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Drug Therapy for the Elderly

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Foreword

> It is much easier to write upon a disease than upon a remedy.
> The former is in the hands of nature and a faithful observer
> with an eye of tolerable judgment cannot fail to delineate a likeness.
> The latter will ever be subject to the whim,
> the inaccuracies, and the blunder of mankind.
>
> William Withering (1741–1799)

When William Withering wrote these words, he never could have imagined that they would still be relevant to the practice of medicine into the next millennium. However, there remains a lingering truth to Withering's words that should humble all those who prescribe medications to older patients. There are many reasons that make geriatric pharmacotherapy especially challenging. Geriatric patients often have multiple coexisting illnesses, leading to the use of complex drug regimens. An increased burden of morbidity often results in polypharmacy; polypharmacy can lead to redundant drug effects and is the most important risk factor for serious drug-drug interactions and adverse drug events. Adverse drug events are often nonspecific and can go unrecognized in older patients. Sometimes, drug side effects lead to the prescription of additional medications, creating a prescribing cascade, and potentially increasing the risk of drug-related problems in older patients even more. Complicating these challenges are the many pharmacologic and physiologic changes that occur with aging, posing additional risks of drug-related injury for geriatric patients. Last but not least, errors in management are extraordinarily common in medication prescribing and monitoring in the elderly, resulting in dangerous near-misses, close calls, and preventable drug-related injuries. All of these challenges are even further complicated by the dearth of evidence that exists around the benefits, risks, and comparative effectiveness of the multitude of drug treatments that are commonly used in older patients.

There is universal recognition of the need to optimize and rationalize the medication regimens of older patients. The editor of this important contribution to the medical literature, Martin Wehling, is an eminent pharmacologist, and he has assembled a distinguished group of experts to create a textbook that should serve as an important reference for health care professionals across the disciplines who wish to provide the very best care to our growing geriatric population.

February 2012

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Preface

Drug therapy is the most important therapeutic intervention by any physician. Even surgeons prescribe numerically more drugs than making decisions on individual operations. The number of diagnoses increases with the age of patients, and so does the number of drugs: Men aged 80+ have 3.24, women of the same age have 3.57 diagnoses in average. As a guideline dealing with one of those diagnoses recommends three drugs on average, it is not difficult to understand why elderly patients often receive ten and more drugs. A U.S. study showed that patients aged 65+ consume five and more drugs in over 50 % of cases, and 10 % of elderly patients even used ten and more. This phenomenon of so-called polypharmacy has grave consequences: For the United States alone, it is estimated that each year about 100,000 patients die of serious adverse drug reactions. The potential of drug-drug interactions increases exponentially with the number of drugs; however, this is not the biggest problem of polypharmacy. Not mentioning costs, which in the light of the demographic revolution is a yet-increasing threat to all health care insurance systems, it reflects the generally insufficient quality of treatment in the elderly. This results—among other reasons—from the fact that most drug therapies have never been tested in the elderly; guidelines often simply extrapolate findings from younger to elder patients if the latter patient group is mentioned at all.

The lack of evidence is one of the major sources of suboptimal treatment in the elderly, and no drug has ever been tested in position 8 or 10 of a list of potentially outcome-relevant drugs. In clinical trials, patient selection aims at those without relevant concomitant diseases and thus medications; this almost automatically excludes most elderly patients from studies, and no drug will be tested on a background of more than four or five drugs. Polypharmacy thus results from extrapolations and simple additions of drugs—a process that often leads to a deadly cocktail. As a consequence, we need not only the systematic generation of data on drug efficacy and safety in the elderly but also an answer to the burning question of how to reduce polypharmacy rationally and consistently in the realm of non-evidence-based drug therapies in the elderly.

In this context, the book has two major aims: to compile the available knowledge on gerontopharmacology and to guide physicians to a rationalistic

approach for successful drug therapy in the elderly. This includes the wide application of a novel classification of drugs relating to their *F*itness f*or t*he *A*ged (FORTA; see chapter "Critical Extrapolation of Guidelines and Study Results: Risk-Benefit Assessment for Patients with Reduced Life Expectancy and a New Classification of Drugs According to Their Fitness for the Aged"), which not only assesses negative drug aspects such as the Beers' list, but also adds the emerging positive experiences in important therapeutic situations. It should be mentioned beforehand that the paucity of data and the yet-early days of an international discussion lead to limitations of this classification, which is only meant as proposal and inspirational attempt; in many instances, it still reflects author opinions only. It applies to chronic therapies for which data in the elderly are more prevalent than for those on acute interventions (e.g., in intensive care situations). This explains that, for example, for stroke as one of the most prevalent diseases in the elderly, only risk factors and preventive measures are addressed, but not the acute treatment, which is mainly done by specialists. In situations in which special knowledge and treatment modalities do not exist for the elderly in comparison to younger patients, we refer to standard books and training; thus, it is conceivable that chapters on gastrointestinal diseases or antibiotics are lacking. This book should concentrate on age-specific problems and not become diluted by the repetition of age-independent standard knowledge that can be found in reference works. Ideally, it should be received as a book supplementing those not devoted to the elderly; thus, the book volume could be restricted to less than 350 pages. Referencing is also very limited and by far not complete. Along this line, basic drug data contained in the *Physician's Desk Reference* or similar national drug listings (e.g., Rote Liste® in Germany) are not repeated unless they are important for age-related issues. Therefore, some chapters appear inadequately small compared to the importance of the clinical entities addressed. This results from the lack of data and reflection thereof in the book, but slim or lacking chapters should also inspire and encourage researchers to generate the data in clinical trials.

An important task for the authors was the thorough reflection of geriatric syndromes directly relating to drug therapy in the elderly, such as dementia, fall risk, and frailty. This includes both the induction of these syndromes by drugs and their treatment by drugs. In addition, more generic aspects of drug therapy in the elderly are addressed, including altered pharmacokinetics or compliance/adherence issues. These topics underlie the disease-oriented chapters (including the "missing" ones), and not notoriously repeated there; for example, it does not need to be reiterated in all chapters that kidney function is essential to the excretion of many drugs. To ease orientation, study acronyms are explained within and at the end some chapters.

The authors hope that this book may positively contribute to one of the most important therapeutic areas of the future: drug therapy in the elderly.

Mannheim Martin Wehling
February 2012

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About the Editor

Martin Wehling is full professor of clinical pharmacology at the University of Heidelberg. He is also an internist (cardiologist) and has long-standing experiences in basic science (cell physiology, steroid pharmacology, nongenomic steroid actions); clinical trials (translating basic science into human studies); and clinical medicine (invasive cardiology, endocrinology, geriatrics). In 2004, he was appointed by AstraZeneca as director of discovery (= translational) medicine. In 2007, he returned to his academic position. In 2000, he founded the Center of Gerontopharmacology (together with the head of the department of geriatric medicine, R. Gladisch), which supports the development of drug therapy in the elderly both scientifically and in daily practice. He has the only outpatient service for gerontopharmacology in Germany.

Potential Conflicts of Interest of the Editor

Martin Wehling was employed by AstraZeneca R&D, Mölndal, as director of discovery medicine (= translational medicine) from 2004 to 2006 while on sabbatical leave from his professorship at the University of Heidelberg. After return to this position in January 2007, he received lecturing and consulting fees from Sanofi-Aventis, Novartis, Takeda, Roche, Pfizer, Bristol-Myers, Daichii-Sankyo, Lilly, and Novo-Nordisk.