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HISTORICAL STUDY OF CHEMICAL DOSIMETRY (1902-1962)

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Chemical dosimetry developed in response to needs created by developments in the field of high-energy radiation. Shortly after the discovery of X-rays in 1895 and of radioactivity in 1896, the deleterious effects of ionizing radiation were recognized. To guard against the injurious effects of radiation in medical application, dose-measuring methods were considered necessary.

The early dosimetric methods were based on what at the time were taken to be the chemical effects of ionizing radiation. In 1902, Guido Holzkecht (1872-1931), a Viennese physician, suggested a method of dosimetry which was based on the coloration of a salt due to irradiation. His proposal, the first of its kind, was followed within about five years by a number of others which were made by other physicians and radiologists and which were based on some visible chemical change. Subsequent developments in chemical dosimetry until about 1915 were concerned mainly with the calibrated scales used

to relate the chemical change to dose, the problem being a lack of a radiation unit of dose.

Further investigations of chemical systems for dosimetry were not made, however, until in the 1920's. In the meantime ionization methods of dosimetry became popular, although some of the earlier-proposed chemical dosimeters were widely in use. The renewal of interest in the chemical effects of ionizing radiation in the 1920's stemmed from the extensive radiobiological research that was conducted owing to the expanded application of higher-energy X-ray units in medicine and in industry. From the research done to understand better the mechanisms underlying biochemical processes, there proceeded several dosimetric systems. The one that proved most reliable was the ferrous sulfate system recommended in 1927 by the biophysicist Hugo Fricke (b. 1892). This renewed research on the chemical effects of ionizing radiation also made some significant contributions for future developments in chemical dosimetry. Most fundamental, both to the developing theories of radiation chemistry as well as to the formulation of many dosimetric systems in the post-World War II period, was the observation made by Fricke and associates that the primary action of the radiation was on the solvent rather than the solute.

The discovery of the neutron and of artificial radioactivity and the development of accelerating devices in the 1930's provided for still further application of ionizing radiation in medicine and in industry which increased the number of persons whose occupation was a source

of radiation exposure. A growing concern for the protection of personnel contributed to attempts at standardizing dosage measurements. Although formal standardization began in 1928 when the roentgen was officially defined as a radiation unit by the International Commission on Radiological Units, it was not until 1962 that the rad was officially restricted as a unit of dose and the roentgen as a unit of exposure. The precision of the terminology contributed to more reliable dosimetry.

The development of reactor technology in the 1940's gave rise to new problems in radiation protection. To monitor the mixed radiation fields present in the vicinity of nuclear reactors, film badges had to be modified for the detection of various forms of radiation. Also, various filter assemblies were introduced into the badge to reduce the energy dependence of photographic emulsions, thus to improve the accuracy of the film dosimeter.

Research in radiation chemistry and in nuclear technology in the post-war period called for dosimetric methods useful over a wide range of dosage and not necessarily as sensitive as those required by research in medicine and radiobiology. As a result, chemical dosimetric systems effective over a range from about 10 to 10^{10} rads were made available. Although many of the systems were formulated on the basis of the indirect action of the radiation on the solute via the solvent, not every system had a comparable reliability nor did each meet all the requirements desirable of a dosimetric system.

Ionizing Radiation and Its Chemical Effects: A
Historical Study of Chemical Dosimetry
(1902-1962)

by

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Note: The various units used throughout this treatise are represented by the symbols which were used by the writers whose works have been studied. These symbols do not always conform with modern accepted usage.

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IONIZING RADIATION AND ITS CHEMICAL EFFECTS: A
HISTORICAL STUDY OF CHEMICAL DOSIMETRY
(1902-1962)

CHAPTER I

IONIZING RADIATION PRIOR TO 1925

During the twentieth century, international organizations have often chosen to hold their conferences or congresses in Switzerland. It is not surprising then that the Fourth International Congress of Radiology met in Zürich in 1934; Zürich was one of the larger cities in Switzerland and enjoyed a certain renown because of the general scholarly achievements of its institutions. What is curious is the emblem that seems to have been accepted as the unofficial seal of the congress.¹ The seal itself is circular and central to it is a smiling sun symbol surrounded by some stylized rays. This radiant sun is further adorned by a background filled with rays symmetrically originating at the sun and diverging towards the periphery of the circle. Superimposed on this symbolic design is a ribbonlike banner on which is printed "The Sun of St. Moritz" in four languages -- French, German, Italian, and English.

The message which the designers of the seal intended it to carry

¹ A picture of the seal may be found in the introductory section of The Trail of the Invisible Light, a historical treatise of the development of radiology (220, p. xviii).

could have been an obviously straightforward one. Perhaps it was meant to call the attention of the congress representatives to the picturesque, recreational resort in the Swiss Alps, St. Moritz. However, there is much more of significance that can be read into the emblem design. Perhaps it was meant to honor the successful work in heliotherapy of Oscar Bernhard, a Swiss physician. While living at St. Moritz in 1902, Bernhard had first used exposure to sunlight as a treatment for a patient suffering from an infected abdominal wound (349, p. 7). The designers of the seal may have considered this application of radiant energy as meaningful to radiologists.

Radiant energy has always been in the service of man. Experienced by him most commonly as light and heat, radiant energy proved useful to man even when the natures of light and heat were not fully apparent to him. When electrical energy was identified through experience, again man found beneficial applications for electricity even at a time when he knew little about electromagnetic radiations. In fact, the actual usefulness of these forms of radiant energy contributed to the development of theoretical notions about them. When ionizing radiation was recognized as a form of radiant energy, it is noteworthy that useful applications were found for ionizing radiation even before much was known about its behavior. Since radiology represents an organized and continuously developing application of ionizing radiation, the emblem on the seal of the Fourth International Congress of

Radiology can be given a meaningful interpretation. The concept of radiant energy does have significance in radiology.

The radiation that was first classified as ionizing radiation was discovered in 1895 (410) and since then, ionizing radiation has taken many forms. This study aims to show the developments in the discovery of these various forms of ionizing radiation as well as the progress made in finding application for them, but only in so far as this development and progress are relevant to a historical treatise of chemical dosimetry.

X-radiation: Discovery and Application

On December 28, 1895, Wilhelm Conrad Röntgen (1845-1923) sent to the secretary of the Physical-Medical Society of the University of Würzburg for publication in the Sitzungsberichte of the society a copy of his work on a new kind of ray (206, p. 14). This announcement would very likely be included in almost any account of the discovery of X-rays since a discovery takes on new proportions when it is no longer confined to the secrecy of the discoverer's laboratory. However, there is one aspect of the statement that may be misleading. The fact that Röntgen chose to notify a medical society² of his

²The Physical-Medical Society of the University of Würzburg was a medical society according to the Eleventh Edition of the Encyclopedia Britannica (454).

discovery must have some significance. It certainly cannot be assumed that since Röntgen was a professor of physics at Würzburg, a university known for its medical school, his choice of the Physical-Medical Society was inevitable. Röntgen was offered his position at Würzburg in 1888. Between 1889 and his announcement of the discovery of X-rays he had published 15 papers, 13 of which he submitted to the Annalen der Physik und Chemie, a journal published with the cooperation of the famous physics society of Berlin, Der Physikalischen Gesellschaft. His choice of the Physical-Medical Society may be indicative, therefore, of his realization that X-rays would prove useful to medicine. In fact, when on the evening of January 23, 1896, Röntgen presented his paper before a session of the medical society, he expressed his willingness to give the benefit of his experiments to anyone in a medical institution interested in investigating the possibility of taking X-ray photographs of internal parts of the human body (204, p. 66).

It happened that as he was testing his conjecture about the possible penetrating power of his rays through a piece of lead, he noted a shadow picture of his thumb and finger on the fluorescent screen. He was then able to report in the communiqué of December 28th that he saw the darker shadows of the bones with the much fainter shadow picture of the hand itself (410). Furthermore he admitted in the lecture of January 23rd that he did not have time to continue experiments in

that direction. As if to provide evidence of this, in his communication dated March 9th he emphasized primarily his work on the property of the rays by which they discharge electrified bodies (411). It seems as if Röntgen were more interested in establishing facts about his rays rather than in finding an application for them. Neither was he particularly interested in theorizing about his rays as is evident in a letter to Ludwig Zehnder (1854-1949), his former student who became one of his best friends. To Zehnder he confided that whether or not X-rays were actually longitudinal light rays was of secondary importance to him; the facts were the important thing (Röntgen's letter to Zehnder is quoted in French translation in 368, p. 65-66).

During 1895 Röntgen had devoted himself exclusively to the study of cathode rays in the tradition of Heinrich Hertz (1857-1894) and Philipp Lenard (1862-1947). Though Hertz had found that metallic film was transparent to cathode rays and Lenard had found that photographic plates were darkened by cathode rays, Röntgen was able to conclude that the emanation from the Hittorf-Crookes tube³ which he was using at the time had to be something other than cathode rays. Since the emanations produced a fluorescent effect on a distant screen, there was evidence of an unusual penetrating power, not only through

³ Many studies of cathode rays were done with the Lenard tube, an ordinary glass discharge tube equipped with a thin aluminum window to allow the cathode rays to penetrate out of the tube. The Hittorf-Crookes tube was an all-glass discharge tube without a thin window.

glass but through more than a meter of free air. It was generally known that only a few centimeters of free air were needed to absorb cathode rays. The emanation from the Hittorf-Crookes tube also affected a photographic plate even if a more or less impermeable substance was interposed between the tube and the plate. Furthermore, no studies of cathode rays produced results as sensational as Röntgen's shadow pictures.

The attention given to this latter aspect of Röntgen's discovery overshadowed perhaps but did not adversely affect the research that was being conducted in almost every physical laboratory where discharge tubes were available. The experiments that Röntgen performed were repeated and modified in an effort to learn more about the nature of X-radiation. Scientific journals like the Philosophical Magazine, the Revue générale des sciences, and the Comptes rendus of the French Academy of Sciences attest to the volume of work done on the properties of X-rays by a great number of scientists in that year following the discovery.

One of the most significant properties was first reported by Louis Benoist (b. 1856), a professor of physics at the Lyceum of Henry IV at Paris, and his Rumanian associate Dragomir Hurmuzescu (1865-1954). On February 3, 1896, they described their observation that the new radiation was able to discharge a gold-leaf electroscope (46). At the Cavendish Laboratory in Cambridge, J. J. Thomson and

Ernest Rutherford in response to this announcement from Paris described their own experiments in which they verified this discharging capability of X-rays. They also proposed an explanation for this discharging power by the notable theory that gases are ionized by X-radiation (495). This explanation was based on an analogy between a dilute solution of an electrolyte and a gas exposed to Röntgen rays. Röntgen rays made a gas conductive; Thomson and Rutherford found that this conductive state could be destroyed if a current of electricity were passed through the gas. The conductive power of an electrolyte solution could also be destroyed if the current that was passed through it was large enough to decompose all of the solution. Therefore, if it were assumed that X-radiation produced negatively and positively charged particles throughout the volume of a gas, then the gas could be regarded as an electrolyte solution. These charged particles would make the gas conductive and thus capable of discharging an electrified body. These charged particles came to be called ions⁴ and thus X-radiation was identified as ionizing radiation within a year of Röntgen's discovery.

Although Röntgen himself was not primarily interested in the usefulness of his new rays, applications with apparent benefit to man were envisioned and attempted within a few months of his discovery.

⁴It was not assumed that the ions in gases were the same as the corresponding ions in electrolyte solutions.

By building up the discovery of shadow pictures, particularly of the human hand, journalists in January of 1896 undoubtedly have had some influence in suggesting applications. The power of this new radiation not only to differentiate between bone and muscle but also to leave a permanent record of that differentiability on a photographic film was more than sufficient to excite great interest. The daily press capitalized on this aspect of Röntgen's discovery

The article that appeared in the January 16, 1896, issue of The New York Times reflected the thoughts that had been appearing in European newspapers from January 5th when the Vienna Sunday Die Presse called the attention of the public to Röntgen's work in an article entitled, "Eine Sensationelle Entdeckung" (photocopy in 162, p. 147). According to The Times, the men of science in New York were awaiting impatiently the arrival of the full particulars about Röntgen's discovery of a method of photographing opaque bodies. What is noteworthy about the article is the fact that The Times gave the impressions of both a physicist and a physician regarding the discovery. The physicist gave his ideas about the nature of the radiation; the physician expressed the opinion that the discovery would lead to a revolution for good in modern surgery (266). In general, the press emphasized the photographic possibilities of X-rays to such a degree that it presented a view of X-ray photography that was entirely out of proportion in relation to what had really taken place at the Physical

Institute at Würzburg. It caused Röntgen to write to his friend Zehnder: "Mir war nach einigen Tagen die Sache veregelt; ich kannte aus den Berichte meine eigene Arbeit nicht wieder. Das Photographieren war mir Mittel zum Zweck und nun wurde daraus die Hauptsache gemacht"⁵ (quoted in 206, p. 87).

That applications of X-ray photography were attempted early in 1896 is evident from the reports of interesting cases of inquiry into this area found in almost every weekly issue of the scientific periodical Nature. For example, in February of 1896 there was the report that the Prussian Minister of War had ordered investigation into the possible application of Röntgen's discovery to army surgery (352). Two weeks later Nature announced that the Paris Academy of Sciences was studying both the chemical and surgical aspects of the discovery (491). Before the month was over, it carried the notice that at McGill University in Montreal the position of a bullet in a leg was photographed with an X-ray exposure of 40 minutes (370).

The penetrating action of X-rays and their photographic effect found almost immediate application even when very little was known about either property. The extended time exposure mentioned above was but one of many instances where lengthy exposures were used just

⁵ After a few days the affair disgusted me; from the reports I did not recognize my own work. For me photography was a means to an end but now it was made the main thing.

to obtain good shadow pictures or radiographs as they came to be called. The problem, commonly admitted, lay in the fact that with the existing types of X-ray tubes procedures could not be standardized. This prompted the American Thomas A. Edison to work with his staff in trying to find the most favorable conditions for taking X-ray photographs (493). From this research came the fluorescent screening device called the fluoroscope (361) which was intended specifically for Röntgen rays (fluorescent screens were familiar to cathode ray researchers). The fluoroscope was a means by which subjects revealed in radiography could be conveyed to the naked eye by the X-rays. Since it made possible the direct observations of skeletal objects, the fluoroscope was more than welcomed by the public and historical accounts of radiology often include classic poses of fluoroscopic viewers. What is significant about these fluoroscopic fans is the fact that they were most intent on viewing the skeletal structure of their own hands (206, p. 201, 204; 220, p. 15-17). This latter possibility became a convenient way of improving radiographic technique. It had become common practice in those days for the X-ray tube operator to place his own hand in front of the tube. When he had a satisfactory fluoroscopic view of his own hand, then he exposed a patient to the X-rays (55, p. 29). This was done for the purpose of obtaining a good radiograph. Such practices hastened the appearance of the deleterious effects of X-radiation and cost many people the skin off

their hands.

During that first year of experimentation and medical applications there were reports of a peculiar dermatitis where hands appeared sun-burned, red, and swollen, which conditions were often followed by a loss of hair and the shedding of the epidermis. One of the first to experience such an "X-ray burn" was Emile H. Grubbé (1875-1960), a Chicago chemist who had been experimenting with and manufacturing vacuum tubes early in January of 1896. Before the month was over he had to seek medical treatment for the ensuing dermatitis that afflicted his left hand (8, p. 212). Elihu Thomson (1853-1937), a Boston physicist, had exposed his left little finger to X-radiation for half-an-hour. This was followed by severe erythema and a blistering condition limited to the finger (206, p. 244). Similar symptoms and effects were described by Dr. S. Fuchs of Charlottenburg, Dr. D. E. Sehrwald from Freiburg, and by Dr. H. D. Hawks at Columbia University in New York (206, p. 242-243).

John Macintyre (1857-1928), a Scottish X-ray pioneer (he seems to have been a fluoroscopist [220, p. 40]), reported a dermatitis of his hands where the severe effects remained for over a fortnight (343). André Broca (1863-1925), a French surgeon, reported a case where exposure to Röntgen rays had produced baldness (372). T. C. Gilchrist of Johns Hopkins Hospital in Baltimore also gave notice of serious deleterious effects of X-rays (143).

Because of such numerous reports of the injurious effects of X-radiation, Alan A. C. Swinton (1863-1930), a Scottish electrical engineer, advised that for living physiological subjects as short an exposure as possible should be used. According to Swinton, a minimum exposure could be attained if a very high vacuum were maintained in the X-ray tube and if it were operated at a considerable voltage (469). By the end of March of 1896 it was reported that the time of the exposure could also be reduced by placing a card covered with barium platinocyanide immediately in front of and in contact with the photographic plate (371).

Although experimental activity was directed at reducing exposure, the possible beneficial use of the serious, harmful effects of X-radiation was also recognized. X-ray therapy was not unheard of in 1896 though it was cautiously and sometimes secretly applied. It seems that the first therapeutic application of X-rays was made by Grubbé on January 29, 1896. Under the direction of the physician who treated his X-ray dermatitis, Grubbé gave an X-ray treatment to a woman suffering from an ulcerous recurring cancer (8, p. 212). There were also cases prior to 1900 where the depilatory action of X-rays prompted the prescribed treatment. The first to recognize the possible beneficial aspects of this action of X-rays was Leopold Freund (1868-1943), the Austrian radio-therapist (162, p. 151-152; 179, p. 13). His experimental patient in November of 1896 was a

little girl who had a huge, hairy, animal-like birth-mark on her neck and back. After Freund subjected the area to X-ray exposure two hours in length for ten consecutive days, he reported that only a circular denuded spot remained of the former disfigurement.

The standardization of diagnostic and therapeutic exposures was greatly advanced by the development of the hot-filament cathode tube at the Research Laboratory of the General Electric Company at Schenectady, New York in 1913. The new tube differed from the type in general use in that the discharge current was purely thermionic in character. This in itself represented a successful culmination of the experimental activity that had been associated with the establishment of a thermionic current in a vacuum tube since at least 1903. At that time the British physicist Owen Williams Richardson (1879-1959) elucidated the relationship between the temperature of a hot body and the emission of electrons (404). The final essential contribution in this research was made in 1913 by the American chemist Irving D. Langmuir (1881-1957). Langmuir demonstrated that electron emission from tungsten filament continued in a vacuum and could be controlled by varying the current which heated the filament (319). William D. Coolidge (b. 1873) succeeded in 1912 in making ductile tungsten from what was regarded as a brittle, non-workable metal (105) and, as director of General Electric's Research Department in Schenectady, he filed for a patent on the hot-cathode, high-vacuum

tube. In providing the applied science of radiation with a tube characterized by a stable performance, applied research, in the words of W. D. Coolidge, had brought "all of the peculiarities of the Röntgen tube into accord with the modern conceptions of electronic conduction and gas molecule decomposition" (105, p. 413).

Use of the Coolidge tube in generating X-rays had certain advantages which provided for a more reliable and a broader applied science of radiation. The hot-filament cathode tube in which a high vacuum was maintained was remarkably stable and permitted regulation of the voltage and the current to the tube. Therefore, the intensity and the penetrating power of the X-rays produced were under the control of the operator. This meant that intense homogeneous primary X-rays of any desired penetrating power could be realized (105). From the point of view of applying the new tube to diagnostic and therapeutic purposes, the X-ray unit could now become an instrument of precision and exposures could be determined prior to treatment.

The introduction of the Coolidge tube was followed by the development of the so-called high-voltage units. Those operating at or near 200 kilovolts due to heavier transformers and added filtrations were few and generally not available early in 1920 (220, p. 104, 108-109). Still the high-voltage units made possible the generation of more penetrating X-rays, and there was a growing demand for high-voltage units for use in deep X-ray therapy.

The application of the hot-filament cathode tube was not limited to medicine. A commercial use of X-radiation was found and reported in January of 1915. Due to the extraordinary ability of the Coolidge X-ray tube to produce highly penetrating radiation, it could be used to detect flaws radiographically in steel castings nine-sixteenths of an inch thick (131). In fact, in six months a reliable technique of radiography was developed for steel thickness up to one-half inch; beyond that thickness, to obtain good radiographs it was necessary to increase considerably either the time exposure or the voltage across the tube. When the porous state of copper interfered with its property of conductivity, copper castings were also studied radiographically to determine the degree of porosity (132).

Radioactivity: Discovery and Application

Among the physicists to whom Röntgen had addressed copies of the reprint of his December 28th paper was Henri Poincaré, professor of mathematical physics at the Sorbonne (204, p. 54).⁶ Poincaré proposed that since the production of X-rays was associated with a strong phosphorescence in the glass vacuum tube, perhaps substances made phosphorescent by sunlight might also emit an invisible radiation

⁶ Röntgen acknowledged to Zehnder how he valued the responses of Poincaré and other physicists to his paper; their expressions of appreciation for his discovery meant much to him (Röntgen's letter to Zehnder is quoted in 206, p. 87).

similar to X-rays (387).

A researcher at the Paris Academy of Sciences was attracted to the very problem proposed by Poincaré. Henri Becquerel, who had previously investigated the phosphorescence of potassium uranium sulfate, now renewed his study in the direction of the new problem. After exposing the fine crystals of the uranium salt to sunlight, he wrapped them in black paper and placed a small silver plate between the crystals and a photographic plate. His first observations were reported to the Academy of Sciences on February 24, 1896, at which time he indicated that the phosphorescent crystals of potassium uranium sulfate emitted a type of very penetrating radiation capable of producing a distinct photographic effect (38). Two weeks later after further experimentation Becquerel reported that though the radiation from the uranium salt had great penetrating power and could discharge an electrified body, it differed from X-radiation in that it was reflected and refracted (42).⁷ However, it was not until March 23, 1896, that Becquerel was convinced that the uranium-rays were not to be associated with visible phosphorescence since the uranium salts kept in the dark emitted the same radiation as the phosphorescent uranium salts (40). From observations he concluded that the uranium salts emitted a form of ionizing radiation different from

⁷ According to Röntgen's original communiqué, X-rays could neither be reflected nor refracted (410, p. 136).

X-radiation and not due to phosphorescence.

Within a very short time experimental physicists acquired a field of interest in addition to X-rays, that of uranium-rays or Becquerel rays as they came to be called. The events that seem to follow each other so rapidly at this time show how experimental activity acquires a direction from a tradition of pursuits, that is, a particular observation may suggest a hypothesis which is further tested by experiments. After the identification of uranium-rays as different from X-rays, the possibility that substances other than uranium and uranium compounds also emitted these new rays was next investigated. Such investigations led to the discovery and isolation of new elements.

Marie Curie, working at the School of Physics in Paris at the time of Becquerel's discovery, undertook a comparative study of a number of minerals containing uranium. Of most importance in the results of her investigations was the fact that pitchblende, one of the uranium minerals, was found to be about four times as active as the metal uranium. Since Mme. Curie considered the radioactivity of uranium as an atomic property, she concluded that the high activity of pitchblende was due to the presence of an unknown element whose activity was greater than that of the then known radioactive elements, uranium and thorium. Working on this assumption, Mme. Curie and her husband Pierre Curie, who was on the Faculty of Science at the

School of Physics, made a systematic chemical examination of the constituents of pitchblende and were able to isolate an active form of bismuth. They recognized that the activity was really due not to bismuth but to the presence of another substance which they named polonium in honor of Mme. Curie's native country (122).

Subsequently they co-precipitated another very active substance with barium. This substance was given the name radium by the discoverers--Marie and Pierre Curie and a collaborator G. Bémont. It was later isolated in pure form as a thesis project by Marie Curie herself and was found to possess the radioactive property to a very high degree. Compared to X-rays and their photographic and electrical effects, the radiation from uranium was extremely weak while that from radium was extremely intense (123). This difference in activity became more impressive when in 1905 it was determined that in minerals the presence of radium is about 3.8 parts in 10^7 parts of uranium (426, 427).

After Becquerel's paper of March 23, 1896, fundamental research was directed not only at studying the activity of uranium and its compounds but also at determining the nature of Becquerel rays and their relationship to X-rays. The subsequent differentiation of Becquerel rays into what were called alpha-, beta-, and gamma-rays⁸ was possible only after a certain amount of evidence had been

⁸Ernest Rutherford was first to note the non-homogeneity of

collected. Deflection of these Becquerel-ray components in a magnetic and in an electric field had to be observed; their relative penetrating power had to be compared; and their ionizing effect on gases had to be noted. When Mme. Curie in 1900 first categorized the easily absorbed alpha-rays as consisting of particles which lost their energy on passing through matter, the alpha-rays were considered non-deflectable by a magnetic field (125). Still R. J. Strutt, the 4th Baron Rayleigh, in 1901 noted similarities between the ionizing effect of alpha-rays and that of canal rays⁹ (466), and although canal rays had been known to be deflected by a magnetic field since 1898, the deflection of alpha-rays was not detected until 1903 by Rutherford, then the MacDonald Professor of Physics at McGill University in Montreal (425). The reason for the delay was the very large radius of curvature of the deviated alpha-ray which was very difficult to observe.

Becquerel rays by observing their absorption in layers of aluminum foil. In 1899 he distinguished two distinct types of rays which he termed for convenience alpha-radiation (that component readily absorbed) and beta-radiation (the more-penetrating component) (426). When in 1900 Paul Villard (1860-1934) distinguished a third component (521), it was naturally termed gamma-radiation.

⁹ Canal rays were so named by E. Goldstein (1850-1930) when in 1886 he observed a luminous stream which seemed to have its source at the anode in a discharge tube. In 1898, Wilhelm Wien (1864-1928) determined the canal rays to be a stream of positively charged particles (536).

The radius of curvature of the deviated beta-ray was not as large. Therefore, the deviation of beta-rays in a magnetic field was recognized as early as 1899 by the German scientist Friedrich Giesel (1852-1927) (202). This observed deflection was confirmed that same year at two different laboratories: by Stefan Meyer (1872-1949) and his co-worker Egon R. Schweidler at the Physics Institute of the University of Vienna (355) and by Becquerel in Paris (34). Such data indicated that beta-rays behave in all respects as cathode rays which were known to be negatively charged particles moving with a high velocity.¹⁰

Before gamma-rays could be identified, a very active source like radium was needed. Initially, from a study of uranium it was shown that the radiation had only two components, the alpha- and the beta-rays (426). In 1900 Paul Villard used a photographic method and showed that radium emitted very penetrating rays that were unaffected by a magnetic field (521, 522). Again this observation was confirmed by Becquerel (36).

When radioactivity was first discovered, it was the photographic and ionizing actions of the uranium-rays which made Becquerel

¹⁰In 1897, J. J. Thomson studied the deflection of cathode rays in an electric and in a magnetic field and concluded that cathode rays were composed of negatively charged particles. From the strengths of the fields and the observed deflections he was able to calculate not only the velocity of the particles but also their charge-to-mass ratio (493).

consider them as similar to X-rays. The discovery of radium and its more intense emissions and the differentiation of uranium-rays into alpha-, beta-, and gamma-rays made further studies of the photographic and ionizing effects possible. Within ten years of Becquerel's discovery, Rutherford wrote that the photographic action of alpha-rays from radium steadily decreased with increasing thickness of absorbing layer. Furthermore, his measurements suggested that there was a critical velocity below which the alpha particles were unable to appreciably affect a photographic plate (423, p. 225).

William H. Bragg (1862-1942) and his collaborator R. Kleeman at the University of Adelaide in Australia found that the ionizing action of the alpha-rays, though very intense in the vicinity of the source of their emission, also fell off rapidly with distance. In fact, the ionizing action ceased abruptly after the alpha particles had traversed 7.06 cm of air (67).

Observations of this kind served to give a structure to the accumulating knowledge about ionizing radiation. It was determined that of the three types of radioactive emissions the alpha-rays had the greatest ionizing effect on a gas, which meant that the ionizing effect varied inversely with penetrating power. Given an unshielded source, the photographic effect was largely due to the beta-rays, again because of their particular penetrating power. The penetration of the alpha-, beta-, and gamma-rays respectively could be

approximated as 1, 100, and 10,000. It was also recognized that the penetrating power of the rays was determined by their energy.

Therefore, ordinary X-rays having less energy and less penetrating power than gamma-rays had a greater ionizing effect on air and other gases. Still if very penetrating X-rays were used, the ionizing effect was proportionally decreased as was evident in the greatly reduced conductivities of some gases.

After careful observations, then, the properties of uranium-rays were identified. Many of these properties were common to X-rays but to a different degree. Although uranium-rays affected a photographic plate, the photographic effect was very feeble compared with the action of X-rays. Therefore, an immediate application of uranium-rays to diagnostic medicine, for example, was not made. With the discovery of radium and its more intense activity, however, the painful physiological effects of radioactivity were readily noted. According to Giesel, the German scientist Walkhoff first observed that radium rays like Röntgen rays caused the shedding of skin. Giesel then demonstrated the physical effects of radium on himself. After he kept a celluloid capsule of radioactive barium bromide on his hand for two hours, it caused an inflammation which was following by the sloughing off of the skin (203). On hearing about these effects of radium Pierre Curie also deliberately exposed his arm to the action of radioactive material and reported to the French Academy that 52

days after the exposure the wound still had not healed completely (43). Marie Curie suffered analogous burns even though the few centigrams of very active material which she carried had been in a thin metallic box. Henri Becquerel was also accidentally burned by some radium-contaminated barium chloride which he carried in a glass tube in his pocket (43). This awareness of the power of radium rays led to a study of the action of radium on animals. In this research Pierre Curie collaborated with two professors of medicine in Paris--Charles Bouchard (1837-1915) and Victor Balthazard (b. 1872) (64). Together they reached the conclusion that radium cured growths, tumors, and certain forms of cancer by destroying diseased cells.

Though extensive use of radium therapy had to await the isolation of radium by an industry just being born and a technique being developed by Marie Curie herself, the first treatments of diseased persons were made with tubes containing a radioactive emanation from radium. This radium emanation was obtained from the laboratory of Marie and Pierre Curie. Although Marie Curie had chosen in 1897 to study Becquerel's rays as the subject of her thesis, she had succeeded in isolating radium by the time she had completed her doctoral studies on "Researches on Radioactive Substances" in 1903 (117, p. 194). The technical process of isolating radium was made available by the Curies to those interested in establishing extraction industries both in France and in America even by the end of 1902 (220,

p. 219).

Within eight years then, ionizing radiation included X-rays and radioactive emission--alpha-, beta-, and gamma-radiation. The relative penetrating power and ionizing effect of these forms of radiation were observed; their physiological effects were noted. Although an understanding of the nature of these rays was still prompting much laboratory investigation, the properties that were recognized found almost immediate application. Diagnostic medicine utilized the penetrability, particularly of X-rays, as well as their ability to affect a photographic plate; therapeutic medicine availed itself of the physiological effects of both X-rays and radioactive emission.

CHAPTER II

CHEMICAL DOSIMETRY (1902-1925)

The deleterious effects of X-rays in diagnostic and therapeutic applications caused radiologists and particularly physicians who prescribed the treatment to be concerned. To make the use of X-rays beneficial and practical, some method of estimating dosage in the administration of X-rays had to be adopted. Since the inflammation of the skin was the first sign of serious physiological effects of absorbed dose, this inflammation naturally became a guide for estimating dosage.

The idea of estimating dosage in terms of the exposure needed to produce inflammation after a latent period¹¹ was not really new or specific to X-ray applications. Termed an "erythema of the skin," such an inflammation was associated with the action of the sun. In 1858, the French neurologist Jean M. Charcot (1825-1893) suggested that this inflammation was due to the active part of the sun's spectrum (348, p. 5-6). He showed that an erythema produced by an arc-light was similar to that caused by the sun, but if the arc-light were passed through a filter which removed the ultra-violet

¹¹ A distinction was made between the redness produced immediately by the thermal action of radiation and an inflammation which usually appeared after a latent period and which was believed due to radiation at the opposite position in the spectrum from heat rays (348, p. 6).

radiation, the filtered arc-light produced no erythema. This identification of the inflammation with the action of the ultra-violet component of the sun's spectrum (called the actinic action) was corroborated perhaps most conclusively by the extensive experiments of the Danish phototherapist Niels R. Finsen (1860-1904) (348, p. 6).

The association by radiotherapists, then, of an inflammation of the skin due to X-rays with the "erythema of the skin" due to ultra-violet rays and the subsequent estimation of dose in terms of the exposure that would bring on the erythema condition seem to be natural outcomes of the similarities between radiotherapy and phototherapy. However, a new problem presented itself as a result of this association. The hazards of overdosage in phototherapy were not as great as were those in radiotherapy. In the latter case, the lack of precise definitions for erythema and erythema dose was soon recognized.

In 1906, Mihran Krikor Kassabian (1870-1910), a Philadelphia medical roentgenologist, made a survey of the practices of some leading X-ray therapists (300, p. 522-526) and showed that there was no uniformity as regards dosage or philosophy of treatment. Some therapists felt that an erythema should be produced, others that it should be avoided. Still others, like John Hall-Edwards (1858-1926) of the British Electrotherapeutic Society, felt that it was impossible to lay down rules which would apply to every individual alike since in dealing with human beings radiotherapists would have to keep in mind

that they were dealing with material that had no mathematical increment (232).

As regards the definition of terms, an example is found in a book on radiotherapeutics by Robert Knox (1867-1928), a British radiation protection pioneer, who stated that "An erythema dose is one which causes slight erythema to appear within fifteen to twenty-one days" (309, p. 424). It certainly does seem that it would be difficult to apply such a definition because of the subjective variability in patients. Knox appears to have been aware of the uncertainty of the end-point in his definition since he qualified it by saying that four-fifths of an erythema dose will, in the majority of cases, cause the hair to fall out. No doubt, definitions like this Knox's were the cause of much confusion. Hall-Edwards made a valid assessment of the situation when he said, "That there is an ever-increasing necessity for a scientific method of measuring dosage in the administration of X-rays for therapeutic purposes is universally agreed" (232, p. 20). Efforts were made to introduce more precision and objectivity into dose measurements, yet it seems as if there were a reluctance among radiotherapists to abandon the erythema concept, possibly because it had, in a sense, a biological basis. Comparative studies as late as 1924 indicate that an erythema dose was used even though, for example, it was known that the French erythema dose was approximately equal to three times the German dose (298).

Most of the early attempts at solving the dosage problem came from the laboratories and medical schools of Vienna. One of the reasons for this response may have been the fact that Vienna was the European center for medical teaching during the second half of the nineteenth century and until the outbreak of the First World War (374, p. 1525; 413, p. 295; 450, p. 285). However, there is another fact which perhaps had significance if considered in conjunction with Vienna's leading role in medicine. At the time of the discovery of X-rays, Franz Exner (1849-1926) was the Director of the Physical Chemical Institute at the University of Vienna (162). Because of the friendship that had developed between Exner and Röntgen during their student days in Switzerland,¹² Exner was among that small circle of friends to whom on January 1, 1896, Röntgen had addressed copies of his paper as well as sample shadow pictures he had taken. This opportunity to become acquainted with the properties of X-rays in advance was especially significant since Franz Exner's brother was the noted physiologist Sigmund Exner. Sigmund was immediately impressed with the importance of the discovery for medicine and on January 10th he presented pertinent information before a meeting of the Society of Physicians in Vienna. A week later on January 17th,

¹²When in 1868 Röntgen worked as an assistant to August Kundt (1838-1894), a professor of physics at the University of Zürich, Exner was one of the advanced students who helped Röntgen with experiments (206, p. 56).

Sigmund Exner exhibited radiographs he himself had taken to show deliberately their specific medical significance. For example, he had prepared a radiograph of a hand to show the distortion of the middle phalanx of the fifth finger (copy of this radiograph in 162, p. 149). Such a prompt demonstration of specific diagnostic possibilities of X-ray photographs by a respected colleague must have had some influence on men interested primarily in medicine and medical research. Any early adoption of X-rays for medical purposes by these men would have made them more aware of the need for methods of dosage measurements.

Most of the dosimetric methods that were proposed and that found any degree of acceptance during this initial development of radiology depended on what was then recognized as the chemical action of ionizing radiation. The chemical effects in substances subjected to irradiation were usually observable because of a change in color, the formation of a precipitate, or the darkening of a photographic emulsion. That any of these effects could be of use in dosimetry would depend on several factors: (1) whether there was a direct relationship between the dose and the observable effect, (2) whether there was a degree of stability in the effect which would make measurement possible, and (3) whether it was an effect that could be related to a calibrated scale. The majority of early dosimeters were based on the change in color of chemical substances.

Developments in dosimetric methods were mainly centered around the third factor listed above, that is, there were attempts at relating the effect to differently calibrated scales for the purpose of improving either the sensitivity or the reliability of the dosimetric method.

Dosimetry Based on Colorimetry

The first to suggest a chemical method of measuring the exact dosage of Röntgen rays was Guido Holzkecht (1872-1931), the Physician-Director of the Röntgen Institute in Vienna.¹³ In 1902, Holzkecht proposed the use of a chemically prepared pastille, a fused mixture of potassium chloride and sodium carbonate, as a chromoradiometer (279). He decided on the solid solution of salts because his research convinced him that the coloration of a mixture of alkaline metal salts due to X-radiation was more pronounced than that of pure salts (280). In addition to the solid reagent, the complete dosimeter included a standard scale which consisted of 12 degrees of graduated tints from colorless to green. The color change was calibrated in an arbitrary Holzkecht unit (H unit) of absorbed dose.

¹³The Medical School of the University of Vienna had associated with it the Allgemeinen Krankenhaus, which could be called the University Hospital in which its interns were trained. The Faculty of Medicine was departmentalized according to personnel specializations; these departments, often called institutes, had their offices and clinics at the General Hospital. Among these was the Röntgen Institute which began as a Röntgen Center in 1898 (162).

Placed at the same distance from the X-ray tube as the part of the body undergoing treatment, the reagent was subjected to irradiation until its color matched the desired tint on the standard scale.

Although Holzkecht did not define an H unit precisely, he did specify that with less than 5 H units of dose the patient would experience excoriation without ulceration (279). Therefore the shade corresponding to 5 H units was to indicate a maximum dose for most applications. Apparently the last tint on the scale was calibrated to represent 20 H units of dose, the recommended dose for the purpose of destroying bacteria. It seems that, in practice, one H unit was considered as equivalent to about one-third the amount of radiation needed to produce an erythema (303). An absorbed dose of 3 or 4 H units had a latent period of about two weeks and produced an erythema of the skin which took a week or two to heal. Such a dose, which was considered a full dose, could not be repeated for several weeks, whereas a dose of 1 or 2 H units could be repeated after about two weeks even if a moderate inflammation were maintained.

The introduction of Holzkecht's chromoradiometer in 1902 meant a new epoch for radiotherapy. Man was then able to assign definite X-ray quantities for different purposes and this helped to do away with many trial exposures. However, although initially the Holzkecht pastilles were serviceable, defects in the dosimetric system soon became apparent (304).

One of the first to propose a remedy for one of the defects in Holz-knecht's chromoradiometer was Leopold Freund, the first Viennese radiation therapist (see p. 12, above). On April 8th, 1904, Dr. Freund, then associated with the Clinic for Venereal and Skin Diseases at the General Hospital in Vienna, addressed a session of the Society of Physicians and proposed a new reagent for dosimetry (178). By his dosimeter which was also based on the colorimetric principle, Freund intended to compensate for the alleged fact that the Holz-knecht radiometer allowed only large doses of radiation to be measured colorimetrically. The Freund dosimeter consisted of a viscous solution of iodoform in chloroform which, initially a yellowish-white solution, becomes a red-violet one under the influence of X-rays, due to the liberation of iodine.

Before proposing the iodoform in chloroform system for dosimetry, Freund determined the condition under which small doses of X-radiation would show any chemical activity. To his satisfaction the variations in color due to irradiation with X-rays of varying intensity and duration were best distinguishable when he worked with a 2% solution of chemically pure crystalline iodoform in chemically pure chloroform. Furthermore, when compared with the Holz-knecht reagent, such a 2% solution showed a distinct color change under a given irradiation after six minutes, though the Holz-knecht reagent showed no color change even after a ten-minute exposure to the same

irradiation (178).

Although the Freund dosimeter was more sensitive than was the Holzkecht chromoradiometer, it did not come into general use both because of the difficulty in maintaining a daylight-excluded environment for its preparation and use, and also because of the great effect of small temperature variations on the reaction (306). Furthermore, the Freund dosimeter had no scale of reference units associated with it. He simply offered some standard liquids where a particular color indicated a certain physiological effect under particular irradiation. In spite of the fact that he did not give his system a degree of mathematical precision, Freund still felt that his dosimeter would be useful in practical roentgenotherapy (178). However, that his dosimeter furnished only a qualitative estimate of dosage may have contributed to its general disuse.

Other problems attendant upon the use of the Holzkecht chromoradiometer proved serious enough to cause the noted French dermatologist Raimond Sabouraud (1864-1938) and his collaborator Henri Noiré (1878-1937) to search for a new reagent for dosimetry. Sabouraud and Noiré had themselves experienced the disadvantages of the Holzkecht reagent since they considered it a necessary instrument in radiotherapy and included the pastilles in X-ray treatments of cryptogamic ringworm¹⁴ (430). The disadvantages which made the

¹⁴In their use of the pastilles, however, it seems that Sabouraud

use of the Holz knecht pastilles inconvenient were: first, the preparation of the pastilles required a special process which had some secrecy connected with it (in France, therefore, and anywhere outside of Vienna the pastilles were very expensive); second, although the pastilles could be reused, they lost some of their precision with each use; and finally, most serious of all, the pastilles continued to change color even after the end of the exposure (431).

In December of 1904, Sabouraud, with the technical collaboration of Noiré at the St. Louis Hospital in Paris, proposed a dosimeter based on the colorimetric principle but one which used barium platino-cyanide as the reagent (431). On being irradiated, the reagent changed from fluorescent light-green to non-fluorescent brown. A fixed geometry of the treatment apparatus involving the dosimeter was required. The pastilles were placed at a distance of 8 cm from the anti-cathode of the X-ray tube, while the exposed tissue was at 15 cm from the anti-cathode. To measure the radiation Sabouraud and Noiré established a brown tint, labeled Tint B, which was reproduced by water-color painting and which represented the shade of brown of one of their pastilles when exposed to a certain quantity of X-rays.

and Noiré were interested in measuring the quantity of X-rays generated in a given time. This shift in emphasis from the quantity of X-rays received by the irradiated tissue to that generated by the X-ray machine is interesting because this represents the beginning of a problem which radiology would eventually have to solve, that is, how to make a distinction between exposure and absorbed dose.

The radiometer consisted of a folio on one leaf of which were two squares designated Tint A (a fresh sample of barium platinocyanide) and Tint B (artificially produced); on the other leaf were the circular pastilles destined to measure the radiation. The skin received a maximum dose which would not produce a dermatitis but only a temporary depilation¹⁵ when the circular pastilles took on a shade corresponding to Tint B. This maximum dose was equivalent to 5 Holzknacht units (431).

There were sources of error in the use of the pastilles which critics soon exposed. First, it was shown that the heat of the X-ray tube had an influence on the color change of the pastilles when it was at the 8 cm distance from the anti-cathode; furthermore, the diameter of some types of X-ray tubes prevented a pastille distance of 8 cm (62). The second source of error concerned the color of the pastilles themselves. Physicians were known who reused pastilles which had already been exposed. It was an accepted fact that light had a restoring effect on the color of the pastilles. It was for that very reason that Sabouraud and Noiré recommended that treatment be carried out in semi-darkness. Still, it was demonstrated that in reality there never was a complete restoration. Investigations indicated that the change

¹⁵It seems that Sabouraud and Noiré standardized their radiometer especially for therapeutic applications on the hair roots of the skin.

of color of the platinocyanides by X-rays was a process of dehydration and that the rehydration with the help of light was never complete (60, 313). Third, it was contested that the reference Tint B, produced by water color, tended to fade with light (59).

Nevertheless the disadvantages of the radiometer were minimal when considered against its relative simplicity, economy, and effectiveness; and it became widely distributed. A contemporary study of the Sabouraud-Noiré radiometer compared to others indicated it was the simplest and best means available at the time of eliminating overdosage as well as underdosage (434). It seems that the Sabouraud-Noiré pastilles remained in general use until at least the 1920's when filtered radiation became available with the construction of higher-energy X-ray units (205, 292). It was then discovered that the proportionality between the color change and the absorbed dose ceased to hold in the case of filtered radiation. Still, years later when chemical dosimetry had taken on a much more quantitative aspect, the Sabouraud-Noiré dosimeter was often the only early dosimeter included in discussions of dosage measurements based on color changes due to X-radiation (458).

After 1904 all dosimeters based on colorimetry were basically modifications of the Sabourand-Noiré technique. The reagent used was still barium platinocyanide, but the calibrated scale which was used to interpret the chemical effect was re-examined and the

technique of making color comparisons was re-evaluated.

Henri Bordier (1863-1943), a Fellow Professor on the Faculty of Medicine at Lyons, was one of those most concerned with improving the accuracy and reliability of the Sabouraud-Noiré radiometer. He began his efforts at standardization by defining a new unit symbolized by I. His definition was in terms of the iodoform in chloroform system in Freund's radiometer (see p. 32, above). Freund's method had no scale associated with it, so Bordier defined the unit I as equal to that amount of X-radiation which acting upon a 2% solution of iodoform in chloroform would liberate 0.1 mg of iodine (502). For this measurement the rays were normal to the surface having a one square centimeter area, and the depth of the solution was but one centimeter. According to this definition, $3\frac{1}{2}$ I were approximately equal to 5 H units. This definition could have been used as the basis of a scale for the Freund radiometer (see p. 33, above), but it seems as if it were intended for an improved Sabouraud-Noiré radiometer.

In 1906, Bordier collaborated with Jean Galimard (b. 1879), also on the Faculty of Medicine at Lyons, and proposed a variation of the Sabouraud-Noiré radiometer (59). In contrast to the Sabouraud-Noiré technique, the pastilles were placed directly on the tissue that was being irradiated or in the same plane with it. Likewise, in place of one tint, Bordier and Galimard constructed a scale with four tints and calibrated it in terms of I units. Tint 1 corresponded to 2 I units

of radiation and was the shade of a clear yellow pastille. The tissue responded to such irradiation by a loss of hair after about 20 days; this was considered a reaction of the first degree. Tint 2 corresponded to $3-1/2$ I units and was the shade of a sulfur yellow pastille. The tissue responded in this case by a strong erythema, a tumefaction, and a final peeling of the skin all after a latent period of from 12 to 15 days; this was considered a light second-degree reaction. Tint 3 corresponded to $5-1/2$ I units and was the shade of a red-yellow pastille. The tissue responded by redness, blistering, and exudation; this was considered a second-degree reaction. Tint 4 corresponded to 10 I units and was the shade of a chestnut-colored pastille. The tissue responded with ulceration which was considered a third-degree reaction.

Besides providing for a fractionated dose by the breakdown of the color change into four tints, Bordier and Galimard provided for reference tints that were obtained by a method which made them lasting and resistant to prolonged exposure to sunlight (59). What the method of preparation was, however, the authors did not indicate in their report. Another advantage over earlier proposed dosimetric techniques came from the fact that Bordier and Galimard included radium in their studies of the pastille responses to irradiation. Therefore, they could claim that their chromoradiometer measured the activity of any radiative source. They also measured the pastille

responses to X-rays of different energies. Although more penetrating X-rays produced a lesser skin reaction and a correspondingly smaller pastille response than in the case of less penetrating X-rays, Bordier and Galimard still felt that their tints could be depended on for comparative purposes.

Jules Curchod (1861-1937), a radiologist-physician from Geneva, also made an attempt at standardizing the Sabouraud-Noiré radiometer. By his device which he presented in 1907 before the Congress of Lyon of the French Association for the Advancement of Science, Curchod proposed to calibrate the Sabouraud-Noiré Tint B (116). He felt that the original calibration in terms of the Holzknecht unit was unsatisfactory because the H unit was too indefinite (see p. 31, above).

His new method consisted of introducing a voltammeter into the secondary circuit of the X-ray generating unit and bringing about the electrolysis of water by the induced current (116). The instrument for the electrolysis was like a reservoir pipette 15 cc in volume. The top had a stopcock and a funnel through which acidified water could be introduced into the reservoir. Its lower end was bent up to an extended volume of about 10 cc in the shape of an open funnel. After the reservoir was filled with acidified water and the stopcock was closed, the water rose in the open branch to a certain level designated zero. Before the water was introduced into the reservoir, two platinum

wires were inserted into the reservoir to act as electrodes to allow the secondary current to pass through the acidified water.

Once the instrument for the electrolysis was inserted into the secondary circuit and the induction coil was set in motion, gases immediately formed at the electrodes (116). Since these gases had no means of escape they forced the water back into the open branch which caused the level of the water to rise from its initial zero position. The number of cubic millimeters of gas liberated raised an equivalent amount of water. Since the electrolysis of water was a dependable phenomenon, it was used to calibrate the Sabouraud-Noiré Tint B. The number of cubic millimeters of gas liberated while a Sabouraud-Noiré pastille at 15 cm from the anti-cathode changed to Tint B was considered a unit which could be subdivided at will in the future without having to use the pastille each time. Such a procedure provided for the measurement of smaller and fractional doses not possible with the Sabouraud method. Besides, the Curchod method had a degree of precision about it which former dosimetric methods seemed to lack.

In working towards standardization of dosage measurements, some radiometrists were concerned more with the proper identification of small color changes rather than with the units used to calibrate a color scale. For example, there were some adaptations of

Lovibund's Tintometer¹⁶ for the purpose of accurately estimating the degree of coloration of the pastilles (309, p. 433-436; 377). The main advantage of these adaptations was the fact that the color standards were composed of permanently tinted glass.

Some original work in this line of dosimeter variations was done in 1914 by Gustav Bucky (1880-1963), a German-American radiologist (71), and by William Hampson (1854-1926), an English radiometrist (234). Bucky applied the theory that each change of color of a non-transparent body was a sign of a change in the wavelength of the light rays reflected by that body. Exact comparison of wavelengths cannot be done normally with the human eye alone but only by means of spectral analysis. By his method Bucky suggested a practical substitute for spectral analysis based on the fact that for the human eye differences in brightness are easier to distinguish than differences in color.

It could be shown that a fresh pastille (light-green in daylight) would appear almost black if observed under a blue and violet light (71). If the same pastille were viewed under a light source composed

¹⁶ Joseph W. Lovibund, a British color analyst, devised his tintometer in 1887 for the purpose of analyzing, synthesizing, matching, and measuring colors. The tintometer consisted of a graded series of colored glass standards, numbered according to their depth of color, and an instrument for holding the standard as well as the object to be measured. The tintometer has had diverse applications from measuring the purity of water to facilitating the grading of oil samples (508).

mainly of green and yellow light, it would appear almost white. Likewise under monochromatic green light, an irradiated pastille (brown in daylight) would absorb the greater part of the light although a fresh pastille would reflect the greater part. With an unfiltered light source, the brightness of an irradiated pastille would also be considered less than that of a fresh pastille, if it were viewed through a filter. This would allow a much easier evaluation of fractional dose since the filter would act to augment the difference in brightness. Bucky suggested that the evaluation of fractional dose would be made still easier if a regularly diminishing scale of gray were used behind the filter when comparing brightness.

Bucky emphasized certain advantages of his dosimetric technique, notably: it allowed evaluation during irradiation; it allowed an evaluation of fractional dose with an exactness of one to two X units¹⁷; it allowed for a pastille protected from daylight throughout the treatment; and it allowed for an exact optical reading with a constant light source and with the elimination of other causes of optical errors.

Hampson's radiometer consisted of 25 graded tints which represented the color change of the Sabouraud-Noiré pastilles on irradiation (234). The tints were numbered from 0 to 24. The 0 tint was the color

¹⁷The X unit was defined by Robert Kienböck in 1905 as being equivalent to one-half of an H unit (see p. 44, below).

of unexposed barium platinocyanide (light-green); the sixteenth tint represented Tint B (brown) of the Sabouraud-Noiré radiometer. The tints were arranged on a circular card which was encased in such a way that only one tint could be viewed at a time and that, under artificial light.

Because of his radiometer, Dr. Hampson was able to reduce the length of exposure for a full dose (234). The fact was that epilation occurred before Tint B was reached, and Hampson's radiometer made possible the measurement of the pastille tint when it was not nearly as dark as Tint B. With this radiometer it was also possible to reuse exposed pastilles even if their initial colors had not been completely restored. It was determined that for a full epilation dose, with the pastille on the patient's skin, the standard color scale was turned through four gradations. Before reusing a pastille then, it was necessary only to match its initial color with the tints in the radiometer because the full dose was known to be four stages darker. Since the darker shades in color were more difficult to observe, it was recommended that a pastille be not reused more than four times in succession.

Even though Hampson's radiometer had a greater sensitivity, a comparative study of the dosimeters in use showed that Hampson's color gradations were not regular (377). The initial changes as well as those from bright to dark brown appeared more slowly, whereas

the middle gradations appeared more quickly. This would have made the four-shades-darker guide mentioned above not very reliable.

Dosimetry Not Based on Colorimetry

Although in 1903 Samuel Stern, a radiotherapist from New York, had suggested the use of photographic film for radiometry (462), Robert Kienböck, a Privatdozent at the University of Vienna, was the first to actually devise a dosimeter which utilized the photographic action of X-rays (306). In 1905, Kienböck introduced his new method of dosimetry before the Roentgen Congress at Berlin.

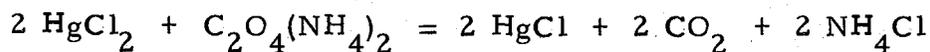
His quantimeter consisted of two parts: first a strip of photographic paper wrapped in black paper and applied to the irradiated tissue and second, a normal scale of graduated tints with which to make a comparison. The scale was calibrated in a unit called X which was equivalent to one-half of an H unit. This method then made possible the estimation of small differences of dosage. In fact, the dosimeter was most effective where small doses were concerned. The scale ranged from $1/4X$ to $15X$ and the greatest distinguishable differences appeared at the bottom of the scale which read: $1/4$, $1/2$, 1, $1-1/2$, 2, $2-1/2$, 3, 4, 5, 6, 7, 8, 10, 12, 15. One-fourth X was the smallest measurable dose when the dosimeter was placed on the skin, but when the distance of the reagent strip from the focus of the tube was decreased, then a correspondingly smaller dose could be

measured. For example, at half the distance a tint due to $1/4X$ at the position of the strip would be a measure of one-sixteenth X at the skin. Besides being more sensitive, the Kienböck strips also provided a permanent record of the exposure for future reference.

Kienböck even felt that his quantimeter could have other uses such as studying the absorptive power of materials used in shields or investigating the activity of samples of radium (306).

Compared with the dosimeters which preceded it--the radiometers proposed by Holz knecht, Sabouraud-Noiré, and Freund--Kienböck's quantimeter had the advantages that it was more sensitive, left a permanent record after the development process, and was inexpensive. These factors must have contributed to its general acceptance (for example, see 222). Even 20 years after they were first introduced, the Kienböck strips were widely distributed and used (377).

In 1907 Gottwald Schwarz (1880-1959), a radiologist at the X-ray Laboratory of the General Hospital in Vienna, proposed another dosimetric method (440). His dosimeter depended on the degree of turbidity caused by the formation of a precipitate of mercurous chloride ($HgCl$) from an ammonium oxalate-sublimate solution [$HgCl_2 + C_2O_4(NH_4)_2$] according to the equation:



Years later Schwarz acknowledged that he began his research on the

dosimeter in 1904 because the Holz knecht chromoradiometer was not considered a satisfactory instrument. Since no other dosimeter was known at that time in Germany and Austria¹⁸, a new one had to be found (339).

In practice the Schwarz dosimeter was placed at half the focus-skin distance. There were two suggested ways of measuring the dose. One method involved the comparison of the degree of turbidity with sealed test cylinders containing liquids distinguished by their turbidity as No. 0, 1, 2, and 3. A turbidity of No. 1 corresponded to an irradiation of 1-1/2 H units; No. 2 to 3 H units; and No. 3 to 5 H units. The other method involved the introduction of a new quantity of dose, the "Kalom". One Kalom was the dose required to bring the initially clear solution to a turbidity of 1. Therefore, one Kalom was equivalent to 1-1/2 H units. Since it was much easier to note the distinction between a clear and a turbid solution than between two solutions of different turbidity, the dosimeter was replaced by a fresh one as soon as it registered a turbidity equivalent to one Kalom. The resulting final dose was the sum of the doses registered by each of the dosimeters used (350).

Schwarz felt that his precipitate-radiometer had definite

¹⁸It seems strange that in 1904 Schwarz would be unaware of the Freund dosimeter, unless the two dosimeters were the results of near simultaneous research.

advantages over other chemical dosimeters. It was a direct, easily observed dosimeter; it did not depend on the temperature or other disturbing factors; and it did away with the colorimetric principle. Schwarz's reasoning shows that there was a recognition of the qualitative nature of the current dosimetric methods and that some of the inaccuracies that proceeded from the subjectivity inherent in the judgment of color-changes had to be removed. Nevertheless, dosimetry based on the colorimetric principle was not simply abandoned. Steps were taken to improve its reliability and precision, but it remained a popular method among radiologists for measuring dosage of X-radiation.

Chemical Dosimetry in Developmental Perspective

Prior to 1908 when Villard proposed that the ionizing effect of Röntgen radiation be used for dosimetry (519), practically all methods of measuring the quantity of radiation for therapeutic purposes depended on what Röntgen and his contemporaries called the chemical action of X-radiation. Not until about ten years after these chemical effects were first recognized was the suggestion made that the chemical action of ionizing radiation was due to the ionizing effect (66). Writing in 1913, Rutherford considered this possibility when he said: "There appears no doubt that the marked chemical action of the α and β rays is connected with the ionization they produce in all kinds of

matter" (422, p. 319). While such opinions provided the impetus for the development of a theory relating to the chemical effects of ionizing radiation, the introduction of the ionization chamber caused the emphasis in dosimetry to shift to the ionizing effect of the radiation.

Chemical dosimeters were still used in actual practice, but there was a decline in independent research in seeking to apply to dosimetry the chemical effects of ionizing radiation on new systems. Although new facts relating to the chemical action of ionizing radiations were accumulating, dosimetry was being expanded to include many physical effects which for more than a decade tended to overshadow the chemical.

For example, in his survey of methods in 1914 (222), the radiologist Dr. G. Grossmann classified the direct dosimetric methods according to their dependence on various properties of ionizing radiation: 1) the electrical charging effect on metallic bodies, 2) a thermal effect, 3) a chemical effect, the coloration of substances, 4) the ionization effect on gases, and 5) the effect on the resistance of selenium. Of these actions of ionizing radiation, Grossmann still included the chemical effect in his selection of those having practical application, however. Charles E. Phillips (1871-1945), a British physicist who did research on ionization methods of dosimetry, did admit in 1920 that for all practical purposes the pastilles and photographically sensitive surfaces were the only indicators in general use

(384).

Therefore, even though new and perhaps more accurate methods of dosimetry were introduced, chemical dosimeters remained in use. Prior to the 1920's, chemical dosimetry was more or less qualitative in nature, that is, the relationship between the extent of the chemical effect and the color change or the darkening of the film was not precisely established. Perhaps the systems which were known to show a chemical effect on irradiation did not lend themselves to precise measurement. Since the reactions themselves in most cases were not expressed in terms of chemical equations, the measurable quantities that could be related to dose were limited. The lack of precision was noted by physicians and radiologists who required dosimetric methods; hence, there were numerous attempts made at improving the accuracy of some systems. However, none of these proposed modifications persisted in use. Although there were about six reported variations of the Sabouraud-Noiré dosimetric method, the original method proposed in 1904 was the only one widely in use even in the 1920's. Of all the dosimeters proposed, only the Sabouraud-Noiré pastilles and the Kienböck strips were generally accepted, if not for their precision at least for their relative effectiveness.

CHAPTER III

IONIZING RADIATION (1925-1942)

The discovery of X-rays in 1895 and radioactivity in 1896 introduced physical scientists to vast new fields of research that gradually revealed the nuclear structure of atoms. In 1911, the first atomic model based on a nuclear concept was proposed by Ernest Rutherford (424). The nucleus was retained by the Danish physicist Niels Bohr in his more developed model of an atom in 1913 (57). The first artificial nuclear disintegration was detected also by Rutherford in 1919 (419). When he bombarded nitrogen with alpha-particles from polonium he observed on a zinc sulfide screen scintillations caused by what were identified as protons because of their much longer range in air than alpha-particles. A decade later artificial disintegration was actually studied with a Wilson cloud chamber¹⁹ (53, p. 34-35). Still what is known as modern nuclear physics did not have a beginning until 1932. In 1932, a fundamental component of the nucleus was identified with the discovery of the neutron. Also in 1932, the first successful nuclear transformation was induced by the use of a high-voltage

¹⁹C. T. R. Wilson (1869-1959), a Cavendish physicist, as a result of research on the formation of liquid droplets in a super-saturated vapor, invented the expansion type of cloud chamber which made possible the study of the tracks of ionizing radiation. Wilson observed the tracks of alpha- and beta-particles for the first time in 1912 (540).

accelerator. The latter provided a means of studying nuclear structure that could be controlled--which control natural radioactivity did not allow. Significant as the last two events were for modern nuclear research, they were also fundamental in broadening the field of ionizing radiation.

Prior to 1932 much was learned, from experimentation, about the nature and behavior of X-rays and gamma-rays. Alpha-rays and beta-rays were also investigated and identified with streams of charged particles--the former, helium nuclei, and the latter, electrons. This led to a study of the behavior of rays of other charged particles as well. Research showed that many of these forms of radiation qualified as ionizing radiation. However, of these forms, the most prominent were X-rays and gamma-rays due particularly to their usefulness in medicine. The development of particle accelerators gave rise to a varied usefulness and application also of other forms of ionizing radiation.

The Discovery of Neutrons

In 1920, Ernest Rutherford, then Cavendish Professor of Experimental Physics at the University of Cambridge, in his Bakerian Lecture on the nuclear constitution of atoms suggested the existence of a proton and an electron in close combination as a neutral doublet, the "neutron" (421). In the years that followed, his suggestion

initiated many experiments aimed at discovering such a particle. At the Cavendish Laboratory a search was conducted for neutrons in a hydrogen discharge tube with the potential varying from 2,000 to 50,000 volts (208). At Trinity College in Cambridge the hypothesis that a much closer combination of an electron and a hydrogen nucleus existed than was known in the hydrogen atom was also tested (408).

Concurrent with the experiments in search for neutrons were those involving nuclear transformations. Following the experiments of Rutherford in 1919 when the light nitrogen nucleus on being bombarded with alpha-particles underwent disintegration with the emission of a proton, many similar investigations were carried out to study the effects of fast-moving alpha-particles on light-weight nuclei. Physicists in Charlottenburg reported in 1930 that some nuclides, when bombarded by alpha-particles from polonium, emitted a very penetrating radiation which they assumed to be of the gamma-ray type (63). Nuclear scientists in Paris (118) and in Cambridge (529) showed that the radiation emitted by beryllium under bombardment by alpha-particles was particularly strong and distinctly more penetrating than any gamma-radiation from naturally radioactive substances was known to be. When the physicists Irène Curie-Joliot (1897-1956) and her husband Frédéric (1900-1958) discovered that the penetrating radiation from beryllium was capable of ejecting protons from hydrogenous substances (119), the British physicist James

Chadwick (b. 1891) at the Cavendish Laboratory was able to show that the very penetrating radiation must have been a beam of neutral particles and the ejected protons very likely recoiling nuclei (81). He came to this conclusion on the basis of the principle of conservation of energy and momentum in collisions. He tested his neutron hypothesis by examining the radiation from beryllium and its effects, first on paraffin wax, and then on thin layers of materials such as lithium, boron, and carbon. The experimental facts could not be explained by the gamma-ray hypothesis unless the principle of the conservation of energy and momentum were abandoned. He concluded that the radiation consisted not of quanta but of particles of zero charge and a mass almost equal to that of protons.

Other scientists at Cambridge quickly assumed the responsibility of elucidating the nature of the neutron and its properties. Chadwick had suggested that because of their extremely small electric field neutrons in their passage through matter would not be deflected unless they suffered collisions with nuclei. Collisions of this kind would produce recoil atoms of short range and great ionizing power (81). The physicist Norman Feather (b. 1904), a Fellow of Trinity College, Cambridge, studied the collisions of neutrons with nitrogen nuclei with the help of an expansion chamber (167). The length of the recoil tracks agreed with the neutron hypothesis; tracks were observed resulting from both elastic and inelastic collisions. The inelastic

collision was evidenced by a nuclear disintegration due either to neutron capture with a resulting alpha-particle emission or to a neutron non-capture but a probable proton emission.

The Scottish physicist Philip I. Dee at Pembroke College, Cambridge, studied the interaction of neutrons with electrons. He came to the conclusion that the production of electron recoils by neutrons was a rare occurrence compared with the production of recoil nitrogen nuclei (142). This behavior was understood on the basis that neutrons being uncharged particles would pass unimpeded through electron clouds of atoms. The only probable interference to their passage would come from the dense atomic nuclei which could slow down or absorb the neutrons depending on whether the interactions were due to a glancing impact or a head-on collision. The interacting nuclei, being charged and often heavier than the neutrons, would recoil with a certain amount of kinetic energy which would quickly be lost by intense ionization along the recoil tracks.

This vastly different mode of ionization of neutron-rays was extensively studied and confirmed with the expansion chamber. Though neutrons themselves left no visible tracks in the cloud chamber, the recoil nuclei and the products of disintegration, if disintegration occurred, left short dense ionization tracks similar to those produced by alpha-rays.

The Early Development of Particle Accelerators

Nuclear disintegrations which were induced in the laboratory by the bombardment of stable nuclei with neutrons and which were observed in a cloud chamber by the ionization tracks of recoil nuclei and charged-particle emissions were a verification of the new form of ionizing radiation--the neutron-ray. Although it was recognized that certain reactions were intense sources of neutrons, it was not an easy matter to measure the number or the speed of the emitted neutrons. However, there was another development at this time which eventually provided for a collimated beam of neutrons of measured intensity.

When the bombardment of stable nuclei was first attempted, the only beam of high-energy massive particles available for projectile purposes was the beam of alpha-particles emitted by naturally radioactive substances. Theoretically, a beam of high-energy protons would have been more suitable for projectile purposes. Compared to a beam of alpha-particles, a beam of protons would have experienced less repulsion of the target nuclei, which fact would have increased the collision probability. At the suggestion of Rutherford, the physicist John Cockroft (1897-1967) of the Cavendish Laboratory with his associate Ernest T. S. Walton (b. 1903) built a high-tension machine that would accelerate protons. They obtained a high voltage

by a voltage multiplier system based on the electric transformer systems. It was generally assumed in scientific circles that for artificial nuclear disintegration, particles with one-million electron volts of energy were needed. Still in 1932 Cockroft and Walton successfully brought about the first nuclear disintegration though they used machine-accelerated particles with energies of only about a quarter-million electron volts (102). As Professor Chadwick wrote, Cockroft and Walton compensated for the low energies by using large numbers of particles (80). The large number of particles increased the chances of penetration. It is important to note that Cockroft and Walton were able to disintegrate only light elements like lithium and beryllium with the accelerating capabilities of their high-tension machine.

Another group of experimenters was concurrently working on a magnetic resonance accelerator, or cyclotron,²⁰ under the direction of the experimental physicist Ernest Orlando Lawrence (1901-1958) at the University of California in Berkeley. Had the physicists at Berkeley any indication that nuclear disintegrations were possible with

²⁰The accelerator at the University of California was initially called the "magnetic resonance accelerator" and in 1935 Lawrence considered the term "cyclotron" to be laboratory slang (326). In an article a year later Lawrence and his collaborator introduced the term "cyclotron" in the text as an alternate for "magnetic resonance accelerator" and used it throughout the article (324). After such a seemingly official recognition, the term "cyclotron" has been generally used.

protons having energies of a few hundred kilovolts, they could have produced the first nuclear disintegration in 1931 (135, p. 46). With their cyclotron, they possessed this capability before the Cavendish team had sufficiently developed the high-tension machine.

The cyclotron, a circular accelerator first proposed by Lawrence in 1930, achieved particle acceleration by giving a particle a relatively small amount of energy in one step and then cycling it through that step many times (325). This indirect method of multiple acceleration was feasible because for a given magnetic field the period of revolution of a charged particle along a circular trajectory is independent of the velocity with which the particle is moving. However, given a specific charged particle, the period of revolution is inversely proportional to the magnetic field. Though the initial demonstration of the cyclotron depended on the uniform magnetic field of a four-inch magnet, the size of the magnet had to be increased in order that high-speed ions with energies in the million-volt range could be produced. The size of the magnet was first increased to eleven inches²¹ and the average magnetic field that was maintained over the path of the ions was such that the accelerated particles traveled successive revolutions in equal intervals of time (325). The

²¹The giant cyclotron at Berkeley today operates with a 184-inch magnet and can accelerate deuterons (heavy hydrogen nuclei) to an energy of 19 million volts (380, p. 577).

science reporter for The New York Times in 1934 described the magnet of the cyclotron at the University of California as being high and wide as a barn door and weighing 85 tons (365). The construction of ever larger cyclotrons at the University of California and elsewhere made possible extensive studies of the interaction of fast-moving particles with matter. At Berkeley, following the announcement of Cockroft and Walton, the bombardment of lithium with high-speed protons was but the beginning of many nuclear disintegrations.

Early in 1934 an announcement from Paris for the second time stunned the group of scientists at the Radiation Laboratory in Berkeley. Irène Curie and Frédéric Joliot had discovered that aluminium exposed to alpha-radiation emitted positrons²² (120) which indicated the possibility that radioactive forms of elements could be produced in the laboratory. In their published announcement the Joliot's speculated on the possibility of producing nitrogen-13, a radioactive isotope of nitrogen, by bombarding carbon with high-speed deuterons. Whether or not this speculation were intended for the Berkeley scientists,²³ it was a possibility they could

²² A positron is a positive electron discovered in 1932 in cosmic radiation by C. Anderson (b. 1905) (11).

²³ Ernest O. Lawrence was the American representative at the Solvay Congress in Brussels in 1933. At this conference of physicists, Lawrence reviewed the deuterium experiments being conducted with the 27-inch cyclotron at Berkeley. Irène Curie and her husband Frédéric Joliot were among Europe's physicists in attendance (92, p. 202-208, 538; 135, p. 58-60).

easily test. Within minutes after they became aware of the possibility, they created the first nitrogen-13 ever known to exist (135, p. 60). This they accomplished by the bombardment of carbon with high-speed neutrons from the cyclotron.

Following this initial creation of nitrogen-13, radioactive isotopes were formed by the constantly improved cyclotron and its beam of ever-more-energetic particles. The improvement of the cyclotron was accompanied by the development of more sensitive instruments for registering all types of radiation resulting from these nuclear investigations. When a beam of high-speed deuterons was used to bombard a beryllium target, the front page of The New York Times could announce that a ray of ten-million neutrons per second flowed through a lead window, the first time neutrons were available in such quantities (365).

The newspaper's interest in the capabilities of the cyclotron to provide intense neutron radiation was due for the most part to the probable medical application of the neutron beam. In fact there is an interesting similarity between this article and the announcement of the discovery of X-rays published by the same newspapers 39 years earlier almost to the date (see p. 8, above). The article of January 16, 1896, emphasized the medical possibilities of X-ray photography and also called attention to the speculation of physicists about the nature of the Röntgen rays (266). The article of January 17, 1935 was subtitled

"New development at the University of California has possibilities in medicine and for building heavy chemical elements from lighter" (365, p. 1, col. 4). The article acknowledged that the use of X-rays in treating deep-buried cancer was limited because of the burning effect of X-rays on the skin and that neutron treatment could possibly overcome that difficulty.²⁴

The Cyclotron in Medicine

Neutron Beams

That a neutron beam should have been considered for therapeutic purposes seems reasonable when its important properties are noted. First, a stream of neutrons possesses great penetrating power, effective even through lead which can stop gamma-radiation. Secondly, a neutron beam would seem to qualify as a therapeutic agent because of its dense ionizing capability when passing through matter. However, it does not seem as if there were any immediate applications

²⁴The article of January 17, 1935, did not overlook the fact that "for the important scientific job of smashing atoms, to learn how matter is made, neutrons are the best projectiles" (365, p. 10, col. 5). The lengthy editorial in the January 18th issue further indicated the scientific nature of the activity at Berkeley when it said: "The truth about the atom may be unknowable. We expect at least a working formula which will partially appease the questioning mind--all that science can ever do for us. The neutron is the name of something that we may never understand. But it is also an aid in devising the formula that we have been seeking ever since we began thinking about the universe" (490, p. 20, col. 3).

or that, in 1934, neutron irradiation was a prescribed treatment. The editorial in the January 18, 1935, issue of The New York Times explicitly mentioned that physicists were aware of the possibility that neutrons might compete with X-rays as therapeutic agents (490). If neutrons were to be used as therapeutic agents, then unnecessary exposure to neutrons would be dangerous. At first, however, the physicists, particularly at Berkeley, seemed not to have been convinced of this radiation danger from neutrons (135, p. 67).

The one man most energetic in forging ahead with neutron therapy was John H. Lawrence (b. 1904), a brother to Ernest. John was a physician who was associated with the Department of Internal Medicine at the Yale University School of Medicine during that memorable first year when the Radiation Laboratory was producing radioisotopes and intense neutron beams. It was John H. Lawrence who, while spending the summer of 1935 at Berkeley, convinced the physicists at the Radiation Laboratory of the radiation danger from neutrons (135, p. 67) and who was responsible for the introduction of the Berkeley team and its projects to medical men and leaders of medical societies.²⁵ He also initiated research on the effects of neutron irradiation on biological functions (327). He, himself, investigated the effects of neutron

²⁵The Radiation Laboratory was to depend for many of its research funds on its chief selling point--the medical promise of the cyclotron (135, p. 68-70, 76).

irradiation on the blood of rats. His results were corroborated by those obtained by Raymond Zirkle (b. 1902) and Paul Aebersold (1910-1964) also at the Radiation Laboratory. Zirkle, a research participant from the University of Pennsylvania, and Aebersold, from the University of California Medical School, studied the growth inhibiting effects of neutrons on wheat seedlings (548).

Such research led to the conclusion that neutrons were more biologically effective than X-rays. The two Lawrence brothers theorized that neutrons were more readily absorbed in substances containing hydrogen, such as biological materials, because in a head-on collision with a proton a neutron was brought to rest while the proton recoiled with the full speed of the neutron. The recoiling-proton, heavy compared to an electron, produced about a hundred times as much ionization per unit distance as that produced by the secondary electrons associated with the action of X-rays (327).

It is significant that at this point in medical history steps had to be taken to convince medical groups of the possible effectiveness of a therapeutic agent. Though a mode of treatment for cancer was very much needed, there was not a general willingness to take risks in 1936 as was the case in 1900. Perhaps this was a response due to experience. In the words of one physician, "Many of the blind alleys [in therapeutic irradiation] investigated in a more or less haphazard way in the case of X-rays would not be explored with such great loss

of time and effort in the case of neutrons" (463, p. 327). This would seem to indicate that the medical profession was deliberately exercising caution and was not intending to endorse neutron irradiation as a form of therapy until sufficient data about its effectiveness was available.

The movement towards the application of neutrons in therapy was aptly summarized by Professor Chadwick in 1938 (80). There was a certain amount of evidence at hand that indicated that, biologically-speaking, neutrons were more effective than X-rays since the effects on individual cells seemed to depend more on ionization density than on the total number of ions formed. Chadwick admitted, however, that the evidence was too meager to permit definite conclusions. A preliminary report from the University of California in 1940 acknowledged that treatment of cancer with neutrons had not been used long enough to report on results (463). The situation was unchanged two years later; in 1942, Ernest Lawrence admitted that his medical colleagues were not yet ready to come to any conclusions as to the relative value of neutrons and X-rays in clinical therapy.(323, p. 72).

If the attitude of the University of California Medical School towards the application of neutron irradiation seems reasonable, then that of the Lawrence brothers was most certainly a bold one. According to one of Ernest's biographers, John Lawrence went so far as to prescribe neutron treatment for his own mother. Early in 1938

Gunda Lawrence, an advanced cancer patient at the age of 65, had been given three months to live by a physician at the Mayo Clinic in Minnesota. The brothers decided to dose her with the neutron beam from the 27-inch cyclotron²⁶ (135, p. 76).

According to the biographer, this was the first neutron treatment ever given a human patient. Specific dates for the treatments were not given, but circumstances seem to indicate that the treatments were given shortly after January of 1938. Since apparently the story of the treatment of Gunda Lawrence had never been publicized,²⁷ the first patient to receive what was considered a safe number of neutron units was irradiated on September 26, 1938 (102). John Lawrence was convinced of the medical value of the cyclotron beam and did not hesitate to prescribe the neutron treatment for other cancer patients. From September, 1938, the cyclotron at the University of California Radiation Laboratory was made available one day a week for therapeutic purposes. To minimize the destruction of healthy surface tissue, every effort was made to regulate the beam and to localize the ionizing radiation. However, fractional doses were not available until after the summer of 1939 when a new cyclotron was completed largely for clinical purposes (135, p. 89).

²⁶ Although there was no apparent change in her condition, Gunda Lawrence did survive and lived to be 83 (135, p. 77).

²⁷ According to a close colleague of the Lawrence brothers, the treatment of their mother was kept completely confidential (135, p. 77).

Radioisotopes

The use of the cyclotron in the production of radioactive elements was another application of great service to biological investigation. Radioactive isotopes had been used as indicators in analytical chemistry many years before the invention of the cyclotron. Initially, the isotopes were used to indicate the amount of labeled material present in inorganic reactions, that is, activity studies provided an alternative to conventional analytical methods. The many artificial radioactive isotopes made available by the cyclotron simply broadened the area of research and application where radioactive labeling techniques could be used. That a radioactive isotope acts like and accompanies its inactive isotope through any chemical process was basic to the studies that were initiated.

The chemist George Charles Hevesey (1885-1966) had done much of the pioneer work with the use of radioactive indicators in the study of chemical processes. The results of his first biochemical experiment--the study of the absorption and distribution of radioactive lead in broad bean plants--were reported as early as 1923 (264). After the development of the cyclotron when Hevesey and his collaborators in Denmark undertook the study of the role of phosphorus in metabolism, they depended upon the Radiation Laboratory in California to supply them with radioactive phosphorus (135, p. 75; 92, p. 475). Since

those early studies dealing with the tracing of phosphorus many other investigations involved, for example, radioactive iodine, iron, calcium, strontium, carbon, water, tagged-hydrogen in fatty acids, and labeled-iodine in insulin. Because of the biochemical and biophysical research made possible by the cyclotron-produced radioisotopes (103, 233, 296), medical science was able to adopt several techniques for diagnosis and treatment, such as diagnosing thyroid malfunctioning with radioactive iodine, treating osteogenic tumors with radioactive strontium, and treating leukemia with radioactive phosphorus.

E. O. Lawrence's main interest in building and improving the cyclotron was for nuclear studies. Originally, he had not foreseen the medical possibilities that would arise because of developments associated with the cyclotron. However, he was very much aware that he needed a tremendous amount of money to finance his projects and medical research at that time stood a much better chance of gathering funds than experimental or theoretical physics. Furthermore, his proposal for a larger cyclotron,²⁸ one designed for an energy range above 100 million volts, was evaluated as impossible due to relativistic limits by some theoretical physicists, notably James Chadwick (81) in England and Hans Bethe (b. 1906) at Cornell

²⁸The 60-inch cyclotron completed in 1939 had the capability of accelerating deuterium ions to an energy of 19 million volts (135, p. 89).

University (52). Therefore, mainly by emphasizing the medical promise of the cyclotron, by providing radioisotopes for medical research, was Lawrence able to gain the financial support of public and private foundations for building ever-larger cyclotrons (135, p. 93-95).

Developments in Medical Radiology

In the early days of therapeutic radiology, X-rays were used for their superficial biological effects. Not until the 1920's when it became possible to generate X-rays in the 200 kilovolt range and above were X-rays considered effective in deep therapy. The existing Coolidge tubes (see p. 13-14, above) could not practically be operated at a kilovoltage higher than 200. Coolidge himself did research in the 1920's to overcome the limitations of the hot-cathode high-vacuum X-ray tube. However, it does not seem as if he were interested purely in generating high-voltage X-rays. Though he was able to modify his tube to attain a kilovoltage of 350 (108), he was also thinking in terms of high-speed particles operating at a potential difference of millions of volts (107).

During the 1920's there were other reports of high-voltage units (68, 322, 506) but it does not seem as if any of these went beyond the model erected for private research for none was in general use for producing X-rays. A Coolidge-type tube designed by the physicist

Arsène d'Arsonval (1851-1940) in 1930 to function under an electrical pressure of 400 kilovolts did seem to have a practical application (129). Still there was a need for more penetrating X-rays. The technological breakthrough came in the early 1930's and curiously the important contribution to therapeutic roentgenology was made at the Radiation Laboratory in Berkeley.

David H. Sloan (b. 1905), from his first days as a graduate student at the Radiation Laboratory in 1930, was interested in developing high voltages. He headed a team which was responsible for several linear accelerators which were developed deliberately, and with E. O. Lawrence's support, to compete with the cyclotron. In 1933, as he was working on an insulation problem for a linear accelerator, his research was temporarily diverted when Lawrence directed him to fill the request of the Medical School for an X-ray machine more powerful than any in existence. With his associate Milton S. Livingston, Sloan redesigned their high-voltage resonance transformer, originally designed for the multiple acceleration of ions, into an 800 kilovolt X-ray machine (452).

Much of the medical research on radium during the first quarter of the twentieth century was directed specifically at the better treatment of cancer. Though many early efforts in radium therapy were simply empirical in nature, as radium became more available (in fractions of an ounce) there were some organized attempts at

therapeutic service. At the Memorial Hospital in New York,²⁹ Giacchino Failla (1891-1961) made an important contribution by his introduction in 1916 of the use of sealed glass capillary tubes of radon (radium emanation) for interstitial irradiation. For several years after the introduction of these slightly filtered "seeds" or implants, the severe local reactions overshadowed the degree of tumor control which was achieved. After much research Failla developed the gold radon seed in 1925 (398). With these filtered implants available, methods of interstitial irradiation and intracavitary irradiation could be standardized. Since 1925, radium therapy has made substantial progress.

Developments in Industrial Radiology

Decades of research in physical laboratories contributed much to the knowledge of X-rays and made possible new and varied applications. X-ray radiography, one of the first recognized applications of X-rays, was expanded considerably. Besides being used in medical diagnosis, it was applied industrially as well. X-ray radiography was

²⁹ Memorial Hospital built the first radon plant in this country in 1917 after Dr. James Douglas, a physician and metallurgist donated a fraction of an ounce of radium to the hospital in memory of his daughter who died of cancer. The plant was dismantled in January, 1970 because now there are other radioisotopes available for attacking cancer cells. Gold-198, iodine-125, and irridium-192 are as effective but not as dangerous as radium and are available commercially (366).

introduced in the foundry shortly after the introduction of the Coolidge tube into X-ray science (see p. 15, above). In 1915 the technique was used on steel castings; in the 1930's it was still used to detect flaws in steel and aluminum castings, but radiographic inspection was not limited to steel and aluminum. At the University of Pittsburg Co-operative X-ray Laboratory it was reported in 1935 that successful examinations of bronze castings containing up to 60% lead were made (265). Since lead acts as a protection against X-radiation, such examinations would require very hard X-rays, that is, those having a high penetrating power. Information gained through inspections of this kind has aided the development of casting procedures.

Welded structures were also inspected radiographically. The importance of sound welds in structures like dams, bridges, and skyscrapers accounts for the extensive use of this technique. The development in the early 1930's of mobile X-ray equipment has made this kind of application feasible (10, p. 19, 64, 87).

Radiography was also applied in the rubber industry, for example, in inspecting reclaimed rubber for its heavy metal content, in examining the adhesion of rubber to cords in tires, and in revealing the symmetry of golf-ball centers (432, p. 158-159). Radiographic examinations have also revealed superimposed pictures or retouchings of old paintings (432, p. 163-164), the heavy metal content of glass (10, p. 97) and defects--cracks, wormholes, knots--in wood to be

used in airplanes (10, p. 107). It was discovered that even assembled particles could be inspected radiographically; this technique exposed the interiors of metallic radio tubes, insulated wires, and any embedded heating elements (10, p. 94-95).

It was recognized, too, that radiographs were not always needed. Therefore, the transmitted X-rays, if allowed to activate a fluorescent screen, made visual examination possible of many completed products, particularly food products (265).

The ability of X-rays to be diffracted also found wide application since X-ray diffraction analysis could be used in industry. It was found that each subdivision of an apparently homogeneous structure diffracted a beam of X-rays in a particular way. The characteristic diffraction pattern was recorded on a photographic plate and analyzed for structural units or aggregates of molecules distinctive of the substance. Such analysis aided in identification and gave valuable data on the constitution of materials (10, p. 230-281).

In metallurgy, diffraction analysis provided information on the mechanism of deformation, on the mechanism and conditions of crystallization, and on the effects of impurities (10, p. 303-309). With such information the metal industry could standardize its techniques and processes. Just as the crystalline structures of elements were being studied in the chemical laboratory and their polymorphic forms were either discovered, verified, or disproved by

X-ray diffraction, so many substances important in industry were subjected to similar analysis. Inorganic substances like lime, plaster, cement, asbestos, and pigments, and organic substances like waxes, soaps, and glycerides were analyzed for their ultimate structures (10, p. 339-350). Such information was useful when certain properties of these substances needed improvement or intensification.

X-ray diffraction also provided textile manufacturers with an inspection tool. By studying the crystallite orientation of the textile fibers, they improved the quality of their materials. Finally, since X-ray diffraction was a means of identifying substances, it was also used to analyze industrial dusts for their content (265). This provided a sure method of identifying the substances responsible for industrial diseases.

Ionizing Radiation in Development Perspective

The ionization theory of gases formulated so brilliantly by Thomson and Rutherford in 1896 (see p. 6-7, above) was meant to account for a property characteristic of the X-radiation which Röntgen discovered in 1895. In less than a half-century many kinds of radiation had been discovered and identified as possessing to different degrees that particular property of X-radiation. Although initially the ionization effect of X-rays was noted by the resulting conductivity

of a gas exposed to X-radiation, the ionization effects of other forms of radiation were eventually observed directly in a cloud chamber (see p. 50, above).

High-energy X-rays and gamma-rays produce ionization by virtue of the electrons which are ejected from atoms and molecules when the X- and gamma-rays are absorbed. Radiation composed of high-energy charged particles, such as electrons or alpha-particles, is capable of ionizing matter directly; the tracks of the charged particles may be observed in a cloud chamber. The radiation composed of neutrons produces ionization by the charged particles which are set in motion as a result of collision processes; the tracks of these recoiling particles may also be observed in a cloud chamber.

By 1942, then, ionizing radiation included X-rays, gamma-rays, streams of alpha-particles or other positively charged particles, streams of electrons, and finally, beams of neutrons. Physical scientists interpreted much of the experimentally verified information about these forms of radiation in terms of valuable insights into the structure of matter. Scientists interested in the practical application of scientific knowledge found in almost every form of ionizing radiation a powerful instrument of service as well. The applied science of medical radiology, whose genesis lay in the very discovery of ionizing radiation, seems to have made the most beneficial use of the properties of ionizing radiation. There were applications in industry

also, but unlike those in medicine, these were developed more deliberately and, because of their nature, were more restricted in scope.

CHAPTER IV

CHEMICAL DOSIMETRY (1925-1942)

Although industrial radiology was not as broad and general in its applications as was medical radiology, the use in industry particularly of X-radiation had led to the control and improvement of many industrial processes and products. Significantly the analysis of industrial dusts by X-ray diffraction served to identify material causes of industrially-related diseases and thus to foster improved working conditions in industry. However, the introduction of X-ray equipment into many industrial establishments also increased the number of individuals whose occupations were a source of radiation exposure. The deleterious effects of irradiation were an ever-present danger. Though overexposure to irradiation had been a recognized problem in medical practice for many years, in the 1920's personnel protection became a broader issue.

Developments in Radiation Protection

During the early part of the twentieth century many countries formed their Röntgen Societies or Institutes of Radiology. However, the first International Congress of Radiology (ICR) was not organized

until in 1925 and met during that year in London³⁰ (484). Since the most serious problem facing radiologists at that time was the lack of standardized radiation units, the first ICR created an organization known as the International Commission on Radiological Units (ICRU) to deal with the problems of standardization in the measurement of radiation (484). In fact the title of the organization was changed later to include "and Measurements" although the abbreviation ICRU was still retained (28, p. 7).

The ICRU, since its establishment in 1925, has aimed to develop internationally acceptable recommendations as regards:

- (1) Quantities and units of radiation and radioactivity,
- (2) Procedures suitable for measurement and application of these quantities in clinical radiology and radiobiology,
- (3) Physical data needed in the application of these procedures, the use of which tends to assure uniformity in reporting (513, p. v).

At the second International Congress of Radiology which was held in Stockholm in 1928, the problem of personnel protection was given prime consideration (483). The International Commission on Radiological Protection (ICRP) was established by the Congress to deal initially with problems of X-ray protection (514, p. iv). Since 1928, the ICRU has cooperated with the ICRP in making

³⁰ Robert Knox (1867-1928), one of the presidents of the British Institute of Radiology, was instrumental in organizing the first ICR (220, p. 254).

recommendations³¹ on radiation quantities, units, and measurements in radiation protection. Standards were set up on an international basis. Any recommendations made by the ICRU and the ICRP were, for the most part adopted by similar national organizations, such as the National Committee on Radiation Protection and Measurements (NCRP) in the United States (512, p. (2)).

Recommendations of the ICRU

A significant first step was taken in dealing with the problem of radiation units when the ICRU met in Stockholm in 1928. The roentgen (r) was adopted as an international unit and was defined in terms of the ionization effect in an ionization or standard air chamber. It was recommended as the unit for that quantity of radiation which, when the secondary electrons were fully utilized and the wall effect of the chamber was avoided, produced in one cubic centimeter of atmospheric air at standard temperature and pressure a degree of conductivity equal to one electrostatic unit of charge at saturation current (487).

This recommended definition for the roentgen lacked clarity because the words "quantity of radiation produced" could be interpreted as referring to the quantity of radiation absorbed in air as

³¹The ICR, the ICRU, the ICRP and similar national groups were not legislative bodies. They were empowered simply to make recommendations (511, p. iv).

well as to the incident radiation intensity. Since the 1928 definition did not specify precisely what was being measured, the ICRU at its meeting in Chicago in 1937 re-defined the roentgen as the unit for that quantity or dose of X- or gamma-radiation such that the associated corpuscular emission per 0.001293 grams of air³² produced, in air, ions carrying one electrostatic unit of electricity of either sign (488). The use of the word "dose" in the revised definition did not really clarify the definition, however, because according to a duality of usage, dose could represent the radiation absorbed in air as well as the incident radiation intensity. In an appendix to its 1937 report the ICRU specifically stated that the dose was not to be confused with the energy actually absorbed by the tissue (28, p. 8). Although there were uncertainties in the interpretation of the roentgen, it served as the standard unit of radiation until the next meeting of the international congress in 1950.

Recommendations of the ICRP

At its meeting in Paris in 1931, the ICRP considered the possibility of introducing tolerance levels of radiation for persons exposed to radiation by reason of their employment (483). No specific

³²The value given as 0.001293 grams of air is equivalent to the mass of air contained in 1 cc of air at standard conditions of temperature and pressure.

recommendations were made, however, until at the next meeting held in Zürich in 1934. At that time the ICRP established what it considered to be a permissible level of radiation exposure of 0.2 r per day. This 1934 recommended permissible level was retained in worldwide use until 1950 (362). Also in 1934 and at the Chicago meeting in 1937, the ICRP specified the thicknesses of barriers of various materials that were to be interposed between a source and an individual to assure adequate protection.

Following the establishment by the ICRP of a permissible dose, a difference in interpretation of that dose was found at some national levels. In 1936, the Advisory Committee on X-ray and Radium Protection³³ in the United States adopted a value of 0.1r per day as the maximum permissible dose (512, p. 1). It seems that in the United States the tolerance dose was taken to represent the dose in air; local practice in Europe and particularly in England included backscatter³⁴ in the tolerance dose. Therefore, since backscatter increases the skin dose considerably, there was very little difference between the ICRP dose of 0.2r per day measured on the skin and the U. S. Advisory Committee dose of 0.1r per day measured in air.

³³The Advisory Committee on X-ray and Radium Protection was formed in 1929 under the sponsorship of the U. S. National Bureau of Standards. The name of the committee was changed to National Committee on Radiation Protection (NCRP) in 1946 (512, p. 111).

³⁴Backscatter is that radiation which has been scattered backward by the patient's body and thus adds to possible exposure (512, p. 6).

Chemical Dosimetry and Stray Radiation

In addition to the useful beam of radiation and any scattered radiation, stray radiation may also contribute significantly to a tolerance dose. By definition, stray X-radiation, for example, includes radiation due to leakage, that is, radiation coming from within the tube housing other than the useful beam, and secondary radiation, that is, radiation emitted by any irradiated material (511, p. 3). When in 1902, the problem was the protection of the patient (see p. 30, above), methods of dosimetry were directed primarily at the useful beam of radiation. Less than 25 years later, concern for the protection of the radiologist centered around methods of measuring stray radiation. Although protection against stray radiation was a recognized need even before 1925 and took the form of shields and barriers placed between the radiation unit and the operator, it seems as if there were no organized procedures for determining whether or not the protective measures taken were adequate. Some radiologists did carry dental film in their pockets, but there was no standard procedure available by which they could interpret the darkened film in terms of dosage.

In 1926, the meeting of the Radiological Society of North America devoted itself to consideration of the problem. Robert S. Landauer (1897-1966), a radiation physicist, offered the radiologist a simple

quantitative solution to his problem in terms of an erythema dose (see p. 26, above). At this time the roentgen had not yet been defined (see p. 77, above), nor was any tolerance dose generally recommended. Landauer made a series of standard films representing fractions of an erythema dose from 0.02% to 1.2%, all readily distinguishable (317). A dose of 1% of an erythema dose per month was considered by some to be a safe tolerance dose. Landauer offered for distribution the standard film No. 6 due to 0.28% of an erythema dose. In preparing the standard he used unfiltered rays of three different degrees of hardness. Each standard was appropriately labeled either as due to (1) unfiltered rays; (2) those rays produced at a peak kilovoltage (kvp) of 125, with a filtration of 6 mm of aluminum, and having a half-value layer (HVL)³⁵ of about 8; (3) those produced at 150 kvp, a filtration of 1/4 mm of copper, and having an HVL of about 10; or (4) those produced at 200 kvp, a filtration of 1/2 mm of copper, and an HVL of about 12. It was suggested that if a radiologist carried a film on his person while being exposed to stray radiation filtered, say, by 1/2 mm of copper he should use the appropriate standard for comparison. If after ten days he first found his film as dark as the standard, this

³⁵ A half-value layer (HVL) was defined as the thickness of a specified substance which, when introduced into the path of a given beam of radiation, reduced the intensity of the radiation to one-half of its original value (8, p. 132). Since Landauer did not specify the standard substance used nor did he attach any units to his HVL measurement, the significance of his HVL values is uncertain.

would indicate that in a month he would be exposed to about 0.8% of an erythema dose. This would give him some assurance that he was working under safe conditions. Landauer felt that the error introduced into the matching process as a result of differences in developing technique on the standard and test films was negligible.

There were no claims in 1926 that the Landauer dosimetric method provided an absolute measurement of stray radiation. It was meant to be a method, very much needed, of estimating exposure to stray radiation (317). Moreover, it was meant to be a method by which the radiologist himself could decide, from his own clinical knowledge, whether or not the stray radiation to which he was exposed was within a safe tolerance level. Even though film monitoring gave only an estimate of the dose received, the convenience of the process very probably facilitated strict adherence to routine procedures which made the method reliable.

Ways were even found for distinguishing the kinds of radiation to which the film was exposed. In its handbook on Radium Protection, the U. S. Bureau of Standards in 1938 recommended that photographic film carried in a pocket could serve as a rough test of occupational exposure (516, p. 3). More specifically it suggested that ordinary "dental film" with a paper clip on it be used. The paper clip served to distinguish between exposure to hard gamma-rays and soft radiation like beta-rays. In 1942 the photographic method of dosimetry was

considered a sensitive and exact method for measuring stray radiation (152).

Chemical Dosimetry and Therapeutics

Measurements of dosage in clinical therapy just prior to 1925 were being made by various methods. In X-ray therapy ionization chambers were popular because they were convenient and sufficiently accurate for most purposes. However, the Kienböck strips and the Sabouraud-Noiré pastilles were still common (192, 292). In radium therapy the ionization methods were not being used to the same extent particularly because of technical difficulties due to the size of the ionization chambers (364). The existing ionization chambers were too large to enable measurements of the radiation in the immediate vicinity of the radium source to be made. Photographic dosimetric methods in radium therapy also were not widely applied because they necessitated intricate manipulation and complicated masks that had to be worn by the technicians.

An erythema dose for the skin variously interpreted and estimated was also a guide³⁶ (see also p. 26-27, above). At the same time many involved in therapeutics began to recognize the problem

³⁶ At the Memorial Hospital in New York the threshold erythema dose in radium therapy was that quantity of radiation which, when delivered at a single sitting, produced in 80% of all cases tested, a faint reddening of the skin, in from two to four weeks after irradiation (8, p. 261).

that a unit of dosage was lacking and that a generally accepted unit of dosage was indispensable. To identify or to define a unit of dosage, something had to be known about the dose actually absorbed by the tissues. Though much was then known about the radiation emitted, very little was known about that absorbed. The clinical and biological acumen of all the pioneers who had the patience and the foresight to still make therapeutics so beneficial to mankind seems to be accentuated by this very lack of knowledge about absorbed dose.

This interest in determining the dose actually absorbed by the tissues probably prompted some of the biological studies in the early 1920's. The knowledge gained by these studies and the efforts made to understand the underlying mechanisms in radiobiology led to renewed studies on the chemical effects particularly of X-rays on aqueous solutions. It was technically difficult to conduct studies on the chemical effects of gamma-rays, important though they were therapeutically, because of their great penetrating power.

The renewal of research on the chemical effects of X-rays in the 1920's is notable from more than one point of view. The research involved departmental groups with various specialties. Some researchers were associated with university laboratories, such as the departments of chemistry, physics, biochemistry, and biophysics. Some groups were associated with institutes of medical research sponsored by various foundations. Some workers were associated

with the research departments in hospitals. Furthermore, the research that was done was of a decidedly quantitative nature, a fact conducive to applications in dosimetry.

Moreover, developments in the ionization method of dosimetry in the 1920's indirectly channeled some of the chemical research that was being done towards specific applications in dosimetry. The ionization method of dosimetry was, in effect, acknowledged as a reliable method when the international unit of radiation, the roentgen, was defined in 1928 in terms of the ionization produced in a cubic centimeter of air under specific conditions. Yet in 1930 a standard air chamber was not available. It was expected by those concerned with dosimetry that even when agreement would be reached on a standard instrument, not very many copies of the primary standard would be available for general use (400). Under the usual procedures in the United States, for example, the primary standard would be kept at the Bureau of Standards and there would be copies of it in only a few major laboratories. Measurements of radiation would, for the most part, be made by some secondary standard which would require calibration. From the practical point of view a method of dosimetry which did not depend upon specialized apparatus seemed most desirable. There were some chemical researchers who felt that a simple, satisfactory method could be developed from a chemical change induced by radiation (188, 400, 460).

In fact, a chemical method of measuring dose would have certain advantages. If the chemical system involved an aqueous solution containing substances made, for example, of light-weight atoms, that solution would have absorption and scattering properties that would closely approximate the behavior of tissue (460). Then, sensitive solutions, once identified, could be sealed in capsules and distributed by a central laboratory. After irradiation under actual clinical conditions, the capsules could be returned to the standard laboratory for analysis. Standardization would be further enhanced because the chemical reaction would act as an integrator of the X-ray output³⁷ over the entire period of irradiation and not just at a particular moment (544).

For a chemical method to be practical value in dosimetry, certain conditions would have to be satisfied (188, 400, 461, 544). First the chemical reaction would have to be sensitive to amounts of radiation in the order of magnitude of those used in therapy. Second, the chemical system would have to be stable enough before and after irradiation so that no spontaneous change would occur for at least several days. Third, the methods of measuring the change would have

³⁷ Apparently the ionization chambers available prior to 1933 generally were calibrated to give the intensity of the radiation in roentgens per second rather than total dose (8, p. 132). Since X-ray sources were known to be inconstant in their output (544) the total dose computed from ionization chamber readings was not always accurate.

to be relatively simple. Although there was general agreement upon these three conditions, other characteristics also considered important by some concerned with dosimetry were: a simple relation between dose and the chemical change it produces (460, 544); easily controlled factors, such as concentration or temperature, upon which the reaction depends (188); a comparable absorption and scattering of the radiation by the solution and by the tissue (460); reagents easily obtainable in required purity (400); and fairly inexpensive reagents which would suffice in small amounts (400, 460).

Of the chemical research that was being done and applied to dosimetry, that of Hugo Fricke (b. 1892), a biophysicist associated with the Cleveland Clinic Foundation in Ohio, was first to utilize the quantitative dependence of a chemical reaction on X-rays (188). In 1927, Fricke and his associates were studying the chemical effects of X-rays in aqueous solutions in order to understand the underlying mechanisms in radiobiology. Their earliest investigations involved the transformation of oxyhemoglobin to methemoglobin under the action of X-rays (189). Hemoglobin, a protein containing only four ferrous atoms per molecule with a probable molecule weight of 68,000, was changed on being irradiated into methemoglobin which contains iron in the ferric state. Since the action of the rays was so selective in having an effect only on the four ferrous atoms in the huge molecule, Fricke and his associate Sterne Morse chose a simpler

system containing ferrous ion--a ferrous sulfate system--for further investigation.

Studies of the ferrous sulfate system, which was composed of aqueous ferrous sulfate in dilute sulfuric acid, revealed that the reaction was independent of the initial ferrous ion concentration from 4×10^{-5} to 10^{-2} M ferrous sulfate in 0.8N sulfuric acid (187, 188). This led to the conclusion in 1929 that the primary action of the rays was on the water³⁸ (187). The activated water molecule, then, transformed the ferrous ions into the ferric. As long as ferrous ions remained in solution, the percent of ferrous ion transformed was linearly related to dose. However, the linearity of the response was also dependent upon oxygen, as well as a certain dose that could not be exceeded. The sharp break in the dosage curves at a dose of 29.0 regardless of the initial concentration of the ferrous ion (see Fig. 1 and 2) was indicative of the complete absence of oxygen or an air-free reaction beyond that point in the curve. Fricke and Morse assumed, then, that the oxidation of ferrous ion and the reduction of gaseous oxygen in solution were somehow related (187).

In addition to showing a linear response to dosage under certain conditions, the ferrous sulfate system had a high relative stability.

³⁸ Further studies in 1934 under the direction of Fricke at the Cold Spring Harbor Biological Laboratory in New York confirmed this "indirect action," of the radiation on the solute via the solvent (181).

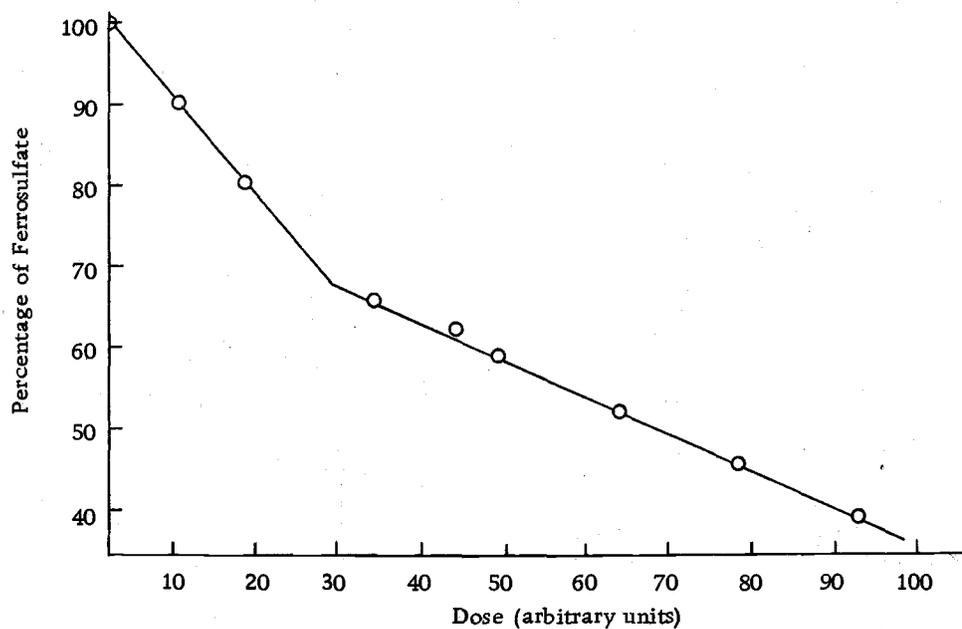


Figure 1. The action of different doses of X-rays on 0.00033 M ferrosulfate in 0.8 N sulfuric acid (187, p. 136).

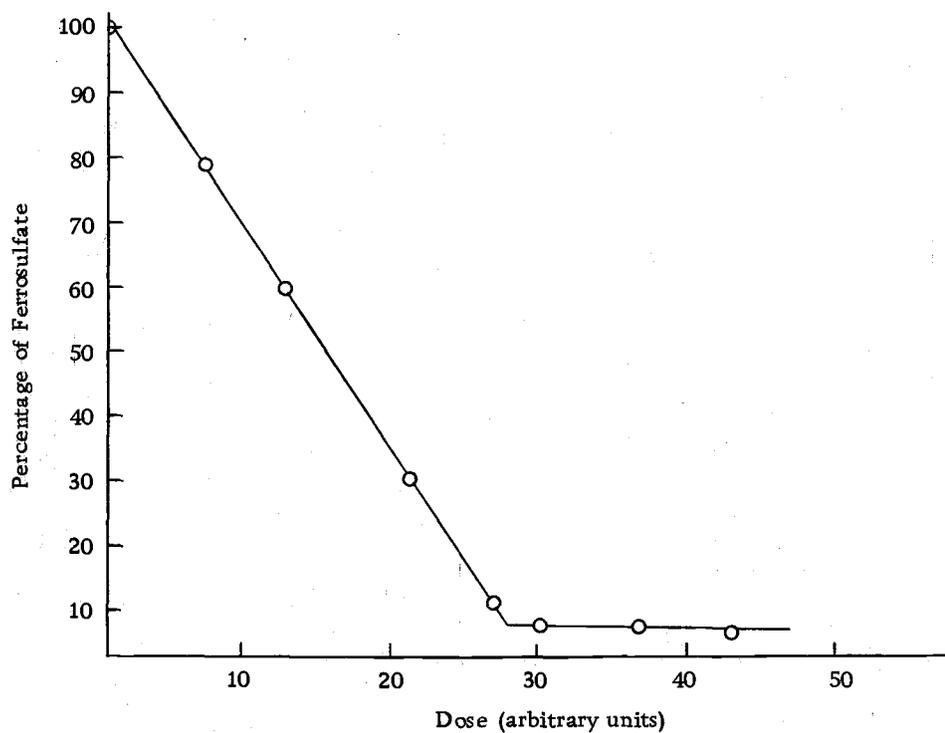


Figure 2. The action of different doses of X-rays on 0.00100 M ferrosulfate in 0.8 N sulfuric acid (187, p. 137).

The irradiated solution showed a spontaneous reduction amounting to only about 1% per day (188). Furthermore, the reproducibility of the reaction on irradiation was most satisfactory. Although in the graphical information (as reproduced in Fig. 1 and 2) which showed the percentage of ferrosulfate transformed the dose was given in arbitrary units, in 1927 Fricke and Morse made a series of laboratory tests with a specified dose of 1.04 kiloroentgens³⁹ (188). After working with numerous test samples, they found that their values for the percentage of ferrosulfate transformed agreed to within 1%.

The validity of the ferrous sulfate dosimetric system was also checked by comparing its performance with that of a standard ionization chamber (187). When exposed to X-radiation within the wavelength range of 0.2 to 0.75 Angstrom units (\AA) and after appropriate corrections were made, the chemical dosimeter agreed with the standard ionization chamber to within 1% in its determination of dose.

There was still another aspect of the ferrous sulfate reaction on

³⁹Since, in 1927, the roentgen had not yet been officially defined by the ICRU, Fricke and Morse probably used the term as it was defined by the physicist H. Behnken in 1924 and adopted by the German Röntgen Society. Behnken's definition is as follows: "The absolute unit of roentgen-ray dose is produced by that amount of roentgen-ray energy which by the radiation of 1 c. c. of air at 18°C. and a pressure of 760 mm. of mercury produces such a conductivity, that the quantity of electricity under saturation conditions amounts to one electrostatic unit. All the secondary electrons produced in the air must be utilized and the effects due to the walls of the chamber must be excluded. This unit is called a roentgen and shall be denoted by r" (quoted in 8, p. 126-127).

irradiation which recommended it as a chemical dosimeter. The oxidation of ferrous sulfate to ferric sulfate was independent of the wavelength of the radiation between the limits of 0.204 and 0.765 Å (187). However, the analytical procedure in the use of the dosimeter was a drawback. The titration which was required to determine the percentage of ferrosulfate transformed was elaborate and required a trained technician. At the same time the given dose of 1.04 KR for a 4×10^{-5} M ferrosulfate solution caused about a 44% transformation of the original concentration of ferrous ion. It seems that the dose required for a conveniently-measurable change was large considering that the system was proposed as a dosimeter for therapeutics.

Subsequent to the detailed investigations of the ferrous sulfate dosimetric system, Fricke directed many other studies of the chemical effects of X-rays on aqueous systems. With his associates he investigated the reduction of the dichromate ion from the hexavalent state to the trivalent state (183), the reduction of oxygen to hydrogen peroxide (180), the oxidation of the nitrite ion to the nitrate ion (186), and even the effects of X-rays on organic compounds (190). Although none of these reactions qualified as well for application to dosimetry as did the ferrous sulfate reaction, results of these studies gave Fricke and his associates valuable insights into the mechanism of chemical reactions induced by radiation. The reduction of the dichromate ion as well as many of the other reactions were accompanied

by the formation of hydrogen peroxide. This confirmed their earlier assumption (see p. 88, above), that the primary action of the X-rays was on the solvent and a secondary reaction effected the change in the solute.

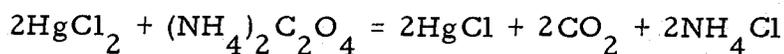
While the work that was begun by Fricke in Ohio was being continued at the Cold Spring Harbor Biological Laboratory in New York, research of a similar nature was being conducted at the Rockefeller Institute for Medical Research also in New York. In 1929, two chemists at the Rockefeller Institute, Ralph W. G. Wyckoff (b. 1897) and Lillian E. Baker (b. 1890), proposed that Eder's solution⁴⁰ be used for dosimetry (544). Eder's solution, composed of aqueous corrosive sublimate (HgCl_2) and ammonium oxalate [$(\text{NH}_4)_2\text{C}_2\text{O}_4$], was suggested for dosimetry as early as 1907 (see p. 45, above). However, prior to 1929 no quantitative information about the sensitivity of Eder's solution to X-rays was available.

The investigation of Wyckoff and Baker showed that the precipitation of calomel (Hg_2Cl_2) from Eder's solution by the action of X-rays was proportional to the dosage (544). However, the proportionality existed only if pure salts were used in making up the Eder's solution. Traces of metallic impurities made the solution

⁴⁰ Ammonium oxalate-sublimate solution has been called Eder's solution after Joseph Eder (1855-1944), an Austrian photochemist, who made extensive photochemical investigations of the system.

sensitive to visible light. Wyckoff and Baker were able to prepare a solution of the required purity by recrystallizing the chemically pure components (four recrystallizations of HgCl_2 and three of $(\text{NH}_4)_2\text{C}_2\text{O}_4$ proved sufficient). Prior to preparing a desired concentration of Eder's solution, then, they determined the exact concentration of the aqueous solution of each salt--that of the HgCl_2 by analysis for the monovalent form of mercury following reduction by phosphoric acid, that of $(\text{NH}_4)_2\text{C}_2\text{O}_4$ by titration with potassium permanganate.

As was known from the previous work of Schwarz (see p. 45, above), the reaction induced by X-rays proceeded according to the following:

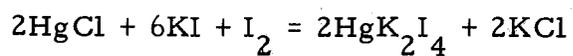


Since the precipitate was very fine-grained and amounted to but a few milligrams, Wyckoff and Baker suggested a special procedure for filtering, washing, weighing, and drying it (544). They proposed that accurate estimates of the extent of reaction, and therefore of dose, could be made by measuring the precipitated HgCl .

However, the curves obtained when the milligrams of HgCl were plotted against duration of exposure were not strictly linear as is evident from a representative curve reproduced in Figure 3. Still, Wyckoff and Baker felt that the curves were essentially straight lines; departures from linearity occurred only after long irradiation. The

curves did not pass through the origin simply because HgCl was slightly soluble in water. The Eder's solution was made more sensitive to X-radiation than is apparent in the data in Figure 3, by increasing the concentration of HgCl₂ in the solution. For example, the dose required for the precipitation of about 3 mg of HgCl was more than doubled when the HgCl₂ solution was only half as concentrated. Under the experimental conditions the lowest dose to give a measurable amount of HgCl was about 870r.

In proposing Eder's solution for dosimetry, Wyckoff and Baker emphasized the sensitivity of the system, the proportionality between the precipitation of the calomel and the dose, and the simplicity of the analytical procedure which they proposed for the measurement of the extent of reaction. However, their analytical procedure presented a problem in that it was too lengthy a process. Edith Quimby (b. 1891) and her associate Helen Downes of the Department of Biophysics and Chemistry at the Memorial Hospital in New York recognized that clinicians would want a more rapid method of analysis. Therefore, in 1930, they suggested a procedure which involved a modification of a known analytical method for estimating mercury as mercurous chloride by means of iodine (I₂) and sodium thiosulfate (Na₂S₂O₃) (400). In the presence of excess potassium iodide (KI), HgCl was oxidized by I₂ to potassium mercuric iodide (HgK₂I₄) according to the equation:



Any I_2 remaining in the system can be titrated with $\text{Na}_2\text{S}_2\text{O}_3$. Comparison with a blank titration of the original solution provided a measurement of the amount of iodine that was required to oxidize the HgCl .

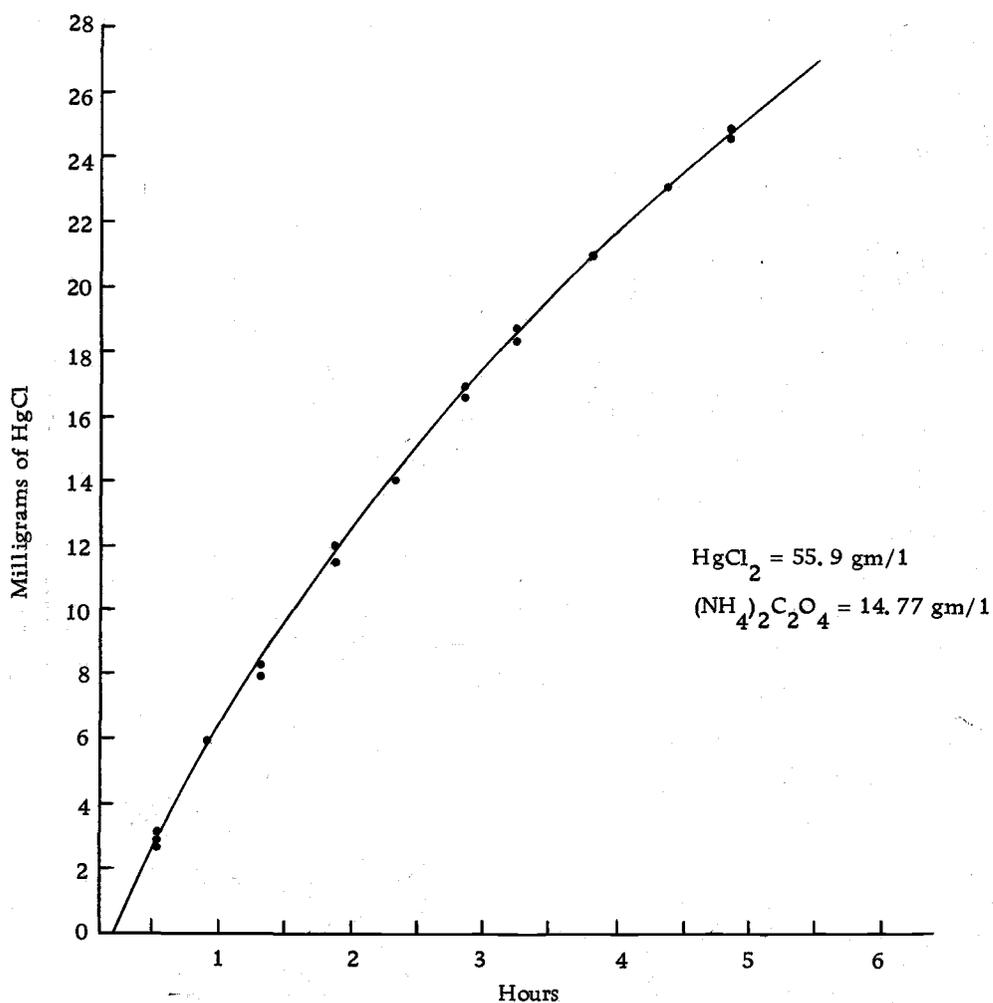


Figure 3. Weights of HgCl obtained by irradiating for different periods of time an Eder's solution of convenient strength (544, p. 552).

When using this analytical procedure much smaller amounts of HgCl could be measured than was possible by the Wyckoff and Baker method. Quimby and Downes reported that 0.35 mg of the precipitate were measured with little difficulty (400). The sensitivity of the analytical method was increased if sufficient iodine were added to the precipitate (this left a readily titrable amount of iodine after the oxidation) and if a strong solution of sodium thiosulfate were used.

By their investigations, Quimby and Downes extended the range over which the Eder's solution dosimetric system was useful. Wyckoff and Baker obtained their data with low-voltage (30 kv) unfiltered radiation (544). Quimby and Downes showed that a proportionality between the amount of precipitate and the dose existed also with 60 kv unfiltered radiation and 200 kv filtered radiation. A curve, typical of their data with 200 kv radiation (see Fig. 4), shows a distinctly linear relationship between the precipitate formed and the length of exposure. The curve also goes through the origin which shows that there was little if any spontaneous reaction.

There were other characteristics of the system that added to its qualifications for dosimetry. Satisfactory results were obtained with volumes of Eder's solution of less than one cubic centimeter. Also, preliminary studies showed that the system could be used for the measurement of radium radiation. The data that was obtained indicated that the system had possibilities as a secondary gamma-ray standard also (400).

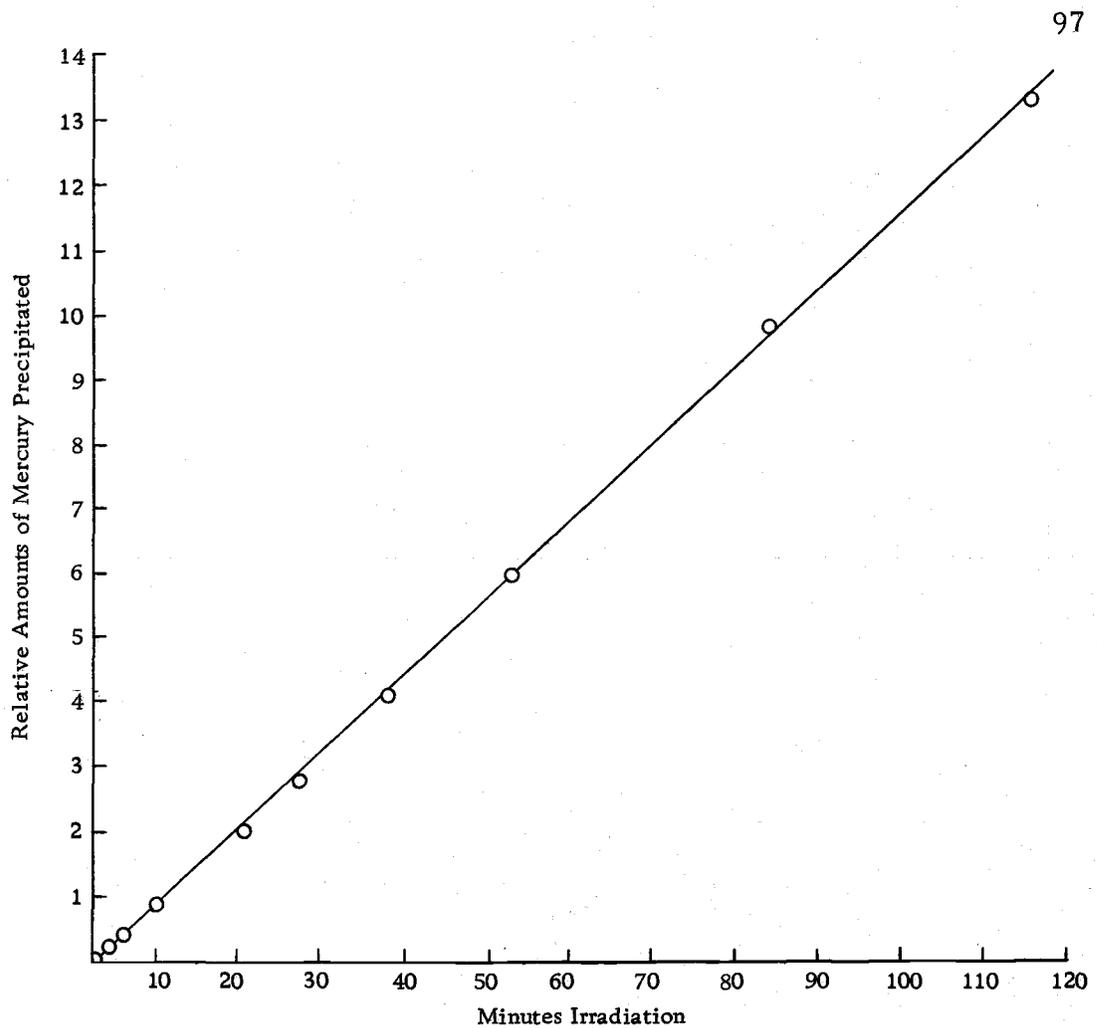


Figure 4. Curve showing relation between amount of precipitate and time of irradiation--all other factors remaining constant (400, p. 469).

While the researchers at the medical institutes⁴¹ were making definite proposals regarding chemical systems for dosimetry and were supporting their proposals with significant data about the desirable characteristics of the systems, extensive research on the

⁴¹Fricke and Morse, Wyckoff and Baker, and Quimby and Downes were all associated with medical institutions.

chemical effects of ionizing radiation was being carried out in the laboratories of the Department of Biophysics at the University of Minnesota. In 1928, under the direction of the biophysicist Wilhelm Stenstrom (b. 1891) studies were made on the effects of radiation on certain amino acids (459). There was a proportionality between the dose and the change in the amino acid and the extent of change showed little dependence on the initial concentration of the acid. Speculation on the mechanism of reaction led to the assumption that the change in the amino acid was caused by the ionized water which was produced by the radiation. The assumption that the chemical reaction associated with irradiation was proportional to the ionization effect on the water seemed to be an accepted line of thought in the late 1920's (see p. 88, above). In fact this very idea prompted the studies on acetylene.

In 1929, although studies were still conducted on biochemical compounds such as cholesterol and tyrosine, investigation of the effect of X-radiation on acetylene and propane in the gaseous state were also made (363). Stenstrom decided to make the latter investigations because of the implications that the assumption about the proportionality between the radiation-induced chemical change and the ionization seemed to have. He felt that if the assumption were valid then the same chemical change should be produced by different kinds of radiation as long as the total ionization due to the radiation was the same.

Since the polymerization of acetylene was caused by alpha-radiation (339), Stenstrom proceeded to test whether or not large doses of X-radiation would have the same effect. The large dose of X-radiation which Stenstrom used in his experiment had an associated total ionization equivalent to that of the alpha-radiation from radium. He reported, however, that even after irradiation for 145 hours there was no observable effect in the acetylene (457).

The extensive studies over a two-year period enabled Stenstrom to classify the irradiated chemical systems into four groups according to differences in the quantitative relationships between the dose and the change produced (457). There were those systems such as cholesterol in benzene that showed no measurable effect due to irradiation, those such as trypsin and also hemoglobin in which the change followed the mass action law,⁴² those such as tyrosine in phenol and also aqueous ferrous sulfate in which the change was directly proportional to dose, and those such as cholesterol in chloroform in which no simple relation between the dose and the change could be found.

In the latter 1920's when chemical systems were being considered for dosimetry, those systems in which the chemical change on irradiation was directly proportional to a given dose were the ones

⁴² According to the mass action law the concentration of the reacting substances determines the extent of the forward reaction.

that were being proposed for dosimetry. The direct proportion was not strictly necessary since systems without such a response could still be calibrated to give reliable measurements. However, with a direct proportion existing between the chemical change and the dose, analytical procedures were usually much simpler.

By 1931, Stenstrom himself channeled his research in the direction of finding a simple method for measuring X-ray dosage (458). Since he thought that some color change might be found for that purpose, he proceeded to investigate the effect of radiation on a number of chromatic substances. Rather than work with a solid as was used in the Sabouraud-Noiré chemical dosimeter (see p. 34, above), Stenstrom felt that aqueous solutions were better because water absorbed and scattered X-rays to about the same extent as tissues and color changes in solutions could be measured accurately by means of colorimeters or spectrophotometers if they were available. Of all the substances tested--methylene blue, potassium dichromate, potassium permanganate, gentian violet, acid fuchsin, 1% ferric ammonium citrate, 1% cupric nitrate, and 1% cobaltous chloride--methylene blue was selected for more detailed studies. A highly diluted aqueous solution of methylene blue (0.00016%) gave a strong color and Stenstrom felt that since very small amounts of substances were changed on irradiation it was necessary to use very dilute solutions in order to have a measurable effect.

The results of the work on aqueous methylene blue were reported at two successive annual meetings of the Radiological Society of North America in 1931 (460) and in 1932 (461). Methylene blue was presented as a means of standardizing roentgen dosage. Stenstrom and his associate Anne Lohmann of the Section of Biophysics and Cancer Institute at the University of Minnesota were cognizant of the accuracy with which measurements could be made with a standard air chamber and how well they could be reproduced with other chambers properly constructed. However, they felt that the standard air chamber was not designed to record the average radiation intensity over a certain area of the skin, but rather the intensity in a narrow beam of rays. Though it was claimed that other ionization chambers were available for the measurement of total radiation at the skin surface, not enough was known about them or whether or not they actually measured the dose given to the tissues (460).

Aqueous methylene blue was suitable for dosimetry because it was rapidly discolored by irradiation and the color change could be measured simply and quickly by means of a spectrophotometer. Stenstrom and Lohmann did not claim to have confirmed the practicality of the system for comparison of dosage at different places. They did experimentally determine a standard curve showing the relation between the duration of exposure and percent decomposition or color change (see Fig. 5). All determinations were made under

the following conditions: 200 kvp, 30 ma, a filtration of 0.5 mm of copper and 1 mm of aluminum, a distance of 50 cm from the focus to the surface of the solution. An ionization chamber recorded an intensity of 82 r per min at the point of interest (460).

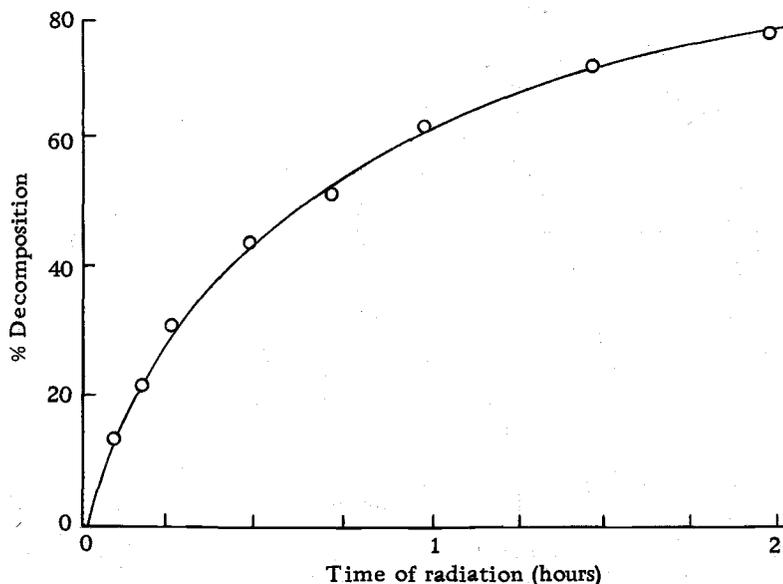


Figure 5: Decomposition of methylene blue by roentgen irradiation (461, p. 307).

Although the methylene blue system had a decided advantage for dosimetry in that it had very nearly the same effective atomic number as water or body tissue and therefore absorbed X-radiation to the same extent, certain precautions had to be taken when using the system for dosimetry. Extreme care had to be taken to keep the system free of organic impurities because they had a pronounced effect in reducing the change produced by the radiation (460). Furthermore, since the color of methylene blue was to some extent affected by exposure to light, especially ultra-violet light, the solution had to be sealed in light-tight containers.

Measurements of the type needed for comparison with the standard curve could only be made where spectrophotometers were available. Stenstrom and Lohmann used a spectrophotometer to determine the concentration before and after the exposure. Though they gave a complete description of their procedure for measuring the absorption at 6700 \AA with the spectrophotometer, they did admit that some training was required to obtain satisfactory accuracy in taking readings. They also recommended that the irradiated capsules be sent to the central laboratory (housing the spectrophotometer) for measurement within 24 hours of the exposure to minimize the effects of any post-irradiation action of light.

Stenstrom and Lohmann did not suggest any mechanism for the reaction behind the color change of methylene blue due to irradiation. They did imply that the effect of the radiation upon the solute was influenced by the solvent, in this case, distilled water. It is not clear whether they were suggesting an indirect effect, however.

While at the University of Minnesota the initial research on the chemical effects of ionizing radiation developed into an intensive study of the color changes produced by the action of X-rays, the physicist James A. Crowther (b. 1883) and his co-workers at the University of Reading in England examined the effects of X-rays from a different point of view. They conducted systematic quantitative studies on colloids subjected to radiation exposure just short of that required

for a chemical change. Again, the aim of their study was to obtain some insight into the mechanism of the effects of X-rays on living matter. From observing the action on simple inorganic colloids, they hoped to infer the effects on complex organic colloids that make up the living cells (112). They began, in 1927, with the colloidal solutions of metals--iron, copper, silver, and gold (112). In 1928, they studied viscosity changes in colloidal ceric hydroxide (164). Measurements of the percent change in viscosity showed that though finally the viscosity increased, initially the viscosity decreased with exposure. They accounted for this by assuming that the increase in viscosity was due to the aggregation of particles that were no longer repelled because the colloidal particles were gradually discharged by the initial exposure.

Later in the 1930's Crowther and his associates worked with colloidal ferric oxide (115) and also with colloidal carbon (114) and colloidal graphite (113). In working with colloidal carbon that had an absorption towards X-rays similar to water, they felt that their study had a possible bearing on the problem of X-ray dosage in therapeutical work (114). They reported that viscosity changes occurred with comparatively small doses of radiation (113). Though doses of this order of magnitude rarely produced chemical changes, they were the doses well within what was known as the therapeutic range. This realization of the comparative dose range between that required for a chemical change and that required for therapy was important from the point of

view of future uses of chemical dosimeters. Furthermore, even if Crowther did not use the principle behind his analytical method for proposing a specific dosimetric system, his technique of observing viscosity changes due to irradiation was a fundamental technique for future dosimeters that would rely on such changes in state.

Some work on the chemical effects of ionizing radiation that was related to dosimetry was also being conducted in the 1920's at the University of Stuttgart in Germany. Richard Glocker (b. 1890), a Professor of X-ray Technology there, directed research on the action of X-rays on an iodoform-chloroform system (31). The research under Glocker expanded upon work done earlier in the century (see p. 32, above) and led to precise measurements not only of the extent of reaction with the duration of exposure, but also of the extent of reaction when the intensity of irradiation was varied. The interval of time during which secondary effects were measurable was also noted. These investigations disproved the claim made in 1904 (178) that the amount of iodine formed was proportional to the energy absorbed during irradiation.

Studies at Stuttgart were also made on the decomposition of hydrogen peroxide by X-radiation (209, 405). It was observed that the action on a peroxide solution in potassium persulfate was dependent on the wavelength of the X-ray. This was expected since irradiation could also be responsible for the formation of hydrogen peroxide (see

p. 92, above).

Extensive work on the chemical action of X-rays that was related to dosimetry was also conducted in the 1930's in the Department of Chemistry at the University of Illinois. Under the direction of George L. Clark (b. 1892) research was carried out on many chemical systems which were considered as possibly significant in interpreting physiological effects (99). The results of some of these studies led to the conclusion that the sensitivity of a system to ultraviolet light was no indication that such a system would be sensitive to X-rays in the region of 0.2 to 0.3 Å (100). Furthermore, reactions involving oxidation and reduction were most affected by irradiation. Also, reactions in the field of organic chemistry showed much larger changes due to irradiation than those in the inorganic area (98).

Clark was interested, as well, in the mechanism of the reactions induced by radiation. To test the supposed influence under irradiation of the formation and decomposition of hydrogen peroxide on chemical reactions in aqueous solutions, he studied the oxidation of potassium iodide in solution in the presence and in the absence of oxygen (the hydrogen peroxide mechanism required the presence of oxygen) (100). He made similar studies of the reduction of potassium nitrate. Since the decomposition of potassium iodide in the absence of oxygen took place to a larger extent but not directly proportional to the dose, Clark concluded that the mechanism of the formation and

subsequent decomposition of hydrogen peroxide was not essential to oxidation in aqueous solutions, but could contribute to it. However, the hydrogen peroxide mechanism played no role in the reduction reaction since the chemical change was a straight-line function of the dose regardless if oxygen were present or not.

Clark and his associates also determined the energy relations in the photolysis of potassium nitrate by X-rays. From their reported measurements and calculations they showed that less than 0.8% of the energy absorbed and utilized in the formation of ions in solution appeared as chemical dissociation of the potassium nitrate molecule (100). Such energy relations were to play an important role in future radiation chemistry. That huge doses of radiation were generally required for a measurable chemical effect would also serve to determine the uses of chemical dosimetry in the future.

Chemical Dosimetry in Developmental Perspective

During the 1925-1942 period chemical dosimetry had taken on a definite quantitative nature compared with the chemical dosimetry of the early 1900's. Perhaps this change in character stemmed from the fact that early dosimetric methods were proposed, for the most part, by physicians or radiologists. These men utilized certain basic observations in developing practical and simple methods of dosimetry which they themselves used in actual practice. Their

attention was directed primarily at the effects of the dosimetry they were advocating, that is, at the development of a science of radiology that would be safe and beneficial to mankind.

During this later period, however, dosimetric methods were proposed, for the most part, by biophysicists or chemists associated with medical research centers connected with hospitals or university laboratories. These scientists were engaged in research and, because of circumstances, they were not exclusively concerned with practical applications as their predecessors had been. The production of a practical dosimetric method was not their sole purpose. Rather, their research was directed at establishing foundations for biophysical and biochemical processes. Although the dosimetric methods proceeded from this research, there is no indication that these scientists themselves used the dosimeters which they developed. The actual use was left to radiologists or technicians.

In fact there are no indications as to the extent to which any of the newly proposed dosimetric systems were used. Keeping in mind the requirements for an ideal chemical dosimeter, it seems that each dosimeter--the ferrous sulfate, the Eder's solution, and the methylene blue--had certain characteristics in its favor. Still, to be judged practical, the dosimeter would have to be used under the actual clinical conditions for which it was intended. The lack of evidence of actual clinical applications would not indicate that the

proposed systems were ineffective in measuring radiation. However, it does suggest that the new dosimeters did not find general acceptance among radiologists.

Some of the scientists referred to above were mainly interested in accumulating data towards a defined goal; others were also interested in accounting for this data. The information that was gathered and compiled led in many instances to new proposals but it also provided evidence to disprove previous claims. For example, the research on the iodoform-chloroform system early in the 1920's at Stuttgart University showed that the amount of iodine formed was not proportional to the amount of energy absorbed during irradiation as was claimed in 1904 (178). The observed liberation of iodine depended on the solvent and proceeded from a secondary reaction whose speed was entirely independent of the source of the radiation, its energy, and its quantity (31). This dependence on the solvent was incorporated later in the 1920's into the concept of indirect action, that is, the action of the radiation on the solute via the solvent, and took on importance during the 1925-1942 period of research. Chemical effects of ionizing radiation were examined from that point of view; in fact, varying the solvent was a way of controlling the chemical effect of the ionizing radiation. This theoretically-based experimental fact was significant for the development of future chemical dosimetric methods. Knowledge that chemical systems usually required huge

doses of radiation for a measurable chemical change was another experimental fact which in the future redirected the uses of chemical dosimeters.

CHAPTER V

IONIZING RADIATION (1942-1962)

Though the forms of ionizing radiation that played an important role in irradiation technology from 1942 until 1962 had been identified prior to 1942, it would perhaps be impossible to duplicate the rapid growth of irradiation technology without the events of December 2, 1942. Those events were succinctly described by Enrico Fermi (1901-1954) when in his December monthly report at the Metallurgical Laboratory in Chicago he wrote: "The chain reacting structure has been completed on December 2 and has been in operation since then in a satisfactory way" (170, p. 270). This "chain reacting structure" had an unusual history. Although in its formation and development military objectives figured prominently, in its final applications it can be evaluated from more than one point of view. The force of circumstances which seemed to be determining the course of global affairs at the end of the 1930's definitely directed the initial use of this "chain reacting structure" for the building of an atomic weapon considered essential for military objectives. At the same time this "chain reacting structure" was recognized by some who were involved in its development as highly useful for research (170, p. 308). It had a high sensitivity for neutrons and was a neutron multiplier of almost

unlimited powers. Potentially, it was a marvelous experimental tool. To others, this "chain reacting structure" represented an unusual source of energy which had obvious promise in satisfying the needs of man.

Prelude to the Manhattan Project

After the demonstration of the existence of the neutron in 1932 (see p. 52-53, above) and after the discovery of artificial radioactivity in 1934 (see p. 58-59, above), much investigation in physical laboratories was directed at methods of producing artificial isotopes by the bombardment of stable elemental forms. The cyclotron and other types of accelerators provided the high-energy particles for such bombardment studies. At the Physical Laboratory of the University of Rome much attention was given to neutron bombardment experiments. Under the direction of Enrico Fermi most of the elements, in the order in which they were listed in the Periodic Table, were bombarded with neutrons from a radon-beryllium source (173). The isotopes which were obtained in most cases were atoms of the elements with the next higher atomic number due to neutron capture and beta-particle emission. When uranium, the last of the known elements, was bombarded with neutrons, again a beta-emitting substance was the product. To the investigators this suggested the possibility of transuranium elements.

This question was taken up for study by a team of scientists working in Berlin at the Kaiser Wilhelm Institute for Chemistry (228, p. 141), specifically, Otto Hahn (1879-1968), Lise Meitner (b. 1878), and Fritz Strassmann (b. 1902). Hahn and the Austrian Lise Meitner had been a research team in an independent department of radioactivity at the Kaiser Wilhelm Institute ever since its founding in 1911. Strassmann joined the two shortly after obtaining his doctorate in 1929. From 1935 until 1938 this group conducted an intensive investigation of the neutron bombardment of uranium and also of thorium. According to Hahn, the data collected in these studies supported the view held by Fermi and others regarding the process of nuclear transformation. The capture of neutrons by nuclei resulted in products which were usually beta-emitters. The products then were isotopes of elements in the immediate neighborhood of the irradiated elements, that is, elements whose nuclear charge was changed by one unit. To quote Hahn: "Prior to 1938 nothing happened to compel anybody to move away from this position" (228, p. 142). When uranium was the target of the bombardment, it was assumed that the product nuclei had higher electric charges than those of uranium atoms. Perhaps this view was taken because the chemical characteristics of the products seemed to identify them as higher homologues of the platinum metals. At that time the transuranium elements were considered to be homologues of the platinum metals.

The experiments on the neutron bombardment of thorium suggested a new scheme of nuclear transformation since both alpha-particles and beta-particles were emitted. Following the neutron-capture event, it was proposed that an isotope of radium was formed by alpha-particle emission. This was followed by beta-emission which gave rise to an isotope of actinium. No steps were taken, however, to isolate either the radium or the actinium isotope until certain complications developed. When further research and countless observations revealed other products whose half-lives and chemical characteristics did not fit into the earlier proposed decay scheme, steps were taken to verify the "radium" isotope experimentally. These experiments in fractional crystallization led to the startling report in January of 1939 that the "radium" isotope had the chemical characteristics of barium (229). Therefore, Hahn and Strassman concluded that if barium were one of the products, the other product must have been one with an atomic weight equal to the difference between the atomic weight of barium and of uranium. The other product in what seemed to be a fission process must have been one of the elements in the middle of the platinum group (ruthenium, rhodium, or palladium).

In the meantime, Lise Meitner fled to Sweden in the spring of 1938 following the invasion of Austria by Adolf Hitler (228, p. 151). Prior to publication, Hahn and Strassman communicated their

conclusion re the fission of uranium to Meitner. Meitner was able to discuss the implications of the communication with her nephew Otto Frisch (b. 1904) of Copenhagen. Together they foresaw the consequences of the large amounts of energy released in the fission process. They also concluded that the unknown product of the fission of uranium was krypton which they determined by subtracting the nuclear charges of barium and of uranium rather than their atomic masses. Sensing the import of their deliberations, Frisch and Meitner immediately notified Niels Bohr of their conclusions which they subsequently verified (353).

Niels Bohr, who was on a lecture engagement at Princeton, left Copenhagen for America before Meitner and Frisch were able to conclude their experiments. Still, there was probably no one more prepared or more qualified with whom Bohr could discuss the implications of the fission discovery than Enrico Fermi, then in America as a refugee⁴³ from fascism. In January of 1939, Fermi was engaged in research at Columbia University. Bohr and Fermi considered the topic at length with other physicists also at the Conference on Theoretical Physics which met in Washington later that month (170, p. 2). After the Washington conference Fermi was determined to

⁴³Since Enrico Fermi was an anti-Fascist, he had chosen not to return to Italy after he had received the Nobel Prize in Physics on December 10, 1938, at Stockholm (441).

pursue the question of possible neutron emission accompanying the fission process. He knew that theoretical considerations suggested an energy release due to fission of the order of 200 million electron volts (354). Although experimentation pointed to a smaller value (17), Fermi saw the possibility of increasing that value many-fold. Fermi felt that if neutrons were emitted as products of fission they could be responsible under precise conditions for further fission reactions. He envisioned a chain reaction and the consequent release of huge amounts of energy. In March, 1939, Fermi and his associates at Columbia reported that neutrons were produced in uranium bombardment with neutrons⁴⁴ (15). Such a report provided the foundation upon which the theory of a chain reaction could be formulated.

The Manhattan Project and the Development of a Reactor

The possibility of a chain reaction and its implication could have spurred scientific imaginations to devise any number of experimental studies. However, the immanence of a war in the spring of 1939, the extent of which was uncertain, focused the attention of scientists and non-scientists alike on the military potentialities of the energy released by a chain reaction. The fission of uranium had been

⁴⁴The liberation of neutrons in the nuclear fission of uranium was verified in an independently published report from Paris (230, 231).

successfully carried out in a number of laboratories in America as well as in Europe after the initial announcement by Hahn and Strassmann. That a chain reaction could be applied in the construction of an explosive weapon was a possibility. American and British scientists and, perhaps even to a greater degree, many refugee scientists from Nazi-occupied territories were concerned when and by whom such a formidable possibility would be first realized.⁴⁵ In October of 1939 after President Roosevelt had received a letter from Einstein⁴⁶ about Germany's capacity of producing an atom bomb, American universities engaged in uranium research were given financial assistance by the U. S. Government and secrecy began officially to cloak all operations (223, p. 10). In addition, the secret efforts of the laboratories involved were placed under the coordinating services of the Office of Scientific Research and Development in Washington.

It was not until June of 1942, however, that the urgency of actual production of nuclear weapons was realized by the U. S.

⁴⁵Fermi later recalled how "Contrary to their traditions, they [the scientists] set up a voluntary censorship and treated the matter as confidential long before its importance was recognized by the governments and secrecy became mandatory" (174, p. 21).

⁴⁶Three Hungarian refugee physicists--Leo Szilard (1894-1964), Eugene Wigner (b. 1902), and Edward Teller (b. 1908)--convinced Einstein in the summer of 1939 that the President of the United States should be warned of Germany's capacity of producing an atom bomb (223, p. 10).

Government. Officially then, there was a transition from the research and development stage into the building of large-scale production facilities, all under the cover of the Manhattan Project.⁴⁷ The decision to build the production facilities, however, really anticipated the completion of the research leading to a controlled chain reaction. Theoretically a chain reaction was possible but this possibility had not yet been demonstrated experimentally. The U. S. Government took the risk that the theory would be reduced to practice and, in effect, demanded an accelerated program to that end. Without the accelerated program which was demanded and, perhaps more importantly, financed by the government, the activities that led to the development of a "chain reacting structure" most probably would have taken a much longer time.

In the research that led to the development of the chain reaction, there were two determined avenues of approach. One involved the separation of the rare isotope, uranium-235, from natural uranium⁴⁸ because uranium-235 was the isotope responsible for the

⁴⁷ Initially, the unit within the Army Corps of Engineers that was assigned the task of administering and supervising the production of a nuclear weapon had its headquarters in New York and was therefore named the Manhattan District. The Manhattan Project included the District as well as all scientific, strategic, and governmental aspects involved in the building of the first nuclear weapon (223, p. 9).

⁴⁸ Natural uranium is a mixture of several isotopes of which only two are considered abundant. Still of the two, uranium-238 is 138 times as abundant as uranium-235.

slow neutron fission of uranium. Therefore, given uranium containing a high percentage of uranium-235 a chain reaction could easily be produced. The difficulty lay in the isolation of uranium-235 on a large scale. One selected method of separation was the gaseous diffusion method being developed by the team at Columbia University (223, p. 19). The other selected method of separation was an electromagnetic process being developed at the University of California (223, p. 36). The objective of these processes was the isolation of a sufficient mass of uranium-235 so that its volume would approach a "critical size," that is, a volume such that the leakage of neutrons produced by fission would no longer counterbalance the trend toward a chain reaction (223, p. 41).

The other avenue of approach leading to the development of a chain reaction made use of natural uranium. In that case, the effective use of the fission-produced neutrons depended on the proper assemblage of the uranium to minimize the loss due to absorption by uranium-238. It was known that uranium-238 absorbed slow neutrons giving rise to the radioactive isotope, uranium-239. This was considered a competitive reaction in taking up neutrons needed to sustain a chain reaction. After the discovery of plutonium-239 at the University of California in the spring of 1941 (302), the competitive reaction which led to uranium-239 took on significance. Uranium-239 disintegrates by two successive beta-emissions to plutonium-239 (by way

of neptunium-239) and, like uranium-235, plutonium undergoes fission by neutron bombardment. In the months prior to the formation of the Manhattan Project, the method using natural uranium was being developed perhaps most intensely at Columbia University under Fermi (172). Related work was also being conducted at Princeton University (223, p. 306), at the University of California (223, p. 149) and at the University of Chicago (223, p. 26). With the launching of the Manhattan Project, all work on the atomic pile⁴⁹ was centralized at the newly established Metallurgical Laboratory⁵⁰ at the University of Chicago under the directorship of the physicist Arthur H. Compton (1892-1962) (223, p. 27).

Since the energy of the fission-produced neutron was of the order of 1 Mev, it was necessary for effective capture to slow down the neutron to an energy as low as that of thermal agitation. Studies at Columbia (12) had shown that absorption of neutrons in graphite was small enough that it would be an ideal material for slowing down neutrons. A series of tests made possible the development of a mathematical method for calculating the life history of a neutron from the

⁴⁹What was later called a nuclear reactor was from the very beginning referred to as the "pile" because of the nature of the assemblage of the device, that is, it consisted of layers upon layers of uranium and graphite.

⁵⁰The name of the laboratory was deliberately intended not to reveal the nature of the work carried on there.

time of its emission as a fast neutron until its final absorption in a column of graphite. This proved important in determining the size of the graphite layers in an atomic pile. Then, to assure as small as possible parasitic loss of neutrons to uranium-238, the uranium was arranged in lumps throughout the graphite (170, p. 119). Since this provided a non-uniform distribution of the uranium, there was less probability that a neutron would encounter a uranium-238 atom during the slowing down process.

The problem of escaping neutrons by diffusion out of a system of finite dimensions was also considered. To quote Fermi: "It was clear in 1941 that the balance of neutrons capable of sustaining a chain reaction, even if at all positive, would be so small as to make it necessary to use a system of very large size in order to eliminate most of the loss of neutrons by escape" (174, p. 23). Since at that time available methods rarely permitted the measurement of nuclear properties with an accuracy better than 10%, calculation alone was inadequate in determining the minimum dimensions of the atomic pile that would be needed to achieve a chain reaction. The critical size of the pile had to be determined empirically.

The first exponential⁵¹ experiment was carried out at Columbia

⁵¹With an atomic pile not of critical size, fission could still occur. However, a plot of the rate of rise of the neutron count due to fission would eventually level off in the form of an exponential curve; hence such trial runs were called exponential experiments.

in 1941 (18). It gave discouraging results in that it indicated that even if the structure were built to an infinite size, there would still be a negative balance of neutrons. During 1942 several other exponential experiments (163, p. 390) were conducted in an attempt to improve conditions of the first trial. Experiments had shown that impurities were responsible for the loss of an appreciable fraction of neutrons. Since by September of 1942 better graphite and practically pure uranium oxide together with some cast uranium metal were available, Fermi drew up the final dimensions of the pile. These dimensions were based on the measurements of "k"⁵² in the exponential piles and on his theory about the life history of a 100 neutrons (see Fig. 6). Fermi further predicted the behavior of the pile in its approach to criticality and he also outlined the function of the controls throughout the operation (170, p. 216). The controls consisted of cadmium rods which could be inserted into transverse slots in the pile. Since cadmium metal was a good absorber of neutrons, a negative balance of neutrons was maintained with the rods in place. In this way the cadmium rods were a means of controlling the chain reaction and guarding against an atomic explosion.

Since the scientists had complete confidence in Fermi's

⁵²This "k" was the number by which one multiplied the number of neutrons of one generation to find the number of neutrons in the second generation.

knowledgeability about the operation, they began the actual construction of the first chain reacting unit according to his direction late in October on the campus of the University of Chicago (223, p. 69).

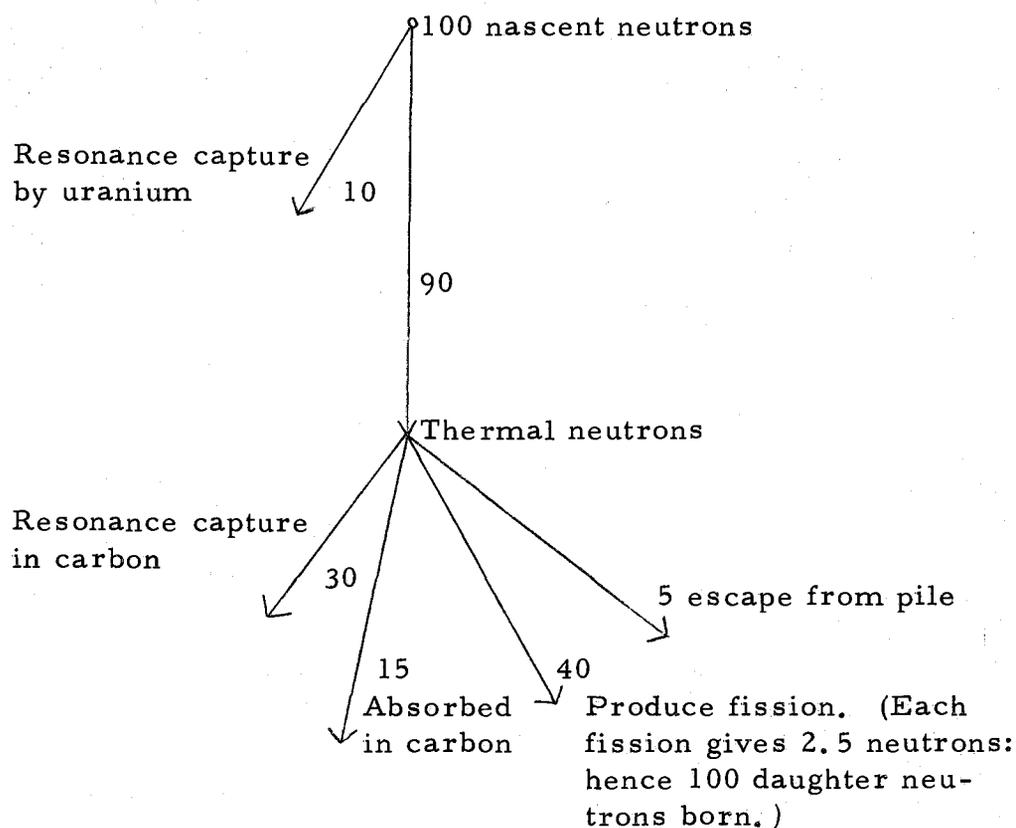


Figure 6. Life history of 100 neutrons (489, p. 225).

It took over a month to build the reactor (170, p. 268-269). It consisted of lumps of uranium spaced regularly in graphic blocks. Each layer of solid graphite alternated with a layer of graphite in which the uranium was embedded. As each additional layer was assembled, the approach to criticality was determined. Since the neutron density could be measured, it provided a positive method for extrapolation to

critical size. The cadmium strips were inserted into their slots when it was judged that criticality was being reached. Periodically the cadmium strips were slowly removed so that neutron density measurements could be made. What kept the pile from going critical on that fateful (!) December 2nd was one last still-inserted cadmium strip. As this last strip was pulled out, first feet, then inches at a time, the rate of rise of the neutron count was watched very closely. Fermi knew that this rate of rise would be constant when the reaction was self-sustaining. On December 2, 1942, this prototype of a chain reacting unit was allowed to go critical for 28 minutes (170, p. 270). That the intensity at which the reactor operated could be adjusted to any desired level with extreme accuracy was demonstrated before the experiment was discontinued. The proceedings at the University of Chicago led to the conclusion that a chain reaction in a graphite and natural uranium assembly was not only possible but easily controlled as well.

In the interest of the Manhattan Project, the chain reaction demonstration in Chicago also showed that the atomic pile was a feasible method for the production of plutonium. As long as the reproduction factor "k" was maintained at a value close to unity, a sufficient number of uranium-238 atoms were capturing neutrons (170, p. 442-443). The final result of this capture was plutonium, a fissionable material which was to be used for an atomic weapon if it

could be produced on a large-enough scale. Even before the successful completion of the experiment on December 2nd, the Manhattan District had selected a site at Hanford, Washington, for the construction of large atomic piles to be operated by Du Pont specifically for the production of plutonium (223, p. 130). When these reactors were actually in operation, the spent fuel (consisting of uranium, plutonium, and fission products) was periodically removed from the atomic piles and reprocessed. The plutonium was recovered by a precipitation technique. The events of July and August, 1945, recording the tests and actual use of nuclear weapons, bear historical witness to the success of the Manhattan Project phase of the development of the reactor.

In just three years of directed and intensive effort, theoretical and experimental physicists had given structure to a nuclear reactor. In a joint venture with scientists from other areas, they put into the hands of applied scientists and engineers a powerful device whose defined purpose was the production of materials of destruction. If this remained the only function of a reactor, then perhaps its value could be considered debatable. Significantly, the very men who breathed a sigh of relief at the successful completion of their experiment on the morning of July 16, 1945, at the Trinity test site in Alamogordo, New Mexico, were among the first to consider a new function for the reactor. In fact, these men, among whom were

Fermi, E. O. Lawrence, Compton, and Teller, urged a thorough examination of the implications of all scientific knowledge gained during the war so that peaceful applications could be made (228, p. xii).

The Atomic Pile: Peacetime Applications

The George Westinghouse Centennial Forum held in Pittsburg in May of 1946 had for its theme--Science and Life in the World. Since Enrico Fermi had an opportunity to address the section on "The Future of Atomic Energy," he chose to discuss the peaceful applications of atomic energy (170, p. 550-557). Within a year of the end of the war he envisioned large central installations in which great amounts of power would be produced and transformed into electrical energy or steam for power consumption. He also saw the possibility that an operating pile, as a source of radioactive materials, could ultimately be the most fruitful field of development.

Source of Useful Power

Harnessing a controlled chain reaction for the production of useful power may appear as an obvious application of reactor technology. Still the technical difficulties for the transition from the wartime plutonium-producing reactors to power reactors that could substitute for a hydroelectric plant were numerous. Even before the conclusion

of World War II Fermi and his associates at the Metallurgical Laboratory discussed the possibility of achieving breeding, that is, producing in a reactor more fissionable material than was consumed (170, p. 411-414, 435-436). They felt that theoretically it was very possible that, in a reactor using natural uranium for fuel, more plutonium would be produced than uranium-235 utilized. However, after the war Fermi recognized the chief technical difficulty standing in the way of breeding reactors. The piles constructed during the war were not made of materials capable of withstanding a very high temperature (170, p. 553). The urgency of their construction left no time for experimentation on that aspect of reactor technology, particularly because it was not necessary for the immediate ends. Therefore, energy was produced at a low temperature. Still, it was evident that the large plutonium-producing reactors at Hanford had produced a good quantity of heat in their cooling waters. The only known practical limitations to the temperature at which energy could be produced by a fission chain reaction was that imposed by the refractory properties of the materials used for the power device which would have to be designed to operate at steady levels.

If the materials used could not withstand high temperatures, coolants would be required. However, any coolant would have a greater or lesser adverse effect on the nuclear reaction (170, p. 554). Including a coolant in the system meant adding material which could

absorb neutrons to a certain characteristic degree. If adding the coolant would cause the reproduction factor "k" to fall below unity, the chain reaction would stop. Fermi felt strongly about the necessity for a technical solution to the problem. Power reactors were desirable, almost necessary, since it seemed that there were fairly large uranium deposits that could be mined at a relatively low cost, whereas it was feared that fossil-fuel sources would be depleted in the not too distant future. Because of Fermi's interest in breeder reactors the first commercial sodium-cooled breeder reactor in the United States was called "The Enrico Fermi Atomic Power Plant"⁵³ (170, p. 411).

The first useful amount of electricity generated from nuclear heat in the United States was produced on December 20, 1951, by the Experimental Breeder Reactor No. 1 developed by the Argonne National Laboratory⁵⁴ at its testing station in Idaho (228, p. xiv). In Britain, the first power reactor was completed in 1956 although the first major experimental reactor, a prototype for several

⁵³The initial loading of the reactor, erected on Laguna Beach off Lake Erie, began on July 24, 1963; criticality was not reached until August 23, 1963 (310).

⁵⁴The Metallurgical Laboratory of the University of Chicago was the predecessor of Argonne National Laboratory. In fact, the original graphite reactor first constructed on the University of Chicago campus was moved and rebuilt with improvements at the Argonne site, located near Chicago. The rebuilt pile reached criticality by the middle of March, 1943 (170, p. 324).

gas-cooled power reactors, was built in 1947. In France, the first reactor for power production alone was constructed in 1957. In Russia where power reactor development emphasized water-cooled systems, a small pressurized-water, graphite-moderated power reactor was in operation by 1954.

Source of Radioactive Isotopes

With the discovery of artificially-produced radioactivity in 1934, radioactive isotopes have found an ever-wider application in medicine, industry, and research. During the 1930's the cyclotron was depended upon as the producer of radioisotopes (see p. 65, above). With the development of reactors in the 1940's the production of radioisotopes in very large quantities was made possible. Some useful radioisotopes were identified among the fission products; many others were produced by the irradiation of target materials in a research reactor.

During the operation of the war-time plutonium-producing reactors, fission products were classified simply as waste products. Reactor fuels had to be purified periodically; after the fuel elements and the plutonium were extracted from the fuel requiring reprocessing, the remaining fission products were stored in tanks as fission waste. Any long-lived isotopes present in this fission waste made storage a problem, particularly if these isotopes were also high heat producers. However, separation methods were not considered

satisfactorily efficient nor economically feasible at that time (542).

In 1948, the development of economically feasible industrial processes was begun for removing certain fission products for which there was a demand, particularly in radiotherapeutics (417). Much attention was especially given to the separation of cesium-137 from reactor wastes since cesium was present in relatively high yield (6%) among the fission products. Cesium-137 which has a half-life of 33 years was recognized as a possible substitute for cobalt-60 in radiotherapy.⁵⁵ Other radioisotopes which were present among the fission products in relatively high yield and for which there was a demand included strontium-90 (half-life of 28 years) and iodine-131 (half-life of 8.05 days). Although the fission products were reprocessed for certain isotopes, full-scale separation methods have not generally been employed because such operations have not been considered practicable.

The radioisotopes produced in a pile by neutron bombardment of target nuclei⁵⁶ have also found wide application in medicine, in

⁵⁵ Compared with cobalt-60 which has a half-life of 5.3 years and emits 1.17 and 1.33 Mev gamma radiation, the use of cesium-137 had certain advantages. Its longer half-life obviated the necessity of frequent source renewal in teletherapy units. Likewise the lower energy gamma emissions of cesium (0.67 Mev) reduced the radiation protection requirements (83).

⁵⁶ Radioisotopes produced in a pile by neutron bombardment are formed either by gamma emission or by proton emission after the target nucleus absorbs the neutron. Gamma emission gives rise to a

industry and in research. They have found wide application mainly because the radioisotopes behave chemically as the stable form of the same element and furthermore they exhibit very constant behavior. They emit a characteristic radiation--alpha-, beta-, or gamma-radiation--which can easily be detected, has a definite energy and is emitted at a certain rate. Therefore, besides being characterized by their half-lives, radioactive isotopes are classified according to their mode of decay, energy of emission, and activity.⁵⁷

The first radioisotope produced in a reactor for medical purposes was carbon-14 (228, p. xxi). It was produced in the X-10 Reactor⁵⁸ at the Oak Ridge National Laboratory and supplied to the

radioactive isotope with the same atomic number as the target nucleus. Proton emission gives rise to a radioactive isotope with a lower atomic number (lower by one) than the target.

⁵⁷The unit of activity is the "curie." In 1962 the ICRU defined the curie (symbol "Ci") as a unit of activity equal exactly to 3.7×10^{10} disintegrations per second (515, p. 3). The curie has been used also as the quantity of any radioactive nuclide in which the number of disintegrations per second is 3.7×10^{10} . This activity is very nearly equal to the rate of disintegration of one gram of radium or the radon in equilibrium with one gram of radium.

⁵⁸The X-10 Reactor, a graphite-moderated, natural-uranium reactor was built at the Oak Ridge site in Tennessee as a pilot plant for the plutonium-producing reactors at Hanford, Washington (401). Although the construction of the X-10 Reactor was begun in February of 1943, the critical loading was not completed until November of 1943. The X-10 Reactor was not large enough for producing plutonium for a bomb but it was able to produce sufficient amounts of plutonium for tests of the chemical separation of plutonium from uranium (170), p. 352). After the war the X-10 Reactor was designated as a research reactor.

Barnard Cancer Hospital in St. Louis, Missouri, August 2, 1946. Ever since the U. S. Atomic Energy Commission was authorized to distribute radioisotopes to those seeking them for useful application, the X-10 Reactor, besides functioning as a research reactor, has also produced radioisotopes for world-wide usage (4). The reactor facilities at Oak Ridge National Laboratory as well as those at Chalk River, Canada, and at Harwell, England, have extensive programs for the preparation and distribution of radioisotopes (3).

Records show that Oak Ridge alone had increased its shipments of radioisotopes from less than 500 shipments during 1946 to more than 10,500 during 1953 (4). Its shipments from August 2, 1946 until December 31, 1953 included about 9,000 curies of cobalt-60, almost 2,000 curies of iodine-131, almost 1,000 curies of phosphorus-32, and about 150 curies of carbon-14. Over the same period 42 foreign countries received a total of 3,406 shipments. Therefore, although not every country took part in the development of reactors and accelerators, radioisotopes were made available by the U. S. Atomic Energy Commission to any institution in any country requesting them if guarantees could be given that users were safe-guarded against health hazards and that the results of scientific investigations with isotopes were made available as widely as possible to other researchers (159). Reports of applications and of the medical research done by recipient countries at the First International

Conference on the Peaceful Uses of Atomic Energy in Geneva in 1955 show the extensive uses made of radioisotopes, particularly iodine-131 and cobalt-60 (144, 159, 299, 373).

The factor that contributed to the development of the use of radioisotopes in medical research was the ease of follow-up and identification of even very minute amounts of radioactive isotopes used as tracers. In such small amounts the isotopes did not appreciably influence the biological or biochemical processes under study, although the isotopes themselves behaved chemically as their corresponding stable elements. In clinical medicine, tracer techniques have been an important part of diagnostic procedures. For example, radioactive iodine-131 has been used extensively in the investigation of thyroid disorders (83; 507, p. 12); radioactive iron-59 in the study of erythropoiesis (507, p. 679; 159); chromium-51 in the labeling of blood cells for the study of circulation (83, 159).

Although radioautography has been a convenient technique ever since radioactivity has been discovered, an application of radioisotopes in radiography was also found to be possible. Certain reactor-produced radioactive isotopes were discovered which emitted the kind of low-energy radiation useful in medical radiography (351). A good example of such an isotope is xenon-133. Xenon-133 is a fission product which emits 81 kv gamma-rays. Present also in the emissions are low energy (35 and 31 kv), characteristic X-rays from

cesium, a product of the disintegration of xenon-133 via beta emission. However, the absence of high-energy beta-radiation which would have given rise to high-energy X-rays made radiography possible with radioactive xenon-133. Satisfactory radiation sources were made by providing for the adsorption of xenon on carbon pellets. Quantities of the order of two curies of xenon gave high contrast radiographs of extremities of the body in a matter of seconds. The small size of the sources together with their non-dependence on electricity made them most valuable where X-rays could not be used.

Therapeutically, radioisotopes are used as internal and external sources of radiation. One approach in the therapeutic internal application of radioisotopes depends on the radiation they emit and their preferential concentration where the radiation is desired (83). For example, phosphorus-32 concentrates in the nuclei of rapidly growing cells and has been used in the treatment of some types of leukemia. Another technique of internal therapy involves the actual introduction of radioisotopes into the body tissues and cavities.

The possibilities of radioisotope teletherapy were not investigated until around 1950 (287, p. 21). After the Second World War it was realized that gamma-ray sources of high specific activity could be made available with high-flux nuclear reactors; such multicurie gamma-ray sources could be used for teletherapy. However, since

at that time large cobalt-60 sources⁵⁹ were not available, iridium-192 was used in a teletherapy unit in Cambridge, England. The short half-life (74 days) of iridium-192 made it impractical for users far away from a reactor. Cobalt-60 teletherapy was made possible when the two 1000-curie sources were made available in 1951. The demand for cobalt-60 radiation sources for teletherapy units⁶⁰ increased rapidly since by August of 1955, high-flux reactors in Canada and in the United States were producing over 100,000 curies per year of high-specific-activity cobalt-60 (3). After the properties of cesium-137 were investigated and sufficient quantities of the cesium isotope were made available by the reprocessing of fission products, many teletherapy units used cesium-137 as a source of radiation (70; see p. 130, above).

Radioisotopes produced in a pile also found extensive application in industry; initially the application was mainly in metallurgical research (255, 456). As such the radioisotopes were used more to

⁵⁹In 1951, the high-flux nuclear reactor at Chalk River, Canada, was the only existing facility capable of producing high-activity sources. Not until 1951 were two 1000-curie sources of cobalt-60 made available by the Chalk River reactor (287, p. 21-22).

⁶⁰For teletherapy units an activity of at least 50 curies per gram is desired (3). If it takes about 18 months in a high-flux reactor to produce a cobalt-60 source with a specific activity of 35 curies per gram (355), then it took very long to produce the 1000-curie cobalt-60 source with a specific activity of 100 curies per gram (in which case only 10% of the stable cobalt was converted to cobalt-60) (3).

investigate existing techniques rather than as a basis for developing new ones. However, as the economic value of isotope utilization to industries began to be realized, the use of isotopes spread to new branches of industry and to other technological processes. For example, the use of isotopes has saved much time for personnel conducting studies on all kinds of wear and corrosion (3). Tracer techniques permit quick and accurate measurement of even very small amounts of wear or corrosion.

A more widespread use of radiographic methods of inspection has been directed at economy in materials of construction (159). Certain isotopes such as cobalt-60, cesium-137, and iridium-198, because of the penetrability of their radiations and their availability as portable sources of radiation, have been increasingly in demand for industrial radiography. Likewise, radioisotope gages, because of their accuracy and convenience in providing measurements of a material without contact, have filled a long-felt need in industry (3). For example, failure to keep thicknesses of sheet materials within tolerance has been a costly error overcome by thickness gages in sheet processing industries such as sheet aluminum and other metals, plastics, paper, cloth, and floor-covering. Similarly, density gages have controlled many processes. Although thickness gages often use radioisotopes that are beta-particle emitters, density gages may rely on those isotopes that are gamma-emitters.

Radioisotopes have also been of benefit to agricultural productivity (3). Tracer studies with a variety of crops have been concerned with the uptake and utilization of nutrients and fertilizers by roots and foliage. Other studies have been directed at plant diseases and at overcoming the tremendous losses due to weeds and insects. In serving agriculture in this manner, radioisotopes have been extremely potent as tools of research.

Besides being employed for research in the applied scientific fields, radioisotopes have also been utilized in basic scientific research such as that conducted by radiation chemists. Although they have not found it advantageous to use reactors directly for research, radiation chemists have depended very much on the radioactive isotopes produced in a reactor. Radiation chemistry⁶¹ by convention has been described as the study of the effects of high-energy radiation on matter. In their investigations the radiation chemists have found it particularly advantageous to use sources of homogeneous high-energy radiation. The high-energy radiation has either been in the form of high-energy protons or high-speed material corpuscles. It

⁶¹ Radiation chemistry can be said to have had an official beginning in May of 1942 at the Metallurgical Laboratory in Chicago. The activities of the chemistry division of the atomic energy project were classified according to four areas of research, one of which was concerned with the effects on the reactor of the radiation it itself was producing. Since photochemistry seemed an inappropriate term for the work being done by that section, the term "radiation chemistry" was coined (74).

has included the emissions of radioactive decay (alpha-, beta-, and gamma-rays, neutrons, and atom and fission recoils) as well as their artificially produced analogues (accelerated protons, deuterons, helium nuclei, electrons, and X-rays). For a source of high-energy radiation, then, the radiation chemists have chosen either natural or artificial radioactive isotopes or some form of particle accelerator.

Of the radioactive isotopes which radiation chemists have used as chief sources of radiation only three are natural; the others are usually produced in reactors. The commonly used natural radioisotopes (polonium-210, radium-226, and radon-222) are chiefly alpha-particle emitters with average discrete energies of 5 Mev. Radium-226 and polonium-210 also furnish some gamma-radiation of an average 0.5 Mev energy. The common artificial isotopes (cesium-137, cobalt-60, hydrogen-3, phosphorus-32, strontium-90, and sulfur-35) are chiefly beta-particle emitters with average energies of 0.8 Mev. Cobalt-60 also emits 1.332 and 1.173 Mev gamma-radiation and cesium-137 emits 0.66 Mev gamma-rays.

As a source of X-rays, either the conventional X-ray machine which furnishes 0.05-0.3 Mev X-rays has been used or one of a number of accelerators depending on the X-ray energy desired. Any of the accelerators--the resonant transformer, the Van de Graaff accelerator, the betatron, and the linear accelerator--which furnish X-rays (total range of 0.1-630 Mev) can also provide monoenergetic

beams of electrons. Other accelerators--the Cockroft-Walton accelerator, the cyclotron, and the linear ion accelerator--provide beams of positively-charged particles (total range of 0.1-400 Mev).

When radiation chemistry came into unofficial being around 1900, the notion of transfer of energy from the radiation to the chemically affected material may have been taken as axiomatic since photochemistry was based on a similar fundamental principle (72). The nature of the chemical effect was not clear, however. There were speculations and suggestions about the mechanism of reactions. After Madame Curie proposed in 1910 that the act of ionization preceded all chemical effects ascribed to high-energy radiation (126, p. 247-248), there were some chemists, Samuel Colville Lind (1879-1965) probably the leader among them, who seemed determined to identify an elementary process in radiation chemistry. They exploited the idea that the chemical yield was related to the number of ion-pairs produced by the radiation and they included M/N ratios in all of their publications (211). The M/N ratio was defined as the number of molecules changed per ion-pair, that is, M represented the number of molecules converted or formed and N represented the total number of ion-pairs produced during the experiment. When radiation chemistry came into official being, as it were, in 1942, M/N ratios were given and discussed for all reactions studied. Since the M/N ratio was the ion-pair yield, a problem arose when liquid

systems were investigated because ionization could not be measured exactly except in the gas phase. This led to an energy-yield expression "G"⁶² which was defined as the number of molecules changed per 100 ev of energy absorbed in the system.

Studies of energy yields and cloud-chamber photographs of the ionization and excitation tracks of various forms of radiation demonstrated that different types of radiation produced different effects. This was analyzed as being due to the differences in the linear density of events along the track of the charged particle. In 1952, the physiologist Zirkle proposed the term "linear energy transfer" (LET) for the "energy transferred from the fast charged particles, per unit length of their paths, to the biological material in or near those paths" (quoted in 28, p. 14). At about the same time, the chemist J. L. Magee and his collaborators used the concept of linear energy transfer and applied it to the primary processes preceding the first chemical effect of ionizing radiation (195, 433). The primary effect of the radiation was considered to be the ionization or excitation of

⁶² According to the radiation chemists Milton Burton of the University of Notre Dame and F. S. Dainton of Nottingham, the idea of energy yield came into being during the Manhattan Project in about 1943 (Burton was at the Metallurgical Laboratory in Chicago and Dainton was at the Evergreen Laboratories in Montreal). It was realized that the concept of ionic yield was not appropriate for liquids. One of the reasons why "G" was adopted as the symbol for the 100 ev yield was the fact that G was not in use for any other purpose in a project filled with code words and letters (468, footnote on p. 36).

molecules.

When these ionized or excited molecules were formed close together, as was true in the case of alpha-particle tracks, the reactive entities were more apt to react with one other than with the medium. The overall yield due to alpha-radiation was then less than in the case of beta-radiation where the ionization and excitations occurred farther apart. This linear density of events along the track provided another way of characterizing ionizing radiation, that is, by its linear energy transfer, or its LET, often expressed in Kev absorbed per micron of track in the medium.

The extent of a chemical reaction was predicted to be a function of the number of active species formed and their concentration along the particle track (433). The latter, in turn, depended on the rate at which energy was lost as the particle was slowed down, its LET. The actual measurement of the rate of energy loss is a complicated process because the rate of energy loss is not constant and the energy lost by a primary particle is not necessarily absorbed locally. However, a rough approximation to the LET can be found by dividing the initial energy of the ionizing particle by its mean range. Although LET values do not strictly apply to X- or gamma-radiation, they are given, however, for the secondary electrons produced by the X- or gamma-rays in a medium.

The physical existence of track effects had been known for some

time (see p. 50, above). However, efforts at explaining regions of energy deposition along a track have contributed to a developing theory of radiation chemistry. These advances probably would not have been made without the reactor-produced radioisotopes which have provided ideal sources of alpha-, beta-, and gamma-radiation.

Ionizing Radiation in Developmental Perspective

The announcements relating to the discovery of uranium fission early in 1939 considerably altered the significance of ionizing radiation for scientific research and application. That ionizing radiation possessed energy which could be variously applied was recognized from the time of Röntgen's discovery of X-rays. In fact, X-radiation and the radiations emitted by radioactive materials were classified as forms of high-energy radiation early in the twentieth century. Scientific genius recognized the research possibilities of radiation of even higher energy and, therefore, deliberately devised ways of increased that energy many-fold. The successive appearance of a variety of accelerators and the uses found for them in the 1930's and the 1940's are indicative of the progress that was made in the field of ionizing radiation.

Man's role in this progress has changed through the years. In a little more than a quarter century he passed from a position of being acted upon to one of acting on ionizing radiation. Initially,

either the physical action, or the chemical effect, or a deleterious physiological response made him aware of the energy and penetrating power of radiation. Through resourcefulness he found applications for this penetrating radiation and even learned to control it. By erecting accelerators man showed that he was confident in his handling of ionizing radiation to the extent that he felt inclined to alter it, to increase its energy. This pre-determined energy of ionizing radiation proved a desirable tool in both basic and applied science.

The discovery of nuclear fission, however, introduced man to much larger quantities of energy than he had ever known. Still, he found it necessary to increase that huge amount of energy many-fold. Once he became convinced of the possibility of a chain reaction involving the fission of uranium, he proceeded to develop a nuclear explosive device which was a function of the energy released by an uncontrolled chain reaction. However, a chain-reacting structure, the reactor, was needed for the building of the nuclear weapon. The development of nuclear reactors within four years of the discovery of nuclear fission put the energy of a controlled chain reaction at man's disposal. What he has done with the reactor, after its initial wartime application, has been most extensive. That the Third International Conference on the Peaceful Uses of Atomic Energy held in Geneva in the late summer of 1964 chose for its theme--reactors and nuclear power--demonstrates the progress nuclear power technology

had made in less than 20 years (393, p. vii). Ever since the immediate post-war period, reactors were developed as possible sources of nuclear power. An important milestone was certainly reached, then, when at the 1964 conference, atomic energy was considered as a world economic reality and was projected as a solution of future world power needs.

The peaceful uses of atomic energy have also been an outgrowth of research associated with high-flux reactor activities. A certain amount of fundamental research was made possible chiefly because such reactors facilitated the production of isotopes. Perhaps most exciting to the scientific imagination was the basic and exploratory research that was made possible by the production of transplutonium elements in sufficient quantity. Likewise, the large-scale production of radioisotopes proved very important to the physical and the life sciences. It seems as if some technology associated with radioisotopes was soon found in virtually every scientific and engineering field. The extensive use of radioisotopes in medical therapy and clinical diagnosis certainly cannot be overestimated.

Although the discovery of fission and the ensuing development of nuclear reactors with their associated programs have been prominent on the scientific scene during this time, there have also been notable advances in other areas of radiation technology. Early X-rays were of relatively low energies when compared with the radioactive

emissions of radium. Even with improvements, X-ray generators prior to 1930 were unable to generate radiation at a voltage higher than about 250 kv. However, there was a growing demand for X-rays to be used in deep therapy. The 1930's, therefore, witnessed first the installation of 800 kvp units (see p. 68, above) and then the erection of Van de Graaff accelerators which could generate X-rays in the Mev-range (92, p. 196). These were followed by other accelerating machines. During the 1940's and 1950's various devices were developed that could furnish supervoltage radiation. By 1950, betatrons, which by their beams of energetic electrons could produce penetrating X-rays with energies up to 22 Mev, were already in use (504).

Synchrotrons⁶³ capable of furnishing X-rays with energies from 20 to 70 Mev, proposed in the 1940's, were actually built in the 1950's (2).

This seemingly unsurpassed period of development of ionizing radiation and of the technology associated with its use could be misinterpreted. Though advances may have been spectacular, they were not indicative of the successful solution of all problems related to ionizing radiation. Probably the most difficult scientific and engineering problems ever encountered in working with atomic energy

⁶³A synchrotron is a charged-particle accelerator which imparts high speeds to the particles by means of a high-frequency electric field (basic to the cyclotron), and a low-frequency magnetic field (basic to the betatron).

were still awaiting solution in the early 1960's. Although research was being conducted on controlled fusion reactors (101), no truly thermonuclear device had, as yet, been constructed. Besides, until a process could be devised whereby the energy generated by fusion would at least equal the energy input, such reactors would be impractical. Controlled fusion promised the benefits of unlimited power for the earth's population for all time. Still, with unsolved problems, no one could be absolutely sure that controlled thermonuclear power could ever be developed. Controlled fission had become a reality sooner than expected by many in the scientific field. Should controlled fusion become a reality, most probably there will be concomitant and resultant developments in the field of ionizing radiation.

CHAPTER VI

CHEMICAL DOSIMETRY IN PERSONNEL MONITORING
(1942-1962)

The expansion of X-ray applications in the 1920's and the 1930's together with the consequent potential hazards of stray radiation made personnel protection an important issue (see p. 80, above). Efforts were made on the national and international levels not only to standardize dosage but also to define a maximum permissible level of exposure as a tolerance dose for radiation workers. Since 1942, the Manhattan Project with all of its post-war extensions and adaptations has contributed a still more serious physiological hazard to a project personnel steadily increasing in numbers. The operation of reactors presented an unprecedented radiation danger because of the high-energy gamma-radiation and high-neutron fluxes that accompanied the process of uranium fission. The required chemical separation of fission products provided an additional source of occupational exposure. The very storage of these fission products became an exposure problem not only for the people then employed but for future generations of workers. Because of mixed radiation fields, radiation monitoring of nuclear energy workers was a much more complex process when compared with the monitoring, for example, of hospital personnel. Still there was a demand by many involved in the

development of reactor techniques and in the handling of large amounts of radionuclides that ample safety measures be taken to avoid injuries in these new fields.

Developments in Radiation Protection

Before radiation monitoring could take on aspects of precision and reliability, further steps had to be taken to standardize dose measurements. Due attention was given to this problem by the international commissions which had been established by the International Congresses of Radiology for that very purpose. Although the ICRU and the ICRP did not hold any post-war meetings until 1950 (in conjunction with the Sixth International Congress of Radiology) (483), progress in radiation protection was made prior to that date by some groups operating at national levels.

At its first post-war reorganizational meeting in 1946, the NCRP in the United States had established a subcommittee to study permissible dose from external sources (482, p. iv-vi). A preliminary report by this subcommittee was prepared during the summer of 1949. The more essential recommendations of this subcommittee were shared, then, with the representatives of the United States, England, and Canada at the first of a series of conferences on radiation safety problems. This first Tri-Partite Conference was held at Chalk River, Ontario, in September of 1949 and emphasized the safety

problems of atomic energy operations (512, p. v). The deliberations of this group became the basis for the recommendations made by the international organizations at their meetings in 1950 (512, p. v-vi).

Conceptual Developments Regarding Dose

In 1937 at its last pre-war meeting, the ICRU had defined the roentgen as a unit of quantity or dose of X- or gamma-radiation (see p. 78, above). Although the use of the word dose was ambiguous (see p. 78, above), the 1937 definition was used to designate a radiological unit through the war years. When the ICRU was reorganized in 1950, there were many reorganizational problems to contend with and there was much information to evaluate. The ICRU recognized the need for an absolute measurement of radiation based on some fundamental technique like calorimetry. This led to important discussions relating to the development of concepts of energy measurement as applied to radiological problems. Although in its final report the ICRU made very few specific recommendations (484), it considered the following recommendations warranted by the information available:

For the correlation of the dose of any ionizing radiation with its biological or related effects the ICRU recommends that the dose be expressed in terms of quantity of energy absorbed per unit mass (ergs per gram) of irradiated material at the place of interest. In the foregoing paragraph by 'energy absorbed' is meant the energy imparted to the material at the place of interest (quoted in 28, p. 11).

This in a certain sense paved the way for the acceptance of a new energy unit of dose proposed in 1953. At the same time, the definition of the roentgen was retained in its 1937 form although there were acceptable arguments in favor of modifying it.

Preceding the Seventh International Congress of Radiology held in Copenhagen in 1953, the ICRU met jointly with the ICRP. Perhaps the most important contribution in the ICRU report (484) of this session was the introduction of a new basic unit of radiation dose, the rad. It was defined as the unit of absorbed dose equal to 100 ergs per gram. The concept of absorbed dose was also clarified. By the absorbed dose of any ionizing radiation was meant the amount of energy imparted to matter by ionizing particles per unit mass of irradiated material at the place of interest. Since the rad was based on energy imparted to matter, it could be applied to all forms of radiation including beta-rays, alpha-rays, and neutrons. Although it was recognized that much more information was needed before the rad could be regarded as a practical unit, it was hoped that the rad would take on importance as a radiological unit and possibly detract from the roentgen. The definition of the roentgen was again left unchanged, not because it was considered physically precise but more because an agreement regarding a change could not be reached.⁶⁴

⁶⁴ Perhaps the "uncertainty of the wisdom of certain decisions" to which Handbook No. 62 of the U. S. National Bureau of Standards attributes the lack of specific recommendations in 1956 (517, p. 2) was also applicable in 1953.

In the 1956 report of its joint meeting with the ICRP in Geneva, the ICRU dealt extensively with the difference between absorbed dose expressed in rads and the exposure dose expressed in roentgens (517, p. 5-7). The concept of absorbed dose as formulated in 1953 was reaffirmed but the term "dose" in the roentgen definition was replaced in 1956 by "exposure dose." There seemed to have been a desire to restrict the use of the word "dose" to the energy absorbed and to divorce its use in connection with the roentgen. However, it was considered necessary to retain the word "dose" (as "exposure dose") for the quantity expressed in roentgens because of long-standing clinical practice and also because all of the existing ICRP recommendations and codes for radiation protection used it (517, p. 9). Exposure dose of X- or gamma-radiation at a certain place was specifically defined as a measure of radiation based on its ability to produce ionization.

The concepts of absorbed dose and exposure dose as formulated in 1956 were retained through the 1959 sessions of the ICRU and the ICRP which preceded the Ninth International Congress of Radiology held in Munich that year.⁶⁵ In its 1962 report of meetings held in

⁶⁵There was concern at this time that the reports and recommendations of the ICRU, originally intended for medical application, should also find application in other fields of science. To facilitate this adaptation it was suggested that "Radiological" in the name of the commission be replaced by "Radiation" to remove any strictly medical connotation from the ICRU reports. The question was not debated but left for further consideration (515, p. vi).

Switzerland (515, p. v), the ICRU recommended that the word "dose" be eliminated and that only the term "exposure" be used for that quantity for which the roentgen was the unit. Therefore in 1962, the official recommendation restricted a special unit to a single quantity, that is, the rad was to be used solely for absorbed dose and the roentgen (at which time the symbol "R" replaced the former "r") was to be used solely for exposure.

In 1956 (517, p. 7) and in 1959 (518, p. 2-3), the ICRU also recognized an RBE dose.⁶⁶ The RBE (relative biological effectiveness) had been a concept used even in the pre-war period to compare the biological effects of various forms of radiation. The RBE dose (in rems) was defined as the product of the absorbed dose (in rads) of the radiation in question and of the RBE factor η . The unit of RBE dose, the rem, carried no precise definition. The RBE concept was considered to have a limited usefulness because the biological effect of radiation depended on many factors. Prior to 1956 it had been suggested that the LET of a particular form of radiation be used as an index of its RBE. Still misgivings were expressed in 1959 about using the same RBE factor in both radiobiology and radiation protection since RBE values would depend on the biological system as well as other variables.

⁶⁶The RBE dose was never included in the ICRU lists of definitions but was considered a recognized symbol (515, p. 3).

The problem was resolved to a certain extent when in 1962 the ICRU recommended that the RBE factor and RBE dose be reserved for radiobiology (515, p. 3). A quality factor (QF), dependent on LET, and other modifying factors were introduced to define the "dose equivalent" in rems. The dose equivalent was defined as the product of the absorbed dose (in rads) and appropriate modifying factors. Furthermore, the dose equivalent was reserved for purposes of radiation protection. It was meant to be a quantity which expressed on a scale common for all ionizing radiation the irradiation incurred by exposed persons.

Changes in Levels of Tolerance Dose

On the basis of the information supplied by the 1949 Chalk River Tri-Partite Conference, the ICRP in 1950 adopted the essentials of the Chalk River recommendations. This meant that the maximum permissible dose (MPD) for radiation workers was lowered to 0.3 roentgens per week. Since 1934 the MPD was equivalent to 1.4 roentgens per week. This lowering of the MPD was not determined by positive evidence that the permissible levels recommended earlier were inadequate. Rather, the change in the MPD was determined by certain trends in scientific opinion which were intended to forestall the recording of such positive evidence (512, p. 1-2).

In its 1953 report (288) the ICRP reaffirmed the basic

permissible exposure level of 0.3 roentgens per week. This value was intended chiefly as protection against over exposure to low and intermediate voltage X-rays. Although the ICRP recognized that protection was also needed against X-rays above 3 Mv, beta-rays, gamma-rays, and heavy particles like neutrons and protons, it felt unprepared to issue specific recommendations in that regard. It did include in its report, however, values of maximum body burden and maximum concentration in air and water of 96 radioisotopes. These values were considered permissible for occupational exposure and the appropriate values depended upon the properties of the radioactive materials and the method of body intake, limited in the report to ingestion and inhalation. The maximum permissible levels of internal dose were based on a calculation of that burden in the body which would result in an average biological dose of ionizing radiation equivalent to 0.3 rad per week to the organ in which maximum concentration occurred.

In 1956, the ICRP recommended an MPD of 5 rems per year or about 0.1 rem per week. Again this was a lowering of the tolerance dose from about 0.3 rem⁶⁷ per week (1953 MPD) to 0.1 rem per week.

⁶⁷ Although an equality does not exist between a roentgen and rem, under certain conditions they are almost equivalent and in literature have been used interchangeably. For example, the physicist L. S. Taylor, the U. S. representative on the ICRP, has reported the 1950 MPD as being equal to 0.3 r per week (483). However, the health physicist K. Z. Morgan at Oak Ridge National Laboratory assigned

Up to that time ICRP recommendations had been made as regards the maximum permissible occupational exposure of the total body to ionizing radiations. Since more had become known about the biological effects of radiations of all kinds, there was concern also for the permissible dose to specific body organs. Distinctions were also made between short-term and long-term exposures. There were even suggested limits of dose for the population-at-large. Such trends indicated the importance that was being assigned to radiation protection measures.

Absorbed Dose Determination

In its 1956 report (517), the ICRU also considered the determination of dose. It restricted its treatment, however, to the calculation of absorbed dose from ionization measurements since that was the method commonly used at that time. Such calculations were based on the cavity ionization relationship.⁶⁸ In its 1959 report (518), the

a value of 0.3 rem per week for the 1950 MPD (362). In general (see p. 152-153, above and footnote 68, below),

$$\text{exposure dose} \times \text{factor} = \text{absorbed dose} = \frac{\text{absorbed dose}}{\text{RBE or QF}} \text{ (rems)}$$

(roentgens) (rads)

⁶⁸ Briefly, this relationship claims that, under conditions of electronic equilibrium, the absorbed dose is proportional to the exposure dose according to the following (517, p. 10-16): absorbed dose = $f \times$ exposure dose, where f is a proportionality constant. When the absorbing medium is air and the average energy required to produce an ion pair in air is 34 ev, then f is equal to 0.87 rads per roentgen for all radiation qualities. For other absorbing media, f varies with

ICRU recognized other methods of absorbed dose determination as well, such as: calorimetric, solid state, photographic, and chemical. Photographic dosimetry, one of the oldest detectors of ionizing radiation was most widely used in 1959 for personnel monitoring (518, p. 59) even though the accuracy of the photographic method was recognized to be relatively low. Still, since ruggedness and low cost were important factors a photographic dosimeter had obvious advantages. If appropriately calibrated, the density of the exposed photographic emulsion could be related to either the exposure dose or the absorbed dose. Although the sensitivity of ordinary photographic film made measurement of small doses possible for monitoring personnel, photographic emulsions were also used for measurements of total exposures up to and beyond 10^4 r (see p. 164, below).

According to the ICRU (518, p. 54-58) chemical methods could be grouped according to their effectiveness in responding to absorbed doses over a certain range. Some systems responded to an absorbed dose from 10 to 10^4 rads. Such systems had dosimetric possibilities not only in research but also in military and civil defense work where rapid dose estimation was required (see p. 212, below). Oxidation-reduction systems were sensitive to doses from 10^3 to 10^6 rads.

the atomic composition of the material according to its mass energy absorption coefficient and also with the radiation quality.

Such chiefly aqueous systems had dosimetric possibilities best applied as secondary standards in a laboratory (see p. 191, below). The ICRU chose to group the rigid chemical systems--the gels--separately. However, in terms of the response within a dose range, gel systems belong in the 10^2 to 10^6 dose range. Finally, the ICRU considered polymeric systems, which usually respond to doses higher than 10^6 rads, under solid-state dosimetry (see p. 242, below).

The classification used by the ICRU in discussing chemical methods of dosimetry illustrates the scope of the research done in chemical dosimetry in the 1950's. There have been many systems investigated during the post-war period for possible dosimetric application. Although there seems to have been no generally accepted definition of a chemical dosimetric system, if broadly defined, chemical dosimetric systems would include photographic emulsions, various aqueous salt solutions, organic solutions, monomers, polymers and gaseous systems. The given dose range for a particular system is a more or less weighted average range because theoretically the addition of certain reagents can often extend the sensitivities of chemical systems to radiation.

Developments in Personnel Monitoring

X- and Gamma-radiation

There are very few chemical systems which respond to an absorbed dose range between 10^{-3} and 10^3 rads. Those that do show this sensitivity, photographic emulsions particularly, have found extensive application in radiological protection. It seems that since about 1940 the use of film badges for personnel monitoring in radiological clinics, industrial radiation centers, and radiation laboratories has become very widespread. That there was a relationship between the density of the exposed film and the dosage received by the film had been long known; that very relationship was the basis of the Kienböck dosimeter in 1904 (see p. 44, above) and of the Landauer standard films in 1926 (see p. 80, above). Although the mechanism for the reduction of the silver ions in the emulsion was not clearly understood, by 1926 the dependence of emulsion sensitivity on X-ray energy was recognized. Landauer himself considered it necessary to prepare standard films for use with X-rays of different energies. When in 1938 the physicists R. W. Gurney and N. F. Mott proposed an explanation for the photolysis of silver bromide (227), their theory also clarified the dependence of emulsion sensitivity on energy.

According to the theory of Gurney and Mott (227) the energy transferred by the ionizing radiation to the photographic emulsion

initiates the reduction of a silver halide grain to atomic silver. This microscopic silver, referred to as the latent image, stimulates the reduction of the whole grain under the action of a special developing solution. The probability that a latent image would be formed increased with the number of electrons set free in the grain by the radiation.

Charged particles transfer their energy to the silver halide grains through collisions which give rise to excitation and ionizations along the paths of the particles. Uncharged particles transfer their energy to the emulsion through the ionization produced by their charged secondaries. However, not all of the energy initially transferred from the X- or gamma-radiation to a silver bromide grain is dissipated in that grain. According to the studies made by the physicist J. R. Greening in 1951 (219), about 90% of the energy of 100 Kev X-rays was dissipated outside the grains. At the same time, part of the energy within a grain came from electrons which originated outside the grain. However, the latter effect did not occur until photon energies were around 1 Mev. The large amount of energy that was deposited by low energy photons (about 40 Kev) in the silver bromide grains gave rise to the most pronounced defect of film as a dosimeter,

that is, the dependence of emulsion sensitivity⁶⁹ on photon energy.

Although the sensitivity of a photographic emulsion depends on various parameters such as type of radiation, its energy, its angle of incidence, and development conditions, the one contributing most to the low accuracy of dose determination by film is the energy of the incident radiation. Some experimenters at the Radiological Institute of the University of Freiburg in 1952 (318) have expressed the opinion that the contributions of the other parameters to error in dose determination has been within an allowable limit.

The extent of this energy dependence was illustrated by some significant experimental data in 1952 by Christian B. Madsen (b. 1906) of the Radium Center at the Municipal Hospital in Aarhus, Denmark (346). According to his report, an exposed film density of 1.0 corresponded to 35 milliroentgens of exposure if the HVL was 0.7 mm of copper, and to 55 milliroentgens if the HVL was 1.3 mm of copper. A half-value layer, as an indicator of the penetration of the radiation responsible for the exposure, is also an indicator of the quality, that is, the energy of that radiation. Therefore, a high HVL indicates high-energy radiation. According to the above data, then, the film

⁶⁹Sensitivity, as a photographic term, has been defined in several ways. As used by the physicist Robert A. Dudley, the term was defined as the reciprocal of the exposure required to produce a net density equal to 0.30, where density is equal to the logarithm of the ratio of the incident radiation intensity to the transmitted intensity (157, p. 316).

was less sensitive to high-energy radiation since it required a greater exposure for a matching density than when exposed to low-energy radiation.

Since the dependence of film sensitivity on the energy of the incident radiation contributed significantly to error in dose determination, developments in photographic X- and gamma-ray dosimetry in this post-war period were due to steps taken to reduce that dependence. One of the earliest approaches to the problem of energy dependence has involved absorbers. Theoretically, an ideal absorber covering an emulsion would attenuate the radiation by a factor which would compensate exactly for film sensitivity at that particular radiation energy. Louis A. Pardue (1900-1963) and co-workers at Argonne National Laboratory were among the first to make studies of filter materials specifically for film badge application in 1944⁷⁰ (378). According to their report, Pardue and collaborators made studies of the effects of lead, silver, and cadmium. They proposed to cover the film with one of these absorbers in order to equalize the extent of film blackening due to radiations of lower quantum energy with that of higher quantum energy. Of the three materials, they discarded lead

⁷⁰ Their report had not been declassified by the U. S. Atomic Energy Commission until in 1947.

because its K absorption edge⁷¹ at 87 Kv was too near X-ray energies commonly used. At the value of its K absorption edge, lead would absorb too strongly and would not achieve the results for which it was intended. Silver and cadmium were more satisfactory in that regard because their K absorption edges came at 25.5 kv and 26.6 kv respectively. Of the two, cadmium was the final choice because of its lower cost.

Pardue and associates also made studies of the proper thicknesses of a cadmium absorber for particular film types (378). They were able to conclude that whether a very sensitive film, like Du Pont No. 502 film, or a less sensitive film, like Du Pont No. 351 film, were used, a 1 mm cadmium filter satisfactorily compensated for the film response to radiation over a wide energy range--from the hard gamma-rays associated with radium emission down to about 60 Kv X-rays. Since the Du Pont No. 502 film normally responded to an exposure range from about 0.03 to 3 r and the Du Pont No. 351 film responded to an exposure from about 3 to 20 r, Pardue decided to use both films in the badge; this made the film dosimeter useful over

⁷¹Low-energy photons are absorbed mainly by photoelectric absorption. As the photon energy increases from a value just below the K shell binding energy (of lead, in this case) to a value just above this energy, photoelectric absorption shows a marked increase. A plot of the photoelectric absorption coefficient against photon energy has a distinct edge (a sharp, vertical rise) at the binding energy (28, p. 142).

an extended range. Only the central portion of the films was covered with 1 mm of cadmium. The unfiltered parts of the film provided for the detection of soft radiation. Although use of the cadmium filter satisfactorily reduced the energy dependence of the films, the film dosimeter in routine dose measurements had an accuracy only of about 25%. However, such an accuracy represented an improvement since film dosimeters were generally rated at about 10% accurate (518, p. 59).

In 1951, Rex B. Wilsey (b. 1889), a researcher at Eastman Kodak Company in Rochester, New York, was also intent on reducing the energy dependence of Kodak X-ray film (538). To achieve this end, he also used cadmium filters. He reported that, with Blue Brand Kodak X-ray film, 1.1 mm of cadmium gave satisfactory film responses for radiation energies from 0.075 Mev and above. With Type K Kodak film, however, 1.85 mm of cadmium were needed to obtain good film responses for radiation with energies from 0.089 Mev and above. Wilsey recognized that, under the usual conditions where film badges were used, stray radiation could strike the film at almost any angle. Therefore, the thickness of cadmium traversed by the radiation would be greater than its measured thickness and the exposure of the film correspondingly less. To remedy this problem, Wilsey recommended that a cadmium filter thinner than that required for perpendicular radiation be used. After further research,

however, Wilsey concluded in 1956 that the variation of film sensitivity with angle of incidence was not a significant factor in film monitoring (539). Only at angles of incident radiation greater than 70° from the perpendicular was the film sensitivity diminished to a considerable extent.

Efforts at decreasing the energy dependence of photographic dosimeters by means of metallic absorbers covering the emulsion surface were also made at the Radiation Physics Laboratory of the National Bureau of Standards in Washington, D. C. In 1951, Margarete Ehrlich (b. 1915) and her associate Stephen Fitch proposed a method of reducing the energy dependence of a four-film dosimeter (160). The four-film dosimeter was composed of four selected emulsions-- Du Pont 510, Du Pont 605, Eastman 5302, and Eastman 5480--to give a dosimeter with a useful exposure range of from 1 to 10^4 roentgens. For absorbers, Ehrlich and Fitch chose a tin-lead combination because tin complemented the effects of lead. Below the K absorption edge for lead, the absorption by tin exceeded the absorption by lead, while above the K edge, lead was the more effective of the two. After finding a suitable thickness of lead and tin for removing the energy dependence of each of the selected emulsions, Ehrlich and Fitch chose a compromise thickness of each (1.07 mm of tin and 0.3 mm of lead) for the four-film combination. In the four-film dosimeter, the pair of absorbers covered the entire emulsion surface. After

much study of methods of modifying the initial radiation spectrum, Ehrlich and Fitch decided that the metallic absorbers had to be used in successive immediate contact with the measuring device--the film. This was the most effective way of reducing the spectral components of the radiation to which the film emulsions were selectively responsive. In this way they were able to reduce the dependence of film sensitivity on energy sufficiently to give their film dosimeter an overall accuracy of $\pm 20\%$ in dosage interpretation (160). By their dosimeter, then, Ehrlich and Fitch not only extended the range over which photographic dosimetry was useful, but apparently they improved the accuracy of the method by about 70%.

While research was being conducted to decrease the energy dependence of photographic emulsions by placing an absorber over the film to attenuate the X- or gamma-radiation, a slightly different approach to the problem was also being pursued. From the Naval Radiological Defense Laboratory in San Francisco in 1950 Eugene Tochilin (b. 1921) and his co-worker proposed a film dosimeter in which the film was covered by an echelon of three metal shields and an open window region (501). The film-density readings were interpreted, then, with the aid of tables relating the ratios of densities under the different absorbers to the dosage in roentgens received by the film. Either Du Pont Type 552 insensitive film or Eastman Kodak Radiatized Type DF-7 dental film could be used in the dosimeter. In order that

the film badge would indicate the effective energy of the radiation striking the film within its energy dependent range, the film was covered with shields. The quadrant labeled Shield A was the open window; B consisted of a shield of 0.020 in. of aluminum; C of 0.008 in. of copper plus 0.020 in. of aluminum; and D of 0.024 in. of copper plus 0.020 in. of aluminum. Once the researchers found that the density ratio of unshielded film to shielded film was a function of the X-ray energy, they set up tables in which they assigned a factor to a density ratio between two adjacent fields. The product of the factor and the net density under one of the shields gave the radiation exposure directly in roentgens. The range of this film badge extended over effective X-ray energies from 15 to 150 kv.

Also in 1950 at the Medical School of the University of California, Rachel Baker and Louis B. Silverman developed a film dosimeter similar in principle to Tochilin's film badge but for more specific application (29). Baker and Silverman proposed that the emulsion (Eastman Kodak Type K film packet) be covered with a silver shield 20 mils thick. However, on the film side of the silver a small lead shield 21 mils thick was also used. Lead and silver were chosen because the ratios of the mass absorption coefficients of lead and silver were found to be very close to unity at low and high energy levels although there was quite a variation around intermediate energies between 150 and 200 kv. This conveniently allowed for

certain energy identification since the exposures encountered at the University of California Medical School were mainly due to 250-Kv and 85-kv scatter X-radiation and radium emission. For example, for the same exposure, 85-kv scatter radiation would give rise to a measurable density under the silver but none under the lead. 250-kv scatter would give rise to a density under the silver and a light density under the lead. A badge exposed to radium would show a silver area density and an intensified lead area density. However, radiation from uranium would not penetrate the silver at all.

Although use of the lead and silver allowed for the identification of radiation of different energies, Baker and Silverman admitted that with the filters the ideal of a density-exposure relationship that was independent of the energy of the radiation was not achieved. By way of compromise, however, the plot of the net density under the silver vs. exposure for 250 kv scatter could act as a master calibration curve for an exposure range from 0 to 2 r. Not only did the net density under the lead due to radium fit this curve, but the net density in the silver area due to 85 kv also coincided with the curve if the plotting values were multiplied by 4.

A filter assembly in a badge similar to that proposed by Tochilin was proposed by H. Langendorff (b. 1901) and collaborators at the University of Freiburg in 1952 (318). They also intended to solve the energy dependence problem of photographic emulsions in the

X-ray region below 300 kv by identifying the quality of the radiation responsible for the film blackening. This group of researchers chose a different metal absorber for each of the three quadrants and then used an unfiltered area for reference. The metal absorbers included 1.5 mm of aluminum, 1.5 mm of copper, and 0.5 mm of lead. By measuring the film density of the areas under the filters they determined the quality of the radiation, that is, whether it was soft, intermediate, or hard. Then by the use of a "hardness factor" which was first proposed by Dorneich and Schaeffer in 1942 (152) they calculated the actual dose received by the film. By the use of the filter assembly and a standard developing procedure, this group at the University of Freiburg obtained an accuracy in dose determination of 15 to 20%.

Four years later, under the Directorship of Professor Langendorff at the same Radiological Institute of the University of Freiburg, H. Dresel proposed that if the same metal were used for all three absorbers, the determination of dose would be more reliable (156). Dresel suggested three copper filters having the following thicknesses: 0.05 mm, 0.5 mm, and 1.2 mm. Only for extremely hard radiation around 1.5 Mev and above did he advocate using a thin lead filter. With filters made of the same metal, Dresel felt that a more conclusive identification of the quality of the radiation was assured.

Of the two approaches used and developed to solve the energy

dependence problem of film dosimetry, that proposed first by Pardue (see p. 161, above) of using a filter to attenuate the radiation to reduce the energy dependence has contributed significantly towards the attainment of better accuracy in photographic dosimetry (see p. 165, above). Still, in 1958 G. Spiegler and R. Davis of the Physics Department at the Institute of Cancer Research in London took an unfavorable attitude toward the absorption method of reducing the dependence of film sensitivity on energy (455). According to Spiegler and Davis there were too many ill-defined factors that made apparent absorption an unreliable indicator of quality. For example, filters failed to distinguish the angle of the incident radiation; in the case of soft radiation, the ratio of filtered to unfiltered dose was so low that absorption could not be measured with low or medium doses; and the amount of secondary electrons recorded in an unshielded area of the film varied with conditions.

For discriminating the quality of the radiation, Spiegler and Davis advocated a method based on the electron emission from metal foils (455). They proposed a new film holder which had a 1.5 mm thick brass front in which was a centralized circular aperture. The 0.6 mm thick steel back was lined with a 0.1 mm lead foil along three-quarters of its length and had an oblong slot across the center. For the evaluation of type of exposure, measurements of the density under the various parts of the film holder were interpreted by making

use of the various features of photon interaction with metals, including the backward and forward ejection of secondary electrons. For example, high-energy radiation was reliably indicated by the negative contrast of the backing slot. The negative contrast of the backing slot was due to a deficiency of secondary electrons within the slot area as compared with the emission of electrons reaching the film from the lead foil due to high-energy radiation. Once the quality of the exposure was known, it was related to dose by an energy factor. Spiegler and Davis claimed an accuracy of $\pm 20\%$ for their method. Although the mean error of absorption methods was much higher than 20% , Ehrlich and Fitch (see p. 165, above) did attain the same accuracy ($\pm 20\%$) with an absorption method. Furthermore, Spiegler and Davis did not report the range of exposures over which their dosimeter was useful. That of Ehrlich and Fitch could be used from 1 to 10^4 r.

In addition to the film-badge modifications that were aimed at reducing the dependence of film sensitivity on energy, there were other suggestions for improving the reliability of photographic dosimetry. However, these suggestions were not the kind that could be generally applied. Often many laboratories improved their film badges for their own benefit, that is, to satisfy their own needs. This was true of the proposals of some researchers who emphasized the type of emulsion used. One such report in 1948 (534) came from Los Alamos Scientific Laboratory in New Mexico where high-energy

gamma stray radiation was the problem. After investigating a number of commercially available films, the group proposed the "Defender Adlux" film as possessing the desired degree of sensitivity. The same Adlux film was suggested by William Herman of Brookhaven National Laboratory in New York in 1951 as a suitable insensitive component of an emulsion combination (263). The presence of the Adlux film with a sensitive Du Pont Type 508 film made a film packet which was more desirable for use in recording accidental high exposures.

In 1954, the radiation physicist Gerald J. Hine (b. 1916) of the Massachusetts Institute of Technology had compiled a list of some film calibrations published by various authors (269). Though it was not intended as a systematic survey of film calibrations, the list does show that there were available emulsion types for all dose levels. The list contained an arrangement of emulsion types according to the exposure in roentgens required to produce a density of 1.0. Kodak Type K film, the lowest on his list, responded to about 0.25 roentgens in the same way as Du Pont Adlux Type 1290 film responded to about 300 roentgens. Therefore, for reliable dosimetry, an emulsion type had usefulness only over a certain range of exposures.

The increase in accuracy and reliability provided by some of the above film-badge modifications accentuated many of the practical advantages of the film badge over other methods of personnel

monitoring. Therefore, photographic dosimetry became increasingly popular during the post-war period. In fact the use of film badges became a small industry in itself. Private groups provided a general service for preparation of the film badges and for the development of the exposed films. This service was made available to all medical institutions and to industrial and research centers. Most probably it has served to standardize film-badge monitoring since closer controls were kept, or at least could be kept, on the development techniques of both the calibration films and the measurement films.

Mixed Radiation Fields

Developments in the field of nuclear energy also gave rise to problems for those interested in the protection of the radiation worker. In the proximity of the numerous reactors and accelerators that were erected, dosimetric measurements were complicated by the presence of mixed radiation fields. Although proper shielding was installed with these devices to prevent the escape of lethal radiation, the monitoring of personnel exposures to stray radiation was still necessary. In fact during the days of the Manhattan Project, the various laboratories took an unprecedented step in actually forming separate organizational sections or divisions whose emphasis was to be the protection of radiation workers against the potential hazards of their occupation (379, p. 1). For example, at the Metallurgical Laboratory

and at Oak Ridge a Health-Physics Section was organized for that purpose; at Hanford it was called a Health Instrument Section; at Argonne the Hazards Evaluation Group was in charge of radiation protection activities. Each laboratory then supervised its own activities that were set up to protect the radiation worker.

The film badges available in the early 1940's were the kind used by radiologists in clinics and hospitals. Such film badges were intended primarily for monitoring exposures to X-radiation or to low-energy gamma radiation. They could not distinguish between exposures to high-energy gamma radiation and to high-energy neutrons. Since exposure to these forms of radiation was possible in the vicinity of reactor installations and since research had shown the different biological effectiveness of these two kinds of radiation, it was desirable and necessary that exposures to the two kinds of radiation could be identified. Research teams under the Health-Physics sections, or their equivalent, in most laboratories devised modifications of the existing film badges to meet these new monitoring needs. Perhaps the secrecy that shrouded the work in each laboratory during World War II contributed to this kind of development. Indeed, it seems as if some of these developments were never published. When reports were published as Atomic Energy Commission classified documents, they may have been distributed among the laboratories involved in the project if the reported information was pertinent to the work being

done at these locations. Once the documents were declassified after the war, they were of particular value to reactor installations just beginning operations. However, existing installations, for the most part, retained their own characteristic personnel badges and modified them as the need arose. It seems reasonable that there would have been duplication of basic film badge types since the scientific principles basic to the required modifications were known. For example, studies on X-ray absorption edges had been reported in 1925 (82). More recently investigations had been conducted at Cornell University in 1938 on the photographic effects of cadmium and other elements under neutron bombardment (275). Data of this kind most probably suggested the direction of any additional research. Therefore, it is probable that modifications of film badges proposed and used by one major reactor establishment were also developed elsewhere to meet similar monitoring needs.

Although the earliest permanent reactor-oriented research centers date back to 1943, apparently regular programs in the monitoring of personnel at these centers were not begun until 1944. The first film badge to be used at Oak Ridge National Laboratory (ORNL) was introduced in 1944 (496, p. 2). A program in personnel monitoring had its inception at Hanford in 1944 (32, p. 1). A film badge system was not begun at the Lawrence Radiation Laboratory in Berkeley until in 1946 (382). Film badges may have been used prior to the

inauguration of a definite program, but records of such uses evidently were not kept.

The first film badge introduced at ORNL was modeled after the one developed at Argonne National Laboratory in 1944 (see p. 161, above). Since that time there were five major changes in the ORNL film badge, each of which was designed by the personnel in the Health-Physics Section at Oak Ridge. The last modification was made in 1959. The major changes involved principally the types of filters and the kinds of film used. The first three badges contained just one cadmium filter on the film in addition to an open window area; the next badge had an echelon of lead, cadmium, copper, and plastic besides the open window; the last two made use only of cadmium which was in reality a cadmium-gold-cadmium combination. The system of filters was meant to overcome the photon energy dependence of the film emulsion.

Apparently the film emulsions used in the badges were actually film packets, that is, they were a combination of sensitive and insensitive films which extended the roentgen dose range of the film dosimeter (496, p. 4-5). Since the second badge type developed in 1949, an additional fine-grained particle emulsion (the NTA film)⁷² was

⁷²The NTA film was produced by Eastman Kodak in 1947 after the introductory research on nuclear track emulsions by the physicist Joseph Cheka (b. 1909) at ORNL in 1944 (334, p. 3).

included in the film section of the badge to measure the thermal neutron dose. This latter emulsion did not suffice when exposure due to neutrons with energies greater than 3.5 Mev were to be monitored. Therefore, the Eastman Kodak NTA film, a packet in itself, was further modified to give a reliable dose response for neutrons with energies up to 10 Mev. A description of the film-packet, proposed in 1954, showing the thicknesses of the component parts is given in Table 1 below. This form of NTA film made the badge useful for monitoring neutrons up to 14 Mev such as may be encountered in the vicinity of accelerators (91).

Table 1. Final NTA-film packet.

| Material | Thickness (mg/cm ²) |
|------------------------------|---------------------------------|
| Cellulose (or front of film) | 76 |
| Aluminum | 85 |
| Cellulose | 24.2 |
| Cellulose (film wrapper)* | 10.3 |
| Aluminum* | 27 |
| Film base* | 28.5 |
| Emulsion* | -- |
| Blank film* | 28.5 |
| Aluminum* | 27 |
| Cellulose (film wrapper)* | 10.3 |
| Cellulose | 24.2 |
| Aluminum | 85 |
| Cellulose | 76 |

* These constituents were present in the packet as supplied by the manufacturer (91, p. 43).

It was not until 1959 that the ORNL film badge was modified for criticality accident applications. Materials were then added which permitted the immediate identification of those who had received medically significant short-term doses of neutrons and high-energy gamma-radiation. The previously incorporated features of the badge provided only for the dosimetry of beta-, gamma-, and low-level neutron doses. In the slide containing the filter assembly, then, provisions were made for other components in the event of a criticality accident: an indium foil, a sulfur pellet, a "bare" gold foil, a chemical dosimeter, and three meta-phosphate glass rods with their associate filters (286).

The filter assembly provided a method for calculating the dose of beta- and gamma-radiation. The activated gold foil permitted a determination of thermal neutron exposure; the one-half gram pellet of elemental sulfur registered any high-energy (greater than 2.5 Mev) neutron exposure. The indium foil was added because it was known that 96% of the natural indium is made up of the isotope indium-115. Indium-115 has a high thermal neutron activation cross section and the resultant indium-116 has a half-life of 54 minutes. In the event of a criticality accident, anyone receiving a significant exposure to neutrons could be identified easily by measurement of the radiation from the activated indium foil in the badge. The activated gold foil, though less sensitive, has a much longer half-life and thus was a

valuable complement to the indium. Of course the dose to the badge and the actual dose to the person was a function of the relative orientation of the badge with respect to the source of radiation.

The silver meta-phosphate glass rods were used to measure gamma radiation doses above 100 rads. Chemical techniques were also used for high-energy gamma dosimetry in the presence of both fast and thermal neutrons. A tubular slot was provided in the badge for a chemical dosimetric system. The system recommended for use in the 1959 ORNL badge had tetrachloroethylene (TCE) as its major component and was applicable in a dose range of from 5 to 2×10^6 rads (286, p. 68-77). When a two-phase aqueous system of tetrachloroethylene is irradiated, water soluble acids are liberated. The amount of acid formed is proportional to the dose within a given range. The acid yields are high with G (acid) values up to 6000; the sensitivity can be reduced by adding some stabilizing agent which could lower the G value to about 30. Significantly a TCE two-phase system produces from 3 to 4% as much acid from a rad of neutrons as from a rad of gammas, but when exposed in a lithium shield, the TCE system provides a relatively accurate value of gamma-dose in the presence of fast and thermal neutrons.

The response of the TCE dosimeter can be evaluated by titration of the acid. If a water soluble pH indicator dye is used in the system, spectrophotometric measurements of pH changes can be

made. The indicator would also serve to give a quick visual identification of exposed persons. The TCE dosimeter had other desirable characteristics. It had good reproducibility and was independent of dose rate up to 10^{12} rads per hour; it was independent of temperature from 5° to 55°C ; and it was independent of energy from 90 Kev to 10 Mev. In addition it had a linear response to doses up to 2×10^6 rads and had a shelf-life greater than nine months.

Although it was not essential to the ORNL badge, the TCE dosimeter had characteristics which made it ideal for the measurement of high gamma exposures. When compared with the first film badge used in 1944, the 1959 type of the ORNL film badge certainly had aspects of complexity about it. It does indicate how every protective measure (one even overlapping another at times) was taken to guard against exposure injury.

Photographic Dosimetry in Developmental Perspective

In its application in the monitoring of personnel, photographic dosimetry has attained a level of reliability by 1960 mostly because ways were found of reducing the energy dependence of photographic emulsions. The use of filters or filter assemblies improved the accuracy of film dosimetry from a low of about 10% to about 80%. Other modifications of film badges made the identification of various forms of radiation possible. Although much has been done in

controlling film response, further developments possibly could come in methods of evaluating the exposed film. For example, in 1960, W. V. Baumgartner of the Hanford Laboratories suggested (33) extending the range of film badges by measuring the silver content of developed films with an X-ray spectrometer. Such measurements would not interfere with optical densitometry. Normally the density of the silver image developed on the film is measured with an optical densitometer. The measurement film is then assigned a radiation dose by comparing its density with that of a standard film whose exposure is known. However, doses greater than 40 roentgens give density readings which often exceed the limits of optical densitometers. The use of an X-ray spectrometer to measure the silver content of the developed film could extend the range of the film to 2,000 roentgens.

During the Symposium on Selected Topics in Radiation Dosimetry sponsored by the International Atomic Energy Agency in Vienna in the summer of 1960, there were reports on personnel monitoring in several countries. It is significant that the use of the film badge did not come into general acceptance in these countries until within a decade prior to the symposium. The methods discussed above for reducing photon energy dependence of the film were adopted or at least followed by these countries.

In Germany (524) film dosimetry was not introduced until in 1952. Since the radiological institutes at several universities in

Germany were responsible for introducing the film badge for personnel protection, the research on the filter technique conducted at the University of Freiburg was utilized (see p. 167, above). In addition, the "double-film" was being used to extend the measurable dose range. The actual dose received by the film was determined by multiplying the apparent dose by a "hardness factor" associated with the quality of the incident radiation. The latter was determined by an analysis of the film density under the filter assembly.

Studies were also made in Germany (524) on the effect of the angle of incidence on the sensitivity of the film. The researchers were mainly interested in the effect that changes in the angle of incidence would have on dose measurement and its significance to radiation protection. Investigation of the doses recorded by film badges worn on various body locations showed that those worn on the chest area always received a dose close to the average dose with a tendency to give higher rather than just average readings. A film badge worn on the lapel of a coat was, then, an effective instrument for radiation-protection purposes. It should also be noted that when neutron film dosimetry was introduced in Germany, the procedures practiced at the Atomic Energy Research Establishment at Harwell in England were followed. However, at Harwell (498) the well-publicized fine-grain emulsion packets (NTA film) proposed by Cheka of Oak Ridge (see p. 175, above) were in use.

At the Swiss Reactor Station in Würenlingen, a tin-lead filter combination (see p. 164, above) was used in the filter assembly for the measurement of gamma-dose (388). However, a rhodium-lead filter combination was also used because studies showed that rhodium responded better to small doses of neutrons than did cadmium. The completed filter assembly had the following sectional components: (1) an open window; (2) 1 mm of plexiglass; (3) 0.3 mm of rhodium plus 0.5 mm of lead, and (4) 0.65 mm of tin plus 0.4 mm of lead. Film density under section 4 was indicative of the gamma-dose. Since that under section 3 indicated the neutron dose plus the gamma-dose, the difference between the densities under sections 3 and 4 gave the neutron exposure. Since the gamma-dose under sections 1 and 2 was identical, the difference between the densities was interpreted as equal to about one-half the beta-dose.

At the same symposium a report from the Industrial Radiology Department at the Electrotechnical Institute in Warsaw, Poland (148), showed concern by those responsible for radiation protection for only X- and gamma-ray dosimetry. Although no specific dates were given in the report, its tone seems to imply that a large-scale program of monitoring industrial workers using sealed radiation sources was introduced in Poland rather recently, that is, just prior to 1960. For use in medical X-ray installations, the photographic method of dosimetry was just being introduced. In fact in 1960, the Central

Laboratory for Radiation Protection in Warsaw was engaged in developing a method for the measurement of dose which would take into account the quality of radiation for what appeared to be a mixed radiation field. In preparation for industrial personnel monitoring, extensive studies were made of the sensitivities of both Polish and German manufactured X-ray films. The final choice of film was the Polish-made "Foton Rentgen Super" film characterized as a high-speed film. Filters were not used for dosimetric purposes. Only one small lead filter which covered a quarter section of the film served to indicate whether the film blackening was due to X- or gamma-rays or to visible light. For gamma-ray dosimetry it was discovered that none of the available films could be used without lead intensifying screens.

Reports like the above from Germany, Switzerland, and Poland show that film dosimetry for personnel monitoring has been patterned after some of the early developments in film badge modifications that accompanied the progress in atomic and nuclear research during and in the immediate post-war period. Early developments in film dosimetry had been based on certain scientific principles. Therefore, reliable procedures for personnel monitoring were established. It seems that, if consistently applied, such procedures should provide an adequate indication of exposure in the future also, unless the need for protection from some yet unknown radiation source should arise.

This does not imply that there is no possibility for improvements in the materials used and in technique efficiency in existing procedures.

Because of the sensitivity of film to small doses, photographic dosimetry has found wide application in personnel monitoring. There have been other areas, particularly in radiotherapy, where film dosimetry has also been employed. Very probably such applications will become more extensive in the future particularly if an adequate and convenient compensator for the energy dependence of a film is found. An application of film dosimetry, related perhaps to personnel monitoring but much more specific, was reported from Lambeth Hospital, London in 1952 (407). There, films were used to estimate the doses received on fingers and hands during the handling of radium. Small Standard X-ray films (1 cm^2 in area), suitably packed in water-proof material, were worn on the fingers and hands during radium manipulations. These films were then compared with a calibrated set of films which had received known doses of gamma-radiation and which were processed with the measurement films. Standard X-ray film was chosen since its response was satisfactory within the range of 0 to 4 roentgens of gamma-radiation.

The photographic method of dosimetry was suggested in 1955 for measuring the distribution of dosage from radium needles and plaques (499). Such a method would obviate the general procedure of mathematically analyzing the distribution of dosage around a linear source

of radium. An experiment was conducted with Eastman Type M industrial X-ray film and radium plaques loaded with needles. Measurements were made in air and also in a phantom of tissue-equivalent wax. No significant differences were found between the two radiation fields. Most importantly, the film measurement agreed with the corresponding mathematical results. Because of the limiting factors of photographic dosimetry, however, any measurements made in tissue-equivalent material were made within 10 cm of the source. This kept the gamma-radiation degradation down to a minimum; otherwise an increased film sensitivity would have been observed.

The possibility of film dosimetry in grid therapy with a cobalt-60 radiation source has also been considered (347). For multiple field dosimetry in radiation therapy with cobalt-60, cesium-137, and X-rays with energies above 1 Mev, the superposition of photographic films has been advocated in 1957 (340). The method of superposition can also be used to measure the depth-dose distribution around a multiple gamma-ray source. A procedure was described in which a tandem with three radium capsules and a colpostat made of two radium containing ovoids were used to treat a carcinoma of the uterine cervix. Calculation of the complete dose distribution would have been a formidable task. According to the superposition of films method, each radium source was used to expose a separate film. The developed films were superimposed corresponding to

spacings of the plane investigated. After the isodensity lines were determined with the help of a densitometer, the films were adjusted to a new spacing of a new plane. This simple method was used to determine the entire series of dose distributions.

These clinical applications of film dosimetry emphasize the practical advantages of a film dosimeter over perhaps a more accurate ionization chamber. Although the dependence of film sensitivity on energy has been a problem in these applications, film dosimetry in these cases has not been as complex as in monitoring situations. However, in the absence of follow-up studies or surveys of such clinical practices, it is difficult to judge whether or not such applications have been or will be accepted as standard procedures.

CHAPTER VII

CHEMICAL DOSIMETRY (1942-1962) - PART I

Photographic emulsions and the associated film badges have been used on a large scale for personnel monitoring in diverse situations. Under normal conditions films are meant to measure exposure to stray-radiation. Other chemical systems generally do not respond to such low-level radiation. Prior to the Second World War chemical reactions induced by radiation were found to require relatively large doses (see p. 107, above). This characteristic of chemical systems led to renewed interest in chemical methods of dosimetry when nuclear reactors and other intense radiation sources were developed. In addition to providing for new and varied applications in radiotherapy and in industry, these intense radiation sources also gave rise to research in radiation biology, radiation chemistry, and nuclear technology. Such developments created a need for the measurement of doses over a wide range. In radiation chemistry and nuclear technology, highly sensitive systems were rarely needed. Although research in radiation biology required lower doses, the measurement of dose by the chemical changes produced in tissue-equivalent material was preferable to, for example, methods utilizing ionization in a gas (137).

Therefore, many chemical systems and their responses to high-energy radiation were examined for dosimetric possibilities. That a chemical system qualify for practical dosimetric purposes, it should possess certain features. Some of these characteristics were recognized as early as the 1930's (see p. 86-87, above). Although variously described in this post-war period and also variously evaluated by researchers, these features included the following: a linear relationship between the chemical effect and an absorbed dose of suitable range; a sensitivity of chemical effect that would fall within the sensitivity of analytical methods; reproducibility; stability before and after irradiation; independence of dose-rate, temperature, and quality of radiation within a certain range; reagents easily available in desired purity; and measurements that could be made simply and interpreted easily (473).

Many of the systems proposed for dosimetry from 1942 until 1962 were based on photoelectric spectrophotometry. In classical colorimetry or visual spectrophotometry the human eye makes the comparison of an unknown substance with a standard; basically, in photoelectric spectrophotometry the photoelectric tube replaces the eye. As early as 1919, photoelectric spectrophotometry was suggested by the physicist K. S. Gibson (b. 1890) as a means of obtaining reliable measurements of transmission or reflection of the blue and violet components of the visible spectrum (197). Although the method

was applied in a few cases (198, 199), data on the precision of the photoelectric method was not available until in 1934 (549). Very probably the method was not utilized earlier for analytical purposes, because many chemists were not that versed in physical optics to set up instruments of that kind. Fortunately in 1929, Arthur Hardy (b. 1895), a physicist at the Massachusetts Institute of Technology, devised an instrument which made use of a photoelectric cell sensitive to light beyond the readily visible part of the spectrum and which was equipped with a recording device (241). Since operation of such an instrument required little specialized training, the General Electric Company used it as a basis for a subsequently developed commercial design (357). General Electric's 1936 model, which also had incorporated in it further suggestions of Hardy (240), was referred to as a new tool for the analytical chemist (357). It was able to give the transmission for each wavelength in the visible spectrum where any one wavelength could be considered to the exclusion of others.

In 1941, Arnold Beckman (b. 1900), a physicist at the National Technical Laboratories in California, proposed his model of a quartz photoelectric spectrophotometer which was the prototype of the famous commercial Beckman instrument (77). In that same year, the physicist Charles Sheard in collaboration with a member of the Research and Development Department of the Central Scientific Company of Chicago (CENCO) devised a concave grating photoelectric spectrophotometer

(443). In the 1940's when chemical systems were being examined for dosimetric purposes, commercial models of photoelectric spectrophotometers were available to the chemist.

Photometric techniques are based on the ability of substances to interact with characteristic energy levels. Since each chemical species possesses certain characteristic energy levels, it absorbs only those frequencies which correspond to excitation from one level to another. The absorption spectrum of an unknown substance would help to establish its identity. Likewise the intensity of the absorption can be related to the concentration of the species in the optical path (465, p. 55-61, 149).

This mode of analysis upon which much chemical dosimetry has been based has made possible the calculation of G values (see p. 140, above). By definition, G (product) is equal to the molecules of the product formed per 100 ev of energy absorbed. Since an energy absorption of 100 ergs per gram is equal to 1 rad (see p. 150, above), then with the proper conversion factors,

$$\begin{aligned} \text{Energy absorbed} &= \frac{100 \text{ (molecules of product formed/g) ev/g}}{\text{G}} (1.602 \times 10^{-12} \text{ ergs/ev}) \left(\frac{1 \text{ rad}}{100 \text{ ergs/g}} \right) \\ \text{(Dose in rads)} & \\ \text{(a) Dose} &= \frac{(1.602 \times 10^{-12} \text{ molecules of product/gram})}{\text{G}} \text{ rads} \end{aligned}$$

If the yield was measured spectrophotometrically, then,

$$\text{(b) } \frac{\text{Molecules of product formed}}{\text{gram}} = \frac{\Delta OD}{\epsilon d} \frac{\text{moles}}{\text{liter}} \left(\frac{1}{1000 \rho} \frac{\text{liters}}{\text{gram}} \right) \left(\frac{6.023 \times 10^{23} \text{ molecules}}{\text{mole}} \right)$$

where ΔOD = the change in optical density

ϵ = molar extinction coefficient (liters/mole cm)

d = optical path length (cm)

ρ = density of the solution

Combining (a) and (b)

$$\text{Dose} = \frac{\Delta OD}{\epsilon d \rho} \frac{(0.965 \times 10^9)}{G} \text{ rads. }^{73}$$

Aqueous Systems

Among the first of the liquid systems to be investigated for dosimetric purposes after the Second World War was the aqueous ferrous sulfate system. The oxidation of aqueous ferrous sulfate in 0.8 N sulfuric acid by irradiation was proposed for dosimetry in 1927 by Fricke and Morse (see p. 87, above). Certain desirable properties of the system as reported by Fricke and Morse were subsequently confirmed by other investigators (184, 444). Among the characteristics emphasized was the independence of the oxidation yield on the initial concentration of ferrous ion. Renewed interest in chemical dosimetry at the end of the 1940's made possible the corroboration of other experimental data. In 1950, Nicholas Miller, a chemical

⁷³The equation as well as its derivation are general and applicable to any type of radiation. An example of its application to a specific chemical system may be found in Radiation Chemistry of Gases (336, p. 59).

physicist at the University of Edinburgh, supported Fricke's claim that the ferric ion yield was independent of quantum energy for 100 kv X-rays to 2 Mev gamma-rays (358, 359). Miller also showed that the yield was independent of dose rate from 0.02 r/sec up to approximately 100 r/sec. This independence of dose rate within a useful range was confirmed in 1952 by another physical chemist, Thomas J. Hardwick (b. 1922) (237).

Although the ferrous sulfate system--the Fricke dosimeter--had many desirable properties, it also had some limitations. Some of the first investigators of the systems had noted in their research that the ferric ion yield was due, in part, to the organic impurities present in the system (444). Therefore, purity of reagents was considered necessary; the water used was triply distilled and the ferrous sulfate was recrystallized. In 1951, Harold A. Dewhurst, a physical chemist, discovered a solution to the problem of organic impurities (146). He found that chloride ions acted as inhibitors to the oxidation of ferrous ion by organic impurities in the system. His proposal that the addition of sodium chloride to the original solution would stabilize it against the actions of organic impurities was the first important modification of the Fricke dosimeter. In addition to contributing to the stability of the system, this modification made the use of the Fricke dosimeter more convenient by eliminating the lengthy process of reagent purification.

In 1952, Hardwick provided for a more sensitive and accurate dosimeter when he suggested that the ferric ion concentration be determined spectrophotometrically by its absorption at a wavelength of 3050 Å (the absorption peak of ferric ion) (237). Fricke and Morse had used a titration process for this determination (see p. 91, above). Not only did absorption spectroscopy provide for more rapid and accurate ferric-ion determinations, but it also placed existing absolute G values for the system under scrutiny. Early investigators had reported a ferric-ion yield of 16 in 1932 (444) and 18.3 in 1935 (185). However, the G value was not specifically defined until approximately 1943 (see p. 140, above). In 1950, using an ionization method, Miller measured the ferric-ion yield due to radium gamma-rays and 200 kv X-rays and reported a G value of about 20.6 (359). Hardwick obtained the same value due to gamma-radiation in 1952 (237). Significantly lower values were reported also in 1952, by the radiation chemists R. W. Hummell and J. W. T. Spinks from Canada (285). For 24.5 Mev betatron X-rays they reported a yield of 15.8 and for radium gamma-rays they measured a ferric-ion yield of 16.8.

Since calorimetry was the most direct, though not the simplest, method for measuring absorbed energy, and since it was not used in any of the reported G value determinations, the chemists C. J. Hochanadel and J. A. Ghormley made a calorimetric determination

of the G value in 1953 at Oak Ridge National Laboratory. Using cobalt-60 gamma-rays they obtained a ferric ion yield of 15.6 (271). Since that time, calorimetric determinations of the G value made by others using cobalt-60 gamma-rays confirmed the Hochanadel-Ghormley value. Yields of ferric ion due to other forms of radiation were also reported.⁷⁴ Since these yields showed a considerable dependence upon the LET of the radiation (see p. 140, above), the appropriate absolute values of the ferric-ion yield had to be chosen when using the equation based on spectrophotometric measurements (see p. 191, above). The appropriate G value was necessary for the reliability of the Fricke dosimeter.

The dependence of the ferrous oxidation upon the oxygen concentration was noted from the very first studies made in 1927 (see p. 88, above). In fact, more recently when the Fricke dosimeter was described as useful within a dose range of 4,000 to 40,000 r, the lower limit was determined by the analytical method used. The upper limit was determined by the supply of oxygen in an aerated solution (530, 532). A possible way of extending the lower limit was presented as early as 1953 by Gösta Rudstam and The Svedberg, nuclear chemists at the University of Uppsala (416). They suggested that iron-59 tracer be added to the solution. According to their method of analysis, ferric

⁷⁴ An illustrative selection of G values for the ferrous sulfate dosimeter as found in literature prior to 1962 is given in Table 2.

Table 2. G Values for the Fricke Dosimeter.

| Radiation | G (Fe ³⁺) | Method of Energy Measurement | Bibliog. Ref. |
|--|-----------------------|------------------------------|---------------|
| 30 Mvp X-rays | 16.3 ± 0.6 | Ionization | 256 |
| 2 Mvp X-rays | 16.0 ± 0.5 | Ionization | 533 |
| Cobalt-60 gamma-rays (1.25 Mev) | 15.5 ± 0.5 | Ionization | 256 |
| | 15.6 ± 0.3 | Calorimetry | 271 |
| | 15.7 | Ionization | 271 |
| | 15.8 ± 0.3 | Calorimetry | 329 |
| | 15.67 | Calorimetry | 276 |
| | 15.9 | Ionization | 442 |
| 2 Mev electrons | 15.45 ± 0.11 | Charge collection | 438 |
| 100 Kvp X-rays | 14.7 ± 0.5 | Ionization | 256 |
| 12 Mev deuterons | 9.81 | Charge collection | 253 |
| 1.99 Mev protons | 8.00 | Charge collection | 253 |
| 3.47 Mev deuterons | 6.90 | Charge collection | 253 |
| 0.63 Mev protons | 6.89 | Charge collection | 253 |
| Polonium-210 alpha-particles (5.3 Mev) | 5.10 ± 0.10 | Absolute counting | 503 |

ion was complexed with thiocyanate and was extracted from the solution with isoamyl alcohol. The ferric ion was then measured radiometrically and the sensitivity of radiometric measurements made the Fricke dosimeter useful down to well below 100 rads.

In 1957, the physicist Gail Adams and his associate at the University of California School of Medicine found a way of extending the lower limit of the dose range by the addition of benzoic acid to the dosimeter solution (1). To 1.0 N sulfuric acid they added 1.4×10^{-3} M benzoic acid and then 7.15×10^{-4} M ferrous sulfate. The benzoic acid increased the G value for the ferric ion yield to about 65, which was determined by spectrophotometric measurements at 2605 \AA , the transmission peak of benzoic acid. The addition of benzoic acid also increased the stability of the pre-irradiated solution. Because ferrous ion was oxidized at a perceptible rate in the absence of radiation (the 0.8 N sulfuric acid in the standard solution was used to retard this oxidation), routine use of the ferrous sulfate dosimeter was not convenient since its shelf life was not very long.

Another modification aimed at extending the lower limit was recommended in 1962 by the biophysical chemist Norman A. Frigerio (b. 1927) (193). He proposed that leucobenzoyl methylene blue be added to the solution. This increased the sensitivity of the system twentyfold owing to the formation of highly colored complexes of ferric ion which increased the reliability of spectrophotometric measurements

of low yields. This modification also made the Fricke dosimeter useful for doses smaller than a 100 rads.

The upper limit of the dose range of the ferrous sulfate dosimeter was extended in 1954 by the chemists Edwin Hart and P. D. Walsh at Argonne National Laboratory (252). They reported that the addition of cupric sulfate to ferrous sulfate at a pH of 2 caused the ferric ion yield on irradiation to fall from 15.6 to 0.66. Oxygen was not consumed in this system. Therefore, much higher concentrations of ferrous ion were used along with correspondingly higher concentrations of cupric ion. Spectrophotometric measurements of ferric ion were still made at 3050 Å without interference from the copper and without having to make adjustments of the acidity (253). The upper limit of the dose range was extended up to 10^7 rads by this addition of cupric ion. The low yield of the cupric-modified ferrous system together with the linear relationship between yield and high doses made it ideal for high-level gamma dosimetry (250).

Although with the various modifications the ferrous sulfate dosimeter is useful within a dose range of a 100 to 10^7 rads, the standard Fricke dosimeter (10^{-3} M ferrous sulfate + 0.8 N sulfuric acid, aerated) has usefulness only within the more limited range of 4,000 to 40,000 rads. However, it has the characteristic of high reproducibility whether in the hands of experienced or inexperienced personnel (532). This reliability of the Fricke dosimeter has made it most

useful for calibrating other dosimetric systems.

The reduction of ceric ion to cerous ion by irradiation was not proposed for dosimetry until in 1952 by Thomas J. Hardwick (b. 1923), a physical chemist at the reactor establishment at Chalk River, Ontario (236). Hardwick reported that the yield of cerous ion was independent of concentration from 3.2×10^{-2} M to 10^{-5} M ceric sulfate in 0.8 N sulfuric acid. The system was also energy independent within a broad range, from 100 kv X-rays to 2 Mev gamma-rays. Working with the beta-radiation from sulfur-35, Hardwick obtained a cerous-ion yield of 3.32 ± 0.8 . The same irradiation applied to a ferrous sulfate dosimeter gave a ferric-ion yield of 20.2 ± 0.7 . The low G value meant that the ceric sulfate system was suitable for the measurement of large doses beyond the normal range of the Fricke dosimeter. Furthermore, the cerous-ion yield was linear with dose and independent of dose rate from 0.5 to 500 r/sec.

Other investigations of the ceric system were then made in an effort to confirm its desirable dosimetric characteristics and to determine any of its limitations in that regard. In that same year, 1952, Jerome Weiss (b. 1922), a physical chemist, confirmed the yield measurements as reported by Hardwick (530). From comparison of the cerium system with the ferrous sulfate system, cerium reacted one-sixth as much as iron did. Weiss determined the ceric ion concentration by spectrophotometric measurements at a wavelength of

3200 Å and reported that the ceric system showed a greater change in optical density per unit change in concentration than did the ferrous system. Therefore, the accuracy that could be attained in determinations made on the ceric system would be better than one could get in measurements on the iron system.

In 1953, reports from the Massachusetts Institute of Technology showed that the ceric sulfate system was independent of initial concentrations over a still wider range from 10^{-2} M to 2×10^{-6} M (136). Although in 1955 the ceric sulfate system was shown to be sensitive to visible and ultra-violet light (367), the system was practically independent of temperature and oxygen concentration (244). In 1959, the chemists J. T. Harlan and E. J. Hart reported the upper limit of the dose range for the ceric system to be 10^8 rads (244, 245). Since the cerous ion concentration in their investigations was quite high (about 0.5 M), Harlan and Hart determined the exact concentration by colorimetric titration of the ceric ion with ferrous sulfate using ortho-phenanthroline as indicator rather than by spectrophotometric measurements. They also recommended that the ceric system be calibrated (against a standard like the Fricke dosimeter) for each situation because it had poor reproducibility owing to its great sensitivity to impurities.

Even before most of the characteristics significant to dosimetry were known about the ceric sulfate system, a modification of the basic

system was reported in 1956 by Thomas Sworski, a chemist at Oak Ridge National Laboratory (470). Sworski showed that the yield of cerous ion from an air-saturated solution of ceric sulfate in 0.8 N sulfuric acid could be increased by adding thalious ion to the pre-irradiated solution. Since the cobalt-60 gamma-radiation induced the reduction of ceric ion by thalious ion, the over-all cerous-ion yield was increased from 2.39 to 7.92. Therefore, the addition of thalious ion increased the reliability of the ceric sulfate dosimeter in the lower-dose range.

To provide an additional dosimetric method for the high-dose range, Ivan Draganić, a physical chemist from Yugoslavia, suggested in 1955 that the decomposition of an aqueous solution of oxalic acid be used for dosimetry (153). Research on the oxalic acid system⁷⁵ enabled Draganić to report its usefulness for dosimetric purposes over the range of 1.6×10^6 to 1.6×10^8 rads (154). The lower limit was set by the small changes in concentration under irradiation and the sensitivity of the analytical method used; the upper limit was determined by the complete decomposition of a saturated solution of oxalic acid at that dose. Concentration measurements originally were made by titration with a potassium permanganate solution. However, when concentrations were low and doses were small, that method proved

⁷⁵ Apparently Ivan Draganić did his doctoral research on this oxalic acid system (132, footnote).

inaccurate (467). Under such conditions hydrogen peroxide formed faster than oxalic acid was decomposed (the hydrogen peroxide effect was negligible at higher concentrations) and, therefore, more potassium permanganate was needed as a control.

To improve the analytical method, Draganić developed a way for direct spectrophotometric determination of oxalic acid by means of cupribenzidine (155). When added to the irradiated solution, the cupribenzidine reagent, a mixture of equal amounts of 1.25×10^{-3} M benzidine hydrochloride solution and 3.75×10^{-3} M copper acetate, formed a complex with the oxalic acid almost instantly. The oxalic acid concentration was determined from the absorption measurements of its cupribenzidine complex at a wavelength of 2460 \AA . These absorption measurements were not affected by any of the other irradiation products. Nevertheless, this new analytical method did have a limitation; the molar extinction coefficient of the complex depended on reagent purity, particularly that of the benzidine hydrochloride. The yield of decomposed oxalic acid was approximately 4.9.

The development of chemical dosimetric systems was not restricted to high-dose levels. An alternative to the Fricke dosimeter for the measurement of lower doses was proposed in 1949 by M. J. Day, a radiotherapist, and Gabriel Stein, a chemist, both from England (139). Day and Stein suggested aqueous benzene and sodium benzoate for dosimetry because irradiation in the presence of oxygen

gave mainly phenolic products. Phenols could be readily estimated colorimetrically after the addition of Folin's reagent (phosphotungstic acid reagent) directly to the irradiated solution. The yield of phenolic products was about 2.6 and was not critically dependent on either pH, concentration, or temperature. In sensitivity the benzene system (which could measure doses between about 20,000 and 60,000 r) was similar to the ferrous sulfate system, but it did have an additional advantage. The solution could be kept, either before or after irradiation, for a long time without deterioration. Subsequently in 1951, Day and Stein reported that the depth of the blue color which developed due to the action of phenols on Folin's reagent was an accurately reproducible linear function of dose to about 60,000 r (137).

Further research showed that the development of the blue color, however, did depend on the freshness of the reagent and the pH and temperature of the solution. This led M. E. J. Carr, a radiobiologist at the Atomic Energy Research Establishment in Harwell, in 1951 to suggest that phenol determinations be made directly by U-V spectrophotometric measurements (76). Since phenol absorbed about 330 times as strongly as benzene at a wavelength of 2700 \AA , small amounts of phenol were easily detected. The spectrophotometric method gave consistent results for doses greater than 5,000 r; however, it was not as sensitive as the colorimetric method for lower doses.

If the benzene solution were not sufficiently aerated, irradiations

of the solution gave rise to products that interfered with the U-V spectrophotometric method. In 1952, the chemist Thomas Sworski at Oak Ridge proposed a new spectrophotometric method of analysis (417). It was based on the difference in the absorption of unbuffered and alkaline phenol solutions. Although unbuffered phenol solutions exhibit an absorption maximum at a wavelength near 2700 Å, alkaline phenol solutions show an absorption peak nearer to 2900 Å. Because there is a relatively considerable difference in optical densities between the two, Sworski's method of analysis minimized the interference of those products of irradiation which showed no appreciable difference in the absorption spectra of their unbuffered and alkaline solutions. The alkaline solution was prepared by adding 3 ml of 0.1 N sodium hydroxide to 5 ml of irradiated solution and diluting the mixture to 10 ml. The unbuffered 10 ml sample consisted of a diluted 5 ml of irradiated solution. Similar alkaline and unbuffered blank samples were prepared. Then the concentration of the phenol was calculated according to the following equation:

$$\text{Phenol concentration (micromoles/liter)} = K [(D_{AS} - D_{US}) - (D_{AB} - D_{UB})] (\text{dilution factor})$$

where the phenol calibration constant K, according to colorimetric methods of analysis (453, p. 352), was equal to $10^6/\epsilon d$. Since at 2700 Å the molar extinction coefficient ϵ of a standard phenol solution was equal to 2495 liters/mole/cm and the path length d of the

photometer cell used was 1 cm, K was equal to 397 micromoles/liter. The term in brackets represented the difference of the differences in optical density between the alkaline (AS) and unbuffered (US) irradiated samples and the alkaline (AB) and unbuffered (UB) blank samples. The dilution factor in Sworski's preparations was 2.

The modification of the Day and Stein method of analysis by Carr in 1951 was aimed at improving the accuracy and ease of phenol determination within the range of dosimetric usefulness established for the system by Day and Stein (see p. 202, above). It did more; it extended the lower limit of the range to about 5,000 r. The modification of the Carr analytical method by Sworski in 1952 was aimed at improving the accuracy and reliability of the phenol determination within this extended dose range of about 5,000 to 60,000 r. Another method of analysis for the determination of phenol yield proposed by the chemist Nathan Klein extended the lower limit to almost 10 r. In 1961, Klein, a member of the U. S. Army Chemical Corps, proposed that the selective coupling of phenol into 2,6-dibromoindophenol be used for analysis (308). Former methods of analysis imposed a lower limit of about 3.3×10^{-5} M on the phenol concentration (associated with a minimum dose of about 5,000 r). The intensely blue 2,6-dibromoindophenol made possible the detection of phenol in the 10^{-8} M concentration range (associated with a minimum dose of about 10 r). To bring about the phenol coupling, Klein proposed that a certain volume of

2,6-dibromo-n-chlorobenzoquinimine be added to a definite volume of the irradiated benzene solution. The agitated solution was allowed to stand for 24 hours. Then a certain volume of n-butyl alcohol was added. The absorbance of the extracted n-butyl alcohol phase was subsequently measured spectrophotometrically at a wavelength of 6500 \AA . Phenol concentrations corresponding to measured absorbances were obtained from a calibration curve prepared with known concentrations of phenol. If the phenol concentration was as high as 10^{-6} M , the butyl alcohol extraction was not necessary. The absorption of the aqueous solution was measured at 5950 \AA . According to the calibration curve (see Fig. 7), the sensitivity of the system was very good.

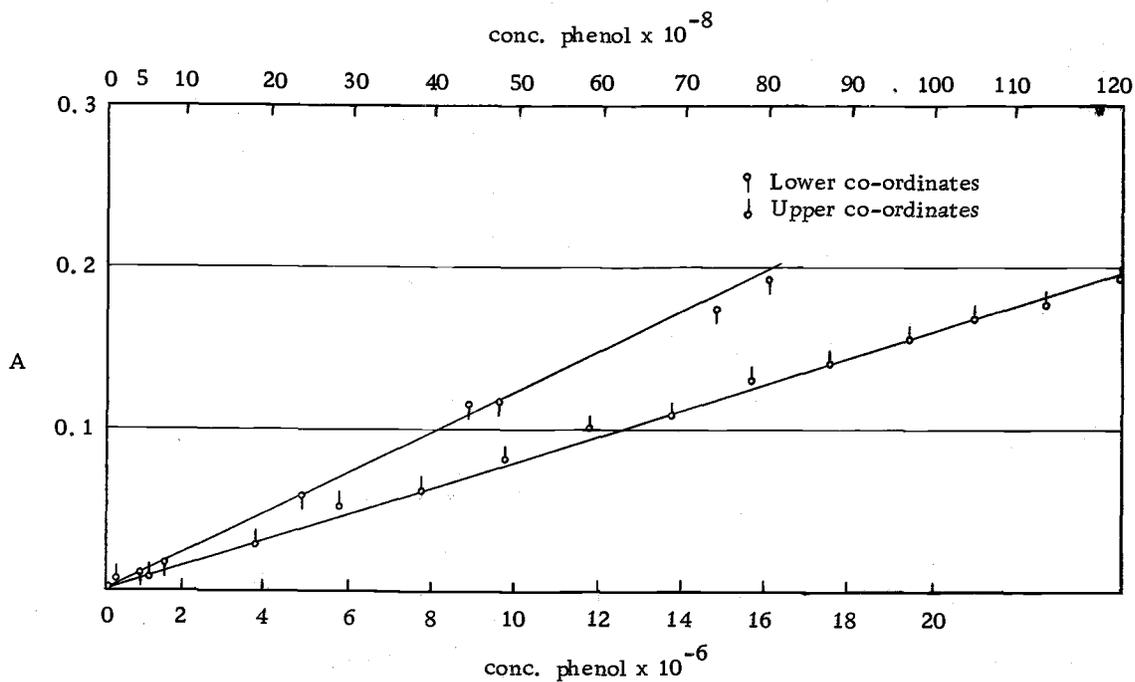


Figure 7. Absorbance at 5950 \AA (lower co-ordinates) and 6500 \AA (upper co-ordinates) as a function of phenol concentration (308, p. 213).

When Day and Stein first proposed in 1949 that the phenol yield was related to the dose which was absorbed by aqueous benzene, they included aqueous sodium benzoate as a system which would also yield phenolic products on irradiation (139). However, when in 1958 William A. Armstrong and Douglas Grant, chemists from Ottawa, suggested that aqueous benzoic acid or aqueous calcium benzoate be used for dosimetry, they were not proposing that the phenol yield be related to dose, but they were proposing a system that could be subjected to a very sensitive analytical method (21). When aqueous benzoic acid or any aqueous benzoate salt was irradiated, salicylic acid was among the radiation products. Armstrong and Grant proposed that the salicylic acid yield be measured since that particular isomeric form of hydroxybenzoic acid fluoresced in aqueous solution and spectrophotofluorometry was a very precise analytical method, capable of accurate measurement at high dilution. They reported that the fluorescent intensity of salicylic acid solutions at a wavelength of 4000 \AA was a linear function of concentration in the 10^{-7} to 10^{-8} M range and was independent of pH in the range 5-11. Spectrophotofluorimetric measurements of irradiated 10^{-4} M calcium benzoate showed that the salicylic-acid yield increased linearly with doses of X- and gamma-radiation over the range 0-100 rads and was independent of dose rate from 4 to 50 rads/min. Furthermore, at the concentrations produced on irradiation, the fluorescent intensity

of salicylic acid was unaffected by the presence of other radiation products (24). This sensitivity of measurement attained by Armstrong and Grant in 1958 on irradiated aqueous benzoic acid was of the same order of magnitude as that attained by Klein in 1961 on irradiated aqueous benzene.

Chlorinated Hydrocarbon Systems

Almost concurrent with the development of the above aqueous dosimetric systems has been the development of systems involving organic halogen compounds. Following the Second World War there was concern about radiation casualties in the event of an atomic war. Even though research and technology were requiring dosimetric systems responsive over a wide range of doses of ionizing radiation, there was a continued search for systems sensitive to doses below and up to the human lethal dose of 600 r (291). One of the first substances to be recognized for its sensitivity to ionizing radiation was a chlorinated hydrocarbon, chloroform (CHCl_3). It was one of the reagents in the Freund dosimeter (see p. 32, above). It is not surprising then that chloroform and other organic compounds with a high chlorine content were considered again for dosimetric purposes at the end of the 1940's.

In 1950, the biophysicist Howard L. Andrews (b. 1906) and the pharmacologist Parkhurst A. Shore (b. 1924), at the National Institute

of Health in Maryland, suggested chloral hydrate for X-ray dosimetry (19). The reaction mechanism for the chemical effect of X-rays on aqueous chloral hydrate $[CCl_3CH(OH)_2]$ was not completely known. However, the increase in pH and electrical conductivity that was noted in the irradiated solution seemed to indicate the presence of an ionized inorganic halide, very probably hydrochloric acid (HCl). Andrews and Shore reported that acid yields were linear with dose and independent of dose rate up to 600 r/min. Still, acid yields did show a dependence on the initial concentration of the chloral hydrate as well as on the temperature. The proposed analytical method for determining acid yields involved the measurement of conductance by means of tungsten⁷⁶ electrodes. In spite of its favorable characteristics, the chloral hydrate system deteriorated slowly on standing, particularly when exposed to light. Solutions that were two or three weeks old could not be used to measure small doses of radiation.

Arthur Hilsenrod, a chemist at the Army Chemical Center in Maryland was interested in the possibilities of the chloral hydrate system for measuring doses below 1000 r (267). He used a Q-meter

⁷⁶The usual platinized electrodes seemed to exert a catalytic action on the process and therefore were replaced by the tungsten electrodes (19).

type instrument⁷⁷ for the conductivity measurements and studied the effects of glucose on the sensitivity of the system. He showed that small amounts of 0.01 M glucose added to dilute solutions of chloral hydrate almost doubled its sensitivity to X-radiation, whereas the same quantity of glucose had no effect on concentrated solutions of chloral hydrate. Large quantities of glucose had a general inhibiting effect on the chemical action of the ionizing radiation.

In 1957, Andrews proposed the chloral hydrate system for depth-dose measurements (20). The technique developed for determining the dose delivered to internal structures made use of a gel composed of 0.05 M chloral hydrate and at least 0.57% agar (the percentage of agar could be increased). Ionizing radiation had the same effect on the gelled chloral hydrate as on the liquid except that acid yields were reduced. Doses were determined either by measurements of electrical resistance or by measurements of pH changes. When pH measurements were to be made, the gel pH was adjusted to 6.5 and methyl red was added to the gel before it set. The light yellow gel (methyl red is light yellow at pH 6.5) turned red on being irradiated and, therefore, spectrophotometric measurements were made at a wavelength of 5400 Å. For spectral absorption

⁷⁷The Q-meter type instrument that Hilsenrod used was devised by the biophysicist John Kanwisher for use in his own chemical dosimeter (see p. 214, below).

measurements, samples of the gel were removed from the dosimeter phantom.

When better spatial resolution was desired, pH measurements were made not spectrophotometrically but by means of glass electrodes which were inserted to any desired point in the phantom and did not require the removal of any sample of the gel (20). Spatial resolution was also attained when measurements were made of the electrical resistance due to absorbed radiation. For this technique the probing electrode consisted of a pair of tungsten wires fused into the tip of a 2 mm glass tube.

The gel dosimeter lacked sensitivity below a dose of 2,000 rads (20). Furthermore, all probing had to be done soon after the irradiation to minimize error due to diffusion. The dependence of the chloral hydrate system on temperature was not a problem in phantom dosimetry, however, since phantoms were at nearly constant temperature throughout and necessitated no temperature corrections.

In 1959, two radiation chemists from Canada, R. F. Platford and J. W. T. Spinks, supplemented the available information on the chloral hydrate system with their report of the action of beta-rays from a strontium-90--yttrium-90 source (386). Not only was the acid yield considerably dependent on temperature, but in this case, it was also dependent on dose rate. Because of the strong attenuation of beta-rays by the solution, acid yield was also dependent on

the depth of the solution. Determinations of acid yield were made by titration using sodium hydroxide and bromcresol purple as the indicator. The microburettes used were graduated to give readings to 5×10^{-4} ml and comparisons were made with unirradiated blanks. The system was also calibrated against a ferrous sulfate dosimeter. The reported G values were always greater than 100 unless the initial concentration of the chloral hydrate was less than about 0.1 M. In spite of the sensitivity of the system, aqueous chloral hydrate did not have suitable characteristics for the dosimetry of beta-radiation.

While the properties and possibilities of the chloral hydrate system were being investigated, George Taplin (b. 1910), a professor of nuclear medicine and radiation biology, and his co-workers at the School of Medicine of the University of California did extensive work on the chloroform and carbon tetrachloride systems. The work was sponsored, for the most part, by the U. S. Atomic Energy Commission. In 1950, they proposed a two-phase chloroform system for dosimetry (477). Chloroform overlaid with a pH indicator dye in pure water had a radiation sensitivity well within the range required (200-600 r) for dosimetric purposes in the event of an atomic war. It also had a relative heat stability. Its shelf-life at 56-58°C was at least twelve weeks and it was resistant to near-freezing temperatures. Since pure water has a pH between 7.2 and 7.4, bromcresol purple was chosen as the indicator because it reacted near that pH. Within

a 6.8-5.2 pH range, bromcresol purple showed a distinct color change from purple to yellow and it was the reduction in pH due to acid yield on irradiation which was the analytical guide. The acid yield was then determined specifically by titration with a standardized sodium hydroxide solution.

The research team under Taplin actually devised an instrument which could properly be called a dosimeter and which utilized the two-phase chloroform dosimetric system (477). The reagent was enclosed in silicone-sealed 2 cc volumetric tubes made of Pyrex glass; the dosimeter consisted of three tubes. Since the sensitivity of the system increased as the ratio of chloroform to aqueous dye increased, a 15:1 ratio of chloroform to dye was recommended as most satisfactory for dosimetry between 200 and 600 r of gamma radiation from a radium source. To make possible a quick classification of atomic radiation casualties, advantage was taken of the decrease-in-sensitivity effect of an increase in the concentration of the dye. One tube contained a 9% dye solution; another tube contained a 20% dye solution; and the third contained a 30% aqueous dye solution. In the tube containing the 9% dye solution, the color change occurred at about 200 r of gamma radiation. Persons exposed to short-term whole-body doses of 200 r were expected to suffer from a decrease in the circulating white blood cells, but in most cases such persons would experience complete recovery. In the tube containing the 20% dye

solution, the color changed from purple to yellow at about 400 r of gamma radiation. Such exposures were expected to cause moderately severe illness to which a small fraction of those exposed would succumb. In the tube containing the 30% dye solution, the color change occurred at 600 r of radiation. This latter dose was considered fatal to about 50% of the persons exposed. Intermediate doses could also be detected by a corresponding color change in more than one tube. For possible medical emergency treatment, the Taplin dosimeter had distinct value in providing for quick visual classification of persons with radiation injury.

Less than a year later, in 1951, Taplin proposed a modification of the two-phase chloroform-dye system of radiation measurement (479). The modification extended the application of the system to the measurement of doses as low as 10 r. This was made possible by the use of alcohol-free chloroform. Alcohol, added to the chloroform as a preservative by manufacturers, controlled the sensitivity of the chloroform. Ten successive washings with distilled water effectively freed the reagent-grade analytical chloroform of its approximately 0.5% ethyl alcohol. The alcohol-free system was sufficiently sensitive to doses as low as 10 r even when low chloroform-dye ratios (2:1) and strong concentrations of dye were used. In fact, by increasing the chloroform-dye ratio and reducing the concentration of the dye, doses of 1 r could be detected. That specific doses could be

measured by the alcohol-free system, certain amounts of sodium hydroxide were added to the dye. This provided for precise measurement of 10, 25, 50 and 100 r. A problem with the alcohol-free dosimeter that needed solution, however, was its instability to heat and ultra-violet light. The ethyl alcohol gave the chloroform system its stability in that regard. What remained to be shown was what concentration of alcohol was optimum for stability as well as for the desired sensitivity.

While the sensitivity of the chloroform-dye system was being modified at the University of California, the biophysicist John Kanwisher (b. 1924) was developing a Q-meter method⁷⁸ for measuring the radiation effect on chloroform (297). In August of 1951, Kanwisher proposed his chloroform-water dosimeter which was based on an indirect method of measuring conductivity changes due to acid yield on irradiation. Since selectively the acid formed entered the water phase, Kanwisher measured the conductivity of the acidified water by determining its absorption of energy from a radiofrequency field. He did this by developing an electronic device of the Q-meter⁷⁹

⁷⁸ Kanwisher's work was sponsored by the U. S. Atomic Energy Commission.

⁷⁹ The ratio of the reactance to the resistance of a coil or the degree to which a coil behaves like a perfect inductance is called the "figure of merit" of a coil or its "Q" value. Q is generally measured by inductance, capacitance, or impedance bridges; hence the term Q-meter (297, p. 15).

type. His instrument was calibrated to give exposure directly. Since it was intended for casualty use it had a full scale range of 600 r. Theoretically, it was possible to increase the sensitivity to a full scale range of 100 r and to decrease its sensitivity to any degree desired.

By means of his instrumental method of analysis, Kanwisher provided for the direct and rapid reading of fractional doses within the casualty range. This method had a decided advantage over the Taplin instrument on which the color change occurred at one value of dosage. Although the Taplin instrument could be read visually and the Kanwisher method required a separate reading instrument, the electronic device developed by Kanwisher was a portable, light-weight unit. With one instrument any number of dosimeters could be read, each reading requiring about five seconds.

Kanwisher sealed the chloroform-water system in a fountain-pen sized, pyrex glass-lined capsule (297). To overcome the system's sensitivity to light, he encased the capsule in black-pigmented polystyrene because polystyrene would not interfere with the conductivity measurements. To overcome the system's dependence on the energy of the radiation, he shielded the plastic case with a 1/64 inch layer of lead. This was effective in bringing 200 kvp X-ray readings to within 10% of the 1000 kvp readings. Since the lead produced no noticeable change in the 1000 kvp readings, the lead shield was

considered satisfactory for casualty dosimetry.

In his report of 1952, Taplin showed that the two-phase chloroform-dye system was sufficiently heat stable and temperature and dose rate independent if it contained ethyl alcohol in 1-2% concentrations (481). Such alcohol-stabilized chloroform systems also were practically insensitive to fast and slow neutron bombardment even when doses were biologically equivalent to gamma exposures of up to 1500 r. This latter observation indicated that the system might be effectively used to identify gamma exposures in the presence of neutrons.

Acid yields were still determined by the previous titration method (481). Calculations of G values from 40-1400, however, seemed to indicate that the primary mechanism of reaction was a chain reaction. This idea was consistent also with the system's dependence on dose rate. Furthermore, samples not stabilized with ethyl alcohol were found to show an after effect when total acid produced was titrated after increasing time intervals. The problem that needed solution before the two-phase chloroform-dye system could be considered most effective in dosimetry was the effect of ethyl alcohol on inhibiting the chain reaction.

In 1954, Taplin reported that resorcinol was the most effective inhibitor of the chain reaction in the chloroform system (474). Systems which contained resorcinol in 0.1 to 0.5% concentration

exhibited adequate thermal stability and also showed an independence of dose rate from 1.25 to 1200 r/min (see Fig. 8). When resorcinol was added to the system in the concentration as given above, the dosimeter also responded accurately to exposure under temperatures varying from 2 to 56° C. Taplin proposed further that the energy dependence of the system be controlled by a shielding of about 0.5 mm of lead (Kanwisher used an equivalent of 0.4 mm of lead for shielding). Although visual colorimetry and titration with sodium hydroxide were still considered by Taplin as methods of estimating dosage, he recommended spectrophotometric determination of the pH changes in the dye phase as the most accurate method of analysis.

In addition to all the specific controls for the two-phase system, Taplin also suggested a single-phase resorcinol-stabilized chloroform-saturated aqueous dye system for dosimetry (474). In the single-phase system, acid yield was independent of dose rate from 5 to 1200 r/min and of temperature from 2 to 52° C. The single-phase system also showed spectral independence when exposed to radiation varying in mean effective energy from 35 kv to 1200 kv. It even showed a relative response to fast neutrons which when compared to the two-phase system's response was about five times more sensitive.

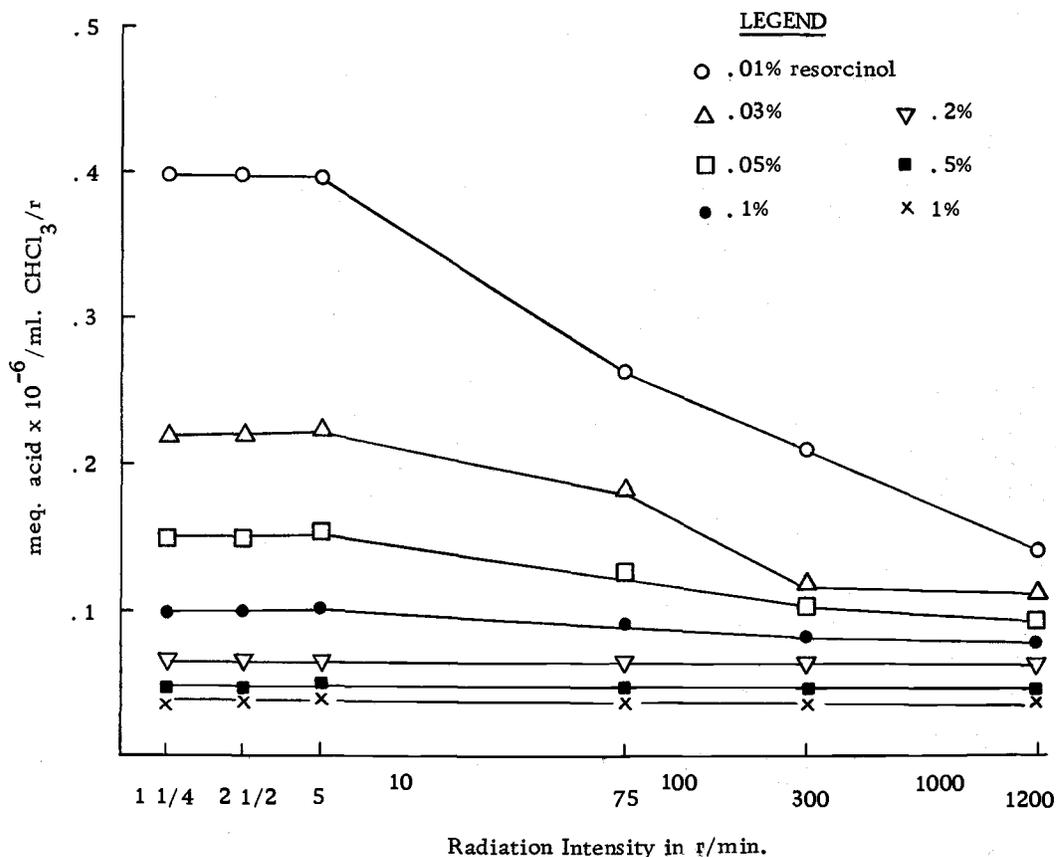


Figure 8. Reduction of rate dependency in acid production from chloroform by varying concentrations of resorcinol (474, p. 24).

Another single-phase system which seemed to be ideal for dosimetry was the system of carbon dioxide-free aqueous phenol red saturated with trichloroethylene (474). In addition to possessing the favorable characteristics assigned to the chloroform systems, it had the added advantage of being many times more heat stable. For example, the two-phase resorcinol-stabilized chloroform system had a shelf life of 12 to 18 months at temperatures below 100°F but resisted a temperature of 212°F for only four or five minutes. The

system consisting of single-phase carbon dioxide-free aqueous phenol red saturated with trichloroethylene resisted boiling temperatures for more than five hours. Although in 1954 Taplin felt that the latter single-phase system was most promising for dosimetry, in 1958 when he obtained a patent for a second commercial dosimeter, it still involved the two-phase chemical dosimetric system (478, 480).

In 1956, Sanford C. Sigoloff (b. 1930), a radiobiologist at the University of Texas, proposed a two-phase chlorinated hydrocarbon system for dosimetry that was very similar to the two-phase resorcinol-stabilized chloroform-dye dosimeter (447). The major difference was in the chlorinated hydrocarbon used. Although Sigoloff admitted that chloroform could be used as well, its volatility made it less desirable at times than tetrachloroethylene (C_2Cl_4). In his system, the acid generated by the irradiation of tetrachloroethylene was also extracted by an aqueous acidimetric dye chlorophenol red. As a method of analysis for dose evaluation, he recommended that the acid yield could be determined by titration with sodium hydroxide or by spectrophotometric analysis. When stabilized with resorcinol, the tetrachloroethylene system was independent of dose rate between 10 and 4250 r/min and of temperature between 5 and 55°C. When shielded with 0.5 mm of lead, the system was also effectively energy

independent between 80 and 600 kev.⁸⁰

In 1960, Sigoloff reported several modifications in his dosimetric system (446). G values in an irradiated non-stabilized tetrachloroethylene system were of the order of 12,000 which indicated that a chain reaction was operative. The chain reaction retarder ionol provided stability for the system but at the same time reduced its sensitivity (G values were about 45). Tetrachloroethylene containing 0.2% ionol showed maximum sensitivity and the highest reproducibility. However, ionol-stabilized systems were still sensitive to light and had to be protected by ultra-violet light absorbers. Ionol-stabilized tetrachloroethylene dye systems were useful for measuring doses between 5 and 5×10^6 rads. To control the decomposition of the indicator dye chlorophenol red at total doses greater than 10^6 rads, 0.2% thiourea (128) by weight was added to the solution.

Although prior to 1956, the dosimeter was evaluated mainly by visual colorimetry or by titration, by 1960 all evaluation was done spectrophotometrically, except in cases of overexposure (446).

Chlorophenol red was chosen as the indicator because its two absorption bands were sufficiently removed from each other and were still in the visible portion of the spectrum. The acid form had an absorption maximum at 4300 Å and its conjugate base at 5730 Å. As the pH

⁸⁰The two-phase tetrachloroethylene-dye system made up the TCE dosimeter included in the 1959 ORNL film badge (see p. 178, above).

of the dye solution changed from 6.0 to 5.0 (red to yellow), the relative transmissions of both bands were related to pH. Theoretically, the transmission of either of the two bands could have been used for an indication of pH. However, Sigoloff recommended that for dosimetric purposes the ratio of the two would be more satisfactory because variations in the diameter, striations, and thickness of the glass would then tend to cancel. When the ratio of the transmissions ($\% T$ at 5730 \AA / $\% T$ at 4300 \AA) was plotted against pH, the center straight-line portion of the resulting curve indicated the useful range of the dosimeter; this was related to dose.

Chlorinated-hydrocarbon dosimetric systems have been investigated particularly as liquid systems, both aqueous and non-aqueous. In 1961, M. S. Potsaid and G. Irie, physicians in the Department of Radiology at the Massachusetts General Hospital, devised a practical in-phantom colorimetric dosimeter (389). However, it also depended on the acid yield of irradiated chloroform. To obtain a three-dimensional isodose picture of absorbed dose, Potsaid and Irie suggested the use of a mixture of solid paraffin and paraffin wax combinations to which different amounts of chloroform were added as well as 100 milligrams of methyl yellow per kilogram of mixture. A 30% chloroform-paraffin-wax mixture (specific gravity around 1.0) was used when material equivalent to tissue was desired. Formed into light yellow slabs in a mold, the dosimetric substance was then

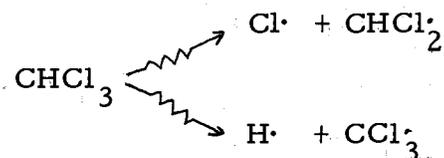
arranged to represent a solid phantom with a particular geometry. Ionizing radiation immediately caused the irradiated portion of the phantom to become red with an intensity proportional to the absorbed dose. This three-dimensional picture of dose could be kept for weeks if protected from direct daylight and ultra-violet light. Storage in a refrigerator helped to reduce the diffusion of the chloroform and to lessen the distortion of the dose pattern. Although the system was sensitive to light, it showed little or no energy and dose rate dependence within moderate ranges (50 to 2000 kvp; 1 to 1,000 rads/min). The phantom dosimeter could easily be sectioned if a more precise determination of absorbed dose were desired. The dose was evaluated colorimetrically, but the development of a quantitative spectrophotometric method for measuring absolute dose by transmittance, absorbance, or reflection using the color changes in a paraffin dosimeter was considered desirable.

The above chlorinated-hydrocarbon dosimetric systems were based on the liberation of acid or hydrogen ions in these systems by ionizing radiation. Although one of the earliest recognized characteristic properties of high-energy radiation was its ability to cause ionization(see p. 6-7, above), high-energy radiation often converts stable molecules into free radicals⁸¹ (468, p. 1). Relatively stable

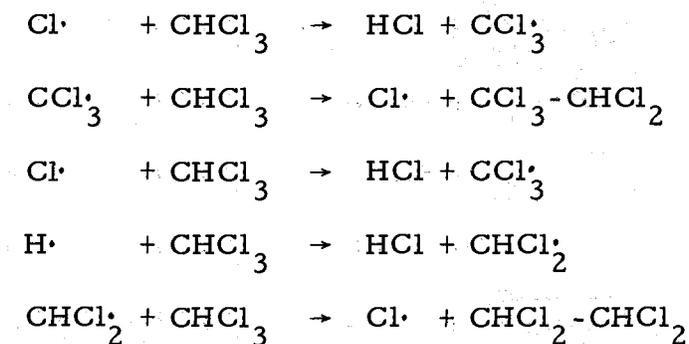
⁸¹Free radicals are atoms or molecules which have one or more unpaired electrons available to form chemical bonds. Free radicals are generally electrically neutral; those that carry a charge are known as free radical ions.

free radicals have been known since 1900 when the triphenylmethyl radical was discovered (215). More recently reactive radicals have been shown to be transient intermediates in many reactions. In radiation chemistry the identification of free radicals and the determination of free radical yields have played an important role in clarifying reaction mechanisms (249, 392).

Although hydrogen ions or hydrochloric acid are among the irradiation products of chloroform, as early as 1930 free radicals have been identified as transient intermediates in this system (110). These free radicals react with each other, with the solvent molecules, or with any solute present. For example, irradiated chloroform can yield:⁸²



The chain reaction mechanism could include the following (110):



⁸² An arrow with a wavy line indicates acted on by ionizing or high-energy radiation. Radicals are shown with their unpaired electrons.

At a sufficiently high concentration of suitable solute species, all the radicals disappear by reacting with the solute species. The number of solute molecules affected is a measure of the number of free radicals formed from the solvent.

The latter principle was the basis for the dosimetric system proposed in 1953 by the physical chemist, A. Chapiro (87). He proposed using the solute diphenylpicrylhydrazyl (DPPH) as a radical scavenger. Since DPPH is itself a stable free radical, it can function as an acceptor of a reactive species to become a saturated molecule. At the same time, on reacting with a radical, DPPH loses its violet color. Chapiro suggested that the color change be related to the absorbed dose of the chloroform. He claimed that the system was sensitive enough to measure doses as low as 100 rads. However, because of the high radical yield, there was a dependence on dose rate. Reproducibility was also poor owing to the effect of impurities as well as the slow continuation of the reaction after irradiation. Chapiro recommended that if a solvent with a lower radical yield were found the problems would be solved. However, he himself did not pursue that line of research and it seems that no one else took it up either.

The chlorine free radical present in both irradiated chloroform and irradiated carbon tetrachloride was believed to be the species

responsible for the dosimetric reactions proposed by George Clark⁸³ in 1955 (95, 96). Dithizone is one of the substances which, as a solute in either chloroform (stabilized with alcohol) or carbon tetrachloride, becomes sensitive to high-energy radiation. The chemical effect of the irradiation is apparent in a color change from a blue-green to yellow. For dosimetric purposes Clark recommended a 5×10^{-5} M solution of dithizone in either solvent as being most suitable of all the concentrations studied because it showed the greatest percentage change with a given amount of irradiation (95). The X-ray decomposition of dithizone was independent of dose rate from 10 to 75 r/sec. The extent of reaction under irradiation was determined by spectrophotometric measurements of the absorption at 6150 \AA when chloroform was the solvent and at 6200 \AA when carbon tetrachloride was the solvent. Although dithizone in both solvents had suitable dosimetric characteristics, the desired sensitivity determined the choice of solvent. In carbon tetrachloride, dithizone was about twice as sensitive to X-radiation than in chloroform. With carbon tetrachloride as the solvent, a dose of 200 r brought about a color change from green⁸⁴ to

⁸³In his research even prior to the Second World War, George Clark, a chemist at the University of Illinois, investigated the chemical effects of X-rays on aromatic colors and dyes (98). For some of his other contributions see p. 106-107, above.

⁸⁴A solution of dithizone in carbon tetrachloride is deep-green; a solution of dithizone in chloroform (stabilized with alcohol) is blue-green.

yellow-green and 300 r caused a complete change to yellow. With chloroform as solvent, a dose of 400 r was needed for a color change from blue-green to green and 600 r for a complete change to yellow.

The sensitizing action of halogenated hydrocarbons due to the presence of chlorine free radicals on irradiation was also necessary in the 2-hydroxy-4-nitrophenyl- β -naphthol (HNPN) dosimetric system and in the resazurin dosimetric system both proposed in 1955 by Clark (96). Of the two organic solvents, carbon tetrachloride and chloroform, carbon tetrachloride was a much better sensitizer for the alcohol solutions of both HNPN and resazurin. G values for both systems were dependent on the concentration of the sensitizer. The color of an HNPN solution changed from purple to red to orange on irradiation. Estimation of dose was made by spectrophotometric measurements of absorption at a wavelength of 5300 Å. The decomposition of resazurin on irradiation appeared as a color change from blue to red. In this case spectrophotometric measurements were made at 6120 Å.

Although both systems showed a sensitivity to light, their sensitivity to high-energy radiation was near the proper range for dosimetric purposes: HNPN in carbon tetrachloride responded to doses in the range 750-1250 r. Resazurin in carbon tetrachloride was most sensitive to doses between 250 and 650 r. In each case the desired sensitivity could be regulated by varying the concentration of solute and sensitizer.

For a dosimetric system possessing the greatest stability on standing and the least sensitivity to light, however, Clark proposed a mixed solute system (96). He recommended using solutions of the same definite concentration of both HNPN and resazurin and mixing them in the ratio of 1 part HNPN to 4 parts resazurin. Such a system was temperature and dose rate independent. At the same time if the vials containing the mixture had light-tight covers, the system was stable for at least four months. To make the system applicable to different dose ranges, four mixtures were proposed, each containing a different concentration of dyes (in the 1:4 ratio) and varying amounts of carbon tetrachloride. Then a color code was set up according to which the dose received by the dosimeter could be estimated (see Table 3).

Table 3. Color changes in four series of mixed indicator solutions (96, p. 304).

| Color | Dosage range (r) | | | |
|-----------------|------------------|---------|----------|-----------|
| | I | II | III | IV |
| Blue | 0-450 | 0-500 | 0- 600 | 0- 700 |
| Purple | 450-550 | 500-600 | 600- 800 | 700- 900 |
| Purple-red | 550-650 | 600-700 | 800- 900 | 900-1200 |
| Red-purple | 650-750 | 700-800 | 900-1000 | 1200-1400 |
| Red or red-pink | 750 | 800 | 1000 | 1500 |

The color code was accurately defined according to measurements made spectrophotometrically. However, for application in atomic casualty cases [which seems to have been the purpose (95, p. 199)] only one mixture of the four showed considerable sensitivity below the human lethal dose of 600 r total-body irradiation. Not one of the mixtures could be used for estimating doses of less than 400 r. Therefore, the mixed solute system had value for indicating critical cases of irradiation but not for giving evidence of exposure to harmful intermediate doses.

CHAPTER VIII

CHEMICAL DOSIMETRY (1942-1962) - PART II

Dye Systems

The change in color of an indicator dye has been the basis of a number of dosimetric systems. However, the change in color was often a secondary effect of the radiation. Systems were formulated in which the radiation products reacted with the dye. This was the case in Taplin's two-phase chloroform-dye dosimeter where hydrogen ion, an irradiation product of chloroform, reacted with the dye (see p. 211-212, above). This was also the case in Clark's carbon tetrachloride-resazurin dosimetric system where the chlorine free radical, an irradiation product of carbon tetrachloride, reacted with the dye (see p. 226, above). Something similar occurred in aqueous dye systems.

The radiation chemistry of water and aqueous solutions has been the concern of chemists from the earliest years when basic observations were made regarding the chemical effects of ionizing radiation (248). Although free radical mechanisms were suggested as being responsible for some of the observations, the activated water hypothesis of Hugo Fricke in the early 1930's with its resulting hydrogen and hydroxyl free radicals (181, 182) was probably the first most effective attempt at explaining much of the available qualitative and quantitative data.

Later, the chemists working at the Metallurgical Laboratory in Chicago from 1942 until 1946 made extensive use of free radical mechanisms in interpreting their water decomposition studies (73). This factor together with the co-ordinated and developed explanation of aqueous radiation-induced reactions by the physical chemist Joseph Weiss (b. 1922) (531) in a certain sense established the functions of the hydrogen ($H\cdot$) and hydroxyl ($OH\cdot$) radicals, as well as molecular hydrogen and hydrogen peroxide, as important intermediates in radiation-induced reactions in water and aqueous solutions.

Since the molecules of organic dyes are large, they possess many sites which are sensitive towards attack by reactive free radicals. One of the earliest aqueous dye systems to be investigated for dosimetric purposes was methylene blue. When it was first recommended for such purposes in 1933 (see p. 101, above), methylene blue was a common laboratory reagent and its color change on irradiation suggested dosimetric possibilities. With the consideration of other redox indicators for dosimetry of biological doses around 1950, the fading of irradiated aqueous methylene blue was again subjected to study. However, detailed reaction mechanisms now served as a guide to those interested in improving the characteristics of the system.

In 1950, the radiotherapist M. J. Day and the chemist Gabriel Stein (b. 1920) reported on their use of gels containing dyes, such as methylene blue, for obtaining three-dimensional distributions of

absorbed energy (138). The gel consisted of a 1% agar solution in water to which 0.003% methylene blue was added. A low concentration of dye was used to assure a radiation-induced chemical reaction and not a photochemical one. The system was based on the reduction of the dye to its leuco⁸⁵ form by the reactive species present in the irradiated aqueous solution of the dye. To increase the post-irradiation stability of the system, Day and Stein recommended that an oxygen-free system was necessary which could be obtained by bubbling nitrogen through the system. In the absence of oxygen, a reversible reaction, that is, a re-oxidation of the leuco compound made apparent by a restored blue color, was prevented. To improve the reduction yield, a 1% benzoate solution was added to the basic system. The hydroxyl free radicals could compete with hydrogen free radicals for methylene blue molecules and thus interfere with the reduction process. The benzoate captured the hydroxyl radicals, thereby increasing the yield of the leuco dye. While Day and Stein reported a satisfactory response of a methylene blue gel to 200 kv X-rays, Bernard Proctor (1901-1959) and Samuel Goldblith (b. 1919), food technologists at the Massachusetts Institute of Technology, reported an equally satisfactory response of the system to cathode rays whose electrons had energies from 300 to 3000 kv (394).

In 1952, Day and Stein emphasized the tissue-equivalent nature

⁸⁵The term "leuco" is derived from the Greek word for "white." In this context it refers to the decolorized form of the dye.

of the methylene blue-agar system as making it ideal for depth-dose studies (137). For such purposes, methylene blue was also preferable to other dyes with higher oxidation-reduction potentials, such as dichlorophenol-indophenol, because of its apparently lower diffusion. The reduction form of the dye was formed nonuniformly in the gel according to the dose distribution. This gave rise to a potential difference which apparently was equalized slowly by diffusion of the dye molecules. The slower the diffusion velocity of the dye, the more suitable it was for depth-dose measurements.

Interested in determining the penetration of high energy cathode rays in the sterilization of foods and pharmaceuticals, Proctor and Goldblith again in 1952 reported on their continued investigations of the characteristics of aqueous and non-aqueous methylene blue⁸⁶ (212). Aqueous methylene blue in the presence of oxygen was completely destroyed by cathode rays having an energy within the range of 2 to 16 Mev. The reaction was irreversible since hydrogen peroxide could not restore the blue dye. The reduction of the dye to its leuco form in the absence of air was a reversible process and an oxidizing agent, such as hydrogen peroxide, could initiate the reverse reaction. Proctor and Goldblith recommended that this effect, the destruction of

⁸⁶ They also recommended a resazurin-agar solution for dosimetry. Although at MIT only qualitative observations of the system were made, the two-stage color change of resazurin from blue to red to colorless seemed to have desirable dosimetric possibilities (212, 394).

methylene blue in aqueous solution, be used for studies of field distribution and also as a chemical method of dosimetry.

Subsequent research at MIT was directed towards determining the range of effectiveness of aqueous methylene blue as a dosimeter (136). The report issued in 1953 showed that doses from 2.5×10^4 to 5×10^6 rep⁸⁷ were effectively measured by the irreversible destruction of methylene blue, assessed by colorimetric techniques. Since doses of the same order of magnitude were used in studies dealing with the preservation of foods with ionizing radiation, the aqueous methylene blue system could be and was practically applied in the Department of Food Technology at MIT.

The other generally acknowledged dosimetric systems--the ferrous sulfate and the ceric sulfate--were more accurate than the methylene blue system (315). However, they required more expensive equipment and much more careful application for good reproducibility. Therefore, advantage was taken of the simplicity of use and

⁸⁷The "rep" as a unit of absorbed dose was equivalent (in the MIT report) to an energy absorption of 83 ergs/gram (136). In 1948 when the roentgen was still considered inadequate as a unit of absorbed energy (see p. 78, above), the rep (roentgen-equivalent-physical) was suggested as a unit of absorbed dose (28, p. 11). It was defined as that dose of ionizing radiation which produces an energy absorption of 83 ergs/cc in tissue. That particular value was chosen because it represented the approximate energy that was dissipated in air exposed to 1 roentgen of hard X-rays. Since the definition of the rep had to be varied with the density of the material, the unit was not used very widely.

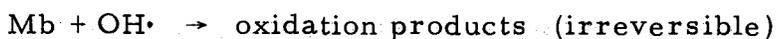
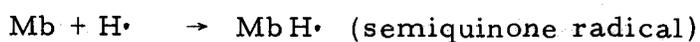
measurement of the aqueous methylene blue system for all routine work in the food technology laboratories and the extent of the practical usefulness of the methylene blue dosimeter was further explored.

Experiments on the effect of temperature on the stability of the system showed that there was an increase in dye content (amounting to more than 30%) of irradiated samples when they were stored at 125° F for 7 weeks (315). Such instability was not considered significant since colorimetric measurements were usually carried out within a few hours after the irradiation and irradiated methylene blue was stable at room temperature. To assure accuracy in the dose measurement the researchers recommended that the irradiated samples be stored at refrigeration temperatures when a delay of more than 24 hours in the colorimetric measurements was expected. Since the non-irradiated methylene blue was found to have almost 100% stability at a temperature of about 35° F, a large number of ampoules could be prepared at one time for the dosimetric work to be carried out within a month or two. Furthermore, irradiation temperatures from 45° to 150° F had no effect on the system. This latter observation may have been due to the shortness of the irradiation process which was usual when working with electron accelerators.

Although the team of workers at MIT did not provide for modifications of the methylene blue dosimeter by the addition of reagents, they contributed to the reliability and accuracy of the dosimeter by defining

the limits within which it was most effective. To improve its reproducibility they recommended that clean glassware and preferably dry colorimeter tubes be used (315). This recommendation minimized the error introduced into the measurement by the previous adsorption of dye on the glass walls of the colorimeter tubes. They further suggested that the same dilution geometry be used for accurate comparisons and that each lot of dye be calibrated since methylene blue powder varied in purity from lot to lot.

While the above studies were being conducted at MIT, Day and Stein were examining the effects of various solutes on the G value of the air-free methylene blue dosimeter (141). The results of some of their investigations are reproduced in Table 4. The G value recorded is the mean for the reduction yields of 200 Kv and 4 Mev X-rays. In all cases the decoloration was linear with dose to about 15,000 rads when bleaching was almost complete. The added organic solutes were about equally more effective than hydrogen in increasing the reduction yield. According to the proposed mechanism of reaction (531), in the absorption of radiation by water the hydrogen and hydroxyl free radicals are formed. The hydrogen free radical is a strong reducing agent whereas the hydroxyl free radical is an oxidizing agent. Therefore, the hydrogen and hydroxyl free radicals (in the absence of air) compete for the organic dye molecule according to the following (468, p. 176-177):



The organic solutes were more effective than hydrogen in capturing the hydroxyl radicals and increasing the reduction yield.

Table 4. Summary of reversible yields under various conditions (141).

| Mb concentration | Solute | pH | G (Reduction) |
|--------------------------------|----------------------|-----|---------------|
| $0.6 \times 10^{-4} \text{ M}$ | Benzoate, 0.2 M | 6.4 | 2.9 |
| $0.6 \times 10^{-4} \text{ M}$ | Ethanol, 0.4 M | 6 | 2.8 |
| $0.6 \times 10^{-4} \text{ M}$ | Lactate, 0.2 M | 7.2 | 2.6 |
| $0.4 \times 10^{-4} \text{ M}$ | H_2 , 1 atm | 7 | 1.7 |
| $0.6 \times 10^{-4} \text{ M}$ | Air, 1 atm | 7 | < 0.0 |
| $0.6 \times 10^{-4} \text{ M}$ | ----- | 7 | 1.0 |

One proposed modification of the methylene blue system was a development of a more sensitive system. Gerald Oster (b. 1918) and Barret Broyde, physical chemists at the Polytechnic Institute of Brooklyn, proposed such a variation in 1959 (375). Unlike the above aqueous dye systems, this one was based on the production of a colored dye by transformation of the leuco form. The reduction or destruction of methylene blue required a minimum dose of the order of 10^3 to 10^4 roentgens. The transformation of the leuco form required a much smaller dose for a perceptible effect. Organic dyes often have sufficiently large extinction coefficients to give the required visual

sensitivity. Even traces of the dyes can be detected. Oster and Broyde proposed a polyvinyl alcohol film which contained the leuco methylene blue. Such a film 1 mm thick showed a blue image of an X-ray beam at doses as low as 0.5 r with the optical density proportional to the dosage. The sensitivity was equivalent to a G value of the order of 10^4 . At room temperature an "after effect" also occurred, that is, the irradiated film did not show the full intensity of color until after five or ten minutes. Therefore, the leuco dye transformation was believed due to slowly-diffusing, oxidizing radicals formed in the polyvinyl plastic. Also, the high G value and the post-irradiation effect of the leuco methylene blue system seemed to indicate that a chain reaction was operative. Although the Oster-Broyde film was highly sensitive, it was only 0.01 as sensitive as an X-ray film. It did have an advantage over the X-ray film, however; it required only a single observation of color for dosage measurement.

By their proposed dosimetric system, W. A. Armstrong and G. A. Grant (b. 1904), chemists at the Defense Research Chemical Laboratories in Ottawa, hoped to obviate the problems that usually accompanied a chain reaction. At the same time they wanted a sensitivity to doses in the range of 25 to 1000 rads (22, 23). Their dosimeter depended on the oxidation of a leuco dye by the reactive species present among the irradiation products of water. The leuco dye acted as a selective radical scavenger and thus kept the free radicals from

reacting with each other to give molecular hydrogen peroxide and hydrogen. In 1958, Armstrong and Grant recommended a 10^{-4} M 4,4'-(5-chloro-2-thenylidene)bis[N,N-diethylaniline] solution as best suited for dosimetric purposes (22). Since the irradiation effects depended on pH, 7×10^{-3} M hydrochloric acid was added to the basic system to maintain a pH of 2.2. This pH was considered optimum for the reaction; the absorption maximum at 6330 \AA of the blue dye formed had a high molar extinction coefficient. Since chloride ion enhanced the reaction (possibly by reacting with hydroxyl radicals to give hydrochlorous acid), 0.1 M sodium chloride was also added to the basic solutions. Neither hydrogen peroxide nor the HO_2 radical (both among the irradiation products) had any oxidizing effect on the leuco dye. Therefore, 10^{-4} M ferrous ammonium sulfate was included in the system because ferrous ion was capable of converting the peroxide and HO_2 radical into hydroxyl radicals, thus increasing the yield. The G yield of dye for the system was approximately 1.1.

With the above described system a dose of about 250 rads was detected visually by the color changes in a cell with a 1-cm path length (22). Doses as low as 140 rads were measured with a spectrophotometer using 1-cm cells. The optical density at 6330 \AA increased linearly with gamma-ray doses up to at least 2000 rads. The system had a pre-irradiation stability of about 2 weeks and a post-irradiation stability of several days. Reproducibility was not a problem if clear equipment

and pure water were used. Furthermore, doses as low as 20 rads were measured with 10-cm spectrophotometer cells.

Further investigation enabled Armstrong and Grant to report later that same year that their proposed leuco triarylmethane dosimetric system was energy independent from 0.16 to 2.0 Mev (23). No dose rate dependence was observed between 4 and 230 rads/min, although at higher dose rates post-irradiation dye fading was observed. The system was only slightly dependent on temperatures below 30° C but markedly dependent on temperatures above 30° C.

Armstrong and Grant certainly identified the important characteristics of their leuco triarylmethane dosimetric system besides providing the basic system with desirable modifications. The linearity of the dosimeter's response, its accuracy and reproducibility, its energy and dose-rate independence, and its sensitivity made it ideal for radiobiological research. It would seem that if used within the defined limits, the 4,4'-(5-chloro-2-thenylidene)bis[N,N-dimethyl-aniline] dosimetric system would be a very convenient laboratory dosimetric method.

The above dosimetric systems composed of organic dyes were dependent upon the radiolysis products of the solvent. Since the change in the dye was brought about by one of the radiolysis products, properly speaking, it was a secondary effect of the radiation. The reduction or destruction yield was high, characteristic of systems highly sensitive

to radiation. However, some dosimetric dye systems were only intended for high-level dosimetry. Their development was not based on reactions by the radiolysis products of the solvent. Any changes in the dye solutes, then, were predominantly due to direct interaction of the radiation and the dye molecule.

In 1954, Ernest J. Henley (b. 1926), a chemical engineer at Columbia University in New York, proposed a system for the monitoring of the radiation sterilization of food (259). For such application, high sensitivity was not needed. Henley recommended a commercially-made, moistureproof, heat-sealable cellophane which contained a dimethoxy-diphenyl-disazo-bis-8-amino-1-naphthol-5,7-disulfonic acid dye as having suitable properties. The cellophane presented no problems in handling techniques. The cellophane strips were encased in aluminum holders specially constructed to fit into the standard Beckmann cell holder. Spectrophotometric measurements of the transmittance of the dye were made at a wavelength of 6550 Å. The observation made indicated that the dosage was a straight-line function of optical readings. Within a dose range of 0 and 3×10^6 r of cobalt-60 gamma-radiation, the optical density was correlated with the dose according to:

$$T = (1.47 \pm 0.03) 10^{-6} r + T_0$$

where

T = % transmission at a dose r

r = dose in roentgens

and T_0 = initial transmission at $r = 0$.

More studies of the system led to the conclusion that the cellophane-dye system was a reliable dosimeter for doses ranging from 10^5 to 10^7 roentgens (262). The system had an unusual stability; it was relatively insensitive to pH, light, and heat. The strips were stored in the dark for about 2 years without showing any optical change. Only after extended periods (about 10 hours) of exposure to temperatures above 60°C did fading occur. The radiation decolorization of the dye was irreversible; the irradiated dye was not affected by acid, base, or oxygen.

Apparently the chemical effects of radiation on the cellophane itself were not significant within the dose range studied. Although Henley made no chemical tests of the irradiated cellophane, researchers at General Electric Laboratories had shown that below 6×10^6 r no detectable effects were noted in irradiated cellulose (328). Therefore, if there were a chemical effect in the cellophane due to irradiation it was not essential to the effects observed in the dye.

Another dosimetric system which was based on direct interaction of the radiation with the dye was proposed by the physical chemist J. F. Kircher (b. 1929) and co-workers at the Batelle Memorial Institute in Ohio (307). They recommended a solution of methyl yellow in cumene for most reproducible results. Intended for high-level dosimetry, the solution was subjected to doses ranging from 4×10^5

to 93×10^7 rads of gamma radiation. The spectrophotometric measurements made at 4060 \AA showed that the change in optical density of the dye with dose was not quite linear. This seemed to indicate that although a decrease in optical density was due to the destruction of methyl yellow by irradiation, a slight increase in the optical density was due to the irradiated solvent. In fact, it was believed that beyond the upper dose studied, any optical change would be determined by the radiation effect on the solvent. The methyl yellow-cumene solution had a stability of about 25 days under normal conditions both before and after irradiation.

Both the cellophane-dye dosimetric system and the methyl yellow-cumene solution appear to have satisfied the requirements for high-level dosimetry. Their sensitivity to radiation was low; measurements were easily performed. The irreversibility of the induced change contributed to their post-irradiation stability.

Monomer-Polymer Systems

Among the many systems which have been proposed and tested for radiation dosimetry, there were some which utilized a visually observable change of state to indicate the absorption of a certain amount of radiation. The change in viscosity due to the polymerization of certain liquid monomers was found to be well-suited to dosimetry because it provided a sharp, irreversible end-point. That ionizing

radiation could be used to initiate polymerization had been discovered in the 1920's. Acetylene was polymerized by alpha-particles (338) and also by beta-particles (106). Although several methods were used to study the extent of polymerization, such as changes in color, refractive index, and viscosity, by the end of the 1930's, changes in density due to irradiation of systems of styrene, vinyl acetate, and methyl methacrylate were followed by a volume dilatometer (282).

Since the Second World War, radiation-induced polymerization as well as the irradiation of polymers has received a great deal of study. The study may have been prompted by the importance that was attached to polymers as engineering materials (435). The topic was of special interest to radiation chemists because the study of the polymerization of dissolved vinyl compounds, for example, was a method of studying the radiation chemistry of water. Since the radicals believed to be present in irradiated water were also considered responsible for initiating the polymerization of vinyl compounds, measurements of polymer yield were useful in detecting and identifying certain reactive species (86, 104, 127).

Probably, the French chemist Annette Prévot was the first one to suggest using volume changes due to polymerization for radiation dosimetry (391). In 1950, Mme. Prévot recommended the monomer acrylonitrile as possessing the desirable sensitivity towards X-radiation. In a volume dilatometer the meniscus of the fluid in a

2 mm-diameter capillary tube was displaced about 1 mm for every 300 r of dose absorbed in 10 min. This method allowed measurements of dose up to 10^5 r to be made consistently with an error less than 5%. Reproducibility was limited only by the impurities present in the acrylonitrile. For greater precision but less sensitivity, Mme. Prévot suggested styrolene as a substitute for the acrylonitrile. Greater precision was obtainable with styrolene because it could be purified to a greater degree than was true of acrylonitrile.

When in 1953 the chemists at the Tracerlab in Boston recommended the polymerization of acrylonitrile for dosimetry, they suggested using the insolubility of the polymer in its monomer as a visual detector of absorbed dose (50). In their experiments on the visual threshold sensitivity they reported that at low rates of 10 to 100 r/hr, the samples gave a clearly visible turbidity after a dose of 20 to 25 r of gamma radiation. At a high dose rate of 9400 r/hr, 200 r were needed for a comparable change. This dependence on dose rate was found to support neither the claim that the rate of polymerization was proportional to the square root of the dose rate (86) nor the claim that the yield was directly proportional to the dose rate (127). However, no simple theoretical expression was found to relate the percent of monomer conversion with the dose-rate dependence. Precision required that the acrylonitrile be free of impurities, especially of oxygen. The polymerization of acrylonitrile was desensitized by even traces of oxygen.

Although the visual detection of polymerized acrylonitrile had dosimetric possibilities, the method was not developed sufficiently nor was it standardized to make practical applications possible. This was not true of the dosimetric system proposed by the radiation biophysicist Frank E. Hoecker (b. 1903) from the University of Kansas (274). In 1957, he proposed a tissue-equivalent, styrene-polyester system as a polymerizable substance for dosimetry. The styrene-polyester liquid was sealed in a dosimeter cell (made of gelatin) along with an air bubble and a small metal sphere. After irradiation each cell was inverted and the final position of the metal sphere from some index line was an indication whether the irradiated object had received the dose for which the dosimeter was calibrated. As such the dosimeter served as a "go, no-go" device. This particular application was possible because during the process of radiation-induced polymerization the viscosity change is insignificant until approximately 97% of the dose is absorbed (272). Gel formation does not occur until during the absorption of the last 3%. The end-point in the dosimeter was that stage during the gel formation at which the air bubble could not move through a network of large molecules.

Hoecker's dosimeter was independent of dose rate (274). When heavy filtration was used for low energy radiation, the system was essentially energy independent. Polymerization was considered complete within 30 minutes after irradiation. To adjust the sensitivity

range of the dosimeter, a radical scavenger was used because it was assumed that the polymerization was the result of radical formation. With iodine as the radical neutralizer the dose range was extended from 1.5×10^4 rads to 2.5×10^5 rads. For measuring an unknown dose, then, a group of cells each having a different dose sensitivity were used as a unit. This showed that the styrene-polyester system was not restricted in application to its use as a "go, no-go" device. The dosimeter had other desirable features. From the practical point of view it could be read by untrained personnel without auxiliary equipment. Furthermore, the dosimeters were easily fabricated from materials whose cost did not exceed one cent per dosimeter.

In 1962, Hoecker defined the limits of the dosimeter precisely as being useful within the extended range of 300 to 10^7 rads (272). The upper dose was not due to the limitation of the system but was the highest dose at which studies were conducted. The extended lower limit was made possible because glass capsules were used for the liquid when measuring doses from 300 to 3×10^4 rads. The glass prevented oxygen from entering the highly purified system. For doses above 3×10^4 rads gelatin cells were used and the oxygen concentration in the dosimetric liquid was in equilibrium with that in the air.

For greater precision as a "go, no-go" device, several monomers, each with a characteristic gel dose were proposed for the dosimetric liquid (see Table 5). The polymerization of each could be

modified in a characteristic way by a number of possible inhibitors: nitrobenzene, resorcinol, diphenylpicrylhydrazyl, and oxygen. At low dose rates from 2.5×10^3 down to 10 r/min, the dosimeters showed a dose-rate dependence. At high dose rates from 3×10^3 to 10^6 rad/min, the dosimeters were dose-rate independent if a monomer with high radiation sensitivity were chosen as the dosimetric liquid and if a sufficient amount of inhibitor were added to the system. Energy dependence⁸⁸ of the dosimeters was negligible for radiation with a half-value-layer greater than 1.0 mm of copper. Although the dosimeters were very stable when stored at low temperatures, the high-sensitivity cells showed a 1% per day change of dose during storage at room temperatures.

Table 5. Gel doses of several monomers at 3000 rads/min (272, p. 382).

| Monomer | Gel dose (rads) |
|--------------------------------|--------------------|
| Commercial polyester* | 6.0×10^4 |
| Allylmethacrylate | 2.8×10^5 |
| Divinyl benzene | 4.2×10^6 |
| Methylmethacrylate | 1.2×10^6 |
| Diallyltumarate | 1.05×10^6 |
| Ethylene glycol dimethacrylate | 5.0×10^4 |

* Polyester of maleic anhydride, phthalic anhydride and propylene glycol dissolved in styrene.

⁸⁸To study the energy dependence of the system, several radiation sources were used: a 250 Kv X-ray unit, a 100-c cobalt-60 source, and electron-beam accelerators furnishing electrons at energies of 7 and 24 Mev (272).

The Hoecker end-point dosimeter seems to have had all the qualities desirable of chemical dosimetric systems. Possibly in industrial applications where routine doses would determine a set number of dosimetric liquids, the dosimeter would be most practical. Otherwise the construction of the many variations of dosimetric systems possible for specific applications would require trained personnel.

Perhaps Hoecker recognized this as a problem when he proposed a modification of the procedure for application of the system as a body-cavity dosimeter (273). The most easily prepared and the most conveniently handled of the dosimetric liquids had a threshold dose of 5×10^4 r. Although this was far above the dose required, such cells could be used because the threshold calibrated dose was known. Therefore, upon removal of the cell after the desired dose was administered, an additional, measured dose would bring about gelation. The unknown dose would be the difference between the threshold calibrated dose and the subsequently measured dose.

The above dosimetric methods were based on the effects of radiation on a monomer solution. Ionizing radiation may have similar effects on a polymer solution. The weight of a macromolecule can be increased by further crosslinkage or by the addition of radicals. However, ionizing radiation may also abstract some species from the macromolecules (75, p. 429). This latter effect was also useful in radiation dosimetry.

The chemical engineer Ernest J. Henley proposed the use of polyvinyl chloride film for gamma-ray dosimetry in 1951 (261). An acid-base indicator methyl violet was embodied in the film. When hydrogen chloride was liberated from the irradiated polyvinyl chloride, the color of the indicator was changed which effect was visually detectable from violet to blue to yellow orange with increasing radiation doses. Quantitative estimates of dosage were made spectrophotometrically at the absorption maximum of methyl violet, 6000 Å. Because the films did not have the same initial transmissions, the fraction X of dyestuff converted was calculated according to the following (261, p. 63):

$$X = \frac{\log T_o - \log T_\infty}{\log T_o - \log T}$$

where T_o = transmission of the unirradiated film

T = transmission of the irradiated film

and T_∞ = limiting transmission after infinite radiation time, that is, after complete conversion of the dyestuff.

Since methyl violet in an inert polystyrene base was unaffected by irradiation, its conversion in a polyvinyl chloride base was a linear function of the hydrogen chloride liberated from the polymer. The latter was proportional to dosage. The dosimeter was most effective for measuring doses in the range of 5×10^5 to 10^7 r.

There was another radiation effect utilized in dosimetry--an

induced ultraviolet absorption in transparent plastics. The radio-therapist M. J. Day and the chemist Gabriel Stein were first to propose this radiation effect as a basis for a dosimetric method in 1951 (140). They recommended the commercially available "Perspex Red 400" (colored polymethyl methacrylate) as a suitable plastic. Irradiation with X-rays gave rise to an absorption band at a wavelength longer than that of the absorption band of the basic dye and irradiation also brought about a decrease in the optical density of the original absorption band. Visually, the radiation effect was detected by a darkening of the color of the plastic.

Day and Stein did not actually formulate a dosimetric method based on the principle of the ultraviolet absorption induced by radiation. They made a few observations, such as --the optical density of the induced absorption band was dependent on the concentration of the dye in the plastic as well as on an oxygen-free system, and suggested that the properties might be applied to the measurement of radiation (140).

A more detailed and defined application of the above radiation effect was made in 1958 by the physicist John W. Boag (b. 1911) in collaboration with the radiobiologist Geoffrey W. Dolphin (b. 1923) associated with the University of London (56). They recommended

using two types of transparent plastics for measuring doses from 10^5 to about 2×10^8 rads. Clear, uncolored⁸⁹ Perspex showed a change in optical density at 2920 \AA after irradiation; the change in optical density was a linear function of dose up to about 3×10^6 rads. The useful range of Perspex was supplemented by that of a plastic with a higher melting point. Melinex⁹⁰ (polyethylene terephthalate) exhibited an absorption band on irradiation at 3250 \AA ; the optical density at this wavelength was a function of dose up to 2×10^8 rads.

Reproducibility was affected, perhaps most significantly, by the variation in thickness of the sheets of transparent plastic (56). Therefore, optical densities were corrected to an arbitrary standard thickness before being used as a measure of dose. Of any contaminants present in commercial plastics, the monomer content exerted the greatest influence on the radiation response. To reduce the monomer content, an approximate heat treatment was recommended.

The ultraviolet absorption showed no dose rate dependence up to about 3×10^8 rads/sec (56). The intensity of the absorption peak of irradiated Perspex was stable for about 24 hours. Then, slow fading occurred at the approximate rate of 10% per month. In the case of

⁸⁹Day and Stein favored colored Perspex because it showed more intense color changes on irradiation than the uncolored Perspex.

⁹⁰Polyethylene terephthalate is manufactured in Britain under the trade name Melinex but in the United States as Mylar.

Melinex, rapid fading of the ultraviolet absorption occurred until a stable level was reached in about 24 hours. The stable level, equivalent to about half the initial change in optical density, remained practically unchanged even after 11 weeks.

Since dosimetry by transparent plastics was entirely empirical, the system had to be calibrated by some other standard method (56). Check calibrations at regular intervals were also recommended because of the variations among different batches of Perspex or Melinex. To take into account the rate of fading of the irradiated samples, Perspex was calibrated at the optical density measured about half an hour after irradiation. Such an optical density reading included any of the "after effects" of radiation. The resulting calibration curve, then, was satisfactory for any readings made within 24 hours. In practice, Melinex was calibrated according to what appeared to be the permanent component of the induced optical density.

In 1961, research on Melinex film showed that the rapidity with which the non-permanent component of the optical density faded depended on the thickness of the Melinex, on the dose absorbed by it, and on the presence of oxygen (406). A 0.00025-inch Melinex film did not exhibit the rapid initial fading, whereas a 0.007-inch film did show fading. Apparently, oxygen diffused easily in the thinner film to make the fading so rapid that it was unnoticeable.

The Perspex-Melinex method of dosimetry was well developed

to provide for accuracy of measurement. Furthermore, it was a more convenient method when compared to colorimetric or any liquid dosimetric method for making routine measurements of radiation at high dose rates.

Although irradiation of a monomer or a polymer may induce polymerization or further cross-linkage, the opposite effect can also occur. Ionizing radiation can degrade or decompose the polymer. Degradation and any variations in the structure of a solid polymer due to irradiation are accompanied by corresponding changes in molecular weight (6, 525). Degradation of polymers in solution results in viscosity changes.

The English radiobiologist P. Alexander (b. 1922) was the first to suggest the use of polymer degradation in dosimetry (7). In 1954, Alexander proposed the use of viscosity measurements of chloroform solutions of irradiated polymethyl methacrylate as a means of measuring doses of 10^6 r and above. The molecular weight of the polymer, determined by the measured changes in viscosity, was inversely proportional to the radiation dose. The method was applicable even when the radiation source provided a mixture of high-energy radiation.⁹¹ From the intrinsic viscosities determined before and after irradiation,

⁹¹ Alexander collaborated with the physicists A. Charlesby and M. Ross at the Atomic Energy Research Establishment in Harwell (7). Test samples of the solid polymer were irradiated in the pile at Harwell.

the radiation dose which the polymer absorbed was obtained from the following relationships (7, p. 400):

$$R = 2.6 \times 10^4 \left(\frac{1}{M_v} - \frac{1}{M_{v_0}} \right)$$

$$r = 1.2 \times 10^6 \left(\frac{1}{M_v} - \frac{1}{M_{v_0}} \right)$$

where R = the dose in pile units of radiation (equivalent to 4.6×10^7 r)

r = the dose in roentgens

M_v and M_{v_0} = the viscosity molecular weights after and before irradiation respectively

and where the proportionality constants were experimentally determined.

With his dosimeter which was based on polymer degradation, the radiation chemist Paul Y. Feng (b. 1926) extended the lower limit of the dose range within which polymer degradation was useful for dosimetry (168). In 1958, Feng proposed a basic system consisting of an aerated solution of polystyrene in carbon tetrachloride. Although Feng did not develop his dosimetric method sufficiently, he did claim that flow-type viscosimetric studies of the system showed that it had a useful range from 10^2 to 10^8 rads. He obtained the extended lower limit because in his system degradation of the polymer occurred by the radicals copiously produced during radiolysis of the halogenated hydrocarbon solvent.

In that same year 1958, some physical chemists at Batelle Memorial Institute in Ohio proposed several solid polymeric systems for high-level dosimetry based on degradation (307). Viscosity measurements of the irradiated polymers in solution in xylene were related to dose; this was not done by way of the changes in molecular weight (a procedure which Alexander had followed in 1954) but by way of the changes in flow-time (a procedure also followed by Feng). With the above dosimetric method, the degradation of solid polyisobutylene was useful for dosimetry over the range from about 10^4 to 10^7 rads. Solid polymethyl methacrylate was useful in the dose range from 10^5 to about 10^7 rads. The solid copolymers of styrene and isobutylene, somewhat more insensitive to irradiation, were useful in the range from approximately 5×10^5 to over 10^8 rads. Again, these solid polymeric substances were suggested as being suitable for dosimetry, but methods involving these polymers were not sufficiently developed to be evaluated.

In 1960, the radiation chemist L. Wiesner from the Institute for Oil Research in Hannover, Germany, proposed a heptane solution of polyisobutylene as a basic system for dosimetry (537). This dosimetric system was also based on depolymerization due to irradiation. The system had many suitable characteristics. Reproducibility of measurements did not depend on the purity of the chemicals. Because the stability of the pre-irradiated solution was high, it could be kept

in dark bottles under laboratory conditions for about two months.

Viscosimetric measurements were simple and required generally from 5 to 15 min per viscosity determination. For measuring doses from 10^3 to about 3×10^6 rads, 20 grams of polyisobutylene (molecular weight about 2 to 3×10^5) were dissolved in a liter of carbon tetrachloride. Since for measuring higher doses more concentrated solutions of lower polymerized isobutylene gave more precise data, about 480 grams of polyisobutylene (molecular weight of 5000) per liter of heptane made up the system for measuring doses up to 10^9 rads. A mixture of polyisobutylenes (molecular weights of 500 and 1500) in heptane made up the system for measuring doses from 10^7 to 10^{10} rads. Quite a comprehensive system for measuring doses from 10^3 to 10^{10} rads, then, was constructed by varying the solute, the solvent, and the concentration of the solutions.

Wiesner further reported that the system was independent of the irradiation temperature between 20 and 80°C (537). The system had to be calibrated against a standard like the Fricke dosimeter. No statement was made about the energy dependence of the system because all studies were conducted only with cobalt-60 gamma-radiation. Since the dosimetric method was intended primarily for application in research in radiation chemistry, future studies of its behavior towards other types of radiation would have to be made.

A much more sensitive polymer degradation dosimeter was

proposed by the chemist A. L. Boni in 1961 (58). As a result of research sponsored by the U. S. Atomic Energy Commission at the duPont Savannah River Plant in South Carolina, Boni proposed a polyacrylamide system as an effective personnel criticality-incident dosimeter. The dosimeter consisted of an 0.078% aqueous solution of polyacrylamide (molecular weight about 6×10^6) in 1.5 ml polystyrene or glass vials. The change in viscosity through the fractionation of the polymer by the radiation products in water was directly related to absorbed dose except for very low doses. Although below a dose of 200 r, the accuracy of the method dropped to $\pm 20\%$, between 5000 and 200 r the viscosimetric readings were obtained with an accuracy of $\pm 10\%$.

The low concentration of polyacrylamide was used to eliminate any cross-linking and to restrict all effects on the polymer to indirect effects (58). The high sensitivity was obtained by using a polymer with a high molecular weight (an approach used by Wiesner). Besides having a high sensitivity, the system had stability over long periods of time in the presence of temperatures at least up to 45°C and towards light (except direct sunlight). The polyacrylamide dosimeter was insensitive to neutrons, was nearly energy-independent over the range from 39 to 1330 Kev gamma-rays, and was dose-rate independent up to 2400 r/hr.

This energy independence over the low range of 39 to 200 Kev

(unusual for a chemical dosimeter) must have contributed to the versatility of the polyacrylamide dosimeter over other comparable systems. Although intended for the monitoring of the gamma-component of mixed radiation fields, the dosimeter had possible application in biological research also because of its range and simplicity.

Certain clear plastics, such as polymethyl methacrylate (140) and polyethylene terephthalate (56), on irradiation exhibited an induced absorption band in the ultra-violet region of their spectra. Since the change in the optical density of this band was directly related to dose, the induced absorption was the basis for a dosimetric procedure. There were other polymeric substances which on irradiation showed quite a pronounced discoloration and a change in optical absorption. Such substances were also useful in dosimetry.

In 1955, the physicist Milton Birnbaum (b. 1920) and his co-workers at the Naval Research Laboratory in Washington, D. C., proposed the use of melamine in the form of a clear plastic as a radiation dosimeter (54). On irradiation, colorless melamine took on a yellow-brown tint and showed a change in optical absorption. Spectral densitometric studies showed that with increasing dose, the greatest change in optical density occurred in the near ultra-violet. A very small change in the blue end of the spectrum gave rise to the visible yellow-brown tint.

The effects of radiation were quantitatively determined by

measuring the changes in the optical density of melamine at wavelengths from 3300 to 4800 Å (54). Analysis of the data collected led to the following procedure. A 1-cm thickness of melamine was used as an X-ray dosimeter for doses in the range of 5×10^5 r; optical density measurements were made at a wavelength of 3400 Å. A 0.4-cm thickness of melamine was used for doses from 3×10^3 to 10^6 r; optical absorption was measured at 3800 Å. A 0.1-cm thickness of melamine measured doses from 3.8×10^4 to 10^7 r and spectral studies were made at 4200 Å. By adjusting the thickness of the dosimeter, then, it was made effective for measuring doses over a broad range. The use of melamine in the dosimetry of X-radiation was advanced by the fact that the dosimeter properties of melamine were roughly independent of X-ray energy in the range of 1 to 11 Mev.

Although Day and Stein found that in an oxygen-free system the darkening of dyed polymethyl methacrylate was linear with dose to about 10^5 r (see p. 250, above), in 1955 other radiotherapists suggested that clear plastics, either polymethyl methacrylate or polystyrene, be used for measuring doses beyond 10^6 r (176). Prior to irradiation these plastics show an absorption at about 2800 Å. Upon irradiation this ultraviolet edge moves up into the visible region of the spectrum, giving rise to a brown discoloration. The increase in optical absorption with dose was found to be linear up to about 2×10^7 r over a considerable range of wavelength.

Another high polymer which discolored with irradiation was polyvinyl chloride in the form of a non-plasticized film (26). In 1958, the chemists Charles Artandi and A. A. Stonehill (b. 1907) suggested polyvinyl chloride film for a dosimeter of electron doses in the 0.5 to 6 megarad range. The film turned amber but the full intensity of color was not reached with irradiation. If the film were kept at room temperature, the color developed after a delay period of about three days. If it were stored at 120°F, full intensity of color was attained after 4 hrs. Optical density measurements were then correlated with absorbed dose.

To facilitate the dosimetric procedure, a standard dose curve (dose vs. optical density) was prepared by irradiating 2-inch slides of the polyvinyl chloride film in 1-megarad increments. After determining the optical density of any subsequently exposed slide, the dose was read directly from the curve. Likewise, slides were irradiated with known doses; these slides served as color standards. The eye could detect 0.5 megarad differences in color; if greater precision were desired, spectrophotometric measurements at 4000 Å showed differences as small as 0.1 megarad.

Subsequent to their first proposal of the film for dosimetry, Artandi and Stonehill established certain useful parameters relating to its application (27). The coloration of the rigid vinyl film began with a greenish color, but gradually turned yellowish-brown,

reddish-brown, or dark brown depending on the absorbed dose. The intensity of color was directly proportional to the absorbed dose in the range of 10^5 to 10^7 rads. The intensity of color was independent of dose rate but was dependent on oxygen in so far as the color was more intense if the irradiation were carried out in a vacuum instead of in air. The coloration of irradiated high polymers was an irreversible process. Still, some fading occurred particularly in those slides where the color was allowed to develop at a higher temperature. Therefore, to obtain reliable dose measurements, the slides were developed under standardized conditions (time, temperature). Since measurements of the absorption at 3960 \AA were most reproducible and sufficiently precise, standard curves were constructed from spectrophotometric data at that wavelength although there were other changes in optical absorption that could have been used.

The dosimetric method of Artandi and Stonehill appears to have been a convenient method, but for reliability it would require rigid standardization. Perhaps this would not be too difficult to achieve in a laboratory situation attendant upon high-level dosimetry for which the method was intended.

Gas Systems

Since the Second World War, chemical methods of dosimetry assumed a new importance because of the demands for dosimetry of

high-level radiation. With the development of irradiation technology, measurements of dose beyond the radiation therapy dose of 5×10^4 r had to be made. Some of the chemical systems described above did qualify as high-level dosimetric systems. The ceric sulfate dosimeter, the oxalic acid dosimeter, the aqueous methylene blue system, and many of the polymeric systems were effective in measuring doses beyond 10^6 r. Although the necessity of monitoring doses beyond 10^8 r was rare, the development of the nitrous oxide system provided an effective dosimetric system in the range of 5×10^4 to almost 10^{10} r (254).

The decomposition of nitrous oxide on irradiation was first suggested for high-level dosimetry in 1956 by the physical chemists Paul Harteck (b. 1920) and Seymour Dondes (b. 1918) at the Rensselaer Polytechnic Institute in New York (254). Nitrous oxide (N_2O) itself had many properties which were highly desirable in a basic dosimetric substance. It could be purified easily; it had an indefinite shelf-life; and it was useful over a wide temperature range from -80 to $200^\circ C$. Furthermore, the decomposition of N_2O was an exactly linear function of dosage to 10^7 r and practically linear to 10^8 r.

The products of decomposition--nitrogen (N_2), oxygen (O_2), and nitrogen dioxide (NO_2)--were always in the ratio of 1:0.14:0.48 which indicated that the products of irradiation did not interact with each other and their yields could be measured at any time after

irradiation⁹² (254). The analytical system for measuring the decomposition yields included vacuum techniques and pressure gages. A colorimeter could be used for measuring the NO_2 . After irradiation the seals of the dosimeters were broken in a vacuum and the condensible oxides were frozen with liquid nitrogen. The residual pressure of N_2 plus O_2 was then measured and the ratio of the amount of N_2 and O_2 formed was measured by burning the oxygen with hydrogen. The oxides were analyzed by measuring the unreacted N_2O at dry ice temperature since at that temperature the NO_2 had almost no vapor pressure. The pressure of NO_2 was finally measured at room temperature (if not colorimetrically). In practice, particularly at low doses, only the N_2 and O_2 were measured. At high doses between 3×10^7 and 3×10^9 r, NO_2 was clearly visible and its measurement sufficed. Above 3×10^9 r the dosimeter was no longer considered accurate since the decomposition of N_2O approached equilibrium with that dose.

When a measurement of thermal neutron dose was desired, 5 mg of uranium-235 oxide powder were added to the reaction vessels (150). The decomposition due to the neutron-induced fission was about one

⁹² Samples of nitrous oxide in sealed 20-cc quartz vessels were irradiated in the Brookhaven National Laboratory Reactor. Other samples sealed in 87-cc Pyrex vessels were irradiated in the BNL cobalt-60 sources (254).

hundred times greater than that due to the beta- and gamma-radiation. Materials like boron, lithium, or natural uranium could be used instead of the uranium-235.

In 1960, two investigators at the Atomic Energy Research Establishment in Berkshire, England, J. A. Hearne and R. W. Hummel suggested that nitric oxide (NO) was an important decomposition product in the nitrous oxide system (257). At the temperature of liquid nitrogen NO reacted with O_2 ; therefore, the measured yield of O_2 was not strictly accurate. The N_2 yield was the most suitable of all the decomposition products for dosimeter application since it was unaffected by the errors inherent in the analytical system as well as by the presence of impurities. Hearne and Hummel also recommended that determining the N_2 and O_2 by gas chromatography would improve the precision of the analysis since it would obviate the necessity of separating the components of the mixture.

When the nitrous oxide dosimeter was incorporated into the dosimetry program associated with the Lockheed Radiation Effects Reactor in 1961, a routine method was developed still based on the analytical technique of Hartech and Dondes (448). Apparently N_2 , O_2 , and NO_2 are the only stable products in the decomposition of nitrous oxide. A determination of yields made routinely within a short time after irradiation would not be affected by any post-irradiation reaction of any NO with O_2 . Any error due to the analytical technique must have been

negligible since the inherent stability of the nitrous oxide dosimeter was considered a definite advantage in its use in area monitoring for integrated dose in fields of high radiation exposure.

Chemical Dosimetry in Developmental Perspective

During the post-war period, radiation dosimetry was no longer limited to personnel monitoring and to measurements for radiation therapy where doses usually did not exceed about 5×10^4 r. Developments in nuclear technology required the measurements of much larger doses of radiation. Extensive chemical research to meet these new demands for radiation dosimetry has made available many chemical dosimetric systems. These systems include gases, liquids, gels, and solids and represent dosimeters that respond to radiation over a total dose range of about 10 to 10^{10} rads. Although only a few of the systems, such as the ferrous sulfate dosimeter and the chloroform-dye system, were widely accepted, many have been applied in special situations.

The formulation of many of the chemical dosimeters has been possible because of the developments in radiation chemistry. In fact prior to 1925, the early chemical dosimeters, for the most part, did not have a chemical theoretical foundation. Then from about 1925 until World War II, investigation of chemical systems for dosimetric possibilities gave rise to a few dosimeters and also to certain assumptions

which proved basic to the developing theories of radiation chemistry. After World War II, the principles in radiation chemistry often served as guides in the research for new dosimetric systems or for variations of those which were formerly proposed.

Most fundamental to many systems was the radiation effect on the particular solvent chosen. Reaction mechanisms based on the theory of the indirect action of the radiation on the solute via the solvent often determined the components of dosimetric systems. Also, the G value of radiation chemistry became a standard way of expressing the yield of chemical change due to absorption of radiation. Indeed modifications of systems often involved steps taken to change the G value. A high G value in radiation chemistry was associated with a chain reaction. Because a chain reaction depended on factors such as temperature, dose-rate, and impurities, dose measurements with a system having a high G value were not satisfactorily reproducible. This gave rise to variations of dosimetric systems into which inhibitors of chain reactions were introduced. A low G value was characteristic of a system with low sensitivity. The use of a system with a low or intermediate G value created a problem when only low doses of radiation were absorbed because precise determinations of low concentrations of products were difficult. The development of spectrophotometry in analytical chemistry provided the necessary analytical tool. Not only was visual and ultra-violet spectrophotometry most useful in measuring

the extent of reactions, but spectrophotofluorometry has made possible the determinations of irradiation products in very low concentrations.

CHAPTER IX

SUMMARY AND CONCLUSIONS

In retrospect, chemical dosimetry developed in the context of certain advances in the field of ionizing radiation. In fact, developments in the field of ionizing radiation created the need for the development of chemical dosimetry. This was especially true following the initial medical applications of X- and gamma-radiation until the 1920's and then, again, following the development of reactors in 1942. During the 1920's and the 1930's, although all developments in the field of ionizing radiation did not directly give rise to a need for developments in chemical dosimetry, discoveries in the field of ionizing radiation indirectly contributed to progress in chemical dosimetry.

The almost immediate application of X- and gamma-radiation in medicine during the first few years after 1895 made dosimetric methods necessary. That the first methods used depended on what apparently were the chemical effects of ionizing radiation is an outcome that might be expected. After all, such effects as the photographic action of ionizing radiation and the coloration of irradiated salts were among the first observed by physical scientists in their investigations of the properties of X- and gamma-radiation. However, little was known about the nature of the chemical action of ionizing radiation or about

the mechanism behind the chemical effect. When the physicians and radiologists first proposed the various chemical systems for dosimetry, they did so because apparently a new chemical entity was formed due to irradiation and, associated with the formation, there was a visible change that seemed to be measurable. This was the basis for the earliest chemical dosimeters; any subsequent developments up to about 1915 were due to the efforts made at improving the methods used to interpret or to measure that visible change.

Beginning in the 1920's, a series of developments in the field of ionizing radiation acted as a series of prods for further study of chemical systems for dosimetric application. However, the research was no longer conducted by physicians and radiologists who were determined to make their practices in clinical radiology safe for their patients. No doubt, among physicians and radiologists, the exigency for devising dosimetric methods became less urgent as one or other of the earlier-proposed chemical dosimeters became a part of routine procedures in clinics and hospitals. Also, the introduction of ionization methods of dosimetry around 1910 made another widely-accepted method of dosimetry available to those in the medical field. In the early 1920's however, the development of higher-energy X-ray units which utilized the Coolidge X-ray tube (1913) and the subsequently expanded application of X-rays in medicine and in industry prompted much radiobiological research. The research in radiobiology led to the renewed

research on the chemical effects of ionizing radiation to determine some of the underlying mechanisms of biochemical processes.

The chemical dosimetric methods that proceeded from this research following the introduction of higher-energy X-ray units were proposed not by physicians and radiologists but by chemists, biochemists, or biophysicists who were not mainly interested in the method for their own immediate use. Rather, these men recommended certain chemical systems for clinical use because they recognized the advantages a chemical dosimeter could have over an ionization chamber. Although only three chemical systems--the ferrous sulfate, Eder's solution, and the methylene blue system--were recommended for dosimetric use, the research of the 1920's and 1930's contributed in other significant ways to future developments in chemical dosimetry. In the ferrous sulfate dosimeter (Fricke dosimeter), proposed in 1927, future radiation chemists found a reliable instrument based on a highly reproducible system which could be used to calibrate other dosimeters. Furthermore, the conclusion reached by Fricke and associates in 1929 that the primary action of the radiation was on the solvent rather than the solute was subsequently reinforced by the observations of other researchers and, after the development of nuclear energy, served as a basis for the formulation of other chemical dosimeters. Finally, the attention given to energy relations between the dose and the chemical effect as well as the introduction of various analytical methods to

measure the extent of reaction contributed to the future development of dosimetric methods.

In addition to high-energy X-ray units, the discovery of the neutron and the development of accelerators which provided beams of high-energy particles and made artificial radioactivity available on a large scale gave rise to considerable expansion in the application of ionizing radiation in medicine and in industry. Consequently, the number of persons whose occupation was a source of radiation exposure was always increasing. Concern for the protection of the radiation workers exerted a decided influence in bringing about the standardization of dosage measurements. The progress made in standardizing dosage in the 1920's and the 1930's indirectly contributed to developments in chemical dosimetry through the identification and definition of radiation units. Although the standardization process began in 1928 when the roentgen was officially defined as a radiation unit, it was not until 34 years later (in 1962) that the rad was officially designated as a unit of absorbed dose and the roentgen as a unit of exposure. However, dosimetric methods were more meaningful when they were based on precise terminology.

The rapid advances made in nuclear technology in the 1940's provided a new impetus for research on chemical dosimetric systems. Again the expanded radiation facilities created a problem in personnel protection, a problem more complex than it was in the 1920's and the 1930's. The presence of mixed radiation fields in the vicinity of

reactors and accelerating devices required that film badges be modified in such a way that they could be used to detect exposure to various forms of ionizing radiation.

Not only were provisions made for monitoring the particular forms of radiation, but steps were also taken to improve the accuracy of photographic dosimetry. The low accuracy of dosimetric methods was attributed mainly to the dependence of emulsion sensitivity on the energy of the radiation. Filtration methods of reducing this dependence of emulsion sensitivity on energy probably could have been developed from the knowledge of the effect of filters on an erythema dose, for example. However, the 1938 Gurney-Mott explanation of the latent image formation in the photographic effects of radiation provided a theoretical basis for such filtration methods because it clarified the dependence of emulsion sensitivity on energy. Since the need for general monitoring by means of film badges did not become very pronounced until the 1940's, the advantage of a theoretical basis for the required modifications was available. The introduction of metallic filters or filter combinations into the film badges improved the accuracy of photographic dosimetry from a low of about 10% with the unfiltered film badge to 20% and in some cases up to 80% with the filtered film badge.

The need for radiation protection was not the only need created by advances in reactor technology. The re-designation of the wartime

reactors as research reactors and the construction of many additional reactor units and accelerating devices for research purposes established a need for dosimeters capable of registering doses of high-energy radiation not only over a wide range but delivered, at times, at high dose rates. Such factors prompted the investigation of many chemical systems for dosimetric possibilities. Although some of the proposed dosimetric systems were intended for application in radiation protection and in medicine, many were intended for measuring doses in radiation chemistry and nuclear technology where highly sensitive systems were rarely needed.

Research on chemical dosimetric systems in the 1950's was based generally on the developing theories of radiation chemistry. The experimentally supported theory that radiation acted directly on the solvent and indirectly on the solute led to many dosimeters utilizing the radiation effects on water as a solvent. Still other dosimeters utilized the radiation effects on chlorinated hydrocarbons as solvents. Some of these dosimeters depended on the liberation of hydrogen ions from the chlorinated hydrocarbon; others depended on the formation of free radicals as reactive intermediates. Chemical dosimetry also adopted the G value of radiation chemistry as a standard way of expressing the yield of chemical change due to absorption of radiation. Modification of systems often involved steps taken to change the G value. In the case of a chain reaction (a system with a high G value),

inhibitors were added to the systems to control the chain reaction, to lower the G value, and thus to improve the reproducibility of the system.

Hence, the theories and reaction mechanisms of radiation chemistry had an important influence on the development of chemical dosimetry. Not only were systems formulated on the basis of the theories, but researchers were often guided in modifying some systems by their knowledge of reaction mechanisms. Much time and research would have been necessary before such systems could have been formulated if the theories of radiation chemistry were not available. At the same time the theoretical foundation of some dosimeters contributed to the simplicity and accuracy of the analytical method used in interpreting the dosage measurement.

Most of the chemical systems proposed for dosimetry in the 1950's relied on absorption measurements as the analytical method of interpreting the extent of a chemical reaction. Such a method was possible because of the progress made in chemical instrumentation in the 1930's and the 1940's. The availability of commercial photoelectric spectrophotometers sensitive to light beyond the visible spectrum added a definite precision to the analytical methods proposed for the interpretation of dosage.

In the post-war period, research on chemical dosimetric systems has been very extensive. It has included gaseous, liquid,

gel, and solid systems which responded to radiation over a dose range from about 10 to almost 10^{10} rads. No single system was effective over this wide range; but such a large dose range was not usually required of a single dosimeter. A combination of dosimeters could be selected to cover the wide range if desired. Not all of the recommended systems had a comparable reliability, however, nor did they meet all the desirable requirements for a dosimetric system. Only a few have been studied in more than one laboratory and it seems as if only a small number have been widely accepted owing to one or other deficiency which each system had for dosimetry. Very likely future research will contribute to improving the reliability and characteristics of some of these dosimeters.

Thus far, the aqueous systems have been most reliable; aqueous ferrous sulfate is even used as a secondary standard. Perhaps a contributing factor to this reliability is that radiation chemists have given much attention to the radiation effects on water. Since the radiation chemistry of water has been considered from several aspects and the various species present in irradiated water have been identified, explanations can be given for oxidation-reduction reactions in aqueous systems. The knowledge of the function of particular entities in the irradiated water must have served as a guide in the formulation or modification of aqueous dosimetric systems. Although much of the early work in chemical dosimetry (1902-1925) was of an empirical

nature, ideas regarding reaction mechanisms were developed along with dosimetric systems in the years that followed (1925-1942). However, in the post-war period, the theories and reaction mechanisms of radiation chemistry figured very prominently in the development of dosimeters. Future developments in chemical dosimetry most probably will rely on further advances made in radiation chemistry.

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