Hans Popper (1903 – 1988) Life and Work

by
H. Thaler and Dame S. Sherlock

Publisher

FALK FOUNDATION e.V.

Leinenweberstr. 5
Postfach 6529
79041 Freiburg
Germany

www.falkfoundation.com

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Cover:
Hans Popper, 1986

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4rd edition 2007

Contents:

Preface 5

Hans Popper in Vienna
Heribert Thaler, Vienna 7

Hans Popper in the United States
Dame Sheila Sherlock, London 25

Hans Popper's Honours and Awards 51

Selected Publications of Hans Popper 52

Major International Falk Symposia on Liver Diseases
1967–1999 59

Preface

As a medical student, I started working at Hans Eppinger's Clinic at the University of Vienna in 1940, just two years after Hans Popper had left the Clinic and moved to America.

My first encounter with Hans Popper took place in Chicago in 1954. I had just completed a research fellowship at the Massachusetts General Hospital in Boston and was touring the East Coast.

The appalling events of the intervening years had done nothing to diminish Hans' sentimental affection for his native Vienna. There were probably several reasons why Hans and I developed a friendship from the very start. I too came from Vienna, had known Eppinger professionally (and visited him only two weeks before his suicide), and shared Popper's interest in liver and hepatic histology. Moreover, I was then running the ward and the histology laboratory where he had worked in Eppinger's department at the University.

After our first meeting, we met often at congresses and conferences, and later traveled together and visited each other socially. Whenever Hans Popper introduced me to a colleague, he would refer to me as "my nephew." I also formed a close friendship with Lina Popper, who retained all of her Viennese charm during their years in the United States.

When we had time to sit and talk, Hans loved to reminisce about his life in Vienna. After his eightieth year, he recorded his recollections on tape. In preparing this recollection, Lina provided me with a copy of the tapes, which proved invaluable when I came to describe his years in Vienna. I have amended a few inaccuracies in Hans' account. He was, after all, recalling events that occurred more than half a century before. Lina also supplied the photographs, except for the picture provided by Immuno AG (Vienna) of Hans Popper's birthplace in Praterstrasse in Vienna. I wish to thank Dr. Herbert Falk for giving me this opportunity to pay my own tribute to Hans Popper.

Heribert Thaler April 1997

Hans Popper in Vienna

Heribert Thaler

According to a family Bible that was lost in the travails of the twentieth century, Hans Popper's forebears lived in Bacharach-on-Rhine during the Middle Ages. In the vanguard of the First Crusade in the year 1096, these ancestors escaped the waves of killing and arson which swept the Rhineland by fleeing to Bohemia. There, the Popper family rose to a respected position in the community. Hans' grandfather, Marcus Popper, was the mayor of Kralowitz and proprietor of a general store (illustrations 1 and 6). His son Carl chose to study medicine. Hans' maternal grandfather, Jacob Grünbaum, converted to Catholicism in order to be appointed a judge in Teplitz, and his daughter Emilie was educated in a convent school. This situation did not deter Emilie Grünbaum from a Jewish ceremony when she married Dr. Carl Popper.

Illustration 1 The general store of Hans Popper's grandfather in Kralowitz

Dr. Carl and Emilie Popper moved to Vienna, where he opened a general practice at Praterstrasse 15 in the 2nd District (illustration 2). It was here that the couple's only child was born on November 24, 1903. The Vienna of Hans' early childhood had, as Max Friedländer once remarked, "the terminal radiance of a fairy-tale city." Fin-de-siècle Vienna lost nothing of its fascination as it teetered with open eyes towards the brink of its annihilation.

Around 1900, the population of Vienna included some 200,000 persons who were Jewish by religion and generally considered themselves to be Austrians and loyal subjects of the Emperor. In addition, at least 400,000 resi-

Illustration 2 Praterstrasse 15 in the 2nd District of Vienna, the house where Hans Popper was born in 1903 and raised. It was one of the few buildings on the street not destroyed during the wartime air raids

dents of the capital – but in all probability far more – had converted from Judaism to Christianity or were closely related to Jews by kinship or marriage. Vienna had always been a melting pot for the many ethnic groups living within the confines of the Habsburg Monarchy. In many cases, it was the elite of these people who migrated to its capital, then the world's seventh largest city. The heavily Jewish population contributed to the literary, artistic, and scientific accomplishments associated with Vienna. The cultural heyday of Vienna endured beyond the collapse of the Monarchy in 1918 and was not finally extinguished until it was ruthlessly crushed by the jackboots of the *Nazis*. Many of the ideas and intellectual assumptions of the modern-day world originated in the traditional cafés and salons of Vienna before World War II.

Hans received a sheltered upbringing from his governess and was thoroughly spoilt by his mother. His father loomed as an imposing figure of authority, unquestionably right in each and every way. Two childhood recollections remained indelibly stamped on Hans' memory. When he was five, the family stayed at the fashionable spa resort of Badgastein when Emperor Franz Joseph visited the town to officiate at the inauguration of the Tauern Railway. Hans was clad in *Lederhosen* and probably bore a close resemblance to his likeness in illustration 3. The little boy was permitted to shake His Imperial Highness' hand. For the rest of his life, Hans held unswerving reverence for Franz Joseph, whom he remembered as a distinguished elderly gentleman. At the outbreak of World War I in late July 1914, when Franz Joseph gave the order for general mobilisation, the 11-year-old Hans and his mother were spending their summer holidays in Reichenau-on-Rax. They were summoned back to Vienna. When they met at the railway station, Hans' father, a captain in the medical corps, looked sterner than ever in uniform. Hans was not to see his father again until after the War.

Under wartime austerity, the family's circumstances became increasingly difficult, but Hans began attending the *Akademische Gymnasium*, an elite school where most pupils were Jewish. Hans always ranked among the best in his class, but the school failed to provide him a real challenge. He was bored. At this stage, his principal interest was not the natural sciences – which figured only peripherally in the syllabus of this decidely humanistic school – but history.

Like most boys of his time, he went through a revolutionary phase. At fourteen, Hans embraced left-wing thinking and studied the writings of Marx, Engels, and Lasalle. Short in stature, untalented in sports, and riddled with feelings of inferiority, he found his opinions taken seriously for the first time (illustration 4). He attended clandestine meetings with his friends, took paramilitary training courses, and delivered speeches. In 1918, he marched alongside the workers and students in protest rallies. On one occasion, he became embroiled in street fighting. His military greatcoat, in which he took

Illustration 3 Hans Popper as a young boy

such pride, was torn, and his left-wing political career likewise lay in tatters. His revolutionary zeal came to an abrupt end. But when the young Emperor Karl stepped down and the Republic of German Austria was proclaimed *(Deutschösterreich)*, he felt a strong sense of personal achievement.

Hard times followed. Inflation eroded his father's livelihood, and the family found itself poor and hungry, like the majority of the Viennese population. For more than half a year, Hans' only warm meals were those provided in soup kitchens by the American Quakers. Like most of his fellow students, he contracted tuberculosis, but recovered without treatment.

He became engrossed in the natural sciences. What fascinated him most was Darwin, Haeckel, and the theory of evolution. Without friends or teachers with whom he could discuss such matters while completing the *Akademische Gymnasium,* he spent his afternoons at the University, where he hoped to learn more. At seventeen, while still in school, he was invited to deliver a

lecture at the University on the evolution of reptiles. Hans recalled this lecture as a major event in his life that gave him a sense of intellectual achievement and worth.

In the early 1920's, innumerable youth organisations came into being. Most of them had extreme right-wing leanings, and Hans Popper joined the *Wandervögel,* took to wearing a brown shirt, greeted his friends with the fascist salute (outstretched right arm), sat around campfires while participating in the general vilification of the Establishment. One of his comrades was Baldur von Schirach, later the head of the National Socialist Youth Movement and ultimately the *Reichsgauleiter* (regional administrator) of Vienna. The way was being paved for the ruinous events to come.

Having completed eight years at the *Akademische Gymnasium* with distinction, Hans Popper enrolled in the Medical School at the University of Vienna. His interests were again changing, and he now opted to follow in his father's footsteps. The young man was starting off in an entirely new direction, leaving far behind his adolescent political ideals and studies of reptile evolution. This time, his interest grew into a deep and life-long passion.

When Hans Popper matriculated, over 8,000 students were enrolled at the medical school in Vienna. Some courses – such as chemistry and anatomic dissection – were obligatory. Otherwise, students were free to attend those lectures that most interested them. The choice was vast, with literally hundreds of lecturers. The best students formed small cliques, and

Illustration 4 Hans Popper as grammar school student and "angry young man." With his parents, Carl and Emilie Popper

Hans found himself in the company of like-minded colleagues. He and his new friends not only studied together, but also went to the theatre and to lectures on general educational topics. But being tone-deaf, Hans actively avoided the concerts and opera.

In l925, the Austrian currency stabilised, and the inflation-prone crown gave way to the gold-backed *Schilling*. This change brought the Poppers' finances back onto a sounder footing. Hans' father, a civilian again, enjoyed the esteem of his patients and colleagues, and soon the family resumed the lifestyle of their years before the War.

The senior Popper felt that Hans should be exposed to more than one medical school, so Hans went off to Paris and attended the Ecole de Médecine at the Sorbonne for half a year. Not that his stay in the French capital did anything to enlarge Hans' knowledge of medicine. With a generous allowance at his disposal, he preferred the colourful bustling life in the cafés of Montmartre to the sterility of the medical school lecture hall. A year later, Hans spent seven months at Christ College in Cambridge, ostensibly to learn English. He developed a marked dislike for the spartan life at college, English mutton, and kidney pie. But he did not waste time at Cambridge. Apart from acquiring the rudiments of English, he made the acquaintance of the English way of life and gained his first glimpse of a far-sighted, global way of thinking. Between journeys to Paris and Cambridge, Hans passed his examinations in Vienna, nearly all with distinction.

The anatomy examination, one of the most difficult in the entire preclinical course, was to take on a special significance in Hans' studies. The examiner was none other than Julius Tandler, the anatomist and distinguished social reformer who gave Vienna the most progressive social welfare system in the world. After the examination, Tandler offered him a post as an instructor *(Demonstrator)*. This position, itself a great distinction, would establish him as one of the elite students; the post of *Demonstrator* was the first rung on the ladder of academic success. When he told his father of Tandler's proposal, Hans was flabbergasted at his father's response. Anatomy, the senior Popper assured his son, might be useful in terms of a career, but in terms of medical knowledge, biochemistry was infinitely more important. This, his father insisted, was where the future of medicine lay. Although Hans considered this advice to be absurd, he bowed to his father's suggestion and what might conceivably be a better insight. He reluctantly declined Tandler's offer.

The Physiology Institute at the University of Vienna contained a Department of Physiological Chemistry (now called biochemistry) which was headed by Otto von Fürth. Hans had no difficulty being accepted into the program. He had all the qualities an aspiring young scientist needed: great diligence, a phenomenal memory, and a remarkable gift for synthesizing facts. He could assemble diverse scraps of information and fashion them into a cohesive concept.

Abeles, a former classmate at the *Akademische Gymnasium,* was one of Hans' fellow students in the Biochemistry Department. In collaboration with him, Hans published his first scholarly article, *"Observations on the distribution of iodine in waste products of the thyroid gland"* in *Biochemische Zeitschrift* in 1925. Hans was then permitted to choose his next research topic on his own.

Insulin had been discovered a few years earlier, and Popper decided to investigate the formation of sugar by yeast under the influence of adrenaline (*"On the effect of adrenaline and related substances on the self-fermentation of yeast,"* l925). He demonstrated that adrenaline did not change as a result of this reaction and inferred that it must have the properties of a hormone. The paper attracted considerable attention, earning Hans the esteem of the faculty at the Institute.

In typical Viennese fashion, the idea for another research project was born at a wine tavern in Grinzing. Hans was sitting and drinking with Warkany, the highly gifted Hungarian, when the wine inspired them to wonder whether tubercle bacteria can form cyclic amino acids. The next morning, their alcohol fumes had cleared, and the two embarked on the project with a vengeance. By adding aspartic acid to the nutrient broth, they did indeed detect tyrosine and tryptophan. Within a single week, their manuscript was finished and ready for publication.

In collaboration with Zacharias Dische, the outstanding chemist, Popper conducted several incisive studies. They introduced a new non-reductive colorimetric method for identifying carbohydrates. This method was to prove enormously important (*"On a new method of microidentification of carbohydrates in organs and body fluids,"* l926) and paved the way for identifying non-reducible sugars. Popper's achievements at this time were all the more remarkable, considering that he was still a medical student and had two more years to go before getting his doctorate.

Hans Eppinger had become the First Assistant at the University First Medical Clinic, which was headed by the world-famous cardiologist Karel Frederik Wenckebach. As First Assistant, Eppinger ranked just below Wenckebach in the Clinic, and was extremely influential. Eppinger asked von Fürth whether the remarkable medical student named Popper could work for him in the laboratory and von Fürth agreed to it. Eppinger made room for Popper, much to the disgruntlement of the doctors working there. Eppinger wanted Popper to work with him on the identification of total carbohydrates and placed all patients in the Clinic at his disposal, establishing Popper as a "child prodigy." But this good fortune was to be short-lived. Eppinger accepted an appointment as Head of the Clinic in *Freiburg im Breisgau*. On the day Eppinger left, Popper – resented by his "colleagues" as an intruder – was thrown out of the laboratory.

There was, of course, no reason why Popper could not continue to study glycogen metabolism and use livers from corpses. He applied for a post

as Junior Assistant at the University Institute of Pathology, headed by Rudolf Maresch. Although Jews were not particularly welcome at the Institute, Popper was accepted. He set about learning pathological anatomy with the same ferocious dedication with which he studied biochemistry. By the end of the summer term of l927, his tenth semester at the University, he took the examination in pathological anatomy, the most difficult required exam in medical school. He passed it with such distinction that Maresch, noted for his reluctance to even converse with his students, offered him one of the few salaried posts at the Institute of Pathology. At the end of the summer holidays, Popper contacted Carmen Coronini Countess Cronberg, the First Assistant at the Institute, who informed him of the requirement that the post be filled by the end of the year. If Popper wanted the post, he would have to pass his remaining eleven clinical examinations within three months. Realizing that he had nothing to lose, Popper made up his mind to attempt the impossible. He would have succeeded had the last examiner, the ophthalmologist, not fallen ill just before the appointed examination date. The authorities at the University turned a blind eye and allowed Popper to take the examination in January. He received his degree as Doctor of Medicine on February 3, l928 and was appointed Assistant Physician at the Institute of Pathology under Maresch (illustration 5).

Illustration 5 The Faculty of the Institute of Pathology at the University of Vienna in 1931, including Hans Popper (second row, seated, second from left), Rudolf Maresch (fourth from left), and Carmen Coronini (fifth from left)

Maresch developed a special liking for Popper and took to calling him by the affectionate diminutive, *"Pöpperchen"*. He installed a chemical laboratory on the premises of the Institute to allow Hans to carry out a series of valuable research projects. Popper also established contacts with the Institute of Pharmacology, where Ernst Peter Pick was working, and began to conduct the histological examinations at the Pharmacology Institute. In pursuing pathology and pharmacology, he was again embarking in a new direction.

In the summer of 1928, Popper spent three months working in Eppinger's laboratory in Freiburg and, the following year, worked for one month at the Charité in Berlin in the Institute headed by Robert R. Rössle, the foremost liver pathologist in the German-speaking world. But Hans was not as interested in pathologic anatomy as in physiological chemistry. The man in charge of physiological chemistry at the Charité was none other than Leonor M. Michaelis, later to give his name to the Michaelis-Menten Equation and the Michaelis-Menten Constant. Hans took this opportunity to study colloid chemistry at Michaelis' laboratory.

The celebrated pathologist Ludwig Aschoff was then head of the Institute of Pathology in Freiburg. Rudolf Schönheimer, later renowned for his use of radioisotopes in biochemical research and for his work on cholesterol metabolism, supervised the prestigious biochemical laboratory until he accepted an appointment at Columbia University in New York in 1932. Aschoff nominated the 29-year-old Popper to be Schönheimer's successor to run the biochemistry laboratory, presumably because Popper was the only pathologist in the German-speaking world who possessed a knowledge of biochemistry. Aschoff's offer was a vindication of Carl Popper's prophetic advice. To evaluate the proposal, Hans revisited Freiburg in 1933. The town had undergone a sinister change since his first visit in 1928 – the streets were now filled with uniformed SA patrols. Horrified and dismayed, Hans returned to Vienna and politely declined Aschoff's offer.

Hans traveled a great deal during those years and learned some important lessons. He came to believe that he – as a Jew – would find it exceedingly difficult, if not impossible, to secure an academic appointment in pathological anatomy in the German-speaking world.

Popper toyed with the idea of switching to a clinical field. The Head of the Otolaryngology Clinic at the University of Vienna was Herschel von Neumann, a friend of Popper's father and a legend in his own time. Neumann declared himself willing to take the young man on, provided that he studied surgery first. The upshot of Popper's new course of study was one of the first papers to examine liver damage resulting from the administration of chloroform as an anesthetic (*"On latent icterus after anaesthetics,"* 1932). However, Popper proved so clumsy with his hands that he decided to return to pathological anatomy, but retained thoughts of entering a different clinical specialty. Erich U. Urbach and Moritz O. Oppenheim, the celebrated dermatologists,

attempted to recruit Popper, but in vain. Years later in Chicago, it was Oppenheim's daughter, Ridi, who introduced Hans and his future wife, Lina.

In the end, political developments in Germany solved the career dilemma for him. Ever since Wenckebach had resigned in order to devote his time to research and his large private practice, the post of Head of the First Medical Clinic had been vacant. Eppinger was the logical candidate, and his name topped the list of possible appointees. Eppinger was probably the most distinguished internist of his day. But during his years as Assistant in Vienna, he had made too many implacable enemies amongst the Faculty. They now opposed his nomination, arguing that he was amoral and unscrupulous. The arguments for and against him left the Faculty in an impasse. The position remained vacant. Professor Hans Elias, a specialist in metabolism and another friend of Popper's father, headed the Clinic in an interim capacity.

(Eppinger came from a family of Prague Jews who had enjoyed special privileges. The so-called "privileged families" were subject to the direct jurisprudence of the Emperor only and could claim a number of other rights.) Eppinger had moved to Cologne in the meantime, but was still hoping to return to Vienna. Hitler's rise to power in Germany on January 30, l933 changed the situation: As Eppinger was about to enter the clinic building in Cologne on April l, l933, his way was barred by doctors and students in SA uniforms. Eppinger realized that it could only be a matter of days before he was officially dismissed. Although Austria was still a sovereign state, the University of Vienna would not appoint a professor who – for whatever reason – had been declared *persona non grata* in the German *Reich*. In desperation, Eppinger cabled the Dean of the Medical School at the University of Vienna, who was then Ernst Peter Pick, to tell him that now was the last possible chance to appoint him. This time, solidarity carried the day over animosity. Pick went straight to Education Minister Kurt von Schuschnigg, who subsequently succeeded Dollfuss as Chancellor of Austria. Eppinger's appointment was announced the next day.

As soon as Eppinger assumed his new post in Vienna, he set about reorganising the Clinic. He asked Maresch, who was still the Head of the Institute of Pathology where Popper was working, to let the young physician come to work with him. Maresch was reluctant to let him go but in the end agreed, realising that he could never offer Popper a career of the kind Eppinger was promising him.

So Popper transferred to the First Medical Clinic to become an Assistant Physician, one of the few available salaried positions. There were hundreds of doctors working at the Clinic, and competition was fierce. Each fought to make a good impression on the Head of the Clinic and to climb to the next rung on the career ladder. This was a tough year for Popper. He started off knowing nothing about clinical medicine; and further, as Eppinger's protégé, Popper was bound to be unpopular. Many of the established doctors at the

Clinic had no compunction about showing their contempt for him. His immediate superiors seized every opportunity to humiliate him, even in the presence of patients. In addition, because of his extra research responsibilities, Popper had to work more and harder than any of his colleagues. Besides the day-to-day hospital chores – in those days, the doctors carried out the haematological tests and urine analyses – he had to keep up with the inundation of laboratory experiments that Eppinger kept proposing as well as writing research papers and studying internal medicine. However, Popper had a decisive advantage over his colleagues: Except for Eppinger himself, he was the only doctor in the First Medical Clinic with a knowledge of histology.

Eppinger worked at least as hard as anybody in the Clinic. Eppinger worked along with Popper on experiments, and Popper later felt that Eppinger was the best experimental surgeon he ever had met. On occasion, Eppinger would help Popper with his experiments, sometimes even washing glassware for him – partly to save Popper time, partly because of his special love for cleanliness.

Again and again, Eppinger would tell Popper that the key to scientific success was unimpeachable accuracy of the collected data and that cross-checking results and repeating tests were essential. Eppinger insisted that experimental possibilities must be explored from every vantage point; only then would the scientist be free to interpret the findings. Provided that an experimental approach had been shown to be feasible and worth exploring, Eppinger refused to accept ethical concerns as limitations on scientific exploration. For Eppinger, despite his established reputation for amoral behavior, it was an unpardonable sin to tamper with data or nudge them in a desired direction. Many of his conclusions proved correct and some were wrong, and Popper put emphasis on his positive contributions. He saw Eppinger's scientific ideas as unfailingly productive and was continually astounded by his remarkable gift for visionary scientific inferences.

Not that Popper was blind to the less reputable sides of Eppinger's character. Eppinger had scant respect for conventions which form the basis of human life and social coexistence. It was often said that Eppinger was endowed with not a single scruple. He pilfered case histories of patients who interested him, even from other clinics. When he came to watch an operation in one of the Surgical Clinics, an extra nurse was assigned to make sure that he did not walk off with any of the surgical instruments. And Eppinger was the only professor in Vienna who was banned from using the University Library; the mystery of who was responsible for cutting pages out of bound journals and books was finally resolved when Eppinger was caught red-handed.

Another episode vividly illustrates Eppinger's effrontery and ethical standards. Wenckebach took an avid interest in beriberi and had studied it first-hand during a stay in Indonesia. A beriberi epidemic had broken out

there after polished rice was distributed to the local population. Once there, Wenckebach had several corpses from Java preserved in formalin and shipped back to Vienna. He examined them in a specially equipped room at the Institute of Pathology, and Popper frequently visited with Wenckebach inside this room. While Eppinger and Popper were conducting an experiment to induce gallbladder edema in dogs, Popper happened to mention that Wenckebach's beriberi corpses also had gall bladder edema. Intrigued by this news, Eppinger said: "Come on, let's go and pay Wenckebach a visit." The great cardiologist gave Popper a warm welcome but virtually ignored Eppinger, whom he loathed. Eppinger whispered in Popper's ear: "Keep talking to him." While Wenckebach was proudly showing Popper his results under a microscope, Eppinger lurked in the background and then disappeared. Returning after a while, he said that he had to go back to his Clinic. Popper was surprised that Eppinger had not even mentioned the gallbladders. When they got back to the Clinic, to Popper's mortification, Eppinger pulled gallbladders out of his trouser pockets. He had simply removed them from the corpses with his notorious penknife. A short while later, Eppinger published a paper on the incidence of gallbladder edema in beriberi patients, thanking an obscure Javanese professor for placing the organs at his disposal.

Eppinger perpetrated countless offenses of this kind and had thereby achieved a high degree of notoriety in Viennese medical circles. But so outstanding were his achievements that people were willing to shrug off their outrage.

Hans Popper upheld Eppinger's scientific tenets while remaining shocked by his amorality. Yet he maintained a lifelong gratitude to his mentor. Popper was well aware that he owed his ultimate synthesis of pathology, biochemistry, experimental pharmacology, and internal medicine to Eppinger.

Popper learned virtually all of the major experimental methods that were current at the time. When a new technique was developed, he went to the relevant Institute to study it. This was how he made the acquaintance of Keller, a newspaper publisher by profession, who had taught himself electrochemistry and electrobiochemistry, and was doing pioneering work in these fields.

As a newcomer to clinical medicine, Popper had spent less than eighteen months performing ward duties under the supervision of an Assistant when Eppinger summoned him and Hans Kaunitz (another Jewish doctor who numbered amongst his favourites) to inform them that he planned to open his own ward and that the two young men would run it under his supervision. Each would be in charge of treating about twenty patients.

Popper was reaching the heights of success in clinical medicine in Vienna, attaining a level of professional seniority that few achieved and then only after many more years of experience. Gratified though he was, his happiness was clouded by tormenting self-doubt. He would soon have nobody to turn to for

advice. Moreover, he would be supervising thirty to fifty doctors from Austria and abroad. They would attend his morning rounds, and he would have to be on his guard all the time. He found the burden of this responsibility almost unbearable. Besides his rotating duties on the day-and-night shift, during which he had the final say in decisions relating to all patients in the Clinic, he had to act as the Medical Consultant to the Surgical, Gynaecological, and Psychiatric Clinics, assess the patients' operability, and take charge when medical complications arose. Understandably enough, Popper's scientific work was no longer the only reason for his lack of sleep. But within a year, even Popper's detractors conceded that he had established himself as a good clinician.

During this period, a farcical episode occurred. Its story has long been retold and is a legend in the Clinic. A young man was running a constant high temperature, and Popper was mystified about the cause. Eppinger was in the habit of visiting the ward at set times. Popper, fearful of making a fool of himself in front of his superior, used to push the young man's bed out of the ward and conceal it in the toilet area before Eppinger arrived. On one occasion, Eppinger appeared earlier than usual and caught his Assistant moving the young man's bed. Striding past Popper, he glanced at the patient and inquired: "Where are you off to with that case of typhoid?"

Eppinger had generated considerable momentum in many fields of internal medicine, but he now became increasingly interested in the liver. The condition then known as "serous inflammation" of the liver developed into something of an obsession with him. The original idea came to him during World War I, when he conducted postmortem examinations of three soldiers who had contracted jaundice but in the end died of tetanus. Examining the liver sections under a microscope, Eppinger observed quite correctly that the sinusoidal lining cells started to detach themselves from the hepatic cell plates, causing the Disse cavity to open wide and fill with serous liquid fluid. Eppinger inferred that this change obstructed the exchange of substances between the blood and the hepatic cells, thereby damaging the cells themselves and ultimately causing jaundice. He carried out animal experiments which produced similar changes by means of various poisons, and he occasionally observed the same changes in liver biopsies conducted either agonally or immediately postmortem. He regarded both observations as confirmation of his theory that nutritional or bacterial poisons or drugs were responsible for this non-surgical form of jaundice.

As a knowledgeable histologist, Popper provided Eppinger with invaluable assistance in this research. Their next objective was to visually locate the protein which appeared to be present in the liquid filling the Disse cavity. Here, they were helped by Max Haitinger, a retired Colonel who conducted pioneering work on fluorescence microscopy in collaboration with Herfried Hamperl. Eppinger provided Haitinger with a laboratory at the Clinic and Popper as his assistant.

The upshot of these studies was the classic book, *Die seröse Entzündung* (Serous Inflammation), which Eppinger wrote jointly with Popper and Kaunitz. Published by Springer-Verlag in Vienna in 1935, it caused a considerable stir in medical circles. Ever since Rudolf Virchow, doctors had used the terms "icterus catarrhalis" or "catarrhal jaundice" (to describe what is now recognized as acute viral hepatitis), and they still believed that a sinister clot of mucus on the Papilla vateri was the cause of the illness. Locating the true cause of this form of jaundice as not in the common bile duct but in the liver itself was an important step in the right direction. It apparently did not occur to Eppinger or his two Assistants that the distension of the Disse cavity which they observed might be, in actual fact, an agonal or postmortem phenomenon. Even this mistake in Eppinger's thinking proved extremely fruitful, prompting closer study of the metabolic functions of biological membranes. Without this groundwork, the modern understanding of membrane physiology and development of the artificial kidney would probably have been much delayed.

When appointed as Head of the Vienna Clinic, Eppinger had given the Dean of the University an assurance – verbally and purportedly also in writing – that he would not promote a Jew to the post of Assistant. By this time, though, Popper was performing all the duties of an Assistant. Eppinger decided to reward Popper for his hard work by making him a *de facto* Assistant, but he did not want to violate his assurance to the Dean. He resolved this dilemma by inventing the post of an "unsalaried Assistant," who would be assigned all the rights and duties of a regular Assistant. By way of recompense, Eppinger permitted Popper to hold medical education courses for American physicians. In those days, the Medical School at the University of Vienna was renowned throughout the world, and any aspiring young doctor would find it easier to climb the domestic career ladder if armed with a certificate from Vienna. Popper offered courses in physiology, pathology, and clinical aspects of the liver and kidneys, receiving between five and ten dollars per hour for each student.

The Clinic did not have a kidney specialist, and Eppinger hit upon the idea of encouraging Popper to study that organ. Indefatigable as always, Popper formed a kidney team by recruiting Emil Mandel, Helene Mayer, and (on a sporadic basis) the neurologist Felix Fuchs. They soon began producing remarkable work. After publishing their paper on the demonstration of creatinine in the blood, they pioneered the important and still commonly used technique of creatinine clearance (*"On the diagnostic significance of plasma creatinine detection,"* 1937; *"Filtration and resorption in renal pathology,"* 1937). Their 1938 publication, *"The flow of blood and fluids in the kidney (On the clinical importance of the renal interstice),"* anticipated the later counter-flow theory that is now the basis of our understanding of countercurrent mechanisms in kidneys.

Meanwhile Popper's courses were a huge success, though he lectured in execrable English (and was blithely ignorant of the fact). His monthly income soon exceeded U$ 500 – a princely sum in those days. His main problem was less in earning money than spending it, especially since he worked right through most weekends. One way or another, though, he managed to get rid of it. On one occasion, he flew to London to visit Sir Thomas Lewis at University College. Now and then, he went off on joyrides to Venice (where else?) in the company of young ladies.

Neither Popper nor Eppinger paid much attention to the storm clouds brewing in world politics. In autumn of 1937, Schiller, the gynaecological pathologist who had emigrated from Austria to the United States to succeed Jaffe at the Cook County Hospital in Chicago, invited Popper to Chicago to take a research fellowship in pathology, at a monthly salary of U$ 250. Popper asked for advice from Eppinger, who in turn asked Risak, his First Assistant. Risak was an ardent National Socialist and held a senior position in the then-illegal Nazi Party, but he liked Popper. Risak cautioned that the National Socialists would seize power in Austria by July of the following year and advised that Popper go to America. When Risak had left the room, Eppinger commented to Popper: "That man is crazy!" In late 1937, Popper declined the invitation to the United States.

Popper retained his ties with Maresch, his old chief at the Institute of Pathology, and was frequently invited to his home. When Maresch fell ill – he was suffering from bronchial carcinoma aggravated by pulmonary abscess – Popper attended to his needs. Popper spent every night at Maresch's house until he died. Maresch's closest friend was Leopold Arzt, the dermatologist who was the Acting Dean of the University and a known anti-Semite. On his death bed, Maresch asked Arzt to confer the academic post of *Dozentur* on Popper. Arzt could not turn down his dying friend's last wish, much as he was loathe to do so – and not only because Popper was Jewish. According to an unwritten law, a candidate for a *Dozentur* had to have worked at a Clinic for a minimum of six years and to be at least 45 years old. Popper had spent less than five years working at Eppinger's Clinic and was still under 35 years old.

The day after Maresch died, Arzt called Popper to his office and told him: "I don't like Jews, but you're going to be Austria's last Jewish *Dozent.*" Arzt was wrong. Only two days later, Hitler summoned Austrian Chancellor von Schuschnigg to a meeting at Obersalzberg near Berchtesgaden. By threatening to invade Austria, the *Führer* forced von Schuschnigg to comply with his demand that the Austrian government include ministers sympathetic to the National Socialists. Von Schuschnigg's response was to schedule a national referendum for March 13, 1938 in an attempt to preserve Austria's independence. The outcome would most likely have been against annexation to Germany – even some declared Nazis had doubts about the wisdom of the

Anschluss. To ward off this likely result, Hitler ordered his forces to cross the Austrian border on March 12, 1938.

It was a Saturday. Popper, on duty at the Clinic, was oblivious to the epoch-making events around him. That evening, one of the Clinic doctors, clad in an SS uniform, opened the door to Popper's office, told him he had been dismissed, slammed the door again, and locked it. Looking out the window, Popper saw that they had stolen a histological stain (eosin) from his laboratory and had used it to turn a red-white-and-red Austrian flag into a swastika flag. It was hoisted from the roof of the First Medical Clinic.

The next morning, the Nazis released Popper from his locked office, but only so that he would be present when his patients were handed over to his successor. He was then summoned to Eppinger's office. With his incorrigible naiveté, Eppinger still believed that the Nazis were harmless hooligans. He told Popper that he had witnessed similar scenes in Cologne and that their bark was worse than their bite. Popper should go home, Eppinger said, take Sunday off, and turn up at the Clinic on Monday morning as usual. Popper was never to see Eppinger again.

As soon as he got home from talking with Eppinger, Popper – who did not share Eppinger's optimism – sent a telegram to Chicago saying that he wanted to accept the invitation after all. There was no way he could continue to work in Vienna. His life had been turned upside down. Ruth Pfaundler, his technical assistant at the Histology Laboratory and daughter of a distinguished Austrian, brought Popper a signed photograph of Eppinger, along with his written attestation that the old Haitinger fluorescence microscope was Popper's personal property and could be taken out of the country. (Popper himself had paid for a new fluorescence microscope, constructed in Vienna, and donated it to the Clinic.) Dietrich Roller, an ardent Nationalist Socialist but sympathetic to Popper, rang to tell Popper that he could collect his private belongings and his scientific papers from the Clinic. Popper objected that he was prohibited from entering the Clinic and didn't dare set foot inside it. Roller promised to guarantee him safe passage, and Popper was not obstructed in any way. Though many friends remained loyal to him, some crossed the street when they saw him coming. It was time to bid his native city farewell.

The telegram arrived promptly from Chicago, with the confirmation of his appointment – albeit for a salary which had dwindled from U$ 250 to U$ 150. Hans was one of the very few to be granted entry to the United States on a "non-quota" visa. There were then no restrictions on the personal effects which could be taken out of the country. The Austrian policemen who monitored Popper's departure advised him to take as much as possible. Popper packed up his belongings, including his fluorescence microscope, thirty suits, paintings, his mother's porcelain collection, and some antique furniture that his parents gave him. All that now remained to be settled was his exit permit,

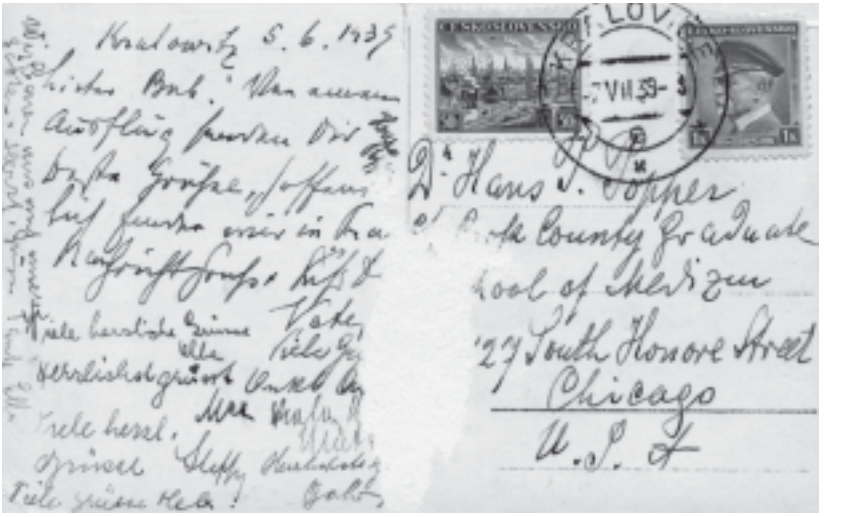
for which he paid the official fees. He booked a first-class berth from Rotterdam on the maiden voyage of the ship in the Holland America Line, the *SS New Amsterdam*.

The ship was scheduled to depart in a week's time. Popper hoped to spend his last few days in Vienna as enjoyably as possible. But the next morning at 4 a.m., his friend Risak from the Clinic rang him up and warned him that the Gestapo was planning to arrest him that day. Arrest meant concentration camp and certain death.

Popper had to get out fast. His parents immediately took him out to the airport, and luckily there was a flight via Munich and Frankfurt to Rotterdam. The aeroplane was packed with men in SS and SA uniforms. With great trepidation, Popper climbed on board, but nobody took the slightest notice of him. The customs inspection in Frankfurt, which he had dreaded, passed without incident, and the German customs officer even carried his hand baggage for him. The plane, now almost empty, took off and crossed the Dutch border. Popper was a free man. It took a while for him to get used to the feeling.

During the Atlantic crossing, virtually everyone on the boat became seasick on the first day, but not Popper. Instead, he ate well in first class. The second day, he fell ill, though the weather was perfect. By the time he landed in America, Popper had all the symptoms of hepatitis. As it turned out, he had merely picked up a viral infection – a briefly lingering and last farewell from his now distant native city (illustrations 6 and 7).

Illustrations 6 Kralowitz, where Hans Popper's father was born.



and 7 The text on the postcard (above) reads, "Kralowitz, June 5, 1939. Dearest Boy, Cordial greetings from an outing. We hope to receive news of you in Prague. Greetings and a kiss, Your Father. Many kisses, Mother."
With the exception of Popper's parents, none of the other signatories of the postcard survived the Holocaust.

Hans Popper in the United States

Dame Sheila Sherlock

For the fifty years between 1938 and 1988, Dr. Popper played an active part in almost all of the original scientific developments in hepatology in the United States and worldwide. The range of his involvement is awe-inspiring and overwhelming. Numerous terms were coined by Dr. Popper, and his prominent influence in the formation of many basic scientific and clinical concepts remains apparent in the language of hepatologists today. Dr. Popper stimulated and was stimulated by countless hepatologists, young and old. Even into his last year, he remained productive and intellectually active, vigorously contributing to research, teaching, clinical consultation, and administration of medical science.

His career spans from the time when he first demonstrated the capacity of single cells to carry on metabolism to the current era of molecular pathology, physiology, pharmacology, and genetics. He is truly the Father of Hepatology.

On his way to Chicago in 1938, he visited Homer Smith, the famous nephrologist, in New York but did not receive the warm welcome that might be expected for a scientist who had made major contributions to this field. Homer Smith later apologized to Dr. Popper, but this incident may have contributed to Dr. Popper's decision to concentrate on liver research, building on his prior work in Vienna.

This was a good time to be investigating the liver. Liver function tests were still exceedingly difficult to conduct, the percutaneous liver biopsy had not been introduced, and hepatology as a discipline was nonexistent. There were no liver societies. In his lifetime, Popper was going to change all this.

In the suitcase he carried from Vienna, he brought Haitinger's old fluorescent microscope. During his early days in Chicago, Popper used this microscope to show the presence of vitamin A in tissues by green fluorescence. This vitamin A research was fruitful and, within two years, he had publications in the *Proceedings of the Society for Experimental Biology and Medicine.* He even lectured at The Mount Sinai Hospital in New York on the distribution of vitamin A in the body (*J. Mt. Sinai Hosp.* 1940; 7: 119). In 1944, Popper obtained a Ph. D. in Pathology and Physiology from the University of Illinois.

During this time, his chief collaborator was Fred Steigmann, a physician also trained in Europe. Together, they published papers on vitamin A, liver function tests *(JAMA 1943; 122:279)*, and jaundice *(Gastroenterology 1943; 1: 645)*.

Dr. Popper soon built the equivalent of a modern liver unit in Chicago at Cook County Hospital. He started "Liver Rounds," where clinical and laboratory findings were discussed with surgical and postmortem input.

These teaching sessions were a sensation, attracting not only collaborators and other physicians, but also many visitors who thronged from other institutions in Chicago and elsewhere. Even laypersons who enjoyed scientific puzzles and intellectual mysteries attended his clinico-pathological conferences. Young co-workers were drawn by his enthusiasm, and their names always appeared on their publications with him.

By age 40, Dr. Popper had acquired two advances professional degrees, made historic contributions in liver and kidney research, escaped the Nazi onslaught, and transplanted himself successfully to a new and receptive home.

Family

Hans' parents eventually joined him in Chicago. Incredibly, at the age of 77, Carl Popper completed an internship at the Michael Reese Hospital, passed the Illinois State Board examination, and started a successful practice in cardiology. Hans evidently inherited his seemingly boundless energy. Also from his father, Hans appears to have inherited his love of people, food, drink, and parties.

In 1942, Dr. Popper married Lina Billig, another Viennese expatriate (illustration 8). They spent their honeymoon in Atlantic City, where Hans presented an exhibit at the Annual Meeting of the American Medical Association. He received an honourable mention, and Lina was delighted. This was her first introduction to Hans' lifestyle. For the next 46 years, Lina was his constant support and companion at meetings, large and small, all over the world.

Marriage to Lina was the best thing that happened to Hans. As Paul Berk has written, "Lina is an exceptional woman who stood beside him for a lifetime. She encouraged him, served as intellectual stimulus, and with charm and grace protected him from enemies, friends and himself." She is a gracious hostess, and there was always fun and laughter at the Poppers' dinner table.

The Poppers had two sons. Frank, born in 1944, is Professor and former Chairman of the Department of Urban Studies at Rutgers University. Charlie, born in 1946, is a child psychiatrist at Harvard Medical School and founding editor of the *Journal of Child and Adolescent Psychopharmacology.*

Chicago and the Hektoen Institute for Medical Research

In 1943, Dr. Popper was appointed Director of the Pathology Department at the Cook County Hospital and Professor of Pathology in its Graduate School. He was determined that Cook County Hospital should become a research center, and persuaded the Hospital Board to found an institute for medical research. This laboratory facility was named after Dr. Ludwig

Illustration 8 Lina Popper

Hektoen, the father of pure medical science, who supported the project wholeheartedly.

At the outbreak of World War II, Popper applied for a commission in the United States Army. He was turned down because he was classified as an "enemy alien," but was told that he could re-apply once he received his citizenship. Dr. Popper directed his research during that period toward the war effort and made important contributions on the use of plasma substitutes in the treatment of shock *(Arch. Surg. 1945; 50: 34)*.

On December 31, 1943, Hans became an American citizen and immediately volunteered for the Armed Forces. He served as a pathologist in the Army between 1944 and 1946. His duties brought him into contact with many soldiers with hepatitis, and his lifelong interest in viral hepatitis began again. He enlarged his knowledge of general pathology and achieved the rank of Major. He became Chairman of the Committee of Medical Research reporting to the Surgeon General of the Army. Among his fellow members were George Gabuzda (of ascites fame), Robert Kark (of Guy's Hospital in

London and then Chicago), Fred Hofbauer (of Minneapolis), Charles Davidson (of the Thorndike Laboratory in Boston), Paul György (the great nutritionist) and C.G. Child (Professor of Surgery, who later graded cirrhosis).

On his return from Army service in 1946, Dr. Popper set about making the Hektoen Institute into an international center of excellence in liver disease. He devoted himself to all aspects, clinical, experimental and pathological. He used all available tools. Perhaps the most important was the liver biopsy, which had become generally available. Dr. Popper became wedded to his microscope and to the interpretation of liver biopsies. He once wrote that "the best research tool is a haematoxylin and eosin-stained slide connected to the brain." Later, he arranged for all liver biopsy specimens at Cook County Hospital to be processed for electron microscopy.

As an exercise in unbiased assessment, he reviewed liver biopsies in teaching conferences while blind to the clinical and laboratory findings. He could reconstruct a patient's history and examination solely from the appearance of the liver biopsy. He had an encyclopaedic knowledge of pathology. His diagnoses were brilliant. He was rarely wrong in his blind readings, and never wrong when he correlated his histological findings with clinical and laboratory data. He could link histological appearances with pathogenesis, an ability that was the basis of many of his fundamental contributions to liver research. Long into retirement, he continued to interpret biopsies and conduct slide seminars, and even retrained the laboratory staff at the National Institutes of Health in Bethesda to prepare slides according to his specifications.

Dr. Popper was particularly interested in the correlation of clinical, biochemical, and histological changes in patients with liver disease. While in Chicago, he published widely on the mechanisms of liver injury, particularly those related to ethionine and bromobenzene.

Fenton Schaffner joined Dr. Popper in 1948 at Chicago and followed him to New York in 1958 (illustration 9). Schaffner wrote that "The 40 year association with Hans was first as my teacher, then as co-worker, friend and father figure." Fenton and Hans traveled all over the world together. Fenton was Dr. Popper's adviser on English usage. An excellent physician, he provided the necessary clinical balance to the team. Dr. Popper published some of his best scientific papers with Fenton Schaffner as co-author.

Dr. Schaffner recalled that writing papers with Dr. Popper was like playing word games. These word games, involving the coining of new words or phrases (such as cholestasis) or finding new uses for old ones, have led to enduring changes in the language of hepatology.

During the post-war period in Chicago, Dr. Popper gained increasing stature as an international leader in medicine. As Director of Pathology at Cook County Hospital, he was able to examine an unusually large volume of pathological material. His clinico-pathological conferences and slide seminars

Illustration 9 With Fenton Schaffner, 1984

continued, his research thrived, the Hektoen Research Institute grew, and he founded The American Association for the Study of Liver Diseases.

Dr. Popper began to engage in extensive international travel. In 1956, his participation in the Fifth Congress of Gastroenterology in Havana led to an international definition of cirrhosis. The details had been worked out at a prior committee meeting, whose attendees were Hans Popper from Chicago, Leon Schiff from Cincinnati, Bernard Sepulveda from Mexico City, Sheila Sherlock from London and Mitchell Spellberg from Chicago. The definition of Havanna included involvement of all parts of the liver, nodular regeneration, fibrosis, and hepatocellular necrosis at some time. This definition has never been bettered.

The Mount Sinai Hospital in New York

In 1956, overtures were initiated to attract Dr. Popper to The Mount Sinai Hospital in New York City. After considerable persuasion from the highly distinguished physicians and the Board of Directors of Mount Sinai, and a great deal of personal and family soul-searching, he accepted the post of Director of Pathology. His challenge was to succeed the legendary Paul Klemperer (illustration 10) as Pathologist-in-Chief at the highly prestigious hospital, and to exchange his Professorship at Northwestern University for

Illustration 10 With Paul Klemperer

one at Columbia University. In 1957, he moved to The Mount Sinai Hospital and began an association that continued for three decades.

Dr. Popper rapidly settled into the New York scene and again attracted an outstanding staff of pathologists, residents, and research fellows from all over the world: Leonardo (Piccio) Bianchi of Switzerland, Nijole Brazenas of Lithunia, Whan Kook Chung of Korea, Helmut Denk of Austria, Stephen Geller of USA, Michael Gerber of Germany, Helmut Greim of Germany, Stephanos Hadziyannis of Greece, Charles Lieber of USA, Fiorenzo Paronetto of Italy, Victor Perez of Argentina, Peter Scheuer of England, Swan Thung of USA, among many others. At least twelve of these "co-workers", as he called them, have become the Chair of the Department of Pathology in their own universities. These co-workers, and others, have become leaders in their own countries and have established the Popper School of Hepatology.

The Mount Sinai Medical School

One of Dr. Popper's proudest achievements was the founding of the Mount Sinai School of Medicine (illustration 11). Although sentiments for developing a medical school had been expressed repeatedly over the years, several factors led to more intense consideration in the late 1950's after

Illustration 11 The Annenberg Building at The Mount Sinai Medical Center, newly constructed for the Medical School

Dr. Popper came to New York. At that time, various studies emphasized the need for more physicians in the United States. Also, after years of exclusion, and this was important, Jewish house staff were finally admitted to prestigious medical schools and hospitals. Consequently, The Mount Sinai Hospital, which formerly had uncontested first choice among gifted Jewish medical graduates, found itself losing some applicants and staff to academic careers in medical schools. This threatened to deprive Mount Sinai of some outstanding

young physicians, including many with the strongest scientific orientation. Also, the Trustees felt an obligation to promote both the research and education opportunities and contributions of the Hospital, and saw that creating a medical school at The Mount Sinai Hospital could reverse this trend.

Dr. Popper believed that the medical stature of The Mount Sinai Hospital would be greatly enhanced by the creation of a medical school. He was concerned about its competitive position in New York City, where the hospitals were the pillars of the prominent medical schools; for example, the College of Physicians and Surgeons at Columbia University was affiliated with the Presbyterian Hospital, Cornell Medical School was linked with The New York Hospital, and New York University School of Medicine had the University Hospital. Dr. Popper was pivotal in helping his colleagues see the new medical school as essential if The Mount Sinai Hospital was to maintain its rightful place in American medicine.

Dr. Popper was the driving force in establishing the medical school. Gustave L. Levy, the Chairman of the Board of Trustees, was a key mover and shaker who worked with Popper in advocating for the new medical school. They worked together, with a lot of perseverance, to overcome the many obstacles.

It was an unusual proposition and unique challenge to start a medical school based on a hospital rather than a university. Since the Flexner Report of 1910, universities were generally viewed as the only legitimate basis for the organization of a medical school. This prevailing dogma, and the fact that The Mount Sinai Hospital did not have a university connection, was one of the earliest and strongest obstacles. Dr. Popper described a meeting with officials at the American Association of Medical Colleges *(Popper, H.: Interview 1966; INT20, Archives of the Mount Sinai Medical Center)*.

We were told point blank that while they would consider Mount Sinai an excellent breeding place for a medical school, they would be afraid that violation of the basic principle in American medical education, recognition that a hospital could make a medical school, would throw back American medical education so much that they would rather sacrifice an excellent school than sacrifice the principle.

To deal with this challenge, Popper promoted the concept that the *integration* of patient care, research, and education should be the cornerstone of the new medical school. He defined a new mission for the hospital and outlined new possibilities for what a medical school could do (*Popper, H. (editor): Trends in New Medical Schools. Grune & Stratton, New York,* 1967). He believed that good science is the primary ingredient of good patient care. He envisaged a medical school with close integration between basic scientists and clinicians.

Dr. Popper articulated "The Mount Sinai Concept," perhaps the earliest formulation of the view that humanistic studies and social sciences can be integrated in an urban setting to create a medical teaching facility with an

emphasis on community care based on scientific research. He wrote of "the balancing of biological thinking in medicine with concern with the whole patient" *(Popper, H.: The Mount Sinai Concept. Clin. Res. 1965; 13 (4): 500)*. In "New Objectives in Medical Education," he emphasized three factors: "the introduction of quantitative biology into community medicine; [the] counteraction of the depersonalization of the organ-specialized physician by broadening the influence of social sciences and human studies; and community medicine which, by experimentation, strives in a setting of specialists to give good care to every person and every disease beginning in the presymptomatic stage" *(Popper, H.: New objectives in medical education. Ann. NY Acad. Sci. 1965; 128: 473–479)*.

Popper coined the term "community medicine," and Mount Sinai established the first-ever Department of Community Medicine. Later, Dr. Popper participated personally in the activities of this department. When Dr. Irving Selikoff, the famous environmentalist, invited Dr. Popper to become part of his Environmental Sciences Division in the Department of Community Medicine, Popper quickly became involved in studying the effects of Agent Orange on the liver.

The charter documents of the Medical School cite Popper as the founding Dean of the Medical School. He served as the Dean from 1962 until 1965 *(Popper, H.: Mt. Sinai: How a hospital builds a medical school. Science 1967; 158 (3801): 614–618)*, but he insisted that a younger individual lead the medical centre by the time that the first medical school class was graduating. With the successful recruitment of Dr. George James, a leader in the nascent field of community medicine, for the first Chair of the Department of Community Medicine, Dr. Popper stepped aside to allow the appointment of Dr. James to the positions of Dean and President (illustration 12). Popper became Dean for Academic Affairs and held that position until Dr. James' untimely death in 1972, when he assumed the roles of Acting Dean of the Medical School and Acting President of the Medical Center (illustration 13).

Dr. Popper was an extremely effective Dean. He maintained weekly contact with Gustave L. Levy, Chairman of the Board of Trustees, with whom he had a splendid rapport. He combined the work of Dean with his duties in the Department of Pathology and never let one intrude on the other. He was efficient, well-organised, pragmatic, and never showed himself under pressure. Popper was an authoritarian yet tactful negotiator.

In 1967, a formal affiliation was started with the City University of New York, and the then-largest federal grant for the creation of a medical school was awarded to Mount Sinai, and The Mount Sinai Medical School graduated its first class.

Over the subsequent decades, Mount Sinai has held its preeminent position in American medicine, and has been central in the establishment of the fields of community medicine and environmental medicine.

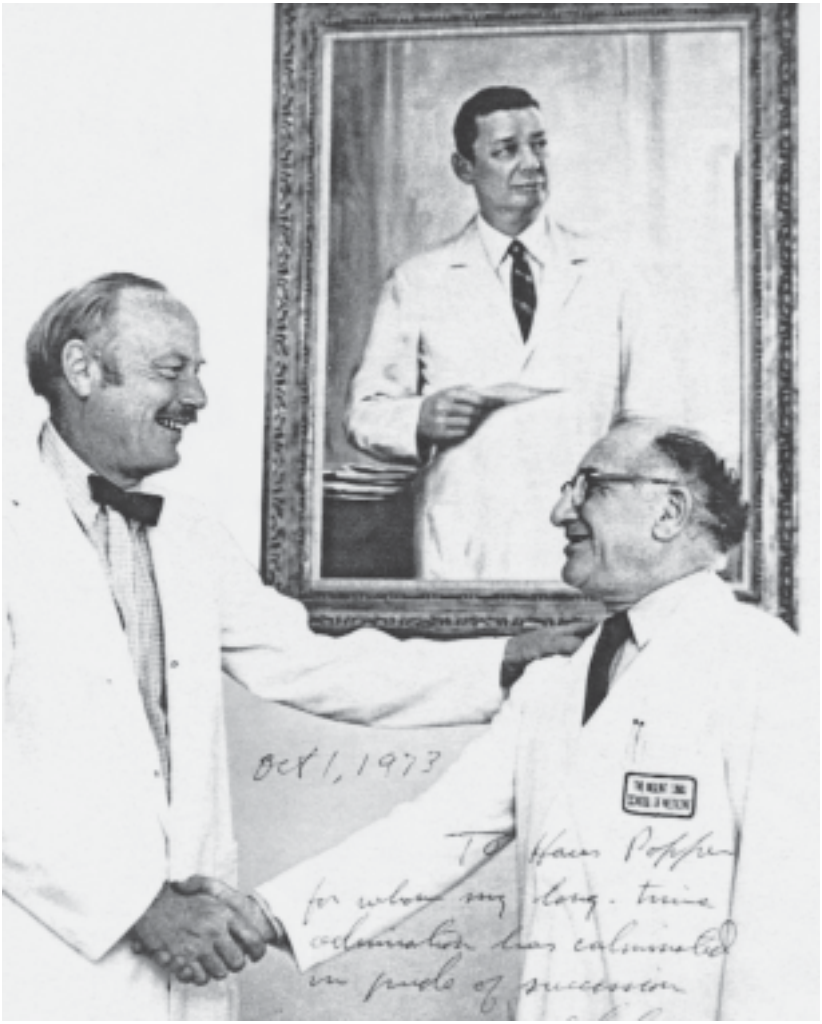


Illustration 12 Three Deans of The Mount Sinai Medical School. With Tom Chalmers, in front of a portrait of George James. The handwritten note by Dr. Chalmers reads: October 1, 1973, To Hans Popper – for whom my long-time admiration has culminated in pride of succession.

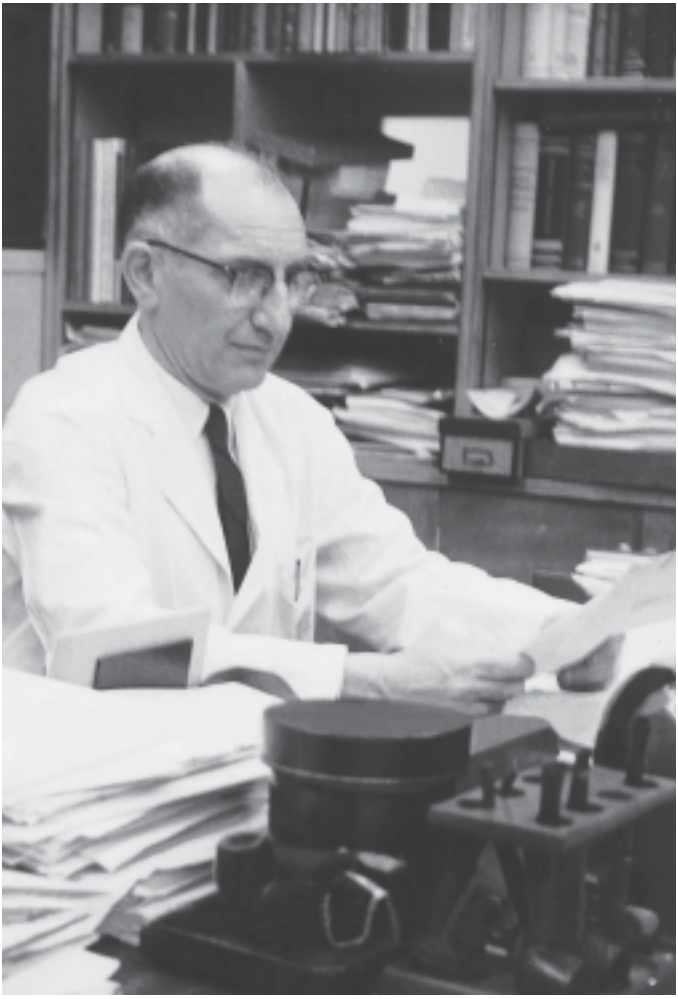


Illustration 13 In his cluttered office in the Antran Building at The Mount Sinai Hospital

In 1973, with the Medical School solidly established, Dr. Popper stepped back from his administrative responsibilities. He became the Gustave L. Levy Distinguished Service Professor at The Mount Sinai Medical Center and maintained this position for fifteen years until his death.

When Dr. Popper moved from Chicago to New York, he brought a valuable colony of rats receiving long-term treatment with ethionine, a protein antagonist. Unfortunately, though, during the flight to New York, the treated rats escaped and fraternised with the placebo rats. Although the cause of some mirth, this episode delayed experimental work for many months.

He soon started again to work on liver injury, particularly the link between hepatocellular damage and fibrosis *(Popper, H. et al.: Studies on the progression from acute hepatic injury to fibrosis of the liver, J. Mt. Sinai Hosp. 1962; 29: 152)*. His concept that *the hepatic sinusoids in alcoholic liver disease become capillarised,* thereby interfering with the exchange of nutrients between blood and liver cell, had profound effects on subsequent investigations of the pathogenesis and progression of alcoholic liver disease *(Schaffner, F. and Popper, H.: Capillarization of hepatic sinusoids in man. Gastroenterology 1963; 44: 239)*. Interestingly, this physiologic interpretation evolved from Dr. Eppinger's and Dr. Popper's early studies on serous inflammation.

Perhaps Dr. Popper's best known concept was *cholestasis.* Defined as the failure of adequate amounts of bile to reach the duodenum, cholestasis functionally represents decreased canalicular bile flow. The term is used for clinical, laboratory, or pathological findings that resemble biliary obstruction. This obstruction might be intra-hepatic, as seen with some drugs such as methyltestosterone, or extra-hepatic due to biliary obstruction *(Popper, H. and Schaffner, F.: Pathophysiology of cholestasis. Hum. Pathol. 1970; 1: 1)*. Popper coined the term *ductule* to describe the connection between biliary canaliculi and the bile ducts, and investigated their function *(Sasaki, H., Schaffner, F., Popper H.: Bile ductules in cholestasis: Morphologic evidence for secretion and absorption in man. Lab. Invest. 1967; 16: 84)*. They reported an interesting appearance of vacuolisation of hepatocytes around the portal tracts in patients with cholestasis. This finding was interpreted as resulting from retention of bile acids, leading to damage in the hepatocellular cytoplasm and particularly the endoplasmic reticulum *(Schaffner, F. and Popper, H.: Morphologic studies of cholestasis. Gastroenterology 1959; 37: 565)*. The cellular injury led to deposition of a combination of phospholipid, cholesterol, and bile acids, perhaps as liquid crystals. This concept of *retained bile acids in the cholestatic patient causing liver injury* had important therapeutic implications. Some forms of chronic intra-hepatic cholestasis, such as primary biliary cirrhosis, are now being treated by ursodeoxycholic acid, a non-toxic bile acid, which is believed to flush out the toxic bile acids retained in cholestasis. Ultimately, ursodeoxycholic acid leads to reductions in serum aminotransferase levels, indicating that they may be improving hepatocellular function, and to increased survival.

The term “primary biliary cirrhosis” was initially used in 1950 by Ahrens and colleagues at the Rockefeller Institute in New York City to describe a rare type of intra-hepatic cholestasis, largely affecting middle-aged women. This term superseded older language, such as “Hanot’s cirrhosis” and “xanthomatous biliary cirrhosis.” Dr. Popper realised that the term *“cirrhosis”* was a misnomer, certainly in the early stages when hepatic zonal architecture was preserved and the nodular regeneration of true cirrhosis was absent. Together with Fenton Schaffner and Emmanuel Rubin, he proposed *the first staging system* for the disease *(Rubin, E., Schaffner, F., Popper, H.: Primary biliary cirrhosis: Chronic non-suppurative destructive cholangitis. Am. J. Pathol. 1965; 46: 387)*. *Chronic non-suppurative destructive cholangitis* was a more accurate but cumbersome description and did not become generally accepted; the old name primary biliary cirrhosis (PBC) continued.

The row of hepatocytes immediately surrounding the portal tract was termed the “limiting plate.” The erosion of this plate was termed *piecemeal necrosis* and was believed to be the mode of progression from chronic hepatitis to cirrhosis *(Popper, H., Schaffner, F.: The vocabulary of chronic hepatitis. N. Engl. J. Med. 1971; 284: 1154)*. Later, Popper believed that *intralobular events were just as important for disease progression,* and that progression was associated with repeated flare-ups with clusters of hepatocytes in an acinar arrangement. This is certainly true of hepatitis virus B and C. Parenchymal changes play a major role in their chronic evolution.

In 1972, Stefanos Hadziyannis from Athens, now Professor of Medicine at the Hippocration Hospital, worked with Dr. Popper in New York. He brought with him liver biopsy slides from patients with acute and chronic hepatitis B. In the liver cells of hepatitis B carriers, large hepatocytes with homogenously appearing cytoplasm were observed and termed “ground-glass hepatocytes” *(Hadziyannis, S. et al.: Cytoplasmic hepatitis B antigen in ground-glass hepatocytes of carriers. Arch. Pathol. 1973; 96: 327)*. These cells were shown, by immunocytochemistry and by immune electron microscopy, to contain abundant hepatitis B surface antigen. They are most numerous in the liver of relatively non-infectious carriers of hepatitis B and are not seen in the acute stage.

Hans Popper was the first to link the severe viral hepatitis of the Amazon Basin and Venezuela with the *hepatitis delta virus* (Santa Marta fever of Colombia, Labrea fever of Brazil). He remembered that, many years earlier, viscerotomy specimens had been taken from supposed victims of yellow fever. A review of the old sections confirmed that the hepatocytes were full of hepatitis delta antigen *(Buitrago, B., Popper, H., Hadler, S.C. et al.: Specific histological features of Santa Marta hepatitis: A severe form of hepatitis delta-virus infection in Northern South America. Hepatology 1986; 6: 1285)*.

Dr. Popper identified the morphology of non-A, non-B hepatitis. Unfortunately, he died before the full recognition of hepatitis C in 1989, but his

interpretation of non-A, non-B histology was eventually shown to coincide with that of hepatitis C virus infections *(Dienes, H.P., Popper, H., Arnold, W. et al.: Histologic observations in human hepatitis non-A, non-B. Hepatology 1982; 2: 562)*.

Hepatitis G is the newest member of the hepatitis alphabet. Fritz Deinhardt in Chicago originally observed a human hepatitis agent that could be transmitted to marmoset monkeys. Dr. Popper provided the histological basis of the study *(Deinhardt, F., Holmes, A.W., Capps, R.B., Popper, H.: Studies of the transmission of human viral hepatitis to marmoset monkeys. I. Transmission of disease, serial passages and description of liver lesions. J. Exp. Med. 1967; 125: 673)*. Again, Dr. Popper was in at the beginning of a major advance in hepatology.

As *drug-related liver injury* was increasingly recognised, Dr. Popper provided the succinct classification and definitive descriptions of chemical hepatitis associated with iproniazid *(Popper, H.: Pathological findings in jaundice associated with iproniazid therapy. JAMA 1958; 168: 2235)*, halothane *(Davidson, C.S., Babior, B., Popper, H.: Concerning hepatotoxicity of halothane. N. Engl. J. Med. 1966; 275: 1497)*, and norethandrolone *(Schaffner, F., Popper, H., Chesrow, E.: Cholestasis produced by the administration of norethandrolone. Am. J. Med. 1959; 26: 249)*.

Immunopathologists Fiorenzo Paronetto and Michael Gerber, together with Popper, published studies on the immune processes involved in a series of liver disorders, including primary biliary cirrhosis, alcohol-related liver disease, and drug reactions.

Aging and the Liver

Dr. Popper was highly supportive of the decision of The Mount Sinai Hospital to establish the first Department of Geriatrics in the United States. When the Department was opened under the leadership of Dr. Robert Butler, Dr. Popper was invited to work on the medical problems of aging. During that time, Popper noted that livers do not age; that is, liver cells do not show the senescent changes seen throughout the rest of the body *(Popper, H.: Relations between liver and aging. Semin. Liver Dis. 5: 221, 1985)*. This scientific observation led to a change in national policy that allowed the livers of older donors to be utilized in transplants, enabling a large increase in the availability of livers for organ transplantation.

Dr. Popper did not live to see the growth of the liver transplant program at The Mount Sinai Hospital. He did, however, vicariously enjoy the success of Dr. Thomas E. Starzl of Pittsburgh, one of his students at Northwestern University in Chicago who went on to become the pioneer of liver transplantation.

Publications

During his scientific career, Dr. Popper wrote 821 articles published in medical journals. Seventy of his most important publications have been selected to illustrate the varied aspects of his scientific life. In addition to serving on numerous editorial boards of medical journals, Dr. Popper was the Editor of *Virchow's Archives in Pathology (Section A, Pathological Anatomy and Histology)* from 1967 to 1984.

Dr. Popper was also the author of 23 books. A major textbook, *"Liver: Structure and Function",* was written with Fenton Schaffner in Chicago and published in 1957 (New York, Blakiston Division, McGraw Hill Book Company Inc.).

The first truly scientific treatise on liver disease was *"The Liver: Biology and Pathobiology",* edited by D. Schachter, D. Shafritz, I.M. Arias, and H. Popper. This historic volume was dedicated by the other editors to Dr. Popper: "His intellect has inspired and stimulated at least three generations of hepatologists. His broad range of interest and sustained desire to bridge the gap between advances in basic biology and liver structure, function and disease exemplify the purpose of this book."

"Progress in Liver Diseases", a series of books beginning in 1961, was a collection of invited reviews on major topics in hepatology. Edited by Hans Popper and Fenton Schaffner, and published by Grune & Stratton, eight volumes appeared during Dr. Popper's lifetime. The ninth volume, published posthumously, was edited by Fenton Schaffner but retained the name of Popper as co-editor. Dr. Popper's wide knowledge of all the advances in liver disease permitted him to select authors at their scientific peak and to persuade them to contribute.

The *"Hepatology Rapid Literature Review",* a compilation of published abstracts concerning the liver, has been published monthly since 1971 by the Falk Foundation e.V. of Freiburg (Germany) and distributed internationally to interested physicians. Abstracts are collected and printed from all over the world. About 8,000 abstracts are published every year. Hans Popper was instrumental in getting this publication off the ground. Every year, he wrote the "Abstract of Abstracts," a year-end summary in which he critically assessed all 8,000 papers and formulated his conclusions.

In 1981, Dr. Popper presided over the birth of *"Hepatology",* the official journal of the American Association for the Study of Liver Diseases. Its first editor was Dr. Irwin M. Arias of Boston, and Dr. Popper continuously offered him support, particularly in selecting contributions in basic science. Dr. Popper gloried in the continued success of this journal.

Societies and Organisations

American Association for the Study of Liver Diseases (AASLD)

In 1947, Dr. Popper conceived the idea of an American liver society. A planning meeting was held in the Library of the Hektoen Institute in Chicago. Among those present were Leon Schiff of Cincinnati, Fred Hoffbauer and Cecil Watson of Minneapolis, Jesse Bollman of the Mayo Clinic, and Sheila Sherlock of London.

The first informal meeting of the society took place in 1948 in the Hektoen Library. Paper presentations were five minutes in length, followed by eight minutes of discussion, and this essentially remains the format today. Attendance was by personal invitation to a small group of Dr. Popper's friends who had made contributions to the field of hepatology: Paul György of Philadelphia, Charles Davidson of Boston, Robert Kark of Chicago, William Bean of Iowa, Franklin Hanger of New York, Stanley Hartroft of Toronto, Richard Capps of Chicago, Gerald Klatskin of Yale, Hans Smetana of Washington, D.C., and Fred Steigmann of Chicago. This list is incomplete because, during the initial years of the AASLD, no records were kept of participants and programmes. Papers to be presented were randomly selected by Hans. Names were placed in a hat and the requisite number selected in a quasi-blind drawing. A clinico-pathological conference held in the Cook County Hospital was usually a part of the meeting. On one occasion, a hirsute alcoholic male was presented to Stanley Hartroft, and the subject turned out to be an experimental rat. Dr. Popper always enjoyed these clinico-pathological conferences.

The Association evolved rapidly. The first official meeting was held in 1950, shortly after its official incorporation, with Leon Schiff as the first President. Hans Popper became President in 1962 and received the Distinguished Service Award of the AASLD in 1983. From its early days, he was a guiding light behind the scenes.

The AASLD holds its annual meeting each November in Chicago. As the conference grew, it moved out of the Hektoen Institute and into increasingly large hotels. It now convenes at the major hotels of downtown Chicago. The attendance at the Postgraduate Course regularly exceeds 2,000, and attendance at the actual meeting has recently exceeded 3,500.

International Association for the Study of the Liver (IASL)

By 1957, the AASLD was functioning well, but the field of hepatology was ready to widen its horizons. In 1957, on the occasion of a splendid liver conference in Perugia, Hans Popper, Adolf Martini (Marburg), and Sheila

Sherlock (London) discussed the possibility of an international liver society. It began with four members from each country, and was intentionally elitist at the start so that no one country would predominate. Of course, this has subsequently been changed. The first meeting took place in Washington, D.C. in 1958, with Sheila Sherlock as the first President. At the second meeting, Hans Popper was President. Since then, the Society has met in many countries, rotating between the North, South, East and West: Australia, Canada, Czechoslovakia, France, Germany, Greece, India, Italy, Japan, Mexico, Spain, Sweden, the United States and Venezuela. Hans and Lina always attended.

The 1996 meeting convened in South Africa to mark the emergence of political freedom. Hans and Lina were much missed. IASL has now taken other Societies under its umbrella, including the British, the Asian Pacific, the African, and the European Associations for the Study of the Liver. There is no longer the same need for the IASL to be a "shop window" for hepatology. Indeed, the goal of IASL is now to be a worldwide society with particular emphasis on speakers and participants from developing countries.

The Gnomes

The Gnomes are a small group of distinguished hepatological pathologists and internists interested in the nomenclature of liver diseases. Membership is a label of prestige. The Gnomes are self-supporting and meet every year in different cities, hosted by one of their members. The group first met in Göteburg in 1967. The 1968 meeting in Zurich led to their title, "Gnomes of Zurich," an analogy to the all-powerful bankers centred in Zurich. The Gnomes met in Leuven in 1969, but Hans Popper did not participate until the 1970 meeting in Copenhagen (illustration 14, The 1975 meeting in Bonn). The classification was then modified and promulgated in Zurich in 1968.

The Gnomes' first task was to make sense of the classification of chronic hepatitis. A classification was formulated at the first official meeting in 1968 *(DeGroote, J. et al.: A classification of chronic hepatitis. Lancet 1968; 2: 626)*. They decided on two main categories: "chronic persistent hepatitis," which was more benign, and "chronic aggressive (active) hepatitis," which was more serious. These terms were widely used and given a prognostic significance they did not entirely deserve. At that time, Hans Popper realised that there was a third category, in which persistent necrosis was scattered through the parenchyma. This was termed "chronic lobular hepatitis" *(Popper, H., Schaffner, F.: The vocabulary of chronic hepatitis. N. Engl. J. Med. 1971; 284: 1154)*.

The discovery of the hepatitis C virus necessitated a change in the classification yet again. It was obvious that chronic hepatitis C was progressing largely through lobular changes. In 1994, a group of internists, pathologists,

Illustration 14 The Gnomes' meeting in Bonn, 1975. From left to right: Gerhard Korb, Heribert Thaler, Hemming Poulsen, Peter Scheuer, Prof. Herwig Hamperl (as guest), Peter Gedigk, Valeer Desmet, Jan DeGroote, Hans Popper, Piccio Bianchi, and Martin Schmid.

virologists, and immunologists came together to consider a new classification. The terms "chronic persistent" and "chronic active" hepatitis were abandoned. Instead, it was recommended that chronic hepatitis should be evaluated in terms of activity and stage. How Dr. Popper would have enjoyed participating in these discussions – there is no doubt that he would have agreed with the conclusions!

Over the years, the Gnomes addressed the nomenclature of other liver conditions, including alcoholic liver disease, hepatic drug reactions, cholestatic conditions, and viral hepatitis. In every meeting during his lifetime, Dr. Popper was the Maestro, drawing on his wide knowledge and formulating new ideas of liver disease. The Gnomes continue to meet every year, and Lina Popper is always an honoured guest.

Hans Popper Hepato-Pathology Society

In 1989, Dr. Popper's colleagues founded this Society in memory of Dr. Popper. At present, Dr. Michael Gerber is the President, Dr. Swan Thung the Vice-President, and Dr. Stephan A. Geller the Secretary/Treasurer. The

Society discusses problems of hepatic pathology and encourages the presentation of papers by Residents and Fellows. It usually meets in connection with national meetings, such as the United States-Canada Academy of Pathology or Dr. Popper's beloved AASLD in Chicago.

Herbert Falk and the Basel Liver Week

The worldwide expansion of hepatology was greatly accelerated by the association of Dr. Popper and Dr. Herbert Falk, founder and president of a large pharmaceutical company that specializes in drugs for liver disease (illustration 15). Drs. Popper and Falk first met in 1965 in Basel, when Dr. Popper was on his way to visit Professor Ludwig Heilmeyer in Freiburg. Thus began a cooperation which lasted twenty-three years. They met again in 1966 at the World Congress of Gastroenterology and the IASL meetings in Japan. It was a perfect symbiosis between the physician-scientist and the physician-businessman who wanted to benefit medical science.

In October 1967, Dr. Falk sponsored the first Falk Symposium in Freiburg; 200 participants were expected but 800 turned up, and it cost half of the net profits of Dr. Falk's company in 1967. Since then, major Falk Liver Weeks have taken place every three years, until 1976 in Freiburg, afterwards

Illustration 15 With Herbert Falk

Illustration 16 Basel Liver Week, 1982. Opening address by Hans Popper

Illustration 17 With Piccio and Emmeli Bianchi

in Basel (illustration 16). Leonardo (Piccio) Bianchi has played a central role as the organising secretary and is assisted by his wife Emmeli (illustration 17). More than 19,000 physicians from 70 countries have attended. Basel Liver Week has been instrumental in introducing physicians, especially Europeans, to the very best speakers on hepatology worldwide. In particular, this extraordinarily international group of physicians have heard basic scientists, consistently of the highest calibre, present their latest research.

Dr. Popper was the guiding genius behind the Basel Liver Weeks. In selecting topics and speakers, he showed exquisite taste in compiling a programme that blended the best of the Old and the New Worlds. He was the life and soul of the meetings themselves. His presence could transform a dull session into a happening.

These meetings always consist of a major symposium on a topic of clinical interest and practical value to all the participants. The symposia are preceded and followed by one or two meetings of a more basic nature, such as “cell-cell interactions”, “collagen metabolism”, “liver cell necrosis” and “membrane alterations as a basis of liver injury.” Dr. Popper usually provided the final oral summation of these basic meetings. This task demanded constant attendance and attention at the meetings, note-taking, synthesising the results, and persuading Mrs. Bianchi to make additional

illustrative slides. Dr. Popper's final synthesis at the meeting on "Structural Carbohydrates in the Liver", given when he was 81 years old, was followed by a standing ovation.

A new event at the Basel meetings is the presentation of the Hans Popper Prize, the international award for liver research. The Hans Popper Prize has so far been awarded to Howard Thomas of London (1989), Mario Rizzetto of Turin (1992), and Michael Manns of Hannover (1995). At the same time, the Hans Popper Förderpreis is given to a young scientist from a German-speaking country.

The Fogarty Center and the National Institutes of Health

Hans Popper formally retired in 1973 by resigning from his positions as the Chair of the Department of Pathology at the Mount Sinai Medical Center and as Acting Dean and President of the Mount Sinai Medical School. Free from administrative burdens, the final fifteen years became the most productive of Dr. Popper's life.

In 1973, Dr. Popper spent seven months as a Fogarty Scholar, living with Lina at the Fogarty Center in Bethesda. This program is directed by the National Institutes of Health and gives time to scholars for the pursuit of research in any field. Fogarty Scholars may engage in any activity they wish at the National Institutes of Health.

This was an exciting time, for research on the hepatitis viruses was beginning. Dr. Popper, among the first to recognise the oncogenic potential of hepatitis B, used the hepadnaviruses in animals as a model to study carcinogenesis in man. Animals such as ground squirrels, woodchucks, or Peking ducks may become infected by viruses related to the human hepatitis B virus and may develop various forms of hepatitis. Woodchucks and ducks may even develop carcinoma of the liver, similar to the cancer that occurs in human carriers with hepatitis B infection. A goal of Dr. Popper's work was to interrupt the transition from hepatitis to cancer with antiviral agents or vaccines.

This work led Dr. Popper to become familiar with modern molecular biology, virology, and immunology. He gained this knowledge by prodigious reading. He soon could hold his own at meetings with experts and indeed at times interpreted the results better than they did. He expanded from his lifelong reliance on the microscope and moved into a functional molecular mode, a fantastic achievement for one in his eighth decade. But he was never very far from his microscope, claiming – only partly in jest – that he had learned to "see DNA" with it. During this period as Fogarty Scholar, he forged links with liver disease researchers at the National Institutes of Health which continued until his death.

Dr. Popper regularly attended the weekly liver biopsy conference at the Armed Forces Institute of Pathology in Washington, D.C. This meeting, presided over by pathologist Kamal Ishak and senior clinician Hy Zimmerman, attracted other senior hepatologists from the city. Hans became a valuable and tactful contributor. His interpretation of slides was brilliant, rapid, even intuitive, and of course based on his long experience. His opinion was remarkably reproducible when reviewed six months later. After he left the National Institutes of Health, he flew in from New York City to attend these weekly meetings.

In 1972, the World Health Organisation asked the IASL to help standardize the nomenclature for diseases of the liver. Eminent hepatologists met at a conference sponsored by the Fogarty International Center in Washington, D.C. Ultimately, some general agreement was reached. The new nomenclature was intended to help students, junior staff, and practitioners talk the same language, and it proved of particular value in developing countries that lacked good library facilities *(Leevy, C.M., Popper, H., Sherlock, S.: Diseases of the Liver and Biliary Tract. Standardization of Nomenclature, Diagnostic Criteria and Diagnostic Methodology. Fogarty International Center, Washington, D.C., United States Government Printing Office, 1977; 22)*. With the support and contributions of members of the IASL, the book was updated, and thes second edition appeared in 1994.

Travels: The Missionary

During his last years, Dr. Popper spent much time traveling through Europe and indeed throughout the world. Herbert Falk was his travel mentor, driver, and organiser. Dr. Popper was like a godfather to the Falks.

Dr. Popper spoke at innumerable medical meetings and visited countless hospitals and medical schools. At each, he insisted on exchanging information with the young house staff. The audience at these lectures numbered 100 to 500. His lecturing record was set in October 1985, when he gave ten talks in ten different places in West Germany, Switzerland, and Austria within twelve days.

Dr. Popper maintained close contact with Korea. He collaborated with Professor Whan Kook Chung in interpreting liver biopsies from Korean soldiers with acute hepatitis and in examining the mechanism of its progression to cirrhosis. In 1982, he participated in the Second International Liver Symposium in Seoul. At that time, the Government of the Republic of Korea awarded him the Order of Mugungwha, a sign of the highest respect from the people of Korea.

In 1980, Dr. Popper attended the inaugural meeting of the Asian-Pacific Association for the Study of the Liver (APASL) in Auckland, New Zealand.

He then made visits to Australian medical centres. Professor Lawrie Powell of Brisbane writes, "Hans Popper will be remembered in Australia particularly for his genuine curiosity about biological events, his vigorous debates, his encyclopaedic knowledge of the scientific literature, for his drive and enthusiasm, and for his constant encouragement of students and scientists."

The Asian trip of 1986 included visits to Singapore for the APASL meeting, Kuala Lumpur, Jakarta, Shanghai and Guilin in China, and Tokyo: five countries in eighteen days!

Dr. Popper's last tour was a visit to Italy and Germany in October 1987. He participated in the meeting of the Italian Association for the Liver held in Ancona on the Adriatic Sea. At this conference, organised by Francesco Orlandi and his wife Anne-Marie Jézequel, Dr. Popper gave an outstanding lecture on viruses and cancer. The lecture became a paper, almost his last, and was published in the *Journal of Hepatology* without peer review. Dr. Popper's last European lecture was delivered on October 23, 1987 at Solko Schalm's Department in Rotterdam, the port city from which he sailed to the United States in 1938.

Honours

Dr. Popper received fourteen Honorary Doctorates from universities worldwide. He derived particular satisfaction from those awarded by German and Austrian universities. The Honorary Degree which gave him the most pleasure came in 1965 from the University of Vienna, on the occasion of the 600th anniversary of the founding of the University.

His native city again honoured him on the occasion of his 80th birthday with a spectacular meeting that was attended by 650 colleagues from 34 countries. A Festschrift was published to commemerate this event *[Brunner, H., Thaler, H. (eds.): Hepatology: A Festschrift for Hans Popper (Falk Symposium No. 39). New York, Raven Press, 1985]*. Dr. Popper gave a splendid speech *(Popper, H.: Vienna and the Liver, Gastroenterology 1984; 86: 183)*. He was bestowed with the Austrian Honorary Cross (First Class) for Science and Art. In addition, the Laboratory in the Institute of Pathology at the University of Vienna – where he had worked 50 years before – was re-named the Hans Popper Laboratory.

Through the generosity of his friend Henry Stratton, whose major medical publishing house, Grune & Stratton, published several of Dr. Popper's books, the Department of Pathology at The Mount Sinai Hospital in New York became the Lillian and Henry Stratton – Hans Popper Department of Pathology in 1985. Clinics in both Freiburg and Nuremberg have been named after Dr. Popper, and a Primate Research Center in Orth-Donau, Austria, was dedicated to him in 1992.

He received innumerable honours from governments, universities, and academic societies throughout the world. In 1976, he was honoured by election to the Deutsche Akademie der Naturforscher Leopoldina in Halle, the most distinguished German academic group. In the United States, perhaps the most important recognition came in 1976 when he was elected a member of the National Academy of Sciences. In 1981, he received the John Phillips Memorial Award of the American College of Physicians, in 1971 the Julius Friedenwald Medal of the American Gastroenterological Association, the highest honour it can bestow. He also received the Distinguished Service Award from the IASL in 1974 and from the AASLD in 1983. In 1967, he received the extremely rare distinction for a physician of being elected to the American Academy of Arts and Sciences.

There were countless others. He received all the awards graciously with an apt comment, always acknowledging his co-workers and his wife Lina.

Conclusion

Despite the traumatic dislocation, Dr. Popper derived much benefit as a result of his move from Europe to the United States. He was accepted, fit in, and enjoyed the American way of life, and Lina provided the Viennese atmosphere. He might not have been so successful and his life might not have been so meaningful to medical science had he remained in Austria.

From his earliest youth, Dr. Popper worked incredibly hard. He needed little sleep. His working day was usually 14 hours, with 8 hours on weekends. He was typically in the hospital from 8 a.m. to 10 p.m. He was highly self-disciplined, pragmatic, and eager to learn to the last.

He had an encyclopaedic mind and read voraciously. It is said that no journal reached the shelves of The Mount Sinai Hospital Library until it had passed through Dr. Popper's hands.

He taught continuously and was the teacher compleat. At Mount Sinai, his slide conferences and gross autopsy review sessions, often conducted late at night, were legendary. On Saturday afternoons until 6 p.m., he met his colleagues and his research group on a one-to-one or small group basis, usually to assess research results and prepare manuscripts for publication. As Michael Gerber and Swan Thung wrote that "This was always a learning experience, even for the most experienced investigator."

Throughout his life, he spanned European and New World medicine. He brought his energy to the land of opportunities and spread it throughout the world. His influence on colleagues was immeasurable. Raised in a disciplinarian culture, Dr. Popper's lectures were meticulously prepared, his slides carefully selected, the text continuously rehearsed; he always kept to his allotted time. He expected his co-workers to do the same.

He was a genial companion, enjoyed friendship, good food, wine and dancing. His conversation was scintillating and often hilarious. He was a Charter Member of the Playboy Club in Chicago. He kept his energy and youthfulness throughout his life, religiously doing Royal Canadian Air Force exercises until the very end.

I have thoroughly enjoyed writing this tribute to the memory of an old and dear friend. I first met him in 1947 while I was a Research Fellow at Yale. When I visited him at the Hektoen Institute, he introduced me to his family, and this initiated our life-long friendship (illustration 18). My thanks are due to Lina Popper. She has supported and advised me and given much biographical material of Hans. She remains one of my best friends.

Hans Popper often cited the words of the angels in Faust, written by his favourite author Goethe. The angels could have composed his obituary:

Wer immer strebend sich bemüht, den können wir erlösen.
Who e'er aspiring, struggles on, for him there is salvation.

Dr. Hans Popper, the Founder and Father of Hepatology, has earned his salvation.

Illustration 18 With Dame Sheila Sherlock

Honours of Dr. Hans Popper

Born: November 24th, 1903 in Vienna, Austria.
Died: May 6th, 1988 in New York, New York.
M. D., 1928, University of Vienna.
M. S. in Pathology, 1941, University of Illinois.
Ph. D. in Pathology and Physiology, 1944, University of Illinois.

Honorary Degrees

1965: M. D. (Hon), Catholic University of Leuven
1965: Ph. D. (Hon), University of Vienna
1965: M. D. (Hon), University of Bologna
1974: M. D. (Hon), Medizinische Hochschule Hannover
1975: M. D. (Hon), University of Turin
1977: M. D. (Hon), University of Tübingen
1978: M. D. (Hon), Catholic University of Seoul
1979: D. Sc. (Hon), The Mount Sinai School of Medicine, New York
1981: M. D. (Hon), University of Lisbon
1981: D. Sc. (Hon), College of Medicine and Dentistry of New Jersey
1981: M. D. (Hon), University of Münster
1984: M. D. (Hon), University of Freiburg
1987: M. D. (Hon), University of Göttingen
1988: M. D. (Hon), The Humboldt University of Berlin (posthumously)

Awards

1967: Fellow, American Academy of Arts and Sciences
1970: Distinguished Lecture Award, American College of Gastroenterology
1970: Charter Member, Alpha Omega Alpha Chapter at The Mount Sinai School of Medicine
1971: Julius Friedenwald Medal, American Gastroenterological Association
1974: Distinguished Service Award, International Association for the Study of the Liver
1976: Member, National Academy of Sciences
1976: Honorary Life Member, New York Academy of Sciences
1976: Gold Headed Cane Award, American Association of Pathologists and Bacteriologists
1976: Member, Deutsche Akademie der Naturforscher Leopoldina.
1983: Distinguished Service Award, American Association for the Study of Liver Disease

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Zur Kenntnis des Glykogengehaltes der Leichenleber.
Virchows Arch. A Pathol. Anat. Histopathol. 279: 819, 1931

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Correlation between cytoplasmic basophilia and the nucleic acid content of the liver.
A. M. A. Arch. Pathol. 51: 399, 1951

György, P., Stokes, J., Jr., Goldblatt, H., Popper, H.:
Antimicrobial agents in the prevention of dietary hepatic injury (necrosis, cirrhosis) in rats.
J. Exp. Med. 93: 513, 1951

Popper, H., Elias, H., Petty, D. E.:
Vascular pattern of the cirrhotic liver.
Am. J. Clin. Pathol. 22: 717, 1952

Koch-Weser, D., de la Huerga, J., Yesinick, C., Popper, H.:
Hepatic necrosis due to bromobenzene as an example of conditioned amino acid deficiency.
Metabolism 2: 248, 1953

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Intrahepatic cholestasis ("Cholangiolitis").
Gastroenterology 31: 683, 1956

Schaffner, F., Popper, H., Dalla, T. M:
Structural alterations in the clinical evaluation of cirrhosis.
Gastroenterology 30: 357, 1956

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Liver: Structure and Function. The Blakiston Division, McGraw-Hill Book Company, Inc., New York, 1957

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JAMA 169: 1447, 1959

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The carcinogenic effect of aramite in rats. A study of hepatic nodules.
Cancer 13: 1035, 1960

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Nature 192: 886, 1961

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Hypertrophic hypoactive smooth endoplasmic reticulum: A sensitve indicator of hepatotoxicity exemplified by Dieldrin.
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Hepatitis after exposure to halothane.
Ann. Intern. Med. 71: 167, 1969

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The social impact of liver disease.
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Major International Falk Symposia on Liver Diseases 1967–1999

Date	*No. of Falk Symposium*	*Topic*	*President*	*Place*
27.–29.10.1967	1	I International Liver Symposium „Jaundice“	L. Heilmeyer	Freiburg
02.–04.10.1970	4	II International Liver Symposium „Alcohol and the Liver“	H. Popper	Freiburg
12.–14.10.1973	13	III International Liver Symposium „Drugs and the Liver“	R. Schmid	Freiburg
08.–10.10.1976	23	IV International Liver Symposium „Liver and Bile“	F. Schaffner	Basel
05.–07.10.1979	28	V International Congress of Liver Diseases „Virus and the Liver“	S. Sherlock	Basel
15.–17.10.1982	35	VI International Congress of Liver Diseases „Liver in Metabolic Diseases“	G. A. Martini	Basel
16.–18.10.1986	44	VII International Congress of Liver Diseases „Cirrhosis“	J. L. Boyer	Basel
12.–14.10.1989	54	VIII International Congress of Liver Diseases „Infectious Diseases of the Liver“	H. Deinhardt	Basel
15.–17.10.1992	69	IX International Congress of Liver Diseases „Extrahepatic Manifestations in Liver Diseases“	R. Schmid	Basel
19.–21.10.1995	87	X International Congress of Liver Diseases „Acute and Chronic Liver Diseases: Molecular Biology and Clinics“	R. Schmid	Basel

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Date	*No. of Falk Symposium*	*Topic*	*President*	*Place*
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