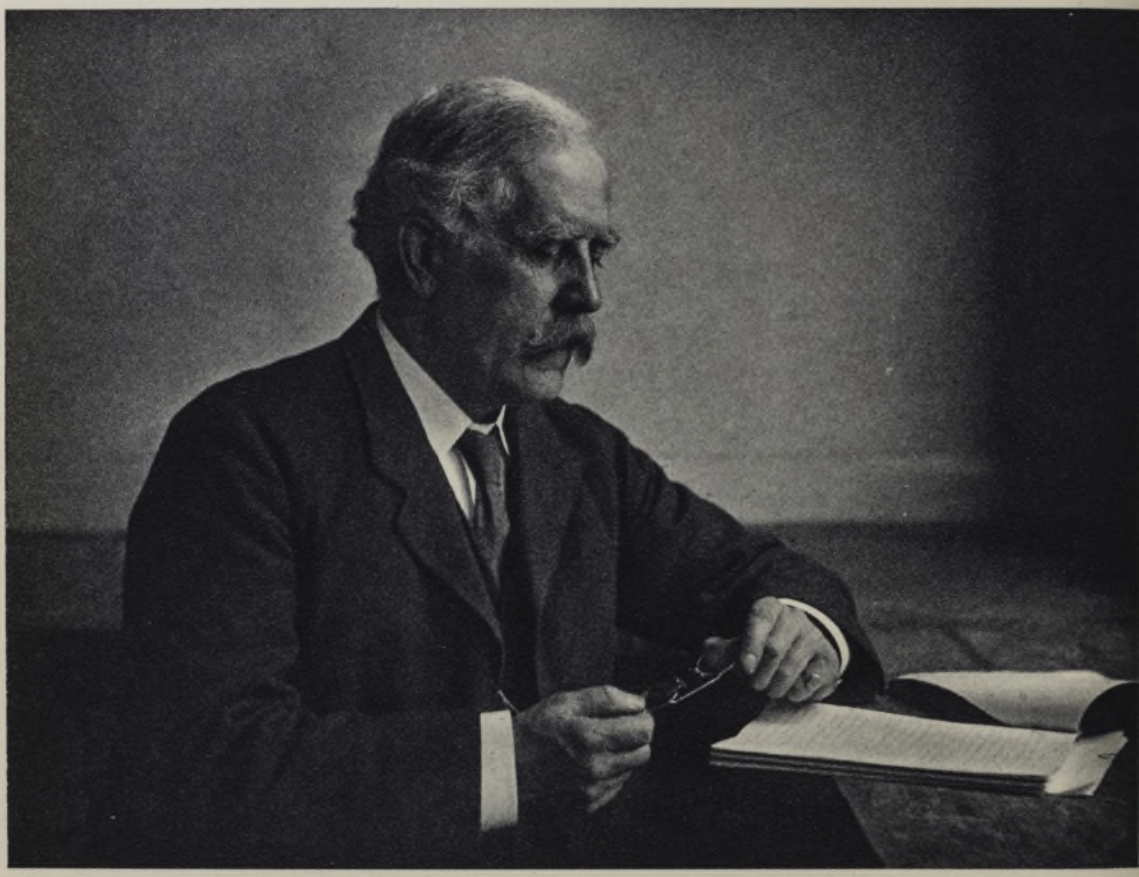

A. E. Garrod.

ARCHIBALD EDWARD GARROD

1857–1936

ARCHIBALD GARROD, born in London on 25 November, 1857, was the fourth son of Sir Alfred Baring Garrod, M.D., F.R.S. The father, a physician well known for his work on diseases of the joints, was himself by nature an able experimentalist who in 1848 succeeded not only in demonstrating the presence of uric acid in the circulation of gouty patients but also in estimating it by weighing the crystals he obtained from a known quantity of blood. His son delighted to recall that this was the first quantitative biochemical investigation made on the living human body.

Garrod was educated at Marlborough and Christ Church, Oxford. He was placed in the First Class of the Natural Sciences School in 1880 and then proceeded to St. Bartholomew's Hospital. After qualifying, he spent some months in clinical studies at Vienna and then returned to a house appointment. His abilities were quickly recognized and he was marked out for the clinical staff. In 1889 he held the post of Casualty Physician, but so few were the changes in the personnel of the St. Bartholomew's Staff during succeeding years that promotion was very slow. He became Assistant Physician in 1903 but Full Physician not till 1912. During the time of waiting, however, he became Assistant Physician to the West London Hospital and later was appointed to the same position at Great Ormond Street where he became Full Physician in 1899. During these years he had relative leisure for work on the problems of chemical pathology which held his interest throughout the rest of his life. After less than three years in the wards of St. Bartholomew's, where he proved himself to be an able and popular teacher of clinical medicine, the War took him to Malta as consulting physician to the Forces there. He saw the patients evacuated from Gallipoli and later from Salonika and his advice was greatly valued. In 1919 he was created K.C.M.G. for his services. On his return to St. Bartholomew's he was chosen as the first Director of the newly established Medical Unit and began with enthusiasm to arrange for clinical research in the wards. It was fated, however, that his energies were soon to be directed into a different channel, for after but one year in charge of the Unit he was called upon to succeed Sir William Osler as Regius Professor of Physic at Oxford in October, 1920.

To the duties of that distinguished chair he gave unremitting attention. Opportunities for clinical work were small and his time was fully occupied with university affairs. The claims and needs of the Scientific Faculties were always his special care, and when in 1922 he became a member of the Statutory Commission he diligently supported their interests. He held the Regius Chair for seven years, retiring at the age of 70.

Garrod's earliest publications were of clinical interest, dealing, like those of his father, chiefly with rheumatism, rheumatoid arthritis, and kindred conditions. He always retained an interest in these and he published no fewer than 26 communications, papers, and lectures dealing with them directly or indirectly. More deeply seated, however, was his interest, hereditary and innate, in the chemical side of medicine. In the nineties of the last century when he began his laboratory studies the technical methods by which we now study quantitatively so many chemical events in the blood and in surviving tissues were yet to be developed, and those interested in metabolic phenomena were still led to look to changes in the urine as a chief field for profitable study. Garrod's wish was to explore the changes in metabolism which are induced by disease and he was early led to take a special interest in urinary pigments. This interest seems to have begun with the finding in 1892 of an unusually coloured urine in a case of chorea. He showed that this was due to *uro-haematoporphyrin*. After working out a successful method for the separation of this substance he showed that in small amounts it is a normal urinary constituent. He found it in varying quantities in a number of pathological conditions and studied its properties and general behaviour with great care. He next dealt with the chief yellow pigment of the urine *urochrome*. Even to-day the nature and origin of this prominent excretory product remain obscure, but Garrod's work removed many erroneous views concerning it. There followed a study of *uroerythrin*, a substance familiar as the pigment in pink urate deposits. No light could be thrown on its actual chemical nature, but its quite exceptional properties were carefully described in much detail and new facts concerning its occurrence and behaviour were discovered.

In 1896 Garrod turned to a study of *urobilin*. He described much that was then new concerning the properties and especially the spectroscopic properties of this pigment. He showed, for instance, that it was not, as had been thought, identical with hydrobiliruben, an artificial reduction product of bile pigment. Its absorption spectra in various circumstances were fully studied and some very interesting points recorded.

Garrod's work on these pigments was essentially descriptive. As pioneer work, however, it was enlightening and valuable. At that

time there was no knowledge of the constitution of any one of them. To-day those of *uroerythrin* and *urobilin* are known.

During 1897 his interest in the urinary pigments brought him into touch with a case of *alkaptonuria*. This fortunate happening was responsible for much of his most influential work and teaching. It was his concern with this relatively rare condition that ultimately led him to think so deeply and to write so brilliantly about what he came to call " Chemical Malformations " or " Inborn Errors of Metabolism ". In *alkaptonuria* homogentesic acid is excreted in the urine. It is derived from the tyrosine and phenylalanine of proteins, and, owing to its oxidation, urine containing it, when slightly alkaline, blackens in the air—a phenomenon by which the condition is usually recognized. The tendency at that time was to suspect infection everywhere in pathology and *alkalptonuria* was supposed to be caused by an organism in the intestines which converted, or assisted to convert, tyrosin into homogentesic acid. One who knew him well relates that one afternoon when Garrod was walking home from the hospital thinking about such problems it suddenly occurred to him that *alkaptonuria* might, after all, be due to some error in the behaviour of the body itself, peculiar to the individual and present throughout life. It might, he thought, be a familial affair. He by now had got into touch with other cases of the condition besides the one he first saw. The mother of a child in whom it was present proved to be again pregnant and Garrod found that her later infant already displayed it on the second day after birth. His hypothesis seemed proved therefore, and later evidence completely confirmed it. In 1899 he published an important paper on this metabolic anomaly in which the data recorded in all known cases were assembled. He here made it clear that the condition was no imposed disease but an individual variation from normal metabolism with a familial distribution. He suggested that it was likely to be present in first cousin marriages. Bateson and Punnett then pointed out that the mode of incidence of *alkaptonuria* is readily explained by looking upon it as a recessive character in the Mendelian sense, a suggestion which Garrod found attractive. He had for some time previously been interested in the abnormalities which occurred as a result of inbreeding, and the records of his cases at Great Ormond Street were of use to Bateson and Punnett in their own work.

By 1903 he had shown that two other conditions, *albinism* and *cystinuria*, were metabolic errors, and that inbreeding was an important factor in their incidence. In 1908 he gave the Croonian Lectures of the Royal College of Physicians with the title " Inborn Errors of Metabolism ". In these he dealt with yet another metabolic anomaly, *pentosuria*, as well

with those he had previously described. The lectures were later published under the same title, and the book, most admirably written, awakened a wide interest. It greatly stimulated thought not among chemical pathologists alone but among all students of biochemistry. A second edition appeared in 1923 and in this two further instances of congenital anomalies were added to those dealt with earlier : *Congenital Steatorrhoea*, on which he had worked conjointly with Hurtley, and *Haematoporphyria Congenita*, studied with L. Mackey. The latter study took him back to one of his earlier interests. With his descriptions of all these conditions Garrod took infinite pains, making always an exhaustive study of the relevant literature, and in every instance adding interesting matter of his own. There can be no doubt that his work on these departures from the normal chemical rhythm of the human body constituted a most important contribution to medical and biological science. He chose indeed a field which has proved fertile in suggestions. After he became full physician at his hospital he had little or no leisure for laboratory experiments, but he guided and encouraged the work of others on the subjects of his interest, and his very numerous published addresses, lectures, and essays were always of the highest quality and always stimulated thought in those who read them.

With all his predilection for experimental science Garrod remained first and foremost a clinician with a deep sense of the dignity and importance of that calling. When speaking, as he often did, of the help that Medicine receives from Science he was always concerned to emphasize the view that this is but a repayment of the debt that Science has owed to Medicine.

He was elected Fellow of the Royal Society in 1910. His father became a Fellow in 1858 and his eldest brother, Alfred Henry Garrod, in 1876. It must have been rare indeed in the history of the Society for a father and two of his sons to attain to its Fellowship.

In 1886 Archibald Garrod married Laura Elisabeth, eldest daughter of Sir Thomas Smith, Bart., K.C.V.O., F.R.C.S. They had three sons and one daughter. The eldest son, Noel, was at hospital qualifying in 1914, but was killed in France in 1916 while serving in the R.A.M.C. ; the second son was killed in France in 1915, while the youngest son, after serving in France for two years, died of pneumonia in Germany after the Armistice. The daughter, Dorothy A. E. Garrod, has been a Fellow of Newnham College, Cambridge, and is well known for her work on prehistoric archaeology. Archibald Garrod died on 28 March, 1936.

F. G. Hopkins.