

Editorial

Introduction to Pharmacotherapy Guidelines for the aged by family doctors for the use of family doctors

In this issue and in the five following issues, the International Journal of Clinical Pharmacology and Therapeutics (IJCPT) is publishing in instalments a series of articles entitled “Pharmacotherapy Guidelines for the aged developed by family doctors for family doctors”. This is a novel step for the Journal and requires some explanation.

The development and use of the guidelines falls within the sphere of “drug utilization research” (DUR), an area of clinical pharmacology. DUR employs the methods of pharmaco-epidemiology and pharmaco-economics with the aim of providing an estimate of the benefits, risks and costs of medication to patients and the population at large, and of conveying the results of the investigations to those who prescribe and use drugs. Thus, the IJCPT regularly publishes articles on DUR which are based on the methods of pharmaco-epidemiology and reports on the benefits and risks of drug use in patients. They address questions such as:

- What do doctors prescribe in certain diseases and does the quality of drug therapy meet scientific standards [Huang WF 2006, Vlahovic-Pelceviski et al. 2007]?

- Is self-medication with the investigated drug efficacious and is it safe [Hinkel et al. 2007]?
- DUR does not only investigate the effectiveness of drugs but also the side effects, such as those associated with iatrogenous morbidity and mortality [McGavock 2004].

For example, one of the first DUR studies uncovered the risks of thalidomide, in which a pharmaco-epidemiological study by W. Lenz in 1966 proved the connection between the indication for a thalidomide-based therapy, prescription of the drug by doctors, drug consumption by the pregnant patient and phocomelia in the newborn baby as an unwanted side effect.

Scarcity of resources in the health system force us in the cost-effective use of drug therapies and to apply the methods of pharmaco-economics. Key questions include:

- What are the costs of pharmaco-therapies in specific diseases? Are there cheaper but equally effective alternatives [Avorn 1996]?
- Can the costs and follow-up costs of therapeutic failures or of drug therapies which do not meet the recommendations of the guidelines be avoided [Mak et al. 2007]?

Although these questions have been identified, the results of pharmaco-epidemiological and pharmaco-economic investigations have proven, that the transfer of evidence-based results from clinical pharmacology research into the daily practice of family doctors does not meet expectations. This can in part be explained by the reduction, for methodological reasons, of clinical studies into simplified research models which do not match the real-life situation of the family doctors and their patients. Some of the main factors are:

- Older patients rarely take part in clinical studies.

- Multi-morbid, chronically ill patients are very rarely included in clinical studies.
- Studies only rarely investigate the effects of general measures such as the effect of a healthy diet and sufficient exercise, which influence the well-being of the patient and thus the effectiveness of drug therapy.
- Studies only rarely take into account the standards of drug therapy management. These include e.g. the continuation and simultaneous evaluation of therapies administered to a patient by different institutions (hospital, specialists), control and adjustment of multi-medication in cases of multi-morbidity, care in the assessment of the development of a therapy, support for the patient's compliance.

For those reasons, the results of clinical studies and the recommendations in many national guidelines are often regarded as inadequate for use by family doctors and because they issue the majority of prescriptions, clinical pharmacology is faced with a problem of great practical significance.

Additional obstacles arise from the fact that pharmaco-epidemiologists and pharmaco-economists pay no great attention to the dissemination of their research results [Grol 1992] but employ only traditional ways of knowledge transfer from lab to surgery. The fact that the dissemination of relevant, more specifically therapeutic knowledge must take into account "implementation" issues, i.e. the day-to-day context in which such knowledge is embedded, is only rarely discussed [Avorn 1992, von Ferber and von Ferber 2005].

The research work within the Family Doctor Guidelines Group in Hesse begins at these self-imposed methodological limits – where drug utilization research stops. It takes the doctor-patient relationship as its starting point and aims at strengthening the sensitivity of doctors to the needs of the patients in order to provide them with the best help possible.

This approach fits within the concept of holistic medicine [Hartmann 1984] but is based on evidence-based therapy. The results of clinical studies are evaluated using all available methods, but always with respect to the concrete situation of the patients. This includes those aspects which pharmaco-epidemiological and pharmaco-economic research excludes for methodological reasons i.e. multi-morbidity, individual risk evaluation and the activation of the personal resources of the patient. However, the aims of the guidelines group is not limited to obtaining the results of its research, it strives for their effective dissemination in order to test its own recommendations. The development of guidelines for family doctors is not solely for the purpose of providing a publication. Although the latter serves to foster critical debate, the development of the guidelines is inseparably bound to the way they are disseminated. Their therapeutic relevance is demonstrated to doctors in structured and moderated quality circles. The circle members in turn evaluate and prove the individual recommendations as well as their implementation and relevance in day-to-day practice [von Ferber and von Ferber 2005].

The publication of the guidelines on pharmacotherapy for the aged, multi-morbid patient contains a research approach that is rooted in drug utilization research but goes beyond the self-imposed limits of its traditional research methods in order to get more closely to the research goals of clinical pharmacology and therapy and thus ensures that pharmacotherapy is more relevant and more effective for patients.

The "Pharmacotherapy Guidelines for the aged" are particularly suitable for introducing this research approach since they demonstrate the need for widening the DUR perspectives and because it investigates the benefit of a therapy for the patient as a whole and not a single disease. Thus it includes the management of all aspects of the aged patient in-

cluding all diseases and their therapy. The “Pharmacotherapy Guidelines for the aged by family doctors for the use of family doctors” summarizes the most important therapeutic problems of aged patients.

The chapter on “general pharmacology” describes the changes in pharmaco-kinetics and pharmaco-dynamics in the ageing body. It also names important age-specific unwanted side effects for commonly prescribed drugs and shows the risks of multi-medication for multi-morbid, chronically ill aged patients.

The chapter “special pharmacology” introduces therapies for some age-specific diseases, commonly encountered in general practice.

A central section of the guideline is dedicated to the “general improvement in the physical well-being of the patient”, his or her diet and his or her exercise regimen, as a basis for an effective drug therapy.

A final chapter of the guideline is dedicated to “pharmaco-therapy management” and includes the assessment and control of therapy development, compliance and cooperation with the hospital, specialists as well as the interactions of the patient with his or her main social contacts, among whom are the family doctor and other therapists.

References

- Avorn, J. Practice-based outcomes research: crucial, feasible and neglected. *Pediatrics*. 1996; 97: 113-114.
- von Ferber L, von Ferber Ch. How should we assess the clinical relevance of guidelines in primary health care? *J Public Health*. 2005; 13: 40-47.
- von Ferber L, Bausch J, Köster I, Schubert I, Ihle P. *Pharmaco-therapeutic Circles*. Results of an 18-month peer-review prescribing-improvement programme for General Practitioners. *Pharmacoeconomics*. 1999; 16: 273-283.
- Grol R. Implementing guidelines in health care. *Quality in Health Care*. 1992; 1: 184-191.
- Haider SI, Johnell K, Thorslund M, Fastbom J. Trends in polypharmacy and potential drug-drug interactions across educational groups in elderly patients in Sweden for the period 1992 – 2002. *Int J Clin Pharmacol Ther*. 2007; 45: 643-654.
- Hartmann F. *Patient Arzt und Medizin. Beiträge zur ärztlichen Anthropologie*. Göttingen: Verlag für Medizinische Psychologie im Verlag Vandenhoeck and Ruprecht; 1984.
- Hinkel U, Schuijt C, Erckenbrecht JF. OTC laxative use of sodium picosulfate – results of a pharmacy-based patient survey (cohort study). *Int J Clin Pharmacol Ther*. 2007; 46: 89-95.
- Huang WF, Lai IC. Potentially inappropriate prescribing for insomnia in elderly outpatients in Taiwan. *Int J Clin Pharmacol Ther*. 2006; 44: 335-342.
- Lenz W. Malformations caused by drugs in pregnancy. *American Journal of Diseases of Children*. 1966; 112: 99-110.
- Mak CF, Choi DKM, Wong RSM, You JHS. Clinical and economic analyses of antimicrobial therapy in fever wards at a Hong Kong teaching hospital. *Int J Clin Pharmacol Ther*. 2007; 45: 654-658.
- McGavock H. Strategies for promoting cost-effectiveness in primary care prescribing and for reducing the pandemic of prescription-related morbidity and mortality. In: Kirch W. (ed) *Public Health in Europe*. Berlin, Heidelberg, New York: Springer Verlag; 2004, p. 101-102.
- Schubert I, Lelgemann M, Kirchner H, von Ferber C, von Ferber L, Ollenschläger G. *Handbuch zur Entwicklung regionaler Leitlinien*. ÄZQ Berlin, PMV Forschungsgruppe Köln, Leitliniegruppe Hessen KVH Frankfurt (ed.); 2006.
- Schubert I, Ihle P, Köster I, von Ferber L. Markers to analyse the prescribing of non-steroidal anti-inflammatory drugs in ambulatory care. *Eur J Clin Pharmacol*. 1999; 55: 479-486.
- Vlahovic-Pelceviski V, Francetic I, Palceviski G, Novak S, Abram M, Bergman U. Antimicrobial use at a university hospital: appropriate or misuse? A quality study. *Int J Clin Pharmacol Ther*. 2007; 45: 169-175.

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Pharmacotherapy Guidelines for the aged by family doctors for the use of family doctors

Part A: Context of the guidelines: evidence categories

Part B: General Pharmacology of the aged

Version 1.07, April 18th, 2007, Revision up to December 2008

Guidelines Group Hesse: Pharmacotherapy Guidelines by Family Doctors for Family Doctors

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Parts A and B are published in this issue. Parts C, D and E will follow in the next issues.

A Context of the guidelines: evidence categories

a) Context, responsibilities and supporting institutions, independence

Membership of the Guidelines Group

The members of the “Guidelines Group Hesse – Pharmacotherapy by Family Doctors” are family doctors practicing within the Hesse region (Germany) of the National Association of the Statutory Health Insurance Physicians. They have been involved as moderators in family doctors’ quality management circles on pharmacotherapy for more than 10 years [von Ferber et al. 1999]. They have developed guidelines on selected conditions of relevance to family doctors and are the authors of the guidelines.

The following institutions have supported the work of the guidelines group [Schubert et al. 2006]:

- The quality circles on pharmacology and the guidelines work are supported by the Hesse Association of the Statutory Health Insurance Physicians (KV Hessen), although the association neither tries to influence nor accepts responsibility for the outcome. The guidelines are published in print by the association.
- The Primary Health Care Research Unit (PMV Forschungsgruppe University of Cologne) acts as chair of the guideline meetings and looks after the concept, guidance and evaluation of the development of guidelines for family doctors.
- The Agency for Quality in Medicine (ÄZQ), Berlin, which was backed by a grant from the Ministry of Health up to May 2003, supported and co-evaluated the project “Guidelines for pharmacotherapy by family doctors for the use of family doctors”. Training in methods in evidence-based-research was also provided. The guidelines are regularly published in the web by the agency and the Research Unit.

The following guidelines have been developed and published by the Hesse group:

- Care of the aged
- Anticoagulation

- Asthma bronchialis and COPD
- Chronic cardiac failure
- Diabetes mellitus Type 2
- Diseases of the fat metabolism
- Communication for Family Doctors
- High blood pressure
- Diseases of the stomach and the intestines
- Pain
- Stable angina pectoris
- Venous thromboses

The Guidelines Group Hesse welcomes recommendations from colleagues concerning their experiences obtained by applying the guidelines in practice. Please address your opinions and recommendations to the PMV forschungsgruppe. Thank you very much in advance.

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Independence

The guidelines group is independent and therefore free from external influence. The members are volunteers and receive only reimbursement of their costs from the association KV Hessen. However, the association does not nominate members for the group, nor does it see the guidelines before they are published. There are no financial or other dependency of the guidelines group to any other institution or interest.

b) Aims and methods

The Hesse guidelines group consists of family doctors with an interest in pharmacology, who have advised colleagues – either individually or in groups (quality circles) – on the quality and efficiency of drug therapies for many years [von Ferber et al. 1999]. The group regards the guidelines as a means of orientation and decision-making for family doctors. The guidelines contain recommendations for typical conditions and therapeutic situations – the “normal” case known to the members of the guidelines group from experience. The group puts a high value on the day-to-day usefulness of its recommenda-

Levels of evidence.

Strength and type of evidence	Emphasis levels of recommendation
Ia Evidence based on meta-analyses of randomized controlled studies	A Based on levels Ia and Ib of evidence type, i.e. the recommendation is based on publications of good quality that contain at least one randomized controlled study.
Ib Evidence based on at least one randomized controlled study	B Based on levels IIa, IIb and III of evidence type, i.e. the recommendation is based on well-designed, non-randomized clinical studies.
IIa Evidence based on at least one well-designed controlled study without randomization	C Based on level IV, i.e. the recommendation is the result of reports and opinions from expert circles, consensus conferences and/or clinical experience of recognized experts. Level C indicates a lack of directly applicable clinical studies of good quality.
IIb Evidence based on one well-designed, quasi-experimental study	
III Evidence based on one well-designed, non-experimental descriptive study (e.g. comparative studies, correlation studies, case-control-studies)	
IV Evidence based on the reports or opinions of expert circles, consensus conferences and/or clinical experience of recognized experts	

tions [von Ferber and von Ferber 2005a,b]. Patients with specific conditions must be treated according to their needs and individual situation. As far as possible, the recommendations are underpinned by studies that in turn are evaluated according to evidence based research [Schubert et al. 2006]. The guidelines group regards the support of non-drug-based, patient-activating measures as important [Schubert et al. 2006]. The fact that these have lower evidence scores does not mean that they are less relevant, but only that they are unsuited to the standardized evaluation methods of evidence-based medicine (such as randomized clinical studies, double-blind studies) and that it is difficult to win financial support for their investigation [Song et al. 2000].

The principles of the guidelines are based on thorough research of already existing guidelines and the supporting literature. If evidence-based guidelines exist, their recommendations on pharmacotherapy that are relevant to family doctors will be accepted. If relevant studies are lacking, consensual recommendations are made on the basis of the therapeutic experience of the participating family doctors. The group presents its working methods in a general report and prepares a specific report for each of its guidelines [Schubert et al. 2006].

Evaluation of the Guidelines

The guidelines and the individual recommendations were discussed between the

members of groups of doctors who base their discussion on quality and efficacy of their own prescribing. The guidelines were evaluated in these groups

The acceptance of the guidelines and its individual recommendations is surveyed among the participants of these groups of doctors [von Ferber and von Ferber 2005a] asking them whether they applied the guidelines in their daily practice.

The effect of the guidelines on the issuing of prescriptions is evaluated by comparison of the prescriptions these doctors issued before and after the discussion of the guidelines. The evaluation took place on the basis of the collected prescriptions and using certain quality markers related to the recommendations in the guidelines [Schubert et al. 2006, von Ferber et al. 1999].

c) Levels of evidence

The decisions regarding the content and recommendations of the Guidelines are the result of a consensus decision by the "Hesse Guidelines Group – Pharmacotherapy for Family Doctors". The findings and recommendations in every guideline are categorized according to evidence in three steps. This is done as follows: Step 1 is a comparison with findings in evidence-based guidelines; the levels of evidence are accepted for recommendations that are effectively identical. For findings that cannot be categorized in this way, the authors – in Step 2– evaluated

the literature and categorized the studies and the recommendations based on them (see above). In Step 3, in the case of findings that currently cannot be proven by studies recommendations are rated C. They are based on the experience of experts who are family doctors and members of the Guidelines Group.

The scheme of levels shown above (evidence types and levels of emphasis of recommendations) is based on that of the US Agency for Health Care Policy and Research (AHCPR, US Department of Health and Human Service, 1993 [Schwabe and Rabe 2004]) as quoted in the guideline of the Scottish Intercollegiate Guideline Network. The Guidelines indicate the levels of evidence in brackets (e.g. {A}).

d) Introduction

Age is the most important determinant of patient morbidity and hence drug use [von Ferber et al. 1995]. The Berliner Altersstudie 2003 (Berlin Age Study) clearly shows the increase in incidence and prevalence of chronic disease among the aged. For example, within the statutory health insurance scheme a 20 – 25 year-old patient receives 96 DDD (defined daily doses) per year, the annual rate for an 85 – 90 year-old is 1,399 DDD [Nink and Schröder 2004].

Multi-medication management in the aged is a constant challenge for doctor and patient because of difficult-to-control interactions in individual cases [von Ferber et al. 1995, von Renteln-Kruse 2004]. For prescription rates such as those quoted above, an increase in undesirable drug effects is to be expected and they are the cause of 5% of hospital admissions in Germany [Thürmann and Schmitt 2000].

Aged and chronically ill patients are mainly cared for by family doctors and specialists in internal medicine. Since chronically ill patients take up more than 40% of the time of a family doctor, guidelines on pharmacotherapy in the aged are urgently sought after by family doctors [Fischer 1992, Klimm 1994].

The following guidelines presents the treatment of disease in the aged in three sections:

- the first section : **General Pharmacology in the Aged** discusses the important aspects and risks of drug therapy in the aged
- the second section: **Special Pharmacology** details the diseases that are particularly common in old age
 - dementia
 - Morbus Parkinson
 - osteoporosis
 - urinary incontinence
 - rectal incontinence and obstipation
- The third section addresses two important **aspects of a sustainable treatment in old age**
 - the management of age associated diseases by family doctors
 - measures to improve health that activate the patient and his/her relatives, because experience suggests that they have a positive effect on drug therapies. These are:
 - nutrition
 - body exercises

B General Pharmacology in the aged

The decisive pharmacological parameters that influence the effectiveness of drug therapy undergo increasing and individual change throughout life. An optimal drug therapy needs to take into account the individual variables as well as physiological changes due to age. Moreover, elderly patients more often require multi-medication, which carries additional risks.

a) Absorption of drugs

[Köppel 2003, Lauterburg 2005, Platt and Mutschler 1999]

A worsening resorption rate with higher age can be shown for many drugs :

- Atrophy of the stomach lining leads to lack of gastric acid (increased pH-value, can also arise from the use of proton pump inhibitors)
- Deterioration in intestinal blood flow (by 30 – 40%)
- Deterioration of the peristalsis (e.g. also from using anticholinergics) reduces speed of resorption
- Chewing disorders due to defective teeth
- Special eating and drinking habits (e.g. low fluid intake, low fiber diet, “custard vegetarians”)
- Occurrence of obstipation or diarrhoea changes the resorption conditions

b) Distribution space

[Beaufriere and Morio 2000, Platt and Mutschler 1999]

Age-related changes in the distribution space:

- Reduction in total water in the body (from 42 to 33% of body weight (in kg), the percentage of extracellular fluids is 29% for infants, 15% for adults and 12% for the aged)
- Increase in body fats (to 15 – 30% in terms of body weight in kg)
- Decrease in muscular mass
- Decrease in plasma proteins (decrease in plasma albumin by 15 – 20%)

influence the distribution of the substances absorbed. The consequences are that (see Appendix 1a – b):

Lipophilic drugs

Lipophilic drugs (e.g. amoxicillin, barbiturates, chlordiazepoxide, diazepam, nitrazepam, oxazepam, prazosin, furosemide) are subject to larger distribution volumes and thus have prolonged efficacy in the aged. They are stored increasingly more effectively and for longer periods in enlarged fat depots.

- Dosage according to body weight may lead to excessive tissue levels whereas their plasma concentration drops.
- This also means that extreme weight reduction (fat reduction) can release excessive amounts of active drug.

Hydrophilic drugs

Hydrophilic drugs (e.g. ACE-blockers, digoxin, lorazepam, metronidazole, L-thyroxine) are subject to a lower distribution volume due to “age-related exsiccosis”. They require sufficient amounts of liquid to be eliminated. Because age reduces the feeling of thirst, leading to lower fluid intake, and kidney activity is also reduced (see below), an accumulation of drug is likely unless the dosage is reduced: it should also be noted that a reduction in the distribution volume as a result of a lower percentage of body fluids due to age causes an increase in drug effects (e.g. digoxin, whose plasma concentration increases, must be given in lower doses) (see Appendix 1a – b).

c) Transport proteins – the carrier system

[Forth et al. 1992, Platt and Mutschler 1999]

Protein synthesis decreases with age, albeit to different degrees in individual patients. Lack of albumin is frequent (see chapter on Diet) and consequently a reduced transport capacity of protein-bound drugs, depending on the strength of the protein bond of the substance affected means that in pa-

tients the free portion of active drug can be surprisingly high. This necessitates an **adequate reduction in the dose of drugs with strong protein bonds in elderly patients**. Multi-medication further intensifies the effects of a deficiency in carrier.

Competition for a carrier system affected by age can lead to dissolution of the protein bond and a subsequent increase in the free proportion of the active drug. (Example: If the strong phenprocoumon-albumin bond of 99% is reduced by only 1% due to simultaneous use of non-steroid anti-rheumatics and/or theophylline, glibenclamide or other substances, the active concentration of the anti-coagulant is doubled and hemorrhage can occur! [Multidisciplinary medication management project 2001]).

Similarly, a reduction in the protein bond increases the free (active) portion of phenytoin, clobazepam, temazepam, desipramine, acetylsalicylic acid and others.

d) Renal elimination

[Müller-Oerlinghausen et al. 1999, Platt and Mutschler 1999]

Rule of thumb: Above the age of approximately 40 years, renal clearance (glomerular filtration rate: GFR) falls by approximately 1% per annum. In patients older than 70, the GFR is reduced by 30 – 50% [Mühlberg et al. 1999].

Important: A normal serum creatinine can mask a reduced renal clearance [Baracskey et al. 1997]. Thus, despite a serum creatinine of 1.2 mg/ml in a patient suffering from muscular regression (and hence a reduced release of endogenous creatinine) the GFR may be only 35 ml/min and not the apparently normal 70 ml/min.

The Cockcroft-Gault formula allows a sufficiently exact calculation of the renal clearance (C_{creat}). (There is a simplified slide rule by the industry.)

Male: $C_{\text{creat}} = (140 - \text{age}) \times \text{weight (kg)} / 72 \times \text{serum creatinine (mg/ml)}$

Female: $C_{\text{creat}} = (140 - \text{age}) \times \text{weight (kg)} / 85 \times \text{serum creatinine (mg/ml)}$

Older patients must be given lower doses of substances with predominantly renal

elimination (e.g. ampicillin, benzyl penicillin, captopril, cefotaxim, cefuroxime, quinidine, digoxin, lithium, metronidazole, tetracycline, theophylline, triamterene). Because of the effects of age on GFR resulting in accumulation, the dose must be reduced to avoid an increase in side effects such as ototoxic effects in the case of amino glycosides (see Appendix 1).

e) Metabolism of substances in the liver and hepatic elimination

[Arzneimittelkommission der Deutschen Ärzteschaft 2003, Forth et al. 1992, Platt and Mutschler 1999]

The effect of age on the liver perfusion (reduction by 40% [Zeeh and Platt 1990]) and on its metabolic function causes variations in hepatic elimination. Thus, there is a risk of reduced elimination and extension of the pharmacological effectiveness.

A reduction of albumin synthesis in the liver is a marker for a reduced liver function (total serum albumin).

All substances with predominantly hepatic elimination and those with a distinctive first-pass effect (which is reduced in cases of liver damage) can have severely altered effects in the elderly (e.g. benzodiazepine, β -blockers, diltiazem, ergotamine, fentanyl, glycerol trinitrate and other nitrates, imipramine, lidocaine, naloxone, nortriptyline, pentazocine, pethidine, prazosin, salicylamide, theophylline, verapamil and others).

⇒ Older patients must therefore receive adequately reduced initial and repeat doses of substances with predominantly hepatic elimination (e.g. paracetamol) (see Appendix 1).

⇒ Equally, substances with a distinct first-pass effect must be given at lower doses (e.g. alcohol, verapamil) (see Appendix 1).

Low hepatic elimination rates as well as reduced first-pass effects have to be observed in the case of barbiturates, quinidine, chloramphenicol, clindamycin, digitoxin, metildigoxin, paracetamol, phenytoin, rifampicin, theophylline (see Appendix 1). When liver function is reduced, patients must be given

lower doses of these substances to avoid accumulation.

Liver perfusion disorders and other endogenous effects of the drugs can lead to unpredictable changes in effectiveness (e.g. increased sensitivity to centrally active drugs such as barbiturates, benzodiazepine, chlorpromazine often require a dose reduction of up to 50%).

Prodrugs, which are normally metabolized into their active form in the liver, on the other hand **must be given in higher doses**, because transformation into their active form is reduced (e.g. amoxicillin, esomeprazole).

Noxious substances such as alcohol, nicotine and also many drugs can accelerate liver metabolism through enzyme induction (see Appendix 2). This leads to a reduced effectiveness of the drugs (e.g. barbiturates, many anti-epileptics (carbamazepine, phenytoin), griseofulvin, isoniazid, preparations made from St. John's wort, omeprazole, rifabutin, rifampicin, sulfapyrazone), which must therefore be given in higher doses (*see Flockhart [2007]: cytochrome p-450. isoenzyme – substances, inhibitors, inducers, and chapter on interactions*).

Because liver metabolic function, especially the system based on the cytochrome p-450-isoenzymes, shows significant individual variation in older patients, the above comments can only hint at the likely changes in drug effectiveness. Individual cases require observation of drug effectiveness over time.

f) Interactions

[Platt and Mutschler 1999, The Merck Manual of Geriatrics 2005]

Because multi-medication is frequent, drug interactions play a major role in the care of the elderly. Drug interactions depend on a number of factors, especially age-related changes. In 3.4% of cases where patients took up to five drugs, unexpected side effects were observed; this rate increased to approximately 25% if more than five drugs were taken [Mühlberg et al. 1999].

Changes in electrolyte levels

Changes in electrolyte levels (e.g. through the abuse of laxatives, wrong diet, exsiccosis)

can retard the effectiveness of water soluble substances. Examples: digitalis (potassium deficiency and/or calcium over-supply can lead to cardiac disorders), lithium therapy requires a balanced supply of electrolytes and fluids (sodium deficiency and exsiccosis lead to toxic increases in lithium levels with, amongst others, dangerous unexpected side effects affecting the heart), ACE-blockers (NaCl-deficiency leads to hypotension).

The enzyme system of the cytochrome p-450

The enzyme system of the cytochrome p-450-system [De Luca et al. 2003, Flockhart 2007, Gysling 2003, Lauterburg 2005, Lazar and Schömig 2005, Schwab et al. 2002, Wilkinson 2005] is especially important for the biotransformation of many endogenous and exogenous substances (e.g. endogenous steroids, estrogens) as well as drugs. Drugs can be substrates of different cytochromes and be blockers or inducers of the biotransformation in question [Flockhart 2007, Gysling 2003].

Although these isoenzymes occur mainly in the liver (90–95%), small amounts are also found in the intestinal wall where they are responsible for the first-pass effect. The expression of a Cytochrome p-450-isoenzyme system is very complex and subject to genetically caused individual variations so that a prognosis of its effect on drug therapy is hardly possible. There are poor, intermediate, extensive and ultra-rapid metabolizers [De Luca and Gysling 2003, Schwab et al. 2002].

The most important group by far is the cytochrome subfamily CYP 3A (CYP 3A3, CYP 3A4, CYP 3A5, CYP 3A7). This group of isoenzymes metabolizes more than half of the commonly prescribed substances and thereby either amplifies or blocks their effectiveness depending on individual circumstances. Racemates of substances can be metabolized by different cytochromes either left- or right-spinning. In humans, there are 18 families of p-450-cytochromes distributed over 57 genes with polymorphic heredity and hence, large variability between individuals.

Currently, pharmacogenetic tests are being developed in order to allow the prediction of therapeutic risks or failures [Lazar and

Schömig 2005, Schwab et al. 2002] (important examples of interactions involving cytochromes can be found in Appendix 2).

Beyond this, there is an increased risk of adverse drug reactions (ADR) in old age, especially for the following ADRs:

- development of an anticholinergic syndrome
- development of acute states of confusion
- development of orthostatic dysregulation, decrease in blood pressure, nausea and syncope
- for an increasing risk of falling

The risk of ADRs is especially increased, if the dosage is too high or inappropriate. The drugs named in Appendices 4–7 are to be used with special caution or, if possible, avoided.

It is important to know that in older patients **the steady-state level of a drug** in the blood is only **reached after 4–5** of its usually extended half-lives [Lauterburg 2005, Schwab et al. 2002]. For some drugs it is possible to measure this level. However, this should be done only after the steady-state level has been reached [Lauterburg 2005].

Measuring is indicated:

- in cases of therapeutic failure despite adequate dosage,
- in cases of altered dosages or new auxiliary medication,
- in cases of therapeutic changes (important e.g. for digitalis, theophylline, lithium, carbamazepine, valproic acid),
- in cases of essential changes to the functioning of the metabolic system or the eliminating organs,
- in cases of expected side effects subject to concentration levels,
- when enzyme blockers or enzyme inducers [Flockhart 2007] (e.g. many drugs, but also St. John's wort, grapefruit juice, alcohol, tobacco smoke) are taken,
- in cases of a suspected wrong dosage (cumulation, suboptimal dosage),
- in cases of non-compliance.

The consequences of these guidelines are: frequent check-ups on medication after discharge from the hospital. Changes to the drug regime will often be necessary, and it should be kept in mind that the blood level will in most cases not have reached the steady-state.

g) Summary

Because a large number of drugs are ineffective due to the pharmacological reasons mentioned above, doctors should base any poly-pharmacotherapy on the effects of each individual substance. If more than three substances are given, it is impossible to predict, when and how much of the substance has reached which compartment and large individual variations will be present. Side effects must be recognized early. “The frequency of undesirable side effects of drug therapy in elderly patients corresponds to the number of prescribed substances.” [Köppel 2003, Mühlberg et al. 1999, Mühlberg 2004, Wen Kwang Lim and Woodward 1999].

In order to attain a suitable and successful pharmacotherapy in elderly patients, the prescribed substances – because their half-lives, either individually or in combination, are unknown – must be given at low and slowly increasing doses and their desirable and undesirable effects must be observed over an extended period. An individual therapy must therefore be adjusted according to its effects. In general, the number and dose of drugs in elderly patients is to be kept low [Cusack and Parker 1996, Mühlberg 2004, Mühlberg et al. 1999, Platt and Mutschler 1999, The Merck Manual of Geriatrics 2005, von Renteln-Kruse 2004].

“**Start low and go slow**” [Cusack and Parker 1996]. The family doctor should always be aware of the discrepancy between what is desirable and what is attainable in day-to-day practice.

References

Part A and Part B

- Arzneimittelkommission der deutschen Ärzteschaft. Arzneimittelverordnungen. 20. Auflage. Köln: Deutscher Ärzteverlag; 2003.
- Bach D et al. Reactivating occupational therapy: a method to improve cognitive performance in geriatric patients. *Age Aging*. 1995; 24: 222-224 (Ib).
- Baracskey D, Jarjoura D, Cugino A, Blend D, Rutecki GW, Whittier FC. Geriatric renal function: estimating glomerular filtration in an ambulatory elderly population. *Clin Nephrol*. 1997; 47: 222-228 (III).
- Beaufre B, Morio B. Fat and protein redistribution with aging: metabolic considerations. *Eur J Clin Nutr*. 2000; 54: 48-53 (eR).
- Beers MH et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med*. 1991; 151: 1825-1832.
- Cusack BJ, Parker BM. Pharmacology and appropriate prescribing. In: Reuben DB, Yoshikawa TT, Besdine RW (eds). *Geriatrics Review Syllabus: a core curriculum in geriatric medicine*. 3rd edition. New York: American Geriatrics Society; 1996, p. 35.
- De Luca A, Gysling E. Zytochrome und ihre Bedeutung für Arzneimittelinteraktionen. 3. Auflage der tabellarischen Zusammenfassung. Will: Infomed; 2003.
- Fick DM, Cooper JW et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med*. 2003; 163: 2716-2724. Erratum 2004; 164: 298.
- Fischer G. Krankheit bei alten Menschen. In: Kochem MM (ed). *Allgemeinmedizin*. Stuttgart: Hippokrates-Verlag; 1992, p. 284-292.
- Flockhart DA. Drug interactions – Cytochrom P 450 Substrates, Inhibitors and Inducers. Internet <http://medicine.iupui.edu/clinical/contact.htm> - drug interactions – P 450 Table – Vers 4.0 Aug. 2007.
- Forth W, Henschler D, Rummel W, Starke K. *Allgemeine und spezielle Pharmakologie und Toxikologie*. 6. Aufl. Mannheim-Leipzig-Wien-Zürich: BI-Wissenschaftsverlag; 1992.
- Gysling E. Zytochrome in der Praxis. *Pharma-Kritik* 2003; p. 10.
- Klimm HD. *Allgemeinmedizin*. Stuttgart: Enke-Verlag, 1994, p. 26ff.
- Köppel C. *Pharmakotherapie im Alter*. Berliner Ärzteblatt; 05.11.2003.
- Lauterburg B. *Grundlagen der Pharmakotherapie* 25.01.05 Institut für klinische Pharmakologie Universität Bern (<http://www.cx.unibe.ch/ikp/lab3/pharmakotherapie/html>); 2005.
- Lazar A, Schömig E. Genetik des Arzneimittelmetabolismus. Bedeutung für Klinik und Praxis. *Gynäkologische Praxis*. 2004; 28: 751-761.
- Mühlberg W. Häufige Arzneimittel-Nebenwirkungen und Interaktionen im Alter (<http://www.alter-nativen.ch/pdf/muehlberg2.pdf>), Autoreferat vom 4. Münsterlinger Symposium zur Alterspsychologie; September 2004.
- Mühlberg W, Platt D, Mutschler E. Neben und Wechselwirkungen von Pharmaka im Alter, In: Platt D, Mutschler E (Hrsg.). *Pharmakotherapie im Alter*. 3. Auflage. Stuttgart: wissenschaftliche Verlagsgesellschaft; 1999. S. 21-32.
- Müller-Oerlinghausen B, Lasek R, Düppenbecker H, Munter KH. *Handbuch der unerwünschten Arzneimittelwirkungen*. 1. Auflage. München-Jena: Urban & Fischer Verlag; 1999.
- Multidisciplinary medication management project*. Top ten dangerous drug interactions in long term care. (<http://www.scoup.net/M3Project/topten/>) (eR); 2001
- Nink K, Schröder H. Arzneimittelverordnungen nach Alter und Geschlecht. In: Schwabe U, Paffrath D (Hrsg). *Arzneiverordnungsreport 2004*. Berlin-Heidelberg: Springer Verlag; 2004. p. 1099-1111.
- Platt D, Mutschler E (Hrsg). *Pharmakotherapie im Alter*. 3. Auflage. Stuttgart: Wissenschaftliche Verlags Gesellschaft; 1999. p. 3-32.
- Schubert I, Leigemann M, Kirchner H, von Ferber Ch, von Ferber L, Ollenschläger G. *Handbuch zur Entwicklung regionaler Leitlinien*. ÄZQ Berlin, PMV forschungsgruppe Köln; 2006. <http://www.azq.de>.
- Schwab M, Marx C, Zanger UM, Eichelbaum M, Fischer-Bosch M. *Pharmakogenetik der Zytochrom-P-450-Enzyme: Bedeutung für Wirkungen und Nebenwirkungen von Medikamenten*. *Deutsches Ärzteblatt*. 2002; 99: A497-504.
- Schwabe U, Rabe T. *Sexualhormone*. In: Schwabe U, Paffrath D (Hrsg). *Arzneiverordnungs-Report 2003*. Berlin-Heidelberg: Springer; 2004. p. 776-798.
- Song F, Eastwood AJ, Gilbody S, et al. Publication and related biases. *Health Technology Assessment*. 2000; 4: 1-115.
- The Merck Manual of Geriatrics*. Chapter 6: Clinical Pharmacology: Pharmacokinetics, Pharmacodynamics, Adverse Drug Reactions, Considerations for Effective Pharmacotherapy. Regularly Updated Version 2005.
- Thürmann PA, Schmitt K. Erfassung und Bewertung unerwünschter Arzneimittelwirkungen. *Med Klin*. 2000; 95: 4-8.
- US Department of Health and Human Services. Agency for Health Care Policy and Research. *Acute Pain Management: operative and medical procedures and trauma*. Rockville (MD): Te Agency 1993. *Clinical Practice Guide No.1*. AHCPR Publication No. 92-0023: 107.
- von Ferber L, Köster J, Schubert J. Arzneimittelverordnungen und Diagnosen bei über 60-jährigen Personen am Beispiel der Herz-Kreislauf-Erkrankungen. *Verlaufsbeobachtungen unter Verwendung von Krankenkassendaten*. *Z Gerontol Geriatr*. 1995; 28: 401-407.
- von Ferber L, Bausch J, Köster I, Schubert I, Ihle P. *Pharmaco-therapeutic circles – results of an 18-month peer-review prescribing-improvement programme for general practitioners*. *Pharmacoeconomics*. 1999; 16: 273 -283.
- von Ferber L, von Ferber C. How should we assess the clinical relevance of guidelines in primary health care? *J Public Health*. 2005a; 13: 40-47.
- von Ferber L, von Ferber C. Wie verbindlich sind Empfehlungen von Leitlinien? – Ein vernachlässigtes Thema der Evaluation. *Med Klin*. 2005b; 100: 340-346.
- von Renteln-Kruse W (Hrsg). *Medizin des Alterns und des alten Menschen*. Darmstadt: Steinkopf-Verlag; 2004. p. 74-76.
- Wen Kwang Lim, Woodward MC. Improving medication outcomes in older people. *Australian J of Hospital Pharmacy*. 1999; 29: 103-107.
- Wilkinson GR. Drug metabolism and variability among patients in drug response. *N Engl J Med*. 2005; 352: 2211-2221.
- Zeeh J, Platt D. Altersveränderungen in der Leber. Konsequenzen für die Arzneitherapie. *Fortschr Med*. 1990; 108: 651-653.
- Zeeh J, Platt D. *Pharmakotherapie im Alter*. Therapie-woche. 1994; 44: 272-282.

h) Appendices Part B

Appendix 1a. Drugs whose dose must be lowered in older patients.

Drugs whose dose must be lowered in elderly patients	Reason
ACE-Blocker	hydrophilic: increase in plasma concentration due to lower distribution volume; special risk because of exsiccosis
Amino glycoside (amikacin, gentamycin, kanamycin, neomycin, netilmycin, streptomycin, tobramycin)	renal elimination: risk of accumulation in cases of kidney failure, higher in cases of exsiccosis, additional risk of ototoxic effects
Amoxicillin	lipophilic: build-up of reservoirs due to increased distribution volumes, extended period of effectiveness
Ampicillin	hydrophilic, see above
Antipyrine	hydrophilic, see above
Benzodiazepine (e.g. diazepam, nitrazepam, oxazepam)	lipophilic, see above; in addition, possibly excessive blood levels due to decreasing metabolism in the liver
Lorazepam	hydrophilic, see above
Benzylpenicillin	renal elimination, see above
β -Blocker	possibly excessive blood levels due to decreasing metabolism in the liver, however, reduced sensitivity in older patients [Bach et al. 1995]
Captopril	renal elimination, see above
Cefotaxime	renal elimination, see above
Cefuroxime	renal elimination, see above
Quinidine	renal elimination, see above
Chlordiazepoxide	lipophilic, see above
Digoxin	renal elimination, see above
Dihydrostreptomycin	renal elimination, see above; additional risk of ototoxic effects
Diltiazem	possibly excessive blood levels due to decreasing metabolism in the liver
Ergotamine	possibly excessive blood levels due to decreasing metabolism in the liver
Fentanyl	possibly excessive blood levels due to decreasing metabolism in the liver
Furosemide	lipophilic, see above
Glyceryl trinitrate and other nitrates	possibly excessive blood levels due to decreasing metabolism in the liver
Imipramine	possibly excessive blood levels due to decreasing metabolism in the liver

Appendix 1b. Drugs whose dose must be lowered in older patients (cont.)

Drugs whose dose must be lowered in elderly patients	Reason
Lidocaine	possibly excessive blood levels due to decreasing metabolism in the liver
Lithium	renal elimination, see above
L-Thyroxine	hydrophilic, see above
Metronidazole	renal elimination, see above
Naloxone	possibly excessive blood levels due to decreasing metabolism in the liver
Nortryptiline	possibly excessive blood levels due to decreasing metabolism in the liver
Paracetamol	possibly excessive blood levels due to decreasing metabolism in the liver
Pentazocine	possibly excessive blood levels due to decreasing metabolism in the liver
Pethidine	possibly excessive blood levels due to decreasing metabolism in the liver
Prazosin	lipophilic, see above, additionally due to decreased liver metabolic capacity, raised blood level possible
Propicillin	hydrophilic, see above
Salicylamide	possibly excessive blood levels due to decreasing metabolism in the liver
Sulfamethiazole	renal elimination, see above
Tetracycline	renal elimination, see above
Theophylline	renal elimination, see above; in addition possibly excessive blood levels due to decreasing metabolism in the liver
Triamterene	renal elimination, see above
Verapamil	possibly excessive blood levels due to decreasing metabolism in the liver

According to [Arzneimittelkommission der Deutschen Ärzteschaft 2003, Lauterburg 2005, Muhlberg 2004, Müller-Oerlinghausen et al. 1999, Platt and Mutschler 1999, The Merck Manual of Geriatrics 2005].

Appendix 2a. Characteristics of combinations of drugs.

Combinations of drugs that cause problems in elderly patients or carry special risks	Reason: cytochrome interaction
Benzodiazepine such as diazepam, flunitrazepam, triazolam + Grapefruit-juice	like many other substances are metabolized through CYP 3A4 contains bioflavines which block CYP 3A4: even sporadic use of these drugs can lead to fatal accumulation
Buspirone + Grapefruit-juice	is metabolized through CYP 3A4 contains bioflavines which block CYP 3A4: even sporadic use of buspirone can lead to fatal accumulation
Citaprolam + 2. SSRI (fluoxetine or paroxetine in low doses)	is a substrate of CYP2C19, 2D6, 3A4 = "extensive metabolizer". In case of insufficient effectiveness, use of an additional SSRI as CYP 2D6 blocker: increase in the plasma level of citaprolam in 10 – 15% of the population with CYP 2D6 reduction = "poor metabolizer", i.e. intended amplification of effectiveness in these patients
Codeine + Tramadol	prodrug, is metabolized in the body to morphine through CYP 2D6 "poor metabolizers" can have very low levels of CYP 2D6: these patients experience only mild analgesia
Clopidogrel + Atorvastatin or + Simvastatin	is transformed into the effective thiometabolite through CYP 3A4 and other cytochromes both block CYP 3A4, the effectiveness of clopidogrel is weakened
Digoxin + Substances made from St. John's wort	elimination through CYP 3A4 weakening of digoxin effectiveness through CYP 3A4 induction of the substances made from St. John's wort
Nicotine + Bupropion	the metabolism is controlled by CYP 2B6, which has a highly polymorphic heredity bupropion for smoking cessation is also metabolized through CYP 2B6: heavy withdrawal symptoms, in some cases relapses
Nicotine, tobacco smoke + Theophylline	tar components of the smoke induce CYP 1A2 und 3A4 metabolism is controlled by CYP 1A2: theophylline effectiveness significantly weakened

Appendix 2b. Characteristics of combinations of drugs (cont.)

Combinations of drugs that cause problems in older patients or carry special risks	Reason: cytochrome interaction
Nicotine, tobacco smoke + Caffeine	tar components of smoke induce CYP 1A2 und 3A4 caffeine is also metabolized via CYP 1A2: lower caffeine effectiveness
Phenprocoumon + Terbinafine hydrochloride + Miconazole + Fluconazole + Griseofulvin	Important metabolism via CYP 2A6, 2C9, 3A4 For treatment of a mycosis of the nails: lowest interactions within the P-450-system unfavorable: inhibits CYP 3A4 unfavorable: inhibits CYP 2C19, 2C8/9, 3A4 unfavorable: induces CYP 3A4
Phenprocoumon + Co-trimoxazole	elimination via CYP 2A6, 2C9, 3A4 inhibits CYP 2C9: phenprocoumon-level rises: danger of bleeding
Phenprocoumon + Substances made from St. John's wort	elimination via CYP 2A6, 2C9 and most importantly via 3A4 Induces P-glycoprotein as well as CYP 1A2, 2C9, 3A4, hence lower phenprocoumon effectiveness
Statins (atorvastatin, simvastatin, cerivastatin, lovastatin) not pravastatin, + polymedication	risk of rhabdomyolysis through interactions via CYP 3A4, because most statins are metabolized via CYP 3A4 (Fluvastatin via CYP 2C19)
Sulfonyl carbamides, glinids, glitazones (not Metformin!) + anti-depressants (e. g. the SSRIs fluoxetine, fluvoxamine, sertraline hydrochloride)	nearly all oral anti-diabetics are metabolized through CYP 2C9 (only metformin is eliminated renally unchanged) these anti-depressants inhibit CYP 2C9: risk of hypoglycemia
Sulfonyl carbamides, glinids, glitazones (not metformin!) + Substances made from St. John's wort	nearly all oral anti-diabetics are metabolized through CYP 2C9 (only metformin is eliminated renally unchanged) induce among others CYP 2C9: increased risk of hyperglycemia

According to [Beers et al. 1991, Fick and Cooper 2003, Gysling 2003, Mühlberg 2004].

Appendix 3a. Drugs or drug combinations that are a problem in older patients.

Drugs that are a problem in older patients	Reason
Aminoglycosides + Furosemide	increased number of undesirable side effects: acute state of confusion through damage to the vestibular nerve with defective sense of balance
Analgesics (morphine, morphine derivatives)	increased number of undesirable side effects: acute state of confusion
Antidepressants, neuroleptics	increased number of undesirable side effects: acute state of confusion , risk increases with sedative potency
Antihypertensives	increased number of undesirable side effects: syncope s, lower sensitivity of the baroreceptors and reduced vein tonicity
Antihypertensives + Psychopharmaca + Nitrates	increased number of undesirable side effects: acute state of confusion due to low blood pressure, especially at start of therapy with exsiccosis and existing high blood pressure
Anti-parkinson agent + Antihypertensives	increased number of undesirable side effects: acute state of confusion in case of higher sensitivity to drugs that affect the CNS
Benzodiazepines	increased number of undesirable side effects: acute state of confusion due to higher sensitivity to benzodiazepines, increased sedative effect, longer reaction time, increased muscle relaxation
Digitalis + Diuretics	increased number of undesirable side effects: syncope s, increased risk of bradycardia due to a lowered excitement threshold of N. vagus. In addition increased digitalis sensitivity with dysrhythmia due to hypokalemia
Diuretics	increased number of undesirable side effects: syncope s, fall in blood pressure , increased loss of fluids with reduced feelings of thirst, low blood pressure beyond hypovolemia due to reduced sensitivity of the baroreceptors
Diuretics	increased number of undesirable side effects: acute state of confusion due to risk of exsiccosis, often falls with fractures of the hip joint
Diuretics, potassium-saving (triamterene, amiloride), if applicable + thiazide-diuretic	increased number of undesirable side effects: acute renal failure especially in combination with thiazides, because the glomerular filtration rate, already low in age, is further reduced by both groups of substances
Diuretic (loop-diuretic) + thiazide-diuretic + low NaCl diet	in therapies of cardiac insufficiency, increased number of undesirable side effects: acute renal failure

According to [Beaufrère 2000, Beers 1991, Lauterburg 2005, Mühlberg 2004, Zeeh and Platt 1994].

Appendix 3b. Drugs or drug combinations that are a problem in elderly patients (cont.).

Drugs that are a problem in elderly patients	Reason
Insulin + Sulfonyl carbamides	increased number of undesirable side effects: acute state of confusion due to hypoglycemia
Midazolam + simultaneous use of opioids	significantly increased risk of breathing and cardiac arrest
Neuroleptics + Antidepressants	increased number of undesirable side effects: acute state of confusion with Morbus Parkinson syndrome, bradykinesia + rigor
NSAIDs	older patients have a four-fold risk of suffering from lethal ulcerative bleeding. increased number of further undesirable side effects: acute renal failure due to vasoconstriction in the kidney resulting from a lack of vasodilating effects of the prostaglandins
NSAIDs + Diuretics at high dosages	increased risk of acute renal failure
Psychoactive drugs + Nitrates	particularly high risk of syncope in case of cerebrovascular insufficiency and long existing hypertension (malfunctioning in the auto-regulation of cerebral perfusion)
Statins (atorvastatin, simvastatin, cerivastatin, lovastatin) not pravastatin	risk of rhabdomyolysis through interactions in cases of poly-medication with substances that are metabolized via CYP 3A4, increased metabolism of Fluvastatin via CYP 2C19 inhibits CYP 2C8/9

According to [Lauterburg 2005, Mühlberg 2004, Zeeh and Platt 1994].

Appendix 4. Drugs that can cause an anticholinergic syndrome.

Drugs that can cause an anticholinergic syndrome	Substance
Analgesics	pethidine
Antiarrhythmics	quinidine, disopyramide, ipratropium bromide, procainamide
Antidepressants	amitriptyline, clomipramine, doxepin, imipramine
Antiemetics	meclozine/meclizine, peremesine
Antihistamines, Sedatives	clemastine, promethazine, diphenhydramine
Anti-Parkinson drugs	biperidin, trihexyphenidyl
Neuroleptics	fluspirilene, haloperidol, thioridazine
Spasmolytics	butylscopolaminium bromide

According to [Zeeh and Platt 1994].

Appendix 5. Drugs that can cause acute states of confusion.

Drugs that can cause acute states of confusion	Risk	Notes on substances
Analgesics, strongly effective	+ + + +	morphine and its derivatives
Antiarrhythmics	+ +	risk highest for lidocaine
Antidepressants	+ + +	risk increases with sedative effectiveness
Antihypertensives	Depending on substance	centrally effective substances: high risk, α - und β -blocker: medium risk, Diuretics, calcium antagonists, ACE-inhibitors: low risk
Anti-Parkinson drugs	+ + to + + +	risk for anticholinergic substances higher than for dopaminergic ones
Antiphlogistics (non-steroidal)	+ +	risk from paracetamol lowest
Benzodiazepines	+ + +	benzodiazepine withdrawal can also cause delirious visions
Corticosteroids	+ + +	especially for doses > 40 mg prednisone equivalent daily over > 1 week
H ₂ -Antagonists	+ to + +	risk highest for cimetidine
Heart glycosides	+ +	
Neuroleptics	+ + to + + +	risk increases with sedative effectiveness
Theophylline	+ +	

According to [Zeeh and Platt 1994].

Appendix 6. Drugs that can cause orthostatic dysregulation, decrease in blood pressure, nausea and syncope.

Drugs that can cause orthostatic dysregulation, decrease in blood pressure, nausea and syncope	Pathophysiology
Antihypertensives	reduced sensitivity of baroreceptors and reduced peripheral vein tonus
Digitalis glycosides	increased risk of bradycardia due to lower sensitivity of the vagus
Digitalis glycosides plus diuretics	in case of hypokalemia increased heart glycoside sensitivity and arrhythmia
Diuretics	increased loss of fluids due to reduced thirst, sudden decrease in blood pressure through hypovolemia due to reduced sensitivity of the baroreceptors, hypokalemia and in addition arrhythmia

According to [Zeeh and Platt 1994].

Appendix 7. Drugs that increase the risk of falling.

Drugs that increase the risk of falling	Effect	Falling mechanism
Long lasting benzodiazepines such as diazepam, temazepam, flurazepam, chlordiazepoxide (cause body swaying when standing still)	reduction in stance and balance	balance impaired, ability to correct stance impaired
Long lasting benzodiazepines (extended half-time causes cumulation, heightened sensitivity in age), also other sedating drugs	sedation	sedation during the day, slower reaction times, muscle relaxation
Insulin, sulfonyl carbamides (especially in cases of poor compliance, concurrent diseases, exsiccosis warning symptoms can be missing!)	hypoglycemia	impaired consciousness, collapse, syncope
Antihypertensives, psychotropic substances, nitrates (especially increased risk at start of therapy, in case of exsiccosis, in case of concurrent diseases, in case of cerebrovascular insufficiency and long existing hypertension with impaired autoregulation of cerebral blood circulation)	hypotension	orthostatic hypotension, postprandial hypotension
Neuroleptics, antidepressants, diltiazem (?) ("rabbit syndrome": perioral twitches)	parkinson syndrome	bradykinesia, rigor (tremor)
Overdose of aminoglycosides, furosemide, acetylsalicylic acid, quinidine or excessive consumption of alcohol	impaired sense of balance	impairment and dysfunction of the vestibularis
Miotics for glaucoma therapy	impairment of vision	miosis

According to [Zeeh and Platt 1994].



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Pharmacotherapy guidelines for the aged by family doctors for the use of family doctors

Part C Special Pharmacology

Version 1.07, April 18th, 2007, Revision up to December 2008

Guidelines Group Hesse: Pharmacotherapy Guidelines by Family Doctors for Family Doctors

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Key words

guideline – pharmacotherapy – measures that precede drug therapy – diet plan – dementia – acetylcholinesterase – memantine – nootropics – Morbus Parkinson – levodopa – MAO-inhibitors – NMDA-antagonists – dopamine-antagonists

Content

C Special Pharmacology for the aged

- a) **Dementia**
- b) **M. Parkinson**
- c) Osteoporosis
- d) Incontinence of urine
- e) Rectal incontinence
- f) Chronic obstipation

Abstract. Part C of the guideline is preceded by Part B General Pharmacology IJCPT. 2008; 46: 600 – 617. Included in Part C are practical guidelines for improving the therapy of some age-specific diseases and problems commonly encountered in general practice. The article in this issue is dedicated to the therapy of Dementia and M. Parkinson. Further guidelines for the other age specific diseases and problems named above will be published in the following issues of IJCPT. An important feature of these guidelines are the inclusion of Levels of Evidence and of the Strength of Recommendations for the therapy which are shown when reliable studies are available. (For both see levels of evidence at the end of this article.)

C Special Pharmacology for the aged

a) Dementia

1) Definition

[Doody et al. 2001, Scottish Intercollegiate Guidelines Network 1998]

Decline in memory and cognitive abilities leading to an impairment of activities in day-to-day living (ADL) (ICD 10) (American Academy of Neurology 2001). Prevalence: 6% of population over 65, increasing significantly with age [Evidence based therapy guidelines of the German Physicians' Drugs Commission 2002].

Types:

- Dementia of type Alzheimer (DTA) 60%
- Vascular dementia 16%
- DTA + Vascular dementia 8%
- DTA + M. Parkinson 8%

Other causes:

- Dementia syndromes (e.g. hypothyroidism, depression, ARD, lack of vitamin B12 etc.) 8%

It is likely that more than 80 % of dementia cases are of a mixed variety!

Stages of dementia

- Initial stage: signs hardly recognizable, occasionally weight loss [Stewart et al. 2005].

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- Intermediate stage: loss of cognitive abilities become apparent.
- Severe or final stage: in need of permanent care, no longer self-sufficient.

Diagnosis

The “Family Doctor’s Basic geriatric Assessment” (2004) comprises:

- Barthel’s index: functional decline, behavior, competencies of day-to-day living
- Methods for the assessment of risk of falling: timed up-and-go test, chair rising test, Romberg’s tandem stance and walk, and other signs of an increased risk of falling
- Psychometric tests for the diagnosis as well as the progression and therapy assessment of dementia: DemTect [Kessler et al. 2000]; MiniMentalStage Test (MMSt), clock-drawing-test [Folstein et al. 1975] {B}, [Harrison 2005, p. 2581], to distinguish dementia from old-age-related depression: TEDDDD-test (test for the early detection of dementia and delineation from depression) [Ihl and Grass-Kapanke 1999].

Dementia and delirium-like symptoms from other causes (about 20% of cases) and from delirium inducing drugs (see Part B General Pharmacology Appendix 5: Int J Clin Pharmacol Ther. 2008; 46: 615) must be ruled out. Patients with damage to the brain, e.g. a multi-infarction syndrome, apopleptic effects, M. Alzheimer and M. Parkinson are at greater risk [Harrison 1989, Müller et al. 2003, Platt 1997].

Determining the patient’s ability to consent to and take responsibility for medical treatment – timely planning of advance directives of the patient [Rendenbach and Engelhardt 2004] (medical will of the patient (Patiententestament), power of attorney (Vorsorgevollmacht))

At advanced stages of dementia the timely determination of life-sustaining measures, e.g. via a PEG-tube, is necessary.

Currently available data do not suggest that a PEG-tube extends the life expectancy of patients with dementia, reduces complications such as aspiration, or even improves the

patients’ quality of life [Mitchell et al. 1997, Peck et al. 1990] {B}*.

2) Measures that precede drug therapy or support it

Repeated mnemotechnical training

[American Academy of Neurology 2001, Evidence based therapy guidelines of the German Physicians’ Drugs Commission 2002] e.g. a daily game of Memory, strategic games etc. [Bach et al. 1995] {Ib}**.

Dementia-adequate communication

(slow and attentive) based on the patient’s biography (family, work, hobbies), attention, eye-to-eye contact, body contact, hearing aid if needed [Bach et al. 1995] {B} {Iib}.

Information and support for carers

[Haupt et al. 2000, Ostwald et al. 1999] with respect to:

- reducing aggressive behavior, de-escalation
- information about manic delusions: no unnecessary correction of a patient’s mistaken view of reality [Haupt et al. 2000] {B} {Iib}
- easing conflicts in relatives caused by unjustified reproaches from the patient
- training program for activities of day-to-day living (ADL), stretching, anti-vertigo-training, prophylaxis against falling
- self-help groups for caring relatives etc. if needed [Ostwald et al. 1999] {A} {Ib}.

Aim: to keep the patient within his/her familiar surroundings as long as possible. Timely planning and preparation for transfer to a care institution if necessary!

Activating care

- Exercise and occupation instead of mere custody
- Structured days: training of recurring routines such as regular meals and rest breaks ([Schwab et al. 2002] {A} {Ib} e.g.:

*{Capital letters} indicate emphasis levels of recommendation;

**{Roman numerals} indicate strength and type of evidence.

[for both see “Levels of Evidence” at the end of this article].

sleeping hygiene (rest, fresh air, monitoring, late meal))

Arranging the surroundings

- Advance organization (e.g. prophylaxis against falling, prevention against running away [Ford 1996] {B} {IIb}, handles, raised toilet bowl, night bowl if necessary, securing of stairs, dimmed night light, alarm systems)
- Control of excrement
- Bright light in the morning improves sleep at night [NIH Consensus Statement 2000] {B} {IIa}

Regular daily diet plan

- Enough fluids (measured) and calories [Wolf-Klein et al. 1995] {B} {IIa}
- Enough fiber (fresh fruit and vegetables)
- Enough vitamins [Sano et al. 1997]
- Control of dental status
- Swallowing exercises if necessary (with help of a speech therapist)
- Instruction and help to stay self-sufficient
- eating as a delight! [Ford 1996] {B} – Respecting preferences
- Instruction and help to maintain cleanliness and table manners
- Alcohol restrictions

Physical and other therapies

- Occupational therapy [Keough et al. 2000] {B}
- Physiotherapy [Pomeroy 1994] {B} {IIb}
- Musical therapy [Lord and Garner 1993] {A} {Ib}

Behavioral therapy

[Thase et al. 2000] {B} {Ib}

At initial stage, especially if behavior shows signs of depression; reality orientation training (ROT) if necessary [Spector et al. 2000] {B}.

3) Drug therapy

1. Dementia of the Alzheimer type

Acetylcholinesterase inhibitors

Studies show that for mild and medium forms of dementia, AChE-inhibitors cause a significant improvement in memory powers though not a reduction in compulsory institutional care [Birks and Harvey 2004, Birks et al. 2006]. There are indications that even severe forms may be positively affected [Winblad et al. 2006]. How much such averages in studies are clinically relevant in individual cases must be determined through an exact progression assessment by the family doctor and neurologist. One should not hesitate to cease therapy if there are no signs of a clinically relevant effect.

For Acetylcholinesterase inhibitors: as regards dosages, interactions and ADR see Appendix 1 and for

Donepezil [Birks and Harvey 2004] {A},
Rivastigmine [Farlow et al. 2000] {A},
Galantamine [Birks et al. 2006] {A}.

Memantine [Areosa Sastre and Sherriff 2004, Reisberg et al. 2003] {A} {Ib}: In a study on the treatment of a moderate to severe M. Alzheimer [Reisberg et al. 2003] memantine significantly slowed the progression of the disease with few side effects. If and how much the slowing effect is of clinical significance, must be determined in each individual case. As regards dosage, contraindication, UDE etc. see Appendix 3.

Important: Progression assessment through repeated identical psychometric test after 12 weeks as well as control of day-to-day living competencies (ADL), overall clinical impression and questioning of nursing staff. If necessary cessation of therapy in the event of no improvement.

If there is a clear progression, the therapy must be stopped. Therapy to only placate relatives or nursing staff is to be avoided.

According to the Guidelines Group, available studies do not merit recommendation of nootropics: piracetam [Ricker and Grimely Evans 1999] {B} {Ia}, nicergoline [Fiovari and Flicker 2001] {B} {Ia}, dihydroergotamine [Olin and Schneider 2000] {B} {Ia} (see Appendix 3), ginkgo biloba [Birks and Harvey 2004] {B} {Ia} (see Appendix 2).

The value of an anti-dementively-based therapy for application by family doctors cannot yet be fully evaluated.

Therapy of behavioral disturbances: (restlessness and aggression, disturbed day-night rhythm)

Neuroleptics

- Classical, highly potent: haloperidol [Lanctot et al. 1998] {A} {Ia}
- Classical, less potent: melperone, promethazine, pipamperone, perazine, sulpiride
- More recent, atypical neuroleptics among others: risperidone, olanzapine, quetiapine [Tariot et al. 2000], aripiprazole [De Deyn et al. 2003] zotepine [Rainer et al. 2004], ziprasidone

Note:

There is as yet no long-term experience with the more recent group of active substances. An increased risk of apoplexia in older patients has been shown for risperidone and olanzapine. The Guidelines Group recommends the preferred use of classical neuroleptics. More recent substances are reserve drugs for patients who do not respond to the tried (classical) neuroleptics [Liebermann et al. 2005].

Benzodiazepines

Appropriate only in individual cases, medium long-term substances (e.g. oxazepam) recommended.

In cases of depressive symptoms

- Citalopram [Nyth and Gottfries 1990] {A} {Ib}, paroxetine, sertraline hydrochloride [Lyketsos et al. 2000] {A} {Ib}, fluvoxamine [Olfsson et al. 1992] {A} {Ib}
- Tri- and tetracyclic antidepressants (esp. in cases of sleeping disorders)

2. Vascular dementia

Causal treatment of underlying diseases (e.g. hypertonia, cardiac arrhythmia, diabetes mellitus, stenosis of the arteria carotis [Forette et al. 1998] {A}, [Hassing et al. 2004] {III}).

According to the Guidelines Group, the available studies do not recommend the following drugs (see Appendices 1 – 3):

- Ginkgo biloba [Birks and Harvey 2004] {B} {Ia}
- “Substances that improve blood circulation” e.g. pentoxifylline [Sha and Callahan 2003] {Ia}
- Donepezil [Mendez et al. 1999]
- Rivastigmine [Moretti et al. 2001] {A} {Ib}
- Galantamine [Maelicke 2001]

3. Mixed forms of dementia

Once treatment options for the underlying diseases (e.g. M. Parkinson, multi-infarction dementia) have been exhausted

- Symptomatic therapy

4) References

a) Dementia

For levels of evidence see Part A b

American Academy of Neurology. AAN Guideline Summary for Point of Care: Detection, Diagnosis and Management of Dementia. *Neurology.* 2001; 56: 1151-1166 s. www. aan.com

Areosa Sastre A, Sherriff F. Memantine for dementia (Cochrane Review). In: *The Cochrane Library, Issue 1, Chichester, UK: John Wiley and Sons, Ltd.; 2004* {meta analysis Ia}.

Bach D et al. Reactivating occupational therapy: a method to improve cognitive performance in geriatric patients. *Age Ageing.* 1995; 24: 222-226 {Ib}.

Birks J, Grimley Evans J. Ginkgo biloba for cognitive impairment and dementia. *The Cochrane Library Issue 1, Chichester Uk: John Wiley and Sons; 2004a* {meta analysis Ia}.

Birks JS, Harvey R. Donepezil for dementia due to Alzheimer's disease. *The Cochrane Library Issue 1, Chichester Uk: John Wiley & Sons; 2004b* {meta analysis Ia}.

Birks JS et al. Cholinesterase inhibitors in Alzheimer's Disease, *Cochrane Review in: The Cochrane Library Issue 1, Oxford Update Software; 2006.*

De Deyn et al. Aripiprazole treatment for psychosis in patients with Alzheimer's disease. Poster presented at: Annual Meeting of the American Association for Geriatric Psychiatry; March 1 – 4, 2003, Honolulu; HI.

Doody RS, Stevens JC et al. Practice parameter: Management of dementia (an evidence-based review): *Neurology.* 2001; 56: 1154-1166 (eR).

Evidenzbasierte Therapieleitlinien der Arzneimittelkommission der Deutschen Ärzteschaft. LL Demenz. Dt Ärzteverlag. 2002; S 141.

- Farlow M, Anand R, Messina J Jr, Hartman R, Veach J. A 52-week study of the efficacy of rivastigmine in patients with mild to moderately severe Alzheimer's disease. *Eur Neurol* 2000; 44: 236-241. Zs.A 575.
- Fioravanti M, Flicker L. Efficacy of nicergoline in dementia and other age associated forms of cognitive impairment. *Cochrane Review*, (CD003159); 2001 {meta analysis Ia}.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method of grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975; 12: 189-198 {III}.
- Ford G. Putting feeding back into the hands of patients. *J Psychosocial Nurse Ment Health Serv*. 1996; 34: 35-39.
- Forette F, Seux ML, Staessen JA et al. Prevention of dementia in randomised double-blind placebo-controlled systolic hypertension in Europe (SYST-EUR) trial. *Lancet*. 1998; 352: 1347-1351 {Ib}.
- Harrison's Principles of Internal Medicine*. 16th Edition German edition. Dielert M, Suttrop N, Zeitz M (eds). ABW Wissenschaftsverlag, Band 2: Differentialdiagnose der Demenz pp 2579, Minimental Status Test p. 2581, 2005.
- Hassing LB, Hofner SM, Nilsson SE et al. Comorbid type 2 diabetes mellitus and hypertension exacerbates cognitive decline: evidence from a longitudinal study. *Age Ageing*. 2004; 33: 355-361 {III}.
- Haupt M, Karger A, Janner M. Improvement of agitation and anxiety in demented patients after psychoeducative group intervention with their caregivers. *Int J Geriatr Psychiatry*. 2000; 15: 1125-1129 {IIb}.
- Hausärztlich-Geriatisches Basisassessment*. Institut für Hausärztliche Fortbildung im Deutschen Hausärzteverband (IhF Köln); 2004, Berlin.
- Ihl R, Grass-Kapanke B. TFDD – Test zur Früherkennung der Demenz mit Depressionsabgrenzung. Schwabe, Karlsruhe; 1999 (s. Book on Demands, 2003: ISBN 3-89811-880-0).
- Scottish Intercollegiate Guidelines Network*. Interventions in the management of behavioural and psychological aspects of dementia; 1998 (eLL).
- Keough J et al. Treating dementia: the complementing team approach of occupational therapy and psychology. *J Psychol*. 2000; 134: 375-391.
- Kessler J, Calabrese P, Kalbe E, Berger F. Dem Tect: A new screening method to support diagnosis of dementia. *Psycho*. 2000; 26: 343 - 347.
- Lancot KL et al. Efficacy and safety of neuroleptics in behavioural disorders associated with dementia. *J Clin Psych*. 1998; 59: 550-561 {Ia}.
- Liebermann JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO et al. for the *Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators*. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*. 2005; 353: 1209-1223.
- Lord TR, Garner JE. Effects of music on Alzheimer patients. *Perceptual & Motor Skills*. 1993; 76: 451-455 {Ib}.
- Lyketsos CG, Sheppard JME, Steele CD et al. Randomized, placebo-controlled, double-blind clinical trial of Sertraline in the treatment of depression complicating Alzheimer's disease: Initial results from the depression in Alzheimer's Disease Study. *Am J Psychiatry*. 2000; 157: 1686-1689 {Ib}.
- Maelicke A. The pharmacological rationale for treating vascular dementia with galantamine. *Int J Clin Prac*. 2001; 120 (Suppl): 24-28.
- Mendez MF, Younesi FL, Perryman KM. Use of donepezil for vascular dementia: preliminary clinical experience. *J Neuropsychiatry Clin Neurosci*. 1999; 11: 268-270.
- Mitchell SL, Kieley DK, Lipsitz LA. The risk factors and impact on survival of feeding tube placement in nursing home residents with severe cognitive impairment. *Arch Intern Med*. 1997; 157: 327-332.
- Moretti R, Torre P et al. Rivastigmine in subcortical vascular dementia: a comparison trial on efficacy and tolerability for 12 months follow-up. *Eur J Neurol*. 2001; 8: 361-362 {Ib}.
- Müller U, Wolf H, Kiefer M, Gertz HJ. Nationale und internationale Demenzleitlinien im Vergleich. *Fortschr Neurol Psychiatr*. 2003; 71: S285-S295.
- NIH Consensus Statement*. Osteoporosis Prevention. Diagnosis and Therapy. 2000; 17: 27-29 (eR).
- Nyth AL, Gottfries CG. The clinical efficacy of citralopram in treatment of emotional disturbances in dementia disorders. A Nordic multicentre study. *Br J Psychiatry*. 1990; 157: 894-901 {Ib}.
- Olfsson K et al. Fluvoxamine in the treatment of demented elderly patients: A double-blind, placebo-controlled study. *Acta Psychiatr Scand*. 1992; 85: 453-456 {Ib}.
- Olin J, Schneider L. Hydergine for dementia. *Cochrane Review*. 1998; Database of systematic reviews 2000; Issue 3; Art. No. C0 000 359. DOI: 10.1002/146 1858. {meta analysis Ia}.
- Ostwald SK et al. Reducing caregiver burden: a randomized psychoeducational intervention for caregivers of persons with dementia. *Gerontologist*. 1999; 39: 299-309 {Ib}.
- Ouslander J et al. Assessment, treatment and management of urinary incontinence in the nursing home. Newbury Park, CA: Sage Publications; 1993. p. 131-159.
- Peck A, Cohen CE, Mulvihill MN. Long-term enteral feeding of aged demented nursing home patients. *J Am Geriatr Soc*. 1990; 38: 1195-1198.
- Platt D (Hrsg.). *Altersmedizin*. Stuttgart, New York: Schattauer Verlag; 1997. p. 284-293.
- Pomeroy VM. Immobility and severe dementia: When is physiotherapy treatment appropriate? *Clinical Rehabilitation*. 1994; 8: 226-232 {IIb}.
- Rainer MK, Mucke HA et al. Zotepine for behavioral and psychological symptoms in dementia: an open-label study. *CNS Drugs*. 2004; 18: 49-55 Zs. A 4083.
- Reisberg B, Doody R, Stöfflen A, Schmitt F, Möbius HJ for the *Memantine Study Group*. Memantine in Moderate-to-Severe Alzheimer's Disease. *N Engl J Med*. 2003; 348: 1333-1341.
- Rendenbach U, Engelhardt J. Patientenvollmacht zur Regelung ärztlicher Maßnahmen. *Notfall- u. Hausarztmedizin* 2004; 30: B105-107.
- Ricker L, Grimley Evans J. Piracetam for dementia or cognitive impairment. *Cochrane Review*. In: The Cochrane Library, Issue 4; 1999 {meta analysis Ia}.
- Sano M, Ernesto C, Thomas RG, Klauber MR et al. A controlled trial of selegiline, alpha-tocopherol, or both as a treatment of Alzheimer's disease. The Alzheimer's Disease Cooperative Study. *N Engl J Med*. 1997; 336: 1216-1222 {A}.
- Schwab M, Marx C, Zanger UM, Eichelbaum M, Fischer-Bosch M. Pharmakogenetik der Zytochrom-P-450-Enzyme: Bedeutung für Wirkungen und Nebenwirkungen von Medikamenten. *Dtsch Arztebl*. 2002; 99: A497-504.

- Sha MC, Callahan CM.* The efficacy of pentoxifylline in the treatment of vascular dementia: A systematic review. *Alzheimer Disease and Associated Disorders.* 2003; *17*: 46-54 {Ia}.
- Spector A, Davies S, Woods B, Orrell M.* Reality orientation for dementia: a systematic review of the evidence of effectiveness from randomized controlled trials. *Gerontologist.* 2000; *40*: 206-212 {Ia}.
- Stewart R, Masaki K, Xue QL et al.* A 32-year prospective study of change in body weight and incident dementia: the Honolulu-Asia Aging Study. *Archives of Neurology.* 2005; *62*: 55-50.
- Tariot PN, Salzman C, Yeung PP et al.* Long-term use of quetiapine in elderly patients with psychotic disorders. *Clin Ther.* 2000; *22*: 1068-1084 Zs. A 1435.
- Thase ME et al.* Treatment of men with major depression: a comparison of sequential cohorts treated with either cognitive-behavioral therapy or newer generation antidepressants. *J Clin Psychiatry.* 2000; *61*: 466-472 {Ib}.
- Winblad B, Kilander L, Eriksson S et al.* Donepezil in patients with severe Alzheimer's disease: double blind, parallel-group, placebo-controlled study. *The Lancet.* 2006; *367*: 1057-1065.
- Wolf-Klein GP, Silverstone FA, Lansey SC et al.* Energy requirements in Alzheimer's disease patients. *Nutrition.* 1995; *11*: 264-268.

5) Appendices

Appendix 1. Acetylcholinesterase inhibitors (AChEI).

- Donepezil
- Rivastigmine
- Galantamine

Indication: light to medium cases of dementia of the Alzheimer type. **Evaluation for family doctors:** success of AChE inhibitor therapy to be documented through progression controls: clinical picture, questioning of relatives, initial psychometric test (MMSt (Mini-Mental-State) or DemTect Test). Minimum time for therapy: 12 weeks. If under therapy the repeat test shows a deterioration of more than 4 points: cease therapy! If therapy is continued: repeat tests in intervals of 3 months.

Daily dose	Donepezil 5 – 10 mg; Rivastigmine 3 – 12 mg; Galantamine 8 – 24 mg
ADR	Nausea, vomiting, diarrhea, bradycardia, dysfunction of the electrical conduction pathways of the heart, problems with bladder emptying, rarely states of excitement, aggressive behavior
Interactions	Substances for the treatment of glaucoma, antihistamines, β -blockers, erythromycin, carbamazepine, phenytoin sodium – beware abuse of alcohol
Contraindications	Relative CI: dysfunction of the supraventricular induction pathways, convulsions, asthma, COPD
Special characteristics	Slow dosage build-up; even after therapy interruption

ADR = adverse drug reactions. For comprehensive information cf. the specialized literature.

Appendix 2. Ginkgo biloba (extract of ginkgo leaves).

Indication: light to medium cases of dementia (DTA). **Evaluation for family doctors:** studies do not merit recommendation.

Dosage	120 – 240 mg daily dose [Birks and Grimley Evans 2004]
ADR	Minor side effects: stomach upset, headache, allergic skin reaction, increased bleeding tendency
Interactions	Higher effectiveness of thrombocyte aggregation inhibitors and anticoagulants
Contraindications	Bleeding diathesis
Special characteristics	Attention: alcoholic solution!

ADR = adverse drug reactions. For comprehensive information cf. the specialized literature.

Appendix 2. Memantine.

Indication: moderate to severe cases of dementia of the Alzheimer type.

Dosage	5 – 20 mg
ADR	Vertigo, headache, constipation, drowsiness
Interactions	Dopaminergics, hydrochlorothiazide, dantrolene sodium, baclofen
Contraindications	Epilepsy, severe kidney disease, severe states of confusion, pregnancy, breast-feeding Relative CI: combination with amantadine

Appendix 3. Nootropics.

- Piracetam
- Nicergoline
- Dihydroergotoxine

Indication: light to medium cases of dementia. **Evaluation for family doctors:** studies do not merit recommendation.

Dosage	Daily dose	ADR and interactions {Ia}
Piracetam [Flicker et al 2004]	Oral: 3 times 800 – 1200 mg max: 5000 mg per day Intravenous: 3 – 12 g per day slowly	ADR: psychomotoric restlessness, aggression, sexual stimulation, gastrointestinal complaints, weight gain, changes in blood pressure, lower convulsion threshold IA: higher effectiveness of other CNS-stimulating substances, including thyroid hormones, possible
Dihydroergotoxine [Olin and Schneider 1998]	4 – 8 mg	ADR: vertigo, lower blood pressure, walking insecurity, nausea, vomiting, “blocked” nose, ergotism IA: drugs to lower blood or influence blood coagulation
Nicergoline [Fioravanti and Flicker 2001]	10 – 30 mg	
Contraindications	Renal insufficiency (creatinine > 3 mg/dl) Relative CI: pregnancy, breast-feeding	
Special characteristics	Reduced dose in cases of renal insufficiency: Creatinine 1.25 – 1.7 mg/dl: 50%, creatinine 1.7 – 3 mg/dl: 75%	

ADR = adverse drug reactions; IA = interaction. For comprehensive information cf. the specialized literature.

b) Morbus Parkinson

1) General

Prevalence

- 100 – 200 cases per 100,000 in the general population [Ricker and Grimley Evans 1999]
- 1,800 cases per 100,000 in the population over the age of 65 [Oertel et al. 2003]
- M. Parkinson with dementia only in 10 – 20% of cases (figures in the literature vary from 10 – 80%) [Biggins et al. 1992]

Types

- Idiopathic Parkinson’s syndrome (primary PS, ca. 75%)
- Symptomatic Parkinson’s syndrome (secondary PS)
- Atypical Parkinson’s syndrome (neurodegenerative PS)

2) Measures that precede or support drug therapy

Timely diagnosis of the heterogeneous disease picture by a neurologist at first suspicion

Physiotherapy (permanent therapy)

- Exercise [Deane et al. 2004a] {A}* {Ia}**
- Ergotherapy, logopedia [Deane et al. 2004b]

Psycho-social therapy

- Nursing care if applicable
- Caveat: danger of mistaking M. Parkinson for dementia
- Treat frequently occurring depressions
- Foster communication [Shimbo et al. 2004]
- Inform relatives, friends, neighbors etc.
- Discuss future therapy (e.g. PEG)

The immobile, paralyzed, “bricked in” patient is not primarily demented!

- Maintain independence and reduce need for nursing care

*{Capital letters} indicate emphasis levels of recommendation; [for both see “Levels of Evidence” at the end of this article].

**{Roman numerals} indicate strength and type of evidence.

for both see “Levels of Evidence” at the end of this article.

Table 1. Basic therapy of the akinetic rigid type and its equivalents.

	Young patient (under 70 years)	Older patient (over 70 years)
Start therapy with	Dopamine agonists	Levodopa
Supplement with	<ul style="list-style-type: none"> – Levodopa – COMT inhibitors – Amantadine [Crosby et al. 2004] {A}, anticholinergic [Katzenschlager et al. 2004] {A} {Ia}, selegiline 	<ul style="list-style-type: none"> – COMT inhibitors – Dopamine agonists – Selegiline
Avoid	<ul style="list-style-type: none"> – Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness)) 	<ul style="list-style-type: none"> – Amantadine (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998]) – Anticholinergics (side effects: cognitive dysfunction, UDE on the bladder, bowel and cardiovascular system)
In case of tremor start with	<ul style="list-style-type: none"> – Anticholinergics – Budipine – Propanolol – Clozapine (81) (take special care) 	<ul style="list-style-type: none"> – Budipine – Propanolol – Clozapine (take special care) – Primidone
Adverse drug reactions (ADR)	Treatment	
Nausea, vomiting, orthostatic hypotension (side effects)	Reduce dose and distribute over the day; if needed, domperidone	
Psychoses [Bayas et al. 2001] (eR):	Atypical neuroleptics (clozapine [Factor et al. 1997, Rabey et al. 1995], olanzapine [Wolters et al. 1996], quetiapine, risperidone)	
Depressions:	SSRI (possibly sertraline hydrochloride [Hauser and Zesiewicz 1997] {B}, tricyclic antidepressants)	
Sleeping disorders:	Sedative antidepressants, short-term benzodiazepines, zolpidem, zopiclone	

Take care with doses for supplementary therapies to treat side effects.
Modified according to Schneider and Richling [2004].

- Avoid secondary diseases (contractures, aspiration, broncho-pulmonary infections, falls)
- Avoid wrong diet and exsiccosis (if necessary, protein-reduced diet because of competition from L-dopa and the neutral aminoacids of the carrier system [Kempster and Wahlqvist 1994])

Recognizing possible symptoms

- Problems with swallowing, PEG?
- Orthostatic hypotension [Pfeiffer 1992]
- Bladder dysfunction (incontinence, residual urine build-up)
- Consequences of an anticholinergic therapy of PS
- Dysmotility of the digestive tract; resorption dysfunction, constipation
- Sialorrhea
- Danger of aspiration
- Infections of the respiratory tract

3) Drug therapy

Start of therapy

A drug therapy is indicated in cases of subjective and/or objective restrictions in day-to-day living; this depends strongly on (i) the quality of life as experienced by the patient and (ii) the objective demands the patient has to meet (Table 1).

For initial dosage setting, controls to adjust therapy and in cases of therapeutic failure a neurologist must be consulted.

Initial dosage setting (cf. Appendix 1 – 3)

Trial therapy with a so-called Nacom-test (testing reaction to L-dopa)

- L-dopa [Parkinson Study Group 2000] {A}
- Dopamine receptor agonists [Parkinson Study Group 2000] {A}
- Monoamine oxidase (MAO) inhibitors [Ives et al. 2004]

- Anticholinergics
- Catechol-O-methyl transferase (COMT) inhibitors
- N-methyl-d-aspartate (NMDA) receptor antagonists
- as well as combinations

Progress control is important, if necessary therapy adjustment by a neurologist. Newly appearing symptoms may be drug side effects!

If drug therapy does not improve an intensifying “on-off-phenomenon”, the current recommendation is: brain pacemaker, stereotactic operation (experimental stadium, no long-term results available yet, risky intervention!)

Avoid inducing a secondary Parkinson’s syndrome by using:

- Classical neuroleptics
- Anti-emetics (e.g. metoclopramide (MCP))
- Reserpine
- Lithium

4) References

b) Morbus Parkinson

- Bayas A, Kornhuber J, Naumann M.* Atypische Neuroleptika und neue Antidepressiva in der Therapie neurologischer Erkrankungen. *Akt Neurol.* 2001; 28: 62-73 (eR).
- Biggins CA et al.* A controlled, longitudinal study of dementia in Parkinson’s disease. *J Neurol Neurosurg Psychiatr.* 1992; 55: 566-571
- Crosby N, Deane KHO, Clarke CE.* Amantadine in Parkinson’s disease (Cochrane Review). The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd.; 2004.
- Deane KHO, Jones D, Playford ED, Ben-Shlomo Y, Clarke CE.* Physiotherapy versus placebo or no intervention in Parkinson’s disease (Cochrane Review). The Cochrane Library, Issue 2. Chichester, UK: John Wiley & Sons, Ltd.; 2004a {Ia}.
- Deane KHO, Whurr R, Playford ED, Ben-Shlomo Y, Clarke CE.* Speech and language therapy versus placebo or no intervention for dysarthria in Parkinson’s disease (Cochrane Review). The Cochrane Library, Issue 2. Chichester, UK: John Wiley & Sons, Ltd.; 2004b.
- Factor SA, Friedman JH.* The emerging role of clozapine in the treatment of movement disorders. *Mov Disord.* 1997; 12: 483-496 (eR).
- Factor SA, Molho ES, Brown DL.* Acute delirium after withdrawal of amantadine in Parkinson’s disease. *Neurology.* 1998; 50: 1456-1458.
- Friedman JH, Koller W et al.* BCLOZ: a double-blind, crossover trial comparing clozapine with benztropine for treatment in Parkinson’s disease (Abstract). *Neurology.* 1996; 46 (Suppl): A 476.
- Hauser RA, Zesiewicz TA.* Sertraline for the treatment of depression in Parkinson’s disease. *Movement disorders: official journal of the Movement Disorder Society* 1997; 12: 756-759 {IIb}.
- Ives NJ, Stowe RL, Marro J, Counsell C, Macleod A, Clarke CE, Gray R, Wheatley K.* Monoamine oxidase type B inhibitors in early Parkinson’s disease: meta-analysis of 17 randomised trials involving 3525 patients. *BMJ.* 2004; 329: 593.
- Katzenschlager R, Sampaio C, Costa J, Lees A.* Anticholinergics for symptomatic management of Parkinson’s disease (Cochrane Review). The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd.; 2004 {Ia}.
- Kempster PA, Wahlqvist ML.* Dietary factors in the management of Parkinson’s disease. *Nutr Rev.* 1994; 52: 51-58 (eR).
- Oertel WH, Deuschl G et al.* Parkinson-Syndrom. AWMF-Leitlinienregister, Nr. 030/010, Entwicklungsstufe 2; Leitlinien für Diagnostik und Therapie in der Neurologie; 2. überarbeitete und erweiterte Auflage 2003; ISBN 3131324120.
- Parkinson Study Group.* Pramipexole versus levodopa as initial treatment for Parkinson’s disease. *JAMA.* 2000; 284: 1931-1938.
- Pfeiffer R.* Optimization of levodopa therapy. *Neurology.* 1992; 42: 39-43.
- Rabey JM, Trevas TA, Orlov E et al.* Low dose clozapine in the treatment of levodopa-induced mental disturbances in Parkinson’s disease. *Neurology* 1995; 45: 432-434.
- Ricker L, Grimley Evans J.* Piracetam for dementia or cognitive impairment. Cochrane Review. The Cochrane Library, Issue 4. Chichester, UK: John Wiley & Sons, Ltd.; 1999 {meta analysis Ia}.
- Schneider D, Richling F.* Checkliste Arzneimittel A-Z; 2. Auflage. Stuttgart: Thieme-Verlag; 2004.
- Shimbo T, Goto M, Morimoto T, Hira K, Takemura M, Matsui K, Yoshida A, Fukui T.* Association between patient education and health-related quality of life in patients with Parkinson’s disease. *Quality of Life Research.* 2004; 13: 81-89.
- Tandberg E, Larsen JP et al.* Risk factors for depression in Parkinson disease. *Arch Neurol* 1997; 54: 625-630 {III}.
- US Department of Health and Human Services. Agency for Health Care Policy and Research.* Acute pain management – operative and medical procedures and trauma. Rockville, MD: The Agency; 1993. Clinical practice guideline No 1. AHCPR Publication No 92-0023:107.
- Wolters EC, Jansen ENH et al.* Olanzapine in the treatment of dopaminomimetic psychosis in patients with Parkinson’s disease. *Neurology* 1996; 47: 1085-1087.

5) Appendices

Appendix 1. Evaluation of selected substances for family doctors.

Substances to treat M.Parkinson: Levodopa and MAO inhibitors.

Levodopa with benserazide/carbidopa	
Effective mechanism	
Dosage	Initial dose: 100 – 200 mg in 3 individual doses, maximum dose: 800 – 1,000 mg/d Dosage to be increased every 3 – 5 days
Advice	Not to be taken with meals! Rapidly soluble forms to treat acute cases of akinesia
ADR	Nausea, vomiting, constipation, vertigo, hypotension, tachycardia, intense sweating, hallucination
Contraindications	Psychoses, decompensated cardiac, renal, endocrine and hepatic diseases, angle closure glaucoma, age lower than 25, lack of contraception, pregnancy, breast feeding
Special characteristics	Not in cases of secondary, drug-induced M. Parkinson

MAO inhibitor selegiline	
Effective mechanism	Monoamine oxidase inhibition, thus higher dopamine levels
Dosage	Initial dose: 2.5 mg/d in the first week maximum dose: 10 mg/d Dosage increased to 5 mg in 1 – 2 individual doses
Advice	In combination with L-dopa
ADR	Restlessness, sleeping disorders, dyskinesia, dyspnea, vertigo, fatigue, headache
Contraindications	Hypertension, renal or hepatic dysfunction, benign prostatic hyperplasia (BPH), angle closure glaucoma
Special characteristics	Not to be taken in the evening!

For comprehensive information cf. the specialized literature.

Appendix 2. NMDA antagonists: amantadine, budipine.

Amantadine	
Effective mechanism	N-methyl-d-aspartate receptor antagonist, thus higher noradrenaline and dopamine levels in the synaptic cleft, antagonistic effect at the glutamate receptor
Dosage	Initial dose: 2 – 3 × 50 – 100 mg/d maximum dose: 500 – 600 mg/d
Advice	Avoid combination with anticholinergics! Sulfate derivative more easily digested than hydrochloride derivative
ADR	Nausea, sleeping disorders, vertigo, dry mouth, cardiac arrhythmia, peripheric edema
Contraindications	Psychoses, acute states of confusion, BPH, angle closure glaucoma, pregnancy
Special characteristics	Intravenous in cases of akinetic crisis (1 – 3(– 6) × 200 mg i.v.)

Budipine	
Effective mechanism	N-methyl-d-aspartate receptor antagonist, thus higher noradrenaline and dopamine levels in the synaptic cleft, antagonistic effect at the glutamate receptor
Dosage	Initial dose: 3 × 10 mg/d maximum dose: 60 – 80 mg/d Dosage increased weekly by 10 – 20 mg/d
Advice	Under strict ECG control (Long-QT-syndrome)
ADR	Nightmares, sensory dysfunction, headaches, sight defects, lack of appetite, nausea, vomiting
Contraindications	Myasthenia, severe cardiac insufficiency, bradycardia, AV block II and III, hypokalemia
Special characteristics	Formal undertaking to be given to drug company, written informed consent

For comprehensive information cf. the specialized literature.

Appendix 3. Dopamine agonists.

Bromocriptine, cabergoline, dihydroergocryptine, lisuride.

This evaluation relates only to the following substances: pergolide mesylate, pramipexole, ropinirole, apomorphine.

Pergolide mesylate	
Effective mechanism	Peripheral and central dopamine receptor agonist, equalization/balancing of "on/off"-oscillations.
Dosage	Initial dose: 3×0.05 mg/d Dosage increased to 0.1 – 0.15 mg every 3 days over 12 days maximum dose: 5 mg/d
Advice	Individual dosage according to clinical symptoms, not to plan!
ARD	Dyskinesia, hallucinations, states of confusion, nausea and vomiting, constipation, diarrhea
Contraindications	Severe liver and kidney disease, pregnancy and breast feeding, restrictions in case of cardiac arrhythmia.
Special characteristics	Monotherapy at early stages and for younger patients, combination with L-dopa at all stages; reduction of side effects through use of e.g. domperidone

Pramipexole	
Effective mechanism	Peripheric and central dopamine receptor agonist, equalization/balancing of "on/off"-oscillations.
Dosage	Initial dose: 0.088 mg/d for 1 week Dosage increased to 3×0.18 mg for 1 week, then 3×0.35 mg maximum dose: 3.15 mg/d
Advice	Individual dosage according to clinical symptoms, not to plan! Beware: sudden falling asleep! Driving ban!
ADR	Dyskinesia, hallucinations, states of confusion, nausea and vomiting, constipation, diarrhea
Contraindications	Severe liver and kidney disease, pregnancy and breast feeding
Special characteristics	Combination with L-dopa at advanced stages; reduction of side effects through use of e.g. domperidone; if discontinued, taper off!

Ropinirole	
Effective mechanism	Peripheric and central dopamine receptor agonist, equalization/balancing of "on/off"-oscillations.
Dosage	Initial dose: 3×0.25 mg/d for 1 week Dosage increased to 3×0.5 mg for 1 week, then 3×0.75 mg and so on maximum dose: 24 mg/d
Advice	Individual dosage according to clinical symptoms, not to plan! Beware: sudden falling asleep! Driving ban!
ADR	Dyskinesia, hallucinations, states of confusion, nausea and vomiting, constipation, diarrhea
Contraindications	Severe kidney insufficiency, pregnancy and breast feeding
Special characteristics	As monotherapy at all stages or in combination with L-dopa; reduction of side effects through use of e.g. domperidone

Apomorphine	
Effective mechanism	Reserve substance in cases of akinetic crisis
Dosage	Initial dose: 2.5 mg subcutaneous, then 4 – 10 mg/h as subcutaneous infusion maximum dose: ---
Advice	Individual dosage according to clinical symptoms, not to plan!
ADR	Severe nausea and vomiting, epileptic convulsions
Contraindications	Infants, toddlers, cardiovascular insufficiency, poisoning with substances that depress breathing, old patients, unconsciousness
Special characteristics	Use only as last resort! Antidote: naloxone. In case of cardiovascular failure: norfenefrine

For comprehensive information cf. the specialized literature.

Levels of evidence.

The schema of levels shown below (evidence types and levels of emphasis of recommendations) is based on that of the US Agency for Health Care Policy and Research (AHCPR, US Department of Health and Human Service, 1993 [Schwabe et al. 2004]) as quoted in the guideline of the Scottish Intercollegiate Guideline Network. The Guidelines indicate the levels of evidence in brackets (e.g. {A}).

Strength and type of evidence	Emphasis levels of recommendation
Ia Evidence based on meta-analyses of randomized controlled studies	A Based on levels Ia and Ib of evidence type, i.e. the recommendation is based on publications of good quality that contain at least one randomized controlled study.
Ib Evidence based on at least one randomized controlled study	
Ila Evidence based on at least one well-designed controlled study without randomization	B Based on levels Ila, Ilb and III of evidence type, i.e. the recommendation is based on well-designed, non-randomized clinical studies.
Ilb Evidence based on one well-designed, quasi-experimental study	
III Evidence based on one well-designed, non-experimental descriptive study (e.g. comparative studies, correlation studies, case-control-studies)	
IV Evidence based on the reports or opinions of expert circles, consensus conferences and/or clinical experience of recognized experts	C Based on level IV, i.e. the recommendation is the result of reports and opinions from expert circles, consensus conferences and/or clinical experience of recognized experts. Level C indicates a lack of directly applicable clinical studies of good quality.



Pharmacotherapy guidelines for the aged by family doctors for the use of family doctors

Part C Special Pharmacology

Version 1.07, April 18th, 2007, Revision up to December 2008

Version 1.00 of Hausärztliche Leitlinie Geriatrie Teil 2 December 2008 was considered

Guidelines Group Hesse: Pharmacotherapy Guidelines
by Family Doctors for Family Doctors

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Key words

osteoporosis – bone density measurement – bisphosphonates – SERM selective estrogen receptor modulator – drugs that increase the risk of falling – incontinence of urine – use of catheters – anticholinergics – α -1 receptor inhibitors – 5α -reductase inhibitors

Content

C Special Pharmacology for the aged

- a) Dementia
- b) M. Parkinson
- c) Osteoporosis
- d) Incontinence of urine
- e) Rectal incontinence
- f) Chronic obstipation

Abstract. The part “Special pharmacology of the aged” of this guideline contains recommendations for typical conditions in the family doctors practice: in the January issue 2009 dementia and Morbus Parkinson, in this issue osteoporosis and urinary incontinence and in the next issue rectal incontinence and obstipation.

This issue of the IJCPT contains the third part of the *Pharmacotherapy guidelines for the aged by family doctors for family doctors. Part 3: Osteoporosis and urinary incontinence.* Osteoporosis is a systematic disease characterized by low bone mass and declining bone structure. Exercise, adequate diet, nicotine abstinence as well as reduction of alcohol consumption may counteract the progression of the disease. Osteoporosis manifests in bone fractures with minimal trauma. Attention must be given to the risk of falling, e.g., by avoiding drugs that increase the risk of falling: e.g., psychotropic agents, analgesic drugs and antiarrhythmic agents. Specific osteoporosis medication e.g. calcium, vitamin D, bisphosphonates and SERM (selective estrogen

receptor modulators) is evaluated by family doctors according to indication, dosage, contraindications, long-term therapy and nature of any fracture. Duration of therapy is at least 3 – max. 5 years followed by reassessment of indication. There are 3 types of urine incontinence (urge-, stress-, and overflow-incontinence). Another standardization of urinary incontinence follows dysfunctions of the pelvic floor: detrusor muscle-dependent, due to sphincter spasm, prostate gland dependent. Urge incontinence with a dysfunction of the detrusor muscle is the most common type. Mixed types are frequent. Non-drug measures (e.g. pelvic muscle training, bladder training, toilet training are first choice treatments. Drug therapy (estrogen, imipramine) are without proven effect.

C Special Pharmacology of the Aged

c) Osteoporosis

1) General

Definition

Osteoporosis is a systemic disease of the skeletal frame characterized by low bone mass and declining bone tissue structure resulting in an increased brittleness of the bones. **It manifests in fractures without adequate trauma** [Therapy Recommendations from the Drugs Commission of the German Chamber of Physicians 2003, WHO Study Group 1994].

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(As regards epidemiological data cf. DVO Guidelines “Osteoporosis in older persons” [DVO 2006a,b])

Risk factors for osteoporosis

Uncontrollable factors

- Age
- Female sex (post-menopausal)
- Familial risk [Soroko et al. 1994] {B}
- Exposure to estrogen < 30 years (early menopause) [Kruse 1994] {B}

Diseases

- Long existing diabetes [Schwartz et al. 2001] {B} (III)
- Renal insufficiency
- Hyperthyroidism (iatrogenic)
- Morbus Cushing
- Hyperparathyroidism
- Extended amenorrheic periods > 1 year

Drugs

- Steroids [Lukert and Raisz 1990] (eR)
- Antiepileptics
- Heparin
- Phenprocoumon
- Thyroid hormones (under substitution the TSH value should be above 0.3 µU/ml)

Lifestyle [DVO 2006]

- Immobilization
- Malnourishment (BMI < 20 kg/m²)

- Inadequate diet, malabsorption syndrome
- Alcohol and nicotine abuse [Cummings et al. 1995, Stewart et al. 2000], abuse of cola drinks

Since osteoporosis is associated with an increased risk of bone fractures, falls should be avoided as far as possible:

Increased risk of falling (cf Appendix 4)

- As a side effect of many drugs, e.g. psychopharmaceuticals, analgesics, antiarrhythmic agents [Leipzig et al. 1999a,b] {B} (sR) (cf. Part B Appendix 7. IJCPT. 2008; 46: 616)
- Polypharmacotherapy (> 4 prescribed drugs).
- Impairment of vision and hearing
- Weakness (chair rising test)
- Insecure gait (impairment of balance and posture and coordination)
- Cognitive disorders or dementia [Kanis et al. 1999] {B}

Diagnosis

- Medical history, drug anamnesis, clinical assessment, in particular decline in body height > 4 cm or > 2 cm over the last year or very low body weight (BMI < 20 kg/m²) [DVO 2006b].
- X-ray in cases of suspected bone fracture and/or for differential diagnosis [DVO 2006b]
- Basic laboratory tests (Ca, P, AP, γ-GT, creatinine, ESR, blood count, proteins electrophoresis TSH) to check for secondary forms of osteoporosis
- Bone density measurement (DXA = Dual Energy X-ray Absorptiometry). This is the only validated method of diagnosis of osteoporosis. Table 1 is designed to assist with the decision on the use of this diagnostic measure. If women or men in the various age groups show the results mentioned, the estimated 10-year fracture risk is 20% or above

2) Measures that precede drug therapy

Exercise

- Top priority: regular exercise
- Muscle toning, balance training

Table 1. Indication for use of specific diagnostics. According to DVO [2006b].

Women	Men	Diagnosis of the following non-relievable indicators
50 – 60 years	60 – 70 years	One or more fractures of vertebrae {A} One or more peripheral fractures (to be decided individually) {C}
60 – 70 years	70 – 80 years	One or more fractures of vertebrae {A} One or more peripheral fractures {A} Fracture of the femur neck in one parent {B} Underweight (BMI < 20 kg/ m ²) {A} Nicotine consumption {A} Multiple falls {A} Immobility {A for proximal fractures of the femur neck in women}
> 70 years	> 80 years	All patients, if therapeutic consequences are intended/possible {A}

Measuring the bone density is not necessary, if X-rays show more than one fracture of the vertebrae typical for osteoporosis.

- Most important goal: fostering patient's self-mobility

Advice on diet and lifestyle

[DVO 2006a,b, Therapy recommendations of the drugs commission of the German Chamber of Physicians 2003]

- Adequate and calcium-rich diet (body mass index > 20 kg/m²)
- Adequate exposure to sun light (at least 30 minutes per day), if necessary supplementation with 400 – 1,200 IU vitamin D – depending on suspected deficit [DVO 2006b],
- Nicotine abstention [DVO 2006a, Steele et al. 1997]
- Alcohol consumption < 30 g/day [DVO 2006a, Steele et al. 1997]

Prophylaxis against falling

[Giada et al. 1998] {A} {Ia}

- Remove stumbling traps
- Improve coordination: balance exercises,
- Height toilet seat
- Walking aids, holding grips
- Night lights, glasses, hearing aid
- If necessary, “falling prophylaxis training” at home, led by a competent trainer [Ricker et al. 1999] {A} {Ib}
- If necessary, hip protectors with adequate training for high risk patients

Evaluating indication for and dosage of drugs that are risk factors for osteoporosis

- Glucocorticoids, phenprocoumon (marcumar), heparin, carbamazepine, thyroid hormones, antiepileptics, high-ceiling diuretics

3) Drug therapy

Determining the indication for a specific drug therapy

Drug therapy in osteoporosis is indicated for the following results:

- Manifest osteoporosis (osteoporosis and fracture without adequate trauma)
- High risk for osteoporotic fractures in cases of prolonged cortisone therapy with at least 7.5 mg equivalent of prednisolone

- Osteoporosis with a fracture risk \geq 30% within the next 10 years (cf Table 2, this situation is indicated as “yes” in Table 2), [DVO 2006a]

Basic medication (cf. Appendix 1)

[DVO 2006a]

- Calcium plus vitamin D: calcium: 500 – 1,500 mg/d, vitamin D: depending on the suspected deficit 400 – 1,200 IU/d (in cases of renal insufficiency other vitamin D preparations may be indicated (e.g. alfacalcidol). Drug therapy with calcium and vitamin D alone is insufficient – supplement of specific medication is necessary.

Pain relief medication

(according to [DVO 2006a])

- Drug therapy for pain relief (WHO scheme), mobilization a.s.a.p. {B}, stabilization with orthosis if necessary.

Specific medication with recommendation level A

(according to [DVO 2006a])

Women:

Biphosphanates are first choice:

- **Alendronate sodium** {A}, risedronate sodium {A}, ibandronate sodium {A} (cf. Appendix 2)

Second choice are the following drugs:

- Raloxifene {A} (cf. Appendix 3)
- Strontium ranelate {A} (cf. Appendix 3)
- Teriparatide (only in cases of manifest osteoporosis in postmenopausal women) {A}
- Estrogens (cf. Appendix 3)

N.B.: a decrease in the number of vertebral fractures has been shown for all drugs {A}.

A decrease in the number of peripheral fractures has been shown for alendronate sodium {A}, risedronate sodium {A}, strontium ranelate {A} and teriparatide {B}.

Men:

- Alendronate sodium, risedronate sodium

Duration of the osteoporosis therapy

At least 3 – max. 5 years, followed by re-evaluation and reassessment of the indication according to the risk situation!

Table 2. Recommendation for a specific drug therapy^{1,2} According to DVO [2006b].

Without vertebrae fracture at age (years)	T-value (applicable only to DXA-values)					
	Men	-2.0 to -2.5	-2.5 to -3.0	-3.0 to -3.5	-3.5 to -4.0	< -4.0
Women	Men	-2.0 to -2.5	-2.5 to -3.0	-3.0 to -3.5	-3.5 to -4.0	< -4.0
50 – 60	60 – 70	No	No	No	No	Yes
60 – 65	70 – 75	No	No	No	Yes	Yes
65 – 70	75 – 80	No	No	Yes	Yes	Yes
70 – 75	80 – 85	No	Yes	Yes	Yes	Yes
> 75	> 85	Yes	Yes	Yes	Yes	Yes
With vertebrae fracture		Yes – swift therapy important because of acute high risk as result of vertebral fracture				

Adaptation of the indication according to individual factors (cf. [DVO 2006a, 2006b]):

¹If one or more of the following risk factors are present (peripheral fracture, fracture of the femur neck in one parent, nicotine consumption, multiple falls, immobility) an adjustment of the therapy to a T value 1.0 lower is recommended.

Example: for a 63-year-old woman with a T value of -2.8 a drug therapy is not indicated; due to an additional risk (e.g. smoking) the therapeutic decision is based on a T value of -3.8 (i.e. 1.0 lower). For this T value a specific osteoporosis therapy is indicated.

²Individual factors (e.g. multimorbidity, short life expectancy) should also limit therapy decisions.

Phytoestrogens

No proven effects have been shown in osteoporosis therapy [Anderson et al. 1998] {B}!

Therapy evaluation

For therapy evaluation osteodensitometry is necessary only in exceptional cases (e.g. cortisone therapy).

An evaluation of therapy needs to address the following questions:

- Is drug compliance evident? Can the necessary modalities of the drug therapy be reliably observed and followed?
- Does the drug therapy show any side effects?
- Has mobility increased?
- Has the diet been changed?
- Have there been recurrent pains?
- Has the patient had a fall?

Ending of therapy

According to current knowledge, the therapy, especially in the case of women with osteoporosis of the hip area, can be finalized after 5 years. In a study that compared 5- and 10-year therapies with alendronate sodium, a lower number of vertebral fractures could be

shown for the longer therapy period; however, that was true only for a high NNT of 172/year [Black et al. 2006].

4) References

- Anderson JJB, Garner SC. Phytoestrogens and bone. *Baillier's Clin Endocrinol Metab.* 1998; 12: 543-557.
- Black DM et al. Effects of continuing or stopping Alendronat after 5 years of treatment. *JAMA.* 2006; 296: 2927-2938.
- Cauley JA, Norton L, Lippmann MR et al. Continued breast cancer risk reduction in postmenopausal women treated with raloxifene: 4-year results from the MORE trial. *Breast Cancer Res Treatment.* 2001; 65: 125-134.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52.705 women with breast cancer and 108.411 women without breast cancer. *Lancet.* 1997; 350: 1047-1059 (III).
- Cummings SR, Nevitt MC, Browner WS et al. Risk factors for hip fracture in white women. *N Engl J Med* 1995; 332: 767-773 (IIb).
- DVO (Dachverband der deutschsprachigen wissenschaftlichen Gesellschaften für Osteologie (DVO) e.V. (Umbrella organization of the German language scientific societies for osteology 2006 (Hrsg)). Evidenzbasierte Konsensus-Leitlinie zur Osteoporose. Prophylaxe, Diagnostik und Therapie bei Frauen ab der Menopause, bei Männern ab dem 60. Lebensjahr. (Evidence-based consensus guideline for osteoporosis – prophylaxis – diagnostic – therapy) Langfassung 2006a. Stuttgart: Schattauer; 2006. http://www.luthershaus-essen.de/osteo/leitlinien-dvo/PDFs/Osteoporose-Leitlinie_Langfassung.pdf; am 10.1.2007.

- DVO (Dachverband der deutschsprachigen wissenschaftlichen Gesellschaften für Osteologie (DVO) e.V.* (Umbrella organization of the German language scientific societies for osteology). DVO-Leitlinie Osteoporose nach der Menopause und im Alter (DVO Guideline Osteoporosis after menopause and in the aged). Kurzfassung der DVO-Leitlinie 2006 zur Prophylaxe, Diagnostik und Therapie bei Frauen ab der Menopause, bei Männern ab dem 60. Lebensjahr. 2006b (http://www.lutherhaus-essen.de/osteo/leitlinien-dvo/PDFs/Osteoporose-Leitlinie_Kurzfassung.pdf); 10.1.2007.
- Giada F, Bertaglia E, De Piccoli B, Franceschi M, Sartori F, Raviele A, Pascotto P.* Cardiovascular adaptations to endurance training and detraining in young and older athletes. *Int J Cardiol* 1998; 65: 149-155 (IIa).
- Hausärztlich-Geriatisches Basisassessment.* Institut für Hausärztliche Fortbildung im Deutschen Hausärzteverband (IhF Köln); 2004, Berlin.
- Hulley S, Grady D et al.* Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. *JAMA*. 1998; 280: 605-613 (Ib).
- Kanis J, Johnell O et al.* Risk factors for hip fracture in men from Southern Europe: the MEDOS study. *Osteopor Int*. 1999; 9: 45-54.
- Kruse W.* Medikamente in der Geriatrie: Probleme bei der Arzneimittelanwendung und Lösungsmöglichkeiten. Expertise im Auftrag des Bundesministeriums für Familien und Senioren. Stuttgart: Kohlhammer; 1994.
- Leipzig RM, Cumming RG et al.* Drugs and falls in older people. A systematic review and meta-analysis: I. Psychotropic Drugs. *J Am Geriatr Soc*. 1999a; 47: 30-39.
- Leipzig RM, Cumming RG et al.* Drugs and falls in older people. A systematic review and meta-analysis: II. Cardiac and analgesic drugs. *J Am Geriatr Soc*. 1999b; 47: 40-50.
- Lukert BP, Raisz LG.* Glucocorticoid-induced osteoporosis. Pathogenesis and management. *Ann Intern Med*. 1990; 112: 352-364 (eR).
- Ricker L, Grimley Evans J.* Piracetam for dementia or cognitive impairment. Cochrane Review. In: The Cochrane Library, Issue 4; 1999 (Metaanalyse Ia).
- Runge M.* Gehstörungen, Stürze, Hüftfrakturen. Darmstadt: Steinkopff; 1998.
- Schwabe U, Rabe T.* Sexualhormone. In: Schwabe U, Paffrath D (eds). *Arzneiverordnungs-Report 2003*. Heidelberg: Springer; 2004. p. 776-798.
- Schwartz AV, Sellmeyer DE, Ensrud KE et al.* Older women with diabetes have an increased risk of fracture: A prospective study. *J Clin Endocrinol Metab*. 2001; 86: 32-38 (III).
- Soroko S, Barrett-Connor E et al.* Family history of osteoporosis and bone mineral density at the axial skeleton: the Rancho Bernardo Study. *J Bone Miner Res*. 1994; 9: 761-769.
- Steele CM, Greenwood C, Ens I, Robertson C, Siedman-Carlson R.* Mealtime difficulties in a home for the aged: not just dysphagia. *Dysphagia*. 1997; 12: 45-50.
- Stewart A, Calder LD et al.* Prevalence of hip fracture risk factors in women aged 70 years and over. *Q J Med*. 2000; 93: 677-680.
- Therapy Recommendations from the drugs Commission of the German Chamber of Physicians (Therapieempfehlungen der Arzneimittelkommission der Deutschen Ärzteschaft).* Osteoporose. 1. Auflage; 2003.
- WHO Study Group.* Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva: WHO; 1994. Technical Report Series 843.

5) Appendices

Appendix 1. Evaluation for family doctors of selected effective substances.

Osteoporosis preparations containing minerals and vitamin D.

- Ca carbonate and vitamin D3
- Active vitamin D3 metabolites: calcitriol and alfacalcidol
- **Indication:** prevention and basic therapy
- **Evaluation for family doctors:** for the prevention and basic therapy of manifest osteoporosis. Current active vitamin D3 metabolites such as e.g. calcitriol offer no advantages except in cases of renal insufficiency and renal osteopathy.

Dosage	Prevention/therapy: 500 – 1,500 mg/d calcium +400 – 1,200 IU/d vit D
Contraindications calcium	Hypercalcemia and hypercalciuria (immobility), kidney stones, nephrocalcinosis, significant renal insufficiency, primary hyperparathyroidism
Contraindications vitamin D3	Hypervitaminosis D (beware of pregnancy), myeloma, bone metastases
Interactions	Increased toxicity of digitalis, hypercalcemia in conjunction with thiazide, 2 – 3 hours before or after taking iron preparations, tetracyclines, fluorides or bisphosphonates
ADR	Hypercalciuria, hypercalcemia if dosage too high, hypophosphatemia, nausea, obstipation

For comprehensive information cf. the professional literature. ADR = adverse drug reactions.

Appendix 2. Osteoporosis preparations containing bisphosphonates.

Bisphosphonates

- **Alendronate sodium**
- Etidronate disodium
- Ibandronate sodium
- Risedronate sodium
- **Indication:** therapy of manifest osteoporosis, bone metastases, iatrogenic osteoporosis
- **Evaluation for family doctors:** effect: inhibition of bone resorption, therapy of choice in cases of manifest osteoporosis and high fracture risk.
- Overview of studies cf. DVO-guidelines [DVO 2006a].

Effective substance	Dosage	Contraindications
Alendronate sodium	70 mg once per week orally or 10 mg/d orally	Delayed emptying of the esophagus (beware: strictures, achalasia, incapacity to stand or sit upright for at least 30 min), hypocalcemia, severe renal insufficiency, pregnancy
Risedronate sodium	Permanent therapy: 5 mg/d orally or 35 mg once per week	
Etidronate disodium	Cyclical 3-months-therapy: 400 mg/d orally for 14 days followed by: 500 mg calcium/d for 76 days followed by repetition of cycle	Osteomalacia, severe renal insufficiency, pregnancy
Ibandronate sodium	150 mg once a month (1 pill) or every 3 months intravenously	hypocalcemia

Interactions	Restricted resorption because of other medication, antacids and calcium (cf. there) or simultaneous intake of food, amplification of gastrointestinal side effects by NSAIDs
ADR	Gastrointestinal complaints, esophagus and stomach ulcerations, pain in muscles, bones and joints, lowering of the serum concentration of calcium
Special considerations	Bisphosphonates are strongly acidic substances and should be taken in the morning at least 30 minutes before breakfast while standing up or sitting down with a large glass of tap water . Do not lie down afterwards!

For comprehensive information cf. the professional literature; ADR = adverse drug reaction.

Appendix 3. Other osteoporosis preparations.

SERM (Selective estrogen receptor modulator)

- **Raloxifene**
- **Indication:** treatment and prevention of osteoporosis in postmenopausal women
- **Evaluation for family doctors:** antiresorptive therapy of manifest postmenopausal osteoporosis with lowering of the re-fracture rate of the spine but no lowering of the rate of femure neck fractures (different to bisphosphonates) shown in studies (studies too small, no significance of results) (Effect visible only after therapy of three years [Cauley et al. 2001]).
- **Beware:** risk of thromboembolism triples (quoted according to [Schwabe et al. 2004])

Dosage	60 mg/d orally (continually)
Contraindications	Thromboembolism in patient history, restricted liver function, severe renal insufficiency, unclear bleeding of the uterus, endometriotic carcinoma, child-bearing capacity
Interactions	Oral anti-coagulants: reduction of prothrombin time, colestyramine impedes absorption
ADR	Thromboembolism, hot flushes, flu-like symptoms, calf muscle cramps, peripheral oedema, increased body weight, gastrointestinal complaints
Special considerations	Estrogen agonistic effect on bones and cholesterol metabolism, increased risk of venous thromboembolistic events, estrogen antagonistic on breast and uterus tissue

For comprehensive information cf. the professional literature.

Estrogens

Evaluation for family doctors (according to [DVO 2006b]).

As a rule, use only if vasomotoric complaints are the main indication. A deliberative process of consultation with the female patient is important because of the increased risk of: thromboembolism [Hulley et al. 1998] {A} (Ib), carcinoma mamma [Collaborative Group on Hormonal Factors in Breast Cancer 1997] {B} (III), endometrium, ovaries, liver), coronary heart disease, heart attack, stroke, weight increase, hypertension, depression

Strontium ranelate

Indication: treatment of postmenopausal osteoporosis to reduce the risk of spine and hip fractures.

Dosage: 2 g/d orally (2 hours after a meal).

Contraindications: severe renal insufficiency. Care is to be taken when used in women with an increased risk or a history of venous thromboembolism.

Interactions: food, milk, milk products.

Appendix 4. Risk of falling.

Procedure for the assessment of the risk of falling

- Timed up and go
- Chair rising test
- Tandem stance / tandem gait

General signs for increased risk of falling

- Clinically recognizable walking dysfunction
- More than two falls or a fall with severe injuries during the last year

Both criteria are not very sensitive, give a late indication and do not permit a component analysis

Qualitative walking dysfunction: difficult to quantify for therapy assessment

Number of falls: not usable for therapy assessment

The five independent factors of a risk of falling

1. Muscular weakness when rising
Test: chair rising test
2. Dysfunction of lateral balance/posture control
Test: tandem stance/tandem gait
3. Severe visual degradation
4. a. Multi-medication (> 4 prescribed substances) – not a causal, but a general disease indicator!
b. Fall-inducing drugs are causal and dosage dependent: neuroleptics, anti-depressants (tricyclics, SSRI), benzodiazepines, anti-convulsives
5. Severe cognitive dysfunctions, cave: risky behavior
(result of significant prospective studies with multivariate analyses [Runge 1998])

Timed up and go test: Patient rises from a chair with armrests, walks three meters, turns, walks back to the chair and sits down again. The time taken for this exercise is to be measured in seconds (e.g. 10.4 sec.). Patient performs exercise at his/her own usual pace, if necessary with walking aids. Use of arm rests to prop oneself when rising is permitted. **Increased risk of falling if time taken exceeds 10 – 12 seconds.**

Chair rising test: patient rises from chair without use of his/her arms five times in as little time as possible. Time taken is measured in seconds (e.g. 9.3 sec.). **Increased risk of falling if time taken exceeds 10 seconds.**

Romberg (parallel feet) / Tandem stance (feet behind each other): risk of falling is increased if less than 10 seconds.

[Hausärztlich geriatrisches Basismanagement; Institut für Hausärztliche Fortbildung in Köln (Institute for Family Doctors CME in Cologne) Berlin 2004].

d) Urinary Incontinence

1) General

Definition

Urine incontinence is defined (International Continence Society) as a state of demonstrable, involuntary loss of urine. This can lead to hygienic as well as social problems. More than 30% of all men and women over the age of 65 suffer from urinary incontinence; for those over 80 years the figure is 40%, for people in aged care up to 80%, for severely demented patients up to 97% ([Füsgen et al. 2000] – with further epidemiological data).

Women are significantly more often affected than men. Incontinence becomes more severe with age and growing multimorbidity [Molander 1993, Mühlberg 2004]; with 50 – 60% of cases dysfunction of the detrusor muscle, usually in connection with motor urge incontinence, is the most common type [Füsgen and Melchior 1997, Füsgen et al. 2000].

Types according to dysfunction

- Detrusor muscle-dependent incontinence (dysfunctional: hypotonic or hypertonic)
- Incontinence due to sphincter spasm (neurogenic bladder dysfunction)

- Prostate gland-dependent incontinence (BPH)
- Mixed types (mostly in women)

Causal analysis through step-by-step diagnosis by the family doctor

- Clinical investigation
- Urine status, elimination of infections (frequent) if necessary
- Sonography of the urinary tract
- (Sonographic) measurement of urine remaining in the bladder
- Stress incontinence is easily diagnosed from the medical history [Nikolaus 1998]
- In cases of unclear results, if conservative therapy shows no signs of improvement and in cases of overflow incontinence: special urological diagnosis of the detrusor muscle and sphincter function (exclusion of stones and tumors, of malformations, of infections etc.) as well as of mixed types, determination whether an operation is necessary

2) Therapeutic measures

- Talk about the problem and free it from being a taboo
- Comprehensive anamnesis, micturition protocol (document time and amount of urine)

Table 1. Types and causes. According to Nikolaus [1998].

Types	Symptoms	Common cause
Urge incontinence	Uncontrollable loss of urine (mostly larger, sometimes varying amounts) due to inability to delay micturition when urge to urinate is felt	Detrusor muscle hyperactivity isolated or in conjunction with one or more of the following causes: local, urogenital variations such as cystitis, urethritis, tumor, stones, diverticles, early subvesical obstruction; reduced contractility of the bladder, diseases of the central nervous system such as apoplexy, demential syndrome, Parkinson syndrome, spinal cord defects
Stress incontinence	Involuntary loss of urine (mostly smaller amounts) occurring when intra-abdominal pressure increases for short periods of time (e.g. through coughing, sneezing, laughing) (mostly in women)	Weak pelvis muscles causing increased mobility of bladder base and proximal urethra weakness of the bladder neck or the sphincter (intrinsic in conjunction with previous traumata, e.g. operations)
Overflow incontinence	Involuntary loss of urine (frequent, smaller amounts) occurring in conjunction with a dilated bladder	Anatomical obstruction through prostate gland, stricture or large cystocele a contractile bladder in conjunction with diabetes and spinal cord lesion

Mixed types are common: thus, e.g., 20% of women with stress incontinence also suffer from motor urge incontinence – especially in cases of bladder infection in later years. The rate of urge incontinence increases to over 60% in older patients [Abbatt et al. 1996, Füsgen and Melchior 1997].

- Exclusion of medication-induced problems (frequent)

Note: urinary incontinence is often a reason for patients to reduce their fluid intake: hence, increased risk of infections, **in case of cystitis permanent bladder irritation with incontinence!**

Information about aids and/or therapy options depending on the amount of urine loss: lining or anatomically formed pads during the day, appropriately sized nappies at night.

Points of advice for the use of catheters

Single use catheter in case of acute obstruction or for intermittent use of catheters.

In case of chronic obstruction, if amount of urine remaining in the bladder > 150 ml: **permanent catheter** if an operation is not indicated.

Permanent catheter

Selection:

- Transurethral: charriere 16 or more with balloon
- Suprapubic: charriere 10 polyurethane catheter, without balloon
- Catheter length: ca. 40 cm for men, ca. 20 – 25 cm for women
- Tiemann catheters (for men) have a curved tip
- Nelaton catheters (for women) are straight
- Foley (balloon) catheters of the varieties mentioned above hold the catheter in the bladder through the balloon

Changing the catheter: depending on bacteria levels about every 2 – 4 (– 6) weeks. In case of incrustation use silicone- or hydrogel-coated catheters or latex catheters; if necessary acidify urine using methionine, lots of fluids.

A permanent suprapubic catheter makes care and hygiene easier. Initial introduction through punctation of the full bladder under local anesthesia, no lubricant, sonographic check of positioning. Change needed depending on bacteria levels or about every 4 weeks (without lubricant).

For chronic release of urine using a permanent catheter, a closed drip system with release clamps should be used in order to avoid infections of the upper tract. Change of drip

system only depending on bacteria levels, or else about every 2 weeks change of container.

Mobile patients should use a container with release clamp attached to the leg during the day.

In case of incrustation use permanent silicone catheter (expensive!), acidification of urine with methionine and increased intake of fluids may help, **avoid flushing catheter** if possible (risk of distributing germs, not very effective) [Harrison 2005].

If possible, always keep urine release system closed and sterile!!

When released from hospital, permanent catheters (that may have been introduced to assist with care), if no longer necessary should be removed. Before **weaning off**, slowly and carefully stretch bladder capacity through temporary disconnection of catheter.

An operation is the measure of last resort for overflow incontinence.

Intermittent use of catheters if necessary in case of atony without obstruction for bladder relief. Assessment of drug effects, if necessary change medication, micturition training.

Introduction of catheter must be sterile [Harrison 2005]

Practical advice for the introduction of a catheter: push back clitoral prepuce, briefly disinfect skin, use sterile lubricant, better without the added chlorhexidine, lidocaine, if necessary sterile NaCl; in cases of pain: Instillagel® or others (contain chlorhexidine and lidocaine).

3) Stress incontinence

Measures that precede or support drug therapy

- Breathing technique
- Pelvic muscle training for women [Berghmans et al. 1998], and also for men, e.g., after prostate gland operation, with exercises for self-training
- Control training success through micturition protocols
- Fluid intake and toilet training: no drinking before exertion, but regular sufficient intake of fluids afterwards, regular visits to the toilet, consult nursing staff
- Supply of aids (see above)

Operation as last resort

Drug therapy

No drug therapy but bladder training [Berghmans et al. 1998]. Use of estrogens for women is to be avoided, because it is risky and without proven effects [Fantl et al. 1994, 1997, Zullo et al. 1998]. No positive effects have been shown for imipramine [Fantl et al. 1996].

4) Urge incontinence

Measures that precede or support drug therapy

- Eliminate infection
- Toilet training (see above)
- Increase intake of fluids [Colling et al. 1994]
- Protocol of micturition to control timely micturition
- Pelvic floor exercise

In most cases of urge incontinence release of urine is contraindicated [Füsgen et al. 1997]; if necessary diagnosis by specialist.

In case of obstruction : ensure release of urine.

Drug Therapy

In case that toilet training or bladder training are insufficient, additional medication depending on detrusor and sphincter function [Burgio et al. 1998].

Because urge incontinence is often due to mixed causes, and if there is no specialist diagnosis from a urologist (cystoscopy, cytomometry, micturition urography, urine culture etc.) or such a diagnosis is not possible, the family doctor must choose a drug therapy on a trial basis by increasing or blocking detrusor function (after an infection has been ruled out).

Tonus decrease through

- Anticholinergics, e.g. oxybutin [Arzneitelegramm 1999, Burgio et al. 1998], tolterodine, trospium [Abrams et al. 1998, Drahi et al. 2003, Madersbacher et al. 1995]

ADR: anticholinergic syndrome in up to 2/3 of patients.

Specific ADR: cardiac side effects, tachycardia, headaches, dry mouth, visual dysfunction, vertigo, obstipation, incomplete draining of bladder, residual urine, cognitive dysfunctions [Abbat et al. 1996, Arzneitelegramm 1996, Drahi et al. 2003]

Cave: avoid anticholinergics in case of glaucoma, prostatahyperplasia, stricture of uretra

5) Overflow Incontinence

Measures that precede or support drug therapy

If necessary diagnosis by a specialist.

In case of obstruction ensure release of urine, if necessary using catheter.

In case of **weak detrusor** additional micturition training, if necessary longer-term intermittent draining of bladder, no drugs.

Beware: Detrusor atonia often is an ADR of e.g. anticholinergics, antidepressives, neuroleptics, muscle relaxants, calcium antagonists, opioids and anti-parkinson-agents.

Drug therapy

In case of incontinence due to sphincter spasms, neurogenic incomplete bladder emptying

- α -receptor inhibitor, e.g. phenoxybenzamine

ADR: poor tolerability, sedation, drug interactions, loss of ability to ejaculate, reflex tachycardia, orthostatic decrease in blood pressure, cardiovascular risks, urine incontinence [Arzneitelegramm 1999].

6) Prostate related incontinence and mixed forms

Measures that precede drug therapy

If necessary diagnosis by a specialist to determine or confirm indication for surgery.

Drug therapy

Prostate related incontinence

- α -1 receptor inhibitors [Arzneitelegramm 1999]: alfuzosin, doxazosin mesylate, tamsulosin, terazosin

Active principle: relaxation of detrusor

ADR: introduce dosage slowly, falling blood pressure, angina pectoris, reflex tachycardia, fatigue, urine incontinence

Cave: Liver and/or kidney failure, **caution:** operation of cataract: important: pre-operative stop of the drug is insufficient

- 5- α reductase inhibitors: finasteride (reserve drug), dutasteride

Active principle: reduction of volume of prostate

ADR: gynecomastia, dysfunction of ejaculation, loss of libido

Look out for individually varying effects [Arzneitelegramm 1999]!

Combination of substances is not sensible

Mixed forms of incontinence:

Therapy depending on effect (cf. therapy for urge incontinence) and/or the result of specialist diagnosis, if necessary surgery.

Herbal and homeopathic agents:

Are occasionally and subjectively regarded as helpful. No evidence of improvements available. Large placebo effect of adequate empathy.

7) References

- Abbutt J et al.* Promoting physical activity with older people. Health Education Authority, Archive for life. London: Hamilton; 1996. p. 1-27 (Guideline not evidence based).
- Abbutt J et al.* Promoting physical activity with older people. Health Education Authority. 1-27. Hamilton House Mabledon Place, London; 1997.
- Abrams P, Freeman R, Anderström C, Mattiasson A.* Tolterodine, a new antimuscarinic agent: as effective but better tolerated than oxybutynin in patients with an overactive bladder. *Brit J Urol.* 1998; *81*: 801-810.
- Arzneitelegramm.* Berlin; 1996. p. 90.
- Arzneitelegramm.* Berlin; 1999. p. 6.
- Berghmans LCM, Hendriks HJ, Bi K, Hay-Smith EJ et al.* Conservative treatment of stress urinary incontinence in women: a systematic review of randomized clinical trials. *Br J Urol.* 1998; *82*: 181-191.
- Burgio KL, Locher JL, Goode PS, Hardin JM, McDowell BJ et al.* Behavioral vs. drug treatment for urge urinary incontinence in older women: a randomised, controlled trial. *J Am Med Ass.* 1998; *280*: 1995-2000.
- Colling H, Owen TR, McCready MR.* Urine volumes and voiding patterns among incontinent nursing home residents. Residents at highest risk for dehydration are often most difficult to track. *Geriatric Nursing.* 1994; *15*: 188-192.
- Dieltl M, Suttorp N, Zeitz M.* *Harrisons Innere Medizin.* Vol. 2. German Edition. Berlin: ABW-Wissenschaftsverlag; 2005. p. 1148.
- Drahi E, Chouillet AM et al.* Prise en charge de l'incontinence urinaire de la femme en medecine generale. Anaes/Service des recommandations professionnelles. May 2003 (eR).
- Fantl JA, Cardozo L, McClish DK.* Estrogen therapy in the management of urinary incontinence in postmenopausal women. A meta-analysis. First report of the Hormon and Urogenital Therapy Committee. *Obstet Gynecol.* 1994; *83*: 12-18.
- Fantl JA et al.* Urinary incontinence in adults: acute and chronic management. Rockville, MD: AHCPR; 1996, Clinical Practice Guideline No. 2. 1996 Update AHCPR Publication No 96 – 0682.
- Fantl JA, Bump RC, Robinson D, McClish DK, Wyman JF.* Efficacy of estrogen supplementation in the treatment of urinary incontinence. *Obstet Gynecol.* 1997; *88*: 745-749.
- Füsgen I, Melchior H.* *Inkontinenzmanual.* New York: Springer; 1997.
- Füsgen I et al.* *Der ältere Patient.* München – Jena: Urban und Fischer; 2000.
- Madersbacher H et al.* Trosipium chloride versus oxybutynin: a randomised, double-blind, multicentre trial in the treatment of detrusor hyper-reflexia. *Brit J Urol.* 1995; *75*: 452-456.
- Molander U.* Urinary incontinence and related symptoms in elderly women. *Acta Obstet Gynec Scand.* 1993; *158 (Suppl.):* 1-22.
- Mühlberg W.* Häufige Arzneimittel-Nebenwirkungen und Interaktionen im Alter [http://www.alter-nativen.ch/pdf/infos/arnzeimitt_interakt2_04.pdf], Autorreferat vom 4. Münsterlinger Symposium zur Alterspsychologie September 2004.
- Nikolaus T.* Harninkontinenz – in der Hausarztpraxis häufig verdrängt. *Fortschr Med.* 1998; *116*: 21-26.
- Schweizerisches Medizinisches Forum Nr.* 27, 20.
- Zullo MA, Olivia C, Falconi G, Paparella P, Mancuso S.* Efficacia delle terapia estrogenica sull'incontinenza urinaria. *Studio metanalitico: Min Ginecol* 1998; *50*: 199-205.



Pharmacotherapy guidelines for the aged by family doctors for the use of family doctors

Part C Special Pharmacology

e) Fecal incontinence f) Chronic constipation

Version 1.07, April 18th, 2007, Revision up to December 2008

Version 1.00, December 2008 "Hausärztliche Leitlinie Geriatrie" was considered

Guidelines Group Hesse: Pharmacotherapy Guidelines by Family Doctors for Family Doctors

F.W. Bergert, D. Conrad, K. Ehrenthal, J. Feßler, J. Gross, K. Gundermann, B. Kluthe, W. Lang Heinrich, A. Liesenfeld, P.G. Loew, E. Luther, R. Pchalek, J. Seffrin, A. Sterzing, H.-J. Wolfring and U. Zimmermann

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non-drug therapy – drug
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exchangers –
stool-forming laxatives –
laxatives with osmotic
effect – stimulating laxa-
tives

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- d) Renal elimination
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Int J Clin Pharmacol Ther. 2008; 46 (12): 600-616.

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- a) Dementia
- b) M. Parkinson

Int J Clin Pharmacol Ther. 2009; 47 (1): 11-22.

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Int J Clin Pharmacol Ther. 2009; 47 (3): 141-152.

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Forthcoming

Chapter

e) Fecal incontinence f) Chronic constipation

Abstract. This article contains the 4th part of the Pharmacotherapy Guidelines for the Aged by Family Doctors for Family Doctors. Part 4 is dedicated to fecal incontinence and chronic constipation. The diagnostic categories are divided according to severity and dysfunction of bowel and pelvic floor, sphincter and neural control. Therapy is also outlined. Importance is given to patient history, in particular the use and abuse of drugs

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that stimulate peristalsis and promote constipation. Therapy in the elderly is guided by the maxim: use the most conservative therapy possible, where stool training has considerable importance. Drug therapy based on symptoms can only be recommended when non-drug measures continue to fail. In patients with fecal incontinence: 1) opiates (which reduce colonic motility), 2) loperamide (which has the capacity to dilate the rectum) and 3) anion exchangers which have the capacity to prevent cholonic diarrhea. In patients with chronic obstipation: 1) stool-forming laxatives (ensure intake of sufficient amount of fluids) 2) laxatives with an osmotic effect and 3) stimulating laxatives (beware abuse, do not use in cases of acute abdomen).

C Special Pharmacotherapy for the Aged

e) Fecal incontinence

Definition

Fecal incontinence (incontinentia alvi) is the inability to withhold bowel contents knowingly and willingly and to induce bowel clearing at the intended time knowingly and willingly [Gregor 2005]. Fecal incontinence is defined as repeated uncontrolled loss of stool over a period of at least 1 month in an individual with a developmental age of at least 4 years [Gregor 2005].

Prevalence in the general population is 0.5 – 1.5%, in patients older than 65 up to 5%, in very old patients with an age-related psychiatric disorder up to 30% [Füsgen et al. 2000], and in patients kept in institutions for care of the aged 47% [Gregor 2005].

Categorization according to severity of fecal incontinence [Pehl et al. 2000] (cf. Appendix 1):

- First degree: inability to withhold soft viscous stool
- Second degree: additional inability to withhold wind
- Third degree: inability to withhold formed stools

Instances of stool smear (loss of very small amounts of stool) do not fall under this definition (cf. Appendix 1)

Measures that precede or support drug therapy

Discuss the problem with the patient and free it from being taboo!

Etiology

[Chatoor et al. 2007, Füsgen et al. 2000]:

- Patient history, if necessary stool diary including history of drug use. Abuse of laxatives? Substances that stimulate peristalsis? Abuse of caffeine, alcohol, nicotine etc.? Indigestible foods (e.g. lactose intolerance)? Inadequate diet? Rule out overflow incontinence in cases of fecal impaction, rule out diarrhea
- Comprehensive body examination
- **Important: digital rectal examination**, if necessary proctoscopy and rectoscopy/ colonoscopy (Perianal changes? Fecaliths? Fistulae? Rectal bleeding? Tumor?)

Consider **psychiatric causes** (anxieties, psychoses, neurotic behavior) only when organic causes have been ruled out.

Check for **diet-related incontinence**: get patient to keep a diet diary to record eating habits (food too cold or consumed too fast?), check for indigestible foods (e.g. alcohol, fat, lactose).

Check **drug anamnesis** with special attention to drugs with laxative effect.

Rule out other diseases such as irritable colon, Morbus Crohn, colitis ulcerosa, perianal fistulae or abscesses, tumors, postpartum damage, deformities and sphincter insufficiency, if necessary consult gastroenterologist or proctologist.

Before beginning therapy, become clear whether the patient suffers from diarrhea or fecal incontinence.

Therapeutic options:

- In older patients use the most conservative therapy possible [Füsgen et al. 2000]: Treat basic diseases first (e.g. diabetes, proctocolitis, hemorrhoids, fistulae etc.)
- In cases with **overflow incontinence**: 40 – 60% of patients older than 65 complain of chronic constipation! [Füsgen et al. 2000]: remove obstruction (subileus, tumor, constipation, fecaliths) with overflow incontinence etc.

- In cases with **sphincter insufficiency:** (more common in women): sphincter training through controlled exercising involving pelvic floor contraction, if necessary reset bowel prolapse, train and organize regular visits to toilet, if necessary neurological examination
- In case of **stress incontinence:** stool training: train regular bowl clearing, “listen to your bowl”
- Lifestyle advice: keep clear of nicotine, alcohol, caffeine, Cola.

Pehl C, Birkner B, Bittmann W, Cluss B, Emmert H, Fuchs M, Passern J, Wendl B, Schepp W, Heitland W. Stuhlinkontinenz. Deutsches Ärzteblatt. 2000; 97: A1303-1308.

In cases with **infectious diarrhea:**

- Treat the underlying disease
- Replace fluid and electrolytes
- Rest
- No food for 1 – 2 days

In cases with **chronic non-infectious diarrhea:**

- If necessary try dietary fiber
- Directed brief treatment with loperamide

Drug therapy

If necessary, therapy according to symptoms [Füsgen et al. 2000]:

- Opiates reduce stool frequency and fluid content, reduce colon motility
- Loperamide: increases resting pressure of inner sphincter muscle as well as capacity to dilate rectum
Beware: uncontrolled long-term therapy with loperamide (OTC drug)
- Spasmolytics such as scopolamine butylbromide lower the resting pressure of the anal sphincter muscle and are usually not useful drugs in such patients
- Anion exchangers: (e.g. cholestyramine) can prevent chologenic diarrhea due to lack of bile-acid reabsorption

References

- Chatoor DR, Taylor SJ, Cohen CR, Emmanuel AV. Fecal incontinence. Br J Surg. 2007; 94: 134-144.*
- Füsgen I et al. Der ältere Patient. 3. Aufl. München-Jena: Urban und Fischer; 2000.*
- Gregor CF. Anale Inkontinenz; Patienteninformation, GIN, Gesundheits-Informationsnetz, Institut für Biostatistik und Dokumentation an der Medizinischen Universität Innsbruck. <http://gin.uibk.ac.at/thema/anale-inkontinenz>; 9.02.2005.*

Appendix 1. Varieties of incontinence [Pehl et al 2000].

Sphincter dysfunction	Disease symptoms
Nerval	Idiopathic, diabetes, postpartum neuropathy of the nervus pudendus
Myopathic	Myopathy of the inner sphincter muscle, congenital myopathy, scleroderma, dermatomyositis, weakening or loss of sphincter function due to advanced age
Traumatic	Injuries, post-surgical, postpartum
Neoplastic	Anal carcinoma, entrenched rectal carcinoma
Inflammatory	Fistulae (e.g. Morbus Crohn)
Drug-induced	Anticholinergics, spasmolytics, calcium antagonists, nitrates, α -blockers, benzodiazepines, abuse of laxatives, magnesium

Sensory dysfunction	
Neural	Idiopathic neurogenic incontinence, diabetes mellitus, cauda-conus syndrome
Traumatic	Spinal cord injury, pelvic fracture with lesion of the nervus pudendus, hemorrhoid surgery
Mechanic	Overflow incontinence due to fecaliths

Reservoir dysfunction	
Traumatic	Coloanal anastomoses
Inflammatory	Morbus Crohn, colitis ulcerosa, proctitis, radiation treatment
Neoplastic	Rectal carcinoma, fecaliths
Dysfunction of the small and large intestine	Diarrhea, irritable colon, proctitis

Dysfunction of neural control	
Anal diseases with or without sphincter spasm	Spinal: spinal cord injury, cauda-conus syndrome, lesion of the nervus plexus, MS, tabes dorsalis, meningomyelocele Cerebral: apoplexy, MS, apallic syndrome

Stool smear	
Proctological diseases	Fistulae, hemorrhoids, anal fibroma
Rectal diseases	Rectal prolapse, fecaliths
Traumatic	Post-surgical keyhole defect
Idiopathic	Long anal channel, rectal sensing dysfunction, dysfunction of the recto-anal inhibition reflex

f) Chronic constipation

Definition

Criteria: hard stool, regular loss of bowel clearing function for 2 – 3 days, frequent futile pressing, frequently painful, incomplete clearing [Füsgen et al. 2000, Pehl et al. 2000]

Epidemiology

24 – 37% of patients older than 65 years suffer from chronic constipation, if asked directly 40 – 60% admit to the complaint. Half of the population over 65 use laxatives [Füsgen et al. 2000]. 75% of elderly patients in hospitals or care institutions receive laxatives to regulate stool movements [Füsgen et al. 2000, Primrose et al. 1987].

Categorization of chronic constipation in line with the “Rome Criteria” [Whitehead and Drinkwater 1989, Whitehead and Chaussade 1991] according to organic and functional causes [Füsgen et al. 2000]:

Organic causes are:

- Neurological diseases (e.g. Morbus Parkinson)
- Endocrine causes (e.g. hypothyroidism)
- Drug-induced causes (e.g. opiates)
- Dysfunction of the pelvic structure (e.g. rectocele)

In cases of **functional constipation** none of the above causes can be detected [Füsgen et al. 2000].

At least two of the following symptoms typical of chronic constipation should be present for a diagnosis:

- Hard pressing for bowel clearing
- Hard stool
- Feeling of incomplete clearing
- Feeling of blockage, manual assistance of defecation (in more than 25% of instances)
- Rare bowel movement (cf. above)

Measures that precede or support drug therapy

- **Comprehensive patient history**
- **Explicitly inquire about use of laxatives!**
- If necessary keep a stool diary
- Sufficient fluids, 1,500 – 2,000 ml per day?

- Physiologically inadequate dietary habits (e.g. preference for sweets, cake, excessive amounts?)
- Thorough history of drug use (drugs that promote constipation?)
- Exercise?

Clinical examination

- Auscultation of the bowels
- Rectal examination (e.g. exclusion of appendicitis and other acute conditions)
- Exclusion of disruptions of mechanical passage (e.g. colon carcinoma, large mucous polyps, fecaliths, fixed hernia)
- Exclusion of endocrinological causes (e.g. hypothyroidism)
- Neurological examination (e.g. MS, various paralyses, apoplexy, dementia)
- Exclusion of post-surgical and post-traumatic pelvic-floor dysfunctions (e.g. after colon surgery, after difficult births)

Interfaces: gastroenterologist, neurologist, endocrinologist, surgeon

Beware: frequent abuse of laxatives is to be avoided!

Control of indication for and use of constipation-inducing drugs: e.g. opiates, analgesics, anticholinergics, β -blockers, diuretics, antidepressants, antacids, steroids!

Dietary advice: Daily amount of fluids ca. 1.5 – 2 liters, fiber (fruit, vegetables, cereal products, yoghurt, sauerkraut, dried fruit)

Stool training: “Listen to your bowel”, i.e. if urge to pass stool is felt, go to the toilet, train regular bowel clearing

Lifestyle advice: Activate! Exercise! (stomach massage, breathing exercises, pelvic floor exercises). Improve constipation-inducing eating habits, reduce coffee and cigarettes.

Therapy for fecaliths: After ruling out contraindications: careful saline enema at body temperature and/or manual removal

Drug therapy

Drug-based laxative measures are indicated only if non-drug measures continue to fail and there are no contraindications

Occasionally, glycerol-based rectal suppositories help in cases of hard stool (not a permanent therapy); if not,

1. trial stool-forming laxatives, so called roughage, also dietary fiber e.g.

- Shredded linseed
- Wheat bran (frequently combined with stimulating laxatives)
- Desert Indian-wheat, combined either with plantago ovata seed, aloe or Alexandrian Senna glycosides

ADR: meteorism

Note: always ensure sufficient amounts of fluid!

If the effect is unsatisfactory:

2. osmotic effect laxatives, e.g.

- Lactulose
- Sodium citrate
- Magnesium sulfate, sodium sulfate
- Saline laxatives
- Macrogol (polyethylene glycol)

If these substances, together with the non-drug measures, do not yield the desired effect then the following measures may be successful (according to [Schneider and Richling 2004]):

3. stimulating laxatives (only for short-term therapy, not long-term!), e.g.

- Anthraquinones (pure senna glycosides)
- Bisacodyl
- Sodium picosulfate
- Liquid paraffin, castor oil: obsolete therapies and mentioned here because of danger of absorption and aspiration – only in cases of acute intoxication

Not in cases of “acute abdomen”, not in cases of (sub)ileus!

Restrict use to 1 – 2 weeks at low dosages!

Beware: stimulating laxatives have a high potential for abuse with a resulting danger of electrolyte imbalance in which a loss of potassium can intensify constipation!

In cases of drug-induced constipation, check indications for constipation causing drugs and their dosage; if necessary, give lax-

atives, especially e.g. in cases of opiate therapy.

References

- Füsgen I et al.* Der ältere Patient. 3. Aufl. München-Jena: Urban und Fischer; 2000.
- Pehl C, Birkner B, Bittmann W, Cluss B, Emmert H, Fuchs M, Passern J, Wendl B, Schepp W, Heitland W.* Stuhlinkontinenz. Deutsches Ärzteblatt. 2000; 97: A1303-1308.
- Primrose WR, Capewell A.E, Simpson G.* Prescribing patterns observed in registered nursing homes and long-stay geriatric wards. Age Ageing. 1987; 16: 25-28.
- Schneider D, Richling F.* Checkliste Arzneimittel A-Z; 2. Auflage Stuttgart: Thieme; 2004.
- Whitehead WE, Drinkwater D.* Constipation in the elderly living at home. J Amer Geriatr Soc. 1989; 37: 423-429.
- Whitehead WE, Chaussade E.* Report of an international workshop on management of constipation. Gastroenterol Int. 1991; 4: 99-113.



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Part D Basic conditions supporting drug treatment

- a) Nutrition in old age b) Body exercise in old age

Version 1.07, April 18th, 2007, Revision up to December 2008.

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Key words

elderly patients – old age – low body weight – malnutrition – lack of fluids – low serum albumin – disease risk physical exercise – chronic disease – cardiovascular disease – degenerative disease of joints

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Abstract. *Physiological changes in old age:* loss of muscle mass; reduction in bone mass; percentage of fat increased; lower amount of body water; lack of thirst; diminishing kidney function (caution: sufficient intake of fluids: 1.5 – 2 l and moderate intake of protein 8 g/kg body weight); reduced secre-

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tion of digestive enzymes, delayed emptying of stomach (which means premature feeling of repletion). Lack of fluids and nutrition is therefore likely. Daily intake of 1,500 kcal and 1.5 – 2 l fluids is necessary. An indicator for *malnutrition* is low body weight (defined for persons older than 65 years of age as BMI < 20) and a protein serum concentration < 35 g/l. Malnutrition carries an increased risk of infections, falling and fractures, bed sores, anemia, decompensation of chronic diseases. 10 – 20% of subjects over 80 years of age show signs of malnutrition, 40 – 60 % of subjects in care institutions or hospitals. There are regressive changes in the locomotor and the nervous system of the elderly which have an effect on *physical fitness*. These changes reduce strength, endurance, proprioceptive capacity (e.g. coordination, balance) and mobility. Exercise in the old and very old should increase skeletal muscle strength in particular and improve coordination and balance. *Regular physical exercise* and moderate training has a positive effect on mobility and thereby improves independence and reduces falls. Moreover, it has a positive effect on cardiac output, maximum heart rate, stroke volume and the risk of a cardiovascular event and mortality can be reduced. Moreover, moderate physical exercise is often more effective in treating chronic disease than drug therapy e.g. heart failure, coronary heart disease, asthma/COPD, stroke, diabetes mellitus Type 2, degenerative diseases of the joints, depression and others. Examine cardiovascular risks in persons over the age of 50 before beginning physical exercise. Avoid maximum stress levels.

D Basic conditions supporting drug treatment

a) Nutrition in old age

Principles for family doctors

- Nutritional requirements and nutritional intake of patients up to 75 years of age are equivalent to those of younger people. In this age group obesity is a bigger problem than nutrition.
- In patients older than 75 years of age instances of malnutrition that go undetected are more frequent. It is necessary to investigate the causes.
- A frequent loss of mobility in old age through osteoarthritis, incontinence or cognitive failure makes shopping, the preparation of food and eating more difficult.
- Psycho-social changes (e.g. the loss of a partner and friends) inhibit the emotional and social satisfaction associated with eating in younger years [Rauscher 1993].
- Malnutrition can trigger decompensation in chronic diseases and lead to a loss of independence and the need for permanent care.
- The number of calories required in the elderly is reduced whereas the need for vitamins, minerals and trace elements remains constant (high nutritional density is required).

Physiological changes in old age

- Loss of muscle mass (reduced basic metabolism, lower calorie requirement) [Murray et al. 1985]
- Larger percentage of fat
- Lower amount of body water
- Reduction in bone mass
- Diminishing immune function
- Lack of thirst [Philips et al. 1984]

Basic metabolism

- Nutrition in a 65-year-old male: ca. 1,400 – 1,500 kcal/day + additional energy requirements depending on activity: a total of 1,750 – 2,300 kcal/day; For a 65-year-old female: ca. 1,500 kcal/day – if warranted by activity: a total of ca. 1,500 – 1,800 kcal/day [World Health Organization 1998]
- Monitor **amount of fluids consumed**: ca. 1,5 – 2 l per day are recommended
- Sufficient intake of **vitamin D and calcium**: ca. 1 g calcium/day
- Sufficient intake of **vitamins and minerals**, if necessary as supplements [Girodon et al. 1999]
- The number of calories required in the elderly decreases whereas the requirement for vitamins, minerals and trace elements (high nutritional density) remains constant

Organic changes

- Diminishing kidney function [Kappel and Olsen 1980] (thus, sufficient intake of flu-

- ids and only moderate intake of proteins, ca. 0.8 g protein/kg body weight/day)
- Delayed emptying of the stomach, premature feeling of repletion
 - Reduced secretion of digestive enzymes
 - Loss of teeth and problems with chewing. According to the German Mouth Health Study (DMS III) 70% of patients aged between 65 and 74 require parodontal or prosthetic intervention [Lenz 1997]. In Germany the requirement for prosthetics is met in about 90%, which represents a very high standard of care in this area [Lenz 1997].
 - Impairment of the senses. Loss of ability to see, to hear, taste and smell (on the other hand the perception of sweet stimuli is well maintained up to a very high age) [Schiffmann 1977].

Conclusion: The feeling of repletion occurs very quickly, whereas the feeling of thirst is reduced. A lack of fluids and nutrition is therefore highly likely [Hesecker 2004].

Obesity

Obesity and a high body mass index are of lesser importance in the elderly (> 75 years). An increased risk of mortality only results from severe obesity (BMI > 40), therefore do not aim to achieve a drastic reduction in weight (caution: malnutrition).

Low body weight, malnutrition

A low body weight frequently develops slowly and therefore is not often diagnosed early enough. Signs of manifest malnutrition are found in 10–20% of those over age 80. In hospital patients and patients in care institutions the incidence is significantly higher (40–60%) [Löser et al. 2007].

An involuntary loss of weight of more than 5% in 3 months or more than 10% in 6 months is an **alarm signal**.

Many elderly patients prefer energy rich foods and therefore consume food which is poor in protein, vitamins and minerals. The so-called “custard vegetarians” [Wagner 2004]. They eat predominantly stewed apple, white bread, cookies and rusks dunked in tea or coffee and soft bread rolls with jam (low

nutrients density). Malnutrition may be present even if the BMI is normal (e.g. in cases with edema, ascites).

Recommended combinations of foods

(following the recommendations of the German Society for Nutrition):

- No rigid rules or bans, enjoyment of and contentment with eating and drinking should be retained! [Elmstahl and Steen 1987, Watson 2002].
- Foods for the elderly patient should be of high nutritional value [Blumberg 1997], i.e. with a low intake of calories and all essential nutrients such as vitamins, minerals and trace elements should be present.
- **A total daily intake of at least 1,500 kcal is necessary.**
- Energy intake should be appropriate to need and monitored through regular weighing (at least once a month).
- Sufficient fruit and vegetables (about 5 handfuls per day, fruit and vegetables also as juice).
- Less sugary products such as cakes, sweets; more wholegrain bread (in the event of chewing difficulties choose Graham bread).
- Low fat milk and milk products (0.25 l low fat milk, butter milk, kefir or yoghurt and two slices of low fat cheese provide sufficient amounts of calcium).
- Fish twice a week and meat without fat (2–3 times a week, mainly poultry).
- **Ca. 1.5–2 l of fluids daily (mineral water, juice mixed with sparkling water, unsweetened herbal or fruit teas, milk are best;** low amounts of alcohol, i.e. < 10 g for women, < 20 g for men).
- Soup counts towards the amount of fluids.
- Liberal use of herbs and spices (stimulate appetite), low amounts of salt, no pickled meats.
- Sparing use of fats.
- In case of chewing and swallowing difficulties: cook food in a small amount of water and then cut finely or mash.

See Appendix 1 for:

- Daily nutrient requirements and recommended relative allocation of nutrients
- Examples of a daily nutritional plan

Low body weight

Definition

BMI < 20 is the limiting value recommended by the WHO as a definition for low body weight in adult subjects > 65 years of age [Richter-Kuhlmann 2004].

Causes of malnutrition [Thomas 1999]

- Medication (e.g. analgesics, serotonin antagonists, digitalis, chemotherapeutics, anticholinergics) [Wilson et al. 1998]
- Chronic diseases [Rudmann and Feller 1989]
- Malignomas [Thompson and Morris 1991]
- Chewing difficulties (poorly fitting dentures) [Vigild 1989]
- Swallowing difficulties [Steele et al. 1997], diminishing appetite
- Social (inadequate meals on wheels) and psychological (loneliness and depression) problems [Morley and Kraenzie 1994]
- Institutional care with frequent lack of attention to individual eating habits [Gallagher et al. 1997] and attractiveness of surroundings [Lutheran Hospitals and Homes Society 1987]
- In Alzheimer patients weight loss is often the result of confusion regarding eating patterns (or even refusal to eat) and oral dyspraxia (chewing difficulties) [Guyonnet et al. 1997, Morley 1996]

Diagnosis

MNA questionnaire (Mini-Nutritional-Assessment)

Assessment of the nutritional status, intake of food and possible causes of refusal to eat, is needed e.g. by means of simple questionnaires [Guigoz 2006] (Appendix 2).

Laboratory parameters

A chemical indicator for the assessment of nutritional status is the serum albumin concentration:

Normal: albumin 45 – 35 g/l; transferrin 3.0 – 2.5 g/l (may also be determined).

The annual mortality rate in patients in institutional care with serum albumin > 40 g/l is 11% and this value increases to 50% for albumin values < 35g/l [Seiler 1996].

A low serum albumin concentration is an indication of a poor nutritional status (loss of body cell mass) and of a high disease risk.

Consequences of malnutrition

- Increased risk of infection, frequently made worse by a lack of trace elements, e.g. zink [Girodon et al. 1999]
- Increased risk of falling and fractures through lack of muscle mass and higher bone fragility (osteoporosis) [Cope 1996]
- Danger of bedsores (decubitus ulcers): a causal connection between bedsores and malnutrition is not proven but likely; a protein-rich diet (or tube feeding) has been shown to accelerate healing in malnourished patients [Langer et al. 2003]
- Anemia (e.g. through lack of vitamin B12) [Nilsson-Ehle 1998]
- Decompensation in chronic diseases (e.g. heart failure)

Step-by-step prevention of malnutrition

- Dietary advice – e.g. in cases of chewing problems
- Swallowing exercises (ergotherapy, logotherapy)
- If malnutrition cannot be rectified, energy-rich supplements should be added to the food or given in liquid form [Larson et al. 1990, Tomaiolo et al. 1981], e.g. vegetable or fruit as well as protein concentrates
- In cases of swallowing problems the rule is to thicken liquids and soften solids; a slightly more viscous mash is easier to swallow
- The head should be slightly bent forward, line of sight straight on when swallowing

Only if these measures are insufficient should tube feeding be considered.

Nasal tubes

Suitable only for short periods of time (max. 14 days). The correct placement of the tube within the stomach is important. Danger of pressure ulcers and oesophageal reflux.

Subcutaneous administration of fluids

This has been tried in some care institutions in patients who lack fluid volume and

found to be well tolerated [Slesak et al. 2003] (Butterfly-needle, up to 1,000 ml/day of lactated Ringer's solution); it is not possible to give nutrients by this route.

PEG (percutaneous endoscopic gastrostomy)

Therapeutic goals:

- Overcoming acute diseases
- Decrease in the mortality and morbidity rate in chronic diseases, if the quality of life attained matches the wishes of the patient.

Indication for a PEG-tube:

In cases of terminal illness a PEG-tube is not indicated.

Tube-feeding may be indicated in cases of

- neurogenic swallowing problems (e.g. for a non-comatose apoplexia patient it may be useful to use a PEG-tube until swallowing exercises have been successful; a nasal tube would interfere with swallowing)
- mechanical obstructions in the upper gastrointestinal tract due to tumors, traumas, operations, radiation, severe burns
- consumption diseases

The indication for a PEG-tube must remain the prerogative of the family doctor who should have knowledge of the wishes of the patient [de Ridder 2008].

Contraindications

- Advanced dementia (according to the literature no proof of improved life expectancy or quality) [German Society for Nutritional Medicine 2003, Gillick 2000]
- Severe malfunction in blood clotting (coagulopathy)
- Peritonitis
- Advanced peritoneal cancer
- Massive ascites
- Severe psychosis
- Significantly restricted life expectancy
- General contraindications for enteral feeding (e.g. ileus)

Aftercare

- Sterile dressing change daily during the first week after PEG-tube has been introduced
- Later change of dressing once or twice per week
- Ability to take a shower after 1 – 2 days
- Tube to be moved inward by 2 – 3 cm for a short time each day to avoid adhesion of the inner holding plate to the stomach wall

Application

- **Avoid pump systems** (expensive and in most cases unnecessary); **exception:** jejunal tube (limited bowel capacity)
- **Bolus feeding** is of limited use
- **Caution:** feeding too rapidly: maximum rate 10 minutes per 100 ml, in the event of vomiting reduce to 30 minutes per 100 ml.
- **Change of tube:** a tube may stay for years [Löser et al. 2007]

Drug application via the PEG-tube

- Preferably only liquid drugs or micro-pellets (e.g. morphine), flush tube afterwards
- Simple uncoated tablets can be crushed, not, however, pills that are resistant to gastric fluids

Problems

Diarrhea: some controversy in the literature, but diarrhea is observed in up to 25% of patients. Soft stool up to 6 times a day is frequent:

- First try a reduction in rate of feeding
- Limit volume of each feed
- Give food at room temperature

Aspiration:

- Slightly lift upper body, if possible up to 45°

Infection at the percutaneous entry point:

- Burn granulation tissue around the percutaneous entry point chemically (if necessary using a "Höllenstein pen" = silver nitrate, avoid touching the tube)

To avoid clogging of the tube:

- alternate regularly between soft and liquid foods

Choice of tube foods

(normally industrially processed foods)

Differentiation:

- **High molecular** tube food (rich in fiber or fiber-free or high-caloric) can be administered if the digestive system is functioning well and the nutrients can still be split up.
- **Low molecular** tube food (to be administered only with a pump system) is necessary if the digestive system is malfunctioning, e.g. in cases of short bowel syndrome or Morbus Crohn.

Usual amounts: ca. 1,500 to 2,000 ml tube food plus 1,000 ml tea per day.

Energy content for standard food: 1 kcal/ml (4.18 kJ/ml) [Domann et al. 2003].

Three kinds of food are functional: normal diet, fiber-rich and high-caloric (the use of other diets, e.g. for diabetics, must be questioned).

There are large price differences for comparable products; a price comparison is worthwhile.

Interface

The family doctor ought to remain in charge of the patient! Frequently patients are set on a path to PEG-tube feeding at the hospital. Industry-paid dietary advisors visit patients at home and determine the type of food and the materials used. The family doctor ought to be part of any decision-making process relating to tube feeding, since s/he is responsible for the indication and prescription.

About 140,000 patients are treated with a PEG-tube in Germany each year.

The decision to use a PEG-tube has severe consequences and should be taken with due consideration. Lack of staff or the wishes of those caring for a patient are not an indication for a PEG-tube. Only the wishes of the patient are relevant (if known, e.g. through an advance directive) or the consent of the legal guardian.

References

- Abbatt J et al.* Promoting physical activity with older people. Health Education Authority, Archive for Life. London: Hamilton House Mabledon Place; 1996. p. 1-27.
- AID Infodienst.* Senioren in der Gemeinschaftsverpflegung. Bonn; 2003.
- Blumberg J.* Nutritional needs of seniors. *J Am Coll Nutr.* 1997; 16: 517-523.
- Cope K.* Malnutrition in the elderly, a national crisis: Contributes to disease, illness, disability, death, escalates health care costs, decreases quality of life. Region X, U.S. Administration on Aging. Publication No. 017-062-00147-2. Washington, D.C.: U.S. Government Printing Office; 1996.
- Domann A, Stehle P, Radziwill R, Löser C, Paul C, Keymling M, Lochs H.* DGEM Leitlinie Enterale Ernährung: Grundlagen. *Aktuel Ernähr Med.* 2008; 28: 26-30.
- Elmstahl S, Steen B.* Hospital nutrition in geriatric long-term care medicine: II. Effects of dietary supplements. *Age Ageing.* 1987; 16: 73-80.
- Gallagher A, Pinteu K, Robinson G, Bellview-Taylor K, Hartery S.* Nutrition. Quality care in the nursing home. St. Louis: Mosby-Year Books; 1997.
- German Society for Nutritional Medicine.* Leitlinie "Enterale Ernährung". *Aktuell Ernähr Med.* 2003; 28 (Suppl 1): 26-35.
- Gillick MT.* Rethinking the role of tube feeding in patients with advanced dementia. *New Engl J Med.* 2000; 342: 206-210.
- Girodon F, Galan P, Monget AL et al.* Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: a randomized controlled trial. *MIN.VIT.AOX. geriatric network. Arch Intern Med.* 1999; 159: 748-754 {Ib}.
- Guidelines Group Hesse; Bergert WF, Braun M, Clarius H, Ehrental K, Feßler J et al.* Hausärztliche Leitlinie – Teil 1 – Allgemeine Geriatrie; 2008. http://www.pmv.forschungsgruppe.de/pdf/03_publicationen/geriatrie_1_ll.pdf
- Guigoz Y.* The Mini-Nutritional Assessment (MNA[®]): Review of the literature – What does it tell us? *J Nutr Health Aging.* 2006; 10: 466-487.
- Guyonnet S, Nourhashemi F, Reyes-Ortega G et al.* La perte de poids chez les sujets presentant une demence de type Alzheimer. *Rev Med Interne.* 1997; 18: 776-785.
- Hesecker H.* Ernährung und Bewegung beim älteren Menschen. In: Deutsche Gesellschaft für Ernährung: Senioren in der Gemeinschaftsverpflegung; 2004. p. 1:2-8.
- Kappel B, Olsen S.* Cortical interstitial tissue and sclerosed glomeruli in the normal human kidney, related to age and sex. *Virchows Arch.* 1980; 387: 271-277.
- Langer G, Schloemer G, Kerr A, Kusas O, Behrens J.* Nutritional interventions for preventing and treating pressure ulcers. *Cochrane Database Syst Rev.* 2003; 4: CD003216.
- Larson J, Unosson M, Ek AC et al.* Effect of dietary supplement on nutritional status and clinical outcome in 501 geriatric patients – a randomised study. *Clin Nutr.* 1990; 9: 179-184.
- Lenz E.* Zahnprothetischer Status bei Senioren. In: Micheelis W, Roth E (eds). Dritte Mundgesundheits-

- studie (DMS III). Ergebnisse, Trends und Problemanalysen auf der Grundlage bevölkerungsrepräsentativer Stichproben in Deutschland. Institut der Deutschen Zahnärzte (IZD). Köln: Deutscher Ärzte Verlag; 1997.
- Löser C, Lubbes H, Mahlke R, Langkisch PG. Der ungewollte Gewichtsverlust des alten Menschen. *Dt Ärztebl.* 2007; 104: A3411-A3420.
- Lutheran Hospitals and Homes Society. Guidelines for Dining; 1987.
- Morley JE. Anorexia in older persons. *Drugs Ageing.* 1996; 8: 134-152.
- Morley JE, Kraenzle D. Causes of weight loss in a community nursing home. *J Am Geriatr Soc.* 1994; 42: 583-585.
- Murray MP, Duthie EH, Gambert ST et al. Age-related differences in knee muscle strength in normal women. *J Gerontol.* 1985; 40: 275-280.
- Nilsson-Ehle H. Age-related changes in cobalamin (vitamin B12) handling. Implications for therapy. *Drugs Ageing.* 1998; 12: 277-292.
- Norton B, Homer-Ward M, Donnelly MT, Long RG, Holmes GK. A randomised prospective comparison of percutaneous endoscopic gastrostomy and nasogastric feeding after acute dysphagic stroke. *BMJ.* 1996; 312: 13-16.
- Philips PA, Rolls BJ, Ledingham JGG et al. Reduced thirst after water deprivation in healthy elderly men. *N Engl J Med.* 1984; 311: 753-759.
- Rauscher C. Malnutrition among the elderly. *Can Fam Physician.* 1993; 39: 1395-1403.
- Richter-Kuhlmann E. Mangelernährung, unterschätzte Gefahr. *Dtsch Ärztebl.* 2004; 101: A623.
- Ridder M de. Medizin am Lebensende. Sondenernährung steigert nur selten die Lebensqualität. *Dtsch Ärztebl.* 2008; 105: A449-A451.
- Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the Short-Form Mini Nutritional Assessment (MNA-SF). *J Geront.* 2001; 56A: M366-377.
- Rudmann D, Feller AG. Protein-calorie undernutrition in the nursing home. *J Am Geriatr Soc.* 1989; 37: 173-183.
- Schiffmann S. Food recognition by the elderly. *J Gerontol.* 1977; 32: 586-592.
- Seiler WO. Malnutrition – multifaktoriell und bedenklich. *Extracta geriatrica.* 1996; 3: 18-20.
- Slesak G, Schnürle JW et al. Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial. *J Am Geriatr Soc.* 2003; 51: 155-160 {Ib}.
- Steele CM, Greenwood C, Ens I, Robertson C, Siedman-Carlson R. Mealtime difficulties in a home for the aged: not just dysphagia. *Dysphagia.* 1997; 12: 45-50.
- Thomas DR. Causes of protein-energy malnutrition. *Z Gerontol Geriatr.* 1999; 32 (Suppl 1): I/38-I/44.
- Thompson MP, Morris LK. Unexplained weight loss in the ambulatory elderly. *J Am Geriatr Soc.* 1991; 39: 497-500
- Tomaiolo PP, Enman S, Kraus V. Preventing and treating malnutrition in the elderly. *J Parent Ent Nutr.* 1981; 5: 46-48.
- Vellas B, Villars H, Abellan G et al. Overview of the MNA – Its history and challenges. *J Nutr Health Ageing.* 2006; 10: 456-465.
- Vigild M. Dental caries and the need for treatment among institutionalized elderly. *Community Dental Oral Epidemiology.* 1989; 17: 102-105.
- Volkeit D. Ernährungszustand, Energie und Substratstoffwechsel im Alter. In: Leitlinie enterale Ernährung der DGEM und der DGG – Teil 2. *Aktuel Ernähr Med.* 2004; 29: 190-197.
- Wagner B. Haben Sie einen kritischen Blick auf betagte Patienten? *Der Hausarzt.* 2004; 6: 38-39.
- Watson A. Food for thought: practical tips about eating, feeding and nutrition for people with Alzheimer Disease. Toronto: Booklet; 2002.
- Wilson MG, Vaswani S, Liu D et al. Prevalence and causes of undernutrition in medical outpatients. *Am J Med.* 1998; 104: 56-63.
- World Health Organization (WHO). Presented at WHO/Tufts University. Consultations on Nutritional Guidelines for the elderly, Boston; 1998.

Appendix 1. Nutritional tables.

When assessing the menus of the (mobile) meal services for healthy seniors (> 65 years of age) it is important to check for the following reference values:

Daily nutrient requirements for seniors: Relative allocation: 15% proteins, 30% fat, 55% carbohydrates			
Calories	1,800 kcal	Vitamin B2	1.2 mg
Proteins	≤ 68 g	Vitamin B12	3.0 µg
Fat	≤ 60 g	Folate	400 mg
Carbohydrates	≥ 248 g	Vitamin C	100 mg
Fiber	≥ 30 g	Calcium	1,000 mg
Vitamin D	10 µg	Magnesium	350 mg
Vitamin E	12 mg	Iron	10 mg
Vitamin B1	1.0 mg	Iodine	180 µg

Example of daily menu

Example of a menu for a healthy senior (> 65 years of age)	
After rising	1 glass of natural water
Breakfast	1.5 slices of wholemeal toast, diet margarine, plum jam, a small amount of fresh cheese with herbs (normal fat variety), 2 cups of coffee
Lunch	1 small schnitzel cooked in rape oil, 3 potatoes garnished with parsley, 1 serving of pea-and-carrot mixture, gravy thickened with flour, 1 small bowl of quark (low fat variety) with blackberries sweetened with sugar, 1 – 2 glasses of apple juice mixed with sparkling mineral water
Snack (between meals)	1 small slice of cheesecake with cherries, 1 cup of coffee
Dinner	1 small bowl of celery and carrot salad with dressing made from lemon juice, rape oil and a small amount of sugar, 1.5 slices of wholemeal bread, diet margarine, 1 slice of cheese (30% fat), 1 slice of ham, 2 cups of peppermint tea
At night	1 glass of water

To ensure a balanced diet it is recommended that the reference values for nutrients amongst the various types of food be as follows (Groups 1 – 6 daily, Group 7 weekly):

Dietary recommendations for healthy seniors (> 65 years of age) according to GSNM	
Group 1: Cereals and potatoes	150 – 250 g mostly wholemeal or dark bread, partly substituted by cereal flakes, ca. 200 – 300 g potatoes, natural rice or pasta (cooked weight) per day
Group 2: Vegetables	400 g of vegetables (e.g. 200 g cooked vegetables, 100 g uncooked and one large serving of salad) per day, frozen and canned vegetables are included
Group 3: Fruits	2 servings or 250 g of fruit per day, frozen or canned products and fruit juices are included
Group 4: Milk and milk products	200 ml low-fat milk or yoghurt (1.5% fat) and 2 slices of low-fat cheese (60 g) per day
Group 5: Fat and oils	50 – 70 g (in prepared foods or as such) fat per day, according to energy requirements
Group 6: Fluids	Ca. 1.5 l of fluids, especially water, mineral water, herbal and fruit teas, vegetable juice, tinned fruit juices, coffee and black tea in moderation
Group 7: Fish, meat, processed meats and eggs	300 – 500 g of (processed) meat per week, e.g. three servings of 150 g each and three times low-fat processed meat, one serving of saltwater fish, in addition use iodized salt, only 2 – 3 eggs per week (incl. eggs in prepared foods e.g. pancakes!)

Appendix 2.



Mini Nutritional Assessment MNA®

Last name: _____ First name: _____ Sex: _____ Date: _____
 Age: _____ Weight, kg: _____ Height, cm: _____ I.D. Number: _____

Complete the screen by filling in the boxes with the appropriate numbers.
 Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

Screening	
A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? 0 = severe loss of appetite 1 = moderate loss of appetite 2 = no loss of appetite	<input type="checkbox"/>
B Weight loss during the last 3 months 0 = weight loss greater than 3 kg (6.6 lbs) 1 = does not know 2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs) 3 = no weight loss	<input type="checkbox"/>
C Mobility 0 = bed or chair bound 1 = able to get out of bed/chair but does not go out 2 = goes out	<input type="checkbox"/>
D Has suffered psychological stress or acute disease in the past 3 months 0 = yes 2 = no	<input type="checkbox"/>
E Neuropsychological problems 0 = severe dementia or depression 1 = mild dementia 2 = no psychological problems	<input type="checkbox"/>
F Body Mass Index (BMI) (weight in kg) / (height in m ²) 0 = BMI less than 19 1 = BMI 19 to less than 21 2 = BMI 21 to less than 23 3 = BMI 23 or greater	<input type="checkbox"/>
Screening score (subtotal max. 14 points) <input type="checkbox"/> <input type="checkbox"/>	
12 points or greater Normal – not at risk – no need to complete assessment	
11 points or below Possible malnutrition – continue assessment	

Assessment	
G Lives independently (not in a nursing home or hospital) 0 = no 1 = yes	<input type="checkbox"/>
H Takes more than 3 prescription drugs per day 0 = yes 1 = no	<input type="checkbox"/>
I Pressure sores or skin ulcers 0 = yes 1 = no	<input type="checkbox"/>

Ref: Vellas B, Villars H, Abellan G, et al. Overview of the MNA® - Its History and Challenges. J Nutr Health Aging 2006;10:456-466.
 Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: Developing the Short-Form Mini Nutritional Assessment (MNA-SF). J Gerontol 2001;56A: M366-377.
 Guigoz Y. The Mini-Nutritional Assessment (MNA®) Review of the Literature - What does it tell us? J Nutr Health Aging 2006;10:466-487.

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 For more information: www.mna-elderly.com

J How many full meals does the patient eat daily? 0 = 1 meal 1 = 2 meals 2 = 3 meals	<input type="checkbox"/>
K Selected consumption markers for protein intake • At least one serving of dairy products (milk, cheese, yogurt) per day yes <input type="checkbox"/> no <input type="checkbox"/> • Two or more servings of legumes or eggs per week yes <input type="checkbox"/> no <input type="checkbox"/> • Meat, fish or poultry every day yes <input type="checkbox"/> no <input type="checkbox"/> 0.0 = if 0 or 1 yes 0.5 = if 2 yes 1.0 = if 3 yes	<input type="checkbox"/> . <input type="checkbox"/>
L Consumes two or more servings of fruits or vegetables per day? 0 = no 1 = yes	<input type="checkbox"/>
M How much fluid (water, juice, coffee, tea, milk...) is consumed per day? 0.0 = less than 3 cups 0.5 = 3 to 5 cups 1.0 = more than 5 cups	<input type="checkbox"/> . <input type="checkbox"/>
N Mode of feeding 0 = unable to eat without assistance 1 = self-fed with some difficulty 2 = self-fed without any problem	<input type="checkbox"/>
O Self view of nutritional status 0 = views self as being malnourished 1 = is uncertain of nutritional state 2 = views self as having no nutritional problem	<input type="checkbox"/>
P In comparison with other people of the same age, how does the patient consider his/her health status? 0.0 = not as good 0.5 = does not know 1.0 = as good 2.0 = better	<input type="checkbox"/> . <input type="checkbox"/>
Q Mid-arm circumference (MAC) in cm 0.0 = MAC less than 21 0.5 = MAC 21 to 22 1.0 = MAC 22 or greater	<input type="checkbox"/> . <input type="checkbox"/>
R Calf circumference (CC) in cm 0 = CC less than 31 1 = CC 31 or greater	<input type="checkbox"/>
Assessment (max. 16 points) <input type="checkbox"/> <input type="checkbox"/> . <input type="checkbox"/>	
Screening score <input type="checkbox"/> <input type="checkbox"/>	
Total Assessment (max. 30 points) <input type="checkbox"/> <input type="checkbox"/> . <input type="checkbox"/>	
Malnutrition Indicator Score	
17 to 23.5 points at risk of malnutrition	<input type="checkbox"/>
Less than 17 points malnourished	<input type="checkbox"/>

b) Body exercise in old age

Physical activity in the elderly [GCIS 2000]

Advancing age is accompanied by loss of physical fitness. The decisive factors for physical fitness are strength, endurance, coordination and mobility.

Epidemiological studies have shown (i) that regular physical exercise has a positive effect on cardiac output, the maximum heart rate when exercising and the stroke volume [Giada et al. 1998, Jeschke and Zeilberger 2004, Perini et al. 2002] and (ii) that through regular physical exercise the risk of an acute cardiovascular event and the mortality can be reduced [Jeschke and Zeilberger 2004, Seals et al. 1994]. In addition, regular training is prophylaxis against falling.

Endurance training

Recommended level of exercise:

- **3 times per week endurance training** (cycling, walking, jogging) for more than 30 minutes, possibly using a cycloergometer or a step-trainer [Green and Crouse 1995, Jeschke and Zeilberger 2004].
- The **exercise intensity** should be at the **aerobic threshold** (lactate levels approximately 2 mmol/l), equivalent to a **pulse of approximately 180 minus age** [Asikainen et al. 2002, Jeschke and Zeilberger 2004, Liesen et al. 1975], minus 10 – 15% for patients who are given β -blockers. This means that the patient is still able to speak whilst doing the exercise.
- If intensity and duration of the exercise are kept at a medium level, aerobic fitness (ability to absorb oxygen) increases and therefore cardiovascular morbidity and mortality decrease [Löllgen 2003].
- Total daily activity (activity around the house and garden, daily walks) contributes to a lowering of the cardiovascular risk [Hakim et al. 1999, Jeschke and Zeilberger 2004].

Strength training

Regressive changes to the

- locomotor system (muscles, bones, cartilage, tendons and joints) and

- nervous system (loss of neurons in the brain and spinal cord [Akima et al. 2001, Jeschke and Zeilberger 2004, Lexell 1997]) determine the level of physical capacity and thus of physical independence in old age.

Consequences of these regressive changes are unstable joints, weak posture, lack of coordination. **The result are frequent falls.** One third of people over the age of 65 years fall at least once a year [Gulich 2008].

An increase in strength through exercise results in higher day-to-day physical capacity (e.g. when climbing stairs) even in the very old (80 – 100 years) and frail patients [Fiatarone et al. 1990, Löllgen 2003].

Amount of training (Appendix 1)

Exercise programs for strength should be competently led (so that they can be continued at home). The emphasis should be on:

- moving and stretching the whole body so that coordination and balance are improved (so-called proprioceptive training) and
- improving the strength of skeletal muscle.

Exercise routine [Mayer et al. 2003]

- At a level of approximately 60% of maximum strength against a resistant force (equivalent to tiring of the person exercising after lifting a weight 10 times)
- Each exercise (with 8 – 10 repetitions) should be repeated after a break of one minute
- A break of 2 – 3 days after each complete routine is necessary.
- **Important: raise intensity of training slowly.**

Use of physical exercise in treating patients with defined disease profiles

Moderate physical exercise (as non-drug treatment) is often more effective in treating chronic diseases than drug therapy, because the muscles are the largest metabolizing organ; e.g. this applies to

- high blood pressure,
- heart failure,
- coronary heart disease,
- asthma/COPD,

- stroke,
- diabetes mellitus,
- degenerative disease of the joints,
- depression
- and others (see exercise recommendations for each disease).

The positive effect of regular physical exercise on the cognitive functions of the brain has been shown. Regular training is advisable to prevent falls [Gardner et al. 2000].

Risks of physical exercise in old age

- The risk of acute myocardial infarction during moderate or light exercise does not increase with age [Jeschke and Zeilberger 2004, Mittleman et al. 1993, Muller et al. 1996].
- It does, however, increase with maximum physical strain (with an additional oxygen consumption up to 6 times of that at rest).
- Strength training will not result in serious injuries if adequate care is taken [Jeschke and Zeilberger 2004].

Summary of recommendations

- **Medical check-up** before training is commenced: patient history with respect to cardiovascular risk factors, clinical examination, ECG, if necessary ergometry, long-term blood pressure monitoring, echocardiography in case of clinically relevant signs that a cardiovascular disease is present, in case of RR > 160/100 blood pressure should be reduced before physical exercise is commenced.
- **Motor function capacity** can be evaluated with simple tests [Jeschke and Zeilberger 2004] (see basic geriatric assessment, risk of falling: This guideline: Chapter Cc Osteoporosis. *Int J Clin Pharmacol Ther.* 2009; 47 (3): 14; [Hausärztlich-Geriatri-sches Basisassessment 2004]; rising from a chair, walking a defined path, stair climbing, balance test: on both legs, on one leg, with eyes open and shut).

Training

- 1 Warm-up before exercising (loosening up, light jogging)

- 2 Avoid maximum strain [Jeschke and Zeilberger 2004]
- 3 Set training levels at pulse rate adequate for the age (170 minus age)
- 4 It may be necessary to increase strength before carrying out endurance exercises
- 5 Avoid impulse exercises, e.g. sprints or jumps
- 6 Avoid long-lasting holding exercises (anaerobic capacity is reduced in the elderly)

Suitable sports for seniors

- Walking (at varying pace and in various terrain (flat country, hills, mountains)), swimming, cycling, running, jogging, home training, table tennis, dancing

Sport under instruction

- Stretching, back-, water- and fitness-gymnastics, relaxation exercises, nordic walking, cross-country skiing, ski walking, tennis, golf

If the patient has been practicing sports since his/her youth, s/he can exercise more intensively (see recommendations on physical activity in Appendix 1).

References

- Akima H, Kano Y, Enomoto Y, Ishizu M, Okada M, Oishi Y, Katsuta S, Kuno SY.* Muscle function in 164 men and women aged 20 – 84 years. *Med Sci Sports Exerc.* 2001; 33: 220-226 {Ib}.
- Asikainen TM, Miilunpalo S, Oja P, Rinne M, Pasanen M, Uusi-Rasi K, Vuori I.* Randomised, controlled walking trials in postmenopausal women: the minimum dose to improve aerobic fitness? *Br J Sports Med.* 2002; 36: 189-194 {Ib}.
- Fiatarone MA et al.* High-Intensity strength training in nonagenarians. Effects on skeletal muscle. *JAMA.* 1990; 263: 3029-3034.
- Gardner MM, Robertson MC, Campbell AJ.* Exercise in preventing falls and fall related injuries in older people: a review of randomised controlled trials. *Br J Sports Med.* 2000; 34: 7-17 {Ia}.
- GCIS.* Guideline for the promotion of active ageing in older adults at primary level. Government Communication and Information System (GCIS) on behalf of the Department of Health; 2000. p. 1-25. Also: <http://www.doh.gov.za/docs/factsheets/guidelines/ageing/aging.pdf> (Guidelines not evidence based).
- Giada F, Bertaglia E, De Piccoli B, Franceschi M, Sartori F, Raviele A, Pascotto P.* Cardiovascular adaptations to endurance training and detraining in young and older athletes. *Int J Cardiol.* 1998; 65: 149-155 {IIa}.

- Green JS, Crouse SF.* The effects of endurance training on functional capacity in the elderly: a meta-analysis. *Med Sci Sports Exerc.* 1995; 27: 920-926 {Ia}.
- Gulich M.* Sturzprävention bei Senioren. Eine interdisziplinäre Aufgabe. *Z Allg Med.* 2008; 84: 116-119.
- Hakim AA, Curb JD, Petrovitch H, Rodriguez BL, Yano K, Ross GW, White LR, Abbott RD.* Effects of walking on coronary heart disease in elderly men. The Honolulu heart program. *Circulation.* 1999; 100: 9-13 {IIb}.
- Hausärztlich-Geriatisches Basisassessment.* Berlin: Institut für Hausärztliche Fortbildung im Deutschen Hausärzterverband (IhF Köln); 2004.
- Jeschke D, Zeilberger K.* Altern und körperliche Aktivität. *Dtsch Arztebl.* 2004; 101: A789-A798.
- Lexell J.* Effects of physical exercise and training on skeletal muscle function in old age. In: Huber G (ed). *Health aging, activity and sports.* Gamburg: Health promotion publications. 1997; p. 98-103.
- Liesen H, Heikkinen E, Suominen H, Michel D.* Der Effekt eines 12-wöchigen Ausdauertrainings auf die Leistungsfähigkeit und den Muskelstoffwechsel bei untrainierten Männern des 6. und 7. Lebensjahrzehnts. *Sportarzt Sportmed.* 1975; 2: 26-30.
- Löllgen H.* Primärprävention kardialer Erkrankungen: Stellenwert der körperlichen Aktivität. *Deutsches Ärzteblatt.* 2003; 100: A987-A996.
- Mayer F, Gollhofer A, Berg A.* Krafttraining mit Älteren und chronisch Kranken. *Deutsche Zeitschrift für Sportmedizin.* 2003; 54: 88-94.
- Mittleman MA, Maclure M, Toftler GH, Sherwood JB, Goldberg RJ, Muller JE.* Triggering of acute myocardial infarction by heavy physical exertion. *N Eng J Med.* 1993; 329: 1677-1683 {IIb}.
- Muller JE, Mittleman A, Maclure M, Sherwood JB, Toftler GH.* Triggering myocardial infarction by sexual activity: low absolute risk and prevention by regular physical exertion. *JAMA.* 1996; 275: 1405-1409 {III}.
- Perini R, Fisher N, Veicsteinas A, Pendergats DR.* Aerobic training and cardiovascular responses at rest and during exercise in older men and women. *Med Sci Sports Exerc.* 2002; 34: 700-708 {IIb}.
- Seals DR, Taylor JA, NG AV, Esler MD.* Exercise and ageing: autonomic control of the circulation. *Med Sci Sports Exerc.* 1994; 26: 568-576.

Appendix 1. Recommendations on regular physical activity

Target group	Activity	Organization
All patients/subjects	Basic program Purpose-oriented daily activities, as long as possible independently. No delegation, no over-protection. Avoid assistance systems for locomotion (climb stairs, do not use lifts, shopping/visits on foot or by bicycle). Stay with motor exercises during leisure time (e.g. gardening) for as long as possible, or take up new ones (e.g. walking a dog).	Independently
Inactive patients Without manifest diseases. Following a general health check by a physician.	Exercise routine Start: exercise coordination, flexibility and strength Frequency: 1 – 3 times/week Duration: 30 – 60 minutes Examples: bench exercises, whole body gymnastics, aerobic exercises (for seniors), Tai Chi, dancing	Group exercise program led by a competent trainer
	Extension/addition: aerobic endurance training Frequency: 3 times/week Intensity: around the aerobic threshold (ca. 2 mmol/l lactate) (moderate) 45 – 65% VO ₂ max; 15 – 30 kJ/min Heart rate: approximately 170 minus age Duration: 15 – 60 minutes to hours Additional energy consumption: ≥ 4,000 kJ/wk (60 kJ/kg body weight/wk) Examples: walking (variation in pace and terrain), nordic walking, ski walking, golf, cycling exercises, cycling in flat country, swimming	Group exercise program led by a competent trainer advisable, at least until routines have been mastered (e.g. nordic walking, golf, ski walking; independently (look for a partner))
Following prior diagnostic by a specialist sports physician	Extension: strength training (concentric, excentric, dynamic, if appropriate static) Frequency: 1 – 3 times/week Intensity/repetitions: 65% RM, 8 – 12 times/muscle group. 75 – 85% RM, 8 – 6 times/muscle group Static: max. 3 sec. holding, 3 – 5 times/muscle group Equipment: body's own weight, small dumbbells, elastic bands of varying stiffness, equipment for training strength Always warm up and cool down with stretching exercises, take breaks	Individual or group exercise led by a competent trainer

VO₂ = oxygen absorption rate; kJ = kilo-joule; RM = maximum load that one can master dynamically only once; wk = week.

Appendix 1. Continuation.

Target group	Activity	Organization
<p>Physically active patients After diagnosis by a specialist sports physician</p>	<p>Complex, seasonal training/sports program Frequency: > 3 times/week Duration: > 1 h/component Additional energy consumption: > 8,000 kJ/wk (120 kJ/kg body weight/wk) Endurance sports: try to retain/improve coordination, flexibility and strength. Games sports: try to retain/improve endurance as well as strength in all body parts</p>	<p>For balancing exercises employ competent trainer, on an individual basis or in a group</p>
<p>Disabled, immobilized, or chronically ill patients Following a general health check by a physician</p>	<p>Motion therapy Coordination, flexibility, strength retention and improvement, improvement of aerobic endurance. Frequency, stationary: daily; partly stationary: 3 – 4 times/week. Group: 1 – 2 times/week. Additionally 3 – 4 times/week independent exercise, especially endurance, for 30 – 60 minutes within set intensity range</p>	<p>Start with individual exercises, later in groups led by competent trainer, if necessary under medical supervision. Stationary, partly stationary, individual physiotherapy, ergotherapy. Groups according to disease: heart, diabetes, rheumatism, asthma</p>

VO₂ = oxygen absorption rate; kJ = kilo-joule; RM = maximum load that one can master dynamically only once; wk = week [Jeschke and Zeilberger 2004.



Pharmacotherapy guidelines for the aged by family doctors for the use of family doctors

Part D Basic conditions supporting drug treatment

Part E Guidelines group, disclaimer, internet addresses

Version 1.07, April 18th, 2007, Revision up to December 2008 was translated.
Version 1.00, December 2008 "Hausärztliche Leitlinie Geriatrie" was also considered.

Guidelines Group Hesse: Pharmacotherapy Guidelines by Family Doctors for Family Doctors

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Key words

elderly patients – management of therapy – family doctors – GP – age-associated diseases – course of illness – chronically ill – multiple medication – patient medication history – age-appropriate dosage – interface hospital – follow up on therapy progress

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C Special Pharmacology of the aged

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Chapter

D c) Management of age-associated diseases in the elderly by family doctors

Abstract. The family doctor plays a special role in the health system. S/he looks mainly after chronically ill, elderly and multi-

morbid patients and strives to control the course of disease of these patients with the aid of their own multiple mostly pharmaco-therapies as well as those of other specialists. Evidence-based recommendations that support G.P's in the therapy of their patients are lacking. Therefore, the Hesse Guidelines Group has put together these guidelines to support family doctor's in the drug therapy of the aged. **General rules for the management of age-associated diseases by family doctors are:** Before prescribing medication for the elderly patient the family doctor is required to carry out a thorough **check of the patient's pharmacotherapy** including self-medication and drugs prescribed by other doctors. Key questions for family doctors are: Is the therapy causal or symptomatic? Can therapy goals be arranged according to priority in order to avoid unnecessary medication? Which interactions and side effects must be expected? Does the patient understand and accept the prescription? **Interface hospital:** As a rule, the family doctor is in charge of managing the therapy and takes sole responsibility for the prescriptions after a patient has been discharged from hospital – (including economic and legal aspects). The framework for choosing medication in an out-patient environment differs from that in a hospital. **Following-up the progress of therapy:** The patient history (questions on previous incompatibilities, additional OTC-drugs taken, drugs prescribed by other doctors), progress checks and close observation of the effects determine the therapeutic approach because at any given time not all possible negative influences on the efficacy of the medication can be known. Elderly patients should always **begin drug therapy with a low dose** in order to reach the required maintenance dose (and steady-state) and which, as a rule, **will be low** without over-shooting.

Part D Basic conditions supporting drug treatment

c) Management of age-associated diseases in the elderly by family doctors

Key questions for family doctors

The pharmacokinetics and pharmacodynamics of drugs in the elderly are particularly variable.

Decisions regarding therapy have frequently to be made without recourse to evidence-based studies because most studies exclude the older, multi-morbid patient (GCP

Good Clinical Practice [Witte et al. 1995]). As a result only limited standardized therapy recommendations are available.

Before prescribing medication for an elderly patient the family doctor is required to carry out a thorough check of the previous pharmacotherapy in the patient and obtain answers to the following questions:

- Is the therapy causal or symptomatic?
- Is a symptomatic therapy necessary?
- In consultation with the patient/relatives: can therapy goals be arranged according to priority in order to avoid unnecessary medication?
- Which drugs can be discontinued so that the patient is not subject to too much medication?
- What other drugs as self-medication or drugs prescribed by other doctors does the patient take? Which of these may be left out?
- Which interactions and side effects must be expected in view of the patient's age and the medication the patient is taking (risk assessment in consultation with the patient)?
- Is the dosage of medication appropriate for the elderly patient? Is it administered appropriately?
- Does the patient understand and accept the prescription and does a relative or a person looking after the patient need to be informed and trained?
- Which of the drugs recommended by hospital physicians should be prescribed after discharge from hospital?
- Can the patient be motivated to undertake activating, non-drug measures (e.g. physical exercise or training, walking, gardening)?

Interfaces

The family doctor is generally in-charge of managing the therapy.

The problems frequently encountered during the long-term care of the elderly following their discharge from (a geriatric) hospital are:

- **Prescriptions after discharge from hospital – the family doctor takes sole responsibility (economically and legally) for these.**

- Accepting the recommendations of hospital doctors does not necessarily result in a safe and sensible therapy.
- Hospital stays are becoming continually shorter but the pharmacokinetics of a drug do not attain a steady state until after 4–5 half-lives. This means that the stay in hospital is often not long enough to ascertain the full efficacy and compatibility with other therapies. If several interacting agents are prescribed, this situation becomes even more acute.
- All hospital pharmacies need to take into account economic considerations when making stocking decisions, e.g. the pharmaceutical industry often makes pharmaceutical preparations available to hospitals gratuitously. Thus, the framework for choosing medication in a hospital environment and in out-patient care differ.

Examples of further interfaces, depending on the nature of the disease:

- Out-patient specialists
- Physiotherapists
- Care services, homes for the aged and day-clinics
- Social services
- Relatives and carers

Social networking

Regular contact with the family doctor has an important social function for the elderly.

In particular, home visits are a chance to gain an insight into the daily life of the multimorbid patient. The altered circumstances after moving to a care institution are critical for health and mental well-being in the elderly and the family doctor will give these patients special attention to assure stable physical and mental health.

Even the consultations at the surgery provide insights into the lifestyle and its possible deficits (e.g. regarding clothing, cleanliness, physical and mental capacities). This is the only way for the family doctor to fulfil his/her role as the patient's agent in coordinating the various care services (see Interfaces).

The social network of older people contracts, mainly due to deaths ("The number of friends among the dead continues to increase." Max Frisch). Chronic diseases, especially physical immobility and mental illness in-

crease. As a result, the elderly experience increasing isolation (lower number of social contacts) and loneliness (the quality of the social contacts does not meet their expectations). This can be overcome through "Assisted living" and other forms of living (e.g. shared housing), daycare, or looking after pets. "Social networking" is one of the tasks the family doctor has to perform in looking after the elderly.

Follow-up on progress of therapy [Köppel 2003]

Family doctors require comprehensive information on the characteristics and possible risks of the medication used (both prescribed and OTC) and the number of agents administered should be as small as possible [Cusack and Parker 1996, Köppel 2003, Mühlberg 2004, von Renteln-Kruse 2000].

Details of the patient history (questions on previous incompatibilities, additional OTC-drugs taken, drugs prescribed by other doctors), progress checks and a close observation of the effects determine the therapeutic approach, because all the negative influences on the effectiveness of a drug or therapy are not known.

Follow-ups are necessary up to the time a steady state has been reached (after 4–5 half-lives) and also later, especially when a therapy is modified after discharge from hospital or when other specialists also prescribe drugs. A further point is that interactions and ADRs are often overlooked since multi-medication is common, self medication increases this problem and co-treatment is often of short duration.

Elderly patients should always begin drug therapy with a dosage lower than the maintenance dose in order to settle on the maintenance dosage slowly (after reaching the steady-state), which, as a rule, will be low. This follow-up is an important task of the family doctor.

Compliance

[Lim and Woodward 1999, Miller et al. 1997, Platt and Mutschler 1999, Williams 2002]

In any drug therapy, in order to attain good therapeutic effectiveness and, thus, good pa-

tient compliance, a doctor should aim to optimize the main effect, recognize unwanted side effects early and modify the therapy accordingly (see General Pharmacology in the aged, Part B Appendix 3: Drugs that are a problem in older patients, IJCPT 46: 613, 614).

According to the Berlin Age Study (Berliner Altersstudie 1996) more than 50% of the over-70s take five or more *prescribed or OTC* drugs simultaneously. The rate for five or more *prescribed* drugs was 24% [Mayer and Baltes 1996 Berliner Altersstudie, Fourth report on the situation of the older generation 2002]. As data from various countries show, 4 – 6% of hospitalizations are the result of ADRs [Hartmann 2003, von Renteln-Kruse 2000].

Since about 50% of aged patients [Bovet et al. 2002, Estler 1997, Sackett et al. 1979] do not comply with prescription instructions [Mayer and Baltes 1996, Reymond and Marty 2003, The Merck Manual of Geriatrics 2005], special efforts by the doctor are needed to foster compliance [Cummings et al. 1995, Reymond and Marty 2003, von Renteln-Kruse 2000, Wen and Woodward 1999] and these are summarized as follows:

- Detailed, patient-oriented information (if necessary, also given to a relative or carer) on the importance and the desired effect of the prescribed medication has been shown to improve compliance [Morisky et al. 1983, Reymond and Marty 2003, The Merck Manual of Geriatrics 2005].
- Simple and clear drug-taking schedules with times of intake appropriate for the elderly have also helped in this regard [Cusack and Parker 1996, Reymond and Marty 2003].
- Aides (e.g. Dosett) for the provision of daily or weekly drug rations are also useful [Lauterburg 2005, Wong and Norman 1987]
- Single daily doses rather than multiple daily doses [Birks et al. 2006, Penfornis 2003, Platt and Mutschler 1999]. An increase in the number of pills to be taken daily reduces compliance [Platt and Mutschler 1999, Reymond and Marty 2003, Fourth report on the situation of the older generation 2002, von Renteln-Kruse 2004].

- The prescription should take account of appropriate packaging and presentation.

The factors which have a negative effect on compliance should be avoided

[Reymond and Marty 2003, Fourth report on the situation of the older generation 2002]:

- Problems associated with child-proof caps [Kendrick and Bayne 1982, Quality medication care group 2004]
- Hard blister packs
- Drop measuring when the patient suffers from impaired vision
- Suppositories when the patient suffers from impaired mobility
- Pills or capsules that are too large for patients who have difficulties in swallowing

In addition

- Main problem: Interactions – (see chapter B of this guideline: IJCPT 46: 604 – 616) Ideally no more than three or four pills [Köppel 2003] should be prescribed although this may not always be possible.
- Pharmacotherapy for aged patients should be restricted to the absolutely necessary [Mühlberg et al. 1999, von Renteln-Kruse 2004].
- Ensure that pills can be cut, beware of “aut idem”-prescriptions, if necessary write dosage on prescription.
- The family doctor and his/her staff should monitor prescriptions and check that the time the medication is being taken is as prescribed [Beers et al. 1991, Platt and Mutschler 1999]
- Introduce alterations in therapy slowly [Cusack and Parker 1996].

Summary of principles

[Fischer 1992, Resnick 1999, Wagner 2004]

a) **The chief parameter here is the biological age** [Fischer 1992, Kruse A 1996]. It is important to distinguish between normal ageing and disease-inducing processes that coincide with ageing. This should be conveyed to the patient.

b) Prior to any pharmacotherapy – especially for aged patients – it must be **ascertained (i) whether such a therapy is neces-**

sary at all and (ii) whether success is likely [Kruse W 1994, Monane et al. 1996, von Renteln-Kruse 2000].

c) No therapy without a comprehensive **patient pharmacotherapy history** [Wagner 2004].

d) **Treat the main underlying diseases**, not the symptoms [Kruse W et al. 1991, McGavock 1995].

e) Consider: a symptom may be the **side effect of pharmacotherapy**.

f) In the case of elderly patients, drugs should always be prescribed **to achieve the desired effect with the lowest possible dose**. No therapy according to the principle “one size fits all” [Wagner 2004].

g) Beware of rare, **unexpected side effects** [Wagner 2004].

h) **Cease pharmacotherapy as soon as it is no longer needed**. No routine permanent therapies [Monane et al. 1996, Wagner 2004].

i) **Monitor compliance**, the mental and physical capacity of the patient and his/her circumstances to ensure that unnecessary therapies are not forced on the patient by the doctor nor carried out because of demands of the patient and those looking after the patient e.g. relatives [Wagner 2004].

“LESS IS MORE!” is often true of pharmacotherapy in the aged. However, this is an ideal and a goal which may not always be attainable. Whenever possible try to administer no more than three substances [Drug Commission of the German Medical Association 1997, Cadieux 1989, Cockgroft and Gault 1976, Resnick 1999, von Renteln-Kruse 2000, Wagner 2004].

References

- Beers MH et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med. 1991; 151: 1825-1832.
- Birks JS et al. Cholinesteraseinhibitors in Alzheimer's Disease, Cochrane Review in: The Cochrane Library Issue 1 2006: Oxford Update Software.
- Bovet P et al. Monitoring one-year compliance to anti-hypertension medication in the Seychelles. Bulletin of the World Health Organization. 2002; 80: 33-39 {Ib}.
- Cadieux R. Drug interaction in the elderly. How multiple drug use increases risk exponentially. Postgraduate Medicine. 1989; 86: 179-186.
- Cockgroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976; 16: 31-41.
- Cummings SR, Nevitt MC, Browner WS et al. Risk factors for hip fracture in white women. N Engl J Med. 1995; 332: 767-773 {Ib}.
- Cusack BJ, Parker BM. Pharmacology and appropriate prescribing. In: Reuben DB, Yoshikawa TT, Besdine RW (eds). Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine, 3. edition. New York: American Geriatrics Society; 1996. p. 35.
- Drug Commission of the German Medical Association. Arzneimittelverordnungen. 18. Auflage. Köln: Deutscher Ärzteverlag; 1997. 754-758.
- Estler CJ. Arzneimittel im Alter. Wissenschaftliche Verlagsgesellschaft Stuttgart; 1997.
- Fischer G. Krankheit bei alten Menschen. In: Kochem MM (ed). Allgemeinmedizin, Stuttgart: Hippokrates-Verlag; 1992. p. 284-292.
- Guidelines Group Hesse, Bergert WF, Braun M, Clarius H, Ehrental K, Feßler J et al. Hausärztliche Leitlinie, Geriatrie – Teil 1; 2008. http://www.pmvforschungsguppe.de/pdf/03_publicationen/geriatrieI_II.pdf
- Hartmann K. Arzneimittelsicherheit. In: Jaehe et al. (eds). Lehrbuch der klinischen Pharmazie. 2. Auflage. Stuttgart: Wissenschaftliche Verlagsgesellschaft. 2003. p. 165-183.
- Jaeschke R, Guyatt GH, Sackett DL. Users' guide to the medical literature. III How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence Based Medicine Working Group. YAMA. 1994; 271: 703-707.
- Kendrick R, Bayne JR. Compliance with prescribed medication by elderly patients. Can Med Assoc J. 1982; 127: 961-962 {III}.
- Köppel C. Pharmakotherapie im Alter, Berliner Ärzteblatt 05.11.2003.
- Kruse A. Gesundheit und Kompetenz im Alter: Aufgaben der Prävention und Rehabilitation im Alter. In: Althoff PG (ed). Präventivmedizin. Berlin: Springer; Loseblatt Sektion 06.02 Geriatrie, 1996.
- Kruse W. Medikamente in der Geriatrie: Probleme bei der Arzneimittelanwendung und Lösungsmöglichkeiten. Expertise im Auftrag des Bundesministeriums für Familien und Senioren. Stuttgart, Berlin, Köln: Kohlhammer-Verlag; 1994.
- Kruse W, Rampmeier J, Frauenrath V et al. Drug prescribing pattern in old age. Eur J Clin Pharmacol. 1991; 41: 441-447.
- Lauterburg B. Grundlagen der Pharmakotherapie 25.01.05 Institut für klinische Pharmakologie Universität Bern [<http://www.cx.unibe.ch/ikp/lab3/pharmakotherapie/html>].
- Lim WK, Woodward MC. Improving medication outcomes in older people. Aust J Hosp Pharm. 1999; 29: 103-107 {eR}.
- Mayer KU, Baltes MM. Die Berliner Altenstudie (BASE). Berlin: Akademischer Verlag; 1996; 2nd edition 1999.
- McGavock H. Precision Prescribing. The Drug Utilisation Research Unit, Queen's University of Belfast; 1995.
- Miller NH, Hill M, Kotke T, Ockene IS. The multilevel compliance challenge: recommendations for a call to action. Circulation. 1997; 95: 1085-1090 {eR}.
- Monane M, Glynn R, Avorn J. The impact of sedative-hypnotic use on sleep symptoms in elderly nursing home residents. Clin Pharmacol Ther. 1996; 59: 83-92.
- Morisky DE, Levine DM, Green LW, Shapiro S, Russell RP, Smith CR. Five year blood pressure control and mortality following health education for hypertensive patients. Am J Public Health. 1983; 73: 153-162 {Ib}.

- Mühlberg W. Häufige Arzneimittel-Nebenwirkungen und Interaktionen im Alter [http://www.alter-nativen.ch/pdf/muehlberg2.pdf], Autoreferat vom 4. Münsterlinger Symposium zur Alterspsychologie, September 2004.
- Mühlberg W, Platt D, Mutschler E. Neben und Wechselwirkungen von Pharmaka im Alter. In: Platt D, Mutschler E (eds). *Pharmakotherapie im Alter*, 3. Auflage. Stuttgart: Wissenschaftliche Verlags Gesellschaft; 1999. p. 21-32.
- Penformis A. Drug compliance in type 2 diabetes: role of drug treatment regimens and consequences on their benefits. *Diabetes Metab.* 2003; 29: 31-37.
- Platt D, Mutschler E (eds). *Pharmakotherapie im Alter*, 3. Auflage. Stuttgart: Wissenschaftliche Verlags Gesellschaft; 1999; p3-32.
- Quality medication care group. Dose administration aids. p. 1-45 [http://www.guild.org.au/public/researchdocs/daalitreview2004.pdf] {eR}.
- Resnick NM. Geriatric Medicine. In: Tierney LM, McPhee SJ, Papadakis MA (eds). *Current Medical Diagnosis and Treatment*, 38. Aufl., Stamford, Connecticut: Appleton & Lange; 1999. p. 45-67.
- Reymond JP, Marty S. In: Jaehde U, Radziwill R, Mühlebach S, Schunack W (eds). *Lehrbuch der klinischen Pharmazie*, Wissenschaft. Stuttgart: Verlags-gesellschaft; 2003. p. 205-212.
- Sackett DL, Snow JC. The magnitude of adherence and nonadherence. In: Haynes RB, Taylor DW, Sackett DL (eds). *Compliance in health care*. Baltimore: John Hopkins University Press; 1979. p. 11-22.
- The Merck Manual of Geriatrics*. Chapter 6: Clinical Pharmacology: Pharmacokinetics, Pharmacodynamics, Adverse Drug Reactions, Considerations for Effective Pharmacotherapy. Continuously updated version. 2005.
- Fourth report on the situation of the older generation*. Sachverständigenkommission der Bundesregierung, Bundesministerium für Familie, Senioren, Frauen und Jugend; 2002. 161-163 [http://www.bmfsfj.de].
- von Renteln-Kruse W. Pharmakoepidemiologie und Erkenntnisse zur Arzneimitteltherapie im Alter. In: Schubert I, Ihle P (eds). *Entdeckungspfade des Public Health*. Essen: Bundesverband der Betriebskassen; 2000. p. 113-130.
- von Renteln-Kruse W (ed). *Medizin des Alterns und des alten Menschen*. Darmstadt: Steinkopf-Verlag; 2004. p. 74-76.
- Wagner B. Haben Sie einen kritischen Blick auf betagte Patienten? *Der Hausarzt*. 2004; 6: 38-39.
- Wen KL, Woodward MC. Improving medication outcomes in older people. *Australian J of Hospital Pharmacy*. 1999; 29: 103-107.
- Williams CM. Using medications appropriately in older adults. *Am Fam Physician*. 2002; 66: 1917-1924 {eR}.
- Witte PU et al. *Ordnungsgemäße klinische Prüfung (Good clinical Practice)*, 4. Auflage. Berlin: Habrich; 1995.
- Wong BS, Norman DC. Evaluation of a novel medication aid, the calendar blister pack, and its effect on drug compliance in a geriatric outpatient clinic. *J Am Geriatr Soc*. 1987; 35: 21-26 {Ib}.

E Guidelines group, disclaimer, internet addresses

a) Information concerning the Hesse Guidelines Group (HGG)

The purpose of guidelines for family doctors

At present, there is a multitude of guidelines, but practical recommendations that relate to the typical cases frequently encountered by family doctors are lacking. Since 1993 the Hesse Association of Statutory Health Insurance Doctors has run regular pharmacotherapy circles. From the group of physicians who chair these circles, the HGG "Pharmacotherapy for Family Doctors" was formed in 1998 in cooperation with Senior Lecturer Dr. Liselotte von Ferber (former head of the Primary Health Care Research Group (PMV forschungsgruppe), Cologne). The Hesse Guidelines Group set out to prepare practical therapy recommendations relevant and applicable to the work of family doctors.

Family doctors regularly look after chronically ill, old and multi-morbid patients and guidelines need to reflect this. When searching the literature for studies that support therapy recommendations, one discovers that such patients are generally excluded from clinical studies for methodological reasons. These studies frequently define an upper age limit and a maximum of just one accompanying disease. This means that the application of study results to a typical group of multi-morbid patients in the care of a family doctor needs to be assessed very carefully [Jaeschke et al. 1994]. In addition, one needs to be aware that common therapies based on multiple medication lead to interactions and compliance problems which are difficult to foresee. The family doctor must therefore select the medication accordingly.

Drug selection according to the Guidelines for Family Doctors

The HGG wishes to support the family doctor in his or her drug selection. As a rule, the group therefore limits its list of substances to those which it considers to be the agents of choice based on the following:

- a) The agent has been given a positive risk-benefit-ratio.
- b) It is well documented.
- c) There is a consensus among the members of the guidelines group on the long-term positive application of the agent by family doctors.

It should be noted that in the event of a contraindication or incompatibility, other substances, indicated but not mentioned in the guidelines, should be chosen. These considerations include the recommendation that a therapy should only be started if it is highly likely that a therapeutic benefit can be achieved in a comparatively large number of patients. The number of patients needed to treat (NNT) to achieve success in just one patient should always be taken into account. Furthermore, the doctor needs to consider the possible harm a substance can do, i.e. must know the number needed to harm (NNH).

Special demands on family doctors

The family doctor is the main contact person for chronically ill patients and he or she must take into account the monitoring of therapeutic success according to clinical standards, age-associated factors, interactions and side effects and aspects other than those concerning the patient in hospital e.g. compliance and the quality of life of the patient as well as shared decision making. The doctor must also consider whether a therapy is economical and this includes the employment of non-drug measures which are rated highly by the guidelines and for which studies and evidences, when available, are presented.

Limiting the list of substances to use is in accordance with strategies to assure the quality of prescription practices by family doctors, as demanded and employed by the WHO [Cockcroft and Gault 1976] and is within the framework of quality-based continuing-education and quality assurance programs in other countries.

Implementation and evaluation of the guidelines

The guidelines prepared by the Hesse Guidelines Group are first discussed with the

moderators of the pharmacotherapy circles, edited if necessary, and then implemented through the circles. Each participant is not only given a copy of the guidelines but also material (so-called manuals) on the topic of the circle meeting containing an introduction to the disease to be discussed and its therapy. The material also includes a prescription analysis based on the participating doctors' prescriptions and diagnoses which, with the aid of key indicators, shows the state of implementation of the recommendations in the guidelines relating to pharmacotherapy.

When the circle completes its work, an evaluation follows, i.e. data describing the prescription practices before and after the work of the circle relating to indicators rating the quality and economy of a therapy are presented and discussed at a circle meeting.

In order to obtain an indication of the relevance and acceptance of the recommendations in the Guidelines, the Primary Health Care Research Group (PMV forschungsgruppe) carries out a brief survey at each circle meeting. The results are presented to both the circle participants and the guidelines group.

b) Disclaimer

Legal points regarding use of the guidelines – disclaimer:

a) Guidelines for family doctors are addressed to physicians. Inquiries from patients cannot be dealt with. The therapy recommendations do not constitute advice for patients on how to treat themselves.

b) The guidelines have been prepared with care by physicians and members of the HGG with reference to the latest literature available. However, no liability can be taken for their correctness or completeness.

c) Details of dosages have been prepared on the basis of the most recent pharmacological literature and information provided by the pharmaceutical companies. However, here too the user takes sole responsibility; prescription decisions are to be made on the basis of the advice provided in the leaflet inside the package and specialist information. Details on interactions and side effects refer only to a selection of those possible.

c) Internet addresses

Free download of the English version of the complete **Pharmacotherapy guidelines for the aged** can be obtained by opening the internet page of the **International Journal of Clinical Pharmacology and Therapeutics** at

<http://www.dustri.com/nc/journals-in-english/mag/int-journal-of-clinical-pharmacology-and-therapeutics.html>

and accessing the various parts of the guidelines in relation to the month of publication or,

alternatively, by going to the internet side of the PMV forschungsgruppe (Primary Health Care Research Group) at

http://www.pmvforschungsgruppe.de/content/03_publicationen/03_a_chrono_2009/oldage_ll.pdf.

This page lists all the parts of the guidelines together.

The newly edited German version of the guidelines “Hausärztliche Leitlinie, Geriatrie – Teil 1, Allgemeine Geriatrie Version 1.0, 2008” can be found and downloaded at

www.pmvforschungsgruppe.de/pdf/03_publicationen/geriatrie1_ll.pdf

“Hausärztliche Leitlinie, Geriatrie – Teil 2, Spezielle Geriatrie Version 1.0, 2008” at

www.pmvforschungsgruppe.de/pdf/03_publicationen/geriatrie2_ll.pdf

The Hesse Guidelines Group and the PMV forschungsgruppe have also published guidelines on:

- Anticoagulation
- Bronchial asthma and COPD
- Chronic cardiac failure
- Communication between the patient and Family Doctor
- Diabetes mellitus Type 2
- Diseases of fat metabolism
- High blood pressure
- Palliative care
- Pain
- Psychosomatic medicine
- Stable angina pectoris
- Thrombosis of the veins

The German version of these guidelines as well as the General Guidelines Report can be found at

<http://pmvforschungsgruppe.de>publikationen>Leitlinien>