Chapter 12

Hermann Holthusen

(1886-1971)

"Not until we are quite clear as to the fundamental phenomena of x-ray effects shall we be able to rise above the empirical point of view and arrive at a rational idea of radiotherapy." (1927)[301]

Hermann Holthusen was born in Hamburg on 22 September 1886, the son of Sophie von Ahsen (1851–1916) and Gottfried Holthusen (1848–1921), senator of the governing body of the Free and Hanseite City of Hamburg. Hermann had an older half-sister, Marie (1873–1940), and brother, Walter (1885–1918). A sister, Agnes (1897–1948), and brother, Claus Gottfried (1896–1974), joined the family later.

Young Hermann had his secondary education in the centuries old Johanneum Gymnasium. His records show he combined good knowledge and natural understanding in mathematics and natural history, and that he had a "vivid interest" in the English language. He was good in gymnastics and excelled in singing, but did less well in Latin and Greek. When Hermann was only nine years old (Fig. 12-1), he heard of Röntgen's discovery from his professor of physics. Within days, on 15 January 1896, his father was much impressed by a public demonstration of X rays by Bernhardt Kurtwalter[B] at the Physikalisches Staatslaboratorium.

After receiving his *abitur* in 1904, young Holthusen spent a year with a London family to learn English. He then studied at the Universities of Munich and Berlin and, after presentation of a doctoral thesis, received his degree of Doctor of Medicine from the University of Heidelberg in 1911.[290] In the winter of 1911–12, Holthusen spent three months in his hometown with Heinrich Albers-Schönberg[B] at the Röntgen Institute of the Sankt Georg Hospital. Holthusen credited this brief association with the inspiring master as having given him a strong professional direction. He was then offered a position in the medical clinics of the University of Heidelberg with responsibility for developing a department of radiology. To prepare him for this task, he was directed to take a course of instruction and experimental work in physics under the eminent professor and Nobel laureate, Philipp Lenard,[B] at the Physikalischen Institut of the university. While serving regularly at the medical clinic, Holthusen continued his study of physics for three years under Lenard, and did some experimental work on the radiation properties of a Lindemann tube.[291] He also engaged in the study of the solubility of radon in the blood of experimental animals, noting the rate of its decay and eventual release.[292,293] He long remembered the weekly visits paid by Lenard to the students for discussion of their projects and the enlightening expressions of the *Geheimrat.* He also remembered the distasteful fact, which he later decried, that the name of Röntgen and the expression "roentgen rays" were not to be uttered at the Physics Institute.

In the first World War, Holthusen served as a medical officer in the German infantry. His mother died in 1916 during his service, and his brother Walter died in the conflict. After the war, he served in an army hospital in Heidelberg. He married Agnes Weizsacker (1896–) in 1917.

In 1919 Holthusen published a paper on the ionization of various media, especially air, by means of radiations. He developed a cylindrical ionization chamber which provided for interesting studies of secondary rays.[295] He maintained that the important parameter of the biologic effects of irradiation was absorption of energy.[294,296,297] In 1920 Holthusen resumed his work at the Heidelberg University Medical Clinic under Professor Ludolf von Krehl (1861–1937). During this period, Professor Röntgen came to be examined at the clinic. It was Holthusen's privilege to submit the discoverer to roentgenologic examination. Meanwhile, he had also renewed his work in physics

Fig. 12-1. Young Hermann Holthusen at ten (1896), shortly after Röntgen's discovery. (Courtesy of Dr. W. Holthusen.)

and radiobiology. He became *Privat-dozent* in radiology at Heidelberg in 1920.

The city of Hamburg underwent a severe socio-economic setback in the aftermath of the war. The victorious Allies requisitioned as reparations all easily-moved property and most of the city's 1500 ships, leaving its docks bare. The resulting massive unemployment was to make the city a focus of proletarian discontent and revolt. Confident of the eventual recovery of his beloved hometown, Holthusen accepted an offer to return to the shores of the Elbe. The Röntgen Institute had entered a new building in 1915. Its founder, Heinrich Albers-Schönberg, died a martyr to his exposure to radiations. In November 1921, Holthusen accepted the position of chief radiologist to the Institute, succeeding Albers-Schönberg. He was to bring additional honor to the already reputable institution through a professional lifetime of dedication. His obligations were in great part radiodiagnostic, but he favored radiobiological research and radiotherapeutics (Fig. 12-2).

In 1922 Holthusen observed in his experimental laboratory that the ligation of afferent vessels definitely diminished the radiosensitivity of certain organs. Within the circumstances of his experiment, he noted that the response was only delayed and that radiosensitivity returned as soon as circulation was re-established.[298] The importance of blood supply in radiosensitivity was also observed by Justin Jolly (1870–1952).[B,343]

Before the end of his second year as head of the institute, with the sponsorship of the Deutsche Röntgen Gesellschaft, Holthusen organized one of the earliest comprehensive courses on radiology (Fig. 12-3). It was attended by over one hundred German and foreign physicians. In 1924 he was appointed professor of the University of Hamburg, but not of radiology: it was simply a title. The prejudice against a chair of radiology was to linger in Germany for many years. Academically, radiology remained subservient to medicine and surgery, and to their respective subspecialties.

In 1925 and 1926 Holthusen contributed several chapters to a textbook on radiotherapy edited by Hans Meyer (1877–1964). These were informative chapters on physics of radiations, qualitative and quantitative measurements, the theoretical basis of radiotherapy, as well as a chapter on diseases of the blood-forming organs.[435] In radiotherapy a means of evaluating the amounts of radiations administered was indispensable for reproducibility and comparison of results. In view of the steady delivery and unchanging quality of radium sources, it became simple to express doses in milligrams/hours. This was "indirect dosimetry," or dose at the source point. However, the dose reaching the normal or neoplastic tissues for the same source dose varied according to whether the application was surface, intracavitary, or interstitial. In roentgentherapy an expression of time of exposure was inaccurate in view of the irreconcilable variables: the unpredictable output of gas tubes, the oscillating milliamperage and voltage, and the changes introduced by distance and filtration.

A rational dosimetry, a "direct dosimetry" at the portal of entry, was slow in coming. Numerous dedicated workers attempted to define an "erythema dose," a visible reaction of the skin. This also proved unreliable as it depended on quality of radiations as well as on fractionation of the quantity administered. At the second International Congress of Medical Electrology in Berne in 1902, Holzknecht, the charismatic Viennese pioneer, presented the first device invented for direct dosimetry. Holzknecht's chromoradiometer was based on the radiochemical change in color of a mixture of sodium carbonate and potassium chloride. He established an arbitrary unit (H) and estimated that the dose necessary to produce a mild skin reaction was 3H. The chromoradiometer with its scale of colors was available commercially. It underwent several model changes and was widely used for over three decades.[319]

Fig. 12-2. Holthusen and his associates with technological and nursing staff (1923). (Courtesy of Dr. W. Holthusen.)

Ringworm of the scalp (*tinea capitis*), a fungus infection of the hair, had been a plague of school children for generations and required segregation. Topical applications of ointments were unsuccessful since the hair grew infected from its root. Epilation by means of radiations became an easy solution, but temporary epilation of all parts of the scalp required some dosimetric precision. Raymond Jacques Adrian Sabouraud (1864–1938), an eminent Parisian dermatologist, and his associate, H. Noiré, introduced in 1904 a new radiochemical dosimetry: tablets (*pastilles*) of barium platinocyanide and a standard colorimetric scale of five degrees.[551] In rapid succession, Leopold Freund (1868–1943),[B] Robert Kienbock (1870–1910),[B] and Gottwald Schwartz (1880–1959), all of Vienna, introduced different radiochemical approaches to dosimetry.[351] There were others as well. In time it was estimated that one Sabouraud unit was equal to five Holzknecht (H) and ten Kienbock units.

Paul Villard (1860–1934), the pioneer French physicist, proposed in 1908 a unit of radiations based on ionization of air: a proposal which went unnoticed. At the Jefferson Laboratories of Harvard University, William Duane (1872–1935)[B] developed an open-air ionization chamber and, since 1914, had utilized an electrostatic unit of intensity (E) measuring five volts in ergs per cubic centimeter.[501] Iser Solomon (1888–1939)[B] the Romanian-French chief radiologist of the Saint Antoine Hospital of Paris, brought forth an ionometer consisting of a closed ionization chamber connected by a cable to an electroscope that registered the passage of electricity. Solomon defined a unit he called the "Roentgen" (R).[42] Despite some gross imprecisions, some 1500 ionometers were sold and used widely. Holthusen had an early interest in radiation dosimetry and favored a measure based on the ionization of air.[596] Hermann Behnken (1889–1945), of Germany, working with a compressed air chamber, adopted an electrostatic unit of energy, which he also called the "Roentgen" (R).

Antoine Béclère, the venerable French pioneer, was a member of the Executive Committee of the first International Congress of Radiology in London in 1926. Beclere made an impassioned plea for the appointment of a Commission on Units and Measures to seek international agreement on a single unit of radiations to be used in radiotherapy.[56] The appointed commission was an authoritative group of competent men with a broadly based representation

Fig. 12-3. The Albers-Schönberg Institut on the grounds of the Sankt Georg Krankenhaus in Hamburg, where Holthusen taught (1925). (Courtesy of Dr. W. Holthusen.)

to assure support for its recommendations. Nobel Laureate Manne Karl Georg Siegbahn (1886–1979) of Sweden was chairman. Edwin Augustus Owen (1887–1973) of England and Hermann Holthusen were secretaries. Hermann Behnken, William Duane, and Iser Solomon were members of the commission that included members from Belgium, Italy, Japan, Switzerland, and the Soviet Union.

At the thirteenth annual meeting of the Radiological Society of North America in New Orleans in November 1927, Holthusen spoke enthusiastically in favor of an international standard measure based on ionization of air, and noted the unreliable character of the erythema dose. He also discussed the potential of the half-value layer as a measure of the quality of radiations.[300] Members of the RSNA at the Roosevelt Hotel in New Orleans devoted an evening to listening to this eloquent German professor. Speaking as a radiobiologist whose knowledge of physics stood him in good stead, he postulated that biologic effects were due to chemical changes caused by the absorption of primary and secondary radiations. He reviewed Regaud's assertion and its confirmation by others, that suitable fractionation of the total dose yielded a greater probability of biologic effects. He concluded that the greater possibility of progress in radiotherapy of tumors lay in appropriate fractionation. He talked of his experimental work with irradiation of *Ascaris* eggs, noting that effects varied with their maturity and observing in passing the increased effects in the presence of oxygen.[301] It was a long evening, but his audience was attentive. Edwin Charles Ernst (1885–1969), of St. Louis, opened the discussion, and was followed by William Edward Chamberlain (1892–1983) of San Francisco, and Francis Carter Wood (1869–1951), of New York. They all appeared pleased by what they had heard. Two days later, at the same 1927 RSNA meeting, Behnken discussed the practicality of standardization of X-ray units, heralding the probability of an international agreement.[74]

In 1927 Holthusen contributed a chapter for the second edition of a widely read textbook of radiotherapy edited by Swiss radiotherapist Paul Lazarus (1873–1957).[413] At the second International Congress of Radiology, in Stockholm in 1928, the Commission on Units and Measures rendered its formal report and proposed the adoption of an international x-ray unit of intensity, the roentgen (r). The proposed unit had similarities to the ones offered by Villard, Duane, and Behnken. In time it was generally adopted.[74]

In Stockholm Holthusen presented a paper on radiotherapy and immunity. In the years that followed, he often wrote on experimental research as it related

Fig. 12-4. Professor Hermann Holthusen (1930).

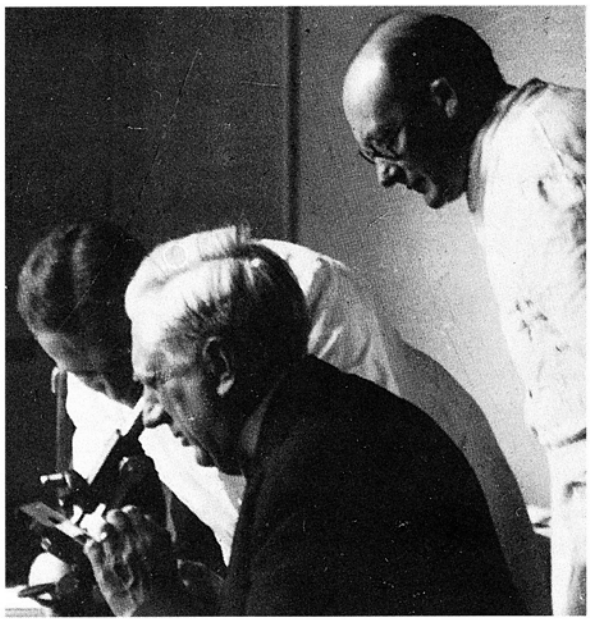

Fig. 12-5. Holthusen looking over the shoulder of Swedish Gösta Forssell in 1938.

Fig. 12-6. Holthusen in the company of Swiss Hans Schinz (1891–1966) at a commercial exhibit (1949).

to radiotherapy. Occasionally, he published in co-authorship with one of his assistants: Anna Hamann (1894–1969)[B] on radiumtherapy,[383] Carl Zweifel on experimental work with *Ascaris megalocephala*, and with Hans Braun on dosimetry.[311] In 1933, with Georg Fedor Haenish (1872–1952) and Adolf Liechti (1898–1946), he produced a textbook on roentgenology for physicians and students which went through several editions in the next two decades.[258]

Holthusen attended and participated in the third International Congress of Radiology held in Paris in 1931 (Fig. 12-4). He also participated in the fourth Congress held in Zurich in 1934.[304] In addition to his work for and contributions to congresses of radiology, Holthusen participated in a number of national and international meetings: the fifth International Congress of Physiotherapy (Liege, 1930),[303] the first International Congress of Cancer (Madrid, 1933), and the Italian Congress of Radiology (Bologna, 1937).[306] He was president of the Congress of Röntgen Societies in Berlin in 1929 and was also president of the Hamburg Medical Society from 1931 to 1935.

Through Holthusen's initiative, stone stelae were erected in the garden of the Sankt Georg Hospital upon which were carved over 150 names of martyrs of radiology. The formal inaugural in April 1936 was attended by radiologists from various countries. Speaking before the group, Antoine Béclère noted that the noble martyrs there remembered did not speak the same language, were citizens of different countries, and belonged to different races. Yet they were all devoted to the same mission: fighting disease at the risk of their own lives.[315]

For the fifth International Congress of Radiology in Chicago in 1937, Holthusen was asked to present a series of four lectures. A composite of these presentations was translated by Ernst Albert Pohle (1895–1965),[B] of Wisconsin, and published in the *American Journal of Roentgenology*.[305] Holthusen touched on a wide range of subjects. He stated his opinion, contrary to that of others, that shorter wavelength radiations had no greater selective effect. He said that prophylactic irradiation of subclinical neoplastic manifestations was effective in doses that would not affect an ostensible neoplastic nodule. In the treatment of cancer of the skin, Holthusen asserted, no dose had been found above which all tumors are always cured and below which recurrences occurred: it is only known that the proportion of cures increases with the dose. He decried the concept of 'tumor dose' and 'tissue tolerance' as fixed factors, maintaining that the margin of safety between effective tumor dose and safe tissue tolerance was dependent on volume of tissue irradiated and fractionation of the total dose. He affirmed that tolerance could be increased by fractionation.[305,306] In Chicago the international committee chose to hold the next Congress of Radiology in Berlin in 1940, with Holthusen as president. The second World War would force the cancellation of these plans.

In the late 1930's, Holthusen continued his work at the Sankt Georg Hospital with Karl Englmann (1900–) as his associate and deputy. Visiting friends

Fig. 12-7. Professor Holthusen, Honorary President of the International Congress of Radiology in Munich (1959).

worried for him because of his outspoken opposition to the regime. It was no longer a time of enlightenment. "His noble, exemplary and dignified posture found recognition abroad," wrote Hans Schinz (1891–1966).[B] "We were afraid for his safety, but our remonstrances with him were quite unavailing," wrote Ralston Paterson (Figs. 12-5 and 12-6).

The city of Hamburg and its population suffered heavily the consequences of war and suffered more than once. Holthusen's oldest son, Gottfried, died in the war. His sister, Marie, also died during the conflict. In 1945, on the one hundredth anniversary of Röntgen's birth, Holthusen wrote a commemorative article.[307] In 1949, with Friedrich Gauwerky (1910–1981), he co-authored a book on radiotherapy of gynecologic cancer and considerations of the pathology of these tumors (subj. note 12.1).[314]

After the war, it was decided to renew the international congresses of radiology and to hold the sixth Congress in London in 1950, with Ralston Paterson as president. Holthusen was honorary vice president and chairman of the German delegation. In London, within sight of the devastation caused by the German V-2's, uninhibited Holthusen was heard to protest the firestorm visited on his own beloved city by the Royal Air Force.

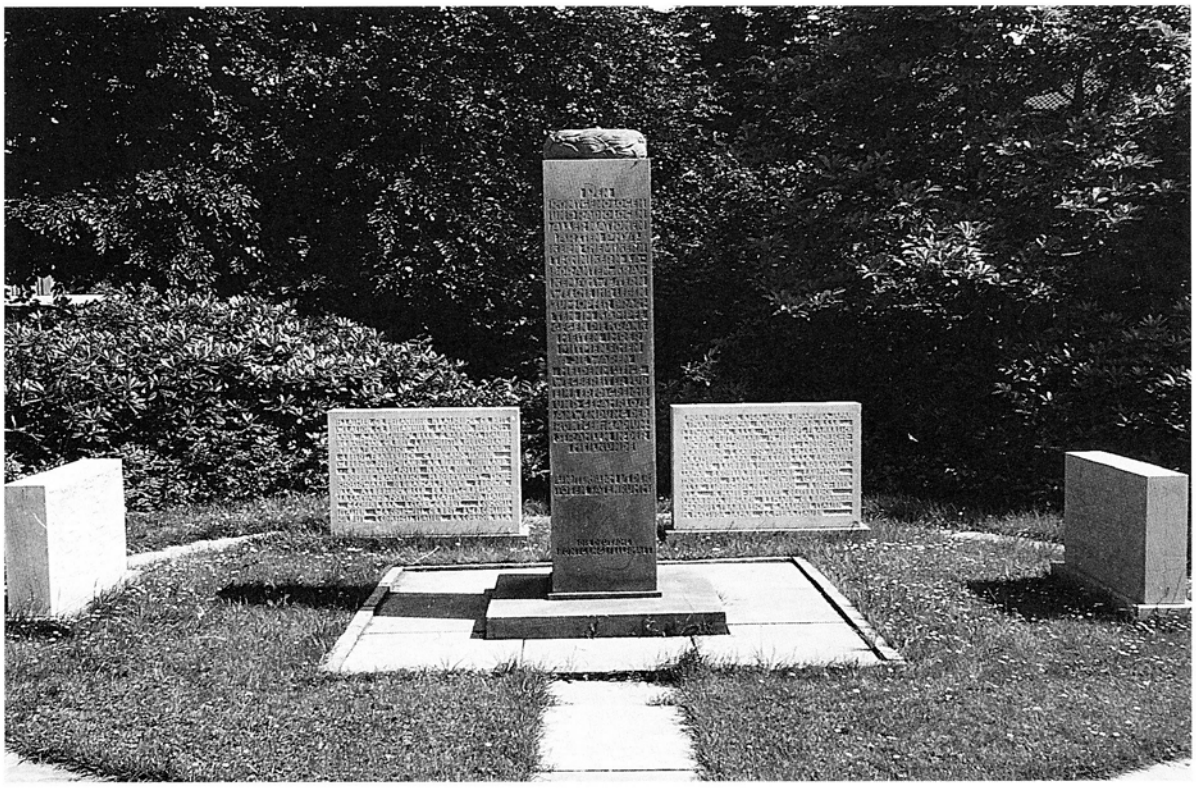

Fig. 12-8. The stelae honoring the pioneers who died victims of their exposures to radiations (1935).

Fig. 12-9. Holthusen in retirement (1967). (Courtesy of Dr. W. Holthusen.)

The University of Hamburg had given Holthusen the title of professor in 1924. In 1951 he was finally appointed *Ordinarius* of Radiology, an historical afterthought. He continued to work as secretary on the Commission on Measures and Units through the congresses of Paris (1931), Zurich (1934), and Chicago (1937). Thereafter he remained a member of the Commission. At the seventh International Congress of Radiology in Copenhagen in 1953, he was again honorary vice president and chairman of the German delegation. He held the same positions at the eighth Congress in Mexico in 1956. The ninth International Congress of Radiology was held in Munich in 1959. A new generation of German radiologists chose a younger man to be president, and Holthusen was honorary president (Fig. 12-7). By then he had become Emeritus Professor and resigned his duties on all commissions of the congress. He had also received two honorary doctorates.

Throughout the years, Holthusen consistently argued that what was important in radiobiology and radiotherapy was not the direct dose delivered but the dose absorbed. This frequently debated concept eventually led to the adoption of the rad (R).[309]

In twenty years, the number of names carved on the stones in the Sankt Georg Hospital garden had more than doubled. In co-authorship with Hans Meyer and W. Molineus, Holthusen wrote a beautiful *Ehrenbuch,* a memorial tribute to the 359 martyrs of radiology whose names remain carved there (Fig. 12-8).[315] This volume has been recently re-edited by Dr. Molineus. The new issue contains the added names of Anna Hamann and of Emil Grubbé, and a total of 404 biographies of martyrs of radiation.

In 1954 Holthusen retired from his position at the hospital and became Emeritus Professor of the University of Hamburg. In retirement, he continued to make steady contributions to the medical literature (Fig. 12-9). In the wisdom of his old age, he apparently feared that interest in new equipment and discoveries diverted attention from the fundamental phenomena: the physical and biologic foundations already available. He wrote comprehensive historical reviews.[308,309,310]

In the winter of 1970, already eighty-four and showing signs of infirmity, the Nestor of German radiology traveled to Würzburg to celebrate the seventy-fifth anniversary of Röntgen's discovery. He spoke at a site where Röntgen had once been honored with a torch parade by university students. In paying tribute to the discoverer, Holthusen reviewed his own experiences, the developments in which he had been

Fig. 12-10. The modern Hermann Holthusen Institute of the Sankt Georg Hospital of Hamburg.

a protagonist, and the problems arising from the wide use of roentgen rays. In paying his respect to the genial discoverer, Holthusen emphasized Röntgen's incorruptible spirit. Shortly afterwards, on 7 May 1971, Hermann Holthusen died. The Sankt Georg radiological institute, originally named after Röntgen and later after its founder, Albers-Schönberg, was divided into radiodiagnostic and radiotherapeutic institutions. The latter, in a new facility, is now named the Hermann Holthusen Institute.

A handsome, impressive, and lovable man, extremely able, courageous, and obdurate, Holthusen was also modest, courteous, and generous. An unquestionable architect of therapeutic radiology, he was an example of honest toil and a figure of equanimity, always to be counted present. Dr. and Mrs. Holthusen had three children: Gottfried (1921–1945), Johannes (1924–1985), and Dr. Wilhelm Holthusen (1923–), who is about to retire after a long practice in radiodiagnosis at the Albers-Schönberg Institute.

Subject Notes

12.1 In addition to those mentioned in the text, the following were collaborators of Holthusen or appear as co-authors in his publications: Otto Asher, A. Becker, A.A. von Braunberens, Gustav Bucky (1880–), R. Determan, Alexander von Essen (1908–), H. Gollwitzen, C. Hegler, Fritz Heinzel, R. Hoppman, H. Jakoby, Robert Janker, A. Schuback, Gustav Schulte, and Hans Richard Sielman (1894–).