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-Pelcevski 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


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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


General practitioners, Association of Statutory Health Insurance Physicians in Hesse (Kassenärztliche Vereinigung in Hessen (KVH) Frankfurt (Main)), Germany

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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 thrombose

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-
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

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
[Beaufreere 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-
patients 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

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 ($C_{\text{creat}}$). (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


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, sulfipyrazole), 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**


Because multi-medications are 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 syncopes
- 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


h) Appendices Part B

<table>
<thead>
<tr>
<th>Drugs whose dose must be lowered in elderly patients</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-Blocker</td>
<td>hydrophilic: increase in plasma concentration due to lower distribution volume; special risk because of exsiccosis</td>
</tr>
<tr>
<td>Amino glycoside (amilacin, gentamycin, kanamycin, neomycin, netilmicin, streptomycin, tobramycin)</td>
<td>renal elimination: risk of accumulation in cases of kidney failure, higher in cases of exsiccosis, additional risk of ototoxic effects</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>lipophilic: build-up of reservoirs due to increased distribution volumes, extended period of effectiveness</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>hydrophilic, see above</td>
</tr>
<tr>
<td>Antipyrine</td>
<td>hydrophilic, see above</td>
</tr>
<tr>
<td>Benzodiazepine (e.g. diazepam, nitrazepam, oxazepam)</td>
<td>lipophilic, see above; in addition, possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
<tr>
<td>Benzodiazepine (e.g. diazepam, nitrazepam, oxazepam)</td>
<td>hydrophilic, see above</td>
</tr>
<tr>
<td>Benzylpenicillin</td>
<td>renal elimination, see above</td>
</tr>
<tr>
<td>\beta-Blocker</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver, however, reduced sensitivity in older patients [Bach et al. 1995]</td>
</tr>
<tr>
<td>Captopril</td>
<td>renal elimination, see above</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>renal elimination, see above</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>renal elimination, see above</td>
</tr>
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<td>Quinidine</td>
<td>renal elimination, see above</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>lipophilic, see above</td>
</tr>
<tr>
<td>Digoxin</td>
<td>renal elimination, see above</td>
</tr>
<tr>
<td>Dihydrostreptomycin</td>
<td>renal elimination, see above; additional risk of ototoxic effects</td>
</tr>
<tr>
<td>Diliazem</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
<tr>
<td>Furosemide</td>
<td>lipophilic, see above</td>
</tr>
<tr>
<td>Glyceryl trinitrate and other nitrates</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
<tr>
<td>Imipramine</td>
<td>possibly excessive blood levels due to decreasing metabolism in the liver</td>
</tr>
</tbody>
</table>
## Appendix 1b. Drugs whose dose must be lowered in older patients (cont.)

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

### Appendix 2a. Characteristics of combinations of drugs.

<table>
<thead>
<tr>
<th>Combinations of drugs that cause problems in elderly patients or carry special risks</th>
<th>Reason: cytochrome interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine such as diazepam, flunitrazepam, triazolam + Grapefruit-juice</td>
<td>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</td>
</tr>
<tr>
<td>Buspirone + Grapefruit-juice</td>
<td>Is metabolized through CYP 3A4 contains bioflavines which block CYP 3A4: even sporadic use of buspirone can lead to fatal accumulation</td>
</tr>
<tr>
<td>Citaprolam + 2. SSRI (fluoxetin or paroxetin in low doses)</td>
<td>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 = &quot;poor metabolizer&quot;, i.e. intended amplification of effectiveness in these patients</td>
</tr>
<tr>
<td>Codeine + Tramadol</td>
<td>Prodrug, is metabolized in the body to morphine through CYP 2D6 &quot;poor metabolizers&quot; can have very low levels of CYP 2D6: these patients experience only mild analgesia</td>
</tr>
<tr>
<td>Clopidogrel + Atorvastatin or Simvastatin</td>
<td>Is transformed into the effective thiometabolite through CYP 3A4 and other cytochromes both block CYP 3A4, the effectiveness of clopidogrel is weakened</td>
</tr>
<tr>
<td>Digoxin + Substances made from St. John’s wort</td>
<td>Elimination through CYP 3A4 weakening of digoxin effectiveness through CYP 3A4 induction of the substances made from St. John’s wort</td>
</tr>
<tr>
<td>Nicotine + Bupropion</td>
<td>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</td>
</tr>
<tr>
<td>Nicotine, tobacco smoke + Theophylline</td>
<td>Tar components of the smoke induce CYP 1A2 and 3A4 metabolism is controlled by CYP 1A2: theophylline effectiveness significantly weakened</td>
</tr>
</tbody>
</table>
### Appendix 2b. Characteristics of combinations of drugs (cont.)

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

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

<table>
<thead>
<tr>
<th>Drugs that are a problem in older patients</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides + Furosemide</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong> through damage to the vestibular nerve with defective sense of balance</td>
</tr>
<tr>
<td>Analgesics (morphine, morphine derivatives)</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong></td>
</tr>
<tr>
<td>Antidepressants, neuroleptics</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong>, risk increases with sedative potency</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>increased number of undesirable side effects: <strong>syncopes</strong>, lower sensitivity of the baroreceptors and reduced vein tonicity</td>
</tr>
<tr>
<td>Antihypertensives + Psychopharmaca + Nitrates</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong> due to low blood pressure, especially at start of therapy with exsiccosis and existing high blood pressure</td>
</tr>
<tr>
<td>Anti-parkinson agent + Antihypertensives</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong> in case of higher sensitivity to drugs that affect the CNS</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>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</td>
</tr>
<tr>
<td>Digitalis + Diuretics</td>
<td>increased number of undesirable side effects: <strong>syncopes</strong>, increased risk of bradycardia due to a lowered excitement threshold of N. vagus. In addition increased digitalis sensitivity with dysrhythmia due to hypokalemia</td>
</tr>
<tr>
<td>Diuretics</td>
<td>increased number of undesirable side effects: <strong>syncopes</strong>, fall in <strong>blood pressure</strong>, increased loss of fluids with reduced feelings of thirst, low blood pressure beyond hypovolemia due to reduced sensitivity of the baroreceptors</td>
</tr>
<tr>
<td>Diuretics</td>
<td>increased number of undesirable side effects: <strong>acute state of confusion</strong> due to risk of exsiccosis, often falls with fractures of the hip joint</td>
</tr>
<tr>
<td>Diuretics, potassium-saving (triamterene, amiloride), if applicable + thiazide-diuretic</td>
<td>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</td>
</tr>
<tr>
<td>Diuretic (loop-diuretic) + thiazide-diuretic + low NaCl diet</td>
<td>in therapies of cardiac insufficiency, increased number of undesirable side effects: <strong>acute renal failure</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drugs that are a problem in elderly patients</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin + Sulfonyl carbamides</td>
<td>increased number of undesirable side effects: acute state of confusion due to hypoglycemia</td>
</tr>
<tr>
<td>Midazolam + simultaneous use of opioids</td>
<td>significantly increased risk of breathing and cardiac arrest</td>
</tr>
<tr>
<td>Neuroleptics + Antidepressants</td>
<td>increased number of undesirable side effects: acute state of confusion with Morbus Parkinson syndrome, bradykinesia + rigor</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>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</td>
</tr>
<tr>
<td>NSAIDs + Diuretics at high dosages</td>
<td>increased risk of acute renal failure</td>
</tr>
<tr>
<td>Psychoactive drugs + Nitrates</td>
<td>particularly high risk of syncope in case of cerebrovascular insufficiency and long existing hypertension (malfunctioning in the autoregulation of cerebral perfusion)</td>
</tr>
<tr>
<td>Statins (atorvastatin, simvastatin, cerivastatin, lovastatin) not pravastatin</td>
<td>risk of rhabdomyolysis through interactions in cases of poly-medi- cation with substances that are metabolized via CYP 3A4, increased metabolism of Fluvastatin via CYP 2C19 inhibits CYP 2C8/9</td>
</tr>
</tbody>
</table>


Appendix 4. Drugs that can cause an anticholinergic syndrome.

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

According to [Zeeh and Platt 1994].
Appendix 5. Drugs that can cause acute states of confusion.

<table>
<thead>
<tr>
<th>Drugs that can cause acute states of confusion</th>
<th>Risk</th>
<th>Notes on substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics, strongly effective</td>
<td>+++</td>
<td>morphine and its derivatives</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>++</td>
<td>risk highest for lidocaine</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>++</td>
<td>risk increases with sedative effectiveness</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Depending on substance</td>
<td>centrally effective substances: high risk, α- and β-blocker: medium risk, Diuretics, calcium antagonists, ACE-inhibitors: low risk</td>
</tr>
<tr>
<td>Anti-Parkinson drugs</td>
<td>+++ to +++</td>
<td>risk for anticholinergic substances higher than for dopaminergic ones</td>
</tr>
<tr>
<td>Antiphlogistics (non-steroidal)</td>
<td>+</td>
<td>risk from paracetamol lowest</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>+++</td>
<td>benzodiazepine withdrawal can also cause delirious visions</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>+++</td>
<td>especially for doses &gt; 40 mg prednisone equivalent daily over &gt; 1 week</td>
</tr>
<tr>
<td>H₂-Antagonists</td>
<td>+ to ++</td>
<td>risk highest for cimetidine</td>
</tr>
<tr>
<td>Heart glycosides</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>+++ to +++</td>
<td>risk increases with sedative effectiveness</td>
</tr>
<tr>
<td>Theophylline</td>
<td>++</td>
<td></td>
</tr>
</tbody>
</table>

According to [Zeeh and Platt 1994].

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

<table>
<thead>
<tr>
<th>Drugs that can cause orthostatic dysregulation, decrease in blood pressure, nausea and syncope</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensives</td>
<td>reduced sensitivity of baroreceptors and reduced peripheral venous tone</td>
</tr>
<tr>
<td>Digitalis glycosides</td>
<td>increased risk of bradycardia due to lower sensitivity of the vagus</td>
</tr>
<tr>
<td>Digitalis glycosides plus diuretics</td>
<td>in case of hypokalemia increased heart glycoside sensitivity and arrhythmia</td>
</tr>
<tr>
<td>Diuretics</td>
<td>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</td>
</tr>
</tbody>
</table>

According to [Zeeh and Platt 1994].
### Appendix 7. Drugs that increase the risk of falling.

<table>
<thead>
<tr>
<th>Drugs that increase the risk of falling</th>
<th>Effect</th>
<th>Falling mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long lasting benzodiazepines</strong> such as diazepam, temazepam, flurazepam, chlordiazepoxide (cause body swaying when standing still)**</td>
<td>reduction in stance and balance</td>
<td>balance impaired, ability to correct stance impaired</td>
</tr>
<tr>
<td><strong>Long lasting benzodiazepines</strong> (extended half-time causes cumulation, heightened sensitivity in age), also other sedating drugs</td>
<td>sedation</td>
<td>sedation during the day, slower reaction times, muscle relaxation</td>
</tr>
<tr>
<td><strong>Insulin, sulfonyl carbamides</strong> (especially in cases of poor compliance, concurrent diseases, exsiccosis warning symptoms can be missing!)</td>
<td>hypoglycemia</td>
<td>impaired consciousness, collapse, syncope</td>
</tr>
<tr>
<td><strong>Antihypertensives, psychotropic substances, nitrates</strong> (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)</td>
<td>hypotension</td>
<td>orthostatic hypotension, postprandial hypotension</td>
</tr>
<tr>
<td><strong>Neuroleptics, antidepressants, diltiazem (?)</strong> (&quot;rabbit syndrome&quot;, perioral twitches)</td>
<td>parkinson syndrome</td>
<td>bradykinesia, rigor (tremor)</td>
</tr>
<tr>
<td><strong>Overdose of aminoglycosides, furosemide, acetylsalicylic acid, quinidine or excessive consumption of alcohol</strong></td>
<td>impaired sense of balance</td>
<td>impairment and dysfunction of the vestibularis</td>
</tr>
<tr>
<td><strong>Myotics for glaucoma therapy</strong></td>
<td>impairment of vision</td>
<td>miosis</td>
</tr>
</tbody>
</table>

According to [Zehe and Platt 1994].
Pharmacotheraphy 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

General practitioners, Association of Statutory Health Insurance Physicians in Hesse (Kassenärztliche Vereinigung in Hessen (KVH) Frankfurt (Main), Germany

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

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].
– 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, apoplexic 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] {B}**.

**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} {IIb}

Behavioral therapy

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

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


Memantine [Areosa Sastre and Sherriff 2004, Reisberg et al. 2003] {A} {IIb}: 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.

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 [Lancot et al. 1998] {A} {Ia}
- Classical, less potent: melperone, promethazine, pipamperone, perazine, sulpiride

**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 risperdone 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**
- Tri- and tetracyclic antidepressants (esp. in cases of sleeping disorders)

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

- 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}.
- 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 and Harvey R. Donezepil for dementia due to Alzheimer’s disease. The Cochrane Library Issue 1, Chichester Uk: John Wiley and Sons; 2004b {meta analysis Ia}.
- Evidenzbasierte Therapieleitlinien der Arzneimittelkommission der Deutschen Ärzteschaft. LL Demenz. Dt Ärzteverlag. 2002; S 141.

Fioravanti M, Flicker L. Efficacy of nicergoline in dementia and other age associated forms of cognitive impairment. Cochrane Review, (CD003159); 2001 [meta analysis Ia].


Pomeroy VH. Immobility and severe dementia: When is physical restraint appropriate? Clinical Rehabilitation. 1994; 8: 226-232 [Ib].


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].


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.

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

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.

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

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.

<table>
<thead>
<tr>
<th>Dosage</th>
<th>5 – 20 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>Vertigo, headache, constipation, drowsiness</td>
</tr>
<tr>
<td>Interactions</td>
<td>Dopaminergics, hydrochlorothiazide, dantrolene sodium, baclofen</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Epilepsy, severe kidney disease, severe states of confusion, pregnancy, breast-feeding</td>
</tr>
<tr>
<td>Relative CI</td>
<td>combination with amantadine</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Daily dose</th>
<th>ADR and interactions (Ia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piracetam [Flicker et al 2004]</td>
<td>Oral: 3 times 800 – 1200 mg max: 5000 mg per day Intravenous: 3 – 12 g per day slowly</td>
<td>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</td>
</tr>
<tr>
<td>Dihydroergotoxine [Olin and Schneider 1998]</td>
<td>4 – 8 mg</td>
<td>ADR: vertigo, lower blood pressure, walking insecurity, nausea, vomiting, “blocked” nose, ergotism Ia: drugs to lower blood or influence blood coagulation</td>
</tr>
<tr>
<td>Nicergoline [Fioravanti and Flicker 2001]</td>
<td>10 – 30 mg</td>
<td></td>
</tr>
</tbody>
</table>

**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%

**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.
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]

---

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

<table>
<thead>
<tr>
<th>Start therapy with</th>
<th>Young patient (under 70 years)</th>
<th>Older patient (over 70 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Levodopa</td>
<td>COMT inhibitors</td>
</tr>
<tr>
<td>COMT inhibitors</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td>Selegiline</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td>Selegiline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supplement with</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Levodopa</td>
<td>COMT inhibitors</td>
</tr>
<tr>
<td>COMT inhibitors</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td>Selegiline</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td>Selegiline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Avoid</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Levodopa</td>
<td>COMT inhibitors</td>
</tr>
<tr>
<td>COMT inhibitors</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
<td>Selegiline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In case of tremor start with</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Levodopa</td>
<td>COMT inhibitors</td>
</tr>
<tr>
<td>COMT inhibitors</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Levodopa doses that are too high (uncertain effectiveness, dyskinesia, monotherapies (for higher doses side effects and uncertain effectiveness))</td>
<td>Antidopa (side effects: development of psychoses, danger of mental confusion if abruptly discontinued [Factor et al. 1998])</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adverse drug reactions (ADR)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting, orthostatic hypotension (side effects)</td>
<td>Reduce dose and distribute over the day; if needed, domperidone</td>
</tr>
<tr>
<td>Depressions:</td>
<td>SSRI (possibly sertraline hydrochloride [Hauser and Zesiewicz 1997] [B], tricyclic antidepressants)</td>
</tr>
<tr>
<td>Sleeping disorders:</td>
<td>Sedative antidepressants, short-term benzodiazepines, zolpidem, zopiclone</td>
</tr>
</tbody>
</table>

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


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}.


### Appendix 2. NMDA antagonists: amantadine, budipine.

#### Amantadine

<table>
<thead>
<tr>
<th>Effective mechanism</th>
<th>N-methyl-d-aspartate receptor antagonist, thus higher noradrenaline and dopamine levels in the synaptic cleft, antagonistic effect at the glutamate receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage</td>
<td>Initial dose: 2 – 3 x 50 – 100 mg/d, maximum dose: 500 – 600 mg/d</td>
</tr>
<tr>
<td>Advice</td>
<td>Avoid combination with anticholinergics! Sulfate derivative more easily digested than hydrochloride derivative</td>
</tr>
<tr>
<td>ADR</td>
<td>Nausea, vomiting, constipation, vertigo, hypotension, tachycardia, intense sweating, hallucination</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Psychoses, decompensated cardiac, renal, endocrine and hepatic diseases, angle closure glaucoma, age lower than 25, lack of contraception, pregnancy, breast feeding</td>
</tr>
<tr>
<td>Special characteristics</td>
<td>Not in cases of secondary, drug-induced M. Parkinson</td>
</tr>
</tbody>
</table>

#### Budipine

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

Bromocriptine, cabergoline, dihydroergocryptine, lisuride.

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Effective mechanism</th>
<th>Dosage</th>
<th>Advice</th>
<th>Contraindications</th>
<th>Special characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pergolide mesylate</strong></td>
<td>Peripheral and central dopamine receptor agonist, equalization/balancing of &quot;on/off&quot;-oscillations.</td>
<td>Initial dose: 3 × 0.05 mg/d for 1 week; dosage increased to 3 × 0.18 mg for 1 week, then 3 × 0.35 mg</td>
<td>Individual dosage according to clinical symptoms, not to plan! Beware: sudden falling asleep! Driving ban!</td>
<td>Severe liver and kidney disease, pregnancy and breast feeding, restrictions in case of cardiac arrhythmia.</td>
<td>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</td>
</tr>
<tr>
<td><strong>Pramipexole</strong></td>
<td>Peripheral and central dopamine receptor agonist, equalization/balancing of &quot;on/off&quot;-oscillations.</td>
<td>Initial dose: 0.088 mg/d for 1 week; dosage increased to 3 × 0.18 mg for 1 week, then 3 × 0.35 mg</td>
<td>Individual dosage according to clinical symptoms, not to plan! Beware: sudden falling asleep! Driving ban!</td>
<td>Severe liver and kidney disease, pregnancy and breast feeding</td>
<td>Combination with L-dopa at advanced stages; reduction of side effects through use of e.g. domperidone; if discontinued, taper off!</td>
</tr>
<tr>
<td><strong>Ropinirole</strong></td>
<td>Peripheral and central dopamine receptor agonist, equalization/balancing of &quot;on/off&quot;-oscillations.</td>
<td>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</td>
<td>Individual dosage according to clinical symptoms, not to plan! Beware: sudden falling asleep! Driving ban!</td>
<td>Severe kidney insufficiency, pregnancy and breast feeding</td>
<td>As monotherapy at all stages or in combination with L-dopa; reduction of side effects through use of e.g. domperidone</td>
</tr>
<tr>
<td><strong>Apomorphine</strong></td>
<td>Reserve substance in cases of akinetic crisis</td>
<td>Initial dose: 2.5 mg subcutaneous, then 4 – 10 mg/h as subcutaneous infusion</td>
<td>Individual dosage according to clinical symptoms, not to plan!</td>
<td>Severe nausea and vomiting, epileptic convulsions</td>
<td>Use only as last resort! Antidote: naloxone. In case of cardiovascular failure: norfenefrine</td>
</tr>
</tbody>
</table>

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)).

<table>
<thead>
<tr>
<th>Strength and type of evidence</th>
<th>Emphasis levels of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia Evidence based on meta-analyses of randomized controlled studies</td>
<td>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.</td>
</tr>
<tr>
<td>Ib Evidence based on at least one randomized controlled study</td>
<td></td>
</tr>
<tr>
<td>IIa Evidence based on at least one well-designed controlled study without randomization</td>
<td>B Based on levels IIa, IIb and III of evidence type, i.e. the recommendation is based on well-designed, non-randomized clinical studies.</td>
</tr>
<tr>
<td>IIb Evidence based on one well-designed, quasi-experimental study</td>
<td></td>
</tr>
<tr>
<td>III Evidence based on one well-designed, non-experimental descriptive study (e.g. comparative studies, correlation studies, case-control-studies)</td>
<td></td>
</tr>
<tr>
<td>IV Evidence based on the reports or opinions of expert circles, consensus conferences and/or clinical experience of recognized experts</td>
<td>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.</td>
</tr>
</tbody>
</table>
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

General practitioners, Association of Statutory Health Insurance Physicians in Hesse (Kassenärztliche Vereinigung in Hessen (KVH) Frankfurt (Main)), Germany

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, biphosphonates 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

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].
(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)

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 precribed 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>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
<th>Diagnosis of the following non-relievable indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 – 60 years</td>
<td>60 – 70 years</td>
<td>One or more fractures of vertebrae {A} One or more peripheral fractures (to be decided individually) {C}</td>
</tr>
<tr>
<td>60 – 70 years</td>
<td>70 – 80 years</td>
<td>One or more fractures of vertebrae {A} One or more peripheral fractures {A} Fracture of the femur neck in one parent {B} Underweight (BMI &lt; 20 kg/ m²) {A} Nicotine consumption {A} Multiple falls {A} Immobility {A for proximal fractures of the femur neck in women}</td>
</tr>
<tr>
<td>&gt; 70 years</td>
<td>&gt; 80 years</td>
<td>All patients, if therapeutic consequences are intended/possible {A}</td>
</tr>
</tbody>
</table>

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 ≥ 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. alfa-calcidol). Drug therapy with calcium and vitamin D alone is insufficient – supplementation 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 orthesis if necessary.

**Specific medication with recommendation level A**

(according to [DVO 2006a])

**Women:**

- Biphosphonates 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!
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


Hausärztlich-Geriatrisches Basisassessment. Institut für Hausärztliche Fortbildung im Deutschen Hausärzteverband (IfH Köln); 2004, Berlin.


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.

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

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

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].

<table>
<thead>
<tr>
<th>Effective substance</th>
<th>Dosage</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate sodium</td>
<td>70 mg once per week orally or 10 mg/d orally</td>
<td>Delayed emptying of the esophagus (beware: strictures, achalasia, incapacity to stand or sit upright for at least 30 min), hypocalcemia, severe renal insufficiency, pregnancy</td>
</tr>
<tr>
<td>Risedronate sodium</td>
<td>Permanent therapy: 5 mg/d orally or 35 mg once per week</td>
<td>Osteomalacia, severe renal insufficiency, pregnancy</td>
</tr>
<tr>
<td>Etidronate disodium</td>
<td>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</td>
<td>Hypocalcemia</td>
</tr>
<tr>
<td>Ibandronate sodium</td>
<td>150 mg once a month (1 pill) or every 3 months intravenously</td>
<td></td>
</tr>
</tbody>
</table>

Interactions | Restricted resorption because of other medication, antacids and calcium (cf. there) or simultaneous intake of food, amplification of gastrointestinal side effects by NSAIDs |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>Gastrointestinal complaints, esophagus and stomach ulcerations, pain in muscles, bones and joints, lowering of the serum concentration of calcium</td>
</tr>
<tr>
<td>Special considerations</td>
<td>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!</td>
</tr>
</tbody>
</table>

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 femur 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])

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

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].

<table>
<thead>
<tr>
<th>Types</th>
<th>Symptoms</th>
<th>Common cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge incontinence</td>
<td>Uncontrollable loss of urine (mostly larger, sometimes varying amounts) due to inability to delay micturition when urge to urinate is felt</td>
<td>Detrusor muscle hyperactivity isolated or in conjunction with one or more of the following causes: local, urgenital variations such as cystitis, urethritis, tumor, stones, diverticiles, early subvesical obstruction; reduced contractility of the bladder, diseases of the central nervous system such us apoplexy, demential syndrome, Parkinson syndrome, spinal cord defects</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>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)</td>
<td>Weak pelvis muscles causing increased mobility of bladder base and proximal urethral weakness of the bladder neck or the sphincter (intrinsic in conjunction with previous traumata, e.g. operations)</td>
</tr>
<tr>
<td>Overflow incontinence</td>
<td>Involuntary loss of urine (frequent, smaller amounts) occurring in conjunction with a dilated bladder</td>
<td>Anatomical obstruction through prostate gland, stricture or large cystocele a contractile bladder in conjunction with diabetes and spinal cord lesion</td>
</tr>
</tbody>
</table>

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 punctuation 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 (cytoscopic, cyto-manometry, 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.


Cave: avoid anticholinergics in case of glaucoma, prostatathyperplasia, 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 week 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 tachycardy, 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-a 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
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.

Schweizerisches Medizinisches Forum Nr. 27, 20.
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,  
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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

Key words
fecal incontinence –  
chronic obstipation –  
non-drug therapy –  
drug therapy –  
opiates –  
loperamid –  
anion exchangers –  
stool-forming laxatives –  
laxatives with osmotic effect –  
stimulating laxatives

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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 chonic diarrhea. In patients with chronic obstipation: 1) trial: stool-forming laxatives (ensure intake of sufficient amount of fluids) 2) trial: laxatives with an osmotic effect and 3) trial: 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

[Chatoo 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 caffèine, 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 bowel clearing, “listen to your bowl”
- Lifestyle advice: keep clear of nicotine, alcohol, caffeine, Cola.

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**


<table>
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<tr>
<th>Sphincter dysfunction</th>
<th>Disease symptoms</th>
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<td>Myopathy of the inner sphincter muscle, congenital myopathy, scleroderma, dermatomyositis, weakening or loss of sphincter function due to advanced age</td>
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<tr>
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<td>Injuries, post-surgical, postpartum</td>
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<td>Neoplastic</td>
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<td>Spinal cord injury, pelvic fracture with lesion of the nervus pudendus, hemorrhoid surgery</td>
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<td>Dysfunction of the small and large intestine</td>
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<th>Dysfunction of neural control</th>
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</table>
| 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       | Fistulæ, 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**


**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**

- 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 paralysis, 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, combines 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-
Pharmacotherapy guidelines for the aged by family doctors for the use of family doctors

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.
Version 1.00, December 2008 “Hausärztliche Leitlinie Geriatrie” was also considered.

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

General Practitioners, Association of Statuatory Health Insurance Physicians in Hesse (Kassenärztliche Vereinigung in Hessen (KVH) Frankfurt (Main)), Germany

Key words

e) Fecal incontinence
f) Chronique constipation


D Basic conditions supporting drug treatment

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

This issue

c) Management of age-associated diseases

E Information

a) Information about the guidelines group
b) Disclaimer

Forthcoming

Chapter

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

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-
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 rusk 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. zinc [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 gastrostomia)**

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)

- **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**


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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:

<table>
<thead>
<tr>
<th>Daily nutrient requirements for seniors: Relative allocation: 15% proteins, 30% fat, 55% carbohydrates</th>
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<tr>
<td>Calories</td>
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<tr>
<td>Vitamin E</td>
</tr>
<tr>
<td>Vitamin B1</td>
</tr>
</tbody>
</table>

Example of daily menu

<table>
<thead>
<tr>
<th>Example of a menu for a healthy senior (&gt; 65 years of age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>After rising</td>
</tr>
<tr>
<td>Breakfast</td>
</tr>
<tr>
<td>Lunch</td>
</tr>
<tr>
<td>Snack (between meals)</td>
</tr>
<tr>
<td>Dinner</td>
</tr>
<tr>
<td>At night</td>
</tr>
</tbody>
</table>

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):

<table>
<thead>
<tr>
<th>Dietary recommendations for healthy seniors (&gt; 65 years of age) according to GSNM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Cereals and potatoes</td>
</tr>
<tr>
<td>Group 2: Vegetables</td>
</tr>
<tr>
<td>Group 3: Fruits</td>
</tr>
<tr>
<td>Group 4: Milk and milk products</td>
</tr>
<tr>
<td>Group 5: Fat and oils</td>
</tr>
<tr>
<td>Group 6: Fluids</td>
</tr>
<tr>
<td>Group 7: Fish, meat, processed meats and eggs</td>
</tr>
</tbody>
</table>
Mini Nutritional Assessment
MNA®

<table>
<thead>
<tr>
<th>Last name:</th>
<th>First name:</th>
<th>Sex:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>A</th>
<th>Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>severe loss of appetite</td>
</tr>
<tr>
<td>1</td>
<td>moderate loss of appetite</td>
</tr>
<tr>
<td>2</td>
<td>no loss of appetite</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>Weight loss during the last 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>weight loss greater than 3 kg (6.6 lbs)</td>
</tr>
<tr>
<td>1</td>
<td>does not know</td>
</tr>
<tr>
<td>2</td>
<td>weight loss between 1 and 3 kg (2.2 and 6.6 lbs)</td>
</tr>
<tr>
<td>3</td>
<td>no weight loss</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C</th>
<th>Mobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>bed chair bound</td>
</tr>
<tr>
<td>1</td>
<td>able to get out of bed/chair but does not go out</td>
</tr>
<tr>
<td>2</td>
<td>goes out</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D</th>
<th>Has suffered psychological stress or acute disease in the past 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>yes</td>
</tr>
<tr>
<td>1</td>
<td>no</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>E</th>
<th>Neuropsychological problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>severe dementia or depression</td>
</tr>
<tr>
<td>1</td>
<td>mild dementia</td>
</tr>
<tr>
<td>2</td>
<td>no psychological problems</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>F</th>
<th>Body Mass Index (BMI) (weight in kg) / (height in m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>BMI less than 19</td>
</tr>
<tr>
<td>1</td>
<td>BMI 19 to less than 21</td>
</tr>
<tr>
<td>2</td>
<td>BMI 21 to less than 23</td>
</tr>
<tr>
<td>3</td>
<td>BMI 23 or greater</td>
</tr>
</tbody>
</table>

**Screening score** (subtotal max. 14 points)

12 points or greater Normal – not at risk – no need to complete assessment
11 points or below Possible malnutrition – continue assessment

**Assessment**

<table>
<thead>
<tr>
<th>G</th>
<th>Lives independently (not in a nursing home or hospital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no</td>
</tr>
<tr>
<td>1</td>
<td>yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H</th>
<th>Takes more than 5 prescription drugs per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>yes</td>
</tr>
<tr>
<td>1</td>
<td>no</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I</th>
<th>Pressure sores or skin ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>yes</td>
</tr>
<tr>
<td>1</td>
<td>no</td>
</tr>
</tbody>
</table>

J How many full meals does the patient eat daily?

- 0 = 1 meal
- 1 = 2 meals
- 2 = 3 meals

K Selected consumption markers for protein intake

- At least one serving of dairy products (milk, cheese, yogurt) per day
- Two or more servings of legumes or eggs per week
- Meat, fish or poultry every day

- 0.0 = if not 1 yes
- 0.5 = if 2 yes
- 1.0 = if 3 yes

L Consumes two or more servings of fruits or vegetables per day?

- 0 = no
- 1 = yes

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

N Mode of feeding

- 0 = unable to eat without assistance
- 1 = self-fed with some difficulty
- 2 = self-fed without any problem

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

P In comparison with other people of the same age, how does the patient consider his/her health status?

- 0.0 = not at good
- 0.5 = do not know
- 1.0 = as good
- 2.0 = better

Q Mid-arm circumference (MAC) in cm

- 0.0 = MAC less than 21
- 0.5 = MAC 21 to 22
- 1.0 = MAC 23 or greater

R Calf circumference (CC) in cm

- 0 = CC less than 31
- 1 = CC 31 or greater

**Assessment (max. 16 points)**

**Screening score**

**Total Assessment (max. 30 points)**

**Malnutrition Indicator Score**

- 17 to 23.5 points at risk of malnutrition
- Less than 17 points malnourished

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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-Geriatriches 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


Hausärztlich-Geriatrisches Basisassessment. Berlin: Institut für Hausärztliche Fortbildung im Deutschen Hausärzeverband (IhF Köln); 2004.


Appendix 1. Recommendations on regular physical activity

<table>
<thead>
<tr>
<th>Target group</th>
<th>Activity</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients/subjects</td>
<td>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).</td>
<td>Independently</td>
</tr>
<tr>
<td></td>
<td>Exercise routine: Start: exercise coordination, flexibility and strength</td>
<td>Group exercise program led by a competent trainer</td>
</tr>
<tr>
<td></td>
<td>Frequency: 1 – 3 times/week</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration: 30 – 60 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Examples: bench exercises, whole body gymnastics, aerobic exercises (for seniors), Tai Chi, dancing</td>
<td></td>
</tr>
<tr>
<td>Inactive patients</td>
<td>Extension/addition: aerobic endurance training</td>
<td></td>
</tr>
<tr>
<td>Without manifest diseases.</td>
<td>Frequency: 3 times/week</td>
<td></td>
</tr>
<tr>
<td>Following a general health</td>
<td>Intensity: around the aerobic threshold (ca. 2 mmol/l lactate) (moderate) 45 – 65% VO$_2$ max; 15 – 30 kJ/min</td>
<td></td>
</tr>
<tr>
<td>check by a physician.</td>
<td>Heart rate: approximately 170 minus age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration: 15 – 60 minutes to hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Additional energy consumption: ≥ 4,000 kJ/wk (60 kJ/kg body weight/wk)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Examples: walking (variation in pace and terrain), nordic walking, ski walking, golf, cycling exercises, cycling in flat country, swimming</td>
<td></td>
</tr>
<tr>
<td>Following prior diagnostic</td>
<td>Extension: strength training (concentric, excentric, dynamic, if appropriate static)</td>
<td>Individual or group exercise led by a competent trainer</td>
</tr>
<tr>
<td>by a specialist sports physician</td>
<td>Frequency: 1 – 3 times/week</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intensity/repetitions: 65% RM, 8 – 12 times/muscle group.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75 – 85% RM, 8 – 6 times/muscle group</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Static: max. 3 sec. holding, 3 – 5 times/muscle group.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Equipment: body’s own weight, small dumbbells, elastic bands of varying stiffness, equipment for training strength</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Always warm up and cool down with stretching exercises, take breaks</td>
<td></td>
</tr>
</tbody>
</table>

VO$_2$ = oxygen absorption rate; kJ = kilo-joule; RM = maximum load that one can master dynamically only once; wk = week.
### Appendix 1. Continuation.

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

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

General practitioners, Association of Statutory Health Insurance Physicians in Hesse (Kassenärztliche Vereinigung in Hessen (KVH) Frankfurt (Main)), Germany

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

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b) Levels of evidence

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b) Distribution space
c) Transport proteins
d) Renal elimination
e) Metabolism in the liver
f) Drug interactions
g) Summary


C Special Pharmacology of the aged
a) Dementia
b) M. Parkinson


c) Osteoporosis
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e) Fecal incontinence
f) Chronique constipation


D Basic conditions supporting drug treatment
a) Nutrition in old age
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c) Management of age-associated diseases

E Information
a) Information about the guidelines group
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This issue

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 pharmaco-dynamics 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 multi-morbid 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 increase. 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**

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**


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].


- 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]
- 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

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-

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 only 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].

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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_publikationen/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_publikationen/geriatrie1_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