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Iatrogenic injuries in hospital: nearly 70% are preventable

The Harvard Medical Practice Study in the State of New York (1990) pointed out that 3.7% of a sample of 30 195 hospitalized patients suffered an adverse event (AE) resulting in measurable disability. Physician experts reviewed 1133 AEs defined as unintended injuries caused by medical management. The AEs were classified as preventable, unpreventable and potentially preventable (i.e. complications reflecting a low standard of care). Nearly 70% of the AEs were found to be preventable and 6% potentially preventable. Negligence was found in 28% of the AEs. No significant age differences were found in the proportion of preventable AEs. Technical errors were the most common cause of preventable AEs (44%), followed by errors in diagnosis (17%), failures of prevention (12%) and errors in medication (10%). Negligence was more commonly an element in diagnostic failure (71%) than in technical errors (20%).

Preventable AEs showed a higher risk for prolonged disability and death than nonpreventable AEs (60% higher risk of dying). Serious medical injury with long disability or death was more often preventable than slight disability (50% of iatrogenic deaths were preventable).

In the USA preventable AEs cost more than 10 billion dollars every year. The authors suggest several areas which should be targeted in hospitals to reduce iatrogenic injury. Identification and reporting methods must be vastly expanded. Hospitals need to rethink the manner in which they deal with human mistakes. Patients' falls in hospital, responsible for a substantial proportion of preventable AEs, demand more attention. The high incidence of technical errors suggests an

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incongruity between the use of complex (and often new) techniques and deficient skills among some of the doctors using these techniques.

Leape LL, Lawthers AG, Brennan TA et al. Preventing medical injury. Quality Rev Bull 1993:144–149.

Avoidable drug-related hospital admissions

As a part of a high-intensity monitoring study of drug events as the cause of admission to hospital, the effects of an educational intervention programme were studied. Overall, the drug-related hospitalization (DRH) as a percentage of all admissions at six departments of internal medicine in the Odense University Hospital (Denmark) was 11.4% during a period of 15 months.

The intervention program included: (1) a letter to the patient's general practitioner summarising the DHR problem, with conclusion and recommendations; (2) distribution of monographs about drug events and their prevention to the GPs in the region; (3) organization of symposia with discussion of DHR.

The intervention program took place at a general and a geriatric department. The 607 pre-intervention admissions were compared with the 703 post-intervention admissions. A modest, statistically non-significant, decrease in DRHs was seen (from 14% to 13%).

However, DRHs classified as definitely avoidable showed a significant decrease of 83%. No relation was found between any one of the three intervention approaches and changes in the pattern of DRHs. It is, however, possible that such an intervention could have had a non-specific effect on avoidable DRHs.

Hallas J, Harvald B, Worm J et al. Drug related hospital admissions; results from an intervention program. Eur J Clin Pharmacol 1993;45:199–203.

Drug-related hospitalization in Taiwan

In a community teaching hospital in Taiwan 2695 patients admitted to the Department of Medicine were studied retrospectively to determine the incidence of drug-related hospitalizations. Drug-related problems were identified in 4% of the patients admitted. The incidence was higher in the group of patients aged more than 65 (5.2%) as compared with the group of patients aged less than 65 (3.2%). 10% of the drug-related hospitalizations were considered as potentially life-threatening. Two patients died. NSAIDs, hypoglemic agents, adrenocorticosteroids, antihypertensive drugs and herbal medicine (12%) were most

often involved. In Taiwan herbal drugs are traditionally used as self-medication. The drug use concerned had been unsupervised in 41% of the drug-related admissions.

Lin SH, Lin MS. A survey on drug-related hospitalization in a community teaching hospital. Int J Clin Pharmacol Ther Toxicol 1993;31:66–69.

Infusion pump technology: benefit and risk

Infusion pump systems are being increasingly used, since many pharmaceuticals are available for continuous parenteral administration (morphinomimetics, antibiotics, oncolytica, total parenteral nutrition). Patients can be treated on an ambulant basis at home. The use of this technology, however, requires careful preparation, training and organisation. The risk of calamities is underestimated. The Netherlands Inspectorate for Health Care investigated the conditions of use of the method in hospitals; many situations were identified in which safety was insufficient. In many hospital departments, various types of infusion pump systems were being employed at the same time. The instructions for use were often not available, or they were written in a foreign language or were otherwise difficult to follow. Procedures were absent or insufficiently studied or understood by nurses and doctors. The role and the responsibility of junior doctors and student nurses was not clear. The author calls for certification and authorization of doctors and nurses who are to use this technology. He also advises using only a single type of infusion pump system in a given hospital department, and calls for central coordination, written procedures and the institution of a log book for every infusion pump, with a record on its use, upkeep and repair.

Spiers WJ. Infuuspomp: tijdwinst of tijdbom? Medisch Contact 1994;49:460.

Björk-Shiley heart valves and strut fractures, a manufacturing problem

In the Netherlands 2303 patients were fitted with a Björk-Shiley heart valve with opening angles of 60° or 70° between 1979 and 1986. During a mean follow-up of 6.6 years 42 strut fractures were reported. The cumulative risk of single-leg strut fractures for large convexoconcave 70° mitral valves after 8 years was calculated as 17.4%. Prophylactic replacement was advised for certain groups of patients.

The explanted valves of 22 patients were examined. The reoperated patients had no signs of a defective valve. Of 24 valves 7 (29%) had a fracture in one of

the legs of the outlet strut. Two valves had features of metallurgical fatigue defects. The conclusion was drawn that the prevalence of strut fractures in these types of valves is higher than suggested before.

The high prevalence of fractures points to manufacturing problems. It appeared that 6 of 7 defective valves had been welded by the same welder.

De Mol BA, Kallewaard M, McLellan RB et al. Single strut fractures in explanted Björk-Shiley valves. Lancet 1994;343:9–12.

Silicone implants and connective tissue disease; another non-disease?

Since 1962 between 1 and 2.2 million women in Canada and the USA have received silicone breast implants. Silicone injections have been administered on an even larger scale. Silicone is also found in many medical implants, syringes, needles, baby bottle teats and elsewhere. In 1992 the US Food and Drug Administration (FDA) banned most silicone breast implants, because of case reports about the relation between silicone implants and connective tissue disease (CTD). Clear evidence about a causal relation was, however, never advanced.

Sánchez-Guerrero et al. reviewed the relevant literature. Only 293 case reports were found of patients with rheumatic symptoms after receiving silicone breast implants. Scleroderma was reported most frequently. In the population at large the incidence of CTD was the same as in the calculated breast implant population.

Gabriel et al. (Mayo Clinic, Rochester) conducted a retrospective population-based cohort study in Olmsted County, Minnesota. A total of 749 women who had received a breast implant between 1964 and 1992 were followed for a mean of 7.8 years (85% silicone implants). They were compared with a control group of 1498 women followed for a mean of 8.3 years. In 5 implant subjects and 10 subjects in the control group a CTD was diagnosed. There was also no significant difference in the incidence of minor symptoms of arthritis in the two groups. The study by Gabriel et al. has some limitations. The case group was too small to detect rare CTD, such as systemic sclerosis; in addition, very late outcomes of CTD could not be evaluated adequately. These data are, however, the best that are available today. Together with the outcome of the Boston literature review, they indicate that an association between silicone breast implants and CTD is more and more unlikely.

Why has the hypothesis that breast implants cause CTD been so rapidly

accepted with so little evidence? Marcia Angell explains in an editorial in the New England Journal of Medicine the consequences of poor scientific discussion in the courtroom. The accumulated weight of anecdotes was taken by judges and juries as evidence of a causal relationship, despite the lack of epidemiologic studies. Multimillion-dollar settlements followed. Four manufacturers of breast implants established a fund of US$4.2 billion to compensate women with CTD after breast implant.

The same doubts arise as regards the FDA. Was the ban, also based on conclusions drawn from anecdotal reports, a carefully taken decision? FDA commissioner David Kessler declared that the FDA had not indicted the implants but had taken the action because the manufacturers had not fulfilled their legal responsibility to collect data on the question. However, Dr. Angell criticizes the FDA action as overly paternalistic and unnecessarily alarming.

CTD caused by silicone breast implants seems to be another non-disease. The story can, however, provide a more general lesson on the way in which scientific issues have to be settled in the courtroom.

Sánchez-Guerrero J, Schur PH, Sergent JS et al. Silicone breast implants and rheumatic disease. J Arthritis Rheum 1994;37:158–168.

Gabriel SE, O'Fallon WM, Kurland LT et al. Risk of connective-tissue diseases and other disorders after breast implantation. N Engl J Med 1994;330:1697–1702.

Angell M. Do breast implants cause systemic disease? Science in the courtroom. N Engl J Med 1994;330:1748–1749.

Kessler DA. The basis of the FDA's decision on breast implants. N Engl J Med 1992;326:1713–1715.

Nutrition in hospital: too little attention

Malnutrition remains a largely underrecognised problem in hospital. Doctors and nurses frequently fail to recognise undernourishment because they are not trained to look for it. In a prospective study at the Dundee Teaching Hospital (UK) 200 of 500 patients were found to be undernourished at the moment of admission. Nearly 10% (47) were severely depleted. Only 96 undernourished patients had nutritional information in their case notes. Often there were no notes as to weight and length. Among 112 patients reassessed on discharge, the nutritional status showed a mean weight loss of 5.4%. Only one of four undernourished patients was referred for nutritional support. However, 80% of the non-referred yet undernourished patients lost further weight during the remainder of their hospital stay.

These data highlight the need for education on clinical nutrition. Patients with a poor nutritional status suffer more complications and heal more slowly. The problem of undernourishment in hospitals is not merely due to lack of learning but also to lack of interest. The management of hospitals are also involved in the problem. A patient who had been fasted for blood tests in the morning, returning from radiology at 2.30 p.m. will miss lunch and, since budgeted catering services have replaced the ward kitchen, he will often have to wait till the evening meal after having fasted for 24 h.

McWhirter JP, Pennington CR. Incidence and recognition of malnutrition in hospital. Br Med J 1994;308:945–948.
Garrow J. Starvation in hospital. Br Med J 1994;308:934.

Suing the doctor: the reason why

A survey of 227 patients and their relatives suing doctors after experiencing adverse events, pointed out that the most important reasons for taking legal action were to prevent similar accidents to others, finding out what had happened and obtaining financial compensation. Although the validity of the results provided by the postal questionnaire which was used can be questioned, the study of Vincent et al. highlights some interesting aspects of the psychological mechanism behind litigation of this type. Over 70% of the respondents stated that they were seriously affected by the incidents in question, which had long-term effects on their work, social life and family relationship. Feelings of anger were expressed by 90% of the respondents. Strong emotions persist for years after the incident. About 40% stated that they never received any explanation and another 40% were dissatified with the explanation provided. Feelings that they had been ignored, neglected or humiliated contributed to the decision to take legal action. Poor communication, lack of openness or willingness to explain seems to be more important than the original mistake in blaming doctors.
A "no-fault compensation" scheme will not take away the emotional feelings of patients about the disturbed relationship with their doctors.

Vincent C, Young M, Philips A. Why do people sue doctors? A study of patients and relatives taking legal action. Lancet 1994;343:1609–1613.
Editorial. Suing the doctor: altruism, naked truth or recompense? Lancet 1994;343:1582–1583.

Alternative dispute resolution prevents litigation

Increasing malpractice litigation is a cause of much concern among American doctors. The change in medical practice in the last 30 years is part of the problem. Progress in medical technology replaced the stethoscope by the MRI. Contact with the patients diminished and something vital was lost. More remote teamwork has replaced the personal relationship with patients. Protocols, standards and rules contribute to the emergence of a businesslike image of the medical profession. At the same time it seems that communication skills have remained underdeveloped.

On the other hand, patients want to believe in the unlimited possibilities of medical progress. They become uneasy by having to accept disappointing outcomes, which they often link to medical mistakes. Doctors are "not allowed" to make errors.

Communication skills are important in the treatment of patients, very especially when the outcome of treatment is disappointing or a mistake has been made. Poor communication is often part of the claim against doctors. All doctors make mistakes but some doctors are never litigated against, while others experience frequent claims.

In Massachusetts a project has been started to keep patients and doctors outside the courtroom in solving disputes relating to medical treatment. An alternative form of dispute resolution, involving expert opinions, can replace litigation. A settlement is possible when all parties involved can reach consensus. Since the introduction of alternative dispute resolution, litigation has decreased by 64% in Massachusetts.

Warshaw AL. A new approach to malpractice dispute settlement. Am Coll Surg Bull 1993;78:7–13.

Effects of risk management

The goal of risk management is to improve the quality of medical care, reduce the number of malpractice claims and keep expenditure within reasonable limits. In emergency departments most events leading to a malpractice claim occur outside office hours, when direct supervision is lacking. In 1987 the pediatric emergency department (PED) of Jackson Memorial Hospital in Miami (Florida, USA) introduced full-time coverage of the unit by a senior physician. In 1994 a retrospective analysis was undertaken of cases leading to malpractice

suits over the period between 1984 and 1990. Although the numbers in the study were too small to produce statistically significant evidence, there was a strong suggestion that malpractice claims and disbursements both decreased (by 42% and 44% respectively) after direct ongoing supervision was introduced. Before 1987 there were twelve malpractice cases and in only two of these had the patient been examined by an attending physician. Between 1987 and 1990 there were seven cases leading to a malpractice suit, and all the patients had been assessed by an attending physician.

In 1989, only 29% of the teaching hospitals in the USA had 24-hour-per-day on-site attending physician coverage of PEDs. The authors plead for full-time attending physicians in the emergency departments of teaching hospitals as a part of a risk management programme, aimed at improving patient care, enhancing resident physician education, teaching better documentation, enhancing efficiency and decreasing the risk of malpractice suits.

Press S, Cantor J, Russel S et al. Full-time attending physician coverage in a pediatric emergency department. Arch Pediatr Adolesc Med 1994;148:578–581.

Incompatible blood and human errors

Unwanted incidents involving blood transfusions include nosocomial infections (HIV, hepatitis b and c) and incompatible transfusions. Most of the deaths immediately after transfusion are caused by human error in procedures preventing AB0 incompatibility. In the USA, errors and death associated with blood transfusion must be reported to the Food and Drug Administration. In Britain no comparable national central system for the registration of such accidents exists.

The Scottish National Blood Transfusion Service sent questionnaires to 400 hospital haematology laboratories about errors associated with blood transfusions. A third of the 245 laboratories responding (a response rate of 61%) reported a total of 111 incidents in 3.3 million units supplied. Six patients died and twelve others had more or less serious reactions. Twenty respondents spontaneously reported 100 near-accidents where erroneous interchanging of blood samples was incidentally discovered in the laboratory. Only 40% of the laboratories used a system for documenting incidents. Information was often provided from memory! Most incompatible transfusions result from giving blood to the wrong patient (errors in identification, faulty labelling of blood samples).

Contreras and De Silva call attention to the common lack of adequate documentation in the operating theatre. They also find that junior doctors, anaesthetists and nurses, with insufficient training or awareness of local and national guidelines on operating procedures, are too often charged with the administration and documentation of transfusions.

Only good procedures, which are carried out in the proper manner, can reduce the number of incompatible transfusion incidents. Hospital risk management needs to establish standard procedures for accurately identifying patients and registering all incidents which occur.

Contreras M, De Silva M. Preventing incompatibele transfusions. Br Med J 1994;308:1180–1181.
McClelland DBL, Philips P. Errors in blood transfusion in Britain: survey of hospital haematology departments. Br Med J 1994;308:1205–1206.

Bedside transfusion errors are underestimated

The SAnGUIS study (Concerted Action for Safe and Good Use of Blood in Surgery) is a multicenter research project of the Medical and Health Research Programme of the European Community. The project provided the opportunity to trace all transfusions relating to six elective surgical procedures carried out in 43 teaching hospitals in 10 countries and to identify the points at which risk arises during blood delivery.

Data from the three participating Belgian university hospitals indicated that the true incidence of bedside transfusion errors (i.e. those happening when blood products have left the blood bank) is underestimated. The medical records of 808 patients transfused with 3485 units of blood, red blood cells or fresh frozen plasma (FPP) were analysed. Errors were identified in 78 records (9.7%) and related to 165 transfused units (4.7%). A distinction was made between major errors (misidentifications, administration of allogeneic products when autologous were available, lack of prescription) and recording errors (misrecording, mislabelling, failures to document transfusions in medical records). Major errors were found with respect to the administration of 15 units (0.4% incidence) to 10 patients (1.2% incidence). One patient experienced a transient transfusion reaction. The major errors occurred variously during non-emergency situations, in wards or intensive care units.

Recording errors represented most of the errors, relating to 150 units given to 68 patients. Many FFP units were found to be given to recipients for whom they had not been ordered (61 errors in 30 patients). In the medical records no trace

could be found of 83 units of red cells or whole blood which were assumed to have been transfused to 38 patients.

Studies on human error in medicine show that active failures are part of a management-related latent failure problem. The errors identified point to failures in the organisation of transfusion management.

Baele PL, De Bruyere M, Denneys V et al. Bedside transfusion errors; a prospective survey by the Belgium SAnGUIS group. Vox Sang 1994;66:117–121.

Too much unnecessary transfusion

Too many blood transfusions are given where they are not needed. In a community hospital and a teaching hospital in Los Angeles (USA) 438 blood transfusions were reviewed by five specialists. Indications for transfusion were judged to be unjustified by four of five reviewers in 18% of transfused patients. Another 17% were considered equivocal. The inappropriate use of blood was considered to be significantly more common in the community hospital than in the teaching hospital (26% vs. 16%). No adequate documentation was available in 39% of the cases. This is a point strongly deserving of attention in hospitals.

Saxena S, Weiner JM, Rabinowitz A et al. Transfusion practice in medical patients. Arch Intern Med 1993;153:2575–2580.

Misuse of fresh frozen plasma

In an editorial in the British Medical Journal, Dr. Hannah Cohen, a London haematologist, warned against misuse of fresh frozen plasma (FFP). In Britain the administration of FFP has increased tenfold in the last 15 years, though firm indications for the use of FFP are few. FFP has no role as a volume expander. It has no place in replacement protocols, in the treatment of protein-losing conditions or as a source of immunoglobulins. Administration is appropriate in some congenital procoagulant factor deficiencies, when a specific factor concentrate is unavailable.

Limited knowledge of the efficacy, ignorance of the risks and the increased availability of FFP are the main reasons for misuse. The risks of inappropriate use of FFP should not be underestimated (infection with HIV, hepatitis b and c, incompabilities, acute lung injury syndrome).

Various recommendations are advanced to improve the situation. Transfusion committees should develop local guidelines for transfusions (based on national

protocols). The widespread British custom of giving 2 units of FFP to an adult in specific circumstances should be abandoned. Transfusion with FFP should be well documented in patients' notes. Safety measures relating to donation, screening and treatment should be developed further. Last but not least, efforts should be directed to identifying the factors in FFP that produce benefit.

Cohen H. Avoiding the misuse of fresh frozen plasma. Br Med J 1993;307:395–396.

Maternal death rate stable in UK

The latest Report on Confidential Enquiries into Maternal Deaths in the United Kingdom records 238 maternal deaths between 1988 and 1990. At 0.01% the death rate has been stable for the last decade. Thromboembolism, hypertensive disorders, haemorrhage and ectopic pregnancy were the most common causes of maternal death. In almost half of the cases of maternal death, evidence of substandard care was found. As was found by the report on peri-operative deaths (NCEPOD), too many cases having major problems proved to have been dealt with by junior doctors working without supervision out of office hours.

In the 27 cases of maternal death due to hypertensive disorders, the care was considered in 90% to be substandard. Similarly, the care provided to half of the cases where death was due to antepartum or postpartum haemorrhage and to 35% of the deaths due to ectopic pregnancy was found substandard.

Again recommendations were given for better protocols in obstetric units. It is disappointing that earlier recommendations of a similar nature failed to lead to an improvement in the death rate. The number of maternal deaths due to haemorrhage and sepsis had indeed doubled since the previous report.

Report on Confidential Enquiries into Maternal Deaths in the United Kingdom 1988–1990. London, 1993.

Puerperal fever due to poverty and medical ignorance: obstetrics in 1845 in Amsterdam

At the beginning of the 19th century a maternity ward was founded in the Amsterdam Binnengasthuis, providing 28 double beds for 56 women. In 1828 a medical teaching school was established at the Binnengasthuis. One consequence of giving practical obstetric education to students was a 3.5-fold rise in

maternal mortality from 2.6% to 9.0% within six years! In 1845 the maternal mortality rate was 8.6%. In an authentic annual report for 1845 the obstetric history of 395 indigent, malnourished and very poor women is provided. Rachitic malformation of the pelvis was common. Many complicated deliveries are described. Perinatal mortality was 12.5%. In the first months of the year an impressive epidemic of puerperal fever broke out; in March the maternal mortality reached 44%. The article gives an insight into the opposing views held at the time as to the dissemination of puerperal fever (the 'epidemic' versus the 'contagionistic' view). The discoveries of Ignaaz Semmelweis reached Amsterdam in 1847, but the reaction of the obstetricians of the Binnengasthuis was tepid and reserved. Aseptic obstetrics were not introduced. Other epidemics of puerperal fever followed until the maternity ward was closed in 1870, because of the high maternal mortality rate.

Pel M, Pel JZS, Boon J. Armoede en onkunde in het Amsterdamse Binnengasthuis in 1845. (Puerperal fever due to poverty and medical ignorance: obstetrics in the Amsterdam Binnengasthuis in 1845.) Ned Tijdschr Geneeskd 1994;137:2649–2653.

Critically ill patients with nosocomial sepsis: high mortality, longer stay in hospital and extra costs

In a pairwise-matched (1:1) case-control study from the Iowa City University Hospitals and Clinics attributable mortality, excess length of hospital stay and avoidable extra costs incurred were determined for critically ill patients with nosocomial bloodstream infection. All 4002 patients admitted to the surgical intensive care unit (SICU) between 1 July 1988 and 30 June 1990 were eligible for analysis. Ninety-seven patients developed 107 episodes of bloodstream infection; 11 of these cases were set aside because of data problems and the remaining 86 cases were fully analysed. In the case group mortality was 50%, versus 15% in the control group. Mortality attributable due to nosocomial bloodstream infection was 35%. The excess length of stay attributable to the infection was 14 days in the hospital and 8 days in the SICU. Counting survivors only, the excess length of stay in hospital was 24 days but excess stay in SICU remained 8 days. Extra cost attributable to bloodstream infection was calculated at $33 000 per patient in the case group and at $41 000 for surviving patients. The eleven rejected cases would not, had they been analyzed, have changed the outcome of the study.

Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. J Am Med Assoc 1994;271:1598–1601.

Hospital admissions: 5% ADRs

A literature review is provided of 49 reports on drug-related admission rates, published in 37 studies between 1966 and 1989. Thirty reports originated from the USA and Canada, ten reports originated in Europe and nine reports were published in Israel, Australia, New Zealand, South Africa and Zimbabwe. The reported proportions of admissions due to ADRs ranged from 0.2 to 21.7%, with a median of 4.9%. The studies concerned a total of 69 187 admissions, 2897 of which resulted from ADRs. Medicines most frequently associated with ADRs included cardiac drugs, diuretics, antibacterials, antipsychotics, NSAIDs and anticoagulants.

Einarson TR. Drug-related hospital admissions. Ann Pharmacother 1993;27:832–840.

Diuretic drug cessation in general practice; most patients need the medication

In the event of long-term drug use, general practitioners often have to make decisions about continuing or stopping medication. In the Netherlands 20% of the elderly use diuretic drugs. The view has been taken in the literature that a proportion of these patients do not really need this medication. Analysis of a postal questionnaire study among 200 Dutch GPs showed that 40% prescriptions of diuretics related to patients with ankle oedema but without signs of congestive heart failure.

In 15 other general practices the effect of withdrawing diuretics in elderly patients was studied. The prevalence of diuretic drug use was found to be 17% (1202 cases). Ankle oedema was the only indication for diuretics in 383 patients (39%). Only in 66 patients (5.5% of all diuretic drug users older than 65 years) were good reasons found to exist to justify continuing the medication.

In a series of 63 patients a randomized study of withdrawal was undertaken; diuretic treatment was stopped in 34 of these and continued in 29. After six weeks, withdrawal was considered to be successful in 26 of the 34 cases. There was a temporary rebound of ankle oedema but no increase in other complaints. Eight attempts at withdrawal failed (because of emergent symptoms of heart failure, hypertension or the patient's insistence on resumption). However, six months after the trial 16 patients (62%) were using diuretics again. The conclusion of the study is that only a certain number of users of diuretics can be

considered eligible for withdrawal. This percentage is lower than supposed in the literature.

de Jonge JW. Diuretic drug cessation in general practice. Academic thesis, University of Limburg, Maastricht, Netherlands, 1993.
de Jonge JW, Knottnerus JA, van Zutphen WM et al. Short-term effect of withdrawal of diuretic drugs prescribed for ankle oedema. Br Med J 1994;308:511–513.