

50 YEARS OF CLINICAL PHARMACOLOGY IN FINLAND

Improving Rational Pharmacotherapy –
50 Years of Clinical Pharmacology in Finland

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50 years ago, Finland was really at the forefront in the development of clinical pharmacology, not only in the Nordic countries but even in the mainland of Europe!

In Finland, the first signs of clinically-oriented perspectives within pharmacology might have been perceptible after the Second World War, possibly reflecting discussions going on in Sweden where the theme had already triggered medical interest. However, clinical pharmacology really took off not until as in the early 1960s when some respected pioneers put this concept firmly on the academic agenda. Thus, the 1960s were the first real decade when we can see the start of Finnish clinical pharmacology.

There were several reasons why it was important to move pharmacology into a clinical direction. There were many new drug innovations, the public became concerned about drug safety and the drug industry required clinically-orientated pharmacologists. Pioneers such as Pentti Peltola, Esko Iisalo and Mauri Mattila imported new ideas from England and Sweden (1965–1968), where modern concepts of therapeutics and drug treatment had already gained academic interest and even some clinical acceptance. There were also other pioneers in clinical pharmacology at that time – e.g. Olli Mustala, Olli Penttilä, Seppo Takki, Pertti Torsti.

1968 WAS THE START POINT OF CLINICAL PHARMACOLOGY IN FINLAND

In the 1960s, there were only four full professorships in pharmacology in Finland: in the Universities of Helsinki, Turku, Oulu and the Veterinary High School of Helsinki. *The first chair in clinical pharmacology* in Europe, outside the UK, was established in Finland, in the University of Helsinki in **1.9.1968**. After the post was advertised, a total of five experienced clinical pharmacologists applied for the professorship: Docent Esko Iisalo, Associate Professor Mauri Mattita, Dr. Olli Mustala, Docent Pentti Peltola and Docent Pertti Torsti. Four of the applicants were also internists. The expert statements about their competence were sought from Arvid Carlsson (Göteborg), Leon Goldberg (Atlanta), Jens

Schou (Copenhagen) and Armas Vartiainen (Helsinki). The expert statements were obtained in autumn 1970. Subsequently, three of the applicants withdrew their applications.

An intense competition occurred between the two top candidates, Mauri Mattila and Pentti Peltola. Finally, in 1971, President Kekkonen appointed Peltola as the first Professor of Clinical Pharmacology. A couple of years later Mattila was appointed as Extraordinary Professor in the University of Helsinki († 2005). He worked in the Department of (Basic) Pharmacology but contributed extensively to clinical pharmacology.

In Nordic Countries, the Department of Pharmacotherapeutics was established in Norway (Oslo) as early as 1964, whereas the next professorships in clinical pharmacology were created in Sweden 1970 (Linköping) and in Denmark the first professor started 1973 in Copenhagen. Even in the mainland of Europe, Finland was really at the forefront in the development of clinical pharmacology,

PROGRESS OF CLINICAL PHARMACOLOGY IN FINLAND

Helsinki

In reality, clinical pharmacology did not thrive until early in the 1970s, when Peltola was appointed to the professorship

Although most of the first clinical pharmacologists were clinicians, the interest of other clinicians was limited. In fact, the official status of clinical pharmacology was not definitively clarified in the administration of the University Hospital. During the next few years, however, the atmosphere started to change slowly. When the Sixth International Congress of Pharmacology was held in Helsinki in 1975, many symposia, and one of the six proceedings books of Congress Proceedings, were devoted to clinical pharmacology. Therefore, even at that time, clinical pharmacology was considered as important not only by the world's pharmacologists but probably also by other medical disciplines.

Initially, the Department of Clinical Pharmacology had only a couple offices and laboratories. Around the middle of the 1970s, it was able to secure more laboratory space and even offices in another building near to the University Central Hospital.

Peltola retired in 1985 († 1987). Once again, there was an intense competition between the two top candidates, Markku Linnoila and Pertti Neuvonen, for the professor's chair in Helsinki. Ultimately, President Koivisto appointed Linnoila as Professor of Clinical Pharmacology in 1988. Linnoila was an eminent scientist who had investigated the effects of alcohol on the brain while working in the US († 1998 – only 50-years old). He did not really perform the duties linked with the professorship and finally resigned from the position in 1991. During Linnoila's absence in the United States, Professor Mauri Mattila acted as Professor of Clinical Pharmacology for more than three years. In 1992, the Medical Faculty invited Pertti Neuvonen, who at that time was Professor of (Basic) Pharmacology in Turku, to take up the Professorship of Clinical Pharmacology in Helsinki. He retired in 2011 but is still working actively. Nowadays there are two Professors in the Unit of Clinical Pharmacology in Helsinki: Janne Backman is Professor of Clinical Pharmacology and Individual Medicine, and Mikko Niemi is the Professor of Pharmacogenetics.

The Department of Clinical Pharmacology and its laboratories have been always housed in the Meilahti campus. Nowadays its offices and laboratories are located in the Biomedicum Helsinki building of the University near to the main building of the University Central Hospital. The Unit has cooperated actively with the clinical laboratory HUSLAB and also with the National Poison Information Center.

Turku

In the University of Turku, internist and pharmacologist Esko Iisalo had been appointed Docent of Clinical Pharmacology as early as 1964. However, the professor's chair was not established in Turku until 1983, almost two decades after it was first proposed that the university should create a chair in clinical pharmacology. When the position was advertised, seven pharmacologists applied for the professorship: Esko Iisalo, Jussi Kanto, Pauli Luoma, Pertti Neuvonen, Erkkä Syvälahti, Heikki Vapaatalo and Pauli Ylitalo. Four of the applicants were physicians who had specialized in clinical pharmacology, and three of them had even another clinical specialty. The expert statements evaluating their competence were sought from the professors of clinical pharmacology in the Nordic countries: Eigill Hvidberg (Copenhagen), Per Knut M. Lunde (Oslo) and Folke Sjöqvist (Stockholm). The common statement of the experts was not received until 1985, and they ranked Iisalo as the most competent applicant. Accordingly in 1986, President Koivisto appointed Esko Iisalo as the first Professor of Clinical Pharmacology in Turku.

Esko Iisalo retired in 1993, and thereafter Mika Scheinin continued as the Professor of Clinical Pharmacology from 1995 until 2004; Risto Huupponen was appointed as Professor of Clinical Pharmacology and Therapeutics in 2007 and he retired 2018.

In Turku, clinical pharmacology has some offices and undertakes clinical activities in the University Hospital. Nowadays, clinical pharmacology is an important component of the integrated Department of Pharmacology, Drug Development and Therapeutics. Cooperation with "basic" pharmacology has been a feature of this department; in this century its research activities have become even more intensive as it has very close links with Clinical Trial and PET Centers in Turku.

Tampere

In Tampere, the medical faculty was established in 1972, and the education in pharmacology started in 1974. The sole Professor in Pharmacology, Heikki Vapaatalo, with the contribution of his chief assistant, was responsible for the activities surrounding clinical pharmacology. After intense lobbying, in the spring of 1987, three pharmaceutical companies, Tamro, Star and Rohto, donated sufficient funds to allow the University to create a professorship in the field of clinical pharmacology and toxicology; the initial funding was for a five-year period. The University promised eagerly to take care of the expenses after this five-year period. Although the University had now the finances to fund the appointment for the next five years, some academic intrigue led to the position being omitted from the University's preference list, even after the list had already been officially accepted and submitted to the Finnish Government. This omission occurred not once but twice, in the years 1988 and 1989. Fortunately, Professor Vapaatalo and the team contacted several eminent Members of Parliament and were successful in ensuring that the chair was funded in the Government's budget list. Thus, the chair was finally established in 1989.

Nine candidates applied for the professorship, and in 1992 President Koivisto appointed Pauli Ylitalo as Tampere University's first Professor of Clinical Pharmacology and Toxicology. After him, Kari Kivistö was appointed in 2007 but resigned in 2013. Today, there is no Professor's chair in Tampere. Instead, the Professor of (Basic) Pharmacology, Eeva Moilanen, and her team have the responsibility for dealing with clinical pharmacology. Professor Reijo Laaksonen, who is a qualified clinical pharmacologist, is responsible for the specialization education of physicians in clinical pharmacology and pharmacotherapy.

In Tampere, clinical pharmacology was a part of the Department of Pharmacological Sciences. From the early nineties up until the last decade, it had also an office and laboratory room(s) in the University Hospital for clinical drug measurements and in training physicians in this specialization. In the 1990s, there were even clinical trial services conducted in the "Tampere Clinical Trial Center" (TCTC) which later was transferred from the University to the hospital district.

Kuopio

In Kuopio, education of medical students started in 1972 followed one year later with an intake of students of pharmacy. Even before the actual education was started, it was planned to establish a Professorship in Clinical Pharmacology, since this office was deemed necessary if the university wished to teach students details of practical pharmacology, pharmacotherapy and drug treatment. However, this professor's chair did not actually come to fruition until 2005, when Risto Huupponen was appointed!

In the earlier decades, the Professor of (Basic) Pharmacology and some docents were responsible for clinical pharmacology education, except for the 1980s and early 1990s; during that time, Pauli Ylitalo, who was Professor of Toxicology and Pharmacokinetics in Kuopio, was also competent clinical pharmacologist and took care of its education. The first actual professor in clinical pharmacology and therapeutics, Huupponen was appointed to the professorship in 2007; after him Tapani Keränen, a physician with specializations in neurology and clinical pharmacology, was appointed Professor from 2009 to 2013. The Professor's chair and facilities were located within the Department of Pharmacology and Toxicology. At the present time, there is no Professor of Clinical Pharmacology in Kuopio, instead, the Professor of Pharmacology, Hannu Raunio, is responsible for the education in clinical pharmacology.

Oulu

The Medical Faculty in University of Oulu is the only one in Finland, in which there has never been a full-time professorship in clinical pharmacology. Nonetheless, the Department of Pharmacology and Toxicology was analysing drugs, hormones and toxins in clinical samples sent from hospitals already in the 1960s. Moreover, the Department provides courses in clinical pharmacology for medical students and it participates in many of the clinical drug trials being conducted in the University Hospital district.

Presently, the University has a Docent in Clinical Pharmacology, and thus it has the necessary qualifications to begin the training of physician specialization in clinical pharmacology and pharmacotherapy. Recently the University has established also a part-time professorship, the selection process for the vacant post is currently underway.

EDUCATION

Students

The education to medical students started already in the early 1960s in Turku and then also in Helsinki. The training has been an obligatory part of the curriculum also in the other medical faculties since the 1970s. The courses have generally varied from two to three credit weeks divided into two or more periods with the courses in different faculties being arranged at different times from the second or third study year to the sixth and final year. There is no strict standard mode of education or core curriculum; in some faculties, most of the teaching has consisted of integrated lectures, whereas in others seminars, demonstrations or working in small groups have been preferred. Kuopio has also organized wide-ranging courses in Pharmacotherapy and Pharmacokinetics/Toxicokinetics for students of pharmacy since the 1970s. Tampere has been responsible for the instruction of the national rules and regulations surrounding drug prescriptions to every physician originating from outside of the ETA countries and wishing to qualify in Finland.

Clinical pharmacologists appreciated that it would be beneficial to produce a national Textbook of Clinical Pharmacology. The initial version appeared in 1994. This was followed eight years later by the first edition of Clinical Pharmacology and Therapeutics, its latest revision was published 2011. This was an important collaborative project undertaken by Finnish clinical pharmacologists. It brought them together, one unified group with a common target – promoting and advancing Clinical Pharmacology.

Specialization

In Finland, Clinical Pharmacology has been an independent and officially recognized specialty for physicians since 1966. The first specialist physicians were very experienced clinicians who had practical and extensive experience of many aspects of clinical pharmacology and drug treatment. They were considered competent for clinical pharmacology and were awarded the specialty without particular training program.

Since the seventies the training program has lasted for six years. It has consisted of three phases: *the first* is 2.5–3 years general training in practical fields of outpatient and drug-intensive hospital clinics, *the second* is 3–3.5 years special training in clinical pharmacology, the *third* is the written examination. Although the present program has changed somewhat since the 1970s, its basic elements are still essentially the same. In the 1960s and 1970s, the specialty was awarded by the National Board of Health, then by the Universities, but now again by the Ministry of Social Affairs and Health (“Valvira”). Thirty-three of the present specialists have been trained and specialized in Helsinki, eleven in Turku, eight in Tampere, three in Kuopio, two in Oulu and one in Norway.

RESEARCH ACTIVITIES

In particular, the research being done in **Helsinki** has gained excellent international recognition. The main interest of the group has been on pharmacokinetics, drug

interactions and pharmacogenetics. One spin-off of these successful research projects is that there is now a Professorship of Pharmacogenetics housed in the Meilahti Campus. The prime mover behind these projects is Pertti Neuvonen; a prominent Finnish investigator who has received several eminent awards. Moreover, we should be thankful to Pertti for leading the national Clinical Drug Research Graduate School and ensuring its financial stability since the middle of the 1990s, at a time when Finland was still in the grip of a financial crisis dating back to the earlier years of that decade.

In **Turku**, the research activities have been also fruitful. These began in the 1960s, when Esko Iisalo was the Docent of Clinical Pharmacology and he initiated many projects in this field. Esko was also internist and focused on cardiovascular drugs and pharmacokinetics. Nowadays, central and autonomic nervous system, diabetes, PET-derived findings and clinical drug trials are being conducted in Turku and very profitable they are too!

In **Tampere**, there have been excellent collaborations with clinicians and the research efforts have focused on pharmacokinetics, cardiovascular drugs, and chemotherapeutics. Because there were few physical resources available to clinical pharmacology, cooperation with the clinics in the University Hospital has been especially important. The collaboration has been most extensive with the units of clinical chemistry and physiology, but there has also been good work done with internists, neurologists, anesthesiologists, pulmonologists and rheumatologists

In **Kuopio**, early clinical studies were essentially centered around pharmacokinetics, with some of them also having a toxicological perspective. Neuropharmacology has been a long time interest of Kuopio pharmacologists, and consequently there has been a special interest in the drug therapy of neurological and psychiatric diseases.

In **Oulu**, the best-known projects have focused on cardiovascular drugs as well as drug metabolism in liver, placenta and fetus. In addition, some clinical drug trials are being conducted as a collaboration with clinicians working in the University Hospital.

HEALTH CARE, REGULATORY AUTHORITIES, PHARMACEUTICAL INDUSTRY

Today (2018), there is a total of 58 physicians holding a specialization in clinical pharmacology (and pharmacotherapy) granted in Finland. Seventeen of them are pensioners. Forty-one of the remainder are in full-time employment, but only 16 of them are full-time clinical pharmacologists with the other twenty-five mainly working as clinicians in large hospitals, in fact 19 of them have an additional specialty. These clinicians have diverse responsibilities in their workplaces. Many of them advise in therapeutic tasks, consult in solving drug problems and contribute to the selection of drugs to be included in the hospitals' formularies. Therefore, their expertise in clinical pharmacology is a major extra benefit for the hospitals, but unfortunately, this has meant that hospital managers do not consider it necessary to employ full-time clinical pharmacologists. Even the pharmaceutical industry and drug advisory agencies have employed sparsely clinical pharmacologists, instead it has recruited many of the less extensively trained physicians who have acquired a "Special Competency in Pharmaceutical Medicine".

THE FINNISH SOCIETY OF CLINICAL PHARMACOLOGY

The Finnish Society of Clinical Pharmacology was founded in 1994. The Section of Clinical Pharmacology was a section within the Finnish Pharmacological Society since 1980. The significant impetus for the founding of an independent society originated from Sweden, where the Swedish Association for Clinical Pharmacology and Therapeutics already existed. The founding meeting of the society was held in Helsinki on May 26, 1994. The meeting was opened by Professor Esko Iisalo, chaired by Professor Pertti Neuvonen and the minutes recorded by Dr. Kristiina Perttunen. The other founding members were Ali Bardy, Risto Huupponen, Mirja Hämäläinen, Asko Järvinen, Timo Kaila, Tapio Kerttula, Tapio Kuitunen, Reijo Laaksonen, Lasse Lehtonen, Mauri Mattila, Eeva Moilanen, Pertti Pentikäinen, Harry Scheinin, Mika Scheinin, Timo Seppälä, Eero Tiula, Olavi Tokola, Pauli Ylitalo.

As soon as it was inaugurated, the Finnish Society joined the European Association for Clinical Pharmacology and Therapeutics (EACPT); it was an independent member participating in EACPT Meetings, which meant that the society was an active participant already at the first European Congress of Clinical Pharmacology and Therapeutics held in Paris in 1995.

During almost all of the Society's first two decades, there was no membership fee, since the Society received its financial support mainly from the Course of Clinical Drug Trials which was organized every year in Helsinki. The Society has generally organized two scientific meetings each year; though varied, their themes have always been focused around drug treatment and therapeutics, clinical drug trials, continuing education, etc. The meetings are often organized in conjunction with pharmacologists and toxicologists. The information about the activities is transmitted to the Society's members through its own newsletter "Transporter". Presently, the Society has 152 members.

FINAL COMMENT

Clinical pharmacology in Finland has enjoyed many highlights during the course of its 50 year history. Altogether 64 colleagues have been granted the specialty in clinical pharmacology (and pharmacotherapy) since its establishment 1966. In education and research, the discipline has a notable status in the Finnish universities, and the Finnish clinical pharmacologists have gained even significant international recognition.

Unfortunately, this status has not always been matched with adequate resources. Thus, in some universities, it is not the case that training in the medical curriculum is being taught by clinical pharmacologists.

In the health care system, the role of clinical pharmacologists has been relatively restricted, and it has not achieved as satisfactory status as hoped. Let us hope now that clinical pharmacology has not yet reached its top stage in the Finnish medical community, instead we will find still new avenues to develop further its therapeutic significance not only in scientific research but also in practical aspects of medicine.