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My life studying steroids

When I came to work on the day that the Research Institute of Endocrinology was established, in January of 1957, the director of the Institute Doc. MUDr. Karel Šilink gave me a choice between studying enzymology or steroids. That time was a golden era of discoveries in steroid chemistry and biochemistry, and most works in specialized endocrinology journals were devoted to steroids. So the choice for me was clear. Even though discoveries in isolating and identifying steroid hormones were the flagship of endocrinology, and the extraordinary attributes of steroids began to be recognized in the clinical sphere (with a Nobel prize in 1950 for Kendall, Reichstein and Hench for their discovery of the therapeutic properties of cortisone in rheumatologic disorders), important laboratory diagnostic steroid analyses were still in their infancy. The rather nonspecific measurement of 17-keto-steroids, 17-hydroxysteroids, estradiol, estriol and pregnandiol in urine were the only tools available at the start of our steroid laboratory. I'm proud that we were able to match the tempo of subsequent steroid laboratory diagnostics during other historic phases – the development of chromatographic methods on paper and thin layer for distinguishing urinary steroids, as well as after laboratory revolution caused by the discovery of immunoanalytic methods enabling the measurement of nanomolar concentrations of compounds in body fluids. Blood sampling thus became routine. Further refinements led to the development of instrumental techniques, with improvements in gas and liquid chromatography, later in tandem with mass spectrometry, eventually to the current status where hundreds of analytes can be determined simultaneously. Today, some top laboratories combine such methods with evaluation by machine learning algorithms for clinical interpretations.

In addition to analytics and the use of results in clinical practice for various endocrine disorders, at the beginning of the 1960s I had the chance to work for a year in Bonn under professor Breuer, working on tissue and subcellular fractionation, experience that I used richly once back home. In 1961, I defended my dissertation on the isolation, identification, and synthesis of a newly discovered 7-hydroxylated C19 steroid from healthy patients, and worked on the biosynthesis of equilin and equilenin, epitestosterone conversions, and the development of steroidogenesis in the human fetus. We first took advantage of the possibility to measure testosterone in plasma in 1970 in men with varicocele, in whom we were the first to discover that it was not just a vascular but also an endocrine disease.

We were interested in testosterone from the point-of-view of male aging and were the first to propose that premature alopecia in men could be the male equivalent of polycystic ovary syndrome. We also studied the influence of endocrine disruptors on male reproductive function. The issue of endocrine disruptors continues to be a relevant, including phytoestrogens that we studied in collaboration with the most well-known international groups in this field. With relaxation of the political environment in the 1960s, internships and participation in congresses provided me the opportunity to make together various friends from both the eastern and western worlds of steroid researchers, many of whom later became important movers in their fields (J. A. Gustaffsson, R. Vihko. H. Adlercreutz, R. Knuppen, J. R. Pasqalini, J. Pankov, C. Shackelton and others). These friendships also resulted in multiple publications, and later lifting of travel restrictions allowed many my young collaborators to take advantage of stays abroad, particularly in Scandinavia and France.

With the so-called "normalization" of the 1970s, our mainstay became cooperation with domestic laboratories, especially with that in Lubochňa. An important chapter in this era was our research describing steroids in various parts of the eye and the role of mineralocorticoids in ensuring mineral equilibrium in non-vascular eye parts. Another rich and productive area was our cooperation with sexologists, particularly on the themes of Klinefelter syndrome and sexual dimorphism.

Currently, much of our work is focused on the steroid metabolome in various situations where some analytes are expected to play roles as neurosteroids. From this point-of-view we have studied depression, phobias, schizophrenia, lactation psychoses, and the effects of various psychopharmacological medications, the influence of smoking, as well as the course of pregnancy,

the small-scale effects of dietary intake, and details of the circadian rhythm. Our laboratory has published more than 2,000 studies registered in PubMed, which have generated several thousand citations. By far our most cited work is our first description of the age-related levels of dehydroepiandrosterone in humans, which because of its strong correlation with aging has been termed the "hormone of youth". Other works with hundreds of citations include a continuation of my dissertation on 7-hydroxy-dehydroepiandrosterone and its role in the brain, and our study of leptin published in Physiological Research. We have also been authors of more than 20 textbooks as well as hundreds of chapters in monographs of other authors.

I'm proud that I was able to provide a research base that was than successfully led by Professor R. Hampl and Dr. M. Bičíková. I am grateful for my cooperation with all my collaborators in the Department of Steroids and Proteofactors at the Institute of Endocrinology, as well as with co-authors from home and abroad for their inspiring collaborations, and I wish all of our younger colleagues much success as they follow in the footsteps of their predecessors.

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