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Ninth Pharmacologic-Historical Forum

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Abstract

The ninth pharmacologic-historical Forum was held online in 2024 in Munich during the Meeting of the DGPT (Deutsche Gesellschaft für Pharmakologie und Toxikologie). Pharmacologists and Toxicologists of all German Universities have carried out excellent work supporting their disciplines and research. Purpose of these Forums is to honour these personalities and to inform our young colleagues about their achievements.

Keywords: Ninth pharmacologic-historical Forum; Pharmacology; Toxicology; Biographies

Introduction

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Ladies and Gentlemen,

I welcome you to this Ninth Pharmacologic-Historical Forum. As you probably know, Roland Seifert initiated the Forum 2014 during the Meeting of DGPT in Hannover. Since then, I organize and direct it. Concerning the purpose of the Forum, I told in Hannover

Pharmacologists and Toxicologists of all German Universities have carried out excellent work supporting their disciplines and research. Purpose of these Forums is to honour these personalities and to inform our young colleagues about their achievements".

In this sense they have been honoured from Marthe Vogt and Edith Bülbring in Hannover to Rudolf Buchheim, Hans-Joachim Dengler and Manfred Göthert last year in Bonn **(Figure 1)**.

Figure 1: Honoured personalities from top left to bottom right: Edith Bülbring, Marthe Luise Vogt, Heinz Lüllmann, Hans Herken, Friedrich Jung, Helmut Coper, Fritz Hauschild, Helmut Kewitz, Wolfgang Heubner,Franz Gross, Ludwig Lendle, Emil Starkenstein. Reinhard Ludewig, Paul Martini, Rudolf Buchheim, Hans-Joachim Dengler, Manfred Göthert. Reproduced from Philippu (2007,2014, 2017).

This Forum is dedicated to pharmacologists and toxicologists of Münich Pharmacology is ingrained in Munich, particularly because Walther Straub studied in Strasbourg by Schmiedeberg, published as student his first paper and belonged to his friends and pupils **(Figure 2).** Peter Eyer will depict the lives and achievements of the pharmacologists,Helmut Greim those of the toxicologists and additionally he will portray the life of Oswald Schmiedeberg.

Figure 2: Oswald Schmiedeberg (second from right) together with some pupils of him and Walther Straub (arrow), Professor probably in Marburg or Würzburg. Section of an illustration, for details see Philippu, 2007.

I cordially invite you to the tenth Forum that will be held 2025 in the Medizinische Hochschule of Hannover, where it was born. In the absence of Athineos Philippu, the Introduction was held by the chairman Helmut Greim.

References

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This overview presents the written version of a lecture given at the ninth pharmacologic-historical forum on March 13, 2024, in Munich. Due to the limited time for an oral presentation and the limited space for the written version, this contribution is only an overview on the development of pharmacology in Munich during the last 130 years. For more details, particularly regarding the appointed lecturers, their fate and major focus of scientific work, the reader may be referred to a former article of the author (Eyer, 2004).

Hermann Tappeiner (1847-1927)

Hermann Tappeiner is regarded as the founder of experimental pharmacology in Munich. He was appointed to the newly elected chair at the Medical Faculty of the Ludwig Maximilians University, Munich in 1883. This chair was established 40 years later than the precedent in Dorpat, who was held by Rudolph Buchheim the acknowledged founder of experimental pharmacology. Notwithstanding, there had been some germinal ancestors in Munich, who gently touched pharmacological topics: e.g., the pharmacist Johann Andreas Buchner, who isolated salicine, the glucoside of saligenin, from the bark of willow in 1828, while his son Ludwig Andreas Buchner succeeded in getting the chair of pharmacy and toxicology in 1852. Both were occasionally depicted as pharmacologists although not adhering to our modern concept of pharmacology in that an experimental analysis of the drug effects proper were still lacking. The same holds true for a medicinal predecessor: the physician Hermann von Boeck who was appointed a lecturer in pharmacology in 1871 with his thesis "On the degradation of proteins in the animal body by morphine, quinine and arsenous acid". In 1876 he obtained an extraordinary professorship and published a 250 pages paper on "Intoxications with poisonous plants" in the Handbook of Special Pathology and Therapeutics edited by Hugo von Ziemssen. However, he received no position at the university and had to earn his livelihood as a practitioner. A chronic liver decease finished his life early. Hence it is Hermann Tappeiner who should be considered as the first pharmacologist in Munich (Goerke, 1972).

Figure 3: Hermann Tappeiner.

Hermann Tappeiner **(Figure 3)** was born in Meran on November 18, 1847, as the son of the famous anthropologist and expert in tuberculosis Franz Tappeiner, to whom we owe the construction of the well-known Tappeiner promenade. After medical studies in Innsbruck, Göttingen, Leipzig, Heidelberg and Tübingen Hermann Tappeiner received his doctorate in Leipzig with an experimental work on "Consequences for the blood stream after ligation of the portal vein." In Munich he was appointed a lecturer for medicinal chemistry at the Physiological Institute of Carl Voigt in 1877 with the title:

"Oxidation of cholic acid by acidic potassium chromate in sulphuric acid".

In 1879 he accepted the chair as professor of physiology and dietetics at the Royal Veterinary School in Munich that did not yet belong to the university. Since the experimental facilities had been rather poor there, he gladly received his appointment as extraordinary professor for medicinal chemistry and pharmacology at the medicinal faculty of the Munich University. Finally, in 1893 he was appointed as full professor and received a new building at Nussbaumstraße 28 in Munich.

Upon opening ceremony Tappeiner sketched out the tasks of pharmacology: "*In the last decades the Materia Medica was swollen to a mess of natural and synthetic products. Only a small part of it had been sufficiently approved bedside. Most of it had been uncritically used upon mystic and natural philosophical speculations or superficial experience and blind belief in authority"…"In contrast, modern pharmacology explores the mode of actions elicited by chemical substances in the organism and contributes to the advances of physiology. Moreover, chemical changes that drugs and foreign compounds are undergone in the body have widened our view on the chemical processes of life."* He proceeded*:" Admittedly even today pharmacology has detected only macroscopically the targets of drug actions and is able to present a kind of topology of drug effects. The molecular events, however, are still obscure and await future elucidation."* No doubt, this kind of view characterizes Hermann Tappeiner as prototype of modern pharmacology (Tappeiner, 1893).

Allow me a short historical excursion: The importance of the discipline of pharmacology was not generally accepted at the end of the 19th century, as Rudolf Buchheim branded in 1876 when he wrote: "Prof. Dr. Billroth (the famous surgeon in Vienna) has mentioned in his recent work 'Über das Lehren und Lernen der medicinischen Wissensch aften an den Universitätendeutscher Nation. Wien 1876.': *"The formerly given lecture on Materia Medica is nowadays disassembled into pharmacology, pharmacognosy, medication prescription, and toxicology. It is of course difficult to employ a full professor sufficiently, if he teaches only this single discipline, since the content of such a lecture has considerably shrunk and the remainder could be easily halved. The lecture in pharmacology should restrict to a brief overview of the most important groups of drugs and demonstrate the action of the most toxic substances. This can be accomplished in 3-4 semester hours. Students should not be burdened with surplus lectures on this topic" (Billroth, 1876).*

During his 36 years direction Tappeiner studied the role of intestinal bacteria, particularly in ruminants, and contributed to better understanding of digestion and enteral absorption. Together with his pupil Oscar Raab he was interested in mechanisms of photodynamic and phototoxic reactions. In addition, Tappeiner became known through his instructions of chemically based bedside diagnostics and his textbook of pharmacology and medication prescription, which appeared 1885 and 1890, respectively. Tappeiner passed away on January 12, 1927, in Munich. He was married with Elisabeth von Ziemssen since 1882, the couple had 4 children (Forth and Klimmek 1994).

Walther Straub (1874-1944)

In 1919, an appointment committee was headed by the then dean of the Medical Faculty, Ferdinand Sauerbruch to find a successor for the 72 years old Tappeiner. The faculty decided to appoint *unico loco*

Walther Straub from Freiburg where he had held the chair for pharmacology over 16 years **(Figure 4)**. After extensive negotiations and an abundant correspondence with Sauerbruch and later Otto Frank, Straub accepted. He was promised the rebuilding of the institute of pharmacology in which a flat for Walther Straub and his family was erected on the uppermost floor. Moreover, the neighboring building of the Institute of Pathology at Nussbaumstraße 26 was assigned to the Institute of Pharmacology. Straub arrived at Munich on April 1, 1923. It took until 1932 when the rebuilding of both institutes was completed. The old Institute of Pharmacology was enlarged and combined with the former Institute of Pathology via a 13 m long bridge made of ferroconcrete and called Straub'sche Brücke (Goerke, 1972).

When Straub came to Munich he was at the zenith of his scientific career and was acknowledged as one of the most important pharmacologists of the first decades of the twentieth century in Germany and even in Europe. In 1920 he provided the impetus for founding the German Pharmacological Society (*Deutsche Pharmakologische Gesellschaft*) and became the editor of the oldest journal of pharmacology: the *Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie*. In 1925, the conference of the German Pharmacological Society was held in Rostock under the heading "Straubismus convergens" – an ironic allusion to the term 'strabismus convergens' as pointed out by Walther Siegfried Loewe, Dorpat (Forst, 1974).

Born on May 8, 1874, in Augsburg, Straub studied medicine in Munich, Tübingen and Straßburg where he started as a medical student some experimental work under Oswald Schmiedeberg on glycosuria following carbon monoxide poisoning (Straub, 1897). After completion of his medical study in Munich he worked on his thesis under Carl Voit in the Department of Physiology and received his degree as Dr.med. On July 18, 1897, which was published in 1899 under the title: "The influence of sodium chloride on the decomposition of proteins" (Straub, 1899). When he became an assistant of Carl Voit, he made the acquaintance with his later friend Otto Frank before he left Munich to enter the laboratories of pharmacology at Leipzig University headed by Rudolf Boehm, the second famous foster father in pharmacology. Within two years he qualified on July 23, 1900, as a Lecturer in Pharmacology with a study on the action of Antiarin on the isolated suspended frog heart. (Antiarin was used as arrow poison due to its digitalis-like properties. Straub, 1900). Immediately afterwards, he visited the Zoological Station at Naples where he had the opportunity to use marine animals, particularly *Aplysia limacina*, a sea snail with a heart devoid of regulatory innervation that was considered to allow physiological studies on the smooth musculature proper. (For details the reader is referred to the comprehensive review of Otto Krayer in the edition of Melchior Reiter, 1998).

Not yet a full professor, Straub in 1905 was appointed to the chair of Pharmacology in Marburg, one year later he followed a call to Würzburg and relinquished this position in 1907 when he was given the opportunity to become the first full professor of Pharmacology at the University of Freiburg. Between 1913 and 1917 a new institute was built, and a very fruitful period started when Straub gathered some very talented coworkers who later became chairs at several German universities.

Much has been written on the scientific oeuvre of Walther Straub (for details see Krayer, 1998; Prüll et

al., 2009). His name relates to an experimental design using the isolated frog heart ('Straub's Frog Heart) or 'Straub's Mouse-Tail-Phenomenon' a bioindicator for morphine-like substances. This phenomenon has been described as catatonic rigidity of the tail that is maximally deflected parallel to the backbone (Straub, 1911). By chance, this phenomenon was observed when the newly synthesized pethidine, designed as a possible anticholinergic candidate, was tested in mice for toxicity. From then pethidine was classed as a morphine-like drug (Schauman, 1940). On occasion of the Second International Congress of Pharmacology held in Prague 1963, a stamp was disseminated showing the Straub's Mouse-Tail-Phenomenon.

Most attention Straub devoted to the mode of action of digitalis glycosides, which were studied in a large kind of differently developed animals. He summarized the pertinent knowledge in his ample legacy (Straub, 1924). The particular merits of his experimental approach center on the quantitative relationship between drug effect and drug concentration. He developed many bioassays to quantify the amount of drug that had been absorbed by a selected tissue. In doing so he had his own views on the mode of drug action that contrasted with the receptor concept as advanced by Ehrlich and Langley (for details see Prüll et al., 2009).

During his decades in Munich, Straub extended his investigations to the smooth muscles of the intestine, to questions of the intestinal transport and characterized the mode of action auf Senna glycosides.

An appreciation of Walther Straub would be incomplete if his many statements to contemporary issues would be ignored. Already before WW I, Straub was eager to immunize practitioners against intolerable advertising promises of pharmaceutical manufacturers. Thus in 1908 he denounced the intense advertising of a new antipyretic/analgesic drug "Pyrenol" that consisted of sodium benzoate, thymol, and salicylic acid "in a particular physicochemical bonding relationship". Straub pulled the blade: "*The manufacturer shows a constitution formula of his product with a fairytale-like connecting hyphen that has only literary meaning. Chemically, this tied construct does not really exist, but a chemical formula is always impressive, and the addressee is clueless and stupid. You could even claim this was the formula of uric acidic glucose"…* "*It's a shame that the many addressees do not realize the fakes and have no longer any knowledge of pharmacology. This shows us that something went wrong and where an improvement is indispensable. The defects are due to our medical teaching and exams, where theoretical aspects are missing out. The major educational goal in pharmacology appears to be the correct medical prescription of drugs*" (Straub, 1908).

On other occasions Straub was a brilliant writer, too, who could hide a lot between the lines. In 1943 Straub, a passionate coffee drinker submitted an article, wisely in Swiss Medical Weekly (*Schweizer Medizinische Wochenschrift*), on "Coffee needs then and now" (*Kaffeenöteeinst und jetzt*). Herein he was sarcastic about the coffee substitutes, which during the war were advertised to the Germans: "These substitutes differ from coffee proper in that they introduce some nutritional compounds, but do not elicit enjoyment at all. From a standpoint of kitchen technology, you should call it flower soup, but not delicacy" (Straub, 1943).

The oppressive time of National Socialism was not without impact on the Pharmacological Institute of

the Munich University. Straub had trouble with the Nazi authorities already in 1933 when he supported his first assistant August Forst who refused to raise the flag with swastika on the roof of the institute when Straub was in the U.S.A. Subsequently, Straub had to struggle for the employment of Forst who was steadfast to remain with his half-Jewish wife, which resulted in the interdiction of exams and refusal of the promotion to an extraordinary professor. In 1935 Straub wrote to the Directorate of the University: "*The Institute of Pharmacology urgently needs a third assistant, because the lectures of Pharmacology have to be enlarged to teach also pharmacists due to the new curriculum. Since the Private Docent Forst is not allowed to hold exams, a substitute is required who can only be an assistant of the institute*."

When Straub publicly criticized amateurish concepts of the responsible Police Inspection how to treat phosphorus burns, he hardly escaped an impeachment during WW II. Straub had detected already in 1903 that $CuSO_4$ was able to inactivate yellow or white phosphorus thus inhibiting self-ignition. His recipe of 1% $CuSO_4$ in a paste of bolus alba was well known to lay press as "Straubsche Paste" and helped to refrain the ill-reputed phosphorus burns from creepiness ("*und half die so übelbeleumundetenPhosphorbrandwundenzuentgruseln*"; Straub, 1944).

The irony of fate would have it that by the air raids in July 1944 three cans, i.e. phosphorus-kindled incendiary bombs ignited the roof-truss of the old building of the former Institute of Pathology, before high-explosive bombs in a later air-raid did the rest. Contemporaries reported that Walter Straub, sitting across the street under a tree had been watching how the building was burning down. Shortly thereafter Straub succumbed in Bad Tölz to a fatal stroke on October 22, 1944 (Forth, 1994).

Straub had become member of the Deutsche Akademie der Naturforscher Leopoldina in 1925, honorary member of the American Society for Pharmacology and Therapeutics in 1929 and in 1935 honorary member of the British Pharmacological Society.

With regard to the personality of Straub we have impressive portrayals by his pupils, e.g., by Gerhard Stroomann, later director of the Sanatorium Bühler Höhe, where Straub took a cure from former stroke-like disorders. All of them stated that Straub was a great teacher. His lectures were vivid and prepared with great care. He insisted that the experiments did function properly and were not cheated. He was convinced that personal witnessing of an experiment was of paramount importance for students, since he was an enthusiastic experimenter himself, a great photographer, and a good amateur painter. For many of his listeners, Straub's lectures and demonstrations were often beautiful and unforgettable events (Stroomann, 1960; Krayer, 1998).

His pupil, Hans Gremels who had obtained the chair in Marburg characterized his teacher as a great cordial genius who provided scientific aid very gently. Thereby he succeeded in producing satisfaction by the own work and responsibility of his coworkers. He usually did not stimulate his assistants with a scientific theme but let them decide according to their own interests (Gremels, 1947). Taken together, it is not surprising that the Institute of Pharmacology was named after Walther Straub at the initiative of Wolfgang Forth (see below).

Since 1904 Walther Straub was married with Dagny, néeLee from Norway; the couple had two children,

Harald and Peter. Walther Straub died on October 22, 1944, in Bad Tölz.

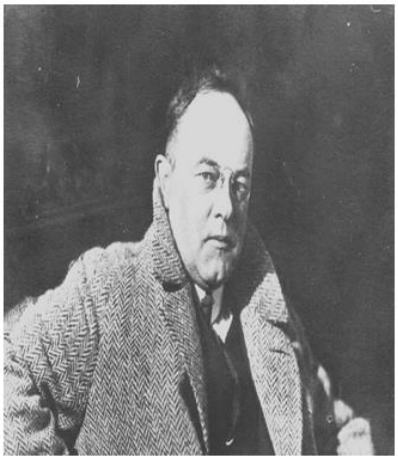

Figure 4: Walther Straub.

August Wilhelm Forst (1890-1981)

After Walther Straub's death, Dr. med August Wilhelm Forst **(Figure 5)** was commissioned by the authorities to lead the Institute in the position of an Assistant, since they refused to appoint him professor of pharmacology. Because of the Nuremberg Laws he was forbidden to give lectures. Justice was done in 1946 when Forst was promoted to full professor and director of the Institute of Pharmacology in Munich. However, his reign was a heap of rubble rather that a building for science and teaching, and it took more than a decade to provisionally repair parts of the building in Nussbaumstraße. 26. Until 1959, the old part of the institute at Nussbaumstraße 28 could be partly used, but the lecture hall that remained for 10 years without a roof could not be saved and was teared down in 1954. Finally, the institute at Nussbaumstraße 26 was reconstructed, simple but appropriate to resume scientific work. The institute at Nussbaumstraße 28 was not renovated and was later substituted by a modern building (Forth and Klimmek, 1994).

August Wilhelm Forst was born in Milano on June 10, 1890. He studied medicine from 1909-1914 in Heidelberg, Freiburg and München and achieved the degree of Dr.med. in 1914 with a thesis on congenital varicose veins. During WW I he served as a medical officer of the mountain regiment in Snowshoe Battalion and was awarded the Iron Cross 1st Class. Thereafter he continued his studies in chemistry und promoted to Dr.phil. under R. Willstätter in 1924 with a thesis on attempts to prepare beta-oxindole-propionic acid. Thereafter he became an assistant of Walther Straub and qualified as Lecturer in Pharmacology in 1928 with the thesis "On the detoxication of prussic acid" (Forst, 1928). Herein he showed that the toxic actions could be rapidly abolished by the intravenous injection of dioxyacetone followed by colloidal sulphur that was responsible for the biotransformation of cyanide to thiocyanate. Forst was engaged with the biological standardization of various drugs, including ergot alkaloids, active agents in the milk of Lactucavirosa, in the blossoms of Arnica montana, Humulus lupulus, and ofopioids. To quantify sedative effects and spontaneous activity Forst designed a suspended running plate (Kippteller) by which movements of

small rodents could be registered on a kymograph (Forst, 1938).

Besides, Forst wrote a comprehensive review on "Bismuth" (Forst, 1935). Finally, he wrote a review on "Detoxication Mechanisms". Unfortunately, the printing plates fell victim to the destruction by air raids shortly before the end of WW II (Forth and Klimmek, 1994). Forst, after having retired decided to write a completely new version that was published in 1966. "Entgiftung" is a German analogue to R.T. William's famous "Detoxication Mechanisms" (Forst, 1966).

Forst together with his secretary Gertrud Sachse saved most books of the library when the institute burned down, was very busy in reconstruction of the destroyed building and served as Dean of the Medical Faculty from 1946-1948 and as Senator of the Ludwig Maximilians University from 1946-1956. In 1951 he was elected as a member of the Bavarian Academy of Sciences. In 1964 he was awarded the honorary doctorate of the Veterinary Faculty of Munich. August Wilhelm Forst has retired in 1961 and passed away in Munich on August 4, 1981. He was married since 1925 with Caroline, née Weidert. The couple had one child, Dr.rer.nat. Dieter Forst.

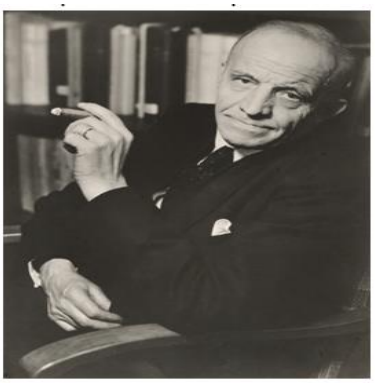

Figure 5: August Wilhelm Forst

Manfred Kiese (1910-1983)

Searching a suitable successor, the Medical Faculty favored a biochemically oriented pharmacologist and selected Manfred Kiese **(Figure 6),** a pupil of Wolfgang Heubner, first choice who headed the Institute of Pharmacology at Tübingen. He obtained the call in 1960 and accepted in 1961. He was accompanied with all assistants of Tübingen except one. Again, negotiations were extensive with regard of a new building that should be erected on the place of the first institute at Nussbaumstraße 28. On occasion of the topping-out ceremony Kiese pointed out in his speech: "*Pharmacology in Munich has suffered many decades from the first Institute that had been erected between 1891 und 1893. When Walther Straub took the chair in 1923, he complaint that the confusing construction plan was a source of constant worry and that the solidity of the building has prevented the justification of its pull down. Moreover, the special constriction by the later erected apartment houses does not allow the necessary enlargement of the complex" (Goerke, 1972). Kiese continued: "In fact there had been serious considerations during my appointment to*

muddle around through the old building that had been ruined by the air raids." Finally, in 1969 the new building could be occupied and the basement in Nussbaumstraße 26 was ready for remodeling. The main usable area of the new complex was around 4.500 m2 and the new lecture hall had a capacity of 420 seats. In addition, Kiese succeeded in his appointment negotiations to gather ample means for instrumental renewal and personal increase. Hence, the Institute of Pharmacology in Munich graduated to the top ones in Germany.

Manfred Kiese was born on June 28, 1910, in Stettin, now Poland, and studied Medicine at the Universities of Hamburg, Frankfurt, München and Berlin where he joined the Institute of Pharmacology (Wolfgang Heubner). In 1935 he was awarded the M.D. for pharmacological investigation of the smooth muscle of the lung, especially with some ephedrine-like substances. Between 1935 and 1937 he was an assistant at the Institute of Pharmacology and studied the oxygen consumption of dog's heart in relation of work and the influence of drugs. In 1937 he became a Rockefeller research fellow at the Department of Biochemical Chemistry, Harvard University (Albert Baird Hastings) studying properties of the carbonic anhydrase. After his return to Heubner's institute he continued the former studies and presented his Habilitation thesis on the effects of carbon dioxide on the isolated guinea-pig ileum, and its sensitivity to drug actions and on isolated enzymes. Probably owing to the beginning WW II he turned his attention to the acute and chronic toxicity of explosives, in particular their effects on blood, which led him to study the mechanisms of ferrihemoglobin formation and its enzymic reduction that was augmented by several dyes. In addition, he was interested in formation and properties of green hemoglobin derivatives (verdoglobins). These subjects found probably support due to war, since there were a lot of victims upon poisoning from explosives. Besides, Kiese collected the pertinent mostly Anglo-Saxon literature dealing with penicillin, a field he was not engaged experimentally. Most probably, the military authorities insisted in this topic to promote a German penicillin production because of the increasing wound infections that were no longer susceptible to the formerly used sulfonamides. Allegedly, this review of Kiese has been transmitted in 1943 to the allied Japan via a submarine by a coworker of the Japanese Ambassy (Kiese, 1943).

In 1945 the Berlin institute was evacuated to the Agricultural School at Kappeln, north of Kiel, where Kiese found shelter with other colleagues from destroyed institutes of the University of Kiel. He continued his studies and published a series of 10 papers showing how phenylhydroxylamine was able to produce many equivalents of ferrihemoglobin in red cells, but not in solutions of hemoglobin. The involved enzymes, responsible for catalytic cycling were analyzed what later became known as the "Kiese cycle". Lectures for students were held on ships which were provided by the British occupation force, since the regular halls were destroyed.

In 1950 Kiese was appointed as full Professor of Pharmacology and the Head of the Institute at the University of Marburg, followed by his appointment at Tübingen in 1956. During this period Kiese discovered first that aromatic amines were N-oxygenated in vivo by isolation of the corresponding nitroso compounds in the blood of dogs treated with arylamines. Formation of N-oxygenated aromatic amines were studied in isolated organs and microsomal fractions. When he became Director of the Institute of Pharmacology at the University of

Munich in 1961, Kiese's group extended studies on microsomal N- and C-oxidation of aromatic amines. Finally, he detected the unique property of 4-dimethylamino-phenol to produce rapidly, but only a defined fraction of ferrihemoglobin in vitro and in vivo that made this hit-and-run drug suitable as antidote in cyanide poisoning. Kiese is author of 200 scientific papers, and his monograph "Methemoglobinemia, a Comprehensive Treatise" is the standard work on this topic comprising 2600 references.

Manfred Kiese was a strict teacher for students and assistants, who relentlessly demanded conscientiousness, scientific honesty, and precise analytical thinking. I vividly remember his vehement combat of whitewashing when using the term "side effect" of a drug ("Neben¬wirkung") when an adverse effect was meant ("unerwünschte Wirkung").

Kiese impressed us by his extraordinarily broad scientific competence and experimental skills when he visited us on the bench almost daily and gave advice until his retirement in 1978.

On the contrary, Kiese refused working in committees, except for his short period as Dean in the Medical Faculty and rarely visited events of the faculty or university. Besides being an enthusiastic scientist, Kiese fatherly lent his ear to personal problems of his coworkers and gave wise advice.

Kiese retired in 1978 and died on February 22, 1983, in Munich. Since 1947 he was married to Edith, née Kunz who had passed 2 years before her husband. The couple had no own children. (For more details the reader is referred to Eyer, 2017b).

Figure 6: Manfred Kiese

Wolfgang Forth (1932-2009)

In 1980 Wolfgang Forth **(Figure 7)** from the Ruhr-University in Bochum followed the call as director of the Pharmacological Institute of the Ludwig Maximilians University in Munich. In contrast to his predecessors, he had been saved the experience of planning or restoring a new building but contended himself with planting magnolias in front of the Institute. Forth initiated the renaming of the Pharmacological Institute. On May 22, 1980, the

Council of the Medical Faculty agreed that – in the honor of Walther Straub – was renamed into Walther Straub Institute of Pharmacology and Toxicology.

Wolfgang Forth was born 1932 in Mannheim and studied medicine at the University of Heidelberg, where he was awarded the M.D. in 1958. The title of his thesis was: "A contribution to analysis of the centrally exciting actions of some sympathomimetic. After his Medical Approbation in 1960 he entered the Institute of Pharmacology and Toxicology of the University of the Saarland in Homburg (W. Rummel). Here, his attention was turned to the movement of ions and water across the membranes of reticulocytes and intestinal mucosa cells in which he studied the effects of laxatives and cardiac glycosides. For these studies he was awarded the Claude Bernard prize in 1966. In addition, his interests soon focused on the mechanisms of absorption of iron and chemically related metals in various segments of intestine, a scientific field for which he became best known. These studies led to his Habilitation thesis in 1967: "Studies on the intestinal absorption of iron and chemically related heavy metals in normal and anemic rats in vivo and in vitro. A contribution to the specificity of the mucosal iron-binding system." In 1974 Forth was appointed to the Professorship and Head of the Institute of Pharmacology and Toxicology at the University of Bochum, and in 1980 he became Director of the Institute of Pharmacology and Toxicology at the Ludwig Maximilians University of Munich, where Forth extended his studies to various metal-metal interactions during transports in the intestinal tract. Forth was author of numerous scientific papers dealing with a broad spectrum of pharmacological and toxicological subjects. In addition, Forth has addressed many therapeutic problems in essays of Deutsches Ärzteblatt, whereby he became known to a broad medicinal public. Finally, Forth was co-editor of *Pharmacology and Toxicology*, a textbook renown in German-speaking countries since 1975 that is meanwhile in its 13th edition, although with a changed team of editors.

Forth was member of many committees and contributed too many discussions in the Medical Faculty. He had particularly high historical interests and literary passions, resulting in separate contributions such as in an Addendum "Building and Men"(Forth and Klimmek, 1994) or "Men and Fugi" (Forth et al. 1997). In fact, he has told us that he had flirted at young age of becoming a journalist.

Wolfgang Forth retired in the year 2000 and passed away on April 12, 2009 in Munich. He was married with Dagmar, néevon Blomberg since 1959. The couple has two sons and two daughters. (For more details the reader is referred to Eyer, 2017a).

Figure 7: Wolfgang Forthamines.

Peter Eyer (1942-)

Although the appointment committee advertised the professorship early in 1998 a vacancy ensued with the retirement of Wolfgang Forth, because the first appointment negotiations were unsuccessful. In the meantime, I had been entrusted with the management of the chair, which unexpectedly dragged on for several years and was stressful for all coworkers.

I had been the head of the department of Biochemical Toxicology and at that time mainly engaged to improve the treatment of organophosphate poisoning. In trying so, we analyzed the kinetic data of the single reactions involved, which allowed in silico simulations, validation in experimental models und finally testing of antidotal strategies in poisoned patients in several clinical studies.

Figure 8: Peter Eyer

Born on June 6, 1942, in Munich **(Figure 8)** I studied medicine in Munich and Freiburg and awarded the medical doctor in 1968 in the group of Dirk Pette with an enzymological thesis: “Purification and properties of glucose-1-phosphate-kinase”. After my medical approbation in 1970 I was allowed to join Kiese’s group that was busy in searching methemoglobin-forming aminophenols as antidote against cyanide poisoning, of which 4-dimethylaminophenol was particularly useful in that

it forms very rapidly methemoglobin to complex cyanide. The particular advantage of this antidote was caused by its hit-and-run kinetics, i.e. methemoglobin formation was complete within a few minutes and stopped rapidly at a given level. My task was to unravel the underlying mechanisms. It turned out that 4-dimethylaminophenol is co-oxidized by oxyhemoglobin to yield a phenoxyl radical that in turnoxidizes ferrohemoglobin to methemoglobin and is reduced back to the parent aminophenol. The catalytic cycle is terminated by disproportionation of the radical giving rise of the quinonimine that rapidly reacts with sulfhydryl groups of hemoglobin or glutathione within red cells. With part of these studies, I've got my Habilitation in 1976 on "Biotransformation and actions of 4-dimethylaminophenol".

Studies of various quinonimines and differently substituted nitrosoarenes with sulfhydryls revealed a variety of reaction pathways hitherto unknown in chemical literature but of major toxicological importance. I've got the tenure professorship (C-2) in 1980 and (C-3) in 1998 at the same institute and headed the Walther Straub Institute temporarily from the year 2000 until my retirement in 2007. (For more details the reader is referred to Eyer, 2014)

During this interregnum several structural problems arose: Early in the 1990s it was stated that the Walther Straub Institute did not meet the fire protection requirements, particularly of the new building that had been erected only some 25 years before. Moreover, the retirement of Forth gave the opportunity to reconsider the future focus of the chair. The majority of the Medical Faculty felt it appropriate that the chair was more intensely aimed at pharmacological issues and less in toxicological ones as in the last decades. In addition, the chair should be personally and consequently spatially reduced. To this end, the chair was considered to move to a floor in the newly built Department of Chemistry and Pharmacy in Munich-Großhadern. This premature plan was impracticable, because several facilities were lacking, e.g., housings for experimental animals, controlled area for working with isotopes and isotope storage facilities. In addition, the main usable area was less than 1/5 of the former. This "offer" deterred the first candidate and further negotiations were stopped. Next, there were plans to install a toxicological dependency at the old place in the heart of the city. Such a gap of 10 km would be impracticable to maintain a vivid corporate identity and was inacceptable for a presumptive successor.

Finally, the faculty agreed to establish the Walther Straub Institute in the completely renewed building of the former Institute of Physiological Chemistry in Goethestraße33 that had moved to the campus of the Biomedical Center in Martinsried/Munich. In turn the Institute of Legal Medicine should be situated in the renewed building at Nussbaumstraße, where a toxicological department of the Walter Straub Institute was hosted. The necessary renovation work was possible, and the staff of the Walther Straub Institute moved into the building at Goethestraße.

New negotiations with an additional candidate dragged on because drastic austerity programs of the Bavarian government led to personnel cuts. Of course, a vacant chair is particularly helpless and target of many desires. Reduced staff at high teaching commitments made the chair increasingly less attractive. Finally, the management of Ludwig Maximilians University and the active support by the Medical Dean, Dietrich Reinhard, succeeded in a third round of appointment negotiations and could

convince Thomas Gudermann from Philipps University Marburg to accept. On May 1st, 2008 Prof. Dr.med. Thomas Gudermann took over the chair. (For details see Eyer &Gudermann 2011).

Thomas Gudermann(1960-)

Born on December 7, 1960, in Lippstadt/Westfalen, Gudermann **(Figure 9)** studied medicine in Münster and Ber Sheba, Israel and awarded the medical doctor in 1989 with an experimental endocrinological work under Eberhard Nieschlag in Münster. After his Habilitation in 1998 in the Institute of Pharmacology at the FU in Berlin (Günter Schulz) on signal transduction of glycoprotein hormone receptors he accepted the appointment of full professorship at the Pharmacological Institute of the Philipps University Marburg. After having obtained the chair in Munich, Gudermann started the conceptual, instrumental and personnel reorganization of the institute, which comprises 17 working groups lead by 7 professors and 3 lecturers. More details are found on the home page of the institute.

Figure 9: Thomas Gudermann

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Oswald Schmiedeberg (1838-1921)

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Oswald Schmiedeberg was born September 29, 1838, as a son of a forester in a small place in Courland, one of the former Baltic provinces of Russia. After visiting the Gymnasium in Dorpat (today Tartu) he studied during 1860 and 1866 medicine at the University of Dorpat. During this time, he became interested in Pharmacology and became a student of Buchheim at the Institute of Pharmacology. After completing his MD thesis (Quantitative measurement and fate of chloroform in the blood) he joined the institute as a scientific assistant. In 1867 he became Privat Dozent, and in 1969 außerordentlicher Professor. During 1869 he visited the physiologist Carl Ludwig at the University of Leipzig to acquire specific experimental tools like the Kymograph and the isolated frog heart, which have not been available in Dorpat. When Buchheim moved to the University Gießen 1871 he was appointed as his successor in Dorpat.

Figure 10: Oswald Schmiedeberg.

Buchheim when studying medicine at the University of Leipzig translated Jonathan Pereira's "The Elements of Materia Medica and Therapeutics" Buchheim revised its content, omitted drugs which he considered to be ineffective, replaced them by others, and tried to give a rationale for therapy. Last but not least by his experimental work for his MD thesis in the Institute of the Physiologist Ernst-Heinrich Weber in Leipzig he realized that there is an urgent need to justify the use of drugs by experimental studies and added a specific chapter"Mode of Action" on drugs in which he described those drugs which have been investigated experimentally to understand the pharmacological effects.This task took him 4 years and in addition with other editorial work and publications1908 (Archive of DGPT)made him well known and on the recommendation of the physiologist Friedrich Bidder, dean of the faculty, 2 years after completing his MD thesis he became chair of Materia Medica, Dietetics and History and Encyclopedia of Medicine at the University of Dorpat in 1847. There he started his experimental pharmacological work in the basement of his own house and in 1860 moved into the newly built Institute of Pharmacology with sufficient facilities for experimental research.

Buchheim has not achieved a specific major discovery but his introduction of experimental studies to explore the effects of compounds led to an improvement of the understanding of pharmacological effects.

After Buchheim left for Gießen Schmiedeberg continued the experimental research. His major achievement between 1871 and 1872 has been the identification of muscarine as the stimulant of the nervus vagus and its antidote atropine. This work published with Koppe presented for the first time? a specific antidote, which has been evaluated in animal experiments suitable for clinical application.

During these years Bernhard Naunyn (1839-1925) moved from Berlin to Dorpat as director of the university clinic of internal medicine, which was the begin of a life-long cooperation and friendship between Naunyn and Schmiedeberg.

In 1872 Schmiedeberg became director of the Institute of pharmacologyof the newly founded Kaiser-Wilhelm University in Strasbourg, which after the French-German war 1870/1871 has been founded in the newly established German province Elsass-Lothringen. It was well equipped with financial resources and had the opportunity to recruit

promising scientists from the German speaking parts of Europe.

Together with Schmiedeberg other renown professors have been appointed: the professor of anatomy Heinrich Wilhelm Waldeyer (1845-1921) who described the lymphatic Rachenring, the physiologist Friedrich Goltz (1834-1902), Felix Hoppe-Seyler (1825-1895) one of the founders of biochemistry and the Zeitschrift für physiologischeChemie, later Hoppe-Seylers Zeitschrift für physiologischeChemie, and the pathologist Friedrich Daniel von Recklinghausen (1833–1910), who described the osteodystrophia fibrosa generalisata cystica, a consequence of hyperparathyreoidism and the neurofibromatosis type 1. In 1888 Naunyn joined from Königsberg and both friends cooperated in Strasbourg until Naunyn retired in 1904 und moved to Baden-Baden.

Schmiedeberg has been the youngest of these in 1872 appointed professors and held this position over 42 years until 1919, when all in Elsass-Lothringen living Germans had to leave. At that time, he was the last of the 1872 appointed professors of the medical faculty of the Kaiser Wilhelm Universität.

During the first years in Strasbourg Schmiedeberg's experimental facilities in the former Faculté de Médicinehave been limited until he moved 1887 to the spacious new institute, which he had planned together with the architect Otto Warth (1845–1918).

Research in Strasbourg included hypnotic effects of urea derivatives and paraldehyde, the action of digitalis on the heart muscle, nicotine as blocker of cardiac vagal ganglia, central and peripheral effects of caffeine, toxicity of heavy metals and their organic complexes, formation of hippuric acid in the kidney and of urea in the liver, detoxication of various organic compounds by forming conjugates with glucuronic acid.

During his time in Strasbourg, Schmiedeberg had about 120 pupils from twenty different countries. Because his advice to faculties was highly appreciated, he helped many of them to acquire good positions. About 40 of them occupied pharmacology chairs throughout the world.

On the occasion of his 70th birthday in 1908 many of his previous pupils, who are presented in the group picture assembled at Strasbourg. Apart from German pharmacologists like Wolfgang Heubner (at that time in Göttingen, later in Heidelberg and Berlin) and clinicians like Oscar Mikowski (professor of medicine in Breslau) many nationalities had come to Strasbourg, as the professors of Pharmacology Cloetta (Zurich), Wallace (New York), Lindemann (Kiev); Herlant (toxicologist at Brussels), Cervello (Palermo), Hofmeister (Prague), Kobert (Dorpat and Rostock), Cushny (at that time in London), and Hans Horst Meyer (Vienna).

Figure 11: Schmiedeberg at his 70th birthday (October 11, 1908) together with his pupils and friends in Strasbourg (Archive of DGPT).

A prominent American pharmacologist, who worked in Schmiedebergs laboratory spent seven years in Germany to complete his pharmacological education was John Jacob Abel (1857-1938). He was borne in Ohio and also worked with Ludwig and Boehm. Returning to America in 1891 on the recommendation of Schmiedeberg, he became the first Professor of Pharmacology at Ann Arbor (University of Michigan) and moved to John Hopkins 2 years later. Working in the laboratory until the age of 80 he had an enormous methodological spectrum and experience, which he conferred to his pupils. His major work has been the purification of adrenaline, pituitary hormones and insulin. In 1909 Abel, 36 years after the Archiv für experimentellePathologie und Pharmakologie, founded the Journal of Pharmacology and Experimental Therapeutics. He has been called the father of the American pharmacology.

Abel's successor in Ann Arbor has been Arthur Robertson Cushny (1866-1926). Born at Fochabers near Elgin, Scottland, he received his medical education in Aberdeen. With a Thompson Fellowship he went to Bern for a year to be trained in physiology by Kronecker (1839-1914). Then he entered Schmiedeberg's department, where after one year, he was appointed to one of the precious assistant positions. After three years in Strasbourg and on Schmiedeberg's recommendation he became the successor of Abel at the pharmacology chair at Ann Arbor. After twelve years he returned to Britain to occupy the newly created chair at University College, London, and in 1920 he went to Edinburgh. He is known for his digitalis studies and for his equally famous work on kidney functions. Cushny published

an extremely successful Textbook of Pharmacology which, after eight editions in his lifetime, was continued by later editors.

Hans Horst Meyer (1853-1939) may have had the greatest impact on pharmacology of Schmiedeberg's pupils. He was born in Insterburg, East Prussia, studied medicine in Königsberg, Leipzig and Berlin and after his promotion to Doctor of Medicine in Königsberg he joined Schmiedeberg's institute in Strasbourg.In 1881 he was appointed to the chair of pharmacology in Dorpat, went to Marburg and finally to Vienna where he stayed until his death. Together with Schmiedeberg he discovered glucuronic acid as the most important rection partner of drugs. He also described the relationship between the lipophilicity of general anesthetics and their potency. A year later Charles Ernest Overton (1865-1933) came to the same conclusion and this correlation became known as the Meyer-Overton hypothesis. Meyer was also one of the founding members of the German Pharmacological Society in 1920. Four of his pupils won the Nobel Prize: George Hoyt Whipple (1934), Otto Loewi (1936), Corneille Heymans (1938), and Carl Ferdinand Cori (1947). Schmiedeberg himself has been nominated repeatedly.

One of his pupils, Otto Loewi (1873-1961), has spent eleven years with Meyer, seven in Marburg and four in Vienna, before he accepted the chair of pharmacology at Graz University. Being Jewish, after the German Anschluss he was forced to leave Austria and eventually immigrated in 1940 to the US, where he had a position as a professor of pharmacology at the New York University. There he worked with George Wallace, a former pupil of Schmiedeberg.

Visiting the Institute of Pharmacology at the University of Graz I found a note of Albert Einstein, living in Princeton, to Otto Loewi's 80th birthday in 1953, which he had to celebrate in New York City:

Heute wünschen wir, dass Du froh und in Seelenruhe diesen Tag begehst und die künftigen. Denn man lernt in der langen Zeit, sich nicht mehr zu giften über die Thorheiten der Anderen, und sich mit Humor abzufinden mit den eigenen.	Today we wish you to celebrate, happy and peaceful, This and many upcoming days, Because one learns over the long journey Not to be bothered by alien foolishness And with humor to tolerate our own.

In 1873 Schmiedeberg, together with the pathologist Klebs (Prague) and the clinician Naunyn (Königsberg) founded the Archiv für experimentelle Pathologie und Pharmakologie. When Naunyn died in 1925, the periodical was named Naunyn-Schmiedeberg's Archiv, from volume 110 onwards. In 1969 the designation 'experimental pathology' was dropped, since nearly all papers submitted dealt with pharmacology.

In 1883 Schmiedeberg publishedthe Grundriss der Arzneimittellehre, latereditshadthe title Grundriss der Pharmakologie in Bezug auf Arzneimittellehre und Toxikologie. Holmstedt & Liljestrand's (1963) History of Pharmacology and Toxicology noted, 'Schmiedeberg was undoubtedly the most prominent pharmacologist of his time'. He had about 120 pupils, about 40 of them occupied pharmacology chairs throughout the world. In the US John Jacob Abel

after his return to the US became the "father of American Pharmacology".

Wolfgang Heubner, who worked in the Strasbourg institute between 1903 and 1908, published an interesting description of Schmiedeberg's persona (Heubner 1956) of which parts are presented:

"To me his persona was imposing and absolutely original. He was of medium stature, had full grey hair, a roundly cut full beard and a rather broad round nose. His gait was like heaving, much as that of a mariner's at seaside. His speech had an unsullied Baltic accent, refreshed yearly during his summer vacations. For my eight years with him, Schmiedeberg's clothing remained the same; he wore a grey suit with long coattails and a flat grey cravat around his white turn-down collar. His hat was a black Italian "Borsalino" with a rather broad brim. Before wearing it he pressed a longitudinal fold along, but after putting it on his head he pulled it down with both hands so that the nice fold bulged up and this hat enthroned more like a pot on his crown.He made extensive use of his university vacations. In early March he always went to Italy, returning by end of April. Early in August he travelled to his Baltic homeland, showing up in Strasbourg only by the end of October. During nice days at his Baltic home he went fishing or hunting, while on bad weather he sat at his desk finding pleasure and concentration in his scientific work."

In 1919 all Germans living in Elsass-Lothringen had to leave the newly established French Department, losing all their private possessions. When Schmiedeberg stood before the railway station waiting for his transport back to Germany Albert Schweitzer saw him standing there with a wrapped package under his arm. Asking whether he could be of help to transfer his furniture to Germany Schmiedeberg only asked him to take the package and try to safely send it to his new address in Baden-Baden. It was the manuscript of his last paper and he feared that it might be confiscated before entering the train. Schweitzer took it, and later on transferred it safely to Schmiedeberg, since then living in Baden-Baden. Oswald Schmiedeberg died on 12 July 1921 in Baden-Baden.

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History of toxicology of the Technical University of Munich (TUM)

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The department of (clinical) Toxicology

Toxicology at the TUM is mainly associated with the Faculty of Medicine at the Klinikumrechts der Isar (KrI). Before the Klinikum became part of the TUM the clinician Max von Clarmann founded the department of (clinical) Toxicology within the II. Clinic of Internal Medicine in 1963. His successors, the Professors Thomas Zilker and Florian Eyer further developed this department to an internationally renowned institution contributing a great number of publications on the identification and treatment of intoxications. Among them are intoxications by organophosphates, mushrooms, cyanide and cyanide via smoke inhalation in fire, colchicine, drug abuse, lithium, alcohol and their treatment and the development and evaluation of new treatment schedules.

Max von Clarmann (1928-2006)

Max von Clarmann was born April 29, 1928. After a 2 years nursing practice at the KrI he studied medicine at the Ludwig Maximilians Universität (LMU) in Munich until 1952. Since then, he continuously has been affiliated with the KrI. Since 1955 he became interested in intoxications and their treatment and his engagement over years became acknowledged by the Klinikum resulting in the foundation of a Dept. of Clinical Toxicology, headed by Max von Clarmann. Under his very effective guidance the department grew rapidly focusing on treatment of intoxications, development of analytical methods and finally establishing a poison information center. The acquirement of simple analytical methods has been considered of great importance to allow a rapid dentification of the poison, which he conceded crucial for the necessary therapeutic measures. Max von Clarmann died in Munich on June 20, 2006.

Figure 12: Max von Clarmann.

The Institutes of Toxicology and of Toxicology and Environmental Hygiene

In 1967 the KrI became the TUM faculty of medicine with the Institute of Pharmacology and Toxicology founded in 1968. Prof. Melchior Reiter the director, formerly Institute of Pharmacology of the Ludwig Maximilian University (LMU), has been interested in mechanisms of glycosides with some activities on

heavy metal toxicity, especially the metabolism of mercury and its organic compounds.

Melchior Reiter (1919-2007)

Melchior Reiter, born in Berlin 1919, studied medicine in Berlin, and in 1944 received his M.D. at the Berlin Institute of Pharmacology of Prof. W. Heubner. Shortly after WW II he received a grant to join Otto Krayer's Institute of Pharmacology at the Boston Medical School. Krayer left Germany in 1933 after he had declined the departmental chair position at the University of Düsseldorf of Philipp Ellinger, who had been removed from the chair on racial grounds. Back in Germany, Reiter received the position of an assistant of the LMU Institute of Pharmacology in Munich, starting his research on the mechanism of amanitin intoxication, published in the Festschrift of W. Heubner's 75th birthday together with Otto Wieland and Hans Georg Fischer. Between 1970 and 1987 he chaired the Dpt. of Pharmacology of the Gesellschaft für Strahlen- und Umweltforschung (GSF) near Munich. 1979 to 1981 he was Dean of the TUM Faculty of Medicine.

Reiter once reported an interesting event during the year before WW II. In 1938 he served as a mountain infantryman of the German army in Berchtesgaden near the Austrian border. When the German army has been ordered to enter Austria, his unit marching from Berchtesgaden uphill to the Austrian border was not so sure whether they will be welcome. Arriving at the border it was their great relief that they have been welcome with music, and behind the musicians happily marched downhill to the Austrian city Hallein.

In 1970 Reiter together with Prof. Friedhelm Korte, Director of the Institute of Ecological Chemistry at the TUM inWeihenstephan proposed the foundation of a working group of Toxicology at the GSF. Prof. Gerhard Lange, also from the LMU Institute of Pharmacology has been appointed as director. Research focused on neurotoxicity and aquatic toxicity, toxicity of of heavy metals and organic pollutants, as well as metabolism and hepatoxicity of persistent chemicals such as polychlorinated biphenyls. After the unexpected death Gerhard Lange in 1973 the development of the group stagnated until Helmut Greim from the University of Tübingen has been appointed as director in 1975. Melchior Reiter died in Prien am Chiemsee on February 18, 2007.

Figure 13: Melchior Reiteralso

Helmut Greim (1935-)

Helmut Greim, born May 9, 1935, in Berlin, studied Medicine at the University of Freiburg and the Free University of Berlin. Based on his experimental work on the digestion of infants with diarrhea he received his MD in 1962, and thereafter joined the research group of Prof. Herbert Remmer at the Institute of Pharmacology (director Prof. Hans Herken) of the Free University. When Remmer in 1970 became Director of the Institute of Toxicology, University of Tübingen, Greim followed him receiving the position of an assistant at the institute. There he continued his research on cytochrome P450 and in 1970 after determining the half-lives of at that time only known two P450 enzymes received his habilitation. Thereafter he accepted the position of a visiting Research Associate Professor at the Department of Pathology, Mount Sinai

School of Medicine of the City University of New York (Chair and Dean Dr. Hans Popper). During this time, he also held the position of Visiting Fellow of Pharmacology at the Yale School of Medicine New Haven, Connecticut. Research at Mount Sinai focused on P450 mediated metabolism of bile salts during cholestasis, of carcinogens and mutagens and the introduction of Phase I metabolic activity into the Ames test. These research activities continued in Tübingen after Greim's return to the institute in 1973. After Greim became director of the GSF toxicology in 1975 the group expanded rapidly and became an Institute in 1978. In 1988 the institute moved into the new and spacy well-equipped building.

Research focused on developing and standardizing in vitro test methods including characterization of metabolizing enzymes of commonly in toxicology used cell lines, establishing rat hepatocytes and V79 cells with competent metabolizing capacity to investigate cytotoxicity, genotoxicity, DNA repair of chemicals.

Studies on mechanism of carcinogenesis and mutagenesis included intercellular communication, cell proliferation and apoptosis, and to extrapolate results from animal studies to humans physiological based pharmacokinetic (PBPK) models have been developed and applied for many carcinogens. Toxicology of metals included molecular mechanisms of copper exposure of infants and biomonitoring of mercury after removal of amalgam fillings.

Participation in the "reactive oxygen club" organized by Prof. E. Elstner, Institute of Biology und Microbiology of the TUM improved the understanding of consequences of inflammation resulting in the reactive oxygen species during inflammation and cytotoxicity.

Together with the toxicologist Frederick Coulston, Albany Medical College, the institute became responsible for the research activities at the former NASA facility in Alamogordo, New Mexico, which kept monkeys and Apes for research purposes. From the German side this has been supported by the Federal Ministry of Research and Development. There, several studies on dioxins in rhesus monkeys have been conducted and on the metabolism of bile acids in apes. After end of these activities several members of the GSF institute of toxicology stayed in the US and received positions at the Institute of Toxicology, Kansas City University. One of them, Dr. Karl Rozman, became member of the US TLV (threshold limit values) committee of the American Conference of Governmental Industrial Hygienists

(ACGIH) and served as liaison-officer between the MAK Commission and the TLV committee.

In 1987 Greim became director of the newly founded Institute of Toxicology and Environmental Hygiene of the TUM. This further expanded research and teaching activities in toxicology for medical students but also for students of chemistry at both Munich universities. By assistance of the president of the TUM Prof. Wolfgang Hermann and the vice-president Prof. Ernst Bayer, both chemists, lectures in toxicology for students in chemistry became mandatory for students of chemistry at German universities.

Greim retired in 2003 and his successor Prof. Dr. Martin Göttlicher became director of both, the TUM Institute of Toxicology and Environmental Hygiene and the GSF Institute of Toxicology, now Helmholtz-Institute of Molecular Toxicology and Pharmacology, specifically investigating molecular mechanisms of bioactive chemicals with the specific aim to develop effective and safe drugs.

In the institutes of Food Chemistry and Analytical Food Chemistry of the TUM School of Life Sciences in Weihenstephan phytotoxins are identified and evaluated regarding their relevance for food safety. Xxxxx

Figure 14: Helmut Greim.

Training courses in Toxicology

Starting in 1975 a postgraduate training program in toxicology has been established by the GSF institute, which since 1980 comprised courses of the 15 major areas of toxicology. These courses are organized on behalf of the German Society of Toxicology and are held in the Munich institutes and competent centers in Germany. They provide the knowledge necessary to finally receive the title "Certified Toxicologist" by the German Society of Toxicology. This title also meets specific requirements in education as well as professional skills and experience for the title "European Registered Toxicologist" (ERT). At present, more than 600 postgraduate students are enrolled to attend the now 17 different courses, which presently are organized by the TUM institute.

Participation in scientific advisory committees

Due to their broad competence in toxicology and risk assessment members of the institute chaired or participated in scientific advisory committees. These include the "MAK Committee" (Senate Commission for the Investigation of Health Hazards of Chemical

Compounds in the Work Area, a permanent commission of the German Research Foundation), the Advisory Committee on Existing Chemicals (BUA), a committee of the Society of German Chemists (GDCH), of both, the scientific secretariates have been in the GSF and TUM institute. Participation in other committees has been the Scientific Committee of Health and Environmental Risks (SCHER) and the Scientific Committee of Occupational Exposure Limits (SCOEL) of the European Commission and the Risk Assessment Committee (RAC) of the European Chemicals Agency (ECHA).

General Discussion

The president of DGP Roland Seifert, who also manages the archive of DGPT asked the audience, if somebody possess important historical material in connection to DGPT to send it to him. Athineos Philippu has promised the entire archive of the six volumes of his book “Geschichte und Wirken der pharmakologischen,klinisch-pharmakologischen undtoxikologischen Institute im deutschsprachigen Raum" consisting of more than 250 hanging folders and 50 gigabytes.

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