Summary and Outlook

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The presentations of this symposium made it quite clear that considerations why and to what extent old age influences the effect of drugs is only part of the more general and much more complex problem of drug treatment in the elderly. In addition, it covers the use and misuse of drugs in the elderly, prescribing habits of physicians, the role of regulatory agencies, self-medication and non-medical influences, morbidity patterns and socioeconomic parameters. Finally, the understanding of the process of aging as such and the relation to disease states particularly prominent in and sometimes almost specific for the aged also form the conceptual background for the problem of drug treatment of the elderly.

There seems to be general agreement that the problem and many detailed questions quoted above have been recognized during the last years even if in many areas research is just about to start and future work will be necessary. This is evidenced by recent official symposia, e.g. Health Care of the Elderly, WHO, Thônex 1980; 9th European Symposium on Clinical and Pharmacological Evaluation in Drug Control, WHO, Drugs for the Elderly, Schlangenbad 1980, and a number of review articles and monographs, e.g. Crooks et al. [1976], Vestal [1978], Crooks and Stevenson [1979], Jarvikei al. [1981].

During this symposium the broader aspects of drug treatment in the elderly were particularly taken care of at the beginning and at the end of the meeting. The introduction by Friedel has put the treatment by medicines in the proper perspective and furnished data on research efforts directed at the influence of age on drug action showing a remarkable increase of publications during the last years. From a geriatrician's viewpoint, Staehelin contributed remarkable ideas of how to define the strategy of treating old people with medicines. His five guidelines should be repeated here as they truly serve as an example of sound clinical judgement: (1) Establish the most accurate diagnosis achievable; (2) Define a therapeutic goal; (3) Establish the hierarchy of medication required to treat; (4) Select appropriate means to communicate aim and medication to patient; (5) Accept noncompliance as feedback to improve your therapeutic goal.

Since Staehelin summarized during his presentation already most of the previous speakers I may concentrate on some selected

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points regarding our main topics, the change of drug effects in old persons.

First of all it became evident that the so-called 'elderly' are a heterogenous group consisting of human beings of different individual ages, with or – rarely – without concomitant disease, smokers and nonsmokers, engaged in different physical activities, found in a varying nutritional status. Any generalization, therefore, needs great caution, wide variations are likely to exist. Secondly, there was apparently general agreement that the whole group of elderly patients is

overmedi-cated or at least at risk of being so. This statement is, however, not as straightforward and as stringent as it stands. Due to multimorbid-ity in old age (consider not only internal medicine but all disciplines) there is almost always a considerable number of medicines which taken all per se and regarding the indication they are intended for seem reasonable and sometimes necessary. It is then a matter of the overall strategy as stated above on which to concentrate and which ones to give low priority regardless of whether they would be justified. A somewhat similar situation holds true for the increased incidence of adverse side effects in the elderly. Here, too, the greater number of medicines taken by these patients and the pattern of diseases occurring in the aged are the main determinants of this increased risk whereas in any case it needs to be established whether a given single drug elicits more side effects in the old. From here we may return to the main topics of this meeting, the influence of age on drug effects. Clearly, there will be at least two possibilities by which age becomes a factor in determining drug action, by (1) pharmacokinetic differences and (2) pharmacodynamic changes with age. It is of general importance that the experience of this meeting has also shown that the existing theoretical framework of a given scientific discipline regulates the achievement when new questions have to be answered. This statement is best exemplified by the case of pharmacokinetics. Certainly, experimental research is necessary to furnish the relevant data and due to the great number of drugs it will be long lasting, but the conceptual background is already extensively elaborated. We, therefore, need only to investigate the influence of age on the various pharmacokinetic parameters in order to predict and – subsequently – to assess experimentally the influence of age on the behavior of a given drug in the aged organism. For this reason we already have a body of data on how different drugs change their relevant pharmacokinetic characteristics with age. A rather similar situation exists as regards drug metabolism. In summary: old human beings often have diminished organ and body clearances of drugs, thus being endangered to develop higher than usual plasma and tissue levels of a drug. The impairment of renal function with age seems to be one of the most important factors. In addition, changes in distribution volume will also greatly influence the disposition of drugs in the elderly. The differences observed in drug metabolism between young and old populations seem to justify the hypothesis that in old age oxidative steps in drug disposition are more likely to be impaired than phase II reactions.

Taking all this into consideration the expectation seems to be non-unrealistic that it will be a matter of time only when the influence of old age on the pharmacokinetics and the metabolism of the relevant drugs for that age will be sufficiently evaluated thus allowing the necessary adaptation of dosage

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schedules and the proper choice of drugs from the viewpoint of drug disposition. It might for instance turn out that drugs being excreted solely unchanged by the kidneys will not be the best candidates for drug treatment in the elderly compared with those which, in addition, are metabolized to a certain extent.

Much more effort will be necessary to define the changes in pharmacodynamics of drugs related to old age. This again reflects the present situation where the quantitative assessment of drug action poses in general more difficulties than the study of drug disposition. In the population of aged patients we have to face the additional requirement that noninvasive techniques are often mandatory and methods will be particularly needed to quantify symptoms like vertigo, tremor,

mobility of joints, memory problems, sleep disturbances and many others. In this area of drug research we may use the experience already available in psychiatry where psychometric methods and the use of scores and scales are widely applied both for nosological problems and in the evaluation of drug effects.

Let us assume now for a moment that the influence of old age on pharmacokinetics and pharmacodynamics is sufficiently defined at least for the medicines most often prescribed for and used by aged patients. Could we then be satisfied as regards drug treatment in the elderly? My answer would be no! What we still need are new medicines particularly tailored for old patients. Some of them can be developed along the way, adapting, for example, drugs with well-defined pharmacodynamic actions to the particular pharmacokinetic situation of old human beings. But we need more, we need new drugs, new principles, for a great number of conditions encountered particularly in old age. Many of them concern psychic performances, others are aimed at 'Befindensstörungen' or neurological symptoms. I am not quite convinced that it depends mainly on the society as Dukes has pointed out in a very readable article whether symptoms in these areas are registered as necessary consequences of old age and as such tolerated by the individual. Several of those symptoms do in fact diminish the quality of life or the feeling of well-being or the social contacts in old people. In consequence, remedies to relieve them would be desirable, and as I think, necessary. In order to develop proper medicines we have – at least to my understanding – to recognize the following points:

Particularly in old age the treatment of symptoms should be regarded as a legitimate goal of medicine.

We should refrain from all dogmatic attitudes regarding the mechanisms by which potential medicines can act. This point is exemplified best by the analogy with anti-anginal drugs. For many years it was almost forbidden in the scientific community to speak of coronary spasms as a cause of angina or – horrible dictu – of myocardial necrosis. Today, reports on the influence of calcium antagonists, on spastic coronary vessels are appearing in every cardiological journal. A similar situation may hold true for drugs claimed to improve 'cerebral circulation', phosphate or glucose transport, oxygen consumption, neurohormonal situation, neuro-transmitter content, etc. Our knowledge is too limited at present to decide clearly for the one or the other approach. More basic research is necessary particularly in neurophysiology and neuropharmacology to define mechanisms responsible for age-related symptoms and for the correction by drugs.

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(4) Governmental regulatory agencies should reconsider their requirements for drugs used in the elderly and should not decide prematurely for or against certain groups of medicines or approaches as regards the proposed mechanism of action. They have a definite – admittedly indirect – responsibility in directing research in the pharmaceutical industry with the possible danger of narrowing the segments on which research is conducted.

(5) Properly timed and not unduly delayed by questionable safety requirements (teratogenicity? influence on fertility?). Clinical trials are needed and methods to assess the efficacy of those drugs have to be developed.

In conclusion, I would like to emphasize that this meeting has demonstrated that the problem of drug treatment in the elderly has attracted the necessary interest and the concern of practical and theoretical medicine. Some of the open questions may be answered in the near future, others

need long-term investments in basic research. An open mind will be necessary to avoid premature options and the firm intention to help the elderly.

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