

nine diabetic subjects intravenously. On separate occasions, insulin was given in amounts designed to produce a depression of blood sugar similar to that obtained after tolbutamide in the same individual. Under these conditions no definite difference in the pyruvate response followed either agent. The lactate changes were related to hypoglycemia. They concluded that differences in blood levels of pyruvate and lactate reflected differences in the rate of blood sugar depression rather than mechanism of action. However, using a method of hepatic vein catheterization they studied the splanchnic assimilations of fructose, glucose, pyruvate and lactate. Their results suggested that tolbutamide depressed splanchnic glucose production or release during fructose administration. Studies on the site of action of sulfonylureas in man by Renold, Martin, Boshell and Thorn⁶ were carried out in an attempt to characterize the hypoglycemia produced by the sulfonylureas as the result of either increased glucose utilization or decreased hepatic glucose release. The decreased conversion rate of fructose to glucose concurrent with sulfonylurea-induced hypoglycemia suggested a decreased rate of hepatic glucose release or synthesis. In addition, these authors, in common with many others, failed to find convincing metabolic evidence of increased glucose utilization as a result of sulfonylurea action, and could not demonstrate

increased levels of circulating plasma insulin under these conditions. They regarded these results as providing clear-cut evidence for an effect of the sulfonylureas on hepatic glucose release *in man*, although the possibility of an additional acute effect upon pancreatic insulin secretion was not considered as excluded. Such an effect on insulin secretion *in animals* appears well established.

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Albrecht von Graefe

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The man most deserving of the title, "Founder of Ophthalmology," Albrecht von Graefe, was born in Berlin on May 22, 1828. His father, one of the founders of German surgery, Director of the Surgical Clinic of the University of Berlin and author of many surgical works, was held in high esteem by the royal family. His renown might have been greater, except that he had an untimely death in 1840, and the great Dieffenbach became his successor.

Albrecht received his instruction at home from private tutors, then entered the French Gymnasium, where he attained proficiency in the French language. He was intensely interested in his studies, and at age of fifteen years entered the University of Berlin in the autumn of 1843. He studied logic and philosophy under Carl Lud-

wig Michelet and demonstrated zeal and intense interest in the natural sciences. The medical faculty at that time consisted of Johannes Muller, Schonlein, Dieffenbach and Juengken, as well as Emil Duboise Reymond, Ludwig Traube, Robert Remak, Rudolph Virchow and Ernst von Brücke. He learned anatomy not only from Muller but also from Schlemm. Among the younger teachers, Graefe was captivated by Virchow.

He had a very happy home and lived in prosperous circumstances. It was his privilege to gain friends quickly and to turn them into enduring friendships. Although his student days were spent in Berlin, he was afforded by his family's wealth and station the opportunity to travel abroad for further studies.

He studied in Prague with von Jaksch, Ditterich and

with Ferdinand von Arlt. Von Arlt was responsible for introducing von Graefe to the study of ocular diseases and surgery, and soon this brilliant young doctor devoted himself to ophthalmology.

The years of 1848 and 1849 were spent in Paris. Much of this time was devoted to study with Claude Bernard, Philippe Ricord and Armand Trousseau. While under the direction of Bernard, he studied intracranial nerves and the extraocular muscles. Clinically, he shared a good deal of time with Julius Sichel from Frankfurt on the Main, founder in 1832 of the first ophthalmological clinic of Paris, and Louis Auguste Desmarres, the founder of the modern French school of ophthalmology.

In 1849 to 1850, von Graefe studied in Vienna. Here he encountered Rokitansky, Bednar, Heschl, Wedl, Brücke, Oppolzer, Bamburger, Hebre and Sigmund. He was especially impressed with the quality of Brücke's lectures on physiology. He also worked on diseases of the eye under Frederick Jager and his son, Eduard. In 1854, Eduard Jager dedicated his book, "Ueber Star und Star-Operation," to his friend, Albrecht von Graefe.

Von Graefe's fame as a teacher and lecturer began in Vienna at that time. A group of young doctors prevailed upon him to lecture to them. He welcomed the opportunity to practice his speaking and teaching.

He left Vienna in July, 1850, and spent two weeks with von Arlt in Prague. From there he went to Berlin and then to London. There have been few finer friendships in the history of medicine than that of von Graefe, Donders and Bowman. It is quite possible that Donders, a physiologist, Bowman, an anatomist, and von Graefe, a clinician, had a significant influence on one another.

Years afterward, in 1886, Donders was selected to present the first Graefe medal, in honor of his lifelong friend, who had since died. In a speech at this presentation, he recalled his first meeting with von Graefe as follows: "I had been enjoying the company of Jaeger for several days, when one morning in Guthrie's Clinic, a young man in full alpine costume burst in. He had only arrived in London a few hours before, and flew into von Jaeger's arms. With the words, 'Here, you two belong together,' the latter literally threw him into my arms. He was not wrong. From early morning after we gathered up a hasty breakfast in Oxford Street and followed the footsteps of the workmen on our way to Moorefield's Hospital until late in the evening when we departed from the hospitable home of our friend, William Bowman, we remained together, inseparable in our search for the common goal. Von Graefe led me in practical matters in which I had, as yet, scarcely delved, and I, in turn,

could help him with many things from the physiologic aspect. There lay for both of us in this mutual complimentary relationship a great stimulus. Those days in which von Graefe gradually displayed the fairness of his nature belong to the loveliest recollections of my life. When I left him after several weeks he had become like a young brother whom I admired and loved." (Donders)

When von Graefe set up his practice in Berlin, there were no free clinics exclusively for eye patients. He modeled his first clinic after that which he had seen in France. This was done in the second story of a house in Behrenstrasse. Shortly thereafter, two simple rooms were rented from a tailor in Johannestrasse, furnished with beds and readied to receive the operated cases. Such was the start of the famous Graefe Clinic, which, after one decade, was to receive patients from all sections of the world. Actually, at this time, there was an advertisement in the daily Berlin newspapers saying, "Dr. Albrecht von Graefe in Behrenstrasse. Eye diseases treated free for the poor." (Adler)

His first cataract extraction was performed on an old inmate of a poorhouse; at the same time, an iridectomy was done on an organ-grinder, who had an old, adherent leucoma, the result of ophthalmia neonatorum. Two nights after the operation, the patient with the iridectomy lost his mental equilibrium as a result of the bandages and attacked the patient with the cataract to such an extent that the cataract patient died. Subsequently, the iridectomized individual recovered and was able to walk unguided for the first time in his life.

By the time von Graefe was twenty-five years old, he had over 1,900 patients recorded in his clinic, and a few years later he had over 10,000 on record. According to Michaelis, von Graefe devoted his mornings to private consultation, operations in the clinic, and then, after lunch, to physiologic studies, and evenings, after hospital visits, to scientific investigations. Later, he adopted a different schedule to which he thereafter adhered. During the mornings he devoted himself to literary pursuits, then lectures, hospital visits and occasional consultations in the city; after lunch, work in the outpatient department and operations and, in the evening, consultations with private patients followed by a visit to the hospital and, finally, a short period of recreation with friends. It is obvious that such a routine must have weakened him and paved the way for his later years of illness. (Michaelis)

Von Graefe transferred the hospital and clinic to 46 Karlstrasse, where both remained until his death. Now a simple tablet announces to the observant visitor. "Hier Wirkte 1852 bis 1870 Dr. Albrecht von Graefe."

In the autumn of 1852, Graefe qualified as Privatdocent der Chirurgie und Augenheilkunde in the medical faculty of the University of Berlin with a treatise entitled "On the Action of the Ocular Muscles." His tie with the University was a very loose one. By virtue of his position as Privatdocent, he was not permitted to post a notice of his course unless he was in charge of the clinic. He therefore devoted his time to teaching the doctors who came to him from all parts of the world. Very few medical students came under his direction or attended his lectures or clinics at that time. After the first few years, by which time his fame as a teacher had spread, he devoted himself chiefly to the clinic and had assistants who gave most of the basic courses.

In 1854, Graefe established the *Archiv für Ophthalmologie*. This journal filled the need of ophthalmology for its own journal, for there was considerable basic scientific investigation now being done in this specialty. The major advance, however, which showed the necessity for such a publication, was the discovery of the ophthalmoscope by Helmholtz. Epstein has recorded the letter which Albrecht von Graefe wrote to Helmholtz about 1852, shortly after his return from his three-year journey to the medical centers of Europe. He was twenty-four years old, and at that ripe young age he recognized the great discovery made by Helmholtz. (Epstein)

Esteemed Professor:

You will pardon the liberty of addressing you, an utter stranger, and requesting a favor concerning a subject which interests me greatly. Last summer, I learned through Professor Brücke in Vienna that you have succeeded in constructing an instrument for examining the retina in the living eye. I even had the pleasure of hearing some of the details by means of which you accomplished this. Professor Brücke was more willing to indicate these to me since we frequently talked over the possibility of such an instrument, and he had previously shown me a scheme of his which had miscarried because of the lack of suitable illumination. Brücke expected to obtain the catoptric and dioptric effects from his instrument by means of a concave glass placed at an oblique angle over the observed eye.

The news of your successful accomplishment was therefore the more welcome to us, and I awaited the publication with impatience until a few days ago, when I was fortunate to find it waiting for me on my table on my return to Berlin after a long journey. To the study of this article I am not only indebted for an exact understanding of the instrument but also for the explanation of other questions in optics which were quite closed

to me, and am therefore going to ask you if you will kindly request your optician to send one or two of your finished ophthalmoscopes to my address in Berlin.

The first number of the journal contains 480 pages, most of which are written by the young editor. Soon he was assisted in the editorship by Arlt, of Vienna, and Donders, of Utrecht.

In 1857, he was appointed Assistant Professor at the University of Berlin. This did not change his activities. In this same year he reported on the possibility of curing glaucoma by iridectomy. His presentation of this information at the International Congress of Ophthalmology at Brussels, in 1857, evoked a storm of applause from the leading scientists of the world. Also in the fall of 1857, he and a few of his friends gathered at Heidelberg to talk over the progress of ophthalmology. Thus was established the oldest local ophthalmological society in existence, the Deutsches Ophthalmologisches Gesellschaft. (Axenfeld)

When von Graefe was thirty-three years old, he was engaged to marry Anna Gräfin Knuth, a charming girl not quite nineteen years old. However, while he was on vacation in the fall of 1861 in Baden Baden, he developed tuberculous pleurisy. Under the excellent nursing care of his two sisters, his bride-to-be and his boyhood friend, Dr. Arndt, and the medical ministrations of Dr. Müller, Professor Friedrich from Heidelberg and Professor Traube of Berlin, the disease was arrested. He continued his convalescence in Nice and finally was married on June 7, 1862. He had several very happy years. His wife often wrote down his dictation until he obtained his own secretary. In the short period of their married life, five children were born. The second child died at the age of six months, and the last child, a son born on July 2, 1869, lived for only a few days. Von Graefe was a modest man who enjoyed good food and drink, but in moderation. He loved company at dinner. He occasionally attended the opera and theater but was rarely seen in public, spending most of his time with his patients and his clinic and his pupils. For him, his greatest pleasure was to be found in his work.

Hirschburg met von Graefe in 1866 and found him to cast a spell over everyone with whom he came in contact. He was impressed with his extraordinary beauty, and remarked on his tall, slender figure, noble brow and classic countenance, ringed by a dark beard and long, curly hair. The sound of his voice and the penetrating keenness of his gaze established great confidence in his patients. (Hirschburg)

In 1866, he was appointed full Professor on the medical faculty of the University of Berlin. His lectures were

not well attended by medical students, perhaps because examinations in ophthalmology were not obligatory. Some have expressed the feeling that his lectures were too intricate for medical students. At the Seventy-First Anniversary of the founding of the Friedrich Wilhelm Institute, Aug. 21, 1865, Graefe devoted his public address to the subject of the importance of ophthalmology in general medicine. He was not very happy with the medical faculty, nor did he receive much support from the faculty or from the government. He did not receive a Directorship of the Konigliche Klinik by his appointment as Professor, and he had considerable difficulty obtaining adequate hospital facilities for the patients who were to be used as his teaching material. In a letter to Jacobson in 1868, he displays his feelings. "My situation is this; I am of course a Professor. I receive as such 500 thaler salary. I do not give examinations, since Papa Juengken still takes care of that in an uncurtailed manner and, naturally also collects remuneration. For this 500 thaler—up to now there has been no talk of the Konigliche Clinic—I have to obtain teaching material for sixty or seventy students, of whom the majority wish to become specialists. Actually I dare not reduce the hospital division of sixty beds in my clinic in order to suffice for their requirements. It costs me in order to have the good fortune to be a teacher of ophthalmology . . . another 5,000 thaler a year." (Jacobson, Perera)

In 1866, Graefe finally became the Head of the Charity Ophthalmologic Clinic, and by 1868, ophthalmology became an essential part of the medical requirements. In the same year, unfortunately, his pulmonary disease became more active. So did his own activities. As disease weakened him, he doubled his efforts to carry out his work. He did not seem concerned with his own illness, but only that of his wife. By 1869, his cough and hemoptysis almost incapacitated him. He was unable to attend the meeting of the Gesellschaft at Heidelberg. Donders called upon him after this meeting to tell him about it, and to sympathize with him. At this time, von Graefe quoted the words of Goethe, "One cannot learn too soon how really unessential he is in the world." On July 20, 1870, he died at the age of forty-two.

It is difficult to select one thing for which von Graefe is famous. He gave great impetus to the development of ophthalmology. He started the *Archiv für Ophthalmologie*. He devised the operation of iridectomy in the treatment of glaucoma, which is still the most widely employed operation for angle-closure glaucoma. The Graefe knife is extensively used for cataract extraction.

He was one of the first to describe the cupping of the optic nerve in advanced glaucoma and to attribute the changes in glaucoma to an increase in intraocular pressure. He described the edema of the nervehead associated with intracranial disease and the signs of blockage of the central retinal artery.

A complete list of his contributions can be found in Perera's review of life and works, in which one will find that he wrote in 1858 on the visual disturbances in diabetes mellitus, describing the diabetic cataract in young and old persons, chronic choroiditis and cerebral amaurosis as complications. In many diabetic patients, he had observed weakness of accommodation. He is probably most widely remembered as the first to use in clinical practice the ophthalmoscope invented by Helmholtz. In Graefe's words, "Helmholtz gave us a new world." He was one of the first to begin systematic plotting of the fields of view in cases of defective vision.

Von Graefe became the first German professor of ophthalmology. In his short, exhausting, but productive life, he did not demonstrate the inventive genius of Helmholtz or the ability to work with minute instrumental detail, as had Gullstrand, but because he had the tremendous ability to apply new methods of examination to their utmost clinical use, to take his clinical observation and deduce with great detail reasons for their existence, he established the scientific foundation of modern clinical ophthalmology. He was one of the first to describe transillumination for the detection of tumors, to use an instrument for the measuring of the tension of the eyeball, to make clinical records of the pathological visual field. There is hardly an area in clinical ophthalmology to which he has not contributed.

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