There was a time when pharmacist and physician were one and the same person, but since the Middle Ages the professions have drifted apart. Now it is time to consider bringing them closer together. The pharmacist has much to offer the physician in deciding on a therapeutic policy, as Professor van Rossum shows.

Optimal pharmacotherapy through close cooperation of physician and pharmacist

During the last few decades an overwhelming development in medicine and pharmaceutics has taken place. Many new and highly effective medicaments have been introduced for the treatment of infections, mental diseases, etc. These medicopharmaceutical advances have had and are still having a great influence on society, our culture and the sciences (Lasagna, 1969).

The availability of very potent drugs which may be used to the benefit of the patient, places a great responsibility on the physician who prescribes such drugs and on the pharmacist who dispenses them. Mankind is challenged not only by the extensive use of chemicals as flavours in food, insecticides on fruit, and environmental pollutants, but also by the inappropriate use of drugs, especially psychotropic drugs.

Historical development of specialists on medicaments

It is obvious that those who deal with the application of drugs should share their specialist knowledge to ensure rational pharmacotherapy.

In Galen's time the exercise of the medical profession and the pharmaceutical profession were still in the same hands. Except for Extr. bella-donnae and a number of poisonous plants, few potent medicines were available.

Gradually a separation of the medical and pharmaceutical profession took place, for which increase in specific knowledge was mainly responsible. Advances in anatomy and physiology were made, while new methods were added to the knowledge of compounding. In the year 1240, Frederic of Hohenstaufen, King of Naples and Sicily, decreed by law that medicine and pharmacy should no longer be practised by the same individual. For ethical reasons there should be no financial connection between the physician and the pharmacist.

In the Netherlands, the remains of the situation existing from before the Middle Ages may still be found in the so-called "pharmacy-licensed physicians". Although it is obvious that individuals with highly specialized academic training are necessary in order to fulfil their task in the Health Services adequately, it is also necessary that they cooperate.

The separate development of medicine and pharmacy is one of the reasons for the insufficient contact that exists between physicians and pharmacists. As a result of the tremendous development of purely medical sciences, the tendency exists with the physician to focus all attention on diagnosis. Once the diagnosis is made, prescription-writing is a matter of seconds.

The pharmacist is too occupied with the quality of the product and he tends to ignore its pharmacology and the patient. But it is not yet too late to share the knowledge of physician and pharmacist for the benefit of the individual patient and the health of mankind.

Drug and medicament

Many drugs are available for all kinds of illnesses and diseases. Not only that but for each specific syndrome various related drugs are at our disposal.

A large number of closely related barbiturates are available for use in a case of sleeplessness, and several antihistamines in a case of hay fever. Several of these drugs are marketed under a variety of proprietary names (see for example Table I). This variety may be a source of confusion, and it could therefore be easier to use the chemical name of a drug. However, the rules for the chemical name are not unambiguous while the chemical name is often complicated, very long and bearing no relation to pharmacological action. Nonproprietary names or generic names, adopted by the World Health Organization, therefore fulfil a purpose (see Table I).

It should be realized that a chemical is in general not given as such to the patient. For instance a bottle containing 20 grams of acetylsalicylic acid is not dispensed; this analgesic is given in divided doses in a particular dosage form. The dosage form—tablet, capsule, suppository—not only consists of the drug proper but also of certain pharmaceutical additives, colouring matter, etc.

It is logical to restrict the word "medicament" or "medicine" to the final product that the patient receives, whereas the word "drug" or "pharmacy" is reserved for the active principle that it contains. The drug should be identified by its generic name and the medicament or drug product by its proprietary name or the number assigned to it by the manufacturer.
Table I Some synonyms of drugs (Marler, 1967). Pity the poor prescriber!

<table>
<thead>
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<th>Chemical name</th>
<th>Generic name</th>
<th>Proprietary name</th>
<th>Chemical name</th>
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<tr>
<td>Acetylsalicylic acid</td>
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In the hospital the climate may be present for fertile cooperation between different specialists and the hospital pharmacist. In several large hospitals in the United States, pharmacists specialize for their consulting role with respect to therapy in internal medicine, pediatrics, psychiatry, etc. They apply their special pharmaceutical knowledge of pharmacokinetics or biopharmaceutics for a rational pharmacotherapy. These clinical pharmacists are patient-oriented, even if they do not in fact treat patients.

The difference between clinical pharmacology and clinical pharmacy lies in the fact that the clinical pharmacologist treats patients and is concerned with the actions of the drug in the patient, whereas the clinical pharmacist advises the clinician with respect to the choice of medicament, the dose, the dosage form and the dosage regimen, while the clinician remains responsible for his patient and has to judge the effect. It has been shown that close contact between the clinician, his nursing staff and the hospital pharmacist considerably improves therapy and leads to the correction of unwarranted therapeutic habits.

During the last few years a great number of articles have been written on the subject of clinical pharmacy. It seems that this way of cooperation leads to optimal pharmacotherapy in the hospital.

Pharmacotherapeutic conferences

The general pharmacist is in control of prescriptions and may bring errors with respect to the prescribed drug, the dose and the dosage regimen directly to the attention of the physician. However, the physician is not likely to learn from his errors if he receives them during a very crowded consultation session. Furthermore, prescriptions that could be improved but are not wrong as such, are not brought to his attention at all. Far better communication may be established in the form of pharmaco-therapy conferences, in which several physicians and pharmacists participate. In association with the Institute of General Physicians, our Department of Pharmacology has initiated such conferences, apparently with great success.

In the following paragraphs, specific information that may be contributed by the pharmacist will be discussed in some detail.
Various medicaments, each containing the same amount of a drug, may differ in pharmacological potency as a result of a different dosage form (potion, tablet, capsule, powder, suppository, etc.) and also because different manufacturers may use different pharmaceutical additives, different crystal form and size of the drug, and different methods of compounding.

Various medicaments, containing the same drug, are not necessarily equipotent; for instance, the rate of absorption and the total amount of the drug that ultimately becomes absorbed may vary considerably. If a drug is given in solution the rate of absorption is in general reasonably good, but absorption may greatly be delayed if an enteric coated dragee is given. This factor is more important for drugs that are rapidly metabolized in the body. For instance, acetylsalicylic acid ($t_{1/2} = 20$ min.) is rapidly metabolized in the body into salicylic acid ($t_{1/2} = ca. 6$ h.), while the former is a more potent analgesic than the latter. Concentration-time curves of acetylsalicylic acid and its metabolite are given in Figure 1a. So acetylsalicylic acid should preferably be given as a calcium or sodium salt in the form of a powder or tablet, while this powder or tablet should be dissolved in water just before oral intake. Enteric coated preparations are of no use (see Figure 1b). The total salicylate concentration following intake of a solution of acetylsalicylic acid is about 80 mg/l. within one hour after administration. Following ingestion of enteric coated tablets, the maximum—less than 40 mg/l.—is reached after four hours.

Knowledge of the influence on biological availability of various factors in compounding is still very scarce. Some general conclusions may, however, be drawn with respect to additives, etc. The relevant information on the drug product should be available to the consulting pharmacist, so that he can judge which product is to be preferred. If such information is not accessible, he had better attend to his own compounding.

**Pharmacokinetics**

In general, drugs produce their effects as a result of the interaction of drug molecules with specific receptors somewhere in the body. The concentration of the drug in the direct environment of the receptor determines the degree of receptor occupation and hence the intensity of the pharmacological effect. The drug concentration in the direct environment of the receptors depends on the concentration of the drug in the blood plasma. The concentration in the blood plasma is a time-dependent function of the dose. The rate of absorption, distribution and elimination mainly determines the shape of the plasma concentration curve. The time the drug persists in the body largely depends on the volume of distribution and the total clearance or elimination. Under certain conditions the biological half-life is a good measure of the time the drug remains in the body. It is obvious that information on the biological half-life is important for the establishment of the correct dosage regimen. Physicians have the tendency to administer most drugs three times a day. For drugs with a long half-life ($t_{1/2} > 24$ h.) this is not necessary.

Drugs that belong to the same pharmacological class may differ greatly with respect to biological half-life. This is for instance the case for sulfonamides. If such drugs are combined one should calculate on differences in half-life. The well-known trisulfa based on a ratio of sulfadimidine: sulfadiazine: sulfamerazine = 1:1:1 is on the basis of kinetic data not correct (see Figure 2). After chronic administration sulfamerazine will accumulate and will be mainly responsible for the bacteriostatic effect of the combination.

The hospital pharmacist in cooperation with the clinician is in a position to gather information on the pharmacokinetics of drugs. It is hoped that kinetic data on the older, generally accepted drugs will become available also.
The unit-dose system

Identification of medicaments is of vital importance to the correct use of drugs. The patient, as well as the physician, should be able to recognize a medicine immediately. For this purpose the so-called unit-dose system has great advantage. Each dosage form, tablet, capsule, etc., is separately packed and labelled.

The various manufacturers of medicaments should adopt a standard system showing on the label the proprietary name of the medicament, the generic name of the active principle and the dose, e.g.:

**BUTAZOLIDIN® tablets**
Phenylbutazone 200 mg.
CIBA-GEIGY Limited

The unit-dose or identi-dose system has the advantage that the physician remains free to prescribe the desired number of dose units, while the medicines keep their identity until the moment of intake. A package insert would then be no longer necessary. The package insert that accompanies packages of a fixed number of dose units contains information for the physician, but the physician should prescribe a drug only if he is aware of its pharmacology and toxicology. It seems unjust that he should obtain such information from a package insert.

**Conclusions**

Through close cooperation between clinicians and hospital pharmacists and between family physicians and community pharmacists, specialist knowledge on drugs may be shared and integrated so that pharmacotherapy may become more rational. Such cooperation is in the interest of the health of mankind.

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**Figure 2**
Plasma concentration curves calculated following chronic administration of a triultra according to a dosage-regimen with a starting dose of 8 tablets of 0.5 g. and a maintenance dose of 2 tablets 6-hourly. The level of sulfadimidine falls off, that of sulfadiazine is maintained, but that of sulfamerazine increases considerably. When drugs are combined the pharmacokinetic data should be taken into account also.