Progress in Clinical Pharmacy

D. Schaaf and E. van der Kleijn
Editors

Proceedings of the 7th European Symposium on Clinical Pharmacy, 1978

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Proceedings of the Seventh European Symposium on Clinical Pharmacy held in Mainz, 2-4 November, 1978.

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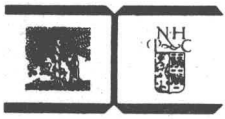

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PREFACE

From November 2nd to 4th, 1978 the 7th European Symposium on Clinical Pharmacy was held in Mainz, Germany in order to give an overview of the continuing development of Clinical Pharmacy. An attempt was made to rationalise the undergraduate curriculum in Europe which has many differences in the health systems and economics of its constituent countries. Since there is a need for such a development, clinical practitioners and scientists from various European countries have come together to attempt to get a professional development to a patient orientated pharmacy and to standardise the movement in the single countries.

In the last decade pharmacotherapy has developed greatly. More and more diseases can be cured and new potent drugs have been developed with the result that side effects or drug interactions are becoming more apparant and individualized dosage prescription and monitoring are of great importance.

Despite this development, pharmacology has remained a peripheral interest for medical and pharmaceutical students, and, despite the provision of information by the manufacturer the knowledge of drugs has diminished with the individual medical practitioner due to the multitude of therapeutics.

Specialists are needed to ensure optimal drug therapy for the future. Both clinical pharmacology and clinical pharmacy are still developing however, and it will not be possible to avoid interferences with the existing disciplines which will basically stimulate progress and delineate functions. In the long run, cooperation and task division will develop since the field is very diverse and can hardly be handled adequately by both groups.

The clinical pharmacist should assume the following role:-

1. his work should be patient orientated e.g. be integrated into the clinic's or hospital's health maintenance team.
2. he should be closely involved in drug distribution to hospital patients and he should develop new drug dispensing systems
3. he should be able to inform the physician, the nurse and the patient about drugs
4. he will develop documentation systems on drugs, their side effects, their interactions and their utilization
5. on the basis of his scientific background he will be involved in interdisciplinary and pharmacokinetic research

A prerequisite for this is an acceptable medical and pharmacological oriented training that has not been achieved up to the present time.

It should be remembered that the pharmacist has the time to assume these new roles since one of his original functions - the production of drugs - has been taken over by industry.

The Editors

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D. Schaaf and E. van der Kleijn, eds.

CLINICAL PHARMACY, MODULE OF A HEALTH MAINTENANCE SYSTEM

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INTRODUCTION

In most European countries nutrition, public health measures and medical care are provided for a larger fraction of the population than most places elsewhere in the world. The major task here is to consider how continuity and progress in the provision of health care can be pursued and how advances can be shared with other people. The past three decades have demonstrated an unprecendented development in health maintenance but at the expense of a still growing proportion of the private and national economy. Efforts to rationalize the distribution and the expenditure of health care have become increasingly important. Health Service Operation Research, and as a subset , Drug Utilization Research, focuses on the identification of deficiencies in existing systems and on proposals for improved or alternative systems. This research has triggered many new areas of investigation in the basic pharmaceutical sciences. With the average number of drugs prescribed or taken per individual simultaneously rising over the past decades, the problems of drug choice, the separation of disease symptoms from drug effects, and quantification of risks versus benefits have become increasingly complex.

PRESCRIPTION ADHERENCE

One of the most striking results of studies in health care research is the number of patients who fail to adhere to prescribed dosage regimens and guidelines. In addition to this well documented problem of patients' poor compliance to prescribtions other prescribing practices have been identified which have both economic and medical impact. These practices include the overuse of drugs with little proven beneficial therapeutic effects (the cerebral vasodilators), concurrent prescribing of drugs with interacting pharmacological effects (coumarin anticoaculants and anti-epileptics), suboptimal combination prescribing (quinidine and procainamide), combinations of drugs influencing each other kinetics, (phenobarbital and valproate,digoxin and quinidine), overprescribing and/or unaudited continuation (anti-biotics, neuroleptics) and

inappropriate selection of drugs(tricyclic antidepressants for situational depression). In hospitals the 'ad hoc' preparation for individual patients and addressing and dispensing prior to administration are all sources for possible non optimal medication. One goal of the pharmacy profession in the future will include the identification of significant prescribing problems and formulating, implementing and evaluating corrective measures. However, the major goal for pharmacy should be original and innovative investigation in developing optimal therapeutics, and methods for the improved preparation and dispensing of medicines.

Although we can be grateful for the present armament against life threatening diseases and diseases that handicap people for a longer or shorter period of time we can not be satisfied with the current state of their application. The cure of diseases is not matter of isolated technical intervention. It has become obvious that drugs can not replace the care and involvement of knowledgable and concerned people. Because of the multifactorial nature of health, increasing emphasis is being placed on the team management approach.

Health management systems depend on a large variety of disciplines to provide adequate care equally available to every one. Pharmacy should identify the drug related needs. It has the capabilities to assume responsibility for resolution.

Policies to extend into primary care also require the training of professionals at all levels of competence on the revision of methods of teaching to include skills for dissemination of instruction and information and documentation of health care practice.

DRUG MONITORING

The monitoring of medication profiles of individual patients in community and institutional practice and the prospective and retrospective surveillance of homogeneous populations have resulted in important information for the improvement of therapy. The identification of fibrotic conjunctivitis and sklerosing peritonitis following chronic practolol treatment, of blood dyscrasia following neuroleptic therapy with clozepine in Finland, the occurrance of lactic acidosis following phenformine hypoglycemic therapy are among the examples that have resulted in withdrawal of these drugs from the market in some countries or have resulted in more careful use in cases when the drug is considered indispensable. This continuing effort on existing and newly marketed drugs will provide better protection of patients especially for those for whom the risk/benefit ratio has yet to be well defined.

Continuous surveillance of all prescriptions but especially those of patients at risks to trace possible errors and chemical and therapeutic imcompatibilities and interactions has ever been a routine effort of pharmacy practice but has improved much by the modern methods of prescription and medication profile processing.

Involvement of other disciplines, including pharmacy, in the clinical evaluation of patients with acute or chronic medical conditions especially in the context of specialized medication guidelines for e.g. such as anticoagulation, epilepsy, psychiatry, antimicrobial therapy, parenteral nutrition, shock treatment, protein supply etc. have been reported to improve therapeutic results,to decrease the incidence of side effects and to enable economic savings in drug use and personnel involvement.

In pharmacy practice emphasis has also been placed on the improvement of drug distribution systems to provide cost savings and improvement of proper destination of therapeutics.

Pharmacy formulation and manufactoring skills also require development which include the latest technology in physical sciences as well as data processing methods, to accommodate individual requirements for dosage, dosage forms and route of administration of medicines for which the proper form is not commercially available.

THE SELECTION OF ESSENTIAL DRUGS

Improvement of the criteria for the choice of the most appropriate drug and its therapeutic regimen has relevance not only for developing countries as recommended by the World Health Organization (1) but also for systems regarded as the best currently available. The objective of voluntary reduction of the proliferation of therapeutically equivalent drug entities increases the possibilities for effective data collection and improved information when appropriate audit and reporting mechanisms are applied.

Promising results suggesting equivalent or even improved utility of a scarce and expensive drug, such as albumin with a substantial, simultaneous reduction in cost can be achieved (2).

Similar planning and audit procedures also seem to be feasable for other groups of drugs. Because of the multifactorial nature of use of anti-microbial drugs it is more difficult to follow drug utilization patterns of isolated drug entities. A decrease in the use of ampicilline antibiotics (figure 1) may be rational based on sensitivity patterns and is not compensated by an increase in cotrimoxazol use.

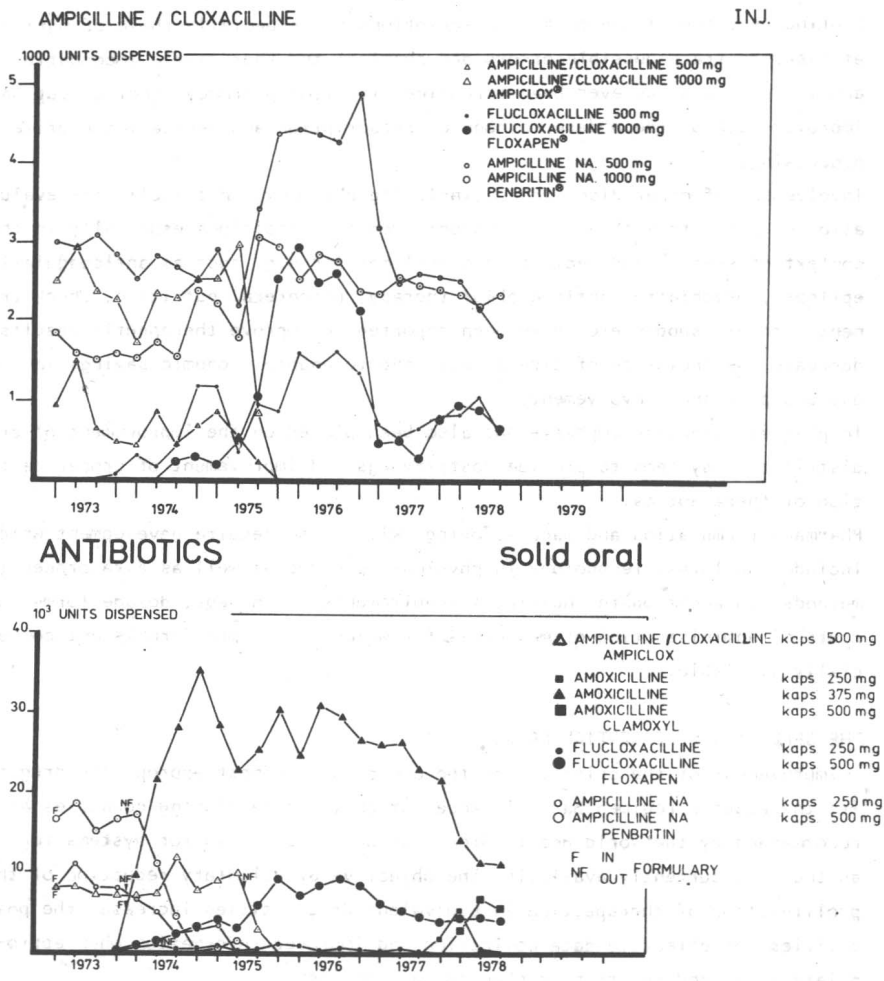

Figure 1. Utilization statistics of Ampicilline, Amoxycilline and Flucloxacilline oral and i.v. preparations respectively.

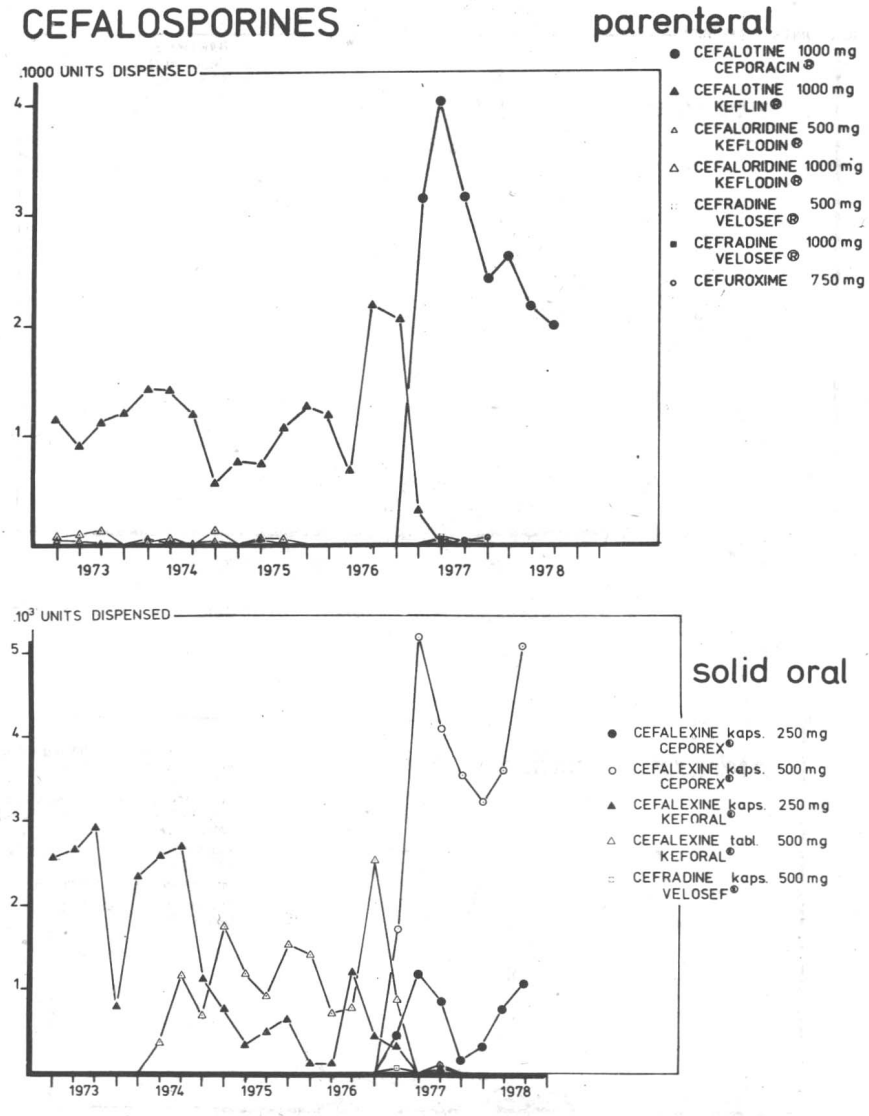

Figure 2. Utilization statistics of cephalexine and cephalotin, oral and i.v. preparations respectively.

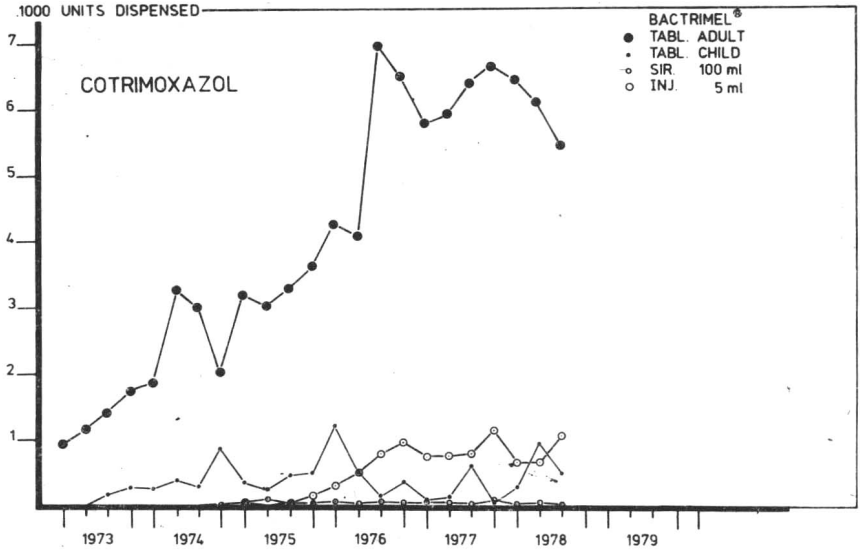

Figure 3. Utilization statistics of cotrimoxazol, oral and i.v. preparations respectively.

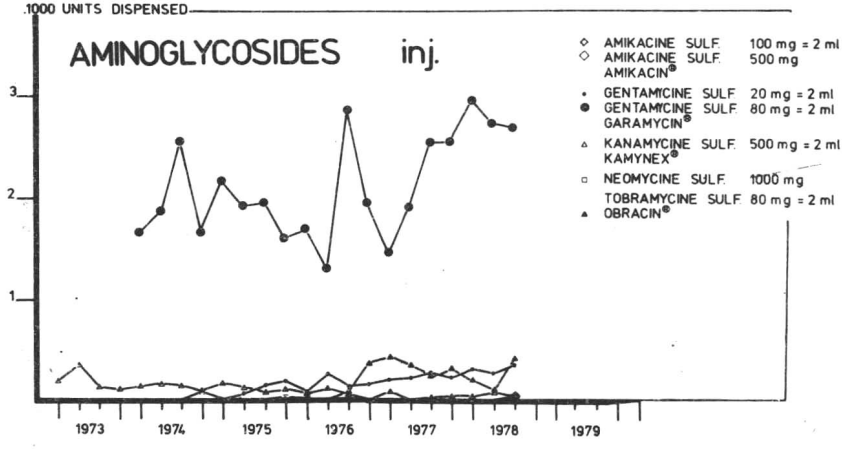

Figure 4. Utilization statistics of Gentamicine injections.

In the groups of β-lactam antibiotics, the use of ampicillines: Ampicilline and Amoxycilline, the penicillanase resistant (Flucloxacilline) and the β-lactamase resistant antibiotics (Cephalosporines) increased sequencially during 1975 and 1976-1977 respectively as a result of guidelines at the Intensive Care Unit in particular in connection with the increased activity in extra corporeal thorax surgery. During 1977 and 1978 a gradual but substantial decrease in Ampicilline and Amoxycilline use could be observed. This declining pattern can also be observed for the parenteral form of Cephalotine during 1977 after a steap rise during 1976. Simultaneously the oral formulations of cephalexine showed an initial decrease during 1977 followed by an increase in the course of 1978. This is a result of the changed policies for post surgical prophylaxis (figure 2). Since its introduction Cotrimoxazol has demonstrated a steady increase in use. In the course of 1978 however a decrease can also be observed (figure 3). The utilization pattern of Cephalosporines that are often given in combination with Aminoglycosides is typical for surgical and medical practice in university hospitals. General hospitals often show a much smaller figure for these products. Although oscillation in use can be observed, the pattern of Aminoglycosides has not changed over the years (figure 4). Tetracyclines show a steady use over the years investigated. The use of oral formulations is only influenced by the choices of the Formulary Committee, but does not show a substantial change in application. The parenteral formulations show a steap decrease in the course of 1975. This decrease must be interpreted as a result of the reduced medication administration frequency required for doxycycline with its relatively longer biological half life. Also the requirement for intravenous bolus injection that can only be performed by a physician in contrast to the oxytetracycline that can be given intramuscularly by nurses may have contributed to this decrease (figure 5). As a general conclusion it can be said that the Formulary guidelines since their introduction in 1971 initially only influenced the qualitative variety of drug products used in the Hospital. In recent years also the quantitative use is influenced, generally leading to a decrease in units used in a period when the intensity of medical care has expanded.

CLINICAL PHARMACOKINETICS

The accumulation of pharmacokinetic data over the past decade as source for better planning of drug schedules and therapeutic guidelines, has markedly improved our understanding of the fate and course of drugs in the body in particular when data is collected in light of all aspects of clinical patient parameters.Knowledge of clearance parameters, product of rate constant for elimi-

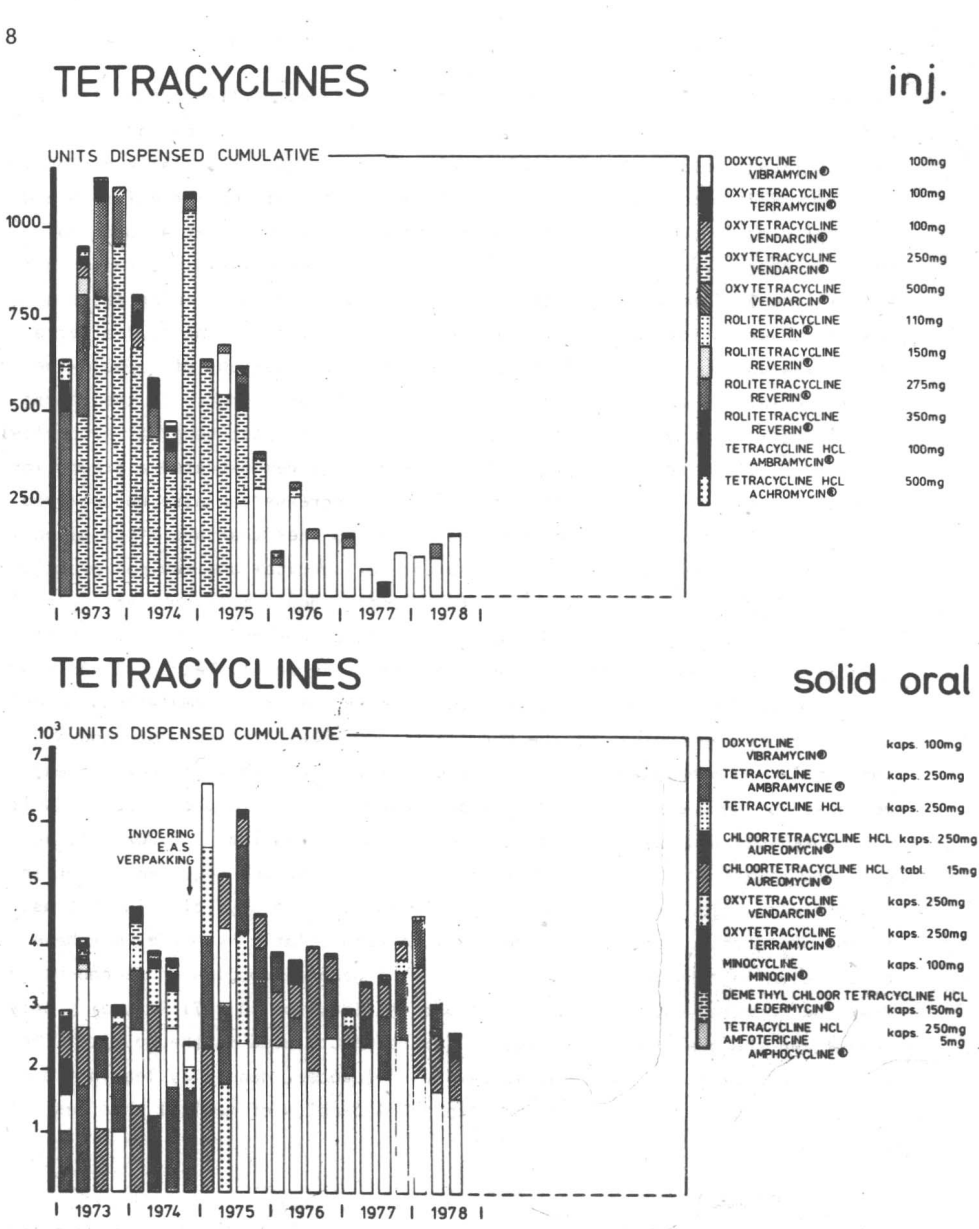

Figure 5. Utilization statistics of Tetracyclines : oral and parenteral preparations respectively.

nation and apparent volume of distribution, and of the concentration range of

drug and/or metabolites able to provide therapeutic effect with statistically evaluated highest probability and the sometimes quantitatively determined factors that influence these parameters enable the calculation of maintenance dosage rate (dose per dosage interval) in (sub)chronic disease conditions.

$$\text{Dose} = C_{therap} \times \nabla' \times \Delta t \times W$$

in which C_{therap} is the 'therapeutic' concentration that is dependent of the diagnosis and the severity of the disease symptoms, and ∇' is the relative total body clearance, sum of all clearance factors such as renal clearance, metabolic clearance, repiratory clearance, etc. In this equation the clearance is related to body weight (W) unless statistics have proven better reference to body surface or other biometric units. The clearance appears to be dependent of many factors.

The most important ones are : age, the relative clearance generally is larger, the lower the age with the exception of newborns. Sometimes when the enzyme capacity responsable for metabolism shows a limited capacity, the clearance may be dose or concentration dependent for which apparent Michealis Menten kinetics may be applied. For the calculation of dosages in acute treatment and for initiation of treatment more or less complicated pharmacokinetic models have been proposed (3,9,10).

Computer technology has made these seemingly intrigated mathematical expressions also feasable at the bedside. Many emotional barriers still have to be taken before physicians will organize their logics for treatment via administration and reproducable algorythms rather than intuitive clinical judgement. Integration of clinical pharmacokinetics consultation in the management of drug delivery, monitoring and surveillance of patients provides a module for health management that in a number of sites has been accepted and proven to be beneficial and economic. The expansion and further development of this approach requires continued education and further research.

CLINICAL PHARMACOLOGICAL RESEARCH

The weakest part in the chain of therapeutic response verses drug chosen in drug delivery and monitoring is the qualitative and quantitative assessment of the clinical effect. Additional emphasis will have to be placed on the scientific classification of appropriate therapeutic response and unwanted drug effect. The development of clinical parameters to study drug efficacy requires the combined efforts or medicine, pharmacy, basic biological sciences, sometimes

behavioural sciences and technology of computer science.

PHARMACY SERVICES SYSTEMS

Efforts to merge the traditional dispensing services of pharmacy with clinical services, patient care and research have taken off in many European countries. Although the profession in every country may have different historical backgrounds, changing pharmacy roles and increased research opportunities are apparent in successful programs reported in Scandinavia, United Kingdom, Spain and the Netherlands. In all European countries groups of enthusiastic professionals are working to improve the quality of therapeutics in health care. University education is slowly responding. Colleges of Pharmacy in Europe are reluctant to expand in patient oriented teaching and research. The demand for new drugs, new therapeutic approaches and more specific, sensitive and accurate drug assay methods would justify a larger input from academic centers. Professional organizations expend their efforts to live up to the new structures of health care management that are created by the pressure to reduce the expenditure and yet improve the individual care of the patient. In most european countries the tools to build and modernize the pharmacy module in the health care management system have been adequatly developed and are available for implementation.

Laboratory methods and applied mathematics are available at a level that now will allow clinical pharmacokinetics to function effectively along with the prescription of potentially hazardous drugs.

After a period of three to four years in which hospitals in the Netherlands where required to pack their own supply by a self developed blister packaging machine, many manufactures, whole salers and contract packers have made their drugs available in the well defined standardized unit of use dosage form (5) (figures 6 and 7).

Labeling technology, stock, turn over, purchase and prescription processing systems are developed for manual and computer application. Local adaptation of these often specially developed systems in many cases requires large efforts of computer and pharmacy experts that reduce the benefits. Structural changes in the professional practice are required that may put stress on the daily performance. The benefits on the long run are such that postponing investments are detremental for the development of the clinical participation of pharmacists. Uniformity in drug nomenclature and codes greatly improve mutual exchange of information and drug identification (7). Drug information and consultatation have matured to a professional level of service in many institutions.

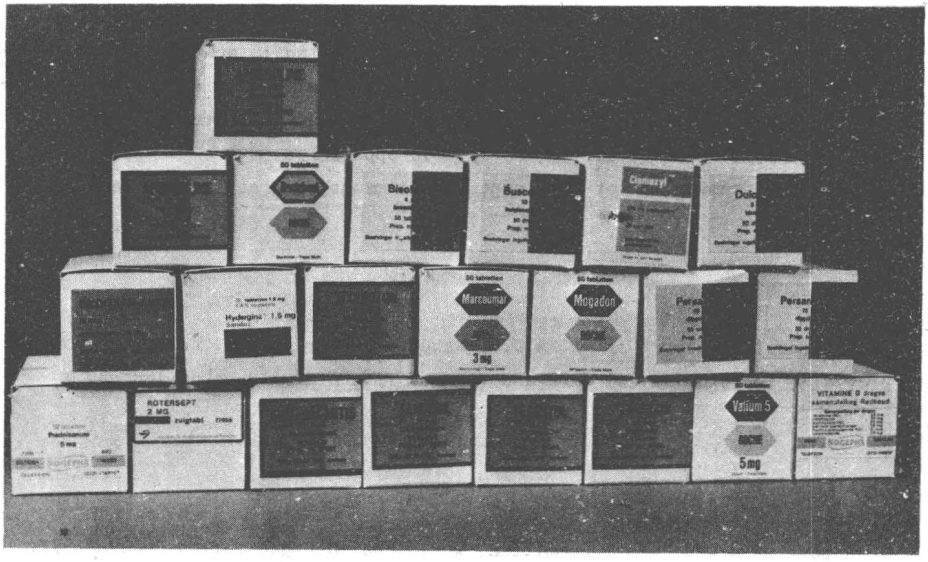

Figure 6. Sample of commercially available Unit Dose Packages in the Netherlands

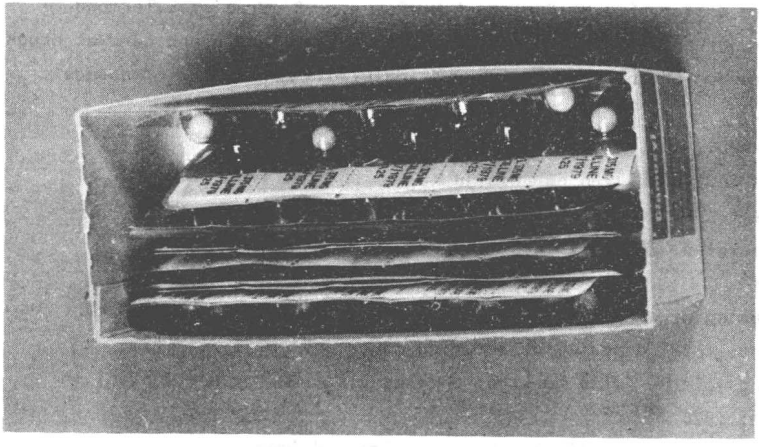

Figure 7. 50 units of use packed in one carton. The Unit Doses are 'push through' blister packed with a self adhesive detachable label with the most essential product identification.

The increased interest and need for individual formulation, manufacturing, dispensing and administration of drugs, have resulted in new drug distribution methods (8). The rate of implementation of these components largely depends on the availability of trained professionals to realize the potentials of more economical, safe and effective therapeutic approaches.
Therefore dissemination of knowledge by all means is greatly welcomed.

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