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Institute, it would be most appropriate time for you to arrive. Looking forward to pleasure of meeting you soon here on Canadian soil.” Szívélyes üdvözlettel: János bátyád. Professor Selye would never miss writing couple of sentence Hungarian at the bottom of his letter written in English or French.

Nevertheless, finally I was there. When I arrived in Montreal late afternoon in September, Professor Selye received me in his office. At this first meeting Professor Selye already presented me with the research options.

“I gladly join in the research work of the Institute- I replied- yet I believe I will have enough time to realize my own research plans as well.”

Hans Selye demonstrated that stress from a variety of sources causes adrenal enlargement and thymus atrophy. The idea that stress alters the immune function gained notable interest among clinicians and scientist and has led to the development of the modern concept of psychoneuroimmunology.

My research conducted in Selye’s institute became the basis of my later research and has proved that the macrophages are the “alarm” cells of the organism, which play a key role in the immune system and the cytokines, the mediators produced by macrophages may start off unwanted reactions damaging the organism similarly to the reactions elements of chronic shock.

**Effect of rare metal salts on reticuloendothelial activity**

One of my first papers published from Selye institute reported that the rare earth metal salts, among the gadolinium chloride, depress the reticuloendothelial activity, and selectively interfere with the function of the Kupffer cells.

These works became determinant in my further scientific work. How is our research work related to the stress concept? Macrophages are the body’s “alarm” cells that synthesize and excrete highly reactive materials. The biological active materials are very important in killing bacteria and tumor cells. However, macrophages not only act as a first line of defense and have pivotal role in regulating immune response.

Nowadays the Kupffer cell blockade induced by GdCl₃ became a generally accepted method for investigation of the physiological and pathophysiological roles of Kupffer cells. Macrophage blockade has the theoretical advantage of abrogating inflammatory responses at an earlier stage of disease and in a specific fashion. It has also been reported that GdCl₃ inhibits the secretion of biologically active substances from the liver Kupffer cells, and decreases the liver-damaging effects of hepatotoxins, ischemia-reperfusion. Furthermore the ablation of the functions of the liver’s macrophages inhibits the development of anaphylaxis, lethal septic and endotoxin shock. GdCl₃ also influences the hypotension induced by immunoglobulin aggregates, and prolongs the survival of a human insulinoma cell xenograft in the liver.

**Pathophysiological rules of Kupffer cells in obstructive jaundice**

Despite advances of intensive care, survival of critically ill patients with obstructive jaundice did not improve over the last decades - and septic complications are still the leading cause of mortality. The Kupffer cell functions are changing after biliary obstruction as well and Kupffer cell-dependent immune modulation may lead to divergent outcomes. Defects in crucial elements of RES function after cholestasis are leading to hypersensitivity to bacterial endotoxin with high rate of septic complications in the long run. However, it has been demonstrated that attenuation of Kupffer cell activity with GdCl₃ might decrease endotoxin-induced lethality and morbidity in obstructive jaundice.

Previously it has been shown that biliary obstruction enhances the inflammatory and microvascular response of the liver to endotoxemia. Our recent observation clearly demonstrates that hepatic microcirculatory dysfunction is significantly exaggerated if obstructive jaundice is
followed by endotoxin administration. The results also show that hepatic Kupffer cells have a pivotal role in this process. Our results that the inhibition of a Kupffer cell-dependent inflammatory response reduces the endotoxin-induced lethality and organ injury in obstructive jaundice suggest a novel application for this experimental treatment modality.

Conclusions

In his book “From dream to discovery” Selye states that timing makes a huge difference, and as far as he was concerned he was fresh and active, and most optimistic especially in the morning. Indeed, Selye arrived at the institute at 6 a.m. before any of employees usually after an early swimming or cycling. The picture shows Selye professor returning cycling around the university campus (Figure 2). From 6 to 8:30 a.m. he was the most intensive and focused work of writing various papers ensued. His productivity is proved by numbers publications, more than 30 books and nearly 2000 articles. Our offices of Sándor Szabó and me were closed to each other. And Professor Selye very frequently visited us in our offices for a short conversation. He very frequently said “Only the Hungarians know the hard-working Hungarian farmers, who start work every day early in the morning when the day is just breaking and stopped at exactly six o’clock in the evening.” At 3 p.m. Selye would start his autopsy meeting, during which he would analyze the results of experiments with his characteristic magnifying glass and head lamp. Usually, these times Professor Selye was invited to deliver a lecture about his experiments concerning the stress. He asked us, Sanyi, Gyuri do you want to accompany me? And we willingly went with him to hear his excellent lectures.

During one year scholarship 15 relevant own papers were prepared in Montreal In Selye’s Institute. After this fruitful scientific year I returned home and continued my work at home with my co-workers.

My work in Montreal has determined my scientific carrier and has been motivated continuously. When I try to recall our life in the company of Hans Selye, my feeling is always that time has stopped and we are young again, full of energy and ambition as we were so many years ago in the old Selye Institute.

REFERENCES


