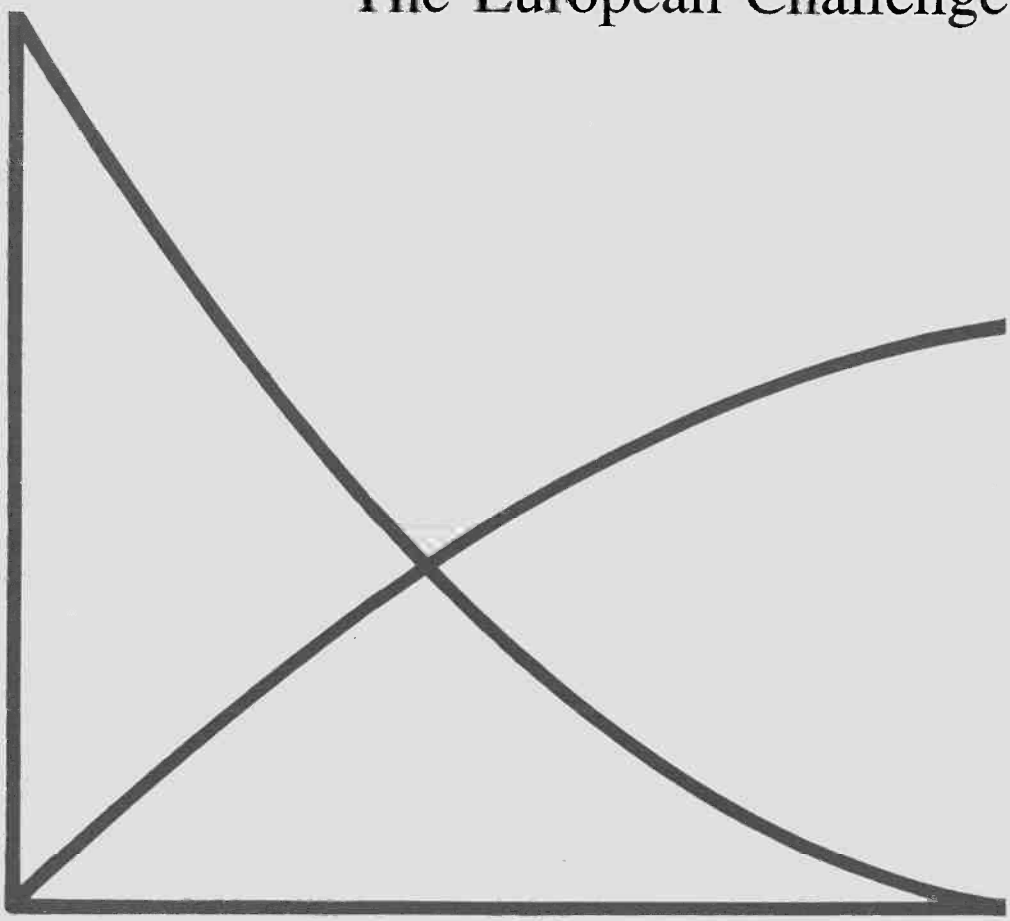
World Health Organization
Regional Office for Europe
Copenhagen

# Clinical Pharmacology

## The European Challenge



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The World Health Organization is a specialized agency of the United Nations with primary responsibility for international health matters and public health. Through this Organization, which was created in 1948, the health professions of some 165 countries exchange their knowledge and experience with the aim of making possible the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life.

The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health problems of the countries it serves. The European Region has 31 active Member States,[a] and is unique in that a large proportion of them are industrialized countries with highly advanced medical services. The European programme therefore differs from those of other regions in concentrating on the problems associated with industrial society. In its strategy for attaining the goal of "health for all by the year 2000" the Regional Office is arranging its activities in three main areas: promotion of lifestyles conducive to health; reduction of preventable conditions; and provision of care that is adequate, accessible and acceptable to all.

The Region is also characterized by the large number of languages spoken by its peoples and the resulting difficulties in disseminating information to all who may need it. The Regional Office publishes in four languages — English, French, German and Russian — and applications for rights of translation into other languages are most welcome.

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[a] Albania, Austria, Belgium, Bulgaria, Czechoslovakia, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, San Marino, Spain, Sweden, Switzerland, Turkey, USSR, United Kingdom and Yugoslavia.

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# Preface

Twenty-one years ago, a WHO study group formulated the principles of clinical pharmacology.[a] Since then, it has become an established medical discipline in a number of countries, notably the Nordic countries (Denmark, Norway and Sweden), the United Kingdom and the United States. Despite the consensus on the need for improvements in the design and conduct of clinical drug studies and in the teaching of the proper use of medicines to medical students in the European Region, clinical pharmacology had a slow start in many countries and initiatives sometimes failed.

It is obviously in the interest of public health and therefore of WHO that drugs be used for the right indications and in the right dosage and that the choice of drugs be appropriate for the patient, his or her environment and the local conditions. Work towards this goal in the Region has mainly emphasized the furthering and improvement of the teaching of the principles of clinical pharmacology and pharmacotherapy to medical students and doctors. These in turn were the purposes of the WHO Working Group on Clinical Pharmacology in Europe, which was set up in 1986.

The Working Group, consisting mainly of university teachers of clinical pharmacology, had broad terms of reference. The Group laid down general principles for the teaching of and training in clinical pharmacology, and formulated general guidelines on the role of the discipline in health care delivery with special emphasis on primary health care. These principles and guidelines were published in three articles in the European journal of clinical pharmacology; the articles are reprinted in this book with the permission of the publisher, Springer Verlag.

In addition, a questionnaire was sent out to medical schools and health ministries about the academic status of clinical pharmacology in the

[a] WHO Technical Report Series, No. 446, 1970 (*Clinical pharmacology. Scope, organization, training*: report of a WHO Study Group).

countries of the European Region. By the end of data collection in July 1990, all countries had responded, with one exception. The responses were then edited by a member of the Working Group, Professor M. l'E. Orme. Although subsequent events in Germany created uncertainty about the data obtained from the former German Democratic Republic, it was decided to present the data as they have been given.

We would like to express our gratitude to the many colleagues in drug administration and universities in the European Region for providing information on conditions in their countries. Clinical pharmacology is still a poorly defined discipline, and definitions of an academic unit or department are necessarily rather vague; thus, value judgements are far from uniform. Assessments of the local situation may therefore be under- or overstated. By redrawing the maps presented with the country reports, however, we tried to provide a picture of clinical pharmacology for the Region as a whole.

This book includes a guide to academic programmes in clinical pharmacology in the European Region as well as a discussion of the role that the discipline could play in medical schools and health care. It is hoped that this fruit of the Working Group's labours will increase interest in clinical pharmacology and thereby improve health care.

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L. Offerhaus

# Clinical pharmacology in Europe: an indispensable part of the health service[a]

*WHO Working Group on Clinical Pharmacology in Europe*[b]

## Introduction

Clinical pharmacology is a medical discipline which, on a scientific basis, combines pharmacological and clinical expertise with the ultimate goal of improving efficacy and safety in the clinical use of drugs.

The central role of drug therapy in many fields of medicine is the background for establishing clinical pharmacology as a separate discipline. The significance of modern drug therapy is undisputed. The availability of effective drugs for the treatment of infections, cardiovascular diseases, neuropsychiatric disorders and certain malignant diseases has radically changed medical treatment.

In 1970 a WHO study group recommended the development of clinical pharmacology as a discipline integrated into the health service system *(1)*. To some extent this action was stimulated by the thalidomide catastrophe and the rapid progress in the drug field through the 1960s, with several important innovations on the drug scene. Clinical pharmacology then developed because of the medical need to establish in scientific terms the benefits of drug therapy relative to its risks. In 1977 a WHO working group further outlined the fields in which clinical pharmacology services were needed *(2)*.

In spite of these initiatives, the development of clinical pharmacology in many countries has been slow. Several other drug disasters, such as the complex adverse reactions to the cardiovascular drug practolol and to the

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[a] Reproduced by permission from the *European journal of clinical pharmacology*, **33**: 535-539 (1988).

[b] Members: J. Bircher, M. Bogaert, M.N.G. Dukes, M. Eichelbaum, L.F. Gram, H. Hüller, M. Orme, F. Sjöqvist, G. Tognoni.

antirheumatic drug benoxaprofen, have further underlined the need for better knowledge in this field *(3)*. Research in clinical pharmacology has further shown that optimization of therapy by pharmacodynamic and pharmacokinetic monitoring may not only reduce the risk of adverse effects, but also improve the efficacy of drug treatment.

Thus, it has repeatedly been recognized that the use of drugs is sometimes associated with severe adverse reactions which are not balanced by the therapeutic gains. The major approach to solving this problem has been the introduction of elaborate central drug control systems, particularly related to the registration of new drugs. However, in spite of a well developed control system in several countries, apparently unpredictable problems still arise when drugs are taken into general use. In all probability only a broader approach, with increasing emphasis on knowledge of drugs among physicians in the hospital and primary health services, can improve the standard of drug use.

In a sense all physicians who are interested in the effects of drugs on their patients may be seen as clinical pharmacologists, but few of them have been properly trained in this role. Clinical pharmacologists are firstly physicians who have received full training in clinical medicine and have also received training in the methods of studying and eliciting drug responses in humans, and of studying the absorption, distribution, metabolism and excretion of drugs, and in the principles of clinical drug evaluation. They will often provide the interface between laboratory scientists and clinicians.

In western Europe the annual cost of drugs per capita is US $50–100 *(4)*. Secondary costs derived from drug-related events, such as adverse drug reactions causing hospitalization, inability to work and other problems add to the total costs. By rationalizing drug therapy in terms of selection of drugs, dosing and treatment principles, substantial costs can be saved, while at the same time the quality of health care may be improved.

Clinical pharmacology as an independent academic discipline was first established some 20 years ago. The developments over the following years have been strikingly different in different countries. In some countries chairs in clinical pharmacology have now been established in most medical schools (German Democratic Republic, Scandinavia, United Kingdom), whereas clinical pharmacology has hardly been recognized as an independent discipline in many other countries.

In this working paper the main functions of clinical pharmacology within *service*, *teaching* and *research* will be described.

## Clinical Pharmacology Service

Clinical pharmacology service may be provided at international (e.g. through WHO), national, regional or local levels. The clinical pharmacology service at a national level is mainly provided in relation to the services of drug regulatory agencies, whereas the service at a local or regional level usually will be associated with a regional clinical pharmacology regulatory centre.

*Central drug regulatory agencies* deal with *drug registration, control of clinical trials, adverse drug reaction monitoring*, and *drug information*, and thus encompass a number of clinical pharmacological functions. The services of clinical pharmacologists are necessary in particular for the following purposes:

— to decide whether animal data on a drug are adequate to justify its administration to humans;

— to decide whether therapeutic trials justify release for general use;

— to develop and conduct drug monitoring programmes;

— to advise on restrictions on the availability of drugs or their withdrawal from the market.

However, and mainly for historical reasons, the participation of clinical pharmacologists in these services has varied and has been limited in most countries. With an increasing understanding of the significant role of clinical pharmacology in those areas, and the increasing availability of clinical pharmacologists, this ought to change in future.

At the *regional and local* level clinical pharmacology has a service role in a number of areas.

*Patient care* is undertaken by clinical pharmacologists as a routine responsibility in some centres (general medicine or drug problem oriented consultations), and more indirectly, through consultative functions, "pharmacotherapeutic rounds", and drug conferences at other centres. This will depend on local circumstances.

Clinical pharmacologists play an active role in providing *information about drugs*. This may be done in collaboration with pharmacists, and there may well be local or regional drug information centres *(5)*. *Drug or formulary committees* have already been established in the hospital sector in many countries, but are now also starting to cover the needs of primary health care in some countries. The activities of such committees are

usually closely linked to the clinical pharmacology service where the latter exists. By carrying out current *drug utilization surveys*, the clinical pharmacologist can fulfil an important task by early detection of changes in prescribing habits that may be undesirable in terms of drug costs or drug effect profiles, and by evaluating the effects of drug information programmes. *Adverse drug reaction* monitoring programmes may serve similarly as an early warning system, which is particularly important for newly introduced drugs, whose potential adverse reactions have not been fully evaluated *(6)*. Clinical pharmacology departments can also provide trained personnel, who can quickly begin investigation of a suspected adverse drug reaction and in some centres can also manage cases of overdose. It should not be forgotten that drug-related problems may account for more than 10% of the admissions to general medical wards *(7)*.

Standard doses of drugs may produce widely different drug concentrations in different patients. *Drug concentration monitoring* is essential, therefore, for some drugs, such as certain antiepileptics and antidepressants, lithium, theophylline and digoxin. In such cases low plasma concentrations may result in therapeutic failure, and high plasma concentrations may produce severe adverse reactions *(8,9)*. The clinical pharmacologist, by virtue of his or her training, is uniquely qualified to organize this service, both in provision and interpretation of the data, as well as in deciding whether further techniques, such as protein binding studies or pharmacogenetic evaluation, are required.

Although some *clinical trials* are carried out by clinical pharmacologists, many are conducted by clinical specialists. The clinical pharmacologist is a source of advice to clinicians who are going to conduct such trials, and clinical pharmacology groups sometimes provide special services, such as drug assays and facilities and personnel for the coordination of multicentre trials.

A major goal of the clinical pharmacology service should be to establish close contact with *general practice*. Primary health care physicians prescribe the majority of all drugs used, and the need for current drug information and consultation is probably even more pronounced there than in hospitals.

## Teaching in Clinical Pharmacology

*Undergraduate teaching* in clinical pharmacology has not, in common with other clinical pharmacology functions, reached such an international level of recognition that general rules can be given. At some medical

schools clinical pharmacologists participate in basic pharmacology courses, usually given early in the clinical part of the study. Later in the curriculum, teaching in clinical disciplines is usually centred on symptoms and diagnosis, and little or no time is given to the principles of drug treatment. Regular clinical pharmacology courses, usually at the end of the course, are included to a varying extent in different medical schools. This may be as formal lectures, integrated clinical teaching sessions or "therapeutic rounds". In general there is increasing understanding of the need for clinical pharmacology courses in the undergraduate curriculum. Medical students should receive a thorough grounding in the principles of clinical pharmacology so that they can appreciate the rational use of drugs. They will then carry with them into their professional lives a framework which will allow them to interpret the actions and uses of new drugs as they are introduced into clinical practice. We believe that clinical pharmacology teaching should be a mandatory part of the medical curriculum and that this teaching should take place during the clinical years.

*Postgraduate teaching* has traditionally been a field in which clinical pharmacologists have played a much more prominent role than at the undergraduate level *(10)*. Drug therapy is a dynamic, rapidly changing field with a corresponding need for continuing education. After qualification doctors need a continuing source of information about drugs, both new and old, and all too often doctors have relied for information on the promotional efforts of the pharmaceutical industry. It is generally accepted that the standard of prescribing and use of drugs is too low in many fields of medicine. Intensified administrative control measures cannot improve this, and we believe that all doctors should undergo mandatory education in therapeutics at regular intervals during their professional lives. Such teaching must be independent of the pharma-ceutical industry, and should be based on comparative evaluation of the best available treatments. The establishment of close contact between clinical pharmacology centres and general practitioners may become an important framework for such continuing education programmes.

## Clinical Pharmacology Research

In all academic medical disciplines, service and teaching are closely related to research, and this link is particularly strong in clinical pharmacology. There will be continuing interaction between these fields, and

research functions must be considered an integral part of any clinical pharmacology centre. The goals of the research will be to improve drug therapy, not only by developing means to avoid unwanted effects, but also by improving the efficacy of therapy through various means of drug and effect monitoring.

*Clinical pharmacokinetic* studies of absorption, distribution, metabolism and excretion of drugs have traditionally had a prominent role in many clinical pharmacology research centres. Research may include kinetic studies during single and multiple dosing, drug concentration/effect studies, and the role of active metabolites in drug action. Central to this research is interindividual variability in pharmacokinetics, which seems to be a major determinant of variations in the effects of many drugs in humans *(11)*. Genetic factors seem to be of considerable importance and they have been particularly well documented in relation to drug metabolism. This may shed new light on the occurrence of rare, severe adverse drug reactions *(12)*. In general, the scope of pharmacokinetic research is to provide a scientific basis for safer and more effective clinical use of drugs by understanding interindividual variability.

*Clinical pharmacodynamic* studies encompass a wide variety of techniques and principles. The measurement of therapeutic drug effects in relation to drug evaluation is a classical problem. The development of more sophisticated techniques for studying drug-receptor interactions *in vivo* and *in vitro* can add new dimensions to clinical pharmacodynamic research, and clinical pharmacologists should play a role in bridging the gap between experimental pharmacology and clinical medicine.

*Drug evaluation and therapeutic trials* aim at defining the potential benefits and hazards of new drugs *(13,14)*. It is increasingly accepted that the requirements for such studies are considerable and demand expertise in various fields, with the clinical pharmacologist in a central role. These requirements relate to the precision with which true differences between new and old drugs can be established in terms of therapeutic efficacy and safety in the smallest number of patients. We see the role of clinical pharmacologists as ideally fitting them to help in the design of clinical trial protocols by which the mechanisms of action of the drugs which are tested, and the reasons for variability of their effects may be systematically explored in carefully defined populations.

*Drug epidemiology/utilization* has been an area of growing concern and research interest during recent years *(15)*. International collaborative studies have shown considerable differences in drug consumption in

different countries, and even within countries pronounced differences often occur. The results, mainly based on sales figures and prescription data, ought to be further examined in relation to morbidity, social and economic factors, patient and doctor attitudes, medical education, and referral and prescription patterns, etc.

## Training of Clinical Pharmacologists

Formal training programmes in clinical pharmacology exist only in countries in which clinical pharmacology has been recognized as a separate medical speciality, but proposed training programmes are available for some other countries.

In general the programmes require an academic degree in medicine (e.g. MD) followed by combined clinical and clinical pharmacological training. We recommend, on the evidence presented above, that the clinical training period should typically include service functions, teaching and research in clinical pharmacology. More specifically, it should include basic clinical service in one of the main clinical specialties, while the emphasis should be in specialist training in clinical pharmacology, which may include experimental pharmacology. The overall training period after the period of residency in hospital will normally be five to six years.

## Clinical Pharmacology Centres

In those countries where clinical pharmacology has been established as a medical discipline, clinical pharmacology departments (units, divisions, centres) have been established at or in conjunction with a university hospital. The departments may have been established either as separate units or within existing departments of pharmacology or internal medicine. In either case the clinical pharmacologists may have direct clinical responsibilities, using, in the latter case, hospital beds which belong to the department. The size of existing clinical pharmacology departments varies considerably, and the optimal organization of clinical pharmacology units within the health system has yet to be defined. The existing departments usually cover regions with populations of 1–3 million, but smaller units have been proposed.

The present location of clinical pharmacology departments in an academic setting in a university hospital dictates a relatively strong

emphasis on research and teaching relative to service. The introduction of clinical pharmacology into district general hospitals would shift the main basis to service functions, as already described. We can expect further developments in this direction in primary health care.

## Perspectives: Use of Clinical Pharmacological Expertise

In the pharmaceutical industry the central role of clinical drug testing in drug development has been acknowledged, and the employment of clinical pharmacologists in the industry is already increasing. Use of more clinical pharmacological expertise in central, national drug control agencies, in conjunction with an improved regional clinical pharmacological service, seems to be essential to achieve a better and more integrated system for the development and control of new drugs. However, the major goal of the development of clinical pharmacology will be to provide service and research facilities to both hospitals and the primary health sector. Precisely how such facilities should be organized has not been generally defined, and local and national circumstances have to be considered. There is, however, a need for definition of the minimal requirements for clinical pharmacological expertise in this part of the health sector.

An integrated development, such as that outlined in this paper, should allow clinical pharmacologists to express more fully their role with respect both to medicine and society. It would also provide the capacity to answer the increasing and justified requests from patients for a more complete understanding of the role of drug therapy in the prevention and treatment of disease.

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# The teaching and organization of clinical pharmacology in European medical schools[a]

*WHO Working Group on Clinical Pharmacology in Europe*[b]

Clinical pharmacology has brought two central themes to the treatment and management of patients, firstly, the reliance on scientific data to make rational therapeutic decisions and, secondly, to try to individualize drug therapy *(1)*. Clinical pharmacology has also contributed much to the research area of drug development. However, the advances in clinical pharmacology have not necessarily found their way into routine medical care as rapidly as they could. It is clear that medical students should receive a good grounding in clinical pharmacology during their undergraduate course so that they can easily understand current therapies as well as evaluate and assimilate new therapeutic advances in the future. However, the status of clinical pharmacology varies from country to country in Europe, and thus in 1983 the WHO Regional Office for Europe set up a task force to try to ascertain the status of clinical pharmacology in the various countries of the Region *(1)*. One of the initiatives of that group was to try to find out about the organization and teaching of clinical pharmacology in European medical schools.

## Materials and Methods

A simple questionnaire concerned with clinical pharmacology teaching was sent to all deans of medical schools in the European Region. The WHO European Region comprises continental Europe (including the USSR) together with Israel and Turkey. The questionnaire was initially sent out in February 1987, and at that time there were 350 medical schools

[a] Reproduced by permission from the *European journal of clinical pharmacology*, **38**: 101-105 (1990).

[b] Members: J. Bircher, M. Bogaert, M.N.G. Dukes, M. Eichelbaum, L.F. Gram, H. Huller, I. Lunde, M. Orme, F. Sjöqvist, G. Tognoni.

in the Region. Reminders were sent out to all schools which had not replied in August 1987 and this was followed by individual approaches to deans of medical schools (or heads of departments) by members of this group in the first three months of 1988.

The questionnaire was designed to be completed easily, either by the dean of the medical school concerned or by the head of the relevant department. The questionnaire was designed to discover if there were departments of pharmacology or clinical pharmacology in the medical school. If there was no clear department of clinical pharmacology, then we (the WHO Working Group on Clinical Pharmacology) wished to know if there were divisions or sections in the subject of clinical pharmacology, although we recognized that the difference between divisions and sections was likely to be arbitrary.

The questionnaire also asked about the number of staff who had received formal training in clinical pharmacology, and about the number of posts in the medical school with "clinical pharmacology" in their title. This question caused some concern since these words are not uniformly used throughout the Region (e.g. in France, units concerned with monitoring adverse drug reactions are called "pharmacovigilance units" but often these units also do clinical pharmacology work). Finally, the questionnaire asked about the number of hours devoted to the teaching of pharmacology, clinical pharmacology and therapeutics and by whom these subjects were taught. The exact definition of these three subjects was left to the respondents, although we envisaged pharmacology as the scientific aspects of the subject taught to preclinical students, and therapeutics as the practical administering of drugs to patients usually taught by clinicians in small group discussions.

## Results and Discussion

Of the 350 questionnaires sent out, a total of 213 were completed and returned. The returns were particularly low from the USSR, with only 8 forms completed out of 89 sent out to individual medical schools. These returns were not evaluated further. Greece and Portugal have both been omitted from the analysis since only one return was received from each country. Thus, the overall compliance rate when these countries were excluded was 82%, with a figure of 84% in western Europe and 74% in eastern Europe. For the purpose of this document, western Europe is operationally defined as including Israel and Turkey. It was originally decided to separate the results of eastern and western Europe because of

the differing evolution of medical care and medical student teaching in those two areas. However, in the analysis, the results from the two regions are not too dissimilar.

Departments of pharmacology were present in 198 out of the 204 medical schools replying. In Italy one medical school, in the United Kingdom one school and in Spain two schools had no formal department of pharmacology, but in each case this was due to amalgamation of the previous department, usually into a department of physiological sciences. Two medical schools in Ireland reported themselves as having divisions of pharmacology. Table 1 shows the number of medical schools in western Europe completing the questionnaire with compliance rates varying between 100% and 50%. The organization of clinical pharmacology is also shown in Table 1 with 43 departments, 30 divisions and 51 sections of clinical pharmacology. The remaining 38 medical schools have no formal arrangement for clinical pharmacology. The departments of clinical pharmacology were all independent but the divisions and sections were in general part of either a department of medicine (32%) or a department of pharmacology (65%) with one section affiliated to clinical chemistry. Table 1 also shows that 330 staff members have been trained in clinical pharmacology in the countries of western Europe, with an average of 2.0 people per medical school reporting. The maximum number was 12 individuals apparently trained in clinical pharmacology in one medical school in Spain. However, many medical schools reported that they had no individual trained in clinical pharmacology. In particular, 10 medical schools in France, 8 in the Federal Republic of Germany and 8 in Italy have no individual trained in clinical pharmacology.

The number of posts in clinical pharmacology throughout western Europe is also shown in Table 1, with an average of 1.3 posts per medical school. A similarly patchy picture is seen, with the largest number of posts being found in one medical school in Sweden (which has two departments of clinical pharmacology), while many schools have no posts in the subject. Thus, in France, 15 schools have no posts in clinical pharmacology as such, though these medical schools tend to concentrate on posts in "pharmacovigilance". In Italy 9 medical schools, in Spain 9 schools, and in the Federal Republic of Germany 19 schools have no posts in clinical pharmacology. In Turkey, clinical pharmacology has little impact since there is only one individual trained in clinical pharmacology in the schools responding, with no formal posts in the subject. In two countries — one in western Europe and one in eastern Europe — the returned questionnaire indicated that a medical school had 12-15 posts in clinical

Table 1. Western Europe: WHO clinical pharmacology questionnaire

| Country | Number of medical schools responding (% of total in country) | Number of medical schools with a department (Dpt), division (Div) or section (S) of clinical pharmacology | Mean number of staff members trained in clinical pharmacology per medical school (range) | Mean number of posts in clinical pharmacology per medical school (range) |
|---|---|---|---|---|
| Austria | 3 (100%) | 1 Div | 3.0 (0 – 8) | 0.3 (0 – 1) |
| Belgium | 6 (85%) | 1 Div, 4 S | 1.0 (0 – 2) | 0.1 (0 – 1) |
| Denmark | 3 (100%) | 2 Dpt, 1 Div | 1.6 ( 1 – 2) | 1.3 (1 – 2) |
| Federal Republic of Germany | 26 (96%) | 4 Dpt, 2 Div, 5 S | 1.6 (0 – 5) | 0.5 (0 – 5) |
| Finland | 6 (100%) | 2 Dpt, 1 Div, 2 S | 2.0 (1 – 4) | 0.6 (0 – 1) |
| France | 28 (80%) | 9 Dpt, 5 Div, 11 S | 1.4 (0 – 6) | 0.8 (0 – 5) |
| Iceland | 1 (100%) | 1 Div | 0.0 | 2.0 |
| Ireland | 5 (100%) | 2 Dpt, 1 Div | 1.4 (0 – 4) | 1.0 (0 – 3) |
| Israel | 3 (60%) | 2 Div | 3.0 (0 – 5) | 1.0 (0 – 2) |
| Italy | 15 (48%) | 1 Dpt, 2 Div, 9 S | 1.0 (0 – 4) | 0.5 (0 – 2) |
| Netherlands | 4 (50%) | 2 Dpt, 2 Div | 3.0 (1 – 4) | 1.0 (1 – 2) |
| Norway | 4 (100%) | 2 Dpt, 2 S | 2.5 (0 – 5) | 2.3 (2 – 4) |
| Spain | 20 (83%) | 2 Dpt, 5 Div, 8 S | 2.5 (0 – 12) | 1.2 (0 – 6) |
| Sweden[a] | 6 (100%) | 4 Dpt, 2 Div, 1 S | 4.0 (1 – 11) | 3.3 (0 – 13) |
| Switzerland | 5 (100%) | 1 Dpt, 4 Div | 2.4 (1 – 4) | 1.7 (1 – 3) |
| Turkey | 6 (55%) | 1 Dpt, 1 S | 0.15 (0 – 1) | 1.0 (0 – 3) |
| United Kingdom | 23 (100%) | 11 Dpt, 2 Div, 9 S | 3.3 (1 – 7) | 3.2 (0 – 6) |
| Total/Mean | 16 (84%) | 43 Dpt, 30 Div, 51 S | 2.02 (0 – 12) (330 staff members *in toto*) | 1.28 (0 – 13) (208 posts *in toto*) |

[a] One medical school in this country has two departments of clinical pharmacology.

pharmacology, but with no individual trained in the subject. This is obviously an error in the completion of the form, and these data have been excluded.

The situation in eastern Europe is shown in Table 2, with 40 medical schools (74% of the total) completing the questionnaire. All had departments of pharmacology. There are 15 departments of clinical pharmacology, of which 12 are independent and 3 are under the control of pharmacology departments. There are also 4 divisions and 12 sections of clinical pharmacology, of which 70% are affiliated to departments of pharmacology and 24% to departments of medicine. There are 92 individuals in these medical schools trained in clinical pharmacology, which gives an average of 2.3 per medical school responding. On average, there are 1.1 posts in clinical pharmacology per medical school. In Yugoslavia, only one medical school (out of seven replying) has posts in clinical pharmacology.

The number of hours of pharmacology, clinical pharmacology and therapeutics taught in western European medical schools is shown in Table 3. These figures represent the total number of hours taught in the subject in the whole course. In most medical schools, pharmacology is taught in the second year of study, but clinical pharmacology may be taught in any of the last four years. On average, 96 hours are devoted to the teaching of pharmacology, which is similar to the mean figure of 133 hours taught in North American medical schools *(2)*. One school in Turkey teaches no pharmacology to undergraduates (it being a postgraduate subject). On average, 28 hours are devoted to the teaching of clinical pharmacology but a number of schools in Austria (2), Belgium (2), France (3), Italy (6), Spain (9) and the Federal Republic of Germany (10) teach no clinical pharmacology. In the latter three countries, there are official governmental moves to take clinical pharmacology out of the undergraduate medical curriculum, which seems a retrograde step with so many therapeutic advances made recently. There is no teaching of clinical pharmacology in the six Turkish medical schools completing the questionnaire. There is a considerable variation in the hours of clinical pharmacology taught in medical schools even in those countries where the subject is well established. Some of this variation may be due to a difficulty in responding to the questionnaire and deciding what is pharmacology, what is clinical pharmacology and what is therapeutics. However, in those medical schools where few hours of clinical pharmacology are taught, there is no obvious increase in the hours of pharmacology or therapeutics taught.

Table 2. Eastern Europe: WHO clinical pharmacology questionnaire

| Country | Number of medical schools responding (% of total in country) | Number of medical schools with a department (Dpt), division (Div) or section (S) of clinical pharmacology | Mean number of staff members trained in clinical pharmacology per medical school (range) | Mean number of posts in clinical pharmacology per medical school (range) |
|---|---|---|---|---|
| Bulgaria | 2 (40%) | 1 Dpt, 1 S | 1.5 (0 – 3) | 0.5 (0 – 1)[a] |
| Czechoslovakia | 7 (58%) | 1 Dpt, 2 S | 1.0 (0 – 3) | 0.8 (0 – 3) |
| German Democratic Republic | 8 (89%) | 6 Dpt, 2 Div | 3.1 (2 – 7) | 2.4 (1 – 5) |
| Hungary | 4 (100%) | 1 Div, 1 S | 1.25 (0 – 3) | 0.75 (0 – 3) |
| Poland | 11 (78%) | 5 Dpt, 1 Div, 3 S | 4.1 (0 – 10) | 1.8 (0 – 10) |
| Romania | 1 (20%) | 1 Dpt | ? | 8.0 |
| Yugoslavia | 7 (70%) | 1 Dpt, 5 S | 3.0 (0 – 10) | 0.4 (0 – 3) |
| Total/ Mean | 40 (74%) | 15 Dpt, 4 Div, 12 S | 2.3 (0 – 10) (92 staff members *in toto*) | 1.1 (0 – 10) (44 posts *in toto*) |

[a] One questionnaire was excluded from this analysis since the school in question claimed 15 posts in clinical pharmacology but had no individual trained in the subject.

Table 3. Number of hours of pharmacology, clinical pharmacology and therapeutics taught in medical schools in western Europe

| Country | Response rate (%) | Pharmacology (mean (range)) | Clinical pharmacology (mean (range)) | Therapeutics (mean (range)) |
|---|---|---|---|---|
| Austria | 100 | 97 (6 – 165) | 2 (0 – 6) | 0 |
| Belgium | 86 | 55 (10 – 120) | 15 (0 – 77) | (0 – 45) |
| Denmark | 100 | 83 (60 – 100) | 43 (20 – 85) | (4 – 10) |
| Federal Republic of Germany | 96 | 88 (10 – 210) | 31 (0 – 70) | 18 (0 – 50) |
| Finland | 100 | 154 (130 – 200) | 36 (18 – 62) | 6 (0 – 22) |
| France | 80 | 45 (12 – 120) | 29 (0 – 110) | 48 (0 – 150) |
| Iceland | 100 | 103 | 42 | 0 |
| Ireland | 100 | 81 (35 – 120) | 23 (0 – 68) | 18 (12 – 32) |
| Israel | 60 | 100 (70 – 161) | 30 (12 – 50) | 0 |
| Italy | 48 | 85 (50 – 300) | 16 (0 – 50) | 22 (0 – 75) |
| Netherlands | 50 | 114 (70 – 190) | 77 (18 – 210) | 61 (16 –140) |
| Norway | 100 | 101 (66 – 135) | 18 (15 – 20) | 29 (10 – 80) |
| Spain | 83 | 97 (30 – 180) | 20 (0 – 60) | 18 (0 – 100) |
| Sweden | 100 | 125 (56 – 320) | 26 (12 – 44) | 24 (17 – 44) |
| Switzerland | 100 | 90 (50 – 150) | 33 (12 – 58) | 18 (10 – 36) |
| Turkey | 55 | 109 (0 – 140) | 0 | 7 (0 – 40) |
| United Kingdom | 100 | 100 (30 – 315) | 40 (6 – 137) | 22 (0 – 100) |
| Mean (range) | 84 | 96 (0 – 320) | 28 (0 – 210) | 18 (0 – 150) |

Therapeutics is taught for an average of 18 hours in western European medical schools but this is likely to be an underestimate, since some teaching in clinical medicine will involve therapeutics. There is again a considerable variation in the hours devoted to this subject both within and between countries.

Table 4 shows the number of hours taught by pharmacologists, clinical pharmacologists and clinicians in western Europe. Pharmacology is almost universally taught by pharmacologists with a little help from clinical pharmacologists. Thus, of the mean 96 hours of pharmacology, 90 are taught by pharmacologists. Clinical pharmacologists are involved in the teaching of their subject to a more varied extent. In many cases, they are involved in teaching pharmacology and therapeutics as well as clinical pharmacology. It is clear that the biggest problems are in France, the Federal Republic of Germany, Italy and Spain, where the lack of trained clinical pharmacologists severely restricts the ability to teach the subject.

Table 4. Number of hours taught by pharmacologists, clinical pharmacologists and clinicians in the teaching of pharmacology, clinical pharmacology and therapeutics in "western European" medical schools

| Country | Pharma-cologists (mean (range)) | Clinical pharmacologists (mean (range)) | Clinicians (mean (range)) |
|---|---|---|---|
| Austria | 84 (6 – 165) | 13 (0 – 40) | 2 (0 – 6) |
| Belgium | 57 (20 – 120) | 15 (0 – 80) | 6 (0 – 45) |
| Denmark | 79 (45 – 108) | 48 (20 – 65) | 7 (4 – 10) |
| Federal Republic of Germany | 104 (0 – 255) | 14 (0 – 42) | 17 (0 – 48) |
| Finland | 133(106 – 170) | 36 (22 – 58) | 5 (0 – 7) |
| France | 50 (12 – 170) | 23 (0 – 85) | 46 (0 – 150) |
| Iceland | 84 | 0 | 61 |
| Ireland | 77 (25 – 120) | 9 (0 – 68) | 36(12 – 104) |
| Israel | 100 (70 – 161) | 30 (12 – 50) | 7 (0 – 22) |
| Italy | 85 (40 – 300) | 13 (0 – 52) | 28 (0 – 50) |
| Netherlands | 114 (20 – 190) | 159 (28 – 280) | 61(16 – 140) |
| Norway | 76 (50 – 92) | 40 (27 – 80) | 25 (0 – 80) |
| Spain | 82 (30 – 120) | 39 (0 – 114) | 13 (0 – 100) |
| Sweden | 128 (56 – 320) | 35 (8 – 68) | 11 (7 – 20) |
| Switzerland | 82 (30 – 150) | 40 (22 – 58) | 19 (10 – 30) |
| Turkey | 109 (0 – 140) | 0 | 7 (0 – 40) |
| United Kingdom | 90 (20 – 315) | 54 (15 – 160) | 16 (0 – 60) |
| Mean (range) | 90 (0 – 320) | 36 (0 – 280) | 21 (0 – 140) |

Clinical pharmacologists teach the most hours in the Netherlands, where very many hours in some schools are devoted to the teaching of all three subjects.

In eastern Europe 124 hours on average are devoted to the teaching of pharmacology (see Table 5) and this subject is taught exclusively by pharmacologists (see Table 6). While there is some variation among medical schools, all countries devote on average in excess of 100 hours to the teaching of pharmacology. Clinical pharmacology is taught for 27 hours on average in eastern Europe, very similar to the figure in western Europe. Most medical schools teach some clinical pharmacology and the subject is usually taught by individuals trained in clinical pharmacology, but there are in general fewer individuals so trained in eastern Europe than

Table 5. Number of hours of pharmacology, clinical pharmacology and therapeutics taught in medical schools in eastern Europe

| Country | Response rate (%) | Pharmacology (mean (range)) | Clinical pharmacology (mean (range)) | Therapeutics (mean (range)) |
|---|---|---|---|---|
| Bulgaria | 40 | 125 (100 – 150) | 30 (30 – 30) | 0 |
| Czechoslovakia | 58 | 107 (70 – 120) | 12 (0 – 20) | 16 (0 – 60) |
| German Democratic Republic | 67 | 131 (0 – 180) | 75 (60 – 90) | 6 (0 – 35) |
| Hungary | 100 | 119 (84 – 150) | 7.5 (0 – 30) | 14 (0 – 40) |
| Poland | 78 | 148 (90 – 240) | 30 (15 – 60) | 1.4 (0 – 15) |
| Romania | 20 | 120 | 15 | 0 |
| Yugoslavia | 77 | 120 (100 – 150) | 21 (0 – 50) | 16 (0 – 30) |
| Mean (range) | 74 | 124 (0 – 240) | 27 (0 – 90) | 7.5 (0 – 60) |

Table 6. Number of hours taught by pharmacologists, clinical pharmacologists and clinicians in the teaching of pharmacology, clinical pharmacology and therapeutics in medical schools in eastern Europe

| Country | Pharma-cologists (mean (range)) | Clinical pharma-cologists (mean (range)) | Clinicians (mean (range) |
|---|---|---|---|
| Bulgaria | 135 (105 – 150) | 10 (0 – 15) | 10 (0 – 15) |
| Czechoslovakia | 107 (70 – 136) | 10 (0 – 20) | 18 (0 – 60) |
| German Democratic Republic | 131 (0 – 180) | 75 (60 – 90) | 6 (0 – 35) |
| Hungary | 119 (84 – 150) | 7.5 (0 – 30) | 14 (0 – 40) |
| Poland | 143 (45 – 240) | 34 (15 – 90) | 1.4 (0 – 15) |
| Romania | 120 | 15 | 0 |
| Yugoslavia | 120 (80 – 200) | 20 (0 – 68) | 9 (0 – 30) |
| Mean (range) | 125 (0 – 240) | 24.5 (0 – 90) | 8.3 (0 – 60) |

in western Europe (see Tables 1 and 2). Few hours are devoted to the teaching of therapeutics in eastern Europe.

It is clear from this survey that pharmacology is well represented in medical schools in Europe, with about 100 hours of teaching performed by pharmacologists. Clinical pharmacology is taught in a much more sporadic pattern. In some countries (Netherlands, Scandinavia, United Kingdom) the subject is taught in every medical school by at least a minimum of trained individuals. However, in other countries, notably Italy, the Federal Republic of Germany and Spain, many medical schools teach no clinical pharmacology, and there is a dearth of individuals trained in the subject, and a lack of established posts from which to teach the current generation of medical students. With the advent of ever more potent drugs for the treatment of disease, this is a situation which must be rectified.

## Conclusions

This survey has highlighted a number of problem areas that need to be tackled if clinical pharmacology is to make progress as a clinical and academic discipline.

1. Clinical pharmacology is taught for relatively few hours on average, compared with those devoted to pharmacology.

2. However, while the teaching of clinical pharmacology is reasonably well developed in some countries (e.g. Sweden, United Kingdom), several countries in Europe have very little teaching time devoted to the subject. This is particularly true in the Federal Republic of Germany, Italy and Spain. In western Europe, 39 medical schools (24% of those responding) devote no time to the teaching of clinical pharmacology, and in a further 20 schools there is less than 12 hours in the whole medical course devoted to the subject. In eastern Europe, there is no teaching of clinical pharmacology in seven of the medical schools (17% of those responding), while a further five schools teach less than 12 hours of clinical pharmacology.

3. There is considerable variation within a country in the hours devoted to clinical pharmacology teaching. In some universities, the subject is developed while in other universities the discipline is not represented at all.

4. There is a lack of individuals trained in clinical pharmacology in Europe. On average, each medical school has about 2 staff members

trained in the subject. However, this figure hides a wide inter- and intracountry variation. There is also a lack of posts in the subject, with on average only one post in the subject in each medical school. In France 15 medical schools (out of 28 responding), in the Federal Republic of Germany 19 (out of 25), and in Italy 9 (out of 15) have no posts of clinical pharmacology.

5. Attention should be focused on the importance of clinical pharmacology as a teaching discipline so that the rational use of drugs can be improved in the Region. This would be achieved by establishing units of clinical pharmacology in those universities where the subject has no current presence and by strengthening those units that are functioning, albeit under considerable strain. The current plans to reduce clinical pharmacology teaching in the Federal Republic of Germany, Italy and Spain thus seem particularly retrogressive.

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# Clinical pharmacology and primary health care in Europe: a gap to bridge[a]

*WHO Working Group on Clinical Pharmacology in Europe*[b]

The great majority of drugs, some 80%, is known to be prescribed and consumed outside academic or other institutional settings, where most drugs have been evaluated. Following the initial clinical trials of a drug and the grant of a product licence, the drug will be promoted for use in primary health care. The physicians involved at that stage will have had little experience in any of the initial trials and will be exposed to promotional information from the pharmaceutical company concerned. Primary health care (PHC) physicians therefore find themselves in a difficult and challenging situation. First, they prescribe a wider range of drugs than their hospital colleagues. Second, their prescriptions may also be for clinical conditions which do not correspond to those which have been subject to controlled evaluation. And third, the PHC physicians are confronted with multiple, hospital-generated prescriptions and have to care for the practice of self-medication. The information available to them is not always pertinent or relevant to their decisions.

These unfavourable conditions of drug use become apparent in connection with major drug problems and occasional surveys of drug use. On those occasions, the need for improved quality of drug therapy in PHC is underlined.

With rare exceptions, clinical pharmacology has developed in the academic hospital setting. In such environments it has proved its value *(1)*. It is logical to assume that clinical pharmacology might contribute substantially to PHC if extended to this discipline. The contribution should involve not only experts in clinical pharmacology but also PHC

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[a] Reproduced by permission from the *European journal of clinical pharmacology*, **38**: 315-318 (1990).

[b] Members: M.N.G. Dukes, P.K.M. Lunde, A. Melander, M. Orme, F. Sjöqvist, G. Tognoni, H. Wesseling.

physicians with training in clinical pharmacology and other health personnel with competence in therapeutics.

In addition to advantages regarding the efficacy and safety of drug therapy, important benefits may be anticipated with regard to public drug expenditure.

## Definitions

The reader is referred to the WHO publications on clinical pharmacology *(2)* and PHC *(3)* for comprehensive descriptions of those disciplines. The following definitions are adopted here.

Clinical pharmacology is a medical discipline which, on a scientific basis, combines pharmacological, clinical and epidemiological knowledge with the aim of ensuring the rational use of drugs. PHC may be described as the level of health care that people first encounter for their health needs (i.e. related to diseases or symptoms), where decisions are made about treatment or the need for further investigation or referral, and where patients are followed up after discharge from hospitals and other institutions.

## State of the Art and Current Problems

### Clinical pharmacology

The development of clinical pharmacology in Europe has recently been reviewed by the WHO Working Group on Clinical Pharmacology in Europe *(1)*. Two points deserve to be stressed in the context of PHC. One is the uneven development of clinical pharmacology within the European Region *(4)* and indeed throughout the world. In many regions the PHC physician has been exposed neither to clinical pharmacology as a concept nor to a clinical pharmacologist. The second problem is that many established departments of clinical pharmacology work in isolation from PHC.

### Primary health care

Physicians in PHC take care of patients who differ from those seen in institutional settings in terms both of the pattern of disease and the demographic variables. The elderly, the handicapped and patients with multiple pathology are well represented in PHC, but are rarely included in most hospital-based clinical trials.

## The Gap between Clinical Pharmacology and PHC

While clinical pharmacology services now exist in many hospital settings, there is still a gap between clinical pharmacology and PHC, although many of the problems of drug use occur in PHC, some being similar to those seen in hospitals, and others unique to PHC. The following aspects should be considered.

### Rational drug use

Drugs are not always used for the purpose for which they have been developed, investigated and approved. They may be used for entirely unproven indications or in cases for which there is no rationale. Doses may be excessive or too low, and multiple prescribing may lead to interactions. There is often too little awareness of individual variation in dosage needs (e.g. in elderly patients or persons with a particular pharmacogenetic constitution). Some drugs may be overprescribed (e.g. antibiotics, hypnotics, sedatives, and antihypertensives in the elderly). Occasionally, there are problems with underconsumption (e.g. when the value of a drug is inadequately known), and some drug doses may be too low.

### Safety–efficacy balance

The safety–efficacy balance of certain drugs and therapeutic strategies is inadequately established in primary health care, if not completely unknown. This is particularly true in PHC when patients with borderline conditions and multiple diseases require many drugs.

Furthermore, many new drugs are accepted too rapidly for PHC, without the systematic adverse reaction monitoring necessary for early detection of serious reactions. Post-marketing surveillance would be of great value here.

### Compliance with the drug regimen

There is a serious problem about patient compliance with therapy, even when there is a clear need for the drug, e.g. in epilepsy and severe hypertension.

### Preventive therapy

The role of PHC physicians in areas where prophylactic long-term drug treatment and non-pharmacological intervention may represent complementary or alternative strategies is largely unexplored, e.g. for cardiovascular and psychogeriatric problems.

### Therapeutic drug monitoring

Existing knowledge of the need for therapeutic drug monitoring is not widely applied in PHC, sometimes because the necessary facilities are lacking, and sometimes because the PHC physician is not aware of the need. On the other hand, inappropriate use of therapeutic drug monitoring without proper assessment of its utility may mislead the clinician and cause unnecessary cost.

### Drug research in PHC

The results and conclusions of trials conducted within hospitals may be inadequate for application in PHC. On the other hand, many trials conducted under PHC conditions are not of such a nature as to contribute to therapeutic knowledge. Studies of drug use in PHC are often scanty. If conducted properly, they could provide valuable epidemiological data on morbidity and the quality of care in different settings, thus forming a basis for educational opportunities and for the promotion of better oriented research projects. The design and assessment of drug studies is a specialized matter, in which the PHC physician is likely to need support to assure validity of the proposed methods and techniques. PHC physicians have much to offer to clinical pharmacologists in collaborative drug research.

### Cost–benefit ratio

Concern is often expressed about expenditure on drugs in general or in special situations. It is difficult to decide whether a particular therapy is cost-effective: the cheapest drug is not always the best in this respect. Moreover, adequate use of modern, allegedly expensive drugs may be highly cost-effective if the need for inpatient care is reduced. On the other hand, inadequate use of inexpensive drugs may lead to extra inpatient care due to adverse effects.

### Influence of commercial versus non-commercial factors on prescribing

In the provision of information to the PHC physician, the pharmaceutical industry plays a dominant role. This activity also extends to the organization of trials, which are initiated by the drug producer, mainly to familiarize the PHC physicians with the drug and to keep them prescribing it (so-called "promotional" or "seeding" trials). The commercial influence often distorts the information, particularly about such issues as the extent to which a drug should be used, or whether the drug produced by the informant or by a competitor should be selected.

## How to Bridge the Gap between PHC and Clinical Pharmacology

It is clear from the problems listed above that various types of interaction between clinical pharmacology and PHC can be conceived, and most or all of them have been used in practice in one country or another. They go beyond the teaching role, which has usually been predominant. The interaction between PHC and clinical pharmacology will depend on needs and on attitudes.

The conventional clinical pharmacologist, who has not worked in PHC, may not have a proper appreciation of its nature and needs. A period in PHC is probably a *sine qua non* for any clinical pharmacologist who wishes to function properly outside the hospital environment.

PHC physicians may not be aware of their needs in this area, or their need may be a latent one, which will only become evident when they discover to what extent they would be aided if clinical pharmacology services were attuned to their work. It is important to know whether they would consult a clinical pharmacologist and, if so, under what circumstances, and with what type of problem. As an example, would they find the clinical pharmacologist useful as a resource person for drug research matters? It is particularly important in this situation to realize that clinical pharmacology is much more than the individual clinical pharmacologist or his or her staff. In fact, it is the entire body of knowledge available about drugs and their proven or suspected effects in humans.

The problems outlined so far may be classified into four broad categories: (*a*) teaching and training, (*b*) service aspects, (*c*) research and (*d*) finance.

### Teaching and training

Teaching in clinical pharmacology should start early in the undergraduate medical curriculum, so that the graduate has a firm theoretical base on which to build future therapeutic advances. A final-year course in practical therapeutics will enable the newly qualified doctor successfully to transfer his or her theoretical knowledge to the everyday clinical setting in hospital.

Postgraduate teaching in clinical pharmacology for PHC physicians should aim to improve their knowledge about rational drug use so that the best use of drug therapy can be achieved at a reasonable cost. Primary health care physicians also learn from their experiences and they should

play a more active role in the therapeutic process by, for example, being members of formulary and therapeutics committees.

A small number of PHC physicians should receive more extensive training in clinical pharmacology and therapeutics than others, to be able to assist and advise their colleagues in practice, thereby serving as "ambassadors" of clinical pharmacology. At that stage, teaching need not be limited to purely therapeutic matters. As examples, questions of drug economics and drug policy will be relevant.

## Service aspects

*Consultative services*

A PHC physician should be able to consult a clinical pharmacologist or other source of drug information for advice about individual cases, particularly when a specific drug-related problem is involved (e.g. evaluation of adverse reactions and other drug problems, information on drugs in pregnancy and nursing, individualization of drug dosage, drug interactions). Drug information centres, staffed by clinical pharmacologists and pharmacists in close collaboration, and building data banks containing problem-oriented drug information relevant to PHC, may be particularly valuable *(5)*.

*Other services*

In some centres, a clinical pharmacology unit will be the site to which the PHC physicians refer patients for certain tests or studies (e.g. phenotyping individual patients for drug metabolizing capacity). In some instances, it will be desirable for the clinical pharmacologist to have a regional function, in order to be accessible to all PHC physicians on demand.

*Drug research*

It may be anticipated that an increasing volume of drug research and clinical trials will be carried out within PHC, even in those countries in which there is no tradition of involving PHC physicians in this respect. The following aspects ought to be considered.

1. Sophisticated studies are needed to assess the safety–efficacy balance of drugs, i.e. the interplay of pharmacological and non-pharmacological preventive and prophylactic measures, and the role of compliance in determining the overall benefit–risk ratios of therapies. Methodological and organizational problems that may be faced in the planning of such studies in PHC may be usefully addressed by close cooperation between clinical pharmacology units and PHC physicians.

2. Many problems, particularly in the pharmacotherapy of diseases prevalent in PHC (e.g. hypertension, atherosclerosis, diabetes, osteoarthritis, minor psychiatric conditions and mental deterioration in the elderly) require formal clinical trials. The joint contribution of specific clinical pharmacological expertise and of the knowledge and control of general care conditions by PHC physicians is likely to create more favourable conditions for research at an acceptable cost.

3. A positive interaction would be of help in the development of an effective and reliable scheme for adverse reaction monitoring.

4. Multidisciplinary skills must be developed both in PHC and clinical pharmacology units, to devise appropriate methods and to produce satisfactory data about the cost-benefit ratio, a field which has only rarely been studied.

5. Studies of drug use require methods which have been well developed by certain clinical pharmacology and other centres. The results can provide valuable support for PHC physicians in evaluating the quality and appropriateness of their practices. Some countries are now able to feed back to PHC physicians details about their drug prescribing, and this is a valuable educational experience.

6. Therapeutic drug monitoring is available for some drugs in virtually all hospitals. However, the value of plasma concentration monitoring in PHC may need to be re-examined in certain circumstances. This could be a useful cooperative endeavour between clinical pharmacology and PHC, both as a research medium and as a way of improving clinical care and optimizing the use of resources.

7. There is little doubt that clinical pharmacology would itself benefit greatly from closer interaction with PHC. Among other aspects, the knowledge acquired about drug use and therapeutic problems of PHC would stimulate new research projects and should suggest strategies of patient care that could lead to better coordination between hospital specialists and PHC physicians in drug selection and drug use.

Because of the structure of most health care systems, clinical pharmacology in Europe could have a unique opportunity to stimulate and promote global research strategies:

— to study neglected therapeutic problems of specific relevance in PHC;

— to compare differences in therapeutic outcome in patients exposed to different treatments because of the differing traditions in various countries;

— to establish research networks oriented to assessment of the epidemiological impact of long-term preventive treatments so far tested only in short-term controlled trials.

*Finance*

A common denominator of many of these plans is financial support. Some support will be needed to expand clinical pharmacology into the PHC area and such an exercise should not be expensive. It may well save money in the long run. There is a good argument that rational drug prescribing in hospitals, while perhaps not reducing drug costs, has markedly reduced the rise in costs that might have been expected. This has come from the use of hospital formularies among other advances. In PHC, the promotion of rational drug therapy, including in many instances the better use of generic prescribing, would be expected to curtail the rising cost of drug prescribing. Drug prescribing in some countries (e.g. the United Kingdom) is currently not cost-limited, and recent governmental moves present an ideal opportunity to improve the input of clinical pharmacology into PHC, while at the same time improving the cost-benefit ratio. The greatest economic benefit of closer collaboration between PHC and clinical pharmacology might be reduction in the indirect cost arising from hospitalization of patients with inappropriate drug treatment.

## Conclusions and Recommendations

Both in the short and the long term, the coming together of clinical pharmacology and primary health care should be planned and carried out with four main objectives in mind, namely *education*, *service*, *research* and *financial organization.*

In creating a more favourable situation, which may differ in detail from one country to another because of differences in the structure of PHC, progress will have to be phased. Initially, the aim should be to make the clinical pharmacologists already established in academic and hospital centres available to provide expertise and support to general practitioners throughout the European Region. Ultimately, the goal must be to have sufficient numbers of individuals trained in clinical pharmacology actually working in primary health care.

Countries that have not instituted clinical pharmacology as a permanent discipline in their universities *(4)* should be urged to do so. They should also be urged to ensure that the development of clinical pharmacology includes individuals collaborating with PHC units.

Countries where the discipline of clinical pharmacology already exists should be asked to allocate resources to those departments to build up units for collaboration with PHC physicians.

In all countries, increased resources may be required, but there is an excellent chance in the long run of financial savings and improved cost-benefit ratios in drug therapy.

Colleagues working in PHC with an interest in clinical pharmacology are cordially invited to respond to our call for collaboration.

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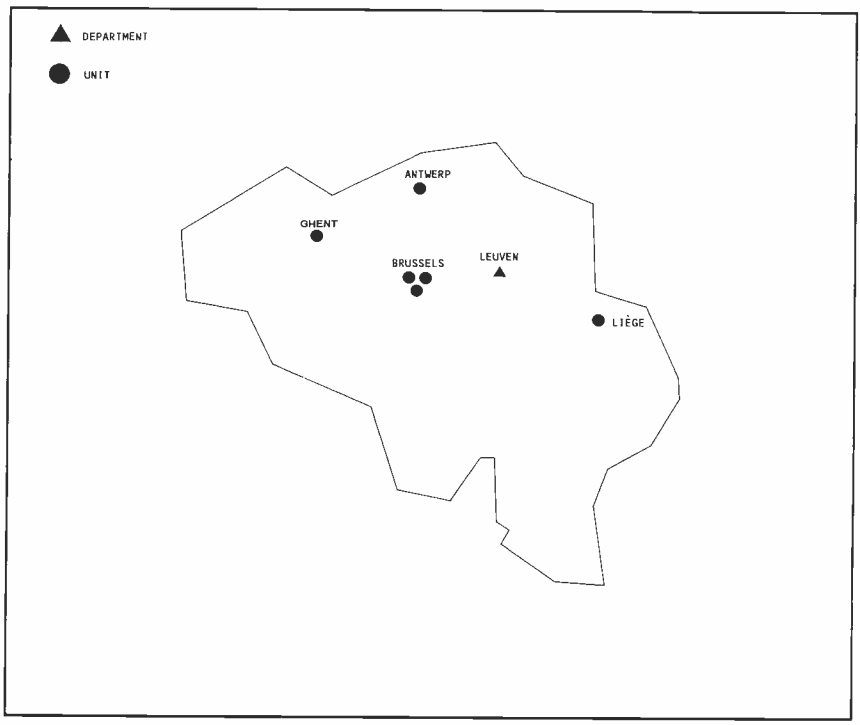
# Country reports

# Belgium




## Teaching, Service and Research

There are six medical schools in Belgium; none has a formal department of clinical pharmacology, although small informal groups exist. There is only one formal post in clinical pharmacology in the country. People interested in the subject or in taking part in clinical pharmacological activities usually have training in both pharmacology and a clinical field: usually internal medicine.

In spite of the absence of formal structures, a number of people are working in clinical pharmacology, usually in academic departments of pharmacology or internal medicine. Most are involved in the undergraduate teaching programme for pharmacology and therapeutics as well as in teaching postgraduates. They are also involved in research and in the provision of drug information.

All the medical schools have departments of pharmacology in which there is an interest in clinical pharmacology. In five of these departments, doctors with training in both pharmacology and internal medicine hold senior positions.

There are no formal training programmes in clinical pharmacology in Belgium. Although clinical pharmacology has little presence in the hospital service, units of clinical pharmacology are active in the pharmaceutical industry.

## Long-term Plans

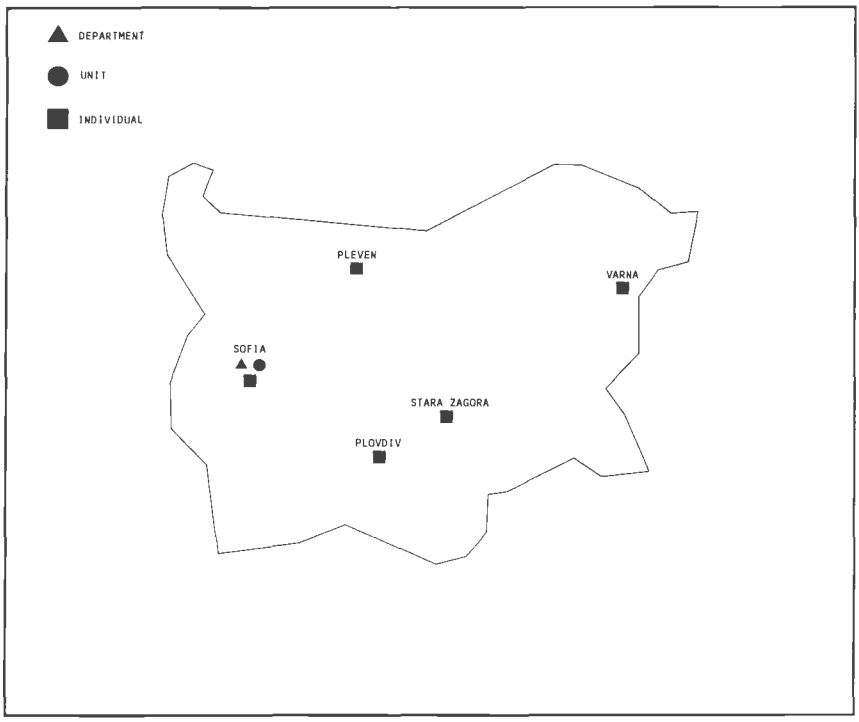
There are no plans for the formalization or further development of clinical pharmacology in Belgium in the near future.

## National Association

The Belgian Society for Experimental and Clinical Physiology and Pharmacology provides a regular forum for most of the people active in clinical pharmacology. The contact person for clinical pharmacology within the Society is:

Professor M. Bogaert
Department of Pharmacology
University of Ghent Medical School
De Pintelaan 185
9000 Ghent.

# Bulgaria




## Teaching, Service and Research

Clinical pharmacology is relatively young in Bulgaria but there is considerable interest in the discipline. The main activities take place in the capital, Sofia, where the Medical Academy has a department of clinical pharmacology, founded in 1981 and headed by a professor of clinical pharmacology. In addition, a clinical pharmacology unit is established at the research institute of the state pharmaceutical enterprise *Pharmachim.* In general, people interested in clinical pharmacology have a background in pharmacology rather than internal medicine. People with interest or duties in clinical pharmacology are present in the medical schools in Pleven, Plovdiv, Stara Zagora and Varna.

Clinical pharmacology is taught in some of the medical schools — usually in the fifth year of study. The subject is also taught at

the postgraduate level to doctors and pharmacists, particularly by the department in Sofia. Research is pursued in a variety of areas and most clinical pharmacologists have responsibility in health care for solving pharmacokinetic problems or therapeutic drug monitoring.

## Long-term Plans

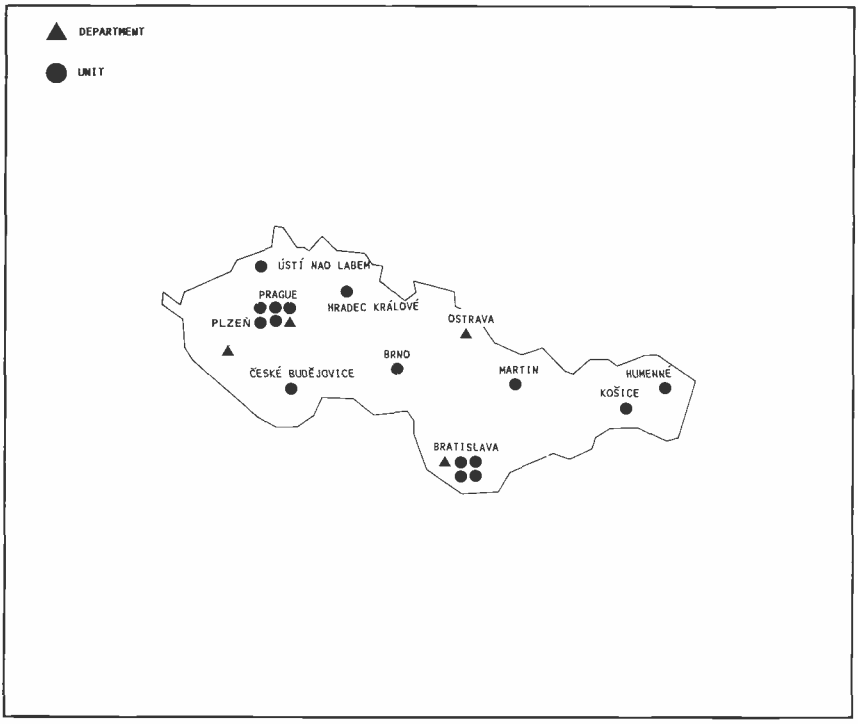
It is hoped to have divisions or departments of clinical pharmacology in all medical schools in the foreseeable future.

## National Association

The Bulgarian Pharmacological Society has a Clinical Pharmacology Section to which most interested people belong. Further information can be obtained from:

Professor V. Vlahov
Belo More Str. 8
1040 Sofia.

# Czechoslovakia




## Teaching, Service and Research

Clinical pharmacology has been developing steadily since the late 1950s. Czechoslovakia differs from most European countries in that this development has mostly taken place at non-academic institutions.

Clinical pharmacology was recognized as an independent specialty in 1976 and this status was confirmed in official documents in 1982. Clinical pharmacology has developed in regional and district hospitals with an emphasis on health care, while the emphasis in state research institutes is naturally on research. There are four departments of clinical pharmacology in Czechoslovakia but only one of these (in Plzeň) is at a university. Recently a special division of the State Institute for Drug Control (SUKL) in Prague has been established to examine the use and adverse effects of drugs.

Since 1981 doctors have been able to specialize in clinical pharmacology as a branch of internal medicine. The initial specialty training focuses on internal medicine or paediatrics, although other disciplines may be included later. Then follow three years of practice in a clinical pharmacology department, one year of which is spent learning techniques in experimental pharmacology.

The teaching of clinical pharmacology in undergraduate medical schools does not reflect its importance in the country. There is no formal course in clinical pharmacology, although some lectures in the subject are given in most medical schools. Postgraduate training in clinical pharmacology is centred on the Czeck and Slovak institutes for postgraduate education in medicine and pharmacy. Here lectures are given and courses arranged for doctors working in clinical pharmacology.

Research in clinical pharmacology addresses all phases of the clinical development of drugs and is directed by the State Research Plan. In the hospital service, regional units of clinical pharmacology provide services such as therapeutic consultation, adverse drug reaction monitoring and drug information. These units also do some drug utilization studies.

## Long-term Plans

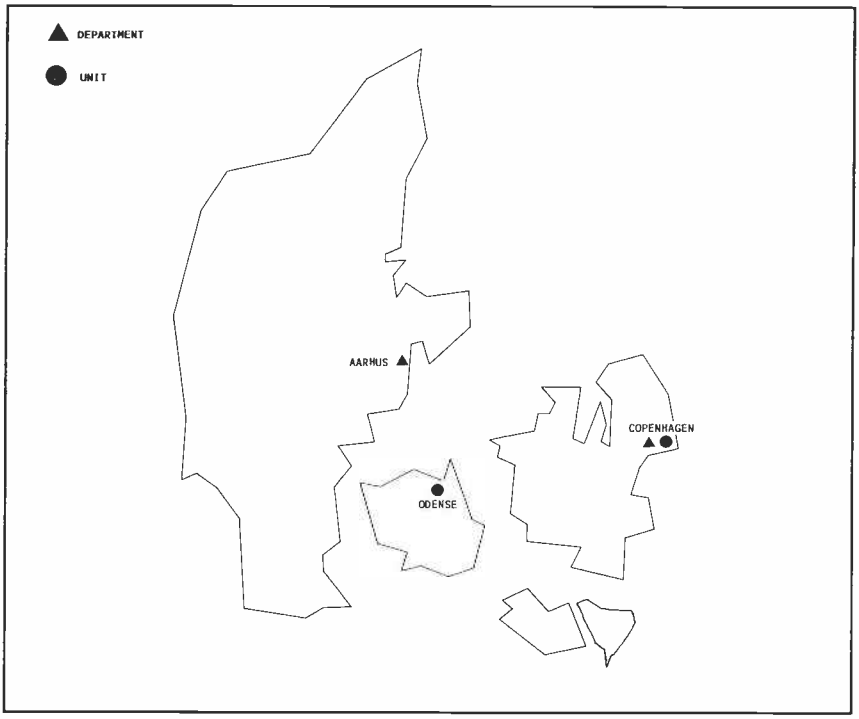
The long-term aims for clinical pharmacology date from 1982. The plan is to have independent clinical pharmacology departments in all the regional hospitals and state research institutes. There are no particular plans for universities or teaching.

## National Association

The Czech and Slovak republics each have a society of pharmacology; each society has a clinical section. Both societies organize conferences on clinical pharmacology. Further information can be obtained from:

Professor Jiri Elis
State Institute for Drug Control (SUKL)
Srobarova 48
10041 Prague 10.

# Denmark




## Teaching, Service and Research

Clinical pharmacology is now established in Denmark as an academic discipline at the three medical faculties at the universities in Copenhagen, Aarhus and Odense. University chairs in clinical pharmacology were established some 8–10 years ago, although that in Aarhus was vacant from 1978 to 1985.

Units or divisions of clinical pharmacology have been organized around the university chairs and within the departments of pharmacology in Odense and Aarhus and the University Hospital in Copenhagen. In the past, other academic personnel have been temporarily associated with these units as research fellows or clinical research assistants. More recently, however, positions for senior research associates have been established in Odense and Aarhus. These clinical pharmacology units

have a formal responsibility for teaching undergraduates and research; they also provide services to the University Hospital and are active in postgraduate training. None of the pharmacology departments has direct clinical responsibilities.

Clinical pharmacology has so far not been recognized as a separate specialty in Denmark. In a proposal to this effect, made in 1982, the Danish Society of Clinical Pharmacology put forward a training programme consisting of about three years' clinical training and four years' training in experimental and clinical pharmacology. Several people who meet these criteria hold positions in pharmacology or clinical specialties.

## Long-term Plans

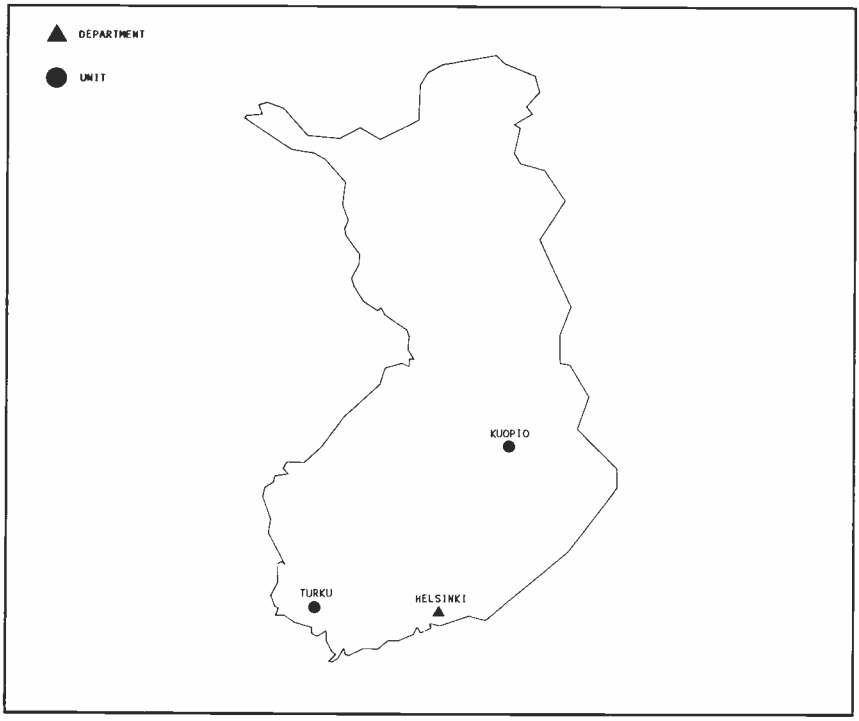
Committees of the national health service (in 1974) and the Danish Society of Clinical Pharmacology (in 1982) proposed that a clinical pharmacology position be established at the general hospital in each county (14–15 in total). In the immediate future, however, clinical pharmacology is likely to develop mainly at the university centres.

## National Association

The Danish Society of Clinical Pharmacology was established in 1978 and has about 100 members. The Society organizes scientific meetings and courses in clinical pharmacology. Further information can be obtained from:

Professor L. Gram
Department of Clinical Pharmacology
Odense University
J.B. Winslows Vej
5000 Odense C.

# Finland




## Teaching, Service and Research

Clinical pharmacology has been an official specialty in Finland since 1966 and it has an accepted role in teaching and research. The development of the specialty in general health care, however, has been very slow. Clinical pharmacology has developed only in the five university medical schools. The department in Helsinki was founded in 1969 and the unit of clinical pharmacology in Turku was started in 1983. The department is responsible for the operation of the Finnish poisons information centre. In addition, individuals are working in clinical pharmacology in other medical schools. A clinical pharmacologist, for example, holds the chair of toxicology and pharmacokinetics in Kuopio.

Medical students learn about clinical pharmacology during the clinical part of the course. In addition to lectures (30 - 44 hours),

demonstrations, seminars and therapy meetings are held. Teaching in clinical pharmacology is also offered to postgraduates from a variety of professions.

Training in clinical pharmacology consists of two years of general professional training in medicine, one year of which is spent in general practice. Specialty training consists of four years in clinical pharmacology, one year of which is often spent in basic pharmacology, clinical chemistry or clinical physiology. Recognition as a specialist follows success in a national board examination. There are three positions in Helsinki and two in Turku for trainees in clinical pharmacology. No funds, however, are available for the training of visiting fellows.

In health care, clinical pharmacology is involved in therapeutic drug monitoring and therapeutic consultations. There is considerable involvement of clinical pharmacology in care in the university hospitals, but there are no beds for which the subject is responsible. Research is actively pursued in all centres and focuses particularly on pharmacokinetics, drug metabolism and clinical trials.

## Long-term Plans

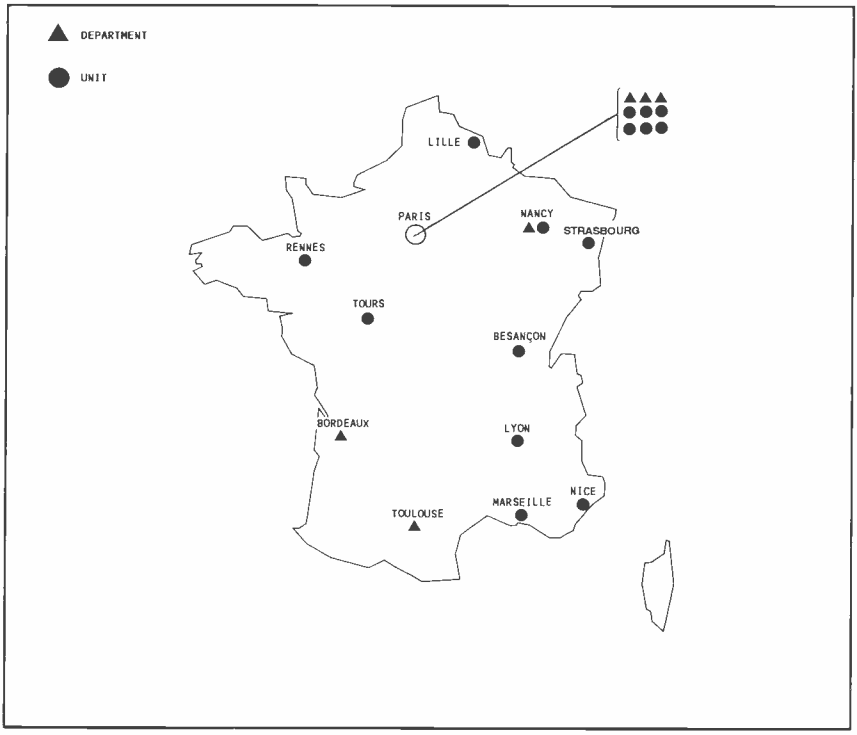
The long-term aim is to strengthen clinical pharmacology activities in universities but more particularly in hospitals. A committee of the Ministry of Health has planned that every district hospital should have a clinical pharmacologist, in addition to those in academic centres.

## National Association

Most clinical pharmacologists belong to the Finnish Pharmacological Society but also take part in meetings of clinical pharmacologists from other countries of the Region. Further information can be obtained from:

Professor Esko Iisolo
Clinical Pharmacology Unit
Turku University Hospital
Kiinamyllynkatu 4-8
20520 Turku 52.

# France




## Teaching, Service and Research

Official recognition of clinical pharmacology as a specialty came in 1981 when the clinical option for university professors of pharmacology was added to the biological option. Since 1981 a dozen chairs in clinical pharmacology have been established in the principal universities of France: those at Bordeaux, Clermont-Ferrand, Lyon, Marseille, Nancy, Paris, Saint-Etienne, Toulouse and Tours. A number of professors of pharmacology appointed to their chairs before 1981, however, have competence in clinical pharmacology and participate equally in its activities.

Clinical pharmacology is taught in the second and third years of undergraduate medical studies. Postgraduates also receive instruction in

a variety of courses, and clinical pharmacologists teach the subject to doctors and specialists in hospitals and in the pharmaceutical industry. A national doctorate in biological and medical science (the pharmacological option) has been established to replace the old doctorate in human biology. Future professors of clinical pharmacology will be expected to hold two doctorates, one in medicine and one in medical and biological science.

The situation of clinical pharmacology in the hospital service varies very much from area to area. Clinical pharmacology services are grouped together in some university hospitals such as those in Lyon, Paris and Toulouse. Such groups are being set up in other areas following an official statement of December 1988 that authorized clinical trials in the voluntary sector. In some areas, departments of medical pharmacology are reorganizing as units of clinical and biological pharmacology. Units of clinical pharmacology in hospitals are involved in all aspects of clinical trials (phases I, II and III), in developing regional pharmacovigilance units, in trying to improve both therapeutics and cost-effectiveness in clinical care, in therapeutic and medical audit activities, and in ethical committee matters. A national research group of 24 centres of clinical pharmacology has been formed at the instigation of the Ministry of Solidarity, Health and Social Protection. The Ministry supplies financial support to these centres, which must reciprocate with an annual report on their scientific and financial activities. Each year a meeting is held to discuss research activities, which are supported by a number of official bodies.

## Long-term Plans

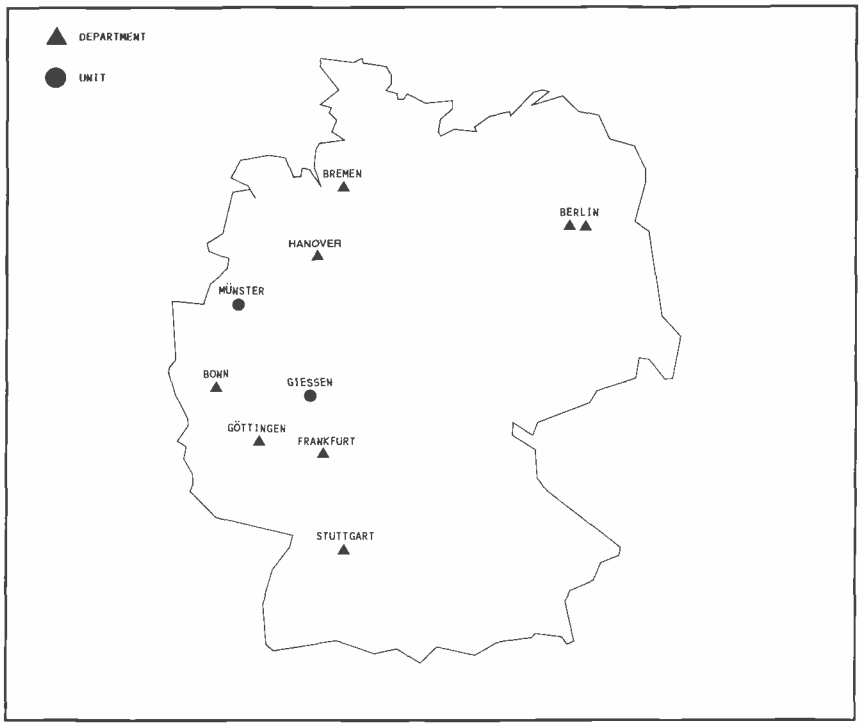
Long-term plans include further strengthening the university units and developing hospital activities. The chief weakness is the lack of hospital services in clinical pharmacology. The Ministry of Solidarity, Health and Social Protection is studying the possibility of establishing hospital units of clinical pharmacology. These units would have beds and would be used both to give care and to conduct clinical trials. Such units would need adequate medical and allied health care staff.

## National Association

The French Association of Pharmacologists has a clinical section that meets regularly for the presentation of scientific papers and the discussion of administrative matters. Further information can be obtained from:

Professor P. Jaillon
Unité de Pharmacologie Clinique
Hôpital St-Antoine
184, rue du Faubourg St Antoine
75012 Paris.

# Germany[a]




## German Democratic Republic

### Teaching, Service and Research

In the German Democratic Republic, clinical pharmacology is an established academic discipline in all universities and medical academies. The subject developed from pharmacology rather than from internal medicine and thus is less involved in direct patient care than in some countries. In the 1980s, activities largely consisted of the education of both undergraduates and postgraduates, improvement in the safety and efficacy of drug treatment, and drug development through clinical trials. There are six departments of clinical pharmacology in the country with three divisions, and small working groups in highly specialized clinics. An

[a]As mentioned previously, the collection of responses to the questionnaire concluded in July 1990, before the unification of Germany.

Institute of Clinical Pharmacology has been funded in the National Academy of Sciences.

Undergraduate medical education in clinical pharmacology is now established in all the medical schools in the country, with 60 hours of lectures and seminars. Dentists receive a shorter course of 30 hours. In addition, most of the academic units undertake postgraduate education. Specialist training in clinical pharmacology is usually given in one of the university or medical academy departments of clinical pharmacology.

After qualification as a doctor, a candidate takes a five-year specialty training programme that includes at least two years in pharmacology and toxicology, one year in a clinical discipline and then a two-year period in clinical pharmacology. An examination concludes the programme and successful candidates are registered as specialists in clinical pharmacology and toxicology.

Clinical pharmacologists are involved in health care through therapeutic drug monitoring and general advice on, for example, adverse drug reactions. Most units conduct research and by law clinical pharmacologists are responsible for phase I and phase II drug trials. Clinical pharmacology is established in the national research plan as a separate mainstream subject.

## Long-term Plans

Although clinical pharmacology is reasonably well established in academic units, these need strengthening, and the hope is to expand the role of clinical pharmacology in health care.

## National Association

Most clinical pharmacologists are members of the Society for Pharmacology and Toxicology and specialist clinical pharmacology activities are organized there. Further information can be obtained from:

Professor H. Hüller
Institut für Klinische Pharmakologie des Bereichs Medizin
Humboldt-Universität
Schumannstr. 20–21
1040 Berlin.

# Federal Republic of Germany

## Teaching, Service and Research

Although the German Medical Association has recognized clinical pharmacology as a specialty in medicine, the discipline has developed rather slowly and from pharmacology rather than from internal medicine.

At present there are four departments of clinical pharmacology, at the universities of Berlin, Frankfurt, Göttingen and Hanover. Three units are affiliated with departments of medicine at the universities of Bonn, Giessen and Heidelberg. Besides these university-based departments and units, there is an Institute of Clinical Pharmacology in Stuttgart, funded by the Robert-Bosch Foundation, and a division of clinical pharmacology at the Cardiology Clinic in Bad Krozingen. In addition, all the major pharmaceutical companies (Bayer, Boehringer Ingelheim, Boehringer Mannheim, Hoechst, Knoll, Merck and Schering) have clinical pharmacology units.

People wishing to specialize in clinical pharmacology must obtain a medical degree and then enter a period of training in experimental pharmacology and toxicology. This lasts three years, after which the candidate requires an additional two years' training at a department or unit of clinical pharmacology. After this period, one year of training in clinical medicine is required. An examination follows the six years of training both in pharmacology and clinical pharmacology; a candidate who passes becomes a specialist in both pharmacology and clinical pharmacology.

Training in clinical pharmacology is usually given by one of the university departments or units of clinical pharmacology. It can also be obtained in a clinical pharmacology unit in one of the major pharmaceutical firms. Candidates who take the second route receive training in pharmacology and clinical pharmacology in accordance with the guidelines set up by the German Medical Association. They do not, however, receive training in clinical medicine.

## Long-term Plans

The development of the discipline has been hampered by the federal system of education in the Federal Republic of Germany. The ministers

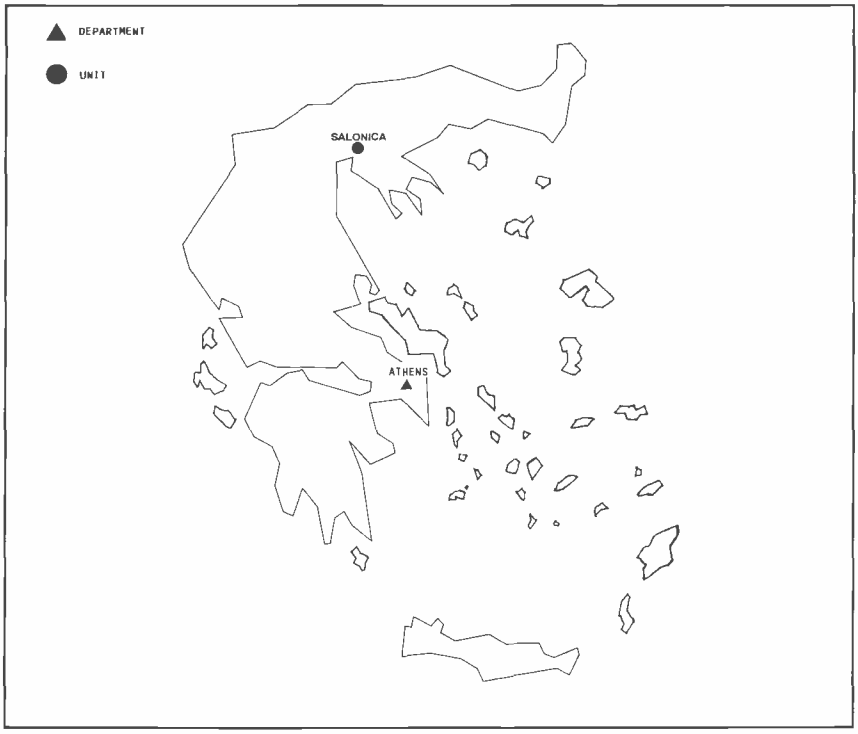
of education of the *Länder* have all agreed, however, that a unit of clinical pharmacology should be established in every university to improve teaching and practice in therapeutics.

## National Association

Most clinical pharmacologists belong to the German Pharmacological Society (GPS), which has a section for clinical pharmacology with about 260 members. The secretary of this section is:

Professor U. Abshagen
Fa. Boehringer Mannheim Gmbh
Sandhoferstr. 116
6800 Mannheim 31.

# Greece




## Teaching, Service and Research

Clinical pharmacology is in its infancy in Greece, but the teaching of clinical pharmacology and therapeutics is established at the National and Capodistrian University of Athens. Basic pharmacology is taught to all medical students in Greek universities, usually in the third year of the course. The medical school of the National and Capodistrian University of Athens has a department of clinical therapeutics where clinical pharmacology and therapeutics are taught to fifth-year medical students in a fifty-hour course. The department also conducts research and has a laboratory for clinical pharmacology. Similar research work is conducted in the departments of internal medicine of the other Greek medical schools.

There is no formal training programme in clinical pharmacology in Greece and the few trained clinical pharmacologists received their training abroad.

Clinical pharmacology is not actively involved in health care in Greece, although some consultations take place in Athens. Therapeutic drug monitoring, where it exists, is carried out by clinical chemists. The monitoring of adverse reactions to drugs is carried out in collaboration with the drug regulatory agency.

## Long-term Plans

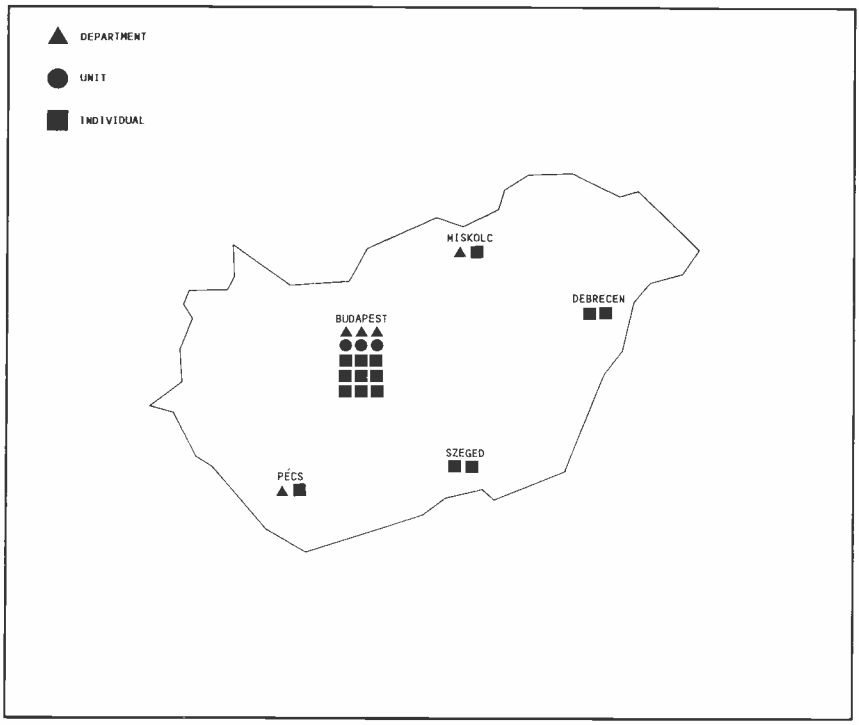
There are no formal long-term plans for the discipline in Greece.

## National Association

A Greek society for clinical pharmacology acts as a national forum for interested people. Further information can be obtained from:

Professor S.D. Moulopoulos
Department of Clinical Therapeutics
Medical School
National and Capodistrian University of Athens
80 Vas. Sofias
K. Lourou Str.
11528 Athens.

# Hungary




## Teaching, Service and Research

A clinical pharmacology network was established in 1967 by agreement between the Scientific Health Council and the ministries of health and industry. Initially the network consisted of a number of small hospital units or university departments that gradually became larger as the facilities improved. It was recently decided to reorganize the discipline by forming a National Centre for Clinical Pharmacology to control the other units while leaving them attached to their mother institutions. Thus the National Centre is to direct the 24 units in Hungary to perform their duties in collaboration with local clinics or hospitals. The reorganization is progressing slowly because of economic difficulties.

Much of the work of the units of the clinical pharmacology network is concerned with the evaluation and registration of drugs. Three units are

specially equipped to do phase I or II studies. One or two new units may be required to study the increased number of drugs coming from the pharmaceutical industry. The systematic monitoring of adverse reactions to drugs was introduced in 1977 and spontaneous reports are submitted by doctors throughout the country.

Clinical pharmacology is not taught to medical students as a formal part of their undergraduate training, although there are courses at the postgraduate medical school. Clinicians working in clinical pharmacology departments for two years after taking their basic specialty degrees (in, for example, internal medicine) can obtain additional certification in clinical pharmacology.

## Long-term Plans

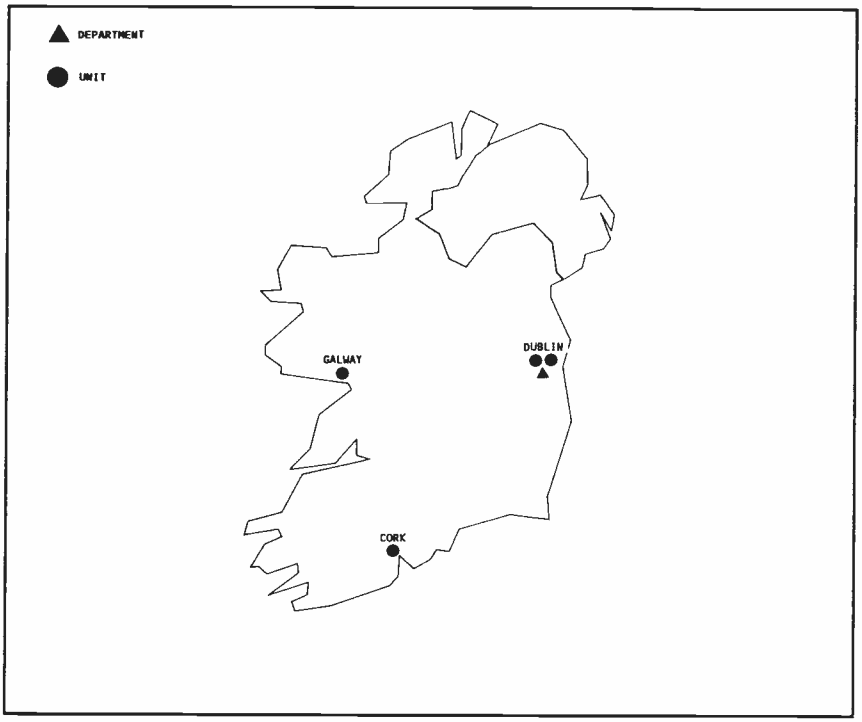
There are no definite plans for the future of clinical pharmacology in Hungary.

## National Association

The Hungarian Pharmacological Society has a section for clinical pharmacology with about 150 members. This is the main forum for meetings. Further information can be obtained from:

Professor A. Kaldor
National Centre for Clinical Pharmacology
Semmelweiss University of Medicine
Scentkiral Y1 U46
1088 Budapest.

# Ireland




## Teaching, Service and Research

There are five medical schools in Ireland; two, those in Trinity College Dublin and the Royal College of Surgeons in Ireland, have a major clinical pharmacology presence. In both cases, clinical pharmacologists chair the departments responsible for the teaching of basic pharmacology, clinical pharmacology and therapeutics. Two other medical schools, in University College Dublin and University College Cork, are setting up clinical pharmacology facilities. In the remaining medical school, in University College Galway, basic pharmacology is taught within a department of pharmacology and applied aspects of pharmacology are taught by two part-time lecturers.

Clinical pharmacologists play an important role in the activities of the national drug regulatory agency: the National Drugs Advisory Board.

## Long-term Plans

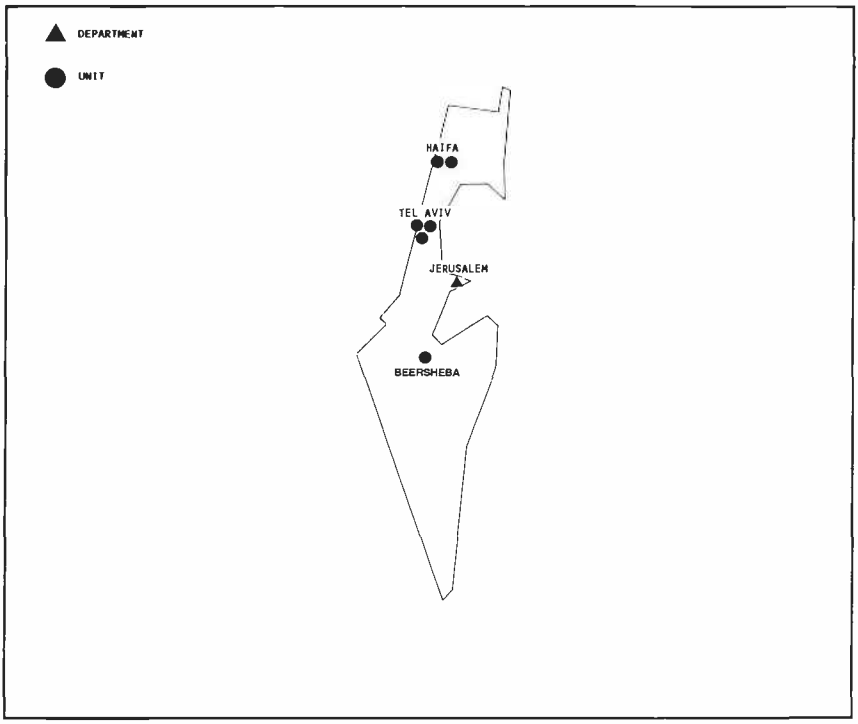
There is no structured plan for clinical pharmacology in Ireland; individual universities decide on their own priorities. In all probability four of the five medical schools will have a major clinical pharmacology facility in the near future.

## National Association

There is no clinical pharmacology society in Ireland. Interested people belong to and participate actively in the clinical section of the British Pharmacological Society. Further information can be obtained from:

Professor K. O'Malley
Department of Pharmacology
Royal College of Surgeons in Ireland
123 St Stephen's Green
Dublin 2.

# Israel




## Teaching, Service and Research

Clinical pharmacology has developed in connection with university teaching hospitals in Israel; the first unit opened in 1974. There are four medical schools in Israel — in Beersheba, Haifa, Jerusalem and Tel Aviv — to which seven units of clinical pharmacology are attached. Five of the units are in departments of medicine while the other two are independent; one of these also provides education in basic pharmacology. The units are run by doctors who are trained in internal medicine and/or pharmacology and have received additional training in clinical pharmacology outside Israel.

Undergraduate medical students are taught clinical pharmacology in their fourth year of studies; this is followed by seminars in the final year. Seminars or short courses are also provided for postgraduates. Doctors in

specialty training can do the six-month basic research requirement in clinical pharmacology. There are no other specialty training programmes in clinical pharmacology and no board examinations.

All clinical pharmacology units have active research programmes and service commitments to hospitals. Areas of clinical work include therapeutic drug monitoring, therapeutic consultations, drug information and adverse drug reaction monitoring.

## Long-term Plans

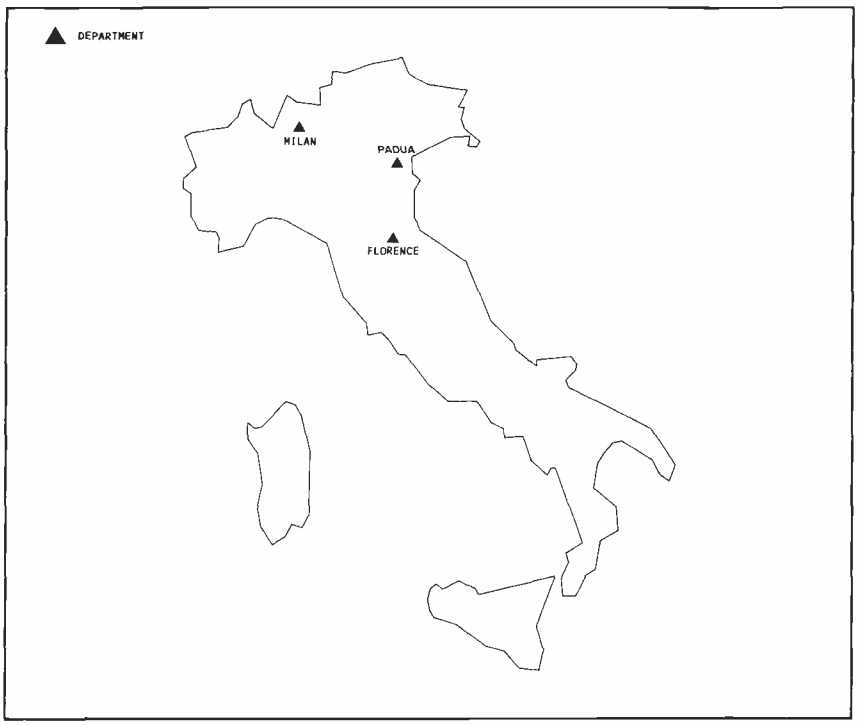
There are at present no plans for the further development of clinical pharmacology. The health and academic authorities accept the role of clinical pharmacology as one distinct from basic pharmacology.

## National Association

The Israel Society of Pharmacology and Physiology has a clinical pharmacology section that is an active forum for scientific presentations and debate. Further information can be obtained from:

Professor Micha Levy
Clinical Pharmacology Unit
Hadassah University Hospital
P.O. Box 12000
91-120 Jerusalem.

# Italy




## Teaching, Service and Research

Clinical pharmacology started to develop in the late 1960s; the pattern of development varied widely. By the middle of the 1980s about 12 medical schools had developed clinical pharmacology programmes including both teaching and research. In 1986, however, the medical curriculum was revised on the national level (the so-called *Tabella XVIII*) and clinical pharmacology was not included in the undergraduate curriculum. Many universities therefore lost their clinical pharmacology teaching programmes and only Florence and Padua universities managed to retain the subject. A second revision followed late in 1989, to allow universities more power in planning their curricula. As a result of this revision and of support from the Italian Pharmacological Society and international agencies, clinical pharmacology is being re-established in Italian universities. At present,

three universities have a clinical pharmacology unit; those of Florence and Padua, and the Mario Negri Institute in Milan.

Training posts in clinical pharmacology in Italy are scarce and many people are trained abroad. Some medical schools have a specialty diploma in pharmacology that may include clinical pharmacology as a subspecialty. Only medical graduates can enrol in the clinical pharmacology programme. The universities of Bari and Padua offer postgraduate research doctorates in clinical pharmacology, run in association with other nearby universities.

Clinical pharmacology has little involvement in health care delivery; there is rarely direct responsibility for beds, for example. In some universities, however, informal consultation is offered. Clinical chemists usually run therapeutic monitoring services without giving advice on drug use.

Research in clinical pharmacology is fairly active in spite of a lack of official recognition. Such research is usually conducted in departments of medicine, pharmacology, neurology or paediatrics, as well as by the pharmaceutical industry and some non-profit organizations.

## Long-term Plans

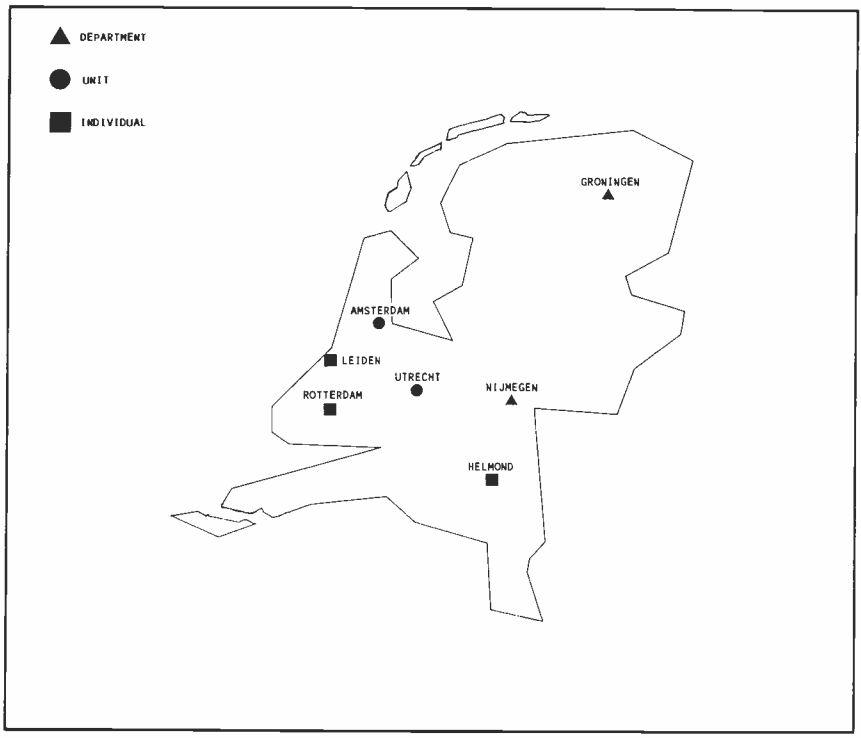
There are no formal plans for the development of clinical pharmacology, but it is hoped that, in view of the recent revision of the medical curriculum, all medical schools in Italy will establish teaching programmes.

## National Association

The Italian Pharmacological Society has recently formed a clinical section that will become the national forum for clinical pharmacology. Further information can be obtained from:

Professor G.P. Velo
Istituto di Farmacologia
Policlinico Borgo Roma
37134 Verona.

# Netherlands




## Teaching, Service and Research

Clinical pharmacology developed in the Netherlands because of Leopold Meyler, who became the first professor of clinical pharmacology. The first initiatives began in the late 1960s and people were sent abroad for training in the subject. A number of attempts to develop clinical pharmacology in universities in the Netherlands failed, however, for financial and other reasons. In the early 1970s, the President of the Health Council formed a committee to report on the subject. After some years of work, the committee recommended founding chairs and departments of clinical pharmacology at all Dutch medical schools, but the recommendations were never implemented.

Departments of clinical pharmacology remain in the State University Groningen and the Catholic University Nijmegen but other units, at

the Free University, Amsterdam and the University of Limburg (at Maastricht), have now closed. The slow and inadequate development of clinical pharmacology in the Netherlands may be primarily due to a surplus of highly trained pharmacists (which led to the closing of two of the four schools of pharmacy). Inevitably pharmacists have taken over some of the tasks normally done by clinical pharmacologists.

Clinical pharmacology is not officially recognized as a specialty in the Netherlands. Discussions continue, however, on the possibility of recognizing six months of training in the subject as an official part of the six-year specialty training in internal medicine. Teaching in clinical pharmacology is not yet an official part of the medical curriculum, although it is incorporated into the pharmacology course in some medical schools.

## Long-term Plans

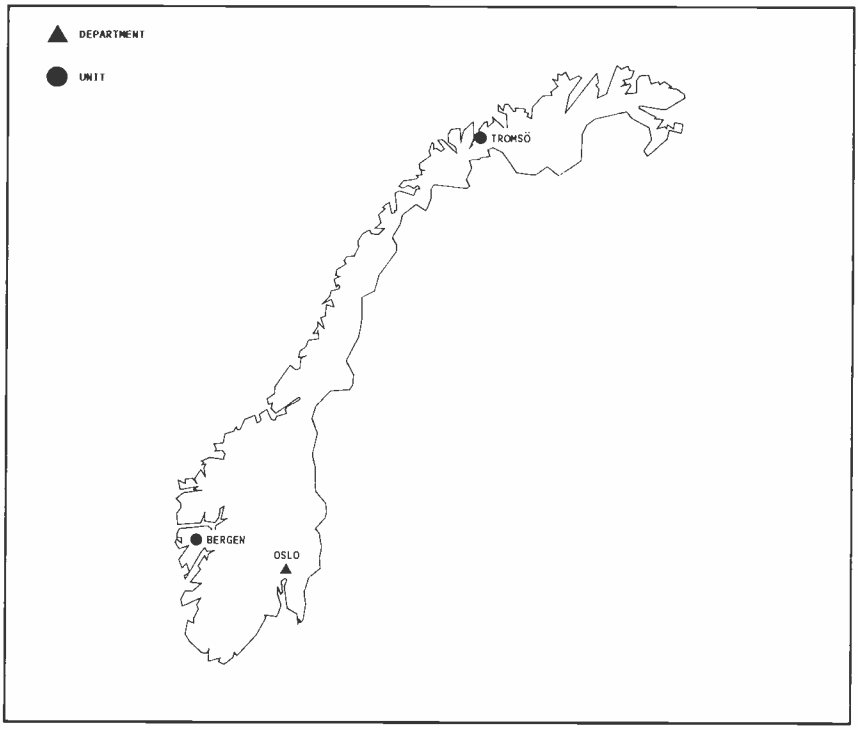
There are no formal plans for the development of clinical pharmacology in the Netherlands.

## National Association

Both clinical pharmacologists and clinical pharmacists are involved in an active society: the Netherlands Society of Clinical Pharmacology and Biopharmacy. It usually meets twice a year. Further information can be obtained from:

Dr T. Thien
Department of Internal Medicine
Sint Radboudziekenhuis
P.O. Box 9101
6500 HB Nijmegen.

# Norway




## Teaching, Service and Research

Clinical pharmacology began in Norway in the 1960s with the training of fellows abroad and the establishment of the first department of pharmacotherapeutics in Oslo in 1964. Since then the discipline has developed according to the recommendations of a national committee on clinical pharmacology that met in 1971. Units have been established in the four universities in Norway (those of Bergen, Oslo, Tromsø and Trondheim). Clinical pharmacology was not formally recognized as a medical specialty until 1987, however, and its development in hospitals has been limited.

Medical undergraduates receive some 70 - 90 hours of lectures in pharmacology in the fourth year of the six-year curriculum. Clinical

pharmacology is taught to a more variable extent in the remaining clinical terms. All clinical pharmacology units are involved in teaching post-graduates (such as general practitioners and pharmacists) and regular national conferences are held on drug-related topics. Some of these conferences are intended for members of the approximately 60 drug and therapeutics committees in Norway. All clinical pharmacology units are actively involved in research. Clinical pharmacology is involved in health care in the major teaching hospitals but less so in district hospitals. No direct patient care is given, but therapeutic consultations are held and therapeutic drug monitoring, adverse drug reaction reports and pharmacokinetic advice are also important.

The recognized specialty training programme in clinical pharmacology lasts five years and about eight people are participating at present. The training includes one year in internal medicine and two years in pharmacology or clinical pharmacology. The programme includes intensive courses in pharmacological methods, clinical pharmacodynamics and pharmacokinetics and issues in clinical pharmacology that are important to society at large (such as clinical trials and drug epidemiology). No funds are available for fellows from abroad.

## Long-term Plans

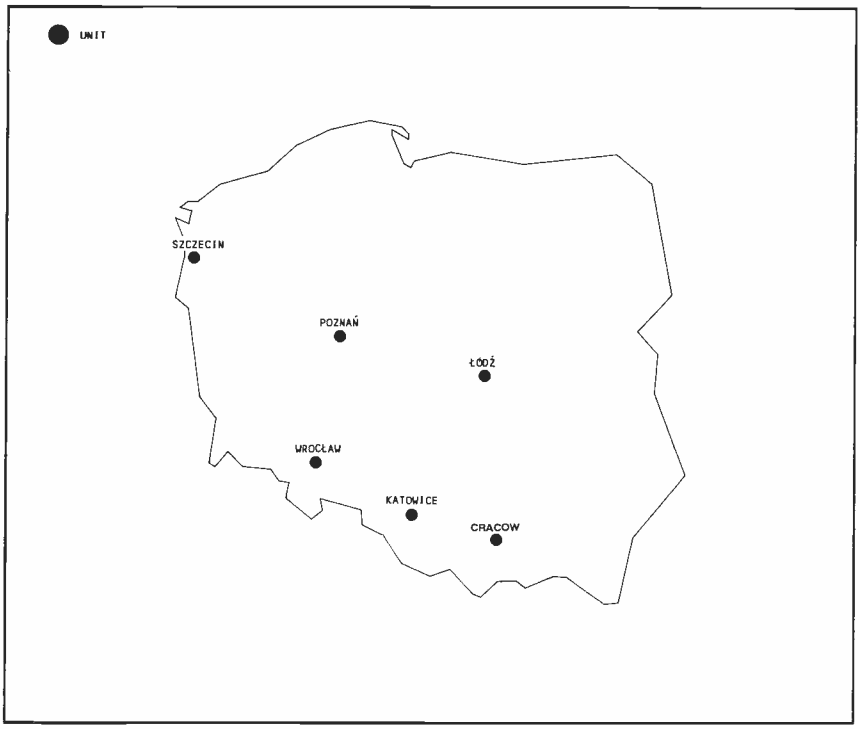
The aim is to establish training posts in clinical pharmacology in each of the regional hospitals. It is estimated that some 40–50 clinical pharmacologists will be needed to provide coverage at county level in the next 15 years.

## National Association

The Norwegian Society for Pharmacology and Toxicology has a clinical section and the Norwegian Society of Clinical Pharmacology (linked to the Norwegian Medical Association) is a forum for scientific presentations and discussion. Further information can be obtained from:

Professor P.K.M. Lunde
Department of Pharmacotherapeutics
University of Oslo
P.O. Box 1065
0316 Oslo 3.

# Poland




## Teaching, Service and Research

Clinical pharmacology is now established in Poland as an independent discipline. The first unit of clinical pharmacology was started in 1974 in Szczecin as a division of the department of pharmacology at the medical academy. Since then the development of the discipline has depended on local conditions. There are five units in the medical academies in Katowice, Lodz, Poznan, Szczecin and Wroclaw and a division in Cracow. Clinical pharmacology has usually arisen from basic pharmacology but the units in Poznan and Lodz originate from clinical medicine.

The duties of units of clinical pharmacology in Poland include teaching at both undergraduate and postgraduate levels. The units are responsible for the teaching of clinical pharmacology to medical students

in their fifth year of study and are involved in teaching the subject to other undergraduates. Postgraduate teaching consists of seminars and lectures for both doctoral and postdoctoral students. In addition, teaching is arranged for doctors and pharmacists and courses are arranged each year at the unit in Szczecin.

The units take part in health care by both looking after patients directly and providing pharmacokinetic advice or therapeutic drug monitoring. Research is actively pursued on a collaborative basis particularly with internal medicine, surgery, urology, neurology, anaesthesiology and oncology units.

## Long-term Plans

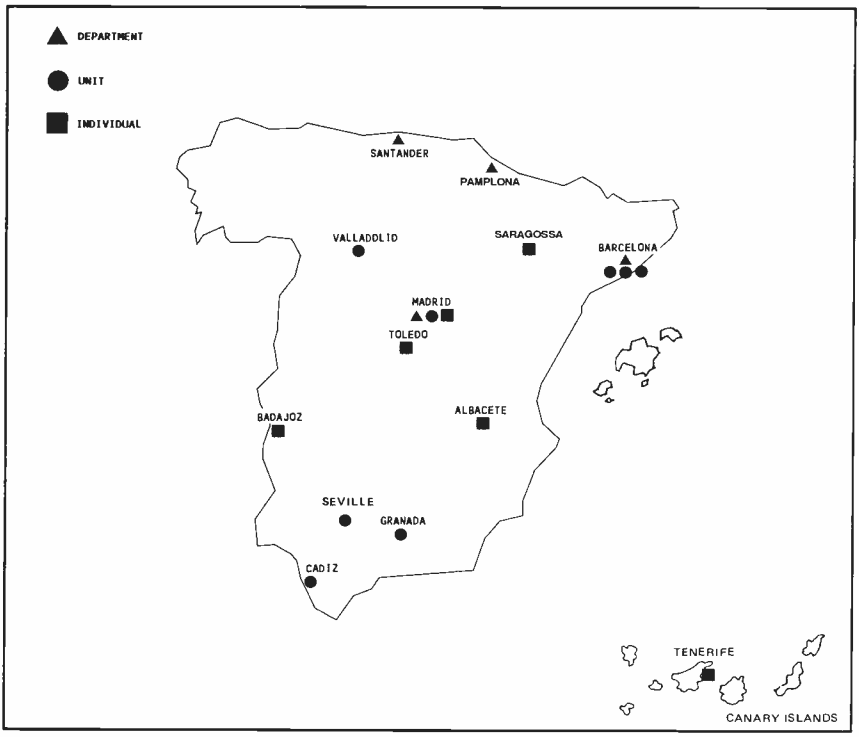
It is hoped that every medical faculty in Poland will have a clinical pharmacology unit. Further progress depends on obtaining the necessary funds both to develop the units and to provide training in clinical pharmacology.

## National Association

Most clinical pharmacologists belong to the Polish Pharmacology Society, which has an active section of clinical pharmacology. Further information can be obtained from:

Professor J. Wojcicki
Department of Clinical Pharmacology
Medical Academy
Powstancow Wlkp 72
70 -111 Szczecin.

# Spain




## Teaching, Service and Research

Twenty-five universities in Spain have medical schools, and one of these universities, in Pamplona, is private. While all the medical schools have a department or unit of pharmacology, clinical pharmacology is much less well developed.

Clinical pharmacology is one of the more than 30 medical specialties officially recognized in Spain. This means that there is an official four-year, full-time postgraduate training programme in the subject. A National Commission in Clinical Pharmacology superintends the training and the accreditation of the approximately 10 hospital units that offer it. The training programme consists of a minimum of 18 months in internal medicine with 6-9 months in five other areas: drug utilization studies, therapeutic drug monitoring, clinical trials, drug surveillance and

therapeutic consultation. After four years, the trainee obtains the title of specialist in clinical pharmacology.

Trainees are selected by means of an annual national examination of residents. Competition for specialty training is stiff, with about 20 000 recently graduated doctors applying for the 2800 places. There are about 20 places for specialty training in clinical pharmacology. No places are allocated for fellows from other countries; interested people need to approach the department of their choice for details. The Spanish Agency for International Cooperation offers grants covering six months to three years of postgraduate training. Recognized training programmes in clinical pharmacology are conducted in Barcelona (at the hospitals of Vall d'Hebron, Sant Pau and Badalona, and Hospital del Mar), Granada, Madrid (at La Paz and San Carlos hospitals), Pamplona, Santander and Seville. Other university or hospital departments with units of clinical pharmacology are located in Badajoz, Cadiz, Salamanca, Tenerife and Valladolid.

A new medical curriculum is under discussion. The most recent proposal includes education in pharmacology during the pre-clinical and clinical periods of the course. Clinical pharmacology is a compulsory subject in only one medical school, and is taught in the sixth year of the course. In another five or six medical schools, clinical pharmacology is an unofficial part of the course. Postgraduate courses in clinical pharmacology (on, for example, adverse drug reactions, clinical trials and therapeutic drug monitoring) are taught in four or five universities and some universities offer "doctorate" courses in basic or clinical pharmacology. A course leading to a master's degree in drug epidemiology is envisaged at one university.

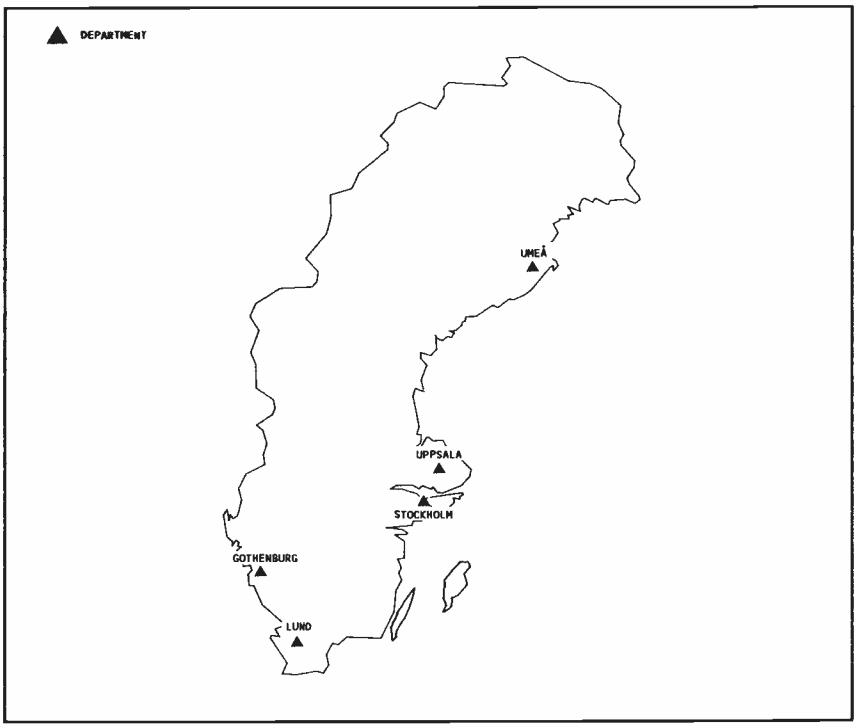
The role of clinical pharmacology in health care is not well developed. Clinical pharmacologists have played a leading role in activities such as compiling a national formulary, which dates from 1980, and extending drug surveillance programmes all over the country, including 11 of the 18 autonomous regions. Clinical pharmacologists also play a major role in the evaluation of drug registration documents and in the evaluation of protocols for clinical trials at the local and national levels.

## National Association

The Spanish Society of Clinical Pharmacology was founded in 1984. The Society meets once each year, designs multicentre clinical trials and other studies, and serves as a forum for the presentation of the results of research. Further information can be obtained from:

Professor J.R. Laporte
Division of Clinical Pharmacology
Faculty of Medicine
Free University of Barcelona
P. Vall d'Hebron, S.A.
Barcelona 32/35.

# Sweden




## Teaching, Service and Research

Clinical pharmacology is well established as an academic and service discipline at all university hospitals in Sweden. It is also involved in the development of health care services in larger regional hospitals and primary health care

Clinical pharmacology began in 1956 with the establishment of readerships in the six medical schools in Sweden. In 1965 these positions were combined with part-time consultancies to various clinical departments. The first chair in clinical pharmacology (combined with a position as head doctor) was created in 1970 at the then new medical school in Linköping. The second chair was founded in 1972 at the Karolinska Institute and based at the new teaching hospital at Huddinge in southern

Stockholm. Chairs were subsequently established at the universities of Lund in 1975, Gothenburg in 1978, Umeå in 1989 and Uppsala in 1990. There are now 13 professorial positions in clinical pharmacology in Sweden including 3 in the drug control section of the National Board of Health. There are seven academic departments (two in Stockholm) with from 10 to more than 50 staff and annual budgets of up to SKr 10 million.

All academic units provide teaching in clinical pharmacology. Medical students receive about 20–70 hours of instruction during their first clinical year. Postgraduate courses for licensed doctors emphasize drug use in primary health care and are held at regular intervals. Specialty trainees receive advanced teaching in clinical pharmacology and research techniques.

The requirements for specialization in clinical pharmacology are a medical degree, two years of internship and five years of specialty training of which four years must be devoted to clinical pharmacology. Most units take foreign scientists for short-term training (1–2 years). Such foreign trainees must usually arrange financing for their studies.

Research is conducted in all units in a wide variety of areas. These include drug metabolism, therapeutic drug monitoring, pharmacokinetics and pharmacodynamics (studies of such drugs as analgesics, anticonvulsants, antidepressants, anti-asthmatics and neuroleptics), drug epidemiology, drug information and drug utilization in primary health care.

The health care services delivered vary from unit to unit but generally include therapeutic drug monitoring, involvement in regional and local drug committees, the provision of drug information, consultation with patients and problem-oriented advisory services to doctors. Regional centres have collaborated on the provision of drug information in recent years and a common database has been created. This database, called Drugline, consists of evaluated case histories of patients with pharmacotherapeutic problems and was produced in close collaboration with pharmacists.

## Long-term Plans

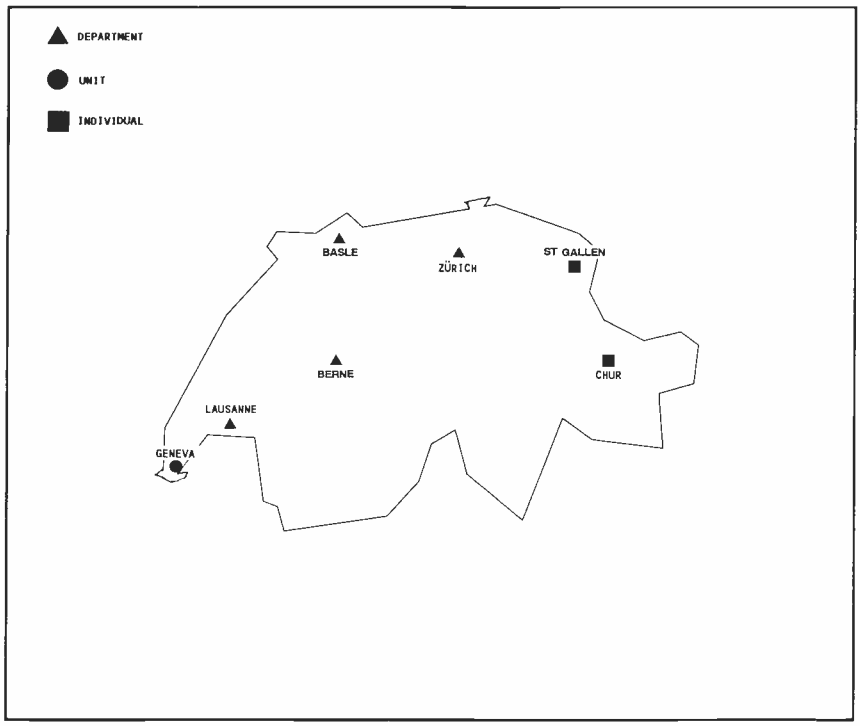
The primary long-term plan is to develop all aspects of clinical pharmacology in Sweden so as to make it competitive enough to retain a firm academic base. An additional aim is to increase the influence of the discipline in new academic hospitals and in primary health care.

## National Association

Clinical pharmacologists belong to the Swedish Association of Clinical Pharmacologists, which holds regular meetings. Further information can be obtained from:

Assistant Professor Curt Peterson
Department of Clinical Pharmacology
Karolinska Hospital
P.O. Box 60500
104 01 Stockholm.

# Switzerland




## Teaching, Service and Research

Clinical pharmacology has developed in the five medical schools in Switzerland and this development has depended mainly on local conditions. There is an independent department in the medical school in Berne University, while clinical pharmacology is integrated into the departments of internal medicine in the medical schools of the universities of Basle, Geneva, Lausanne and Zurich. All units have general teaching and service functions in addition to research activities in specialized fields. The service functions vary according to the particular interests of the unit. The teaching programmes are coordinated nationally on a voluntary basis. Clinical pharmacology is taught at the end of the course for undergraduates in medicine and knowledge is assessed by a common examination. Teachers of clinical pharmacology wrote a general text on the subject

that was included in the Swiss national drug formulary; this is an important source of information for students and doctors. A committee including members of the Swiss Society of Clinical Chemistry has produced recommendations for the determination of plasma concentrations of drugs.

There are no formal training programmes in clinical pharmacology in Switzerland. Because the Swiss Society of Physicians did not create specialty board examinations in clinical pharmacology, the clinical pharmacology section of the Swiss Society of Pharmacology and Toxicology created its own diploma. The diploma is granted to doctors who are already specialists in a clinical field and who then undertake a two-year programme in clinical pharmacology. The diploma may include special skills acquired in their specialty or in industry. In addition, candidates must show their research skills by substantial publication in international peer-reviewed journals.

There are no clinical pharmacology activities outside university hospitals, but several very active units of clinical pharmacology are to be found in the pharmaceutical industries based in Switzerland. These units occasionally accept fellows for training.

## Long-term Plans

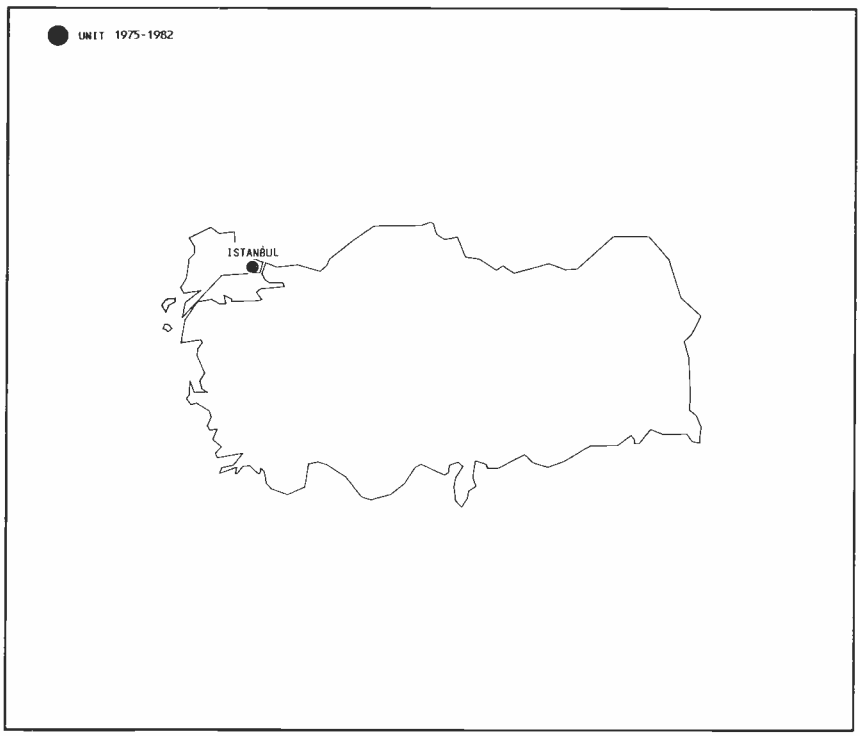
There are no long-term plans for clinical pharmacology in Switzerland.

## National Association

The clinical pharmacology section of the Swiss Society of Pharmacology and Toxicology meets annually with the Federation of Biological Sciences and from time to time with other clinical societies. Further information can be obtained from:

Professor Ferenc Follath
Abteilung Klinische Pharmakologie
Department für Innere Medizin
Kantonsspital
Universität Basel
Petersgraben 6
4031 Basle.

# Turkey




## Teaching, Service and Research

Six universities in Turkey have medical schools but none of them has a formal department of clinical pharmacology. The Department of Pharmacology in the Faculty of Medicine at Istanbul University was renamed a Department of Pharmacology and Clinical Pharmacology in 1975. After the reorganization of universities in 1982, however, the department reverted to its original role. There are pharmacology departments in all medical schools and some have staff interested in clinical pharmacology. Such people have usually specialized in internal medicine. There are no formal clinical pharmacology activities outside the universities and no defined training programmes.

Clinical pharmacology is taught on a less formal basis than previously. Prior to 1982 some universities taught a clinical pharmacology

course, but only basic pharmacology was included in the formal programme after the reorganization. Seminars in clinical pharmacology, however, are taught on an informal basis.

## Long-term Plans

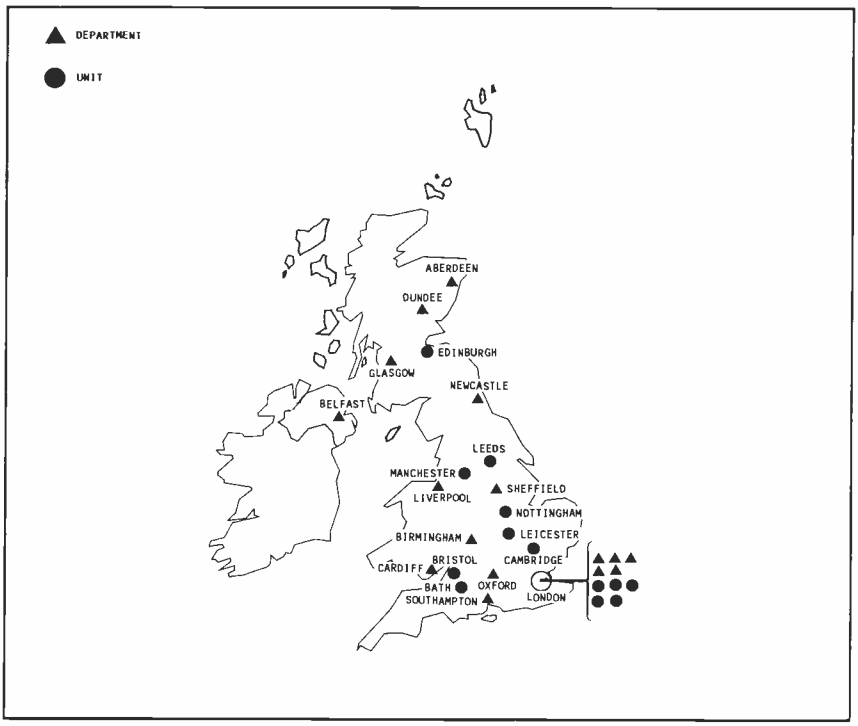
There are no plans for the further development or formalization of clinical pharmacology in Turkey in the near future.

## National Association

People interested in clinical pharmacology attend the meetings of the Pharmacology Society of Turkey. Further information can be obtained from:

Associate Professor Mustafa Ilhan
Department of Pharmacology
Faculty of Medicine
Hacettepe University
Sihhiye
Ankara.

# United Kingdom




## Teaching, Service and Research

Clinical pharmacology is well established as an academic and service discipline in most universities in the United Kingdom. Most university medical schools now have a department or division of clinical pharmacology and give the clinical pharmacologist an acute service role. This often means a direct responsibility for both inpatient and outpatient care. In other cases, clinical pharmacologists are responsible for outpatients and perhaps have a role in providing pharmacokinetic advice, or the monitoring of plasma concentrations of drugs. The teaching of clinical pharmacology to both medical students and postgraduates is a major responsibility and all units have active research programmes.

Outside the universities, a number of smaller units, usually with one or two trained clinical pharmacologists, work in the National Health

Service. (The map does not show such units.) There are 75 consultant posts in either pure clinical pharmacology or general internal medicine with an interest in clinical pharmacology; 54 of these are in the university setting. There are 24 posts for specialty training in clinical pharmacology.

As a specialty, clinical pharmacology developed from internal medicine rather than from pharmacology, as has occurred in some other European countries. Thus, people wishing to specialize in the field need to obtain a medical degree and then a period of general medical training. The next step is three or four years of specialty training, during which the MRCP diploma is usually obtained.

Specialist training in clinical pharmacology is usually undertaken in one of the university departments of clinical pharmacology, therapeutics or materia medica. The trainee occupies a post of lecturer or research fellow (or an equivalent) and holds honorary registrar or senior registrar status in the National Health Service. He or she takes a full part in the clinical service role of the university department, teaches both undergraduates and postgraduates, and is closely involved in the research work of the department. Trainees usually conduct research projects (under supervision) and often present their work as an MD thesis. The exact nature of the work involved varies between departments. Trainees' research and service work is likely also to give them experience in another discipline such as gastroenterology or endocrinology. The Joint Committee for Higher Medical Training (JCHMT) recognizes all suitable posts for training in both general medicine and clinical pharmacology. Recognition is increasingly given, often *ad personam* for additional specialty training.

## Long-term Plans

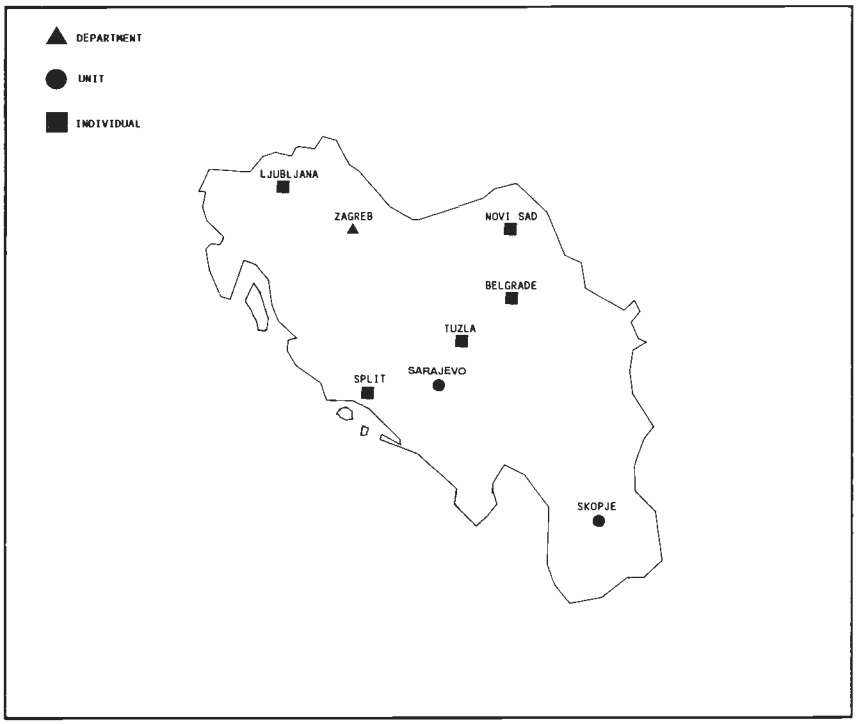
It is hoped that all district general hospitals will have a clinical pharmacologist on the staff in the foreseeable future. This has been agreed in principle with the Government but funds are lacking. Meanwhile, progress in this direction is slow.

## National Association

Most clinical pharmacologists belong to the British Pharmacological Society (BPS), which has a very active clinical section with 600 members. Many European clinical pharmacologists have joined the Society. The Honorary Secretary for the clinical section of BPS is:

Dr P. Routledge
Department of Pharmacology and Therapeutics
Welsh National School of Medicine
Heath Park
Cardiff CF4 4XN.

# Yugoslavia




## Teaching, Service and Research

Yugoslavia consists of six republics, one of which (Serbia) has 2 autonomous provinces (Kosovo and Vojvodina), and has 10 medical schools. All republics are responsible for their own health affairs and as a result the development of clinical pharmacology has varied between republics. In Croatia, clinical pharmacology developed from internal medicine and the university department of clinical pharmacology in Zagreb has clinical responsibilities for 15 beds and outpatient services; the unit in Split also has clinical responsibilities for beds and oupatient facilities. In contrast, in Bosnia-Herzegovina (Sarajevo and Tuzla), Macedonia (Skopje), Serbia (Belgrade) and Vojvodina (Novi Sad) clinical pharmacology developed from pharmacology and activities are largely based in the pharmacology departments of the medical schools.

The place of clinical pharmacology in the medical curriculum also varies between republics. In many medical schools it is included in lectures on pharmacology given early in the course. The recent extension of undergraduate medical education from five years to six, however, gives an opportunity for clinical pharmacology to be taught in the last year of studies. Clinical pharmacology is also taught to postgraduates such as pharmacists and doctors.

Clinical pharmacology is present outside universities, with a few trained clinical pharmacologists working in hospitals or in the pharmaceutical industry. There are also people who have received one year's training in the laboratory, but they cannot really be called clinical pharmacologists.

## Long-term Plans

It is hoped that clinical pharmacology will spread slowly and steadily to all the medical schools in Yugoslavia. Then, stimulated by the 1987 federal drug law, it may expand in the bigger hospitals. Several paragraphs in the new law mention the importance of the principles of clinical pharmacology.

## National Association

The Pharmacological Society of Yugoslavia has a clinical section which is an active forum for clinical pharmacologists. In addition, the Physicians' Association of Croatia has a pharmacotherapy section. Further information can be obtained from:

Professor B. Vrhovac
Section of Clinical Pharmacology
Department of Medicine
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41000 Zagreb.

It is obviously in the interest of public health, and therefore of WHO, that drugs are used for the right indications and in the right dosage, and that the choice of drugs is appropriate. Work in this direction in Europe has mainly concentrated on teaching the principles of clinical pharmacology and pharmacotherapy to medical students and doctors, and this in turn was the purpose of a WHO Working Group on Clinical Pharmacology in Europe set up in 1986.

The Working Group laid down general principles for the teaching of and training in clinical pharmacology, and formulated guidelines on the role of the discipline in health care delivery, with special emphasis on primary health care. It is these principles and guidelines that form the first section of this book.

In addition the book presents, country by country, the results of a questionnaire sent out to medical schools and health ministries about the academic status of clinical pharmacology. As such, it represents a guide to academic programmes in clinical pharmacology in the European Region, as well as a discussion of the role that the discipline could play in medical schools and health care.

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