

OPENING REMARKS

Mr. President of the Republic, President of the Congress, Ladies and Gentlemen, on behalf of the International Organizing Committee I would like to express our most sincere thanks to you for making it possible to organize the 4th International Congress on Hormonal Steroids here in Mexico City. We are particularly pleased and delighted, since there is hardly any other city on earth which had such an important historic rôle in the development of the steroid field.

Since man began to speculate on what forces regulate the course of life, the idea occurred to him again and again that not only external forces dominate him, but that the vital processes have their origin in the body itself. Our savage ancestors tried to solve the riddle of life by the idea of powerful divine beings who arbitrarily pushed them around and whom they must cajole if they wished to preserve their health. However, our ancestors soon discovered the important role of certain internal forces, the role of internal secretions, when they observed the far-reaching metabolic and psychological effects of castration. They noticed major changes in fighting instinct and in personality following the removal of the testes. This is the *first step* in the history of any biologically active steroid, the observation that the removal of a gland induces a state of deficiency, and Aristotle in his *Historia animalium* around 350 B.C. describes very well the effects of castration on birds, beasts and men. The *next step* is always to show that the administration of an extract of the gland can restore the normal condition; although the Indian Ayurveda of Susruta in 1400 B.C. as well as Plinius in ancient Rome recommended the administration of testicular tissue for the cure of impotence and Mesüe, the Elder in the 8th Century prescribed such a diet as an aphrodisiac, it is doubtful that this therapy had any effect, except perhaps a psychological one. It is first John Hunter in England, who in 1762 reports on the transplantation of testis in the fowl, followed by Professor A. Berthold in Göttingen, who in 1849 claims to prevent the effects of castration in roosters by transplanting their testicles into another part of the body. Fifty years later, in 1899, the 79 year old Professor Brown-Séquard injects himself with extracts of crushed dog and guinea pig testicles and enthusiastically describes to his astonished and incredulous colleagues in the French Academy the rejuvenating effect of such therapy, which he calls "la puissance dynamogénique". A few years earlier, in 1894, the Russian scientist A. Poehl isolated a crystalline substance, Spermin, which was then believed to be the testicular hormone, but soon proved to be ineffective. This is the time when commercial exploitation starts, and during the decades which follow tons of Spermin and of aqueous extracts of bull testes are sold all over the world by ambitious men to ambitious men.

My next note is from 1920; the first World War is over and Steinach publishes his famous book on his equally famous rejuvenating operation, which consists of the ligation of the Vas Deferens; even this turns out to be of doubtful, or in the best case of temporary value, just as the next step in the drama. In 1923, Professor S. Voronoff publishes his book *Greffes testiculaires*; he implants monkey testes into ageing men, hoping, in vain, that the glands

resume their function when transplanted into another species. Reading this book is a moving experience; one sees the "trial and error" approach of man in operation and one recalls Elbert Hubbard saying "truth is an imaginary line dividing error into two parts . . .".

And now the *third* and *fourth* phases in the discovery of a steroid hormone: the method of assay, isolation and identification. McGee in the U.S.A. describes effective extraction procedures for the active substance from bull testes in 1927, and Gallagher and Koch in Chicago develop a quantitative method for the testicular hormone in 1930. Now, one can assess the effect of every step in the purification procedure, and already the following year, in 1931, Adolf Butenandt in Germany isolates from male urine a steroid, androsterone, which is believed to be the male hormone. Another error, but a very close guess, and in 1935 Professor Ernst Laqueur's group from Holland reports on the isolation of testosterone, the main steroid of the testis. With this crystalline material clinical studies are started all over the world; large quantities of material are needed and chemists start to synthesize testosterone and even more active compounds. These chemical modifications of the molecule soon lead to the development of the first oral contraceptives by Carl Djerassi and his colleagues in 1952; however, it is impossible to discuss this chapter of History without considering the role of Mexico, and Professor Castelazo-Ayala is much more qualified than I am to do so. Rather, I would like to mention that I could show you, Ladies and Gentlemen, the same historic process, with the same cardinal steps, deprivation, substitution, method of assay, isolation, identification and synthesis in the case of virtually all biologically active steroids. I could show you how the method of Allen and Doisy enabled the Doisy group to isolate the female hormone, estradiol, and how the method of Corner and Allen helped Fels and Slotta to isolate progesterone, the hormone of gestation. I could also tell you that the story of the testicular hormone is by no means finished, that ongoing research suggests the existence of another hormone, "inhibin" in the testis, and I could call your attention to the words of Shakespeare that "what is past is prologue".

What is perhaps more important is to realize in a humble way that science is a continuously self-correcting process and to remember the words of George Sarton, saying that in the final analysis "the acquisition and systematization of positive information is perhaps the only human activity which is really progressive".

Mr. President, Ladies and Gentlemen, communication is perhaps one of the most complex and most important functions of the human mind. The local Organizing Committee has provided us with the most excellent facilities to communicate with each other and to exchange information during this week and we are very grateful for this opportunity. On behalf of the International Organizing Committee, I would like to thank once more for all help, generous assistance and effort by our hosts and colleagues in Mexico, which will make this Congress a successful and most memorable one.

EGON DICZFALUSY