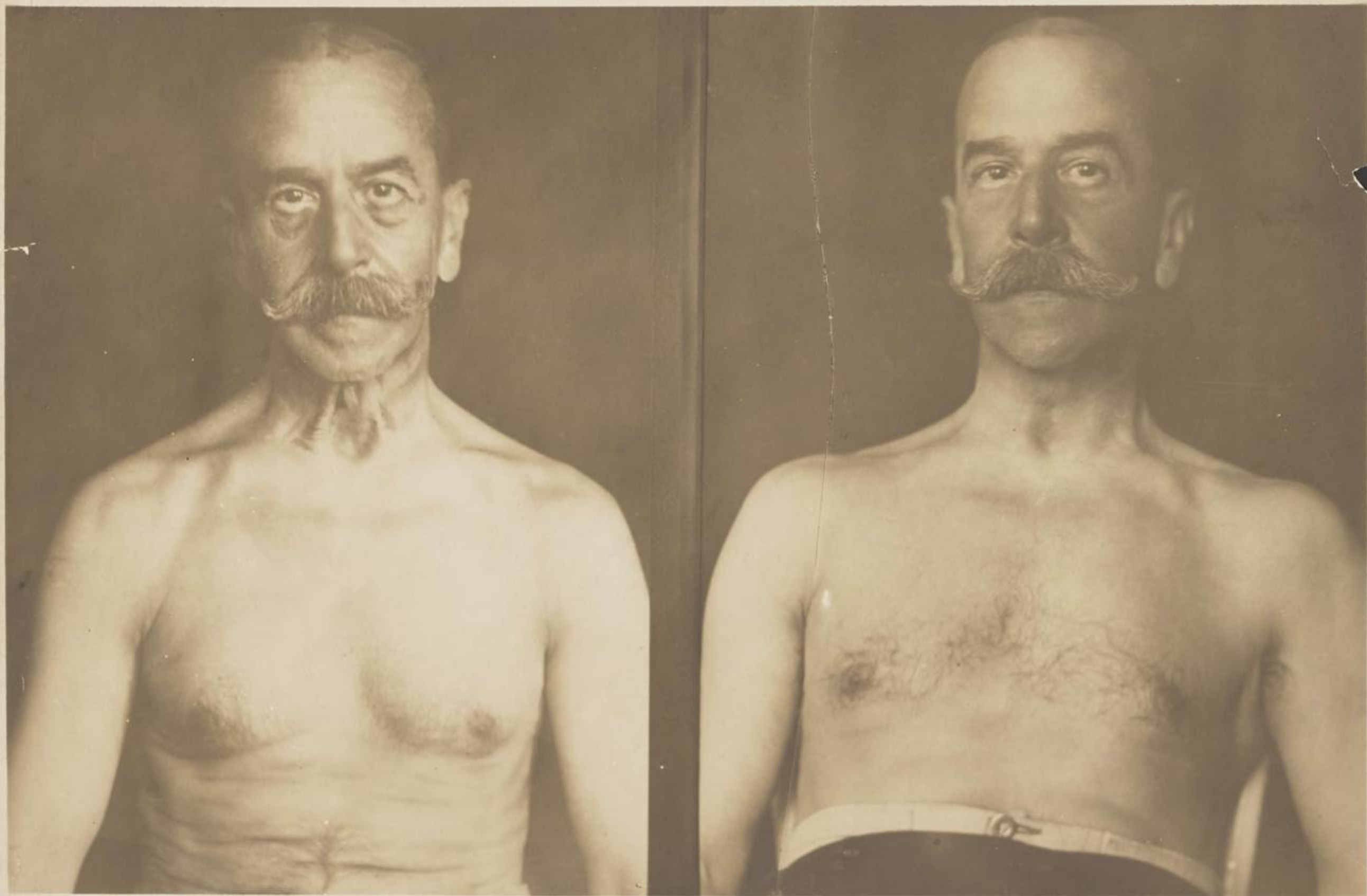
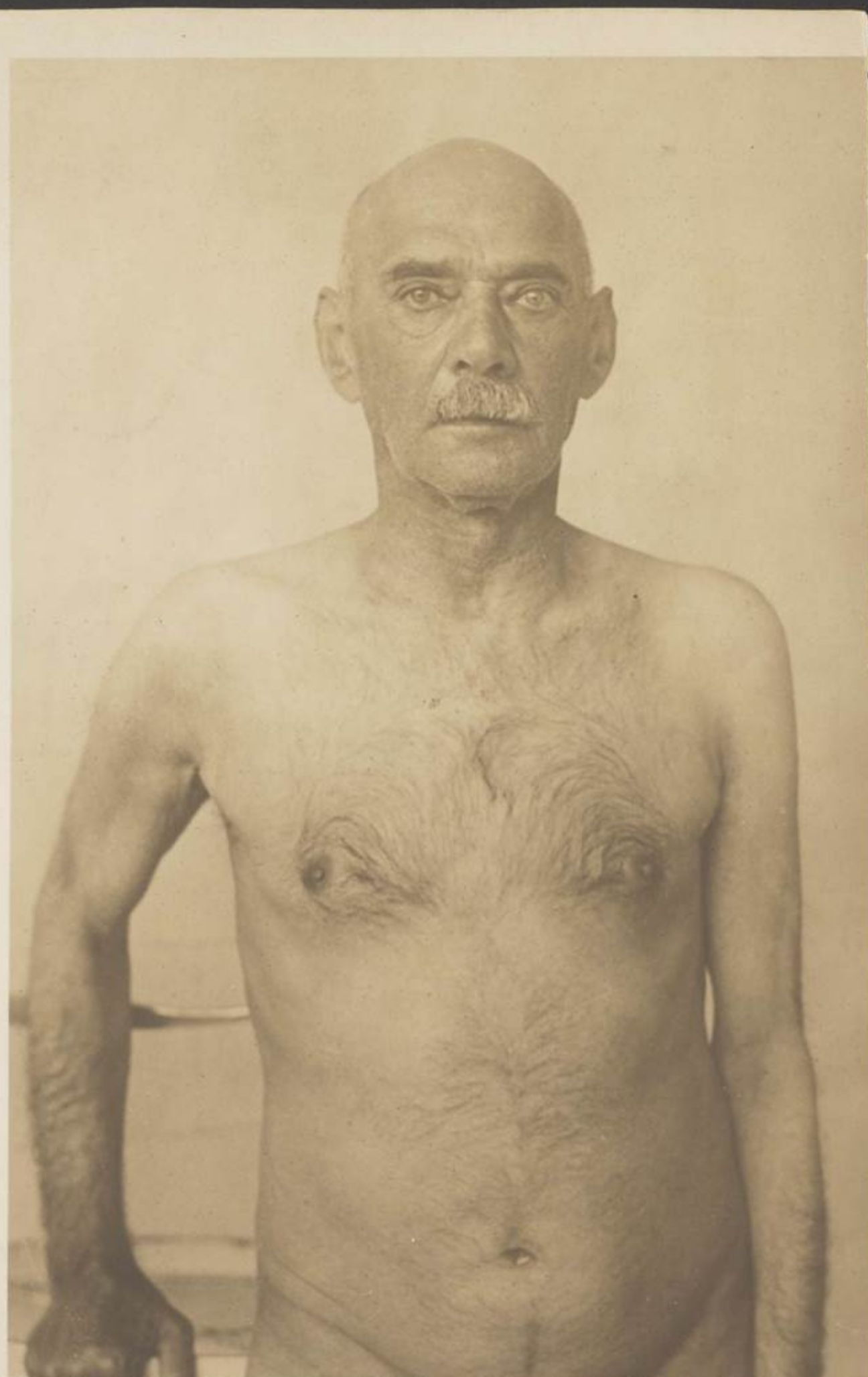
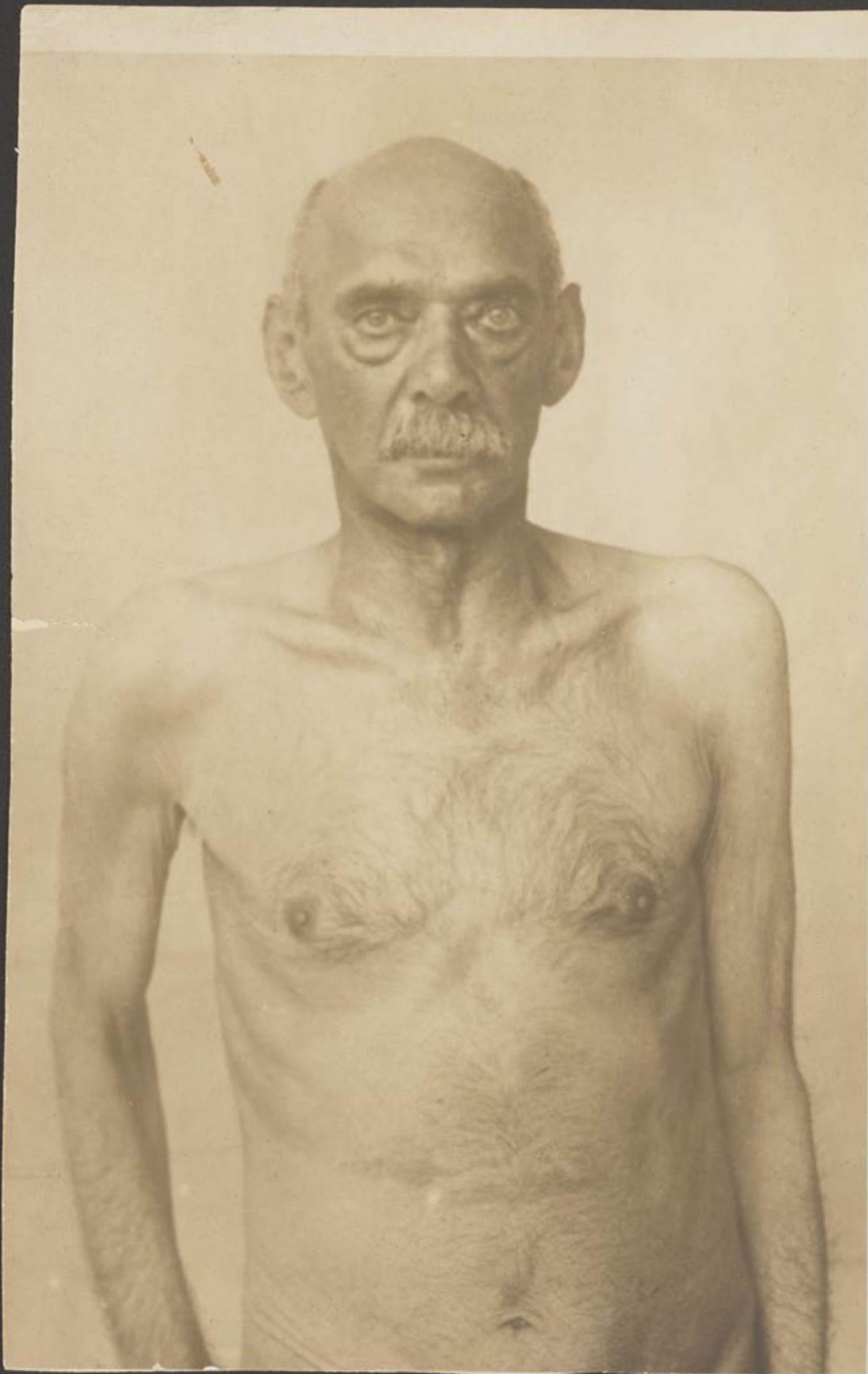






EUGEN STEINACH, 1861-1944: A LIFE OF RESEARCH

By HARRY BENJAMIN, M.D.

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THIS is the story of revolutionary medical research. It is also the story of a scientist who dared to penetrate the primeval forest of human prejudices and sex taboos and who added immeasurably to human happiness. He earned but little gratitude in his lifetime. Through his investigations and discoveries, he laid the cornerstone for a new medical specialty: the endocrine treatment of old age. Now called gerontotherapy, it endeavors to add life to years; maybe, also, years to life. Who knows?

The closing years of the last century had witnessed a profound change in the philosophy of medicine. Medical science had outgrown the preceding period of a purely speculative natural philosophy, and a new era had begun in which life in all its manifestations was interpreted chiefly in mechanistic and chemical terms. Life was regarded as a chemical accident; the human body as an immensely complicated machine subservient to the laws of physics and biochemistry. Such was the new world of scientific thought when Eugen Steinach entered his special field of medical research by publishing the first original investigations that dealt with the physiology of sex. The year was 1894, and Steinach was 33 years old. It was the birth year of a new field of scientific research.

Physiologists already knew Steinach from numerous and varied publications, but it was a turning point in his career when his series of three articles on the "Comparative Physiology of the Male Sex Organs" appeared in *Pflüger's Archiv*. The first of these investigations can be called a "negative" one, and according to Steinach's own statement it was based on an "accident." He had seen an article by Tarchaloff in which the theory was proclaimed that the sexual "embracing re-

flex" of the frog was due to a nervous mechanism elicited by the tension of completely filled seminal vesicles. Steinach set out to test this theory. He removed the seminal vesicles not only of frogs but also of rats and found that sex instinct and sexual response were in no way altered. Therefore, the seminal vesicles could not possibly have the significance that Tarchaloff had ascribed to them, and so his theory was conclusively disproved.

But if this was not the explanation for the release of the sex instinct, what then could it be that influenced the psyche in this specific manner and led to the characteristic manifestations of sex? This was the question Steinach asked himself; to answer it he set in motion a chain of experiments that determined almost his entire life's work. One novel experiment followed the other, and each was the logical outgrowth of the preceding one. From then on, Eugen Steinach was inseparably identified with the biology of sex. All his previous researches in other fields of physiology receded into the background.

PRE-SEXGLAND PERIOD

Born on January 27, 1861, in Hohenems, a small town in the Austrian Alps, young Eugen grew up in an atmosphere of medicine. His father as well as his grandfather were practicing physicians. The grandfather was also an enthusiastic and successful cattle-breeder, a fact which bore fruit many years later when his grandson did research work on sterility in cows.

After finishing high school Steinach went to Geneva, Switzerland, to study natural sciences and soon afterward to the University of Vienna to devote himself to medicine. In 1886 he graduated and became doctor of medicine. During the following two years he worked as assistant in the Physiological Institute in Innsbruck and published a few minor contributions, such as "Studies on the Blood Circulation of the Kidney"; "Time-Reaction of Temperature-Sensations," and

* The illustrations of experimental animals in this biography are reproduced from Steinach's *Sex and Life* with permission of the Viking Press, Inc., New York. The autographed portrait of Professor Steinach at his desk is taken from Dr. Heinrich Meng's *Psyche und Hormon* with permission of the author and the publisher; i.e., Medizinischer Verlag Hans Huber, Bern, Switzerland.

"Experiments to Measure Temperature and Pressure-Sensation Time."

His deep interest in physiology soon brought the young research scientist under the influence of Ewald Hering, one of the greatest physiologists of his time, and in 1889 we find Steinach as his pupil and first assistant in the Physiological Institute of the German University in Prague. Here began the first period of Steinach's scientific career, a period which can be designated as "pre-sexgland." It extended roughly to 1910, and, up to this time, the only sex-physiological investigation was the one previously mentioned dealing with the male sex organs.

Steinach remained in Prague over 20 years. He became *Privatdozent* two years after his arrival and five years later was named *ausserordentlicher* professor of physiology. In 1907 the University of Prague conferred on him the *ordentlicher* professorship. Steinach, then 46 years old, was able to look back already on a distinguished, though hardly exceptional, career. He had ambition, initiative, and originality, which were particularly demonstrated in 1902 when he created and organized a laboratory for "general and comparative physiology," the first of its kind in German-speaking countries.

It was principally in this laboratory that a great number of various researches were conducted. Among other subjects they dealt with "Visceromotor Functions of the Posterior Roots of the Medulla Oblongata" and "Chromatophore Muscles of the Cephalopods." In "True Contractility in Motor Innervations of Capillaries" (*Pflüger's Archiv*, 1903) Steinach described original observations of electrical stimuli on the circular muscles of capillaries with photographic studies. In 1908 he published a noteworthy contribution on "Summation of Singly Ineffective Stimuli as a General Phenomenon of Life."

More important than these, however, were earlier series of researches on the "Comparative Physiology of the Iris," which appeared in *Pflüger's Archiv* in 1890 and 1892. They reflect clearly the influence, if not the pressure, of Steinach's great teacher Hering, who himself had contributed so much to the physiology of the eye and the problems of vision.

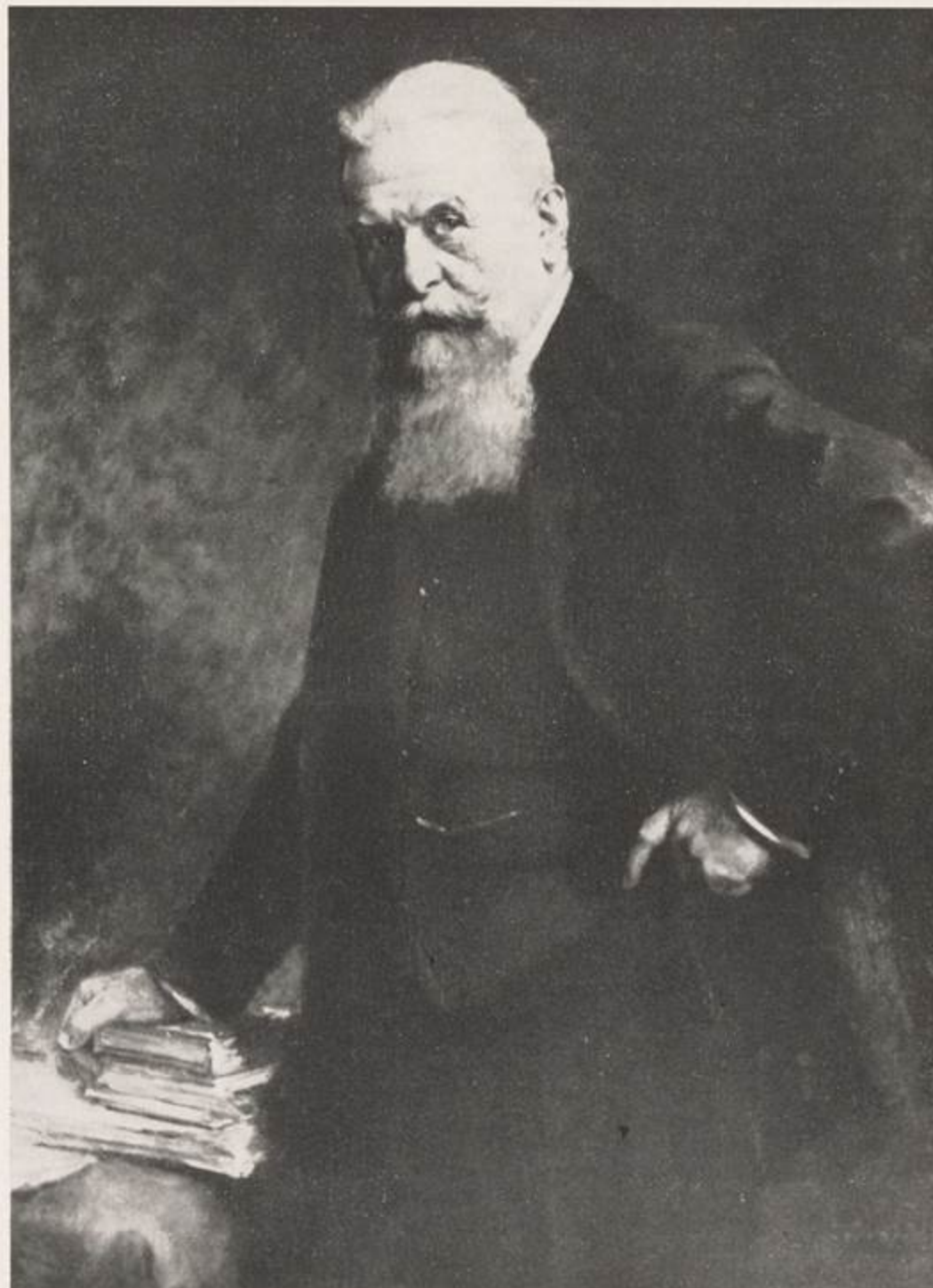
In later years, when Steinach's name had become world famous as a sex biologist, he used to refer to the work in the "pre-sexgland period" with hardly more than a shrug of the shoulders. He considered the experiments "not entirely satisfactory" and once said to his assistant and collaborator, H. V. Klein: "When there is not enough love and devotion to one's work, one can hardly expect much of a success."

PHYSIOLOGY OF THE TESTIS

Although this unduly pessimistic attitude toward his own work applied to the first period of Steinach's career, the extreme opposite prevailed in later periods. He was then "heart and soul" in his studies of sex biology to which he devoted more and more time during the later years of his stay in Prague. These studies, which were principally concerned with the physiology of the testis, initiated the second period in Steinach's research life. It was during this time—roughly, from 1910 to 1920—that Steinach's original mind led to his greatest accomplishments and his most brilliant success.

The year 1910 saw the 49-year-old scientist still in Prague teaching physiology and conducting or supervising experiments. Among the latter were already those in sex biology which paved the way for the coming work in Vienna and which laid the foundation of his future fame.

The consequences of castration, well known for a long time, were in these years no longer explained by a severance of nerve fibers connecting brain and testes when the latter were removed. This theory had been exploded. The physiologist von Berthold, by his transplantation experiments on roosters in 1849, had furnished evidence that something in the circulating blood constituted the link between sexgland and brain. Unable, however, to identify the particular agent any closer, Berthold could go no further, and his experiments were soon forgotten. Besides, they had one great drawback that detracted from their scientific reliability: The testes of fowls are most difficult to remove completely, as they are not surrounded by a firm capsule like those of mammals. If, therefore, even the smallest part of testicular substance re-



EUGEN STEINACH, 1861-1944

remained *in situ*, full castration had not taken place and valid conclusions could not be drawn.

Therefore, Steinach used male rats for his transplantation experiments and showed, first of all, more conclusively than ever before, how the gonads influence the secondary sex characters, including the sex instinct. This influence, however, did not mean a complete dependence. The first fundamental publication on the subject appeared in the *Zentralblatt für Physiologie*, 1910, and was called "Sex Instinct and True Secondary Sex Characters as a Result of the Endocrine Function of the Gonads." Although emphasizing the biological pre-existence of male or female sex and their respective secondary sex characters, Steinach showed that growth, maturation, and preservation of the latter were definitely controlled by the internal secretion of the testis. Remove the testes, and the seminal vesicles and prostate shrink; sexual lethargy develops. Implant a testis somewhere else in the body, and the physical as well as the psychic sex characters are restored.

All this sounds trite and commonplace now, but 35 years ago it was an important discovery, or at least a final confirmation of what had so far been mere assumption.

The Puberty Gland. The next logical question that Steinach now asked himself was: In what part of the testis does the internal secretion develop? Is the male hormone a product of the spermatogenic tissue (that produces the spermatozoa) or is it secreted by the interstitial (Leydig) cells (forming the rest of the testicular tissue)? This question had been asked before, notably by two French scientists, Bouin and Aneel, in 1903. Through vasoligature experiments on rabbits and guinea pigs, they had come to the conclusion that the internal secretion was a function of the interstitial tissue. They called it *Glande interstitielle* and regarded it as the source of the hormone that controlled secondary sex characters. Their theory was accepted in some quarters and rejected in others. Steinach seized the opportunity presented by his own transplantation experiments (1910) to try to settle the question.

He had been the first experimenter who succeeded in transplanting a testis in such a way that it became vascularized and remained functioning in its new site. Infantile animals had been used. When they were castrated, they remained infantile. But they developed normally when the re-embedded gonad remained alive in the body. What kind of a gland was it now, that continued its function somewhere under the skin instead of in the scrotum? Years later, in his book *Sex and Life*, Steinach described the histological structure as follows:

The spermatogenic (germinal) tissue proved to be more sensitive and was unable to adapt itself to the altered conditions of blood supply, and therefore perished. The hormonal tissue, on the other hand, proved to be more robust and not only adapted itself readily and completely to the new environment, but also increased. The space made available by the atrophy of the germinal tissue was occupied by proliferating interstitial cells. Thus, as an incidental result of my transplantation experiments in 1910 and succeeding years, I found that I had changed testicular tissue into a gland consisting wholly of interstitial cells.

Since this gland promoted the maturing process, Steinach named it the "puberty gland."

The older, inconclusive experiments of Bouin and Aneel were now evidently confirmed, and the internal secretion of the testis had to be ascribed to the Leydig cells. In taking a decided stand in favor of this theory, Steinach entered the first of several scientific controversies in which he was a leading figure, if not the actual storm center. Objections to the "puberty gland theory" persisted in several scientific circles, where the internal secretion was still ascribed to the spermatogenic tissue or to the Sertoli cells, which are a part of this tissue.

It would be only of historical interest to go into the details of this controversy, although it played undoubtedly a great role in Steinach's scientific trials and tribulations. It was finally decided in Steinach's favor (and naturally in favor of Bouin, Aneel, and their adherents) when two of his principal opponents withdrew their objections in 1926 and 1933, respectively. Steinach had to wait over twenty years for this recognition, but when it finally came—in a rather dramatic episode—it was one of the highlights in his

career. It was in Berlin in the fall of 1926 when the First International Congress of Sexual Research took place, and Steinach had delivered a lecture on "Sex Hormones, Their Biology, Physiology, Pathology, and Therapy." At that time he was already a world-famous figure in medicine on account of his publication on "rejuvenation" and was the "star speaker" of the Congress. The auditorium was crowded to overflowing. No discussion had been scheduled after Steinach's paper, but Dr. Albert Moll, the president of the Congress, arose and congratulated the speaker on his results, which he compared in fundamental importance to the Mendelian laws of heredity. After him, Dr. Oscar Riddle, distinguished biologist of the Carnegie Institution, who was chairman of this session, spoke briefly to recall the debt which the biology of sex owed to Steinach for his important contributions.

Everybody expected the meeting to close after these remarks, when Dr. Moll rose once more and announced that Professor Benda had asked for the floor to make a brief statement. The famous pathologist of the Berlin University had been known for years as one of the most bitter opponents of Steinach and of his "puberty gland" theory. The large audience expected another scathing attack—this time orally—and the tenseness was distinctly uncomfortable. I happened to be present, sitting next to Dr. Peter Schmidt, Steinach's foremost pupil in Germany, who whispered, "Watch the fireworks."

In this electric atmosphere Benda's words amounted to a near sensation. Instead of dissenting, he paid high tribute to Steinach and stated in so many words that, following new experiments of his own, he was ready to withdraw his objections and concede the correctness of Steinach's claims. When the two scientists then shook hands the applause amounted to a demonstration.

Benda's declaration had shaken the stronghold of Steinach's opposition, but the victory was only complete when the second great opponent, the anatomist B. Romeis, of the University of Munich, likewise revised and altered his standpoint in 1933 (*Klinische Wochenschrift*, No. 42) and in a truly scientific spirit admitted his error.

Let us return to the year 1912 when Steinach's stay in Prague came to an end. His publications had made a sufficiently deep impression in the scientific world to cause his appointment as research director in the Physiological Department of the Biological Institute of the Academy of Sciences in Vienna. At the same time the University of Vienna bestowed on him the title of *ausserordentlicher Professor*.

Steinach was 51 years old when he came to Vienna. With his striking head (on a pyknic body) and his impressive reddish-blond beard, he was soon a familiar figure in Vienna's *Prater*, where the Biological Institute was located. The Viennese called it the "Vivarium." Steinach was still a bachelor. He was a conscientious hard worker, who demanded much from his assistants. In all his scientific work he insisted upon logic in thought, clarity in expression, and uncompromising adherence to the purpose on hand. But away from the laboratory he was a man of the world, full of genuine humor and of a vitality that let him enjoy the good things in life to the fullest. Here, in Vienna, his greatest wish was at last realized: he could concentrate entirely on research and was no longer distracted by obligations to teach students.

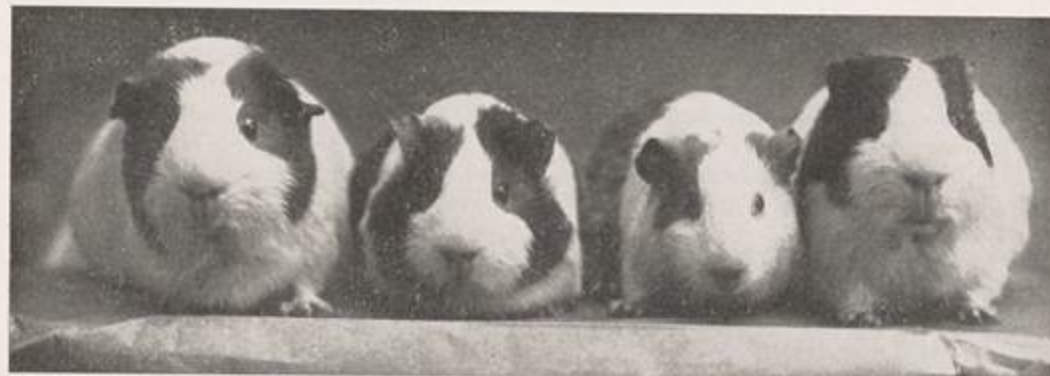
Reversal of Sex Characters. The year of Steinach's removal to Vienna also saw the publication of his classic research work on "Intentional Transformation of Male Mammals into Animals with Pronounced Female Sex Characteristics and Feminine Psyche." These experiments were a natural outgrowth of the former investigations as to the significance of the sex hormones. Were these hormones unspecific as to sex, like the hormones of the thyroid, the adrenals, etc., or were they sex-specific? That is what Steinach wanted to know.

Infantile male guinea pigs were castrated. Into the resulting "neuter" an ovary was implanted. The developing sex characteristics were not those of the congenital masculine *anlage* but definitely feminine. The "foreign" female gland proved stronger than the male *anlage*. Milk-producing nipples appeared; the penis remained rudimentary,

resembling a clitoris. Body growth and configuration was more like those of a control sister than of the normal control brother. The forms of chest and head changed to the feminine type. The rough unkempt hair of the male was replaced by the softer, shorter hair of the female. Even the internal structures of the originally male animal, as revealed by the X-ray, were now like its sister and quite different from its twin brother.

furthermore, were pursued by the normal males that attempted intercourse. They radiated genuine feminine attraction.

The opposite experiment was equally successful and striking. The young castrated female, under the influence of an implanted testis, turned into a "male" and grew a penis; even its voice assumed a characteristic masculine guttural sound instead of the well-known squeak of the female. This



CHANGING THE SEX CHARACTERS OF GUINEA PIGS

Above: MASCULINIZATION. Left to right: MASCULINIZED SISTER, SPAYED SISTER, NORMAL SISTER, NORMAL MALE. Below: FEMINIZATION. Left to right: CASTRATED BROTHER, NORMAL SISTER, FEMINIZED BROTHER, NORMAL MALE.

More astonishing even than the physical transformation was the change in the psyche. Normally, male guinea pigs show no paternal instinct. They repulse the young ones. But the "feminized" male behaves like a mother and actually suckles the young. When Steinach demonstrated these animals and their behavior before a Physiological Congress, they created a sensation. They made medical history. These feminized males,

masculinized female, like a normal male, also secrete a female in heat, pursues her, and attempts sexual contact. It was this erotization of the brain in the "sexgland-specific direction" that impressed Steinach most and led to many future inquiries into the nature of the sex urge. For the first time the relationship of hormone and psyche was brought into focus. Steinach and Freud (who had met years ago as students) had now found a

contact in their respective researches—the one proceeding from the soma, the other from the psyche. The body-mind problem was moving closer to a solution.

After the appearance of classic "Feminization of Males and Masculinization of Females" (*Zentralblatt für Physiologie*, 1913) Steinach's name as a foremost sexologist was firmly established. The technique of his experiments was impeccable, combining imagination with strict discipline. In many laboratories the experiments were repeated and confirmed. Knud Sand in Copenhagen feminized roosters and masculinized hens. Their pictures can be found together with Steinach's guinea pigs in many scientific textbooks.

Studies of Homosexuality. Numerous investigations and publications followed in consequence and in elaboration of the classic experiments of sex reversal. In collaboration with the renowned Viennese roentgenologist Holzknicht, Steinach tested the effect of X-rays on the ovaries of infantile female guinea pigs (1916) and found that these rays in small ("stimulating") doses caused an acceleration of growth of uterus, mammary glands, and nipples, that is to say, an experimental precocity. In a publication "Puberty Gland and Hermaphroditism," Steinach reported the effect of simultaneous implantation of testicle and ovaries into infantile castrates and described the resulting "experimental hermaphroditism" (*Archiv für Entwicklungsmechanik*, 1916). These investigations were in turn the cause of two further groups of experiments: "Inquiries into the Nature of Homosexuality" and "Proof of the Antagonistic Effect of Male and Female Hormones."

In 1918 (*Münch. Med. Wochenschrift*) Steinach and the Viennese urologist Lichtenstern published a paper with the optimistic title "Conversion of Homosexuality through Exchange of Puberty Glands." This was a practical application of Steinach's researches. Homosexual men were castrated and another man's cryptorchid (undescended) testicle, which consists of predominantly interstitial tissue, was implanted. The homosexual tendencies disappeared and a normal

(heterosexual) libido developed. Such, at least, was the conclusion that the authors drew from the report of their patients.

In the light of a modern concept of homosexuality, which sees an endless variety of combinations between homosexual and heterosexual tendencies, and between constitutional and psychological factors, this assumption of an exclusive endocrine etiology of sex inversion and its clinical cure by endocrine therapy must be taken *cum grano salis*. Organic cases of intersexuality may indeed be influenced by glandular methods, but Steinach's and Lichtenstern's generalization is hardly justified.

Another controversy resulted from Steinach's histological examination of testicles of homosexual men, which he described as showing the following abnormal characteristics (*Archiv für Entwicklungsmechanik*, 1920): "Atrophy of spermatogenic tissue, partial degeneration of the male interstitial cells, presence of large cells, differing widely from the former and approaching in appearance and structure the female cell types." Steinach referred to them as "F cells," but to this day their existence has not been generally recognized.

Antagonism of Sex Hormones. Also in the *Archiv für Entwicklungsmechanik*, 1920, appeared a series of articles dealing with "Artificial and Natural Hermaphrodite Glands and Their Analogous Effects." In the first and most important part, on "Antagonistic and Sex Specific Effects of Sex Hormones," the author comes to these conclusions: Sex hormones are sex-specific, that is, the male hormone develops the *anlagen* of male characteristics, the female hormone doing the same for the female *anlagen*. Hand in hand with this effect on the like sex goes an antagonistic (inhibitory) influence on the characteristics of the opposite sex. Their development is prevented, retarded, or even brought to involution.

Opposition to this theory of the physiological antagonism of sex hormones still exists but remains unconvincing in view of many corroborating experiments, especially those of Alexander Lipschuetz.

The year 1920 also saw the publication

of a rather extensive study "Climate and Puberty" by Steinach in collaboration with the zoologist Paul Kammerer (whose outstanding work in heredity is as well remembered by his colleagues as is his tragic death in 1926). The authors showed that rats kept in higher temperatures developed a proliferation of interstitial cells in their testes and consequently an enlargement of secondary sex characters together with a high degree of sexual excitability. It was not difficult to find the analogy of these "heat-rats" with the proverbial sexual ardor of men and women in the Tropics. Steinach and Freud had met once more.

Rejuvenation. As far as publications are concerned, 1920 was undoubtedly for Steinach not only the most fruitful but also the most fateful year of his research life. In this year appeared his little book *Rejuvenation Through the Experimental Revitalization of the Aging Puberty Gland* (J. Springer, Berlin), and almost overnight Steinach became one of the most talked-of men of science all over the world.

In the medical profession he was soon



REVIVIFYING EFFECT OF HORMONE TREATMENT ON A RAT

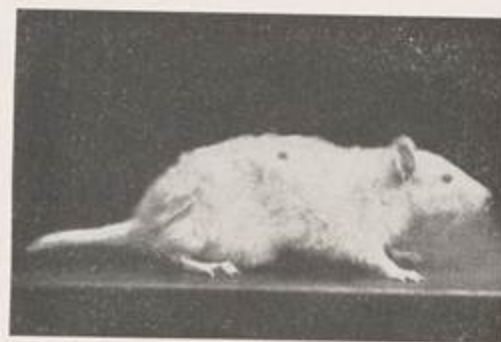
Left: SENILE FEMALE RAT BEFORE ADMINISTRATION OF A FEMALE HORMONE. Right: THE SAME AFTER TREATMENT.

praised as a genius by some and condemned as a quack by others, while the laity saw in him a modern Ponce de León on the one hand and a violator of sacred laws of nature and morality on the other.

Steinach's thoughts and studies on the problem of old age date back to 1912 when a paper "Investigation of Youth and Age" was submitted to the Vienna Academy of

Sciences but remained buried there for nine years. Steinach had observed and, for the sake of priority, described in this early paper the striking resemblance of the effects of castration and those of senility. In both instances the lack of sex hormones produced the similarity of the clinical pictures. The inevitable thought then occurred that both conditions could be remedied by supplying the missing hormones.

The transplanting of a foreign gonad into a castrate had proved successful in curing or ameliorating the characteristic signs of deficiency. Gland transplantation into an aging body was, therefore, the first method to be considered, inasmuch as it had been successful in numerous animal experiments. The injections of hormone solutions in the manner of Brown-Séquard was another possibility. Steinach did not favor either one. Transplantation would be impractical on a larger scale. Where should all the glands come from? (Voronoff, in Paris, tried to solve this problem by resorting to the use of testicles from anthropoid apes). Hormone solutions were too uncertain in their effects and also difficult to procure in those early days,



long before the advent of biologically tested or synthetic androgenic preparations. Steinach wanted a wider human application, not one that could benefit only aging rats and guinea pigs.

Thus arrived the moment when this ingenious scientist had a truly "royal" thought: foreign materials should not be employed to reactivate the senescent system

but the person's own sex gland should be made to produce the necessary hormone increase. The body's own resources must be mobilized. This is the principle underlying all those therapeutic methods which justly deserve the designation "Steinach therapy."

Vasoligation was the first practical result of this idea, and the small operation soon bore Steinach's name. Bouin and Ancel had

touched off nevertheless another scientific controversy, this time especially vehement on account of its practical clinical implications, namely, the claim that vasoligation "rejuvenates" not only animals but men as well, though to a lesser degree.

Steinach had waited for years with this pronouncement, and therefore the storm in the medical world broke only after the afore-



REVIVIFYING EFFECT OF VASOLIGATION ON A RAT

Left: SENILE MALE RAT BEFORE LIGATING ITS VAS DEFERENS. Right: THE SAME ANIMAL AFTER THE OPERATION.

used the ligation of the vas deferens previously but for experimental and theoretical purposes only. Now Steinach wanted to apply it in the practice of medicine and to combat old age by taking advantage of its effect on the histological structure of the testis.

The vas deferens is the canal through which the spermatozoa reach the outside (i.e., the urethra). If this canal is sealed through a permanent ligature, the spermatozoa are dammed back into the gland, gradually causing a pressure atrophy of the very delicate germinal epithelium from which they originate. This, at least, was Steinach's reasoning. The place of the disappearing cells is taken by the much harder interstitial cells which—according to the Steinach school—proliferate and consequently produce more hormone. At the height of the atrophy of one tissue and proliferation of the other the testis was said to resemble a cryptorchid or a transplanted gland.

Although this theory of the histological consequence of vasoligation seemed amply supported by exact laboratory studies, microscope slides, and animal specimens, it

mentioned book on rejuvenation appeared in 1920. It dealt at length with all the preliminary animal experimentation but also contained case histories of "rejuvenated" men.

The Theoretical Controversy. The opposition to the "Steinach operation" was twofold. One was directed against the theory of the proliferation¹ of interstitial cells following vasoligation, therefore concerning the laboratory worker. The other was of a clinical nature. The reactivating effect of the operation was denied, for animals as well as men, more often for men only, thereby limiting the debate to the medical profession.

It would be quite impossible to review here the enormous scientific literature that emanated from laboratories and operating rooms all over the world. Among others, Romeis in the *Handbuch der Innern Secretion* (1931) made a complete survey of this literature, and so did Lipschuetz in his book *The Inter-*

¹ According to experiments by Romeis, Schinz and Slotopolsky, Moore, and others, this proliferation is not real but appears to be such only in comparison to the atrophied spermatogenic tissue. The number of Leydig cells are declared to remain the same although their individual size may increase.

nal Secretions of the Sex Glands and Allen in *Sex and Internal Secretions*. It seems that a majority of the authors generally confirmed Steinach's histological findings, although many found themselves in variance as to explanation and the degree of the changes that occurred in the testicle after vasoligation. In the United States a group of zoologists in Chicago roundly denied that any hypertrophy of interstitial cells took place after the vas deferens was ligated and, therefore, declared not only that Steinach's theory was wrong but also, consequently, that no clinical effects could be expected from the operation. If anyone claimed to have seen such effects, they said, he was just fooling himself and others. This disapproval of Steinach's research claims was the determining factor for a similar disapproval of their clinical application by the American Medical Association.

In justice to Steinach and the many "pro-Steinach" investigators, one should recall an old truth in medicine which can likewise be applied to physiological experiments: Positive findings are of greater significance than negative ones. Positive findings are a reality that call for explanation. Negative findings mean little in comparison. Therefore, it seems logical to ascribe more credence to those authors who saw changes after vasoligation than to those who did not see them.

Several factors may explain the divergence of findings: The technique of the operation, the period of time that elapsed between the ligation and the examination of the testis (under the influence of an increased hormone production from the "puberty gland" a regeneration of atrophied spermatogenic tissue is said to take place), the type and age of the animal, the method by which the changes were evaluated. In any event, the final word as to the effect of vasoligation on the structure of the testis is still to be spoken.

"Within modest limits, the process of aging can be influenced." Such was Steinach's own summarization of the result of the operation. Two points were emphasized before he recorded the effects: First, the proper technique of the operation that must seal the vas deferens permanently and must preserve

blood and nerve supply to the testis. Secondly, the proper selection of the patient. A favorable response would then "revivify" the entire glandular system, and a mental, physical, and, incidentally, sexual invigoration could take place.

Steinach himself never operated, nor did he consider himself a competent clinical investigator. He was the research scientist first and foremost. He recorded merely the objective and subjective changes that clinicians had observed in their patients and depended upon their statistics which gradually began to appear in the international medical literature. The reports were by no means uniform. There were enthusiastic confirmations; there were almost complete denials of any beneficial results; and there were guarded reports with the usual appeals to reserve judgment until more experience had been gained. "Positive" reports were generally based on much larger statistics than "negative" ones, which is understandable from the physician's point of view.

In some reports like those from Russia (Eiber and Uspensky) the benefits on physical strength and endurance of laborers were emphasized, while in the majority of others dealing predominantly with the intellectual classes the restoration or preservation of mental faculties was in the foreground.

A few individual cases received wide publicity, such as that of Professor Adolf Lorenz, the famous Viennese orthopedist, who ascribed his return to active practice at the age of 72, after his retirement, to a successful "Steinach."

Known in Vienna but not published was the fact that during the 1920's well over 100 university professors and teachers underwent vasoligation, among them Sigmund Freud, in order to improve their health and extend "the platform of their efficiency." Freud, as well as others, was emphatic that such had been accomplished, but exact scientific data are missing.

The Clinical Controversy. Exclusive of these honest and independent members of the medical fraternity who reserved judgment as to the value of the operation because they had no personal experience and did not

feel competent to express an opinion, there were roughly three different groups of physicians who took a stand in the controversy: First, there were those who roundly denied any results from the operation, simply because they had not seen any or considered Steinach's theory to be faulty. They pronounced the benefits reported by others as due to "autosuggestion," and the successes with animals were denied or ignored. Secondly, there were those who likewise believed Steinach's theory to be wrong but did not deny clinical benefits, which they ascribed, for instance, to absorption of degenerating spermatogenic tissue. In accordance with this theory they claimed that the benefit to the patient was only of relatively short

duration. Finally, there were those who believed Steinach to be most likely correct in his theory because, with it, they could best explain the invigorating and re-energizing results on body and mind that they had observed in their patients (or some of them in themselves), especially if this result seemed to last for many years.

But the opposition to Steinach was powerful and persistent in its arguments. The term "rejuvenation" easily invited criticism. It was unfortunately chosen, as Steinach found to his regret, for it led to exaggerated expectations of patients and doctors and consequent disappointments, and it produced an unavoidable echo in the lay press and a publicity that wallowed in sexual implications. Later Steinach replaced "rejuvena-



REVIVIFYING EFFECT OF VASOLIGATION ON A DOG
Left: EIGHTEEN-YEAR-OLD DOG BEFORE VASOLIGATION. Right: THE SAME DOG AFTER THE OPERATION (WILHELM).

tion" by the more appropriate term "reactivation," which was first proposed by this writer in *American Medicine*, August 1922. The only "sexual" factor in "rejuvenation" was the use of the sex gland. A restoration of sexual potency was incident to the general re-energization of aging men and was only mentioned as such. But this could never satisfy a sensation-hungry press and public or quiet the vaudeville comedians who were untiring in confusing the methods of Steinach with "monkey glands." Consequently more criticism arose, and the serious scientific efforts of Steinach and his co-workers were severely handicapped.

Then came the "Steinach Film" and the wide publicity it created in 1922. A German film concern made a full-length moving picture record of some of Steinach's outstanding experiments. There was an authorized scientific version as well as a popular one. The public loved it, but the medical profession in Germany and Austria frowned. Steinach was raving mad and claimed never to have given consent for the popular form.

Some of Steinach's co-workers indulged in uncritical praise of the effects of vasoligation. Their overenthusiasm and that of lay-writers on medical subjects was then rivaled by equally uncritical opposition on the part of some medical editors and authors. Steinach and his collaborators were, for instance, blamed for a publicity and an exaggerated public interest that was clearly due to the nature of their work. Again, in justice to

Steinach, we must remind ourselves that there are always critics in every branch of human endeavor who write their comments not in the light of facts and logic but in the twilight of their individual prejudices, their own likes and dislikes.

Neither Steinach nor some of his pupils can be absolved entirely from responsibility for the fact that the controversy was often conducted in an undignified manner. Occasionally, rejuvenation claims were attributed to Steinach which he had never made (the newspapers had done so), and straw men were set up and knocked down. Unnecessarily sharp rejoinders followed. The acrimony of the debate betrayed its high emotional potential. Steinach, whose vanity was easily hurt, suffered greatly under all these attacks, some of them surely unjust. They left their mark on him psychologically throughout the rest of his life. He became unduly suspicious even toward his friends and easily antagonized people. He was too deeply hurt himself to realize when he hurt others.

Now the controversy over the "Steinach operation" has died down. The development of the synthetic testosterone has reduced interest in the operation. Steinach had the satisfaction of having watched its great popularity and of having heard from many supporters and grateful patients. He had the disappointment of its lack of universal recognition. He himself blamed this failure on prejudices and enmity in the profession, on a frequent faulty technique of the operation, and also on puritanical influences which opposed sex in all its implications, even in utilizing the sex gland for promoting better health in later years. By way of illustration, he liked to show a letter which he had received from a Swedish clergyman who threatened him with Hell and damnation if he continued any longer to interfere with the divine laws of nature.

After the portentous year 1920, Steinach published one more brief paper on the "rejuvenation" operation. He had to take issue with the argument that his rats were suffering from mange but were not old when they were used for rejuvenation experiments; that disease, not senility, accounted for their hair

changes. Steinach had to bring proof that these rats were undoubtedly senile, as they had grown old in the laboratory under constant control and that their loss of hair was natural and not due to infection. ("Mange and the Combat of Senility," *Wien. Med. Woch.*, 1921.)

For the following five years no publication came from Steinach's laboratories, although research was never entirely interrupted. Those were the years of monetary inflation and of Austria's greatest economic plight. Government subsidies had practically ceased for all research work, and Steinach had to keep the laboratory with several assistants going the best he could out of his own pocket. Fortunately, patients came to him from all over the world for consultation and operation. Though he did not operate himself (except on animals), he was nevertheless present during all operations, which were performed by such competent surgeons as Robert Lichtenstern and Erwin Horner. In Steinach's waiting room, laboratory, or hospital the rich and the famous from abroad met with the poor and the famous from home. Those were Steinach's busiest years. It was often a problem to do justice to his clinical, research, and literary work and yet allow time for the many visitors, both doctors and laymen.

Steinach was now in his early sixties. A few years earlier he had married the cultured widow of a noted attorney. With her command of English and French she was an invaluable assistant. Who does not remember her as the gentle soft-spoken "secretary" anxious to please everybody, not the least (and not the easiest) the *Herr Professor*? Steinach was sometimes "difficult" indeed. He was a man who made enemies easier than friends. He was touchy, quick-tempered, and—having been "burned" too often—forever suspicious. The *Frau Professor* frequently had a hard time trying to smooth ruffled feelings.

On other occasions Steinach, in his ambivalent nature, was depressed, looked at himself as a martyr, and became resigned to being misunderstood. Fortunately, his moods were of a passing nature, and he was able to forget his irritation and his mistrust, to be again a

sincere friend, a liberal teacher, a sympathetic physician, and a gracious host. A moderate prosperity had come to him, and, being a man who forever said "yes" to life, he enjoyed his hobbies and pleasures fully. He loved horses. For many years he could be seen in the *Prater* on horseback or driving a carriage. He was a handsome man in spite of his short stature. His white hair, his graying beard, and sparkling dark eyes, which could flash so angrily and smile so kindly, were not easily overlooked or forgotten.

BIOCHEMISTRY OF THE HORMONES

The Female Hormone. The third period in Steinach's research career, which roughly extended from 1920 (or 1925) to 1938, began with an interest in the female hormone and in female reactivation.

The use of the X-rays in small doses as worked out with Holzkecht for the maturation of infantile animals had occasionally good results in aging women but was not the final answer to the problem. Nor was it the transplantation of ovaries. "Steinach therapy" (the stimulating "autoplastic" method) had to be replaced or supplemented by a "homoplastic substitution therapy." Moderately effective ovarian hormone solutions had already been made by others, but to Steinach belongs the credit of developing the first standardized preparation of high potency and also of using such female hormone for the purpose of reactivation.

The test for such an ovarian preparation was its ability to "initiate the sexual cycle, to develop sex characters, and to reactivate the senile female organism." This was essentially the title of the publication in *Pflüger's Archiv* in 1925 (Steinach, Henlein, and Wiesner) which described the experiments on female rats, using an extract derived from ovaries and placenta. This preparation could be standardized in units and tested according to the vaginal smear method of American physiologists (Allen and Doisy, Long and Evans, Papanicolaou, et al.). It laid the foundation for future work culminating in the production of "Progynon."

After Steinach had succeeded with his preliminary work on the female (now known as



BEFORE THE WAR
STEINACH AND HIS FAVORITE HORSE IN VIENNA, 1937.

"follicular") hormone in attracting the attention of the chemical industry, the work of purification and concentration made rapid progress. It was the Schering-Kahlbaum Corporation in Berlin (Professor Schoeller) that lent help through their own research laboratories, and the result was "Steinach's Progynon," the first purified highly potent and standardized female sex hormone that was put at the disposal of the medical profession. Today's "Progynon," so popular in the United States, is a partly synthetic product. In this respect it differs from the original preparation, but it owes its existence nevertheless to Steinach's original research work, a fact now rarely remembered.

The years 1925 to 1928 were devoted principally to the study and elaboration of the effects of the follicular hormone. If it was injected into infantile males an inhibition of the development of their sex characters took place, while their retrodevelopment was observed in adults. These experiments, published in collaboration with H. Kun, confirmed once more the "Antagonistic Effects of the Gonadal Hormones" (*Biologia Generalis*, 1926).

In 1928 two publications appeared in *Pflüger's Archiv* on the female hormone. The first, written in collaboration with Dohrn, Schoeller, et al., was entitled "Bio-

logical Action of the Female Sex Hormone" and described its influence on the mammary gland (its growth and milk secretion) and on the uterus. The second, with Kun and Hohlweg as coauthors, dealt with the "Reactivation of the Senile Ovary and of the Female Organism through Hormonal Influence." Here the hormone's favorable effect on hair growth and red blood cells was recorded and also the restoration of fertility. As an additional aid for the reactivation of women, Steinach somewhat later advocated the use of diathermy to the ovaries to produce hyperemia. With simultaneous injections of the hormone, substitution and stimulation therapy were combined.

The Pituitary and the Central Nervous System. In the late 1920's the pituitary gland began to assume some of the importance that later researches so fully substantiated. Steinach's interest was readily aroused and led to important studies and conclusions. In 1928 he published a paper (*Mediz. Klinik*) with one of his favorite collaborators, H. Kun, on "The Significance of the Hypophysis as Activator of Gonadal Secretions." With the then crude extracts from the anterior pituitary lobe, the authors induced precocious maturation in infantile male rats. They explained it by the activation of the Leydig cells which were said to increase in numbers. In eunuchoid and senile animals they effected a restoration of atrophic sex characters and concluded that the pituitary was chiefly responsible for the "mechanism of development" and for a "biological law of puberty."

Deviating briefly from glandular studies, Steinach and Kun conducted experiments and published them in 1929 and 1930 (*Mediz. Klinik*) which revealed the presence of a specific *Reizstoff* (excitant) in the central nervous system. This so-called "centronervin" increased the excitability in frogs and the fly-catching ability of tree toads. The authors suggested its possible therapeutic use by employing brain and spinal cord tissues.

In 1931 Steinach returned to the studies of the ovary, but this time experimenting with the corpus luteum. He found two luteal

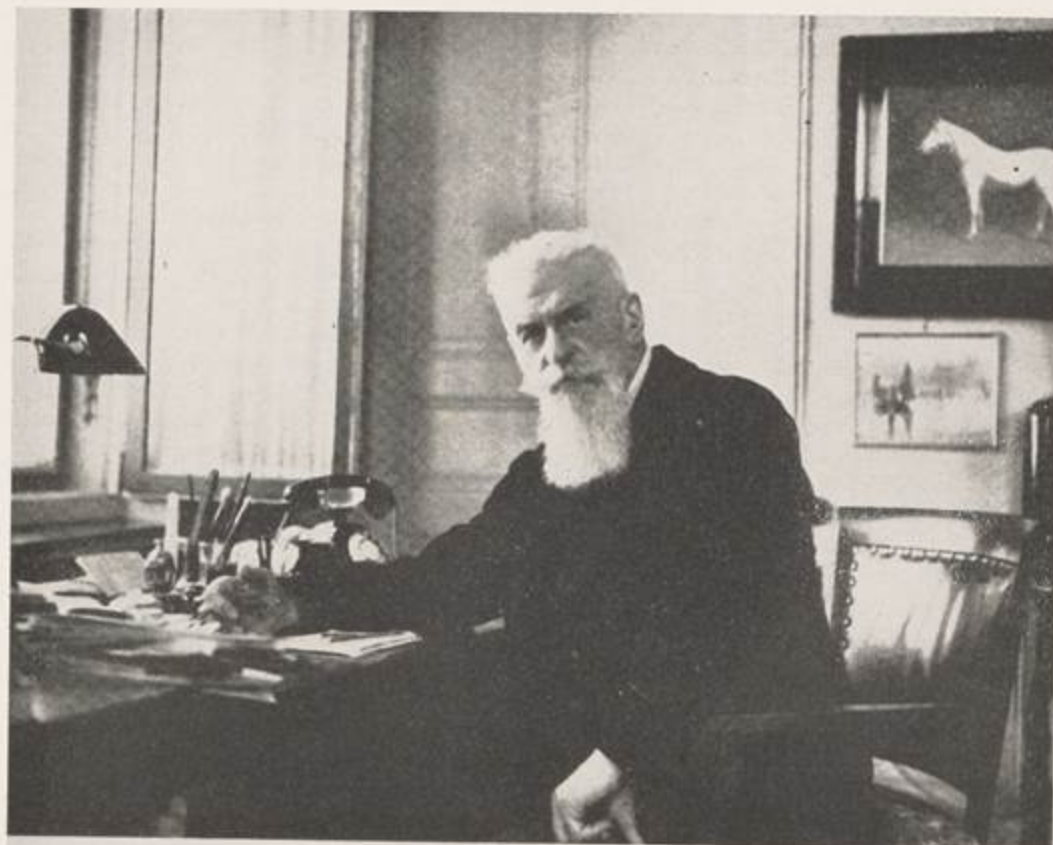
hormones—one, sex-specific, affecting the uterus; the other of masculine characteristics capable of influencing secondary sex characters just like the male hormone. He spoke, therefore, of the "hormonic bisexuality" of the ovary (*Pflüger's Archiv*).

The Male Hormone. In the meantime male sex hormone preparations had been developed: first, androsterone from urine (Funk and Harrow, Laqueur, etc.) and then testosterone from testicles (Koch, Butenandt, Ruzicka). Steinach tested the latter, stressing the effect on psychic functions (erotization) in addition to the known somatic influences (*Anz. Acad. Wissenschaften*, 1933).

The following year saw Steinach in Switzerland collaborating with the veterinarians Staeheli and Grueter in the "Correction of Sterility in Cattle and Hogs" (*Wien. Klin. Woch.*, 1934). (The grandfather's cattle-breeding had planted the seed for this new interest.) One or two injections of "Provetan" (which was the "Progynon" of veterinary medicine) initiated oestrus in sterile cattle. These original experiments received wide attention, confirmation, and elaboration in veterinary circles.

Several summarizing publications on the "Analysis of Sex Hormone Effects" (Steinach, Kun, and Peczenik, *Wien. Klin. Woch.*, 1936) and on the "History of the Male Hormone" followed. In another series of articles (*Wien. Klin. Woch.*) the hyperemia produced by the sex hormones was especially emphasized. This hyperemia, Steinach thought, was the mechanism through which the results on body and mind must be explained. These studies readily led to the experiments on hypertonia in the same year (*Wien. Klin. Woch.*). A suitable combination of male and female hormone was used for the treatment of hypertension. Elaborate and interesting charts showed the reduction of blood pressure in a number of cases.

Likewise, in 1936, Steinach, Kun, and Peczenik published "Diagnostic Test for Disturbances of Male Sexual Functions Due to Endocrine Causes and Its Clinical Application" (*Wien. Klin. Woch.*). The creatine content of the urine after a test meal was used to differentiate impotence of an endo-



E. Steinach

crine nature from purely psychic impotence. The former would be indicated by an increase of creatine output. The reactivating effects with the synthetic testosterone on men in various age groups were also recorded.

Except for a few minor articles (*Lancet*, 1937 and 1940) dealing with the male sex hormone, only two other publications by Steinach deserve to be recorded, because they appeared exclusively in the United States. One is an article in the *Medical Record* (New York), 1927, "Biological Methods against the

Process of Old Age," a summarization of laboratory and clinical data, and the other is his book *Sex and Life (Forty Years of Biological and Medical Experiments)*, which the Viking Press published in 1940. It is a somewhat autobiographical record of his life's work.

LAST YEARS IN EXILE

Steinach's scientific work ended with the end of an independent Austria. When Hitler marched into Vienna (how easy it is to speak

of it now after VE-Day), Steinach and his wife happened to be in Switzerland. They never returned to their home. At 77, Steinach was an exile, like Freud and so many others. In Zurich, his new home, he bore up bravely under his personal tragedy, which was deepened by his wife's death. Fortunately, he had no economic problems, and he still had his indestructible zest for life, his science, his hobbies. His philosophy of life allowed him to make the least of what he had lost and the most of what he retained.

The Swiss Government had granted him permanent residence, but his enforced idleness was a heavy burden. He suffered under personal and scientific loneliness. His fertile mind with his ever-youthful curiosity was constantly filled with new ideas for experiments, and it was not surprising, therefore, that an old wish to visit America became a new and ardent hope. In America there would be a chance to start research work once more. Many efforts were made through universities, research institutions, and private organizations to have him invited to the United States. Promises were given but not kept. Various excuses were found for not opening the doors to him. Some said he might be too old; others said the physiologist had nothing to offer anymore. "If Steinach would be a biochemist, we would go to any length to bring him here" was one statement. In another instance fear was expressed that too much publicity would result from Steinach's arrival. "You know the American Medical Association. They would not like it," was another statement. And so Steinach never came.

It was his last disappointment. His powerful vitality, which he retained to the last (for he fought senility in himself as he had fought it in others) finally succumbed to

stronger forces. A lonely, uprooted, and somewhat embittered man, Steinach died on May 14, 1944, in his eighty-fourth year, during a sojourn in Territet near Montreux. His cremation in Zurich on May 17 was the occasion for impressive services when leading Swiss scientists honored the memory and work of their great colleague.

Like every true pioneer, Steinach had relatively few immediate followers for the simple reason that he was ahead of his time. It matters little that some of his theories have not been verified and some of his experiments were not fully confirmed. Neither were Darwin's, nor Virchow's, nor Freud's. Steinach has nevertheless shown new ways and created new foundations on which subsequent researches were built, although this fact is often forgotten, especially in this country, conveniently by some, carelessly by others.

Professor Heinrich Meng, of the University of Basel, in his recent fascinating book *Psyche und Hormon* emphasizes and conclusively shows the fundamental importance of Steinach's lifework for all sex hormone research and therapy of today.

When Steinach approached the "dangerous" problem of sex physiology, all the sex taboos and prejudices of his day were arrayed against him. Many cried "heresy," just as they did in the times of Copernicus and Galileo, of Darwin, Haeckel, and Freud. Man has forever fought against the recognition of his own status in nature, and "original sin" has blighted for centuries the life of the individual. Steinach's work began in the shadow of the Victorian era, but he himself (to speak in psychoanalytic terms) had conquered the castration complex and was able to approach sexological problems with the fortitude and objectivity of a true scientist. "He found a road, because he dared to walk it."

