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MY PATH TO PHARMACOLOGY

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When I first came to Oxford I was occasionally surprised when I heard myself addressed as a pharmacologist, for when I began my research career it was in a very different field. Of course, nothing has really changed in the forty-five years since I began my work. What has probably changed is pharmacology: It has moved closer to my own interests.

Here I want to tell how it all started. First of all, I was most fortunate in my home background. I come from a family of doctors. When I began to demonstrate in the histology class at Cambridge, after my arrival there in 1934, I was surprised to find that the students immediately accepted me as an expert. Eventually I discovered that their text, Schafer's *Essentials of Histology* (1), contained a picture with the legend: "Section of Skin of Heel (Blaschko)." I cannot remember now if I ever revealed that this was a reference to Alfred Blaschko (1858–1922), my father who, as a young man almost fifty years earlier, had published a paper on the anatomy of the human skin from Waldeyer's laboratory in Berlin (2). A picture of my father has recently appeared in the *British Journal of Dermatology* (3) in connection with a paper on the "lines of Blaschko" (4).

By the time I was old enough to remember, my father's chief interests had shifted to problems of social medicine, especially the control of leprosy and of venereal diseases. He was a well-known figure in Berlin, especially in the working-class districts where he had practiced all his life and where he had been a pioneer in the field of social insurance; however, he always retained his interest in natural science and its modern developments, and we learned much from him. He was a keen naturalist and he knew the flora of his native countryside, the area around Berlin, intimately. We were very inquisitive, and he was always conscientious in finding answers to our innumerable questions.

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Many of his friends were well-known doctors and scientists. I never knew Paul Ehrlich, who gave him salvarsan for trials before it was released for general practice, but I met Albert Neisser (1855–1916), the discoverer of the gonococcus. Most important for me was Arnold Berliner (1862–1942), the founder of *Naturwissenschaften,* a magazine responsible for much of my early introduction to science. It was through Berliner that we met Max Born (1882–1970), the physicist, who in his recently published autobiography has lovingly described the influence my father exerted on him (5). Much later Max Born's son Gustav, now professor of pharmacology at King's College London, worked in my laboratory here at Oxford.

Through Max Born I have met many of the great physicists of our time; including Albert Einstein, James Franck, Enrico Fermi, and Fritz London.

My own introduction to laboratory work came early. During the First World War we were allowed to take our school-leaving examination early provided that we intended to do work considered essential to the war effort. I was not keen to go into a munitions factory; instead my father found a place for me in the spring of 1917 with Nathan Zuntz (1847–1920), a pupil of Pflüger, who was then director of the Institute of Animal Physiology at the Agricultural Academy in Berlin. Years later, at Cambridge, Joseph Barcroft told me that he had gained his first experience of high altitude physiology with Zuntz. That had been in 1910, on an expedition to the Pic of Tenerife (6). Later, in 1924, I accompanied Zuntz's principal co-worker, Adolph Loewy, on his studies at Davos, in the Engadin and on the Jungfraujoch (7).

As a laboratory assistant in 1917, I learned simple techniques like weighing and titrating. Zuntz's task was to report on the nutritional value of innumerable ersatz foodstuffs. I had to carry out many Kjeldahl determinations and Soxhlet extractions. I did not mind the repetitive nature of this part of my job, and I enjoyed the freedom of the laboratory atmosphere. There were occasional distractions. For instance, I had to collect the frogs for the physiology class which were easily caught in the flood meadows near the Berlin rivers. On one occasion, based on the suggestion that the seeds of shepherd's purse (*Capsella bursae-pastoris*) might serve as a useful source of oil, I was given the task of collecting seeds in the cobbled streets near our home, a back-breaking job that took several hot and sunny days in 1917. I then did the determinations in the laboratory and found that the seeds were indeed rich in fat; however, it was concluded that the task of collecting them was too onerous.

I enjoyed my medical studies which I started, at first part-time, in the autumn of 1917. During my time as a medical student I formed friendships that have continued throughout my life. The medical course at Berlin was old-fashioned, still based firmly on anatomy. For two winters we were kept busy dissecting the human body, an occupation that I found tedious at first but that began to interest me as I became more skillful. Unfortunately the lectures were boring. Waldeyer had just retired at the age of eighty—I still remember listening to him once in the University, where he gave a course on anatomy for artists, and I can see the old man drawing on the blackboard a picture of a neuron, the structure to which he had given that name many years before. The new professor was R. Fick, a son of the famous physiologist and a very poor lecturer. Our professor of histology was Oskar Hertwig, who had first described fertilization of a sea urchin's egg. He was old and ailing and often absent; his deputy at that time was Poll, to whom we owe the term *phaeochromocytoma*. I most enjoyed the lectures of the two botanists: Haberlandt was the plant physiologist, and Correns, the geneticist, one of the rediscoverers of Mendel's laws. I met Correns again as the director of the Dahlem Institute, which I joined in 1925.

I am afraid I was not a model student. I used to go to the lectures that interested me but would skip those that I found unprofitable. German students enjoyed privileges that we very much cherished. There was much freedom in the choice of lectures, a privilege I made much use of. For instance, I went to a course of popular lectures by Albert Einstein, and I took part in a seminar led by the psychologist Wertheimer, one of the founders of Gestalt theory. I became quite friendly with him. I had first met both Wertheimer and Einstein through Max Born.

German students also had freedom of movement. At the end of each semester we were free to move from one university to another, and so I divided my time between my native city, Berlin, and the university of Freiburg im Breisgau, where I spent four of my ten semesters.

In Freiburg I found some of the professors more interesting than in Berlin. In contrast to Berlin, Freiburg had a Department of Biochemistry, under F. Knoop, whose lectures and practical classes I found useful. I was most attracted by the physiologist, Johannes von Kries (1853–1928), a pupil of Ludwig and Helmholtz. At the end of my preclinical period, I did most of the experiments for my MD thesis in his laboratory; I must have been his last student.

I stayed on for a while in Freiburg after my preclinical period ended. I attended the pharmacology lectures given by W. Straub. He was a little uneven as a lecturer, but when he was in good form he was worth listening to, and I did profit from what I learned from him. He took much care over the demonstrations that accompanied his lectures. By far the most stimulating academic teacher that I have encountered was Ludwig Aschoff, the pathologist. Not only was he a very good morbid anatomist, but he had assimilated modern cytological and biochemical ideas, and was outstanding at conveying his own thoughts to the students.

Because I found the system of clinical instruction boring, my attendance at the clinics was rather poor. In German medical education, clinical work, like the preclinical course, was based on the university terms and on lectures, and lecture demonstrations. The professor demonstrated a case, had a proforma dialogue with a few selected students, and after a cursory examination of the patient lectured for the remainder of the hour on the subject of the disease he had just shown. There were some good academic lecturers among the professors, e.g. the ophthalmologist Axenfeld in Freiburg and one or two of the internists in Berlin, but on the whole they were in the minority, and altogether this method of teaching was very wasteful. Most of what we learned of clinical medicine was picked up during the long vacations between the semesters, when we hired ourselves out as assistants, chiefly in the municipal hospitals that were often understaffed and where there were greater opportunities for work involving responsibility. In Freiburg the clinical students, dissatisfied with the curriculum, appointed a committee for curriculum reform. I was briefly a member of this committee until my father's illness necessitated my return to Berlin. In March 1922, shortly before his death, my father had a visit from Abraham Flexner. I told Flexner of my interest in curriculum reform, and he told me of his own studies of medical education in Europe and the United States. I still own the two volumes, published under the auspices of the Carnegie Foundation, that he sent me after his return to the United States (8, 9).

At the end of my preclinical studies I was not sure whether I should continue my medical course or switch to biology. I am glad I followed my father's advice to remain in the course and get my medical qualification. Much of my later life has been spent teaching medical students, and my own work has gained by an awareness of its relevance to medicine.

After my final examinations in 1922, I had to spend a year in a hospital as an intern to gain my qualification. On the advice of Max Born, I decided to go to Göttingen, where I spent about 18 months in the Medical Clinic of the University Hospital, under Erich Meyer (1874–1928). Eric Meyer was an outstanding representative of the great German tradition of clinical medicine and was the best clinical teacher I ever had. His own outlook and his teaching were based upon his understanding of modern physiology, biochemistry, and pharmacology, and he was able to use this understanding as the basis for his clinical lectures and presentations, which were models of clarity. I owe him much, and he gave me the opportunity for responsible work, unusual in Germany at that time. So, before I left Göttingen I was put in charge of one of the medical wards for the periods when my immediate superior was on holiday. Also, Erich Meyer sent me to the small town of Alfeld an der Leine, halfway between Göttingen and Hannover, where a severe typhoid epidemic had broken out, in order to assist one of the two local practitioners there. The few weeks that I spent there in the winter of 1923–1924 were full of experiences that have inprinted themselves firmly in my memory, maybe because this was almost my last contact with the practice of medicine.

Göttingen at that time was one of the world's great centers of mathematics and physics, and through the Borns I met many of the people whose names are now familiar to all students of modern science.

A coincidence determined my subsequent history. One of Born's friends was Richard Courant (1888–1972), professor of mathematics with whom I became friendly (see 10). One day he asked me, "What are your plans for the future?" Haltingly I tried to describe to him that I would like to do research, and if possible in the borderline field between physiology and biochemistry. After a little thought he asked me, "Have you ever heard of Otto Meyerhof?" I told him I had read an article of his in *Naturwissenschaften*; that was all. He told me, "He might be the right man for you; I know him because we worked for a while in the same office during the war. If you would like me to, I could write to him."

Shortly afterwards a colleague introduced me to a friend of his who was on a visit to Wolfgang Heubner, our professor of pharmacology. This friend was Rolf Meier (1897–1966), on leave of absence from Heubner's institute in order to work at Kiel with Otto Meyerhof. I still remember Rolf Meier's tales of the laboratory at Kiel; he was convinced that this would be the right place for me.

Rolf Meier eventually became a director of CIBA at Basel, and he is remembered by many pharmacologists as the founder of the firm's modern pharmacological laboratory.

The coincidence of these two experiences was much in my mind when I left Göttingen. I first went to Switzerland, where I finished my work with Loewy on the Jungfraujoch, and I then went to a meeting at Innsbruck. I have recently described my first experience there of Otto Loewi (11). When I returned to Berlin I found the search for a place to work a discouraging experience. So I remembered Courant's promise and I asked him to get in touch with Meyerhof on my behalf. He promised to do so.

The outcome was that on January 1, 1925, I started work at Dahlem in Meyerhof's laboratory in Berlin. Meyerhof had received the Nobel Prize in 1923 jointly with A. V. Hill, and he had moved from R. Höber's institute at Kiel to the Kaiser Wilhelm Institute for Biology a few months before my arrival.

Much has been written in recent years about the Dahlem of the 1920s (12, 13). As for myself, I could not have arrived at a better place, and most of my remaining time in Germany was spent in Meyerhof's laboratory, first at Dahlem and later at Heidelberg. My active period of work with Meyerhof was twice interrupted by longish periods when I was laid up with pulmonary tuberculosis, with deleterious effects upon my output.

I have always considered my period of apprenticeship with Meyerhof as one of the great formative experiences of my life. The work was determined by Meyerhof's research interests, which centered around the energetics of muscle. There were usually only about four or five people in the department, most of these visitors from abroad. At first I found Meyerhof a little unapproachable; he spent most of his working day at the bench, and one did not like to interrupt him too often, but I remember a number of occasions when we discussed the general implications of the work I was doing. Once his interest was aroused and he began to "think aloud," it was possible to have a long and fruitful conversation that left one with a feeling of satisfaction and eager to carry on with the program of work.

Much of the stimulus of the laboratory came from my contemporaries. Meyerhof's laboratory has given me many good friends.

When I came to Dahlem, Karl Lohmann (1898–1978) was already in the laboratory. He is best remembered as the discoverer of ATP, but he was a great biochemist, who made many important discoveries, all of them in the stimulating environment of Meyerhof's laboratory. Lohmann was a modest man. I owe him much; in a quiet and unobtrusive way he helped me along and taught me chemical technique. And later there came David Nachmansohn, Ralph Gerard, Frank O. Schmitt, Severo Ochoa, Fritz Lipman, Karl Meyer, and many others. Under the same roof, with Otto Warburg, there was Hans Krebs whom I had already known when we were medical students at Freiburg in 1919. We had a good time together, and the continuous contact with bright and lively contemporaries is one of the gains from my period with Meyerhof.

Dahlem was an exciting place. The Institute of Biology had several other departments, in addition to Meyerhof's and Warburg's. The director was Correns and there was another geneticist, Rudolf Goldschmidt. Viktor Hamburger, later professor of zoology at Washington University, had the laboratory next to mine. Close by there were the Institutes of Chemistry, with Hahn and Meitner; Physics with Haber, Freundlich, and Polanyi; and Biochemistry with Neuberg. We had a seminar in our own institute; I particularly remember an exciting talk by Correns on non-Mendelian inheritance, and another one by Jollos on relative sexuality. Then there was the renowned seminar presided over by Haber which we attended regularly. This was a great occasion, and we admired Haber's grasp of a great variety of subjects and his ability to force the speakers to speak clearly and understandably. Most of the topics discussed I have forgotten. One of Haber's aims at the time was to extract gold from sea water, in the hope of paying the reparations that had been imposed on Germany at the end of the war. One occasion that I still remember is Freundlich's talk in which he described and named the phenomenon of *thixotropy.*

On the other hand, we had no contacts with the university departments; we were separated from these by a considerable distance.

Meyerhof, although older than Warburg, had begun research in Warburg's laboratory; that had been before the war. Meyerhof came late to science, having first studied philosophy and only later taking up medicine, I believe, in order to become a psychiatrist. When he met Warburg in Heidelberg, the latter persuaded him to join his laboratory. When I went to Meyerhof in 1925 he still very occasionally did some work on topics that were essentially in Warburg's sphere of interests. My paper must have been the very last in this line (14). I studied the reversibility of the cyanide inhibition of a number of so-called autoxidation reactions, reactions that, as Warburg had shown, were in reality metal-catalyzed. This modest piece of work later assumed great significance for me when I chose my own line of study.

Of course, all the work of the department was determined by Meyerhof. I remember that while we were still in Dahlem, I asked him if I could do some work on the effect of caffeine on muscle. He was not enthusiastic about this, for he thought this might become too much like pharmacology! In view of the work done on the effect of caffeine in recent years, it still seems to me that we might have discovered something worthwhile. Also, I might have had my introduction into pharmacology at an earlier stage.

In Dahlem Meyerhof could offer only one salaried position; this was held by Lohmann. When he accepted me in 1925 he warned me that he would never be able to pay me a salary. I told him I had not expected a paid job; at that time it was quite usual to have no pay during one's apprenticeship. After a few months he told me that he would be able to give me a modest grant. However, when in 1928 I was asked by E. von Skramlik, who was going to Jena as Professor of Physiology, whether I was interested in the University assistantship vacant in his Institute I thought I should accept his offer. I had met von Skramlik in Freiburg where he had been a lecturer in the Institute of Physiology.

The chair in Jena had become vacant through an unusual accident. It had been held for many years by Biedermann, who had done good work in electrophysiology as a young man. One of the assistants, Professor Noll, wanted to write a congratulatory article on the occasion of Biedermann's seventieth birthday, but there was some doubt about the exact date of his birth. The University authority gave a date in summer, but Biedermann seemed to remember that his mother had told him his birthday was in

January. Noll thereupon wrote to the Burgomaster of Bilin in Bohemia, Biedermann's birthplace, to find out. The Burgomaster wrote back saying he was pleased to learn that a son of his town had done well, and that Professor Biedermann was quite right: his birthday was in January. However, he also had to tell Professor Noll that the birthday that Biedermann was going to celebrate was not his seventieth but his seventy-second! The congratulatory article was never written, and Biedermann, when he was told, was delighted and retired immediately.

For me, the time at Jena might have been a complete loss had I not been given much of the responsibility for preparing the demonstrations for the Professor's lectures and also for the work in the practical classes. This experience I found useful when I came to Cambridge in 1934, where I had to demonstrate in the practical classes in physiology.

The gloomy prospects for my future at Jena were relieved when Meyerhof offered me a position in the new Kaiser Wilhelm Institute for Physiology at Heidelberg, where he moved in 1929. I gladly accepted, but I was first sent for one year to University College London, to learn methods in the laboratory of A. V. Hill, with whom Meyerhof had shared the Nobel Prize in 1923.

My first piece of good luck was to have been raised in the right family environment, the second was to have been accepted by Otto Meyerhof. The third stroke of luck was to work with A. V. Hill. I had been happy enough in Meyerhof's laboratory, but the spirit of freedom and friendship that I experienced during my year with A. V. Hill, 1929–1930, was exceptional. The close and friendly contact with Hill was very different from what I had experienced before. Every day, when he came to the lab, he used to come to my room, and we discussed everything that seemed to matter, from the leading article in the *Times* to the experiment to be done. One was not only entirely in the picture about the general implications of what one was doing but also aware of everything important that was happening in the world. My relationship with A. V. Hill was an experience that I still treasure and that was reinforced in the years to come. Also, I owe to Hill the first independent piece of research that I have done. During his visit to the International Physiological Congress in Boston I worked in Plymouth at the Marine Biological Laboratory on the mechanism of facilitation in the adductor muscle of the crustacean claw (15). I returned to Plymouth again in the summer of 1930. In 1929 I worked there with J. L. Kahn, a visitor to A. V.'s laboratory from Moscow, and in 1930 with McKeen Cattell, later Professor of Pharmacology at Cornell Medical School. The piece of work that Kahn and I had started in 1929 owes much to Cattell's great knowledge and skill.

I visited Meyerhof once during this period, a few days before Christmas 1929, just after he had moved to his still unfinished Institute in Heidelberg. He told me of a letter that he had from Denmark, from Einar Lundsgaard (1899–1968), who reported his observations on the alactacid contraction of the muscle poisoned with iodoacetic acid (16). The school led by Gustav Embden had maintained for some time that the lactic acid formation was not coincident with the muscle's contraction, but followed it. Meyerhof had always stoutly repudiated that claim, chiefly because the evidence brought forward was considered inadequate. But Meyerhof could not see any flaw in Lundsgaard's experiments, and I was impressed with his readiness to give up his long cherished ideas. He told me that Lundsgaard was expected to arrive in Heidelberg in the spring of 1930.

When I came to Heidelberg, in May 1930, Einar was already there. He told me that when the first experiment did not come off, Meyerhof again became doubtful, but that the second experiment worked! As a matter of fact, I was able to clear up that point after my return: The critical effective concentration of iodoacetate in winter frogs and in summer frogs differed by a factor of about ten.

Lundsgaard was the first of many visitors to Meyerhof's Heidelberg laboratory. He was one of the most impressive of all my contemporaries. We soon became friends, and his friendship lasted until his untimely death in 1968. Although his great discovery of 1929 is probably his best-known work, he made other contributions of great importance. For instance, I remember the paper he read to the International Physiological Congress at Rome, in 1932, in which he showed that phosphocreatine breakdown could also be made to lag behind muscular contraction, provided the experiments were carried out at low temperature. It was this discovery that pointed to ATP breakdown as the ultimate source of energy for contraction, although Lundsgaard was too careful to say so. In 1930 I was fortunate to have Lundsgaard as a traveling companion to Plymouth. There he studied the effect of iodoacetate on the crustacean muscle, where phosphoarginine replaces phosphocreatine (17).

In the much bigger laboratory at Heidelberg, Meyerhof was able to accommodate more visitors, and the list of those who worked with him there covers many names well known in biochemistry: Severo Ochoa, Alex von Muralt, Andreé Lwoff, and George Wald. The other assistant, Hans Laser, is still at work at Babraham (Cambridge) at the time of writing.

My own output at Heidelberg was again affected by illness. Little of the work that I did there was published; much of it appears in the form of footnotes in other people's papers. The advent of the Nazi regime in 1933 found me again in hospital, this time at Freiburg im Breisgau, where Hans

Krebs was one of my physicians, a particularly apt coincidence, since Freiburg was the place where we had first met in 1919. While convalescing I improved my skill in manometry in his laboratory.

While still in hospital, a letter from A. V. Hill arrived, inviting me to return to University College London. I did not hesitate, and so in May 1933 I was again installed at University College. I could afford to do this, as my English relatives were willing to offer me hospitality.

So here too was another bit of good luck. I had been very happy in my first year at University College and had made many friends in England. Thus my emigration was unlike that of many of my contemporaries: It felt more like a homecoming. Also, in the last year or two I felt that I had been with Meyerhof long enough, and I was ready for the day when I could start finding my own field of research.

That day, however, was yet to come. I was still convalescing, and most of that year in London I was busy assisting A. V. Hill with his work for the Academic Assistance Council (now the Society for the Protection of Science and Learning). This body was founded by Archbishop Temple, Sir William Beveridge, and A. V., as an organization to help refugee scholars. This organization still serves a much needed function in a world that is still a far from perfect place.

In 1933 it was necessary to interview new arrivals, mainly from Germany, to help them with their initial language difficulties and to help A. V., who interviewed many of them for the purpose of directing them to suitable places. This was work that at the time took precedence over my own research. Also, it taught me a new aspect of A. V.'s conception of the scientist's duty, an experience that has stayed with me throughout my life.

By 1934 I was fit to start doing some work of my own. A. V. Hill and Hans Krebs decided that I should leave London, and so I was glad to accept an invitation from Joseph Barcroft (1872–1947), then Professor of Physiology at Cambridge; at the same time I was given a grant from the Academic Assistance Council. I held this grant for two years, and although I did not get a permanent position until 1946, I managed from then on to maintain myself by teaching, both in the Physiological Laboratory and through giving tutorials.

Coming to Cambridge was another of those fortunate events that happened to me at the right moment. The German centers of learning were already under the threat of extinction, and what Dahlem and Göttingen had been in the 1920s, I found again at Cambridge in the 1930s. I did not have much contact with the physicists except that I had the use of Rutherford's glassblower, the latter also a German expatriate, but the Physiology Department with Barcroft, Adrian, Roughton, Matthews, Rushton, and Willmer was the Mecca for physiologists. Biochemistry under Hopkins had equally become the leading center in the world. I became particularly friendly with David Keilin (1887–1963), who at the Molteno Institute had built up a fine center of enzyme research. I had constant support from him, particularly when I was despondent about my future.

I began with some work on catalase and catalase inhibitors (18, 19). I had bought, with my last German money, a manometer bath and some Warburg manometers, and it was this precious possession that for quite a while dictated my choice of topics. Barcroft, who, jointly with J. S. Haldane (20), had been one of the initiators of manometry, was interested in what I was doing. I much enjoyed my close contacts with that interesting and lovable man. My laboratory adjoined his, and at the end of the day he often showed me the results of his experiments. One day he asked me, "How is adrenaline destroyed?" He had seen some differences in the time course of the pressor response to adrenaline in mother and fetus. I knew nothing about adrenaline, but I promised to look it up in the library. After all, adrenaline was a substance that had been around for a long time, and I felt certain that the answer to Barcroft's question could readily be looked up in the library. However, when I went to the Biochemistry Library, I soon discovered to my surprise that the fate of adrenaline was not known. The textbooks said adrenaline was a readily autoxidizable substance, and it was obvious that its actions were evanescent.

Autoxidation was what I had been concerned with in Dahlem in 1925, and I thought that my experience might possibly be useful in helping to answer Barcroft's question. Moreover, I was sharing a laboratory with Hans Schlossmann, until recently a lecturer in Pharmacology at the Medical Academy of Düsseldorf, who had just written a long article on methods of bioassay (21). So I proposed to Schlossmann that we might have a go at this problem.

My hunch that the Dahlem experience from 1925 might prove useful was soon proved to be right. The "autoxidation" of adrenaline was readily inhibited by cyanide. However, when one incubated the adrenaline with tissue homogenates, an inactivation of adrenaline remained that was resistant to cyanide. This cyanide-insensitive inactivation reaction was an oxidation reaction in which half a molecule of oxygen for each molecule of adrenaline was consumed. It could easily be shown that this inactivation had the characteristics of an enzymic reaction.

This is how the action of monoamine oxidase on adrenaline was discovered. We were fortunate: A few weeks after we started we were joined by Derek Richter, who was working in the Dunn School of Biochemistry, under Hopkins. It was Hans Krebs who introduced us to Derek, who had taken his PhD with O. Wieland at Munich, where he had become familiar with oxidation reactions.

We soon established that both noradrenaline and dopamine were oxidized similarly to adrenaline. Derek Richter knew of earlier work, carried out in Hopkins' laboratory by Miss Hare (later Mrs. Bernheim) on "tyramine oxidase" (22, 23). In a few weeks the identity of our enzyme with tyramine oxidase was established (24, 25). Actually, Mrs. Bernheim had tested adrenaline as a possible substrate, but without success. I suspect she too had run into difficulties over the autoxidation, like some other earlier authors.

We had been most fortunate in the timing of our work. The acceptance of the idea of humoral transmission of nervous impulses had prepared the way for biochemical studies in this field, and I had immediate reactions from many physiologists and pharmacologists; these included, as I have recently described (11), Otto Loewi, then still professor of pharmacology at Graz.

The work of many observers was required before the physiological role of monoamine oxidase in the biological inactivation of adrenaline could be fully established. This is not the story I wanted to tell here; my aim has been to describe how I was led to pharmacology.

However, my tale is not yet quite complete. I was still in Cambridge, in the physiological Laboratory. I was still without a job, and from 1937 onward I was working again on my own. I had, most of the time, no laboratory assistant, and I had to do all my own work, including the washing of glassware. At the beginning of each term I had to wait until I knew whether there would be enough teaching for me to earn my living. However, when the War began and the more active and enterprising people left for more exciting work, I even made myself quite useful. In addition to the work in the laboratory, I acted as supervisor in physiology for St. John's College, an occupation I enjoyed because it brought me into closer contact with younger people. When Joseph Barcroft came back from his war work in 1942 at the age of seventy, I even got a part-time research grant from the Agricultural Research Council.

In the autumn of 1943 I had an offer from J. H. Burn to join him in his department at Oxford. He had just returned from the United States, where he had worked as a reporter for the Medical Research Council. There he had witnessed the upsurge of biochemistry and the contributions that biochemical methods had made to pharmacology. These experiences are described in his letters to the Medical Research Council. When I moved to Oxford early in 1944 copies of these letters were precious reading matter for us, because we had been very much cut off from contacts with our colleagues overseas.

Burn had promised me an established position at Oxford and it was this offer that determined my move to Oxford. Also, I had had a very large teaching load at Cambridge during the war, and I was very tired. The job at Oxford was mainly a research appointment.

So, at the age of 44 I was for the first time housed in a Department of Pharmacology. The established post had to wait until 1946, since once again I was laid up and out of action for a period of nine months. That was the last time my work was interrupted by a spell of pulmonary tuberculosis. However, thanks to the help given by Ruth Duthie and Isabel Wajda the work in the laboratory did not entirely come to a standstill while I was out of action. From then onwards I never again worked entirely on my own.

The present story comes to an end with my transfer to Oxford. As far as my research work was concerned this made little difference at first. I had brought two major problems with me from Cambridge, and they were both essentially pharmacological: monoamine oxidase and adrenaline biosynthesis. Both these lines were continued. Also, shortly before I left Cambridge, I had discovered an enzyme, L-cysteic acid decarboxylase (26), and we continued to do some further work on this enzyme (27, 28). However, this line was not continued. The biological significance of taurine is a problem that remains unsolved.

Berlin, Freiburg, Göttingen, Dahlem, London, and Cambridge, these were the stages that brought me to Oxford and to pharmacology. I can trace my interest in pharmacological problems to a very early period, but it took a long time for me to get there. In the meantime I have been very fortunate in having had many close personal encounters with outstanding people, from an early age onward and right through my development. These experiences not only have helped to shape my own outlook but also have enabled me to hand on a tradition to those who are continuing where I left off.

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