2014; Höftberger, 2015). Not only is the pathogenesis different, but the PNS is also more severe and often presents a broader range of clinical symptoms (Maverakis et al., 2012). A large number of cancer patients show CNS involvement (Höftberger et al., 2015). The first report of a paraneoplastic syndrome has been attributed to a French physician, M. Auché, who described peripheral nervous system involvement in cancer patients in 1890 (Auché, M., 1890).

Autoimmune Reactions and the Immune system presents an overview of the immune system. For the first time a schema with all the elements of the immune system was possible due to all the evidence-based material meticulously gathered in centuries of medical science. This schema has been elaborated with a new perspective on the immune system, encompassing not only the fight against viruses, bacteria, parasites and fungi, but as the system organizing the processing of the cells of the body. A perspective shifting from fighting to protection and ultimately to exchange between the human body and its surroundings. To enable this broad perspective a fourth pathway of complement activation was developed, the melatonin-pathway.

Dr. Martine F. Delfos is a scientist active in a broad scientific area, combining different scientific fields, who also works as a practitioner.

From the foreword of Prof. Dr. Dick Swaab: Martine Delfos is one of those exceptional people who, at a very early stage in her career, successfully started to build bridges between the fields of psychology, medicine and neuroscience. For a long time she was one of the few psychologists truly interested in neurobiology. She is a scientist by trade but corroborates her scientific insights as a clinical psychologist and a therapist. As she says: "A scientist needs to be confronted with his mistakes through real life". Martine contacts me a couple of times a year with in-depth biomedical questions. Her questions always concern a very different topic, are never easy to answer, and are always original and force me to look at a problem in a new way. The latest fruit of her labours is the present volume 10 of her PICOWO-series on 'Autoimmune Reactions and the Immune System'.





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