Clinical Pharmacology: A Future Perspective for Congolese Hospitals

 **ABSTRACT**

Pharmacology, briefly defined as the science of medicine, is a discipline that evaluates the interaction between drugs and biological systems. While there are many sub-branches of pharmacology, clinical pharmacology, identified as the study of drugs in humans, has a distinct ground and importance within the field. In this review, the historical development, definition and content of clinical pharmacology will be defined, information on its position in the world and its status in Turkey will be apprized and suggestions regarding the development of this discipline in Congo will be discussed.

**Keywords:** Clinical pharmacology, Congolese Hospitals,

 **INTRODUCTION**

Pharmacology, which is briefly defined as "pharmacology", is a discipline that studies the interaction of drugs with biological systems.one. Under the lens of these reviews,homo sapiens. There are also other animals, including bioactive molecules, organelles, cells, tissues and organs.in vitroor on experimental animals or volunteer humansin vivo research is carried out using methodsone(Abernethy, 2004). The ultimate goal of all these studies is to find new chemicals for the diagnosis, prophylaxis, treatment and other medical purposes of diseases, to develop them as drugs and to determine the treatment principles of established drugs (Mc Lean & lecouteur,2004). Although there are many sub-branches of pharmacology such as pharmacodynamics and pharmacokinetics operating within the framework of these goals, clinical pharmacology, which means "studying drugs in humans", has a separate place and importance( Hochnaus et al, 2000). In this review, basic information will be given about the historical development, definition and scope of clinical pharmacology, its position in the world and its situation in Democratic Republic of Congo, and suggestions will be made on how this discipline can be developed in our country( Lecouteur et al, 2006).

**History of Clinical Pharmacology**

Aside from its current descriptive name, the first traces of clinical pharmacology can be found today in the work of traditional Chinese, Indian and Peruvian physicians who discovered the activity of herbal medicines containing substances known as artemisinin, reserpine and quinine. William Withering's publication in 1785 describing the use of foxglove in heart failure is an important record for this discipline, but it took 200 years for digitals to be accurately studied with clinical pharmacology methods( Fried et al,2006).

Although it is disputed who first used the term clinical pharmacology, according to the Anglo- Saxon literature it was Harry Gold, professor of pharmacology at Cornell University in the 1940s( Reuben et al, 2010). However, in 1914 Hans Horst Meyer and Rudolf Gottlied wrote a German resource book called "Pharmacology, Clinical and Experimental". Paul Martini, also a professor at Bonn University, published his monograph titled "Methodology of Therapeutic Research" in 1932( Ferruci et al, 2013).

In the United States (USA), where the most diligent efforts have been made for the development of clinical pharmacology, an important development in this field was made by Goodman and Gilman, whose first edition was published in 1941(Guralnik et al, 2015). The Pharmacological Basis of Therapeuticshas been a book. In these times, experimental pharmacologists had to be on their toes because a pharmacologist builds his own tools and isolates his drugs, They created measurement methods, anesthetized animals and covered their drums with soot. When we look at today, it seems that the clinical pharmacologist should be skilled in many disciplines such as pharmacology, biochemistry (in terms of drug metabolism), mathematics and statistics (in pharmacokinetics and clinical trial design), experimental medicine, safety analysis and pharmacovigilance( Ried et al, 2016).

After the attack on Pearl Harbor, when the Japanese invaded Indonesia, the main source of hatred, a crisis broke out in the American army, which was operating in the Pacific Islands, where malaria is common. Thereupon, James Shannon was assigned to Goldwater Memorial Hospital in New York to find synthetic antimalarial drugs and establish a laboratory. Studies in this area have led to the publication of many publications on drug disposition and metabolism and the discovery of acetaminophene( Gray et al, 2003).

In 1949 Shannon became director of the National Institutes of Health (NIH: the National Institutes of Health), the chemical pharmacology laboratory was established, and the cytochrome P450 enzymes responsible for drug metabolism became its major focus. In 1953 Shannon appointed Albert Sjoerdsma as the head of the newly established Experimental Treatment Department at NIH, this center became the training base of qualified clinical pharmacologists in the USA with the early 1960s, and those who came out of this center started to establish clinical pharmacology research and training centers in the country( Beers, 2018).

In Europe, which lacks a centralized base such as the NIH, the development of clinical pharmacology has taken place multi-centre, with the contribution of research-savvy doctors working with pharmaceutical companies. In particular, research on antipsychotic drugs such as chlorpromazine and drugs used in the treatment of hypertension has been carried out by clinicians in France and the United Kingdom (UK), while the development of clinical pharmacology in Sweden has been through the efforts of some distinguished pharmacologists. Although there is now significant convergence, the fact that clinical pharmacology originated primarily in internal medicine in the UK and the USA and in pharmacology in the Scandinavian countries underlies the differences in practice and financial support that persist today(Hanlon et al, 2010; Onder et al, 2015).

The 1950s and 1960s, when many new and important drugs started to appear, were the years when it was started to be realized that more systematic and comprehensive drug research should be done in humans. During this period, many departments were opened in the UK, USA and Sweden and financial support was provided by the NIH, Medical Research Council (MRC: Medical Research Council) and major pharmaceutical companies. The World Health Organization (WHO) held many meetings and prepared reports on the development of clinical pharmacology, the first of which was in 1969( Savo et al,2010;Flather,2000).

In the first of these reports, the expected functions of clinical pharmacology at that time were defined (Table 1). It is stated that thanks to these functions, the profit-loss ratios of drugs will increase as a result. Moreover,British Journal of Clinical PharmacologyClinical pharmacology units were established within new associations or existing associations( Agostini et al, 2010). Clinical pharmacologists have spread around the world from these sources, clinical pharmacology internships have been added to undergraduate students' training programs, and various centers have organized postgraduate training programs and workshops(THompson et al, 2014).

Clinical pharmacologists have played an important role in establishing and operating both local and national pharmacovigilance systems, as well as reporting and analyzing adverse drug reactions. A clinical pharmacologist, if available, has been included in recently established hospital formulary committees. Many clinical pharmacologists have opened front-line clinical services within internal medicine, often with a cardiovascular bent, as well as psychopharmacology. When they did not open a service of their own, they structured the hospital consultation services to solve the problems related to drugs. All these developments have occurred as the budgets of research and clinical services have increased rapidly, but with the shortage of university and hospital budgets in the 1990s, many of these services began to be devastated( Dobkin,2010; McLung et al,2011).

Many disciplines contribute to the understanding of the efficacy and safety of drugs in humans. In parallel with the increasing amount of drugs over the years, the number and importance of these disciplines has increased.

Both basic and clinical pharmacologists and clinicians have begun to identify significant inter-patient differences in therapeutic efficacy and the occurrence of side effects, and have recognized the importance of drug metabolism in explaining this inter-individual variation.

The concept that the drug effect is determined by the concentration of the drug in the blood rather than the dose and the variation between patients is caused by the differences in drug concentrations in the blood has created an instrumental situation for clinical pharmacology. In fact, as this topic has evolved, many of the fundamental studies have been done in biochemistry and molecular biology laboratories.

**Table 1. Functions of clinical pharmacology (WHO 1980 meeting report).**

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| --- |
| Improving patient care by supporting safer and more effective drug use Increasing |
| Research  |
| Education |
| Drug Analysis and information |
| Drugabusetracking |
| Consultance from the experimental design of clinical drug trials |

Two pioneers in drug metabolism have been Tecwyn Williams at St Mary's Hospital in London and Bernard Brodie at NIH. The interest of the first was on the biochemistry of drug metabolism, while the second was on the effect of metabolism on drug action and toxicity. Brodie's lab at the NIH has become the world's center for drug metabolism research( Nair,2000).

The scientists here demonstrated for the first time the inhibition and induction of drug metabolism, purification of the responsible enzymes and the importance of metabolites in toxicity. A breakthrough development was the discovery in 1962 of the existence of the enzyme cytochrome P450 and its isoforms(Leouintee et al,2005).

In the nineteen eighties, it was realized that the chirality of drugs was important both in effect and disposition, and it was discovered that R and S enantiomers, especially warfarin, were responsible for interpersonal differences. Similarly, in addition to the liver, it has been observed that the intestinal wall also contributes to the presystemic elimination and may play a role in active transport in absorption.

Through the discipline of pharmacogenetics, the founder of which is Canadian Werner Kalow, the existence of slow and fast metabolizers due to genetic polyformism in some enzymes responsible for drug metabolism has been determined and a reason for the control of blood pressure has been determined.

Thus, it has been understood that there is a very wide range between doses of antihypertensive drugs. On the other hand, it has become a routine task to evaluate the effects of metabolism pathways and enzyme polyformism of a drug under development in the pharmaceutical industry. Probably the direction of clinical application will be towards the provision of diagnostic chips for the most common polymorphisms in drug metabolism.

Although the term pharmacokinetics is derived from an article by Dost in 1953, the terms redistribution and pharmacokinetic models date back to 1847 and 1937, respectively. Since then, developments and studies on topics such as absorption kinetics, dose-dependent kinetics, pharmacokinetic/pharmacodynamic (PK/PD) analyzes, clearance concept, importance of chirality, carrier proteins, blood-brain barrier, liver pumps and population PK/PD analysis. followed each other(Leouintee et al,2005).

Although so-called clinical trials are as old as human history, Lind demonstrated the most primitive example of controlled clinical trials with his mini controlled clinical trial on scurvy in 1747. But real credit should be given to Austin Bradfort Hill, who was one of the founders of clinical pharmacology for his clinical research at the MRC in 1947 on the treatment of tuberculosis( Walker & Wynne, 2015).

As regulatory authorities began to require detailed protocols and documentation regarding efficacy and safety, pharmaceutical companies began to include operational personnel in their teams who would specialize in clinical pharmacology, clinical trial design, statistical analysis and legislation, as well as monitor matters such as paperwork, clinical trial supplies, and quality of trial sites. Parallel to these developments, while the contribution of academic clinical pharmacologists to drug discovery has decreased, those in the pharmaceutical industry have increased( Beyth & Shoor,2020)

As the costs of clinical trials have increased a lot over the years, companies have started to conduct these studies in eastern Europe, Asia and South America, where the cost is lower. On the contrary, basic research on drug discovery has shifted to the USA, where the large market and the NIH's anomalous investments have supported this reversal.

**Table 2. Fields of interest of clinical pharmacology Research**

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| --- |
| **RESEARCH**  |
|  Pharmaco-cinetic, Pharmacodynamic, Pharmacogenetic |
|  Drug clinical researchs |
|  Controle of Therapeutic drug  |
|  Pharmacovigillance |
|  Pharmacoepidemiological studies |
|  Pharmacoeconomic’s Control |
|  **EDUCTION** |
|  Before and After Graduate |
| **PATIENTS CARE** |
|  Drugs and Traitment comities |
|  Analysis of critical drugs |
|  Toxicology’s Service |
| **PHARMACEUTİCAL INDUSTRİES** |
|  Development of product |
|  Phase,I, II,II,IV researchs |
|  Pharmacogenetic studies |
|  Pharmaco epidemiological studies |
|  Pharmacovigillance and Pharmacoeconomie |
| **STATE RESPONSABİLİTİES** |
|  Organisation of the hospitals and clinics |
|  Consulting committees. |

**Definition and Scope of Clinical Pharmacology**

WHO defined clinical pharmacology in 1988 as “a medical discipline that seeks to combine pharmacological and clinical experience to improve efficacy and safety in clinical drug use”. Alternatively, clinical pharmacology can be briefly defined as “a scientific discipline that examines all aspects of the relationship between humans and drugs”.The term clinical pharmacologist is used professionally for physicians with expertise in clinical pharmacology, who have received long postgraduate training in topics such as clinical trial theory, drug evaluations, pharmacoepidemiology, pharmacoeconomics, pharmacogenetics, pharmacovigilance, and clinical drug toxicity (Leouintee et al,2005).

The scope of clinical pharmacology can be roughly divided into two: i) Testing and evaluation of chemical substances that have been thoroughly studied in experimental animals in healthy and sick volunteers according to certain rules, licensing the appropriate ones as drugs and following up after marketing, ii) examining the treatment principles of drugs. In connection with these, the fields in which clinical pharmacology plays a role can be classified under five headings: i) Research, ii) education, iii) patient care, iv) pharmaceutical industry, v) government (Table 2).

**Research**

Under the title of research, there are pharmacokinetic, pharmacodynamic and pharmacogenetic studies conducted in volunteers, and in these studies, the mechanism of the drug's effects on the organism and the organism on the drug is tried to be clarified. Apart from the identification of metabolism and excretion pathways, these studies focus on genetically inherited differences in drug targets, drug transporters, and metabolism-related enzymes that are responsible for intra- and inter-individual differences in drug predict and differentiate genetic and non-genetic factors that affect the outcome of drug therapy( Bordet et al, 2001).

 There are two main approaches to pharmacokinetic studies: i) an approach in which many drugs are measured in a few volunteers at a given time period, ii) an approach based on rare drug measurement from each subject in a large population (population pharmacokinetics). While both are useful in identifying subpopulations with impaired or increased elimination capacity, population pharmacokinetics can also be applied in pharmacokinetic-pharmacodynamic analyses.

When it comes to clinical drug analysis and phase I-III drug research, phase I studies in healthy volunteers are often undertaken by clinical pharmacologists working in the pharmaceutical industry or private clinical research services. Phase II studies may also be conducted by clinical pharmacologists, given their training. Randomized controlled trials (RCTs) led by clinical pharmacologists are the gold standard for demonstrating the efficacy of a drug, and phase III studies are no longer only under the jurisdiction of clinical pharmacologists, but physicians from all fields of expertise can play a role here. It is also worth noting that clinical drug research is a multifaceted field with legislation (laws, good manufecture practice (GMP) guidelines, helsinki declaration), ethical committees, regulatory authorities, contract research organizations, independent data monitoring committees and sponsoring pharmaceutical companies( Boredet et al, 2018).

Therapeutic drug level monitoring is a scientific medical technology in which clinical pharmacology makes significant contributions. The studies are important for safer drug use in the elderly, children, and risky patients with kidney or liver failure. In addition, these studies have helped to detect and manage drug-drug interactions and to understand the effects of genetic polymorphism in drug elimination pathways. Clinical pharmacologists need to understand the principles of laboratory methods, although they are not required to practice them. The main responsibility of the clinical pharmacologist in research related to formulate a clinically relevant problem, design a study to understand this problem, be medically responsible for the volunteers, and adapt the results to clinical practice( Carbonin et al, 2010; Huurtwitz,2010).

Clinical pharmacologists play an active role in drug utilization studies, defined as an eclectic collection of descriptive and analytical methods for understanding and evaluating the processes of prescribing, dispensing and consuming drugs. This area is also concerned with testing interventions to improve the quality of these processes.Pharmacoepidemiology can be defined as the study of drug benefits and effects in large populations. The purpose of research may be to detect a signal, to determine the risk , or to test a hypothesis by cohort or case-control studies. The results of the study can serve to advise health organizers or individuals, or to formulate a policy for the optimal use of drugs. For the continuation of the development of this discipline, it is important that some part of pharmacoepidemiology is closely linked to clinical pharmacology(Kellaway & Mc Crae, 2020).

Pharmacoeconomics is a scientific discipline that evaluates the clinical, economic, and humanistic aspects of pharmaceutical products, services and programs, and other healthcare. The aim is to generate valuable information to health decision makers, producers and patients for the allocation of health resources and optimal outcomes. Clinical pharmacologists play an important role in this field as actors formulating medically relevant research questions and designing medically relevant outcomes. Also, other roles are to examine the relevance and quality of clinical trial data and to assess whether a treatment has a clinical advantage over another currently available treatment and to reach an objective conclusion in terms of cost-effectiveness(Leouintee et al,2005).

**Education**

First of all, it should be emphasized that clinical pharmacologists should provide rational drug use training at all levels. Closely related to this, prescribing is an ingenious task with significant risks as well as benefits. Many studies have shown that in serious drug therapy cases, prescribers have insufficient education and awareness about drugs. Recent graduates cite prescribing as the most challenging and most unprepared activity of their professional life. It is clear that all medical graduates must master the practical prescribing principles on which the discipline of clinical pharmacology forms the basis. In order to achieve this, it is important that pre- and post-graduate training is given by clinical pharmacologists.

Many medical faculties give the first of basic and clinical pharmacology education in the 2nd and 3rd grades, while the second one is offered somewhere between the 4th-6th years.

Similarly, in the medical faculty where the author of this article is assigned, basic pharmacology is given as a theoretical course in the 2nd and 3rd grades, taking into account the needs of the first step, and clinical pharmacology is given in the 5th grade theoretically and practically in the form of a 1-week internship based on the principles . In undergraduate education, essential drug lists should be prepared under the leadership of clinical pharmacology, various training styles and electronic training procedures, especially problem-based, should be developed, validation evaluation systems should be established, and external quality controls and quality controls of trainings should be provided (Kellaway & Mc Crae, 2020).

Clinical pharmacology and prescribing education should be continued after graduation due to the continuous emergence of new drugs and the renewal of knowledge. The time problem that arises at this point is a situation that can be overcome with flexible internet-based learning methods. Unlike pharmaceutical companies, it is important that non-promotional training events are organized by clinical pharmacologists with other actors. Education comes to the fore especially in terms of gaining the ability of inexperienced physicians to prescribe effective and safe drugs.

The training of clinical pharmacologists is a topic in itself and is discussed below. Pharmaceutical companies are at the forefront of assisting the training of clinical pharmacologists, particularly in clinical research.4. However, in order to make a long- term career in these companies, some more skills are required, for which special training is inevitable.

**Patient care**

Examination of the treatment principles of drugs, which is one of the main subjects of clinical pharmacology, is an area related to patient care and its application area may vary from country to country. Clinical pharmacologists are needed in patient care, as their focus is on drug evaluation and in this context, it would be appropriate to take a role in the following areas.

Drug and treatment committees (DTCs) are the organizations that clinical pharmacologists should take part in, as they form the basis of the principles of RDU. The training of DTC members and the provision of evidence-based advice should be the responsibility of clinical pharmacologists.

This local type of committees, clinical pharmacologists, preparation of hospital formularies, etc. can be active in. They may also hold various roles in health technology expertise at the national level, drafting therapeutic guidelines, establishing the national pharmacopoeia, and regulatory authorities.

Critical drug analysis is an application area that gains importance especially when new and expensive drugs are introduced, plays a central role in clinical consultations and judgments about drug information, is a cornerstone and is fundamental to patient care. Drug use studies and pharmacoepidemiological services are structures that are closely related to DTC functions and include clinical, pharmacoepidemiology and clinical pharmacology specialists, which play a role in the systematic introduction and monitoring of new drugs and health organizations in determining future drug preferences. Drug information services should be seen primarily as structures that evaluate and resolve drug problems in patients. Although a pharmacist can do the descriptive part of the job, it is best that the problem-focused provision of service be delivered by a properly trained clinical pharmacologist (Kellaway & Mc Crae, 2020).

Therapeutic drug level monitoring (TDLM) and pharmacogenetics servicesideally provided by clinical pharmacology departments. Drug blood level measurements can be performed in any laboratory, but the actual TDLM service also includes clinical interpretation of data, taking into account diagnosis, drug interactions, renal function, and pharmacogenetics. Dose adjustments are important, especially in elderly patients, taking into account the loss of kidney function, and personal therapy has been growing in recent years, especially in cancer therapy.

Toxicology services, these are the structures where clinical toxicologists who are accredited as clinical pharmacologists at the national level or in the hospital work and where drug poisoning is investigated, diagnosis and treatment are provided.

An optional 1-year clinical toxicology module is included in the clinical pharmacology curriculum in the UK, and it is aimed that residents gain experience by participating in the treatment of patients either in the national poison center or other centers or in their own hospitals. Although treatment with antidotes is limited, correct identification of the responsible drug, follow-up and future

to prevent poisoning or abuse, it is important. On the other hand, many hospitals prefer clinicians from many disciplines to be involved in these works rather than employing clinical toxicologist specialists.

Although clinicians without specific clinical toxicology training are sufficient in many cases, the contribution of poison centers is very important in accessing the information needed about thousands of substances that patients are exposed to, their clinical results and appropriate treatments. In some countries, clinical pharmacologists are involved in systems established to prevent athletes from abusing doping substances such as anabolic steroids.

Direct patient servicesare units where clinical pharmacologists provide care to patients in different ways. In some countries, clinical pharmacologists may assume a direct responsibility in the care of patients with a specific problem (Ex. intensive care), those with a specific disease such as hypertension, stroke and epilepsy, and those in specialized fields such as pediatrics and geriatrics. In other countries, clinical pharmacologists are used for their ability to evaluate clinical drug problems such as therapeutic failure, ADRs, drug interactions, and inappropriate polypharmacy.

Electronic pharmacology services with the widespread use of the internet and smartphones, advice on drugs has started to become tools that provide information about drug interactions, drug use in pregnant and lactating women, ADRs and similar problems related to drugs, and eventually integrate evidence-based information with clinical practice.

**Pharmaceutical industry**

Pharmaceutical companies have until recently played a central role in the discovery, development and marketing of new or established drugs. Clinical pharmacologists have a broad perspective on drug discovery and use, and more importantly, they can integrate preclinical and clinical data with knowledge of drug target and disease pathogenesis to guide drug developmet (Leouintee et al,2005).

Information from clinical pharmacology studies, if properly prepared, can differentiate a product from its competitors, as well as enable it to be used safely in various and complicated patients. During clinical development, clinical pharmacology seeks to elucidate the exact relationship between the desired and undesirable effects of a drug (Table 3). In this context, basic skills related to pharmacology, clinical pharmacology, biological sciences, systems biology, experimental medicine, mathematics, translational medicine and clinical medicine should be integrated in drug development.

**Table 3. The roles of clinical pharmacology in drug development: Drug exposure and clinical effects.**

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| **Drug administration** |
|  Formulations |
|  Administrations’ ways |

Traditionally, clinical pharmacologists are involved in the planning, design, execution, analysis, interpretation, and reporting of clinical drug trials during the early phases of clinical drug research, such as phases I (first-time human trials) and II (proof-of-concept work). As for specific roles, these include preclinical development, pharmacogenetics, pharmacoepidemiology, pharmacovigilance, pharmacoeconomics, and phase III (confirmation studies).

Apart from these, clinical pharmacologists may hold other positions in the industry: i) Legislation (preparation of applications, negotiation with regulatory authority), ii) outsourcing (relationship with contract research organizations and academic institutions), iii) consultation (setting and management of scientific and clinical advisory boards). and relationship with scientific and clinical leaders to develop suitable products), iv) intellectual property administration (patent preparation, contact with patent attorneys and office), v) due diligence activities (participation in scientific and clinical analysis of data, assessment of market potential of firms and products) , vi) managerial and financial activities (infrastructure and human resource planning)

**State**

By the nature of their training, clinical pharmacologists are suited to many issues of public concern, such as drug licensing, post-marketing surveillance, preparation of national treatment guidelines, reimbursement decisions, and ethical evaluation of research projects.

 If governments want the population to have a more effective and safe treatment, that is, to implement the principles, clinical pharmacologists must be consulted both in hospitals and in regulation. authorities and health technology analysis institutions. In addition, clinical pharmacologists have an important role in the implementation of the WHO's “National Drug Policy Development Guideline”, the main goal of which is to ensure: i) drug quality, efficacy and safety, ii) equitable access to drugs by the entire population,
iii) rational/quality use of drugs, iv) viable and robust local pharmaceutical industry. The state and its related institutions are obliged to take all measures to ensure that their citizens are not harmed and their basic human rights are not violated in the researches they are involved in.

 Ethics committees and regulatory authorities may employ clinical pharmacologists for this purpose. The presence of clinical pharmacologists familiar with drug-focused research, especially in ethics committees, will make invaluable contributions. In addition, clinical pharmacologists should be involved in the design and use of electronic health records, which can make a very important contribution to pharmacovigilance, as these systems have the potential to contribute to future studies and drug safety.

**Organization of Clinical Pharmacology**

As noted earlier, the discipline of clinical pharmacology historically sprouted from pharmacology or internal medicine departments, but today it exists as an independent specialty in some countries. Depending on the situation, clinical pharmacology may be an independent department or a sub-section (a science) affiliated to the pharmacology or internal medicine department. On the other hand, if the clinical pharmacology discipline is a small organization, it may be more appropriate to define it as a "unit". No matter how it is organized, clinical pharmacology is located in the university hospital and carries out its main duty research, education and patient care activities.

In some countries, clinical pharmacology is so developed that it operates as an independent division. In this type of departments, in addition to clinical pharmacology specialist, employment of basic pharmacologists, pharmacists, nurses, computer experts, statisticians, laboratory technicians and secretaries is required to sustain many activities of the discipline. In many countries, the clinical pharmacology discipline is organized under a clinical department, as the minimum number of clinical services or the amount of staff required for the services these services will provide is insufficient. However, trying to evolve towards a full-fledged division should be the long-term goal. In some cases, clinical pharmacology is organized as a subdivision or unit of it, as it develops from the basic pharmacology division. Whatever form clinical pharmacologist drug information services (primary pharmacologist, pharmacist, nurse), pharmacoepidemiology and pharmacovigilance (epidemiologist) and (personnel trained in analytical methods) have to cooperate with a wide range of professionals.

**Clinical Pharmacology in the developped countries**

The USA can be considered as one of the most important countries that has been a pioneer in the development of clinical pharmacology. First, in 1900, with the initiative of 20 physicians, the “American Therapeutic Association” was established in Washington and after the 70s, it continued on its way as the “American Clinical Pharmacology and Therapeutic Association”.

Similarly, the "American Society for Pharmacology and Experimental Therapy" was founded in 1909. The American Board of Clinical Pharmacology was established in cooperation with these two associations above and the American College of Clinical Pharmacology in cooperation with the following three purposes: i) to evaluate individuals' educational qualifications, scientific research and learning achievements, ii) to prepare and administer exams for individual certification in clinical and applied pharmacology. iii) approve and accredit training programs in clinical pharmacology14. The requirements for taking the board exams are determined separately for physicians and non- physicians.

Accordingly, the most important criteria that physicians must meet are as follows: i) To have a medical degree (MD: Medical Doctor; DO: Osteopathic Medicine Doctor) obtained from the USA, Canada or an equivalent accredited institution outside the USA, ii) in the USA or Canada. have a license to practice medicine, iii) have a specialty certificate under the auspices of the American Board of Medical Specialties, iv) complete a two-year postdoctoral fellowship in a training program approved and accredited by the American Board of Clinical Pharmacology to qualify for certification, v ) documenting contributions to clinical pharmacology (such as publications), vi) participating in clinical pharmacology educational activities as a student or instructor16. On the other hand, in the eligibility criteria of non-physician candidates, the first one is "PhD degree in life or medical sciences from the USA, Canada or an equivalent accredited institution outside the USA" and the other criteria are the same. As it can be understood from these criteria, there is no obligation to be a physician in order to receive clinical pharmacology training in the USA. Institutions providing clinical pharmacology training in this country are listed on the website of the relevant institution.

Clinical pharmacologists take part in many national and regional committees and make important contributions to the evaluation of new drugs, preparation of national treatment guidelines, reimbursement, decisions and preparation of national drug lists. In addition, many clinical pharmacologists work in critical positions at the Danish Medicines Agency under the Danish Ministry of Health, such as drug licensing and marketing, approval of clinical trials, issues related to pharmacovigilance and medical devices, monitoring good clinical practices and establishing pharmacy infrastructure. Apart from these, clinical pharmacologists in Denmark conduct clinical research in many areas such as drug-drug interactions, drug metabolism in liver failure, pharmacogenetics and pharmacoepidemiology. In addition, clinical Pharmacology education is given to medical faculty students in different ways in different universities. Many important scientists have played a role in the development of clinical pharmacology in the Russian Federation, and clinical pharmacologists first began to emerge in the late 1990s. The practice of clinical pharmacology is regulated by the ministry of health, and a 1997 directive defines the basic structure and duties of clinical pharmacology services and the positions of physician-clinical pharmacologists (Leouintee et al,2005).

Accordingly, the roles of physician-clinical pharmacologists in hospitals are as follows: i) development of drug formulations, ii) pharmacoeconomic analysis, iii) pharmacotherapy evaluation for patients (efficacy and safety assessment of drug-drug interactions and adverse event records), iv) hospital practices related to drugs. v) organizing conferences, seminars and new reports on pharmacotherapy, vi) working on hospital commissions (administrative and ethical commissions), vii) participating in thematic reviews, viii) assisting departments in the completion of emergency medical kits, ix) other health care services participation, x) evaluation of drug applications in other health services, xi) conducting pharmacogenetic and pharmacokinetic studies and giving consultations. The training of clinical pharmacologists is carried out after graduation, after obtaining a degree in medicine or pediatrics, either through residency in medicine or general development in clinical pharmacology.

Contrary to the developments and organizations in the world, clinical pharmacology discipline in Turkey has not been officially established in its original form, apart from individual academic and practical applications in some faculties and hospitals. Medical pharmacology departments in medical faculties in Turkey are organized within the internal sciences department and specialty training in medicine, which only medical faculty graduates can enter, is carried out for 4 years. Medical pharmacology specialty (MPS) training, as such, is similar to clinical pharmacology specialist (CPS) training in Europe. Both MPS and CPS trainings are carried out in the form of residency, not doctoral training. Secondly, being a physician is a prerequisite for applying to both specialization programs, and at the end of the training, the person becomes a specialist physician. However, there is a gap between CPS in developed countries and MPS in Congo in terms.

When these definitions are viewed from a bird's eye view, the deformation created by including non-physician pharmacologists on the pharmacologist member in clinical research ethics committees, where physician-pharmacologists must play a central role, will be clearly seen. In this respect, in official regulations in Congo as well as in the world, the responsible researcher in clinical research is defined as "the physician or dentist who has completed his/her specialty or doctoral education in the field related to the research subject and is responsible for the conduct of the research". As can be clearly seen, only physicians can be principal investigators, while other professions can be (assistant) researchers defined as "the person involved in clinical research under the supervision of the responsible investigator". Consequently, it is futile for non-physician pharmacologists, who cannot even be principal investigators, to act instead of physician-pharmacologists who play a central role in clinical research ethics committees. For this reason, the relevant article in the regulation should be changed as “a physician who has specialized in clinical pharmacology, otherwise a physician who has specialized in medical pharmacology, or if he does not exist, a doctor with a doctorate in medical pharmacology” and physician-pharmacologists should be made indispensable again(Leouintee et al,2005).

**Conclusion and Recommendations**

It is clear that there is a long and arduous road ahead for the discipline of clinical pharmacology to be fully established academically and formally in Turkey, similar to the one in the West. When we look at the historical development of clinical pharmacology in D. R. Congo, it will be seen that first of all, the legislation in the field of clinical research has started to be structured and then a few centers where bioavailability/bioequivalence and phase I researches are opened with individual efforts. There are no rights violations in clinical research, except for the problematic situation explained above, regarding the membership of physician-pharmacologists in clinical research ethics committees.

When it comes to patient-oriented clinical pharmacology practices, which come second in historical development, it can be determined that polyclinic and/or counseling services have been opened in some university and state hospitals with the individual efforts of physician-pharmacologists. However, since these newly established units are foreign to Congole's health system and are not officially defined by the Ministry of Health, problems arise in making any payments for these transactions.

This causes the chief physicians to look at these services that do not “make money”. On the other hand, in university hospitals, income can be obtained for hospital revolving funds through "private examination". In recent years, these patient oriented services offered by physician-pharmacologists have been has begun. It is obvious that clinical pharmacists are trying to incorporate these patient-oriented services completely into their own structure.

The process started a long time ago in the field of clinical research and in recent years, it has begun to spread to other areas of clinical pharmacology with the efforts of a new generation of physician-pharmacologists.

It will be obligatory for these units, whose number and quality have increased over time, to achieve a common and minimum standardization after a point. Thus, clinical pharmacology disciplines under medical pharmacology departments will be included in the medical specialization education system as minor branches. Perhaps, within years, clinical pharmacology departments will be able to be established separate from medical pharmacology as in developed countries. However, this takes much longer to happen. For this reason, it would be appropriate to focus on rational and realistic goals. In the event that a clinical
pharmacology sub-branch can be established under the medical pharmacology department in the future, the clinical pharmacologist title should be
given to physician-pharmacologists with both and doctorate degrees who prove that they are related to clinical pharmacology. However, if the new generations from below want to become clinical pharmacologists, they should first receive training and then clinical in the
event that a clinical pharmacology sub-branch can be established under the medical pharmacology department in the future, the clinical
pharmacologist title should be given to physician-pharmacologists.



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