Diagnosis, Treatment and Prevention of the Diabetic Foot Syndrome
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Preface

We warmly welcome Dr. Stephan Morbach’s practical book on the diagnosis, management and prevention of diabetic foot problems. Over the past two decades, interest in this “Cinderella” specialty has increased. Numerous diabetic foot conferences have been organised and books and papers written. However, this book is a very useful addition to the literature.

The diabetic foot is a great problem world-wide, and patients with diabetic foot disease are at very high risk of major amputation of a leg. In this volume, Dr. Morbach describes with clarity and precision, the interventions needed to improve outcomes for patients.

The book is beautifully illustrated by colour photographs. It is compact enough to be easily portable, and will be useful both for community physicians and healthcare workers as well as for multi-disciplinary, hospital-based teams. The contents are very efficiently organised, and Dr. Morbach has not confined himself to common areas of management, but also leads the reader through often neglected realms of psychological and socio-economic aspects, quality of life and epidemiology. However he does not neglect the more practical aspects of classification, risk factors, diagnosis and management of patients with neuropathic and ischaemic ulcers, infections and necrosis. Wound care, dressings and use of advanced products such as living human skin equivalents are covered in detail, as are the management of peripheral vascular disease, Charcot’s osteoarthropathy and pressure off-loading.

This very practical book will be valued by all members of the diabetic foot team, be they physicians, surgeons, podiatrists, nurses or orthotists, working in community or hospital and should help to improve outcomes for diabetic foot patients.

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Foot lesions affect more than 10% of patients with diabetes mellitus at some point in their life and are amongst the most dreaded complications of this disease. They can cause prolonged periods of immobility and discomfort and some never heal. Year after year, one in every 200 diabetics loses a leg. The cost of foot ulcerations to the individual and to society are considerable.

One of the reasons why foot injuries in diabetics represent such an extraordinary problem is the large number of different factors that contribute to the aetiology and progression of such lesions. Another relates to the management and treatment of diabetic foot ulceration. Optimum treatment assumes the knowledge and experience of a specialist multidisciplinary team, but such teams are unfortunately not widely available. The majority of all foot injuries in diabetics, however, are treated by medical professionals who have neither received specific training nor have sufficient experience. This book has been written for them. It is intended as a practical guide to the diagnosis and management of the lesions found in the diabetic foot.

Another section outlines the strategies for prevention of such lesions. This book is based on experience with diabetic patients in the outpatient foot clinic and on the wards of the Marienkrankenhaus in Soest (Germany) over the past eight years and on the knowledge and experience imparted to me by the “Greats” of the diabetic foot, such as Prof. Ernst Chantelau (Düsseldorf) and Dr. Mike Edmonds (London).

Many questions relating to the diabetic foot still remain and many procedures have yet to be scientifically confirmed. This book is nevertheless an attempt to combine practical guidelines with the current level of knowledge on the subject.

Dr. Stephan Morbach
Diabetes mellitus – an introduction

Diagnosis and classification of diabetes mellitus

Over the past few decades considerable knowledge has been acquired about the aetiology and pathophysiology of diabetes mellitus. This knowledge places a burden on the individual and society – because without doubt it is a very common, serious and cost-intensive, chronic disease. There are now many options in terms of diagnosis and treatment to help sufferers. Many studies have been directed at improving the metabolic status and treating the secondary complications of diabetes.

Despite these encouraging developments, there are unfortunately clear indications that a large number of patients with diabetes mellitus are at present undiagnosed and effective treatment programmes have yet to be implemented universally. Improved detection rates and the greater incidence of the disease will increase the costs of diabetes dramatically in the next few decades. In the years between 1958 and 1993, the number of people diagnosed with diabetes multiplied five-fold\(^1\). In 1995, 135 million patients world-wide were living with diabetes mellitus. By the year 2025 it is estimated that this figure will have increased to more than 300 million\(^2\). In Germany it may be assumed that there are currently at least 4 million known diabetics (5% of the population) and a further 3 to 4 million who are undiagnosed\(^3\).

Diabetes mellitus is a chronic metabolic disorder, predominantly of carbohydrates, which has hereditary and environmental factors. According to the criteria of the WHO and the ADA (American Diabetes Association) of 1997\(^4\), a diagnosis can be established on the basis of fasting plasma glucose levels of:

1. 7.8 mmol/L (126 mg/dl) or above (with or without the presence of the classic signs, such as polydipsia, polyuria, tiredness, unexplained weight loss or pruritus).
2. 11.1 mmol/L (200 mg/dl) and above measured at random and coexisting with the disease symptoms mentioned previously
3. 11.1 mmol/L measured two hours after a standardised oral glucose tolerance test.
Under this classification, four types of diabetes may be distinguished. Type 1 diabetes involves destruction of the pancreatic insulin-producing cells, usually resulting in an absolute insulin deficiency. Type 2 diabetes covers a broad range from marked insulin resistance with relative insulin deficiency to a marked impairment of insulin secretion with slight insulin resistance. Type 3 relates to genetic, endocrinological, infectious and immunological underlying diseases, diseases of the pancreas and iatrogenic or chemically induced forms. Type 4 (gestational diabetes) occurring during pregnancy and disappearing again post partum. Type 1 and type 2 are the most common.

Well over 80% of all diabetics can be classified as type 2.

The distinction between type 1 and type 2 diabetes based previously on age of onset (“juvenile diabetes”, “senile diabetes”) is difficult to make in individual cases. In the following situations, the diagnosis of type 1 diabetes is suggested, even in more advanced age:

1. Normal bodyweight with further weight loss
2. Absence of family history of diabetes mellitus
3. A labile metabolic status on oral antidiabetic medication
4. The appearance of ketone bodies in the urine
5. The detection of auto-antibodies to pancreatic cells or their components (GAD = Glutamic Acid Decarboxylase; ICA = Islet Cell Antibodies) in the blood suggest a diagnosis of type 1 diabetes, even with a more advanced age of onset.

### Diagnostic guideline values for establishing diabetes mellitus (ADA 1997)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Fasting plasma glucose</th>
<th>Random blood sugar with symptoms</th>
<th>Oral glucose tolerance test (75 g glucose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>≥7.0 mmol/L</td>
<td>≥11.1 mmol/L</td>
<td>≥11.1 mmol/L after 2 hours</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td></td>
<td></td>
<td>≥7.8–&lt;11.1 mmol/L</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>≥6.0–&lt;7.0 mmol/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;6.0 mmol/L</td>
<td></td>
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</tbody>
</table>
New aetiological classification of diabetes mellitus
(American Diabetes Association, ADA 1997)

I. Type 1 diabetes
β-cell destruction, usually resulting in absolute insulin deficiency
A. immunologically mediated
B. idiopathic

II. Type 2 diabetes
Type 2 diabetes can range from marked insulin resistance with a relative insulin deficiency to marked secretory impairment with insulin resistance.

III. Other specific types
A) Genetic defects of cell function
B) Genetic defects of the action of insulin
C) Diseases of the exocrine pancreas, e.g. pancreatitis, haemochromatosis
D) Endocrinopathies, e.g. acromegaly, Cushing’s syndrome
E) Drug or chemical induced, e.g. glucocorticoids
F) Infections
G) Rare immune-mediated forms, e.g. anti-insulin receptor antibodies
H) Other genetic syndromes, e.g. Down’s Syndrome, Klinefelter’s syndrome

IV. Gestational diabetes (GDM)

Treatment and self-monitoring of diabetes mellitus

The treatment of diabetes mellitus has the following aims:
1. Prevention of acute metabolic disorders (hypoglycaemia, symptomatic hyperglycaemia, hyperosmolar and ketoacidotic diabetic coma)
2. The avoidance of diabetic complications, both microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (coronary heart disease, peripheral and cerebral arterial occlusive disease).

The incidence rate (rate of new occurrences) of diabetic ketoacidosis is currently between 5 and 8 per 1,000 patients annually and the related mortality well below 1%. In the largest prospective study on the treatment of type 2 diabetes (UKPDS, almost 4,000 patients, 15 year observation period) only one insulin-treated patient died during an episode of hypoglycaemia. Commensurate with the origin of the disease, only insulin therapy
is available for the treatment of type 1 diabetes. A distinction is drawn here between conventional insulin therapy (CT) with the administration of long-acting or mixed insulin once to three times daily, and intensified conventional insulin therapy (ICT) on the basal bolus principle (covering basal requirements with administration of long-acting insulin once to four times daily and an injection of normal (short-acting) insulin at mealtimes depending on the quantity of carbohydrates ingested. The insulin analogue ("designer insulin") Humalog® and Novo Rapid® (insulin lispro and insulin aspart) has been available for this purpose since 1996. If basal and mealtime requirements are provided constantly via a pump, then this is referred to as continuous subcutaneous insulin infusion (CSII) or insulin pump therapy.

The success of treatment is measured by the proportion of glycosylated haemoglobin to total haemoglobin (HBA1c value). This value is maintained below 7% to prevent vascular diabetic complications in accordance with the results of the DCCT study7 and the UKPD study6, corresponding to near-normoglycaemic blood sugar control.

Since the end of the DCCT study in 19937, ICT has been considered the gold standard in the treatment of type 1 diabetics. Compared to conventional insulin therapy, the occurrence or progression of vascular complications has been reduced by 50 to 70%. Similar reduction rates have been published for an “intensive treatment” regime in type 2 diabetes. In obese patients, treatment with insulin or oral antidiabetics (e.g. glibenclamide6, metformin8) is compared to less intensive (mainly dietary) therapy with less specific target criteria. In this case the early institution of insulin therapy is frequently necessary to achieve the desired HBA1c value. Self-monitoring by diabetics nowadays goes well beyond the self-measurement of blood and urine glucose values:

1. Blood pressure self-monitoring
2. Weight control
3. Self-determination of protein elimination in the urine
4. Regular foot inspections for diabetic ulcer.

Patient training and instruction to increase self-help (empowerment) is necessary as a further pillar of diabetes therapy and should no longer be withheld from any diabetic.
Secondary complications of diabetes mellitus

Sustained hyperglycaemic blood sugar values are the underlying pathological factor in the development of secondary diabetic complications. In type 1 diabetes, the diagnosis is established shortly after the onset of hyperglycaemia and several years of inadequate metabolic compensation are generally necessary for any secondary complication to become apparent. The onset of type 2 diabetes often passes unnoticed and the disease can be diagnosed four to seven years too late. During this phase of undiagnosed diabetes mellitus, excessive blood sugar values result in the development or progression of microvascular (diabetic retinopathy, diabetic nephropathy and diabetic neuropathy) and macrovascular (coronary heart disease, peripheral arterial occlusive disease, cerebral arterial occlusive disease) complications. These complications of diabetes are associated with certain life habits (sedentary lifestyle, smoking, alcohol) and other disorders of a metabolic (lipid metabolism disorders, obesity) and haemodynamic (hypertension) nature. In asymptomatic patients with often only slightly raised blood sugar values, doctors with insufficient experience in diabetology are reluctant to diagnose diabetes mellitus and to institute appropriate therapy at an early stage.

At the time of diagnosis, a cardiovascular complication or neuropathy is already present in about 10% of diabetics and nephropathy or retinopathy in 20 to 30% of patients. Forty percent of newly diagnosed diabetics in the UKPD study had arterial hypertension (in most cases untreated). Inadequately treated hypertension is at least as important a risk factor as excessive blood sugar values, particularly for macrovascular complications but also for the progression of an existing diabetic nephropathy. Combinations of microvascular disorders, i.e. retinopathy and neuropathy, and the formation of foot ulcers are described at the time of diagnosis. In the first four years following diagnosis, about 20% of diabetics suffer from peripheral diabetic neuropathy, which increases to 50% or more after 15 years. Diabetic retinopathy is found in 20% of type 2 diabetic at the time of diagnosis. Again at 15 years, a background retinopathy is found in 97% of all type 1 diabetics and about 70% of type 2 diabetics. A proliferative retinopathy necessitating treatment is found at this stage in 30% and 15% of patients, respectively.
In the worst-case scenario, diabetic nephropathy can result in terminal renal insufficiency and the need for haemo dialysis in the early stages. In Germany no less than 35% of all dialysis patients in 1996 were diabetics, (more than 90% of them type 2 diabetics). With annual treatment costs of about 40,000 EUR per dialysis patient, this complication alone generates direct treatment costs of more than 500 million EUR annually\textsuperscript{13}. Peripheral arterial occlusive disease affects diabetics four to ten times more often than non-diabetics, and the rate of CVA is approximately threefold. Half of all deaths among diabetics are due to a cardiac disease\textsuperscript{1}. Some information about the differing risk of micro- and macrovascular complications may be deduced from the patient family history. Late diagnosis of diabetes and genetic predisposition appear to put an individual at increased risk of secondary microvascular lesions. Macrovascular problems are more likely to occur in patients with lipid metabolism disorders, obesity and an increased incidence of hypertension in the family\textsuperscript{14}.

Screening of risk groups for early detection of diabetes mellitus and subsequent treatment of hyperglycaemia and hypertension are cost-effective\textsuperscript{15}. It also reduces the complications of diabetes dramatically. Early diagnosis then allows regular follow up examination of patients in order to delay or prevent end organ damage (blindness, renal insufficiency, amputation), which incurs great costs to the health care system.
Definition and history of the diabetic foot syndrome

The concept of diabetic foot syndrome incorporates various clinical pictures characterised by different aetiologies and pathological mechanisms. Common to all is the fact that injuries to the foot of the diabetic patient can result in complications that may lead to amputation of the whole limb if treatment is delayed or ineffective.

Pryce described “a case of a perforating ulcer in diabetes and atactic symptoms” as early as 1887. In the first half of this century, foot lesions in diabetics, which frequently lead to amputation, were considered an unavoidable complication of diabetes associated with arteriosclerosis and were classed under the heading of “diabetic gangrene.”

In 1934, Elliot Joslin, one of the pioneers of diabetology, published an article entitled “The menace of diabetic gangrene.” According to his observations, diabetic gangrene as a cause of death in diabetics had increased from 2% before 1914 to more than 12% by 1926, only a few years after the discovery of insulin. Although impaired circulation and the consequent diabetic gangrene was considered the main cause of diabetic foot complications, Joslin described in detail the now well-known common causes of diabetic foot lesions, i.e. burns from hot water bottles, ill-fitting new shoes and lack of foot hygiene. He vehemently advocated the intensive education of patients about cleanliness and care of their feet in order to minimise the occurrence of impending diabetic gangrene. “Consequently it has been forced upon me”, he wrote, “that gangrene is not heaven-sent, but is earth-born”.

However, it was not until the 1950s that diabetic neuropathy, ischaemia and infection, were finally recognised as precondition of foot complications in diabetics – facts that still hold good today. The good prognosis for local surgery in neuropathic lesions and the confinement of radical surgical interventions to ischaemic changes was also described first at that time.

The need for specialised care of diabetics with foot problems became increasingly apparent in subsequent years and it was recognised that many approaches to treatment (pressure relief, shoe provision) could be
derived from the procedures adopted in another disease associated with a neuropathic impairment of sensory perception, leprosy\textsuperscript{20}. In the 1970s, special programmes to improve the prognosis in diabetic foot complications were introduced for the first time in Atlanta, USA. The amputation rate in diabetics was reduced by 50%. Institutions with similar success rates were subsequently set up in Europe, firstly in Geneva and London\textsuperscript{22}, and then in Germany in 1983 (\textit{Prof. Ernst Chantelau, Dr. Maximilian Spraul and Prof. Michael Berger at the University Hospital of Düsseldorf}\textsuperscript{23, 24}). In 1989, the St. Vincent Declaration\textsuperscript{25} set a target of halving the amputation rate in diabetics within a five-year period. Subsequently, outpatient foot departments were created. In 1993 these joined together to form an association, the Diabetic Foot Working Group, affiliated to the German Diabetes Society.

Increasing interest in the diabetic foot was also reflected in research activities. In the journals of the American and British Diabetes Societies the number of articles on subjects related to diabetic foot syndrome in each case doubled between 1982 and 1996, while at the American Diabetes Congress, three times as many contributions dealt with the subject in 1996 as in 1980. Since 1998, a medical journal “The Diabetic Foot,” published four times a year in England, has been devoted to the subject. International meetings on the topic of diabetic foot problems lasting several days are held annually in San Antonio (Texas, USA) and every two years in Malvern (England). An international symposium was organised on the diabetic foot for the first time in 1991 in the Netherlands, attended by 500 participants from 46 countries. The third and most recent was held in May 1999\textsuperscript{26}. 
Diabetes treatment and research in Europe: The St. Vincent Declaration (1989)

Five-year aims of the St. Vincent Declaration:

– Implementation of effective measures for prevention of costly complications

– Reduction of the rate of new cases of blindness due to diabetes by one third or more

– Reduction of the numbers of people entering end-stage diabetic renal failure by at least one third

– Reduction by one half in the rate of limb amputations for diabetic gangrene

– Cut morbidity and mortality from coronary heart disease in the diabetic by vigorous programmes of risk factor reduction

– Achieve pregnancy outcome in the diabetic woman that approximates to that of the non-diabetic woman

Despite all these activities, the care of patients with diabetic foot problems in Germany has still not been satisfactorily resolved, and further urgent improvements are required.
Epidemiology of the diabetic foot syndrome

A quarter of the diabetic population is at increased risk of foot injuries as a result of the presence of diabetic neuropathy or an arterial circulatory disorder. Every year 3 to 7% of diabetics suffer a foot lesion for the first time. Following healing of the injury, the risk of suffering a further ulceration (relapse) increases annually to between 30 and 100%, depending on the quality of the after-care. Like previous amputees, these patients must also be regarded as high-risk patients and require very intensive, structured monitoring and care. In Germany, more than 20,000 foot lesions in diabetics still culminate in amputation per year. Following an amputation, mortality is approximately 20%. Within 3 years 50% of the surviving patients also undergo an amputation on the contralateral side. The five year survival of patients after amputation is low, approximating 25%.

More than four million diabetics are known to be living in Germany today. If patients at risk of diabetic foot complications are defined as those diabetics who suffer from diabetic neuropathy and/or in whom two or more foot pulses cannot be felt, then 25% of the diabetic population belong to this risk group. In the case of Germany, this yields an estimated 1.25 million diabetic patients at risk of lesions of the lower limb. The most negative consequence of such an injury, amputation, affects diabetics of various age groups up to 100 times more frequently than their non-diabetic peers.
Sensorimotor and autonomic diabetic neuropathy and peripheral arterial occlusive disease must be regarded as the most common underlying conditions for diabetic foot complications. These can lead to foot injuries in diabetics either alone or in combination. In 600 English patients with ulceration, neuropathy was found to be the cause in 45%. Fortyfive percent of these patients exhibited both diabetic neuropathy and a circulatory disorder, and only 7% suffered exclusively from a peripheral circulatory disorder. In aetiological terms, neuropathy proved to be responsible for 90% of injuries. In 260 of our own patients with foot injuries, neuropathy was found in 80% of cases, and of these 43% had accompanying circulatory disorders. As in the British study, an isolated arterial occlusive disease occurred in only 10% of patients.

Diabetic neuropathy must therefore be seen as a predisposing factor to diabetic foot lesions. This may be due to external (e.g. ill-fitting footwear) or internal pressure (limited joint mobility) foot deformities and severe foot pressure. Increased foot pressure is to be found in 20% of patients even without a clinically detectable neuropathy and can be used to identify patients at risk of ulceration. Almost 30% of patients with increased foot pressure suffer from ulceration during the following two years. The incidence of symptomatic diabetic neuropathy varies with the patient's age and the duration of diabetes: 5% of diabetics aged between 20 and 29 years exhibited neuropathy. This rises to 40% between the ages of 70 and 79 years. At the time of diagnosis, 7% of patients in the UKPD study were suffering from neuropathy. Five years after diagnosis, 20% of the patients had detectable neuropathy and this figure increased to approximately 45% with the longer duration of the disease (40 years or more).

Diabetic neuropathy was found in half the type 2 diabetics aged over 60 years. Although the lack of pain from injuries predisposes to the development of diabetic foot complications, pain in the lower extremity does not in any way preclude neuropathy ("painful-painless leg"). Veves found a painful neuropathy of this nature in almost half of neuropathic patients and a third of patients with foot ulcer.
Among non-selected patients in general practice, an arterial occlusive disease is found in about a third of diabetics, about four times as often as non-diabetics\(^{34}\).

Preliminary signs of ulcer disease (prelesions such as a hard callus with or without maceration) are detected in approximately one in seven patients with an existing diabetic neuropathy. In these patients, the development of a perforating ulcer of the foot (classic neuropathic pressure ulcer) can be avoided with adequate and early treatment\(^{35}\). In a regional study in Rhineland-Palatinate, hyperkeratosis was found in almost 70% of patients, of whom half showed additional subcallosal suggillations. In this study involving almost 900 patients, 8% exhibited a florid, open foot lesion, and almost 15% of those studied reported a previous history of such lesions\(^{36}\).

When a lesion of this kind is healed, there is still a lifelong risk of recurrence of the ulcer because of the ongoing underlying disease. In a large Swedish study recurrent ulceration was found in 34%, 61% and 70% of ulcer patients after 1, 3 and 5 years, respectively. Fifty percent had suffered another lesion within two years\(^{37}\).

Foot ulceration is the most frequent cause of amputations in diabetics\(^{38}\). The risk of an amputation of a limb varies according to the patient’s age, race and sex\(^{39,40,41}\). Common to all, however, is the fact that the risk of undergoing an amputation is 20 to 40 times higher (in some age groups up to 100-fold) than in comparable non-diabetics\(^{39,42,43}\). However, the idea that a limb amputation is an event that occurs late in the course of diabetes is incorrect. According to an English study, 20% of amputations occur in the year in which the diabetes is diagnosed\(^{44}\). The level of amputation is particularly important for a later independent lifestyle and the prognosis of the patient. After amputations of the toes and forefoot (minor amputations) between 5% and 7% require permanent care, whereas in the case of major amputations (lower and upper limb) 36% require permanent care.
The probability of survival and the risk of an amputation on the opposite side are also closely correlated to the amputation level. Mortality after two amputations is approximately 3%, whereas this figure rises to 20% after major amputation\textsuperscript{45}. The 5 year survival rate after amputation is 27% which compares to 60% of patients whose foot lesion is healed with conservative treatment\textsuperscript{37}. The probability of a limb amputation on the opposite side following a successful major amputation is 12% in the first year and more than 50% after three years.

If the aim of reducing amputation by half is to be achieved, the diabetic patient must be advised to avoid any situation that might result in foot ulceration.
Socio-economic significance of the diabetic foot syndrome

Costs due to foot complications in diabetics

When talking about medical topics, it is not possible to ignore the associated costs. Few data are available on the costs resulting from diabetic foot syndrome in Germany, but the extent of the problem can be illustrated using data from Scandinavia, Great Britain and the USA. Overall, the costs generated by diabetes are about three times as high as those produced by non-diabetics. Foot complications constitute a major proportion of these: every fifth hospital admission for diabetics is a result of foot problems. As the inpatient period can be prolonged, foot complications are responsible for almost half of all inpatient days for diabetics. In Great Britain, hospitalisation as a result of diabetic foot complications alone results in annual costs equivalent to 375 million EUR. Inpatient treatment costs are the most significant single factor. With primary healing, about 30% of the total cost derives from hospitalisation, but where amputation is required this figure is 65% to 80%. The average healing duration for diabetic foot lesions is about four months. Ten percent of all lesions persist for more than one year, which incurs further costs for outpatient care. Fifteen percent of all foot ulcers in diabetics do not heal before the patient’s death.

Beside the long period of inpatient care that is frequently required, the high likelihood of an amputation and the risk of life-long disability are important cost-generating factors. The average costs of a superficial diabetic foot ulcer are estimated at approximately 4,500 EUR. In the presence of a deep infection this increases to 23,500 EUR and with the occurrence of gangrene may rise to 50,000 EUR. In the case of primary healing, expenses amounting to some 7,500 EUR are incurred, but this could be multiplied sixfold where an amputation is required.
The costs of antibiotic treatment (less than 1% of the overall costs) or technical orthopaedic measures (about 3% in the case of primary healing) are relatively small\textsuperscript{50}. The costs of local wound treatment are less determined by the use of certain wound dressings, but to a much greater extent by the frequency with which bandages are changed.

When calculating the actual financial burden resulting from diabetic foot problems, it is essential to take a long-term view. The potential risk of recurrent ulceration, amputation or the patient’s death must be incorporated in the calculations. Over a 3-year period, a primarily healing neuropathic ulcer incurs costs of about 15,000 EUR overall\textsuperscript{51}. With a conservatively healed ischaemic lesion, the costs rise to about 25,000 EUR. If amputation of an extremity is necessary, in the following three years on average about 40,000 EUR annually are required simply for domestic care. In the USA, the direct costs of an amputation are put at 15,000 to 50,000 EUR depending on the amputation level required\textsuperscript{52}. If the indirect costs resulting from loss of productivity are added to this, the figure is more than doubled\textsuperscript{53}. A recent American study calculated the annual total costs resulting from diabetic foot problems in the United States to be 5,000 million EUR\textsuperscript{54}.

As outlined earlier, the diabetic foot syndrome incurs massive financial costs to the health services and the patient. Just as impressive as the costs incurred, are the calculations of the potential savings that can be made from preventive strategies in the treatment of the diabetic foot syndrome. In the USA in 1998 the annual savings resulting from the avoidance of amputations as a result of structured patient information was estimated at 3 to 4,500 EUR per patient\textsuperscript{52}. Calculations by Assal in Geneva suggest that for every dollar invested in educating diabetics, savings of three to four times that amount may be expected. Savings made as a result of avoiding nine limb amputations could finance the treatment of 400 diabetic patients for a year, 820 hours of group training, further 1,100 hours of individual training for diabetics and an additional 1,500 foot visits\textsuperscript{55}.

One cost item, however, does not feature in any of these calculations, namely the “cost” to the patient themselves in terms of the emotional trauma suffered and the loss of quality of life and independence.
Psychological aspects and effect on quality of life

“Quality of life is a descriptive concept that is intended to provide information about the degree of satisfaction with life or those factors which make life worth living” (from: J.M. Last: A Dictionary of Epidemiology). In medicine, the concept involves three dimensions:

1. Physical capacity
2. Subjective well-being
3. The individual’s social relations with his environment

Since purely objective findings are insufficient for assessing the quality of life, the patient's subjective well-being and his own assessment of his condition increasingly need to be included in the medical evaluation and given due consideration in the treatment of a disease.

Logically, the effect of diabetic foot injuries on the quality of life of both the patient and their relatives should be considered jointly. The few studies that have been published to date on this subject are unanimous: the decisive factor that affects the quality of life of patients with diabetic foot problems is the restriction on their mobility. This adversely affects their social situation and can result in various psychological responses.

One example of this is the fact that patients who are mobile after amputation rate their quality of life more highly than patients with florid foot lesions. The restriction on the sphere of activity impinges on the patient's occupational and social situation and can lead to feelings such as guilt (“being a burden on others”). The resultant anger and frustration (loss of independence) are associated with fear and worry (“How long will this go on for?”, “Will it result in amputation?”). Relatives on the one hand become the target for the patient's unhappiness and imbalance and on the other hand have to assume new roles in the patient's life (transport to medical appointments, taking over everyday activities previously undertaken by the patient themselves). Opportunities for social contacts and the scope for movement (e.g. travel and holidays) are equally limited for patient and relatives.
Tension in relationships is therefore unavoidable. A few sufferers, however, regard the more intensive contact with their relatives, even if involuntary, as a positive factor and acquire more patience in dealing with other everyday problems as a result of handling this particular situation. The ability to cope with these changes is influenced by the patient’s age and social origins\textsuperscript{58}. Among younger patients, the anxiety of losing one’s job, impending financial losses and the reduction in self-esteem take precedence. Elderly sufferers rate social isolation as more serious. Physical effects on the quality of life are elicited in the form of side effects to any antibiotic treatment required and the tiredness and exhaustion that result from the increased expenditure of energy needed for moving about\textsuperscript{57}.

Fear of the consequences of foot ulceration can channel the patient’s behaviour in various directions: a depressive mood or paranoia-like fixation on the foot injury may result. Equally there may be total denial of the situation, associated with non-attendance at outpatient appointments or failure to attend in the event of new injuries\textsuperscript{60}. It is at this point that the diabetic foot team can provide targeted, patient-oriented information about the disease and avoidance of unrealistic expectations on the part of the patient. This effort of the team, together with the provision of therapeutic certainty are important bases for the successful treatment of patients with foot lesions. Disappointment and failure can thus be minimised, avoiding the incorrect behaviour pattern in patients.

Psychological problems affect the clinical course and the subsequent outcome of treatment of patients with diabetic foot complications. Members of treatment teams should be aware of such stresses on the patient-therapist relationship, be willing to review treatment, and, if necessary, change their own patterns of behaviour and expectations in this respect.
Risk factors for foot complications in diabetics

The main risk conditions for the occurrence of foot lesions in diabetics are the loss of protective mechanisms in the presence of a diabetic neuropathy and the absence of sufficient tissue perfusion as a result of an arterial occlusive disease (AOD).

The most important risk factors are:
Bony foot deformities, the existence of increased plantar pressure, impairment of vision and mobility and a previous history of a diabetic foot lesion.
Infections play a minor role in the genesis of a diabetic foot lesion, but assume considerable importance in existing injuries as a risk factor for progression to amputation.

Reduced sweat gland activity, loss of the plantar fat pad and impaired joint mobility in diabetic neuropathy, together with the resultant callus formation, lead to callus haematomas at exposed sites if the pressure is not relieved.

One of the most effective means of preventing diabetic foot complications is a regular foot examination as well as the identification of risk indicators. Unfortunately, foot examinations in diabetics are only rarely performed. And when they are performed – in both outpatient and inpatient settings – then they are often inadequate. A thorough foot status is established in only about 10% of all diabetics during routine outpatient visits. Even among patients who are admitted to hospital for a diabetic foot ulcer only 14% are adequately examined in terms of their foot findings.

61
The following section begins by presenting the different risk factors for foot lesions which may lead to amputations in diabetics and their importance, before going on to investigate in detail the causative factors of foot injuries.

Although different authors ascribe different significance in their studies to the various risk factors for diabetic foot lesions, the same basic risk factors are implicated:

1. Peripheral neuropathy
2. Bony foot deformities
3. Existence of increased plantar pressure
4. History of ulcer
5. Peripheral arterial occlusive disease.

Peripheral sensorimotor neuropathy represents the most important risk factor for the occurrence of foot ulcerations and amputation in diabetics. Patients rarely develop a diabetic foot ulcer in the absence of neuropathy. The loss of the protective perception of pain and pressure is the underlying cause of foot complications in diabetics. The occurrence of a foot ulcer in the great majority of cases is a multifactorial and complex process in which various risk factors play a role. Neuropathy is found as a subsidiary factor in about 90% of cases\(^6^2\). The risk of suffering ulceration of the foot increases ten-fold in the presence of signs of diabetic neuropathy (detected by the pathological monofilament test and pathological vibration sensation in the biothesiometer test) compared with neurologically healthy diabetics\(^6^3\).

In addition to the reduced awareness of injury resulting from the impairment of the sensory nerve fibres, two other major risk factors are involved:

1. The occurrence of bony deformities of the foot
2. Increased plantar pressure

These factors also lead to atrophy of the small muscles of the foot with the consequent impairment of balance. The impairment of autonomic nerve fibres leads to a failure of sweat gland function and consequently to loss of skin elasticity.
Foot deformities, together with severe hyperkeratosis (callus formation) contribute to foot ulceration in about 60% of cases, and increased plantar pressure in 50%. Reduced adaptability and increased pressure loads arise through a variety of mechanisms: changes in the skin and peri-articular structures (e.g. joint capsules) result in an impairment of joint mobility. The resultant increase of approximately 30% in foot pressure values, combined with the loss of protection due to neuropathy, considerably increases the risk of an ulcer formation.
Ischaemic diabetic foot syndrome with pressure necrosis on the sides of the foot and toes, associated with dry gangrene of the third toe.

This is supported by studies of rheumatoid arthritis patients with foot deformities, but without concurrent neuropathy. More recent studies indicate hardening of the peri-articular connective tissue and increasing atrophy and fibrosis of the plantar fat pad as independent risk factors, particularly in recurrent lesions. Such changes are found in the presence of even mild neuropathy, but their intensity increases proportionately to the severity of underlying the neuropathic disease. An effect on the capillary blood flow as a result of the increased plantar pressure load and increased fibrosis as a result of a chronic inflammatory irritation are suggested as possible pathological causes. Fibrosis and atrophy of the plantar fat pad affect the biomechanical properties of the sole of foot in the same way as the frequently observed increased callus formation. Removal of the callus reduces the pressure load on the sole of the foot by about 25% and hence reduces the risk of subcallous haematoma, as well as subsequent ulcer formation.

Finally, patients with a previous history of diabetic foot ulcer are at highest-risk of relapse, because of the constant risk conditions and the structural foot changes described (less resistant and less flexible tissue or change in the pressure-bearing surface following minor surgery). The risk of suffering a relapse is tripled following primary ulcer healing and increases to about 50-fold following surgical treatment.
Ischaemia as a consequence of peripheral arterial occlusive disease represents a minor contributory factor to the occurrence of diabetic ulcer (23 to 35%62,71), but assumes increasing significance as a risk factor in the progression of a foot ulcer towards amputation38. Critical limb ischaemia (CLI) is present in 50% of all diabetic foot lesions that end in amputation. Whereas ulcer formation is a multifactorial process, ischaemia in itself can be sufficient to result in amputation.

While peripheral arterial occlusive disease in non-diabetics is the reason for amputation in the majority of cases, several factors are usually involved in diabetics, both in the occurrence of an ulcer and also in the subsequent progression to amputation. In 80% of cases, there is an identifiable, acute cause, mainly footwear-related or thermal trauma (burn, excessive cold). Subsequent ulceration and insufficient wound healing contribute to the amputation of all or part of a limb38. Peripheral oedema (40%), ignorance about foot care (25%) and lack of social integration (20%) are further factors leading to amputation.

In 80% of cases the initial insult that results in ulcer formation and ultimately amputation can be identified 38,62,72, a fact that appears extremely important in relation to the advice given to patients in order to prevent recurrence.

Infection plays a minor role in the causation of diabetic foot lesions (less than 1% of cases71), but is a major risk factor for amputation (involved in 60% of cases)38. What is important here in diabetics is the frequent absence of the classic signs of infection (fever, leucocytosis, increased erythrocyte sedimentation rate, [ESR]) because of the existing immunopathy73. Despite multi-disciplinary care, surgery is unavoidable in almost 90% of diabetics with deep foot infections. In 34% of cases this involves minor amputations and in 10% a high-level limb amputation.
The probability of a major amputation is increased by the presence of:

1. Pain (the relative risk increases 13-fold)
2. Progressive gangrene (14-fold)
3. Pre-existing intermittent claudication (6-fold).

None of these signs, however, precludes primary healing or healing following minor surgery. The risk of having to undergo an amputation is also increased in the presence of an additional cardiovascular disease, diabetic neuropathy, reduced arterial ankle pressure (less than 80 mmHg) or toe pressure (less than 45 mmHg). Male patients are also at higher risk. A further important risk factor for the occurrence of foot ulceration is impaired vision and reduced mobility, as these factors limit the patient's ability to co-operate in foot inspections and foot care. Eighty percent of sufferers are totally unaware of this restriction. In a study by Assal, impaired vision was found in 70% of diabetic ulcer patients studied, 10% of the patients with neuropathy but no ulceration, and only 5% of non-neuropathic diabetics.

Inadequate visual acuity (defined as patient's incapability to observe a lesion of 3 mm in diameter at the minimum eye-foot distance) was found in 50%, 5% and 3% of patients, respectively. Impaired vision also constitutes an independent risk factor for fractures with the subsequent formation of Charcot's deformity as a result of the increased risk of spraining and tripping.

In a large Italian case-control study possible risk factors for ulcer formation were:
1. Male sex (the relative risk increases 3-fold)
2. Lack of family involvement (1.4-fold)
3. Difficulty attending follow up appointments (2-fold)
4. Lack of diabetes education (3-fold)
5. Irregular compliance with foot inspections.
In central Europe, the occurrence of diabetic foot ulcerations is preceded in 28%\textsuperscript{78} to 55%\textsuperscript{79} of cases by shoe-related injuries. Eighteen percent are the consequence of injuries related to foot care, while 3% are preceded by other minor trauma. Thermal traumas, particularly burns, are relatively rare (2% of all cases), but are significant because of the risk of hypertrophic scar formation and delayed recovery. At temperatures of 44°C, a theoretical exposure of six hours is required for necrosis formation, whereas at a temperature of 50°C, only a five-minute exposure is sufficient\textsuperscript{80}. In diabetics, a disorder of hot and cold perception is found in the hands as well as in the lower limb. In other regions of the world, causes of diabetic foot injuries include rat bites\textsuperscript{81}, worm infestations\textsuperscript{82} or burn injuries from the use of alternative medical methods such as moxibustion, a traditional Chinese medical procedure\textsuperscript{83}.

As previously mentioned, certain constantly recurring sets of circumstances can result in foot ulcerations\textsuperscript{71} and amputations\textsuperscript{38}. An understanding of these facts is essential for the successful employment of preventative strategies. A distinction is drawn here between contributory factors which, together, might result in the event (ulcer or amputation), and “sufficient causes” which can produce such an event in themselves. The causal factor can be found in 80% of ulcers and 86% of amputations.
Three frequent pathways, which together account for 60% of all ulcers, are:

1. Neuropathy, deformity, callus formation, increased pressure
2. Penetrating minor trauma
3. Ill-fitting shoes

The combination of minor trauma, skin ulceration and delayed wound healing with or without the co-existence of infection or gangrene results in amputation in 70% of cases. Eighty-four percent of all amputations are preceded by ulcer formation.

Diabetic foot ulcerations are a significant problem because:

1. They are very common
2. They are cost-intensive
3. They can identify patients at risk of amputation
4. They adversely affect the functional status and well-being of the patient concerned
5. They can be avoided in many patients by preventive foot care and the use of specifically designed footwear

Early identification of the risk factors and appropriate implementation of preventive and therapeutic measures would dramatically reduce the occurrence of foot complications and their consequences in diabetics.
Concurrent diseases in diabetics with foot complications

The average age of diabetics with foot injuries is more than 65 years. Mediocre response to treatment in these patients is due in part to the multimorbidity of sufferers. Patients with foot lesions suffer to a considerable extent from macrovascular disease and the consequences of diabetic microangiopathy. Diabetic retinopathy, autonomic diabetic neuropathy and diabetic nephropathy are more frequently found in type 1 diabetics than in type 2 diabetics with foot lesions, who have a greater incidence of coronary vessel disease and peripheral arterial occlusive disease (PAOD). In 243 patients from the Dortmund Hospital, neuropathy was found in 80% of ulcer patients. Nephropathy, retinopathy and coronary heart disease were found in 50% of patients. Involvement of the arteries supplying the brain in 22% and PAOD in almost 70%. Similar figures were obtained in our own patient population: neuropathy 80%, nephropathy 65%, retinopathy 55%, myocardial infarct 19%, stroke 20% and PAOD 56%.

The risk of a concurrent disease of the coronary vessels in patients suffering from PAOD is increased two and a half times compared with patients without disease of the leg vessels. The disease is frequently asymptomatic, particularly in women. Prognostically, the occurrence of gangrene of the toe in particular may be considered an extremely adverse sign in terms of patient survival rate. The mean survival time of these patients following the onset of gangrene is on average less than 18 months. In the study quoted, smokers (82% smokers vs. 45% non smokers) and patients requiring an amputation (64% amputated vs. 27% non amputated) were found significantly more often among patients who died early than among those with a more favourable prognosis for survival.

There is an obvious relationship between increased protein loss from the kidney (micro-albuminuria, proteinuria) and the occurrence of ulcers in diabetics. Although the abnormal excretion of albumin from the kidney in type 2 diabetics is of renal origin, it reflects a vascular process that involves the nephron and the tunica intima of the large vessels. Micro-albuminuria is therefore,
a marker of a progressive renal disease and a predictor of a generalised arteriosclerosis and early death. Increased albumin excretion occurs most frequently in patients with ischaemic and neuro-ischaemic lesions. It is also found to a greater extent in patients with purely neuropathic ulcers, as compared to ulcer-free diabetics.

Diabetic retinopathy is an important finding in foot patients for several reasons. Firstly it represents a risk factor for the development of foot injuries (see also chapter “Risk factors for foot complications in diabetics”). Secondly, the concurrent presence of the two diseases is increasingly found at the time of diagnosis in type 2 diabetics. If an arterial occlusive disease is present at the time of diagnosis, then the survival rate in these patients is markedly reduced. After five years less than 20% survive. The occurrence of both disease states at the time of diagnosis of type 2 diabetes is particularly common among smokers.

Typical fundoscopic findings in proliferative diabetic retinopathy: diabetic retinopathy is considered a risk factor for foot complications because of the impairment of vision.
The high incidence of concurrent micro- and macrovascular disease in patients with foot ulcers shows the urgent need for the use of all available options for early diagnosis and appropriate treatment, not only to increase the chances of a positive outcome of the foot lesion, but also to have a beneficial effect on the overall fate of the patient affected.
Diagnosis and differential diagnosis of the diabetic foot syndrome

Diagnosis of sensorimotor and autonomic diabetic neuropathy and diabetic neuropathic osteoarthropathy

The human nervous system consists of the peripheral nervous system (PNS) and the central nervous system (CNS). The CNS comprises the brain and the spinal cord. The somatic and autonomic nervous systems are distinguished in terms of their functions. Somatic nerve fibres conduct stimuli to the muscles and conversely from the sensory receptors to the CNS. Neurons that are not subject to voluntary control are grouped together under the heading of the autonomic nervous system. In the lower limb, they exert a particular action on the regulation of vascular tone and the secretion of sweat glands. Neuropathies are characterised by a progressive loss of nerve fibres, which can be detected by non-invasive tests of nerve function. The early identification and education of patients with a loss of sensory perception in the lower limb would be the most effective way of avoiding foot injuries and amputations in diabetics.

The NEURODIAB Working Group of the European Association for the Study of Diabetes (EASD) agreed guidelines in 1998 for the annual follow-up of diabetics with regard to their neurological status. As opposed to the consensus guidelines of the San Antonio conference, only simple and universally available investigations, in addition to clinical examination, were proposed to establish nerve function. Diabetic neuropathy is defined as “the presence of signs or symptoms of peripheral nerve function disorders in diabetics following the exclusion of other causes.”

Three sensory modalities can be easily tested:
1. Vibration sensitivity (tuning fork test and biothesiometry)
2. Pressure perception (Semmes-Weinstein monofilaments)
3. Temperature discrimination (Tip Therm)
These tests provide information about the degree of neuropathy and hence the risk of diabetics developing foot lesions.

Disorders of autonomic innervation of the foot may be suspected in the presence of dry, cracked skin, fissures and hyperkeratosis. The acetylcholine test (“sweat spot test”) is a suitable test method ⁹⁸. Electrophysiological investigations (e.g. nerve conduction velocity) serve more to differentiate neuropathies of different aetiology than to provide additional findings in diabetic foot syndrome. These tests do not add to the diagnostic value of the methods described above. Abnormalities of nerve conduction velocities, moreover, are not consistent with the clinical signs in diabetic neuropathy ⁹⁹.

Two clinical methods have become increasingly accepted in Germany: the examination of vibration sensitivity with the calibrated Rydel-Seiffer tuning fork and the recording of pressure sensitivity with the 5.07 Semmes-Weinstein monofilament (10 gram application force).

Of the various manifestations of diabetic neuropathy, three are of relevance to the lower limb ¹⁰⁰: the acute sensory, chronic sensomotoric and autonomic neuropathies. A progressive, stocking-shaped, predominantly symmetrical loss of vibration, temperature and pain perception is typical of the chronic sensorimotor form of the disease. A lack of proprioceptive reflexes and
atrophy of the small foot muscles with a claw toe position and prominent metatarsal bones may be considered signs of involvement of motor nerve fibres.

The progressive glycosylation of the plantar aponeurosis with an increasing loss of elasticity and an eventual rupture may contribute to these deformities\textsuperscript{101}.

Autonomic nerve fibres are involved in a large number of cases in patients with foot ulcerations\textsuperscript{102}. Particularly in patients with a diabetic neuropathic osteoarthropathy (DNOAP), involvement of the autonomic nervous system is observed in more than 90\% of cases\textsuperscript{103}. Severe acute and isolated autonomic neuropathies are rare manifestations\textsuperscript{99}. About two-thirds of diabetic neuropathies which follow are asymptomatic. Hence, the absence of symptoms does not necessarily mean that the patient has healthy feet\textsuperscript{100}.

Loss of vibration sensation is the most common and earliest sign that nerve fibres are affected in diabetic neuropathy. Normal ageing has an effect on vibration sensation, so have patient co-operation and motivation. Its usefulness in elderly patients is doubtful\textsuperscript{104}. In addition, proprioceptive reflexes cannot be detected in about 70\% of all elderly patients (including non-diabetic patients).

The 128 Hz tuning fork is marked with a scale that is subdivided into eighths. An impairment of age-related impairment of sensation was found in 20 of 26 patients with foot ulcerations in a tuning fork test. A reduction to less than 4/8 occurred in 95\% of ulcer patients\textsuperscript{105}. In another study, a reduction in vibration sensitivity to 2/8 or less was found in all patients with foot lesions\textsuperscript{94}. The semiquantitative measurement of the vibration sense yields valuable information for patients under 60 years of age. Evaluation of the quantitative vibration measurement (determination of the vibration threshold) by biothesiometer yielded a threshold of normal sensation of 25 V (volt). The risk of ulceration in the group of patients with a sensitivity of between 25 and 33 V was increased eight-fold, while with values of more than 42 V it increased more than twenty-fold\textsuperscript{95}.

While the vibration sensation test is used in screening for neuropathy, it is the loss of temperature discrimination and pain perception that is responsible for foot injuries in diabetics. The test of pressure sensitivity with the 5.07 (10 gram) nylon filament is superior to the biothesiometer
measurement because of its higher sensitivity (100% vs. 79%). Nylon filaments with a standardised application force (1, 10 and 75 gram) are applied at specific points on the patient's foot, bent and their perception tested96.

Temperature discrimination can be tested simply, economically and reproducibly with the Tip Therm (Axon, Düsseldorf). This is an instrument similar to a thick pencil with a plastic side and a steel side. All 26 patients with a previous determined temperature discrimination threshold of less than 10°C recognised the different temperature on the two sides of the Tip Therm. In contrast, 20 of 24 patients with impaired temperature perception (threshold greater than 10°C) were incapable of doing so97. With a combination of the tuning fork test, the monofilament test and the temperature discrimination (Tip Therm), the neurological risk status of each diabetic can therefore be determined rapidly and cheaply.

A rare but important complication of diabetic neuropathy is diabetic neuropathic osteoarthropathy (DNOAP) which is found in at least 0.1 to 0.5% of all diabetics. Cavanagh et al. (1994) even found evidence of osteoarthropathy in about 10% of all patients with diabetic neuropathy106, i.e. in about 3% of all diabetics.

Such changes were first described by Musgrave, 1703, as a consequence of sexual transmitted diseases107. In 1868, Charcot, after whom the final stage of osteoarthropathy with marked deformities was also named, described painless neuropathic joint changes and bone destruction in patients with tabes dorsalis108. Diabetes mellitus is the most common disease underlying such changes today. Such findings also occur in patients with leprosy, syringomyelia, in alcoholics and in patients with congenital insensitivity to pain. The exact pathogenetic background of DNOAP has yet to be fully elucidated107. In the current state of knowledge, the autonomic neuropathy observed in almost all patients with diabetic osteoarthropathy results in increased blood flow as a result of arteriovenous shunts, and ultimately in osteopenia. The reduced bone density can often be detected even before the clinical onset of the disease109.
Acute diabetic osteoarthropathy with swelling, redness and excessive heat and incipient deformity of the right foot.

The muscular imbalance caused by the presence of a motor neuropathy and the potential for concurrent traumas due to the sensory deficit, result in repeated peri-articular fractures with impaired healing and the possible end-state of a severely deformed foot. In addition to the swelling and redness of the affected extremity, a temperature difference of more than 2 °C from the opposite side is indicative of an active osteoarthropathy.

According to Sanders, five forms of diabetic osteoarthropathy may be distinguished on the basis of their different localisations. Forms I, II and III involving the anterior and middle parts of the foot constitute more than 80% of all cases. Sella distinguishes four disease stages. The intention here must be to identify this clinical picture despite its relative rarity and to prevent extensive foot deformities through early diagnosis (clinical features, X-rays, CT scans) and the resultant appropriate relief of pressure. In addition to this, initial findings from adjuvant therapy with bisphosphonates provide promising results.
Diagnosis of arterial occlusive disease

The most significant single factor affecting the risk of amputation for diabetics is ischaemia of the affected extremities following an arterial occlusive disease. In a large proportion of cases, degenerative arteriosclerotic vessel processes underlie arterial circulatory disorders, resulting in a loss of elasticity of the vessel and ultimately occlusion of the lumen. Appropriate and early diagnosis of circulatory disorders and an understanding of the specific features of the disease in diabetics are essential to avoid unnecessary amputations.

The prevalence of arterial circulatory disorders in Germany in the 55- to 64-year-old age group is about 10%.112 This rises to 21% in type 2 diabetics113. Other risk factors include the patient's age, hypertension and heavy smoking. Although the incidence of peripheral arterial occlusive diseases (PAOD) is increased in diabetics and the disease manifests itself at an early age, the disease course is similar to that in non-diabetics114.

The misconception of an occlusive microangiopathy, the pitfalls of instrumental diagnosis in the presence of Mönckeberg's arterial sclerosis and its significance for the particular pattern of distribution of PAOD in diabetics are presented below in further detail. This is followed by a description of the clinical features in the presence of an associated sensorimotor diabetic neuropathy, together with a step by step procedure for the diagnosis of arterial occlusive disease.

The primary task in assessing diabetic foot lesions is the differentiation of neuropathic and (neuro-)ischaemic findings. The underlying difference between the two forms is the existence (or absence) of foot pulses. The most important basic diagnostic measure is therefore the palpation of foot pulses. Doppler examination of the peripheral arteries using an occlusive pressure measurement (determination of the ankle-arm index of arterial blood pressure)115 and, where necessary, an oscillographic examination or hydrostatic toe pressure measurement116,117,118 in the presence of media calcification are non-invasive examinations that yield further information.
**Clinical and instrumental diagnosis in diabetic foot syndrome**

<table>
<thead>
<tr>
<th>Neuropathic status</th>
<th>Arterial vascular status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previous history:</strong></td>
<td><strong>Previous history:</strong></td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>Clinical signs of an arterial occlusive disease such as resting pain or intermittent claudication (pain on exercise – both of which are often undetectable when a neuropathy is present simultaneously)</td>
</tr>
<tr>
<td>Clinical symptoms of neuropathy</td>
<td>Vascular risk factors such as hypertension, smoking, obesity and lipid metabolism disorders</td>
</tr>
<tr>
<td>(“positive symptoms” such as nocturnal or resting pain, “negative symptoms” such as impaired or absence of sensitivity to vibration, pain, pressure, temperature or touch) microvascular diseases of the eye and kidneys, plus alcohol abuse</td>
<td></td>
</tr>
<tr>
<td><strong>Inspection:</strong></td>
<td><strong>Inspection:</strong></td>
</tr>
<tr>
<td>Warm, dry, cracked skin</td>
<td>Cool, pale or livid, atrophic skin</td>
</tr>
<tr>
<td>Atrophy of the internal musculature of the foot with foot deformities</td>
<td>Loss of integumentary appendages, hair loss</td>
</tr>
<tr>
<td>Hyperkeratosis and subcallus haematomas</td>
<td>Typical acral necrosis</td>
</tr>
<tr>
<td><strong>Examinations:</strong></td>
<td><strong>Examinations:</strong></td>
</tr>
<tr>
<td>Reflex test (ATR)</td>
<td>Palpation of foot pulses</td>
</tr>
<tr>
<td>Vibration perception (Rydell-Seiffer Tuning fork, biothesiometer)</td>
<td>Doppler examination with occlusive pressure measurement (ankle-arm index, hydrostatic toe pressure)</td>
</tr>
<tr>
<td>Semmes-Weinstein monofilament (10 g)</td>
<td>Duplex ultrasonography</td>
</tr>
<tr>
<td>Temperature perception (Tip-Therm)</td>
<td>Transcutaneous oxygen measurement</td>
</tr>
<tr>
<td></td>
<td>Invasive and non-invasive radiological procedures (DSA, angiography, CO₂-angiography, MRI angiography)</td>
</tr>
</tbody>
</table>
In occlusive pressure measurements, an ankle-arm index of less than 0.9 is an indicator of arterial occlusive disease, irrespective of the existence or otherwise of medial calcification. Calcification of the tunica media of the arteries, described for the first time in 1909 by Mönckeberg and named after him, is found in a high percentage of diabetics. As a result the vessels become rigid and the occlusion pressures measured by Doppler pressure measurement are false. The presence of an occlusion of the vascular lumen or a reduction in the circulatory reserve due to calcification cannot be excluded.

Evidence, however, has been found of a correlation between medial calcification and the primarily more distal type of distribution of PAOD in diabetes patients. Patients with existing medial calcification exhibit tibial or peroneal occlusive localisations of PAOD significantly.
more frequently than diabetics without medial calcification or non-diabetics. Depending on the literature source, the arteries are assumed to be incompressible with an ankle-brachial index (ABI) of 1.35 or 1.5\[123].

Indices of more than 1.2 may be considered indicators of the presence of medial calcification\[122]. The most definite evidence is provided by taking an X-ray of the forefoot in which the medial calcification is visualised as a classic “tramline finding”\[120].

Media-calcification is a feature that is also increasingly found with advancing age, even in non-diabetics. In diabetics, however, the presence of diabetic neuropathy predisposes to its early onset, particularly where autonomic nerve fibres are also involved (loss of modulation of vessel tone)\[120]. The degree of calcification of the arteries correlates with the vibration perception and the duration of the diabetes\[124]. In patients with pronounced diabetic osteoarthropathy, in which the involvement of autonomic nerve fibres is typical, media-calcification is found in 80–90% of cases\[120]. As has already been mentioned, hydrostatic toe pressure measurement\[116,117,118] may be used for diagnostic purposes, as well as oscillography. In diabetics, there is often a physiologically lower pressure in the area of the toe arteries, relatively little calcification of the media and the unmasking of media calcification on elevation of the extremity above heart level. Values of more than 70 mmHg may be regarded as normal findings in this case.

In summary, Mönckeberg’s arteriosclerosis is a non-occlusive angiopathy typical of diabetes mellitus and specific to the presence of diabetic neuropathy. It is possibly of prognostic significance for the subsequent appearance of a peripheral arterial occlusive disease (PAOD) and the occurrence of fatal myocardial infarction\[125].
The significance of microcirculatory disorders at the capillary level in the onset and course of diabetic foot lesions is still a matter of debate. The presence of lumen-occluding processes in the microcirculation of diabetics\textsuperscript{126,127} was used before as justification for early and extensive limb amputation. Today, the presence of occlusive disease can be measured and hence excluded. However, functional abnormalities of the microcirculation with deterioration of haemodynamic, endothelial and cell function as a consequence of poor blood glucose control, must be considered definite\textsuperscript{128}. These conditions impair healing. At present, capillary microscopy, laser flow measurement and transcutaneous oxygen measurement are standard procedures used in the investigation of microcirculatory problems. Therefore the presence of gangrene with palpable foot pulses in patients with diabetic foot syndrome should no longer be considered a consequence of an occlusive microangiography, but much more as evidence of a neuropathic infected foot with the presence of septic emboli, and hence treated accordingly\textsuperscript{120,129}.

Fontaine's staging of PAOD is often of only limited use in diabetics when it is accompanied by diabetic neuropathy involving loss of pain perception. Measurement of the classic ischaemic pain following exercise (Fontaine stage II) and the presence of resting pain (Fontaine stage III) have limited significance. Occasional neuropathic irritation states are sometimes difficult to differentiate from resting pain in arterial occlusive disease. The essential aim should therefore be appropriate clinical examination and directed investigation. Ultrasound imaging of the arteries and further angiographic investigations (conventional angiography, digital subtraction angiography, MRI angiography\textsuperscript{130} and CO\textsubscript{2} angiography\textsuperscript{131}) according to the guidelines of the European Consensus Paper of 1990 should be performed in primarily neuropathic lesions with delayed healing before any amputation is recommended in diabetic foot ulcers or gangrene. The imaging should always include the foot arteries\textsuperscript{115}. MRI angiography may be expected to replace current angiographic methods in the medium term due to its superiority in detecting occlusion distances and its high cost efficiency\textsuperscript{130}. CO\textsubscript{2} angiography also exhibits marked advantages over the procedures currently used through its non-allergising method and the absence of renal toxicity\textsuperscript{131}. 
Classification of diabetic foot lesions

The optimum treatment for diabetic foot syndrome involves the multidisciplinary team. It assumes clear communication between the various members of the treatment team and requires a clear classification of diabetic foot lesions. The requirements made of classifications are illustrated below, the most frequently used classifications presented and their clinical significance described.

Co-operation and communication are mutually dependent and assume clarity and accuracy in the classifications used for planning therapy and for subsequent comparability.

A clinical description is a specific snapshot of a particular lesion and changes as the clinical situation improves or deteriorates. An effective description should not only provide someone else with an indication of the best possible immediate therapy, but should also indicate the urgency with which such treatment should be undertaken. A classification, however, should be applicable at all times and to a variety of lesions. A good clinical description of foot lesions should include details about the patient (including social aspects), the affected foot (side, localisation, cause of lesions) and the lesion itself (size, severity, infection, stage of wound-healing).

One difficulty in establishing classifications of diabetic foot lesions lies in the fact that they must be simple enough to be understood by all team members (specialist or non-specialist). Also, they must be flexible enough to cover all conceivable lesions and at the same time specific enough to be able to define an individual lesion clearly. A good classification also makes it easier to establish the prognosis for diabetic foot lesions.

Described in 1976 by Meggit and further refined by Wagner in 1981, the so-called Wagner classification has become one of the most widely used classifications of diabetic foot lesions world-wide. It comprises six stages (0–5). Grade 0 corresponds to the pre-lesion (e.g. callous formation or condition following a healed foot lesion). Grade 1 and grade 2 describe surface and deep ulcerations. Grade 3 severity involves the presence of deep ulcerations complicated by infection of bone and joints. Grades 4 and 5 describe localised and extensive necrotic developments. The classification has the
advantage of being very simple, but the disadvantage of being imprecise. Modifications by Harkless (supplemented with the suffix B for ischaemic extremities) or Reike (indication of the main aetiopathogenetic factors) have further refined these classification in terms of their use in practice.\textsuperscript{133,136}

**Wagner’s classification**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No lesion, possibly foot deformity or cellulitis</td>
</tr>
<tr>
<td>1</td>
<td>Superficial ulceration</td>
</tr>
<tr>
<td>2</td>
<td>Deep ulcer as far as joint capsule, tendons or bones</td>
</tr>
<tr>
<td>3</td>
<td>Deep ulcer with abscess formation, osteomyelitis, infection of joint capsule</td>
</tr>
<tr>
<td>4</td>
<td>Limited necrosis in forefoot or heel region</td>
</tr>
<tr>
<td>5</td>
<td>Necrosis of whole foot</td>
</tr>
</tbody>
</table>

The University of Texas Wound Classification System has been available as an alternative to this since 1996.\textsuperscript{137} In this classification 4 degrees of severity are distinguished (0, I, II, III). Severity grade 0 describes a pre- or post-ulcerous state with complete epithelialisation. Grade I refers to a superficial wound, and Grade II to a wound that has extended to the tendon or capsule. Grade III describes a wound with bone or joint involvement. All grades then have the suffix B appended in the presence of an infection, suffix C for concurrent ischaemia and suffix D for the concurrent presence of an infection and ischaemia. For example grade III D would be a lesion with ischaemia and infection in the presence of bone involvement. Grade II A would be a superficial wound without signs of infection or ischaemia.
The authors *Lavery, Armstrong* and *Harkless* evaluated the system in 1998 while studying more than 360 patients\(^{138}\). A grade III lesion (bone or joint involvement) indicated an eleven-fold increase in the risk of amputation. Patients with ischaemia and infection (stage D) exhibited a 90-fold higher risk of amputation.

*Rischbieter* and *Reike* in 1998 presented a similar evaluation for the modified Wagner classification. Patients with lesions of Wagner stages 4 and 5 (localised and generalised necrosis) had a nine-fold greater risk of amputation than patients with lesions of Wagner stage 0 to 3\(^{136}\).
## University of Texas San Antonio – Diabetic Wound Classification
**(Armstrong’s classification)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Completely epithelialised pre- or post-ulcerous lesion</td>
<td>Wound with tendon or capsule involvement</td>
<td>Wound with bone or joint involvement</td>
</tr>
<tr>
<td>A</td>
<td>Superficial wound without tendon or capsule involvement</td>
<td>Wound with tendon or capsule involvement with infection</td>
<td>Wound with bone or joint involvement with infection</td>
</tr>
<tr>
<td>B</td>
<td>Complete epithelialised pre- or post-ulcerous lesion with infection</td>
<td>Wound with tendon or capsule involvement with infection</td>
<td>Wound with bone or joint involvement with infection</td>
</tr>
<tr>
<td>C</td>
<td>Complete epithelialised pre- or post-ulcerous lesion with ischaemia</td>
<td>Wound with tendon or capsule involvement with ischaemia</td>
<td>Wound with bone or joint involvement with ischaemia</td>
</tr>
<tr>
<td>D</td>
<td>Superficial wound without tendon or capsule involvement with infection and ischaemia</td>
<td>Wound with tendon or capsule involvement with infection and ischaemia</td>
<td>Wound with bone or joint involvement with infection and ischaemia</td>
</tr>
</tbody>
</table>
## Diagnosis structure in diabetic foot syndrome
(modified by H. Reihe)

1. Underlying disease
   (neuropathy, arterial occlusive disease, mixed form, osteoarthropathy)

2. Localisation
   (e.g. toes, forefoot, heel region, scar regions)

3. Extent of injury
   (e.g. Wagner’s stages 0–5; Armstrong’s classification)

4. Wound healing stage
   (cleaning, granulation and epithelialisation phase)

5. Infection
   (yes/no; limb threatening, non-limb threatening)

A precise description and classification of diabetic foot lesions is essential for planning therapy, establishing the prognosis and comparing diabetic foot changes and should therefore be recorded meticulously.
Basic principles of the treatment of diabetic foot lesions

At present, treatment procedures for diabetic foot syndrome considered to be of proven efficacy include:
1. Pressure relief of the affected parts of the foot
2. Repeated and adequate mechanical débridement
3. Phase-specific moist wound treatment
4. Medical and surgical treatment of infection
5. The use of reconstructive and interventional procedures to improve blood circulation (with due allowance for the specific features of arterial occlusive disease)

Procedures such as the use of hyperbaric oxygen (HBO), the application of bio-engineered tissues and growth factors or biomechanical wound treatment with the use of fly larvae (where strictly indicated) may be regarded as supplements to the basic therapy but not as a replacement for it.

Possibilities of pressure relief

As has already been mentioned, biomechanical changes are a frequent consequence of diabetic neuropathy, resulting in an altered pressure load on the sole of the

Partial foot relief shoe (forefoot relief shoe, Thanner company) to maintain the mobility of patients with plantar and acral lesions during the recovery phase
foot. The combination of diabetic neuropathy and foot deformities increase the risk of ulcer formation. Therefore consistent pressure relief is an essential precondition for the prevention and healing of foot ulcers.

There is evidence of accelerated and persistent healing with various treatment approaches, such as bed rest, wheelchairs, the use of a total contact cast (plaster treatment) and partial relief shoes. The advantages and disadvantages of the latter two procedures will be presented below in greater detail.

Plaster treatment in the form of a total contact cast (TCC) currently represents the gold standard in the USA and Great Britain for pressure relief in plantar pressure lesions of the diabetic foot. The benefit or relatively short healing time, approximately five weeks with a pressure reduction of 75% to 85% contrasts with the high cost (about 200 dollars), the need for regular changes of the cast and the risk of infection with
increased difficulty of detection. Probably the most extensively used method of pressure relief in Germany is the use of so-called partial foot relief shoes. These walking aids are considerably cheaper than plaster therapy, but slightly less effective in terms of healing rate and degree of pressure relief. In a case control study, 96% of wounds in patients with forefoot relief shoes healed within an average of 70 days, whereas in patients without such walking aids only 59% of ulcers healed (mean healing time of 118 days). Hospitalisation was necessary in half the patients without walking aids, but in only one out of 26 patients fitted with forefoot relief shoes. The principal difficulties encountered by patients from the use of such accessories include:

1. The development of blisters or pressure points
2. Pain in the joint area
3. Difficulties in walking because of the difference in height from the contralateral shoe
4. Tearing of the walking sole

Other options for pressure relief in specific cases (e.g. deformity in osteoarthropathy with ulcer formation) in our outpatient department include the use of Allgöwer walking apparatus, aircast splints or custom-made two-layer orthoses.

**Structured wound treatment and importance of interactive wound dressings**

Wound healing in diabetic foot syndrome is a complex process, the purpose of which is to fill the tissue defect that has occurred, restore sufficient strength to the tissue and re-create the physiological barrier between the internal and external environment. In the course of this, complex cellular biochemical processes result in the formation of low-grade scar tissue. Wound healing usually occurs in three phases:

1. wound cleansing (*inflammatory phase*)
2. the granulation phase (*proliferative phase*) and
3. the epithelialisation phase (*differentiation phase, wound closure*).
Differences are found between diabetics and metabolically healthy patients in all three phases and these are described in greater detail below.

Immediately after an injury local blood coagulation occurs with the formation of a fibrin network. This then dissolves to allow the unimpeded extension of the ensuing granulation tissue. In diabetics, these fibrin coatings occasionally persist beyond the first phase\textsuperscript{144}.
Subsequently a local inflammatory reaction develops, in which first neutrophils (which release proteases and are capable of phagocytosis) and then macrophages migrate to the wound area where they release messenger substances, known as cytokines (such as PDGF or TGF-β). These mediators stimulate cell activities such as angiogenesis, autolytic débridement, keratinocyte migration, matrix formation and fibroblast formation.

There are deficiencies in diabetics in respect of both the bactericidal activity of the neutrophils\textsuperscript{145} and the properties of the fibroblasts\textsuperscript{146,147}. High glucose and lactate levels cause disruption of the rate of fibroblast division and resistance to growth factors. In addition to these acquired changes of immune function, there is also assumed to be a genetically predetermined disorder of immunocompetence in diabetics\textsuperscript{148}. As a result of the proliferation of vascular
endothelial cells and fibroblast formation, a shiny red granulation bed is formed and collagen synthesis is increased.

Finally, wound closure occurs through epithelialisation. The formation of an epidermis serves as protection, though it does not improve the strength of the new tissue any further.

There are two types of wound healing.

1. Primary wound healing occurs through primary adaptation with only small quantities of granulation tissue.
2. Secondary wound healing takes place in infected and necrotic tissue, whereby wound closure occurs mainly by contraction. In the second form, adaptation can be assisted by the use of Omnistrip® wound suture strips for example.
Disruptive factors in wound healing may be systemic or related to local conditions in the wound area. They are listed here:

**Possible causes of impaired wound healing in diabetic foot syndrome**

**Systemic factors:**
- Hyperglycaemic metabolic situation
- Malnutrition
- Obesity
- Nicotine abuse
- Anaemia
- Renal insufficiency/uraemia
- Patient’s age
- Drugs (steroids, antirheumatic agents).

**Local factors:**
- Ischaemia and hypoxia of affected tissue
- Pressure load
- Repeated trauma
- Inadequate local wound treatment
- Infection
- Necrosis
- Oedema formation
- Foreign body in the wound

Successful local wound treatment must fulfil the following conditions:

- It must:
  1. Support normal biological healing processes,
  2. Prevent infection and/or reduce the microbial count,
  3. Prevent necrosis formation and/or eliminate existing necrosis,
  4. Be based on a phased wound healing process,
  5. Be cost-effective
  6. Be well tolerated by the patient and applicable for outpatients.

In the therapy of chronic wounds, moist wound treatment using modern differentiated wound therapy has now replaced the previous conventional wound treatment – consisting of various dyes, local administration of antimicrobial substances and sterile dressings.
In the first phase of wound healing, the mechanical or physical removal of necrotic tissue, the provision of drainage for exudate and where necessary the resection of infected bone sequestra take precedence. In addition, deoxyribonucleases (e.g. Fibrolan®), streptokinase-streptodornase (e.g. Varidase®) or collagenases (e.g. Iruxol® N) may be used. There are at present no studies that confirm the efficacy of these preparations.
In terms of special wound dressings, alginates (e.g. Sorbalgon®) are used at this stage for wounds with profuse exudation and are also suitable for deep and gaping wounds. Wound healing complications have been described in individual cases with alginate therapy in undiagnosed deep wound infections, osteitis or minimally exudative wounds\textsuperscript{149,150}.

In non-infected wounds of Wagner stages 1 and 2 with only mild to moderate exudation, the use of hydrogels (e.g. Hydrosorb\textsuperscript{®}) or hydrocolloids (e.g. Hydrocoll\textsuperscript{®}) may be considered for moist wound treatment. The hydrogels are polyurethane meshes with a 60% or higher water content, depending on the product. In contrast to the hydrocolloids, they do not form a gel and therefore absorption of exudates is possible. As a result of the high water content, the main effect of hydrogels in diabetic foot syndrome lies in the softening of necrotic tissue and wound coatings.

By reducing the frequency of dressing changes, treatment with special wound dressings becomes cost-effective. Despite the difficulties of comparability between studies (due to use of different preparations in different stages of healing), the application of hydrocolloids resulted in reduction in costs by 60% in comparison to dry or moist gauze dressings\textsuperscript{151}. In addition to the dressings described, Ringer's solution administered either as a continuous irrigation or in carrier media such as superabsorbent polycrylate (e.g. TenderWet\textsuperscript{®}) is suitable for moist wound treatment in the late cleansing and granulation phase. Because of its mechanical protective action, the continuous release of the absorbed Ringer's solution and its high absorption capacity for wound exudate, this product is particularly suitable for the outpatient treatment of diabetic foot lesions. Lastly, epithelialising wounds are covered with a non-medicated, ointment-impregnated gauze.

As the skin of neuropathic patients is very fragile, wound dressings and bandages in our hospital are secured exclusively with gauze bandages and gauze dressings. In ambulant patients, tubular dressings are also applied to prevent the primary bandage from slipping. Direct contact of the fixation plaster with the patient's skin is avoided where possible because of the tendency to
macerate. The lack of adequate studies on the phase-specific use of sufficient wound dressings results on the one hand in inappropriate use by unspecialised users\textsuperscript{152}, and on the other in a constant debate among experts about the risks of using specific wound dressings in diabetics\textsuperscript{149,153,154}. In a large English survey on the use of specific wound dressings in diabetic foot syndrome, five to eight different wound dressings were mentioned by each user, among which hydrocolloids, hydrogels and alginites were the most widely used. None of the products, however, had more than 30% support in any of the wound healing phases. This survey was unable to clarify whether this finding is due to a lack of information, or to the belief on the part of the users that there are no essential differences between the various dressings\textsuperscript{152}. Encouraged by individual case reports, the use of hydrocolloid dressings in diabetic foot syndrome has become a subject of debate in recent years.

Problems identified in the use of hydrocolloid dressings include:
1. Rapidly progressive infections under occlusive dressings
2. Gel particles incorporated in wounds as foreign bodies
3. Maceration and pressure injuries of wounds have been described.

Pre-existing infection of the wound and weekly changes of dressings were common to all the case reports with fatal outcomes. By complying with the contra-indications and observing shorter intervals between changes of dressings, such complications could definitely be avoided. In contrast to these case reports, an infection rate of only 2.6% under occlusive dressings has been observed in large-scale studies, which compared to 7.1% with conventional dressings\textsuperscript{155}.

Stage-specific application of the treatment principles, regular débridement and strict monitoring of the wound status in the initial phase (at least twice daily changes of dressings in infected wounds) are essential preconditions for successful treatment. An important component of treatment also involves actively including the patient and their relatives at this early stage and preparing the way for the transfer of individual responsibility.
Moist wound treatment

In wounds healing by secondary intention, moist wound treatment is now considered the standard and has become accepted in particular in the treatment of chronic problem wounds. The scientific bases for moist therapy were established in the studies by Winter (1971). He showed that a moist and permeable dressing made the wound heal quicker than a dry wound exposed to air. This fact is also confirmed by more recent studies. According to Turner (1990), permanent moist wound therapy results in a significantly faster reduction in wound area and a larger quantity of granulation tissue than in controls. Accelerated re-epithelialisation is also observed. In addition, moist wound dressings exhibit a good wound healing effect without damaging immunocompetent cells.

Wound dressings for moist treatment

A series of wound dressings are now available for the practical implementation of moist wound therapy, covering the whole spectrum of therapeutic requirements in terms of a treatment system.

**TenderWet – Wound dressing pad with superabsorbent core**

TenderWet is an extremely efficient wound dressing for the treatment of chronic infected and non-infected wounds during the cleaning phase and at the beginning of the granulation phase. The basis of its high degree of efficacy is a special principle of action that allows continuous “rinsing” of the wound.

TenderWet is a multilayer wound dressing pad containing a superabsorbent polyacrylate core as its central component which has irrigating properties. The superabsorbent core is activated before use with a suitable volume of Ringer’s solution, which is then delivered continuously to the wound over a period of twelve hours. This constant supply of Ringer’s solution actively softens and detaches necrotic tissue (1).

At the same time, the absorbent core reliably takes up and retains germ-laden wound exudate. This exchange is possible because the superabsorbent core has a greater affinity for protein-containing wound exudate than for salt-containing solutions (Ringer’s solution). The wound exudate therefore displaces the Ringer’s solution
from the wound pad (2). Thus, TenderWet continuously renews the film of Ringer’s solution over several hours and simultaneously absorbs micro-organisms, released detritus and toxins. Hence, the wound is “rinsed” and rapidly cleansed.

As soon as the factors that inhibit wound healing are eliminated and the wound area is clean, granulation tissue can build up through the migration of cells and the regeneration of vessels (3). In the course of this, the moisture and the electrolytes in the Ringer’s solution, such as sodium, potassium and calcium, contribute to cell proliferation.

TenderWet has no contra-indications and can also be used in infected wounds. In individual cases, an apparent enlargement of the wound occurs following initial cleansing with TenderWet. This means that undetected devitalised tissue has also been eliminated by this method.

The amount of Ringer’s solution necessary to activate the absorbent/ rinsing core depends on the size of the dressing. In deep wound conditions, TenderWet should be packed loosely to ensure the direct contact that is required for fluid exchange to occur. The physical properties of the superabsorbent compound, combined with the covering of knitted fabric, give TenderWet the necessary packing properties. In extensive wounds, the TenderWet wound pads should be applied so that they overlap slightly. They can then be covered as necessary with a gauze fixation dressing.

TenderWet is available in various shapes and sizes to ensure good adaption to the various wound conditions. TenderWet is activated with Ringer’s solution directly in the sterile peel – off package (right).
TenderWet has no contraindications and can be used in all wound conditions, both infected and non-infected. The “rinsing effect” of TenderWet is optimal during the cleaning phase and at the beginning of the granulation phase. The examples show TenderWet used in the care of a venous (1) and an angio-pathic/diabetic ulcer (2).

TenderWet dressings as a rule should be changed twice daily, i.e. every 12 hours. TenderWet 24 can be used at 24 hour intervals. TenderWet 24 is made of the same materials as TenderWet, but is designed so that the Ringer’s solution absorbed is released more evenly and the absorption/rinsing action persists over 24 hours. In addition, a moisture-repellent layer is incorporated inside the dressing to prevent moisture penetrating and thus provides a dressing that offers excellent moist therapy.

Sorbalgon – conformable calcium alginate dressings

Sorbalgon is the ideal wound dressing for cleansing and for expediting the build-up of granulation tissue in fissured wounds and those that are difficult to manage. Sorbalgon is highly adaptable and thus ensures effective wound cleansing and management, even in deep wounds.

Sorbalgon is a non-woven dressing of high-grade calcium alginate fibres which is applied to the wound in its dry state (3). On contact with sodium salts, such as are found in the blood and wound exudate, the fibres swell and are transformed to a moist, absorbent gel that fills the wound (4). Sorbalgon approximates closely to the wound surfaces, therefore micro-organisms even at a deep level are absorbed and incorporated safely in the gel structure (5). This results in efficient microbial reduction and helps prevent recontamination. Wounds are rapidly cleansed, so that Sorbalgon has become established in the treatment of chronic and infected wounds in particular.

The gelatinous consistency of Sorbalgon also acts like a moist dressing, preventing dehydration of the wound. A favourable microclimate for wound healing arises, promoting the formation of granulation tissue and keeping the wound surfaces supple.
As Sorbalgon is able to be transformed into a gel, it does not adhere to the wound and changes of dressing can be made painlessly. The complete transformation of the calcium alginate fibres to a gel requires sufficient exudate. Thus, where fissured wounds with little exudate require packing, Sorbalgon should be moistened with Ringer's solution. Any fibres remaining in the wound can be rinsed out with Ringer's solution, otherwise the gel plug is removed from the wound with forceps.

The frequency with which dressings are changed depends on the individual wound conditions. In the wound cleansing phase, one or two changes of dressing are necessary, depending on the degree of exudation. Later, with granulation formation, a change of dressing every 2 to 3 days may be sufficient. Sorbalgon is supplied in square dressings of two sizes. Sorbalgon T ribbons are available specifically for larger wounds.

**Hydrosorb – hydrocellular gel dressing**

Hydrosorb is especially suitable for moistening and protecting granulation tissue and young epithelium and is hence the optimum wound dressing for phase-specific treatment following TenderWet or Sorbalgon therapy.

Hydrosorb is a ready-to-use gel made of absorbent polyurethane polymers which has a high water content (60%). Thus, from the very beginning Hydrosorb automatically provides a moist environment for the wound for several days (1). At the same time, Hydrosorb absorbs excess exudate, which is then incorporated in the gel structure. This exchange guarantees the optimal level of moisture for wound healing and thus accelerates granulation formation and epithelialisation (2). The germ-proof and waterproof surface of Hydrosorb also guarantees protection against secondary infections.
Hydrosorb does not stick to the wound and can be removed even after prolonged application without the risk of irritation to the wound. Unlike hydrocolloids, Hydrosorb can be removed in one piece since the gel structure is not dissolved by the absorbed wound exudate. No residues are left on the wound and the wound condition can be assessed safely without prior rinsing.

One particularly practical advantage of Hydrosorb is its transparency, which lasts even after prolonged application. As a result the wound can be inspected without removing the dressing. This ensures rest for the wound which is so important for healing, as well as a high degree of cost effectiveness because of the reduced frequency of dressing changes.

Hydrosorb is available in two forms: Hydrosorb and Hydrosorb comfort. Both hydrogels have the same principle of action, but differ in terms of methods of fixation. Hydrosorb does not have a self-adhesive border and as a rule is secured by means of a fixation dressing, adhesive plasters or a dressing retention bandage.

Hydrosorb comfort has a hypoallergenic adhesive film border to ensure it stays firmly in place and to prevent bacterial penetration. This, together with the germproof and waterproof surface of Hydrosorb comfort, simplifies daily hygiene.

*Hydrocoll – absorbent hydrocolloid dressing*

Hydrocoll is a self-adhesive, absorbent hydrocolloid dressing for the cleaning and management of non-infected wounds.

The term “colloid” comes from the Greek and means "a substance that is incorporated in a matrix in a very fine distribution". Hydrocoll consists of absorbent and
expandable hydrocolloids incorporated in a self-adhesive elastomer with a semipermeable film that serves to prevent the penetration of bacteria and moisture. Upon absorption of exudate from the wound, the hydrocolloidal particles swell to form a gel that expands into the wound and maintains a moist wound environment (1). The gel remains absorbent until the hydrocolloids are saturated. Saturation of the hydrocolloids is indicated by a blister-shaped protrusion of the dressing (2), whereupon the Hydrocoll must be changed.

Due to the adhesiveness of the elastomer, Hydrocoll can be laid on the wound like a plaster. With the formation of the gel, however, the adhesiveness in the area of the wound surface is lost, so that Hydrocoll is attached only to the intact border and thus does not affect the wound. In addition, when the dressing is removed, it can be removed without leaving residues of gel on the wound. Prior irrigation is not necessary for assessing the wound after a change of dressing. Hydrocoll has a high absorbency due to the special material composition. Excess contaminated exudate is rapidly absorbed and safely retained in the gel structure as a result of the swelling process. In this way the microcirculation in the wound area is simultaneously improved, so that the body’s own cleansing mechanism is reactivated, especially in those chronic wound conditions where healing is delayed.

During the granulation phase, the moist wound environment under Hydrocoll particularly stimulates the activity of fibroblasts, which are responsible for initiating the process of tissue regeneration. During the epithelialisation phase, the division and migration of epithelial cells is supported. If there are no complications, Hydrocoll can remain on the wound during this phase for several days until the epithelialisation process is completed.

The germproof and waterproof top layer serves as a reliable barrier against bacteria and protects the wound from contamination and penetration of moisture. Ambulant patients can shower with the dressing in place.
<table>
<thead>
<tr>
<th>Product characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Zetuvit</strong></td>
</tr>
<tr>
<td>Wound-compatible absorbent dressing pads with non-adherent material covering and an absorbent core of cellulose fluff</td>
</tr>
<tr>
<td><strong>Cosmopor steril</strong></td>
</tr>
<tr>
<td>Self-adhesive wound dressing with waterrepellent microgrid wound contact layer, absorbent pad of pure cotton wool and soft non-woven fabric coated with a hypoallergenic polyacrylate adhesive</td>
</tr>
<tr>
<td><strong>Comprigel</strong></td>
</tr>
<tr>
<td>Impregnated, non-adhering gel dressing with integrated absorbent core in medicated cotton</td>
</tr>
<tr>
<td><strong>Atrauman</strong></td>
</tr>
<tr>
<td>Wound-compatible water-repellent polyester tulle, impregnated with a selfemulsifying, neutral ointment, non-adherent</td>
</tr>
<tr>
<td><strong>TenderWet</strong></td>
</tr>
<tr>
<td>Superabsorbent polyacrylate wound pad with an absorbing/rinsing core, activated before use with Ringer’s solution which is delivered to the wound in exchange for wound exudate</td>
</tr>
<tr>
<td><strong>Sorbalgon</strong></td>
</tr>
<tr>
<td>Conformable, non-medicated dressings made of calcium alginate which form a moist gel in contact with wound exudate</td>
</tr>
<tr>
<td><strong>PermaFoam</strong></td>
</tr>
<tr>
<td>Hydroactive foam dressing with a high level of water vapour permeability top layer; but liquid- and germ-proof</td>
</tr>
<tr>
<td><strong>Hydrocoll</strong></td>
</tr>
<tr>
<td>Self-adhesive, absorbent hydrocolloid dressing with semi-permeable, germproof and waterproof layer.</td>
</tr>
<tr>
<td><strong>Hydrosorb</strong></td>
</tr>
<tr>
<td>Absorbent hydrogel dressing with high water content in the gel structure, covered with semi-permeable transparent germproof and waterproof layer</td>
</tr>
</tbody>
</table>
Properties and use

- **Commercial forms**

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zetuvit</td>
<td>sterile and non sterile</td>
<td>10 x 10, 10 x 20, 15 x 25</td>
</tr>
<tr>
<td>Cosmopor</td>
<td>7.2 x 5, 10 x 8, 15 x 6, 10 x 8, 15 x 8, 20 x 8, 20 x 20, 25 x 10 and 35 x 10 cm</td>
<td></td>
</tr>
<tr>
<td>Comprigel</td>
<td>5 x 7.5, 10 x 10 and 10 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>Atrauman</td>
<td>5 x 5, 7.5 x 10 and 10 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>TenderWet</td>
<td>4, 6.5 x 5.5, 7.5 x 7.5 and 10 x 10 cm</td>
<td></td>
</tr>
<tr>
<td>TenderWet 24</td>
<td>4, 6.5 x 5.5, 7.5 x 7.5 and 10 x 10 cm</td>
<td></td>
</tr>
<tr>
<td>Sorbalgon</td>
<td>5 x 5, 10 x 10 and 10 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>Sorbalgon T tamponade ribbon</td>
<td>sterile, 1g/30 cm and 2g/30 cm</td>
<td></td>
</tr>
<tr>
<td>Hydrosorb</td>
<td>5 x 7.5, 10 x 10 and 20 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>Hydrosorb comfort</td>
<td>7.5 x 12 cm</td>
<td></td>
</tr>
<tr>
<td>Hydrocoll</td>
<td>5 x 5, 7.5 x 7.5, 10 x 10, 15 x 15 and 20 x 20 cm; Hydrocoll sacral, 12 x 18 cm; Hydrocoll concave, 8 x 12 cm; Hydrocoll thin, 7.5 x 7.5, 10 x 10 and 15 x 15 cm (all sterile)</td>
<td></td>
</tr>
<tr>
<td>PermaFoam</td>
<td>10 x 10, 15 x 15, 10 x 20 and 20 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>PermaFoam comfort</td>
<td>45 x 11, 15 x 15, 10 x 20 and 20 x 20 cm</td>
<td></td>
</tr>
<tr>
<td>Hydrocoll thin</td>
<td>7.5 x 12.5, 11.5 x 24 and 21.5 x 24 cm</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of infection

Inflammation is a physiological reaction of the body designed to protect the tissues and to aid the elimination of harmful agents. These harmful factors may be microorganisms or chemical substances (acids or bases), but they can also be friction, pressure, foreign bodies, or of a physical nature (e.g. an effect of temperature). Infection in this context means the transmission, adherence and penetration of micro-organisms to and into a macro-organism. This can result in the development of an infection, depending on the infectious and pathogenic properties of the micro-organism, but also on the defensive and offensive forces of the macro-organism (immunity). Infection is not a primary cause, but the most severe complication in diabetic foot syndrome and is associated with impaired wound healing and an increasing risk of amputation. The best prophylaxis against wound infections is the destruction of the favourable living conditions for pathogenic micro-organisms through drainage of the exudate and elimination of necrosis, but also through specific drug therapy and early (minor) surgery, where necessary.

Superficial and deeper, uncomplicated neuropathic forefoot ulcers (Wagner stages 1 and 2) heal as rapidly with standardised, phase-specific therapy without the administration of antibiotics as they would with antibiotic therapy. The mean reduction in ulcer size in this case is 0.25 mm/day\textsuperscript{156}. In patients in whom specific disease conditions point to the possibility of a modification of the natural healing process (patients with severe ischaemia, with renal insufficiency or immunsuppressant diseases), antibiotic treatment should be considered at an early stage, even with this degree of severity\textsuperscript{156,157}. At the same time, the importance of long-term antibiotic therapy of foot ulcer patients in the development of multiresistant organisms should not be underestimated (e.g. a methicillin-resistant Staphylococcus aureus – MRSA). This micro-organism now constitutes up to 25% of all staphylococcal infections in diabetic foot syndrome\textsuperscript{158,159}. In foot infections in which preservation of the extremity is not threatened and which can be treated on an outpatient basis, aerobic Gram-positive cocci (e.g. Staphylococcus aureus) are found in almost 90% of cases,
and constitute the sole pathogenic agent in about 40%. Gram-negative aerobes (e.g. Klebsiella or Pseudomonas) and anaerobic micro-organisms are found in 36% and 13% of cases respectively, always in conjunction with polymicrobial infections. In the study quoted, clindamycin and cephalosporins were used for antibiotic therapy, which in our outpatient department are replaced where necessary by Fluoroquinolones following the results of cultures and in the absence of improvement in local findings. Ninety percent of infections are healed with these agents, 75% of them within two weeks.

The aim here is to prevent the development of deep infections or osteomyelitis (or more accurately osteitis, since initially it is the bone cortex that is affected and the most commonly affected small bones of the foot contain hardly any marrow). Osteitis is mainly a polymicrobial infection (about 80% of cases), between 50% and 80% of which involve staphylococci.

Drug therapy in deeper soft tissue infections and osteitis should be based on sensitivity tests of the microorganisms isolated from the tissues concerned (obtained by wound swab, aspirate, curettage or surgical excision). Again clindamycin may be considered here. With purely conservative therapy, long-term treatments of eight to twelve weeks are necessary. The safest way of obtaining long-term eradication of bone infection without threatening the integrity of the foot appears to be early surgical removal of affected sections of bone. Early surgical intervention should be considered, particularly if the infection fails to respond to targeted antibiotic therapy, not least because an unhealed infection involves the risk of an arthropathy occurring later in the course of the disease.
There are a variety of expensive imaging procedures for the diagnosis of osteitis in diabetic foot syndrome, such as leucocyte scans, Tc99m bone scan, magnetic resonance imaging (MRI) and standard X-rays. A simple and cheap method with at least as high a positive predictive value for the presence of osteitis (89% versus 75%–85% with leucocyte scans and 50%–93% with MRI) is the “tube test”. Access to the bone via the existing lesion with a sterile rinsing tube indicates the presence of osteitis with a high degree of accuracy. Clinical signs (reduced pain perception due to neuropathy) and biochemical indications of osteitis are much less reliable in diabetics. Fifty-four percent of all patients with osteitis in an American study were within the normal range in terms of the leucocyte count, while in 82% of the affected patients the oral temperature measured was normal.

Targeted action, however, presupposes an adequate diagnosis. In a follow-up study of patients with infected diabetic foot lesions in an American teaching hospital, documented examinations of the wound for the involve-
ment of deeper structures were found in only 10% of cases and a lack of foot X-rays was observed in 33% of patients. Blood cultures were arranged in 62% of cases but tissue cultures from the wound in only 51% of cases167.

**Vascular and surgical interventions in the diabetic foot syndrome**

Primarily neuropathic lesions usually have a tendency to heal rapidly following complete pressure relief, débridement, drainage of soft tissue infections and, where necessary, antibiotic therapy. In other cases where additional ischaemia is found, immediate Infection control and consideration of Reconstructive or interventional surgery to improve perfusion should be attempted. Then, if unavoidable, borderline zone resection or Amputation, sparing as much tissue as possible, is performed (IRA principle according to Vollmer168). It is essential that a complete clinical and instrumental examination is performed before every amputation in diabetics to identify those patients who will benefit from vascular surgery169. This is made more difficult as concurrent diabetic neuropathy reduces the detection of ischaemic pain and traditional methods of investigating blood circulation are of limited predictive value in the presence of media calcification.

There is as yet no documented evidence in large, controlled studies of an improvement in the prognosis for patients with diabetic foot syndrome from drug therapy with prostaglandin derivatives. These products have not been shown to have any specific effects in diabetics. A large Italian study showed a short-term improvement in the critical blood circulation of a limb and a reduction in the risk of amputation with prostadil (Prostavasin®). After six months’ observation, however, only moderate differences were found between treated and untreated patients170.

In a small study involving eight patients with a disorder of the arteries of the lower leg and rapid progression of the foot lesion, urokinase therapy showed good short-term success. However, in the long-term a bypass operation had to be undertaken in half the patients to preserve the extremity171.
It is thus apparent that patients with lesions of ischaemic origin should be examined as rapidly as possible with a view to establishing their suitability for a surgical procedure (e.g. angioplasty, graft).

Some differences from non-diabetics are apparent with both treatment approaches as a result of the particular anatomical circumstances. In principle, the results of vascular surgery in diabetics are comparable to those in non-diabetics. In particular, a leg preservation rate of 77% was found after 1½ years with the dilatation of circumscribed occlusions or stenoses of lower leg vessels\textsuperscript{172}. In patients in whom a balloon dilatation remains technically unsuccessful or in whom the leg condition fails to improve despite an initially successful operation, bypass surgery procedures should always be considered\textsuperscript{173}. Overall, the pool of patients who can be helped by vascular surgery is increased by the isolated dilatation of lower leg vessels. Advanced age, a long history of diabetes and a high degree of severity of the circulatory disorders have an adverse effect on the results of this method in diabetics. Regular examinations to identify asymptomatic vascular processes and the implementation of surgical measures prior to the occurrence of serious complications should therefore become standard procedures\textsuperscript{174}. Interventional (e.g. dilatation) and reconstructive (e.g. bypass surgery) procedures should be employed as supplementary measures to preserve the extremity in diabetic foot syndrome. In 22% of patients from the Augsburg Clinic in whom a cruromalleolar bypass was performed between 1986 and 1992, the blood supply had previously been optimised by a percutaneous transluminal angioplasty (PTA) of the femoral artery.\textsuperscript{175}

Because of the particular anatomy (the lower leg is frequently affected by PAOD, while the ankle and foot arteries are spared), crural (bypass to a lower leg vessel) or pedal (bypass to foot arteries) bypass procedures have increasingly obviated the need for amputation in diabetics over the past few years. Previously, the creation of a femoropopliteal bypass in combination with a transmetatarsal borderline zone amputation was the therapeutic procedure of choice in ischaemic diabetic foot syndrome. There has been a marked reduction in the number of amputations required in diabetics post
the introduction of bypass procedures. In both the USA\textsuperscript{176} and Denmark\textsuperscript{177} the number of amputations in diabetics more than halved between 1984 and 1989, while bypass surgery, angioplasty and above all the use of distal bypass grafts in each case more than doubled. In addition, in those amputations that have still proved necessary, the level of amputation has increasingly moved distally. The amputation rates in Germany in centres using such procedures\textsuperscript{175,178} are less than 10\% for major amputation. The extremity is preserved in 75\% and 71\% of cases after 2 and 5 years, respectively. The patency rates of the bypasses created are about 60\%. This means that even short-term bypasses are frequently sufficient to save a jeopardised extremity. As the diameters of the vessels in the lower leg and foot are small, autologous materials, i.e. the patient’s own veins, should predominantly be considered for bypass material. In individual cases, however, synthetic crural bypasses with survival periods of several years have been observed in our hospital. Peri-operative mortality of 1 to 2\% in such procedures must be regarded as favourable\textsuperscript{175,178}, when compared to primary amputation as an “alternative method” which has a peri-operative mortality rate of 8\% in minor amputations and 18\% in major amputations\textsuperscript{175}.

A precondition for the use of such procedures is good angiography, with visualisation of the foot arteries\textsuperscript{76}. Foot arteries that are suitable for bypass-surgery can be found in a large proportion of diabetics. Even in the absence of any angiographic evidence, a suitable vessel for a bypass can be found in half the remaining patients by Doppler examination\textsuperscript{179}. 

\begin{center}
\textit{Creation of a distal vein bypass to preserve the extremity}
\end{center}
Surgical measures in the treatment of the diabetic foot syndrome are not simply based on amputation. If vascular surgical principles are applied, then extensive mutilation can be prevented. If an amputation cannot be avoided because of insufficient perfusion or uncontrollable infection, the principle that is now applied is to preserve as much tissue and function as possible.

Slight residual necrosis in the large toe…

…and non-irritant, secondarily healing wound following resection of the necrotic fifth toe

The classical amputation lines of previous years are no longer binding and borderline zone amputations that are as non-mutilating as possible are the procedure of choice, subject to local perfusion conditions.

In the toe region, especially the large toe, partial amputations are also beneficial for postural reasons. Transmetatarsal amputations in the forefoot area, as opposed to surgery of the mid-foot and hind-foot, have the advantage of yielding better muscle balance with-
Forefoot stump which can be well catered for by orthopaedic measures (left) compared with a functionally unfavourable result following amputation of the first, second and fourth toe with a considerable risk of occurrence of further foot lesions (right).

While the long-term outcome of surgical interventions on non-weight-bearing osteolytic sections of bone (e.g. resection of proximal interphalangeal joints) is non-problematic, pressure ulcers in the neighbouring areas or the induction of diabetic neuropathic osteoarthropathy are occasionally observed in surgery on weight-bearing sections of bone (e.g. metatarsal resection). With the long-term presence of ulceration (on average nine months), Griffiths was able to heal all patients by resection of the metatarsals within an average period of three months. No relapses were seen in any patient during a fourteen-month long follow-up observation phase.

A 70% reduction in pressure following resection of metatarsal I and 40–50% following resections of metatarsals II to V was measured. In our own patient population, plantar recurrences have been seen on isolated occasions in patients in whom individual metatarsals were resected, but not in patients in whom metatarsals II to V were completely removed.

Successful revascularisation is the determining predictive factor in the healing of partial foot amputations. Without prior revascularisation, 70% of partial foot
amputees must be re-operated, whereas after a successful revascularisation this applies in less than 20% of cases. In contrast to patients with major amputations, patients with amputations at the foot and ankle level have a markedly higher probability of survival of almost 90% after four years and more than 75% after eight years. However, re-ulceration occurs or further surgery is required in more than 50% of patients. The whole group of such patients is characterised by high morbidity with a further period of ulceration in almost 20% of cases following a successful amputation. With appropriate care, however, further surgery can be avoided in 52% of patients over an eight-year period. More than 2/3 of patients can be rehabilitated following a transmetatarsal borderline zone amputation and are able to walk without impairment. In contrast to forefoot amputees, patients with amputation of the posterior foot area (by the Chopart, Pirogoff and Syme methods) are not capable of walking without a prosthetic device, but these operations allow the lower leg to be preserved. The prognosis for a Syme amputation depends in particular on good local perfusion. With good circulation, 90% of Syme amputations heal and can be fitted with a prosthesis. After 2½ years, two-thirds of patients still wear their prosthesis throughout the day. Among patients with a lower leg amputation, 66% are able to walk with a prosthesis. Upper leg amputated patients are capable of walking with a prosthesis in 46% of cases, whereas bilaterally amputated patients can be mobilised with a prosthetic device in only 19% of cases.

The mean survival time following major amputations is slightly more than three years and 50% of patients are threatened with the loss of the other extremity within five years. Good aftercare of limb-amputated diabetics is essential. This involves care of the contralateral limb and also good social reintegration.

In the case of extensive skin defects, the possibility of plastic surgery to cover the defect should be considered at an early stage. Split-skin grafts, mesh grafts or island flaps are available for wound closure.

**Importance of adjunctive treatment methods**

**Hyperbaric oxygen therapy (HBO)**

Hyperbaric oxygen therapy has been debated for some years as a possible supplementary method for the treatment of poorly healing wounds. On the assumption
that the combination of hypoxia and infection is responsible for the delayed healing of diabetic foot lesions, the oxygen tension of the affected tissue should be increased through the application of hyperbaric oxygen in high-pressure chambers. It is thought that oxygen tension remains high for a prolonged period after exposure. Thus the development of necrosis in the affected tissue is reduced. In addition, a direct inhibitory effect on the growth and toxin production of anaerobic microorganisms and a potentiating effect on angiogenesis are postulated\textsuperscript{192}. This is offset by the frequent side effects of such therapy (barotraumas in 1 to 2%, transient lung and eye damage in 15 to 20% of treatment cases) and the as yet far from convincing data on the treatment of diabetic foot syndrome with hyperbaric oxygen (HBO)\textsuperscript{193}.

A small randomised study in patients with, mostly neuropathic ulcers showed no effect on the reduction in size and colonisation of the ulcerations during a 14-day treatment cycle. The healing rate was even lower in the treatment group\textsuperscript{194}. Another study in 1996 concluded that HBO therapy in patients with diabetic foot syndrome contributes not only to a significant increase in transcutaneous partial oxygen pressure (TCPO\textsubscript{2}), but also to a significant reduction in the number of major amputations required (8.6% versus 33% without HBO therapy)\textsuperscript{192}. On careful analysis of the data, however, it became apparent that only one of three amputated patients in the treated group had amputation without previous revascularisation, whereas in the control group this was the case in 7 out of 11 patients. The contribution of HBO therapy to reducing the number of amputations thus remains questionable\textsuperscript{195}.

A consensus conference on the subject in 1998 came to the following conclusion:

1. The effect of hyperbaric oxygen therapy for radiation induced wounds appears proven and there are good data for osteomyelitis and soft tissue infection in animal models and non-diabetics.
2. There are still no large randomised studies for diabetic foot syndrome.
3. Ulcerations of Wagner grade 3 to 5 treated unsuccessfully by standard methods in multidisciplinary establishments and for which an amputation is imminent may be considered for such treatment.
4. Careful follow-up of patients for diabetic retinopathy is necessary.

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4. Careful follow-up of patients for diabetic retinopathy is necessary.
5. Cost-effectiveness, quality of life and the endpoints of limb preservation, duration of hospitalisation and healing rate must be determined in the studies to be performed\textsuperscript{196}.

**Use of growth factors and bio-engineered tissues**

As has already been mentioned, deficits in immuno-competence play a significant role in the pathophysiology of wound healing disorders in the diabetic foot. In immunosuppressed patients suffering for example from neutropenia as a result of chemotherapy, treatment with granulocyte-stimulating factor (G-CSF) has become established. Studies have also recently been conducted into the efficacy of these products in immunosuppressant diseases without neutropenia. A study along these lines in patients with diabetic foot syndrome found an ulcer healing rate within 7 days of 21\% versus 0\% with placebo as evidence of a supportive effect of such therapy on wound healing\textsuperscript{145}. This isolated result, however, is a matter of dispute\textsuperscript{197}.

Treatment with growth factors and bio-engineered tissues has come to the fore in the last years. While a clinical study with fibroblast growth factor (bFGF) showed no advantage over standard therapy\textsuperscript{198}, studies with recombinant platelet derived growth factor (rhPDGF-BB, Regranex\textsuperscript{\textregistered}, for example, revealed significantly improved healing rates and a faster reduction in wound diameter than with conventional wound treatment during a 20-week observation period\textsuperscript{199}. Preliminary clinical results of the treatment of diabetic foot wounds with bio-engineered tissues (Dermagraft\textsuperscript{\textregistered}) were published in 1998. Dermagraft\textsuperscript{\textregistered} consists of neonatal, dermal fibroblasts that are cultured in vitro in a bio-absorbable mesh. A viable, metabolically active tissue is produced containing matrix proteins and cytokines. After application to diabetic foot ulcers once a week, a healing rate of 50\% was obtained within 12 weeks as compared to 8\% in the reference group. During a 14-month follow-up observation period, no patient in the Dermagraft\textsuperscript{\textregistered} group suffered a relapse. One explanation for this might be found in the more flexible replacement tissue compared to traditional scar tissue.

In a follow-up study in six patients with “poorly-healing ulcers” (mean duration of 43 weeks), 50\% were healed within 12 weeks. As a result of the accelerated healing and the lower tendency to relapse, treatment
with Dermagraft® is regarded as cost-effective despite the high costs of the product\textsuperscript{200}.

While the results of studies on wound treatment with individual growth factors in diabetic foot syndrome have been unconvincing, treatment involving products with a more complex composition of growth factors or with bio-engineered tissues offer interesting new prospects in problem patients. Treatment with growth factors is not yet considered standard.

**Biomechanical wound treatment**

Biomechanical wound treatment (BMT) has in some institutes acquired a certain value recently as a supplementary measure in the therapy of chronic wounds.

Described for the first time in 1931, treatment with fly larvae (maggots) was a commonly used form of therapy in the treatment of infected skin injuries in the 1930s and 1940s in the USA. With the introduction of antibiotic therapy, this method of treatment was to a large extent

*Use of fly larvae (maggots) following the exhaustion of all conservative and operative possibilities and the imminent loss of an extremity*
forgotten before undergoing a resurgence of interest in the 1980s in the USA and since the mid-1990s in Great Britain\textsuperscript{202}.

The mechanism of action by which the larvae of Lucillia sericata (greenbottle fly) contribute to the cleaning and healing of necrotically coated or infected wounds has yet to be fully elucidated. The production of an antibiotic-like agent (also effective against micro-organisms resistant to conventional antibiotics), the presence of growth factors in the larval secretion, the destruction of bacteria by absorption and a change in the pH value of the wound are postulated\textsuperscript{201}. The provision of full and detailed information to the patient and an explanation of the principle of therapy are essential. Surprisingly, problems of acceptance are occasionally to be found less on the part of the patient than on that of medical staff\textsuperscript{202}. This method is being used following exhaustion of conventional treatment procedures, as is the case in our hospital. In future, earlier use might mean faster wound healing and the avoidance of the need for systemic antibiotic treatment\textsuperscript{201}.

Similarly, positive results are reported from individual centres with the use of leeches (Hirudo medicinalis) in amputation surgery. Because of their local anti-inflammatory and antithrombotic effect due to the formation of hirudin, they are used in areas of critically impaired circulation or in the development of hematoma. Very peripheral borderline zone amputations even in ischaemic limbs should therefore be possible with good results\textsuperscript{203}.
Tertiary prevention of the diabetic foot syndrome

Patients with DFS remain extremely high-risk patients throughout their life. Their education must include information about what to do in the event of an injury or impending amputation in addition to preventive foot care aspects. Regular aftercare in special institutions considerably reduces the risk of recurrence of lesions and subsequent amputations in these patients. Successful tertiary prevention must also include risk-centred and phase-adapted shoe provision for patients and the organisation of injury-free, professional foot care for those affected.

Effects of educating risk patients

Although value has been placed on the education of diabetics since the beginning of the insulin era, education was not considered an essential part of the treatment of diabetics insofar as there was no convincing evidence of its therapeutic efficacy. Preventive foot care programmes in which patient education represented an important component were among the first to show a clear benefit in this respect.

A diabetes programme was instituted in California as early as 1969, involving educational measures and a telephone hotline. In Los Angeles the number of weekly attendances for severe foot problems decreased from 320 to 40. Assal in Geneva found a complete lack of any previous information about preventive or early treatment measures in 22 of 23 lower-leg amputated patients, whereas all eleven patients in whom surgery of the foot area had sufficed had received previous education. These were not controlled studies, but extensive programmes involving different treatment approaches, including educational input. The contribution of the educational components to the success of treatment was therefore difficult to distinguish from the improved medical care. However, further data about the importance of educational measures were obtained from studies which identified 40% of hospital admissions for diabetic foot problems as the consequence of psychological problems or inadequate information.
In the late 1980s, a series of studies were carried out, firstly to establish the effect of patient education alone and secondly to compare different types of foot training programmes in terms of efficacy.206

The effect of a simple one-hour education programme was examined in a prospective study in which the trained group were shown slides of foot lesions in diabetics. After one year, the incidence of ulcers and the amputation rate in the control group without any education was in each case three times higher than in the trained group.207 Comparing a straightforward lecture with a presentation involving practical exercises, the latter form of education showed a marked improvement in the short term. There was improvement in the patients' knowledge and induction of behavioural changes, particularly in nail care and daily foot inspections.208 Simple educational measures involving a single hour of instruction about the foot, was compared to instruction spread over four weeks with 1 1/2 to 2 1/2 hours' instruction per week and involving a chiropodist and a psychologist. The latter method had a sustained effect on patients' behaviour, as well as increasing their knowledge. The number of foot problems that occurred fell markedly and the routine performance of the patient's own foot care and compliance with advice to consider professional foot care were observed much more often in the intervention group.209

Patient education should be simple, relevant and consistent (the same verbal and written statements) and repeat the central message. The simplicity of relevant training measures cannot be emphasised enough since many of the patients who develop foot problems are non medical people who will not be helped by confusing vocabulary and complicated training programmes. Training programmes must take account of the social background and the level of education of the patients concerned. A problem-oriented approach should be adopted and the patient should experience the urgent need of having to know certain things, rather than simply having the feeling of being forced to learn.
The aim and form of training should be tailored to the patient and their requirements, because education is only successful if it manages to change habits and patterns of behaviour. Particularly in elderly people who are often no longer capable of undertaking simple foot inspections on their own. Partners, relatives or carers should be included in the training. Finally, intensive foot education should be directed towards specific target groups most at risk. The “over-education” of healthy diabetics may in the worst case even prove counterproductive. 

Evidence for the lack of education of affected patients is not difficult to find: 25% of all type 1 and 50% of all type 2 diabetics do not consider the loss of sensation in the lower limb a consequence of diabetes mellitus. Only about 30% of all foot ulcer patients consider themselves at risk of foot injuries and a similar small number have ever received information about foot and nail care before suffering their lesion. Risk conditions, such as diabetic neuropathy or arterial occlusive disease which increase the risk of amputation by 40% and 160% respectively compared with healthy subjects, do not result in the increased prescription of foot care or the provision of more intensive education for these patients by their doctors. Only the presence of a foot injury or even a prior amputation (11-fold increased risk of further amputation!!) mean that these patients receive more intensive medical care. Non-standardised treatment is often the cause of a dramatic deterioration in the foot disorders in diabetics as lack of care on the part of the patient. Education must therefore be directed equally to members of the medical professions (doctors, nursing staff, physiotherapist, occupational therapist) and to patients and their relatives. The recognition of an “at risk foot” and of early signs of pathological changes in the feet of diabetics are the most important responsibilities in the outpatient management of diabetic foot patients. The greatest barrier to this is a logistical one, namely that of giving the patients the opportunity and regularly encouraging them on their visit to the doctor to take off their shoes and stockings. Abnormal foot findings were detected in only 20% of patients who wore shoes and stockings on their visit to the doctor. In contrast, 60% of existing foot problems were detected in patients who presented themselves barefoot to their doctor. A foot examination is an extremely effective, but unfortunately much too infrequently used preventive measure. In a New Zealand study, lesions (ulcers, foot injuries) or predisposing changes (fungal infections, maceration or
callus formation) were found in 50% of a group of unselected diabetics. Only 40% of patients with existing blisters or foot ulcerations had undergone a foot examination in the 12 months prior to this examination\textsuperscript{214}.

In addition to the provision of information to the patient about the risk to their feet and the principles of proper foot care, educational measures for high-risk patients must include information about the correct action to take when foot injuries occur and how to react if the doctor recommends amputation of a limb. No amputation in diabetics should occur today without a full circulatory examination (including angiography of the foot arteries). Patients should always be encouraged to obtain a second opinion before a planned amputation, where possible from a specialised centre\textsuperscript{215}.

**Importance of professional foot care**

Foot care in diabetics is of particular importance, but also requires particular knowledge and skills. Treatment errors can have serious consequences. Between 13\%\textsuperscript{216} and 30\%\textsuperscript{217} of all foot lesions are related to foot injuries (either self inflicted by the patient or by professional chiropodists). Inadequate foot care or poor hygiene also contributes greatly. The use of keratolytics (products that remove horny skin), incorrect or wrongly used foot care instruments (tweezers, scissors, razor blades, “special tools” such as callosity files), and excessively long or hot foot baths are possible causes of foot care related lesions.

Appropriate foot care treatment includes:
1. Care of callus
2. Removal of clavi (corns)
3. Care of interdigital spaces
4. Treatment of fissures, macerations and fungal diseases
5. Nail care and the careful correction of nail deformities.

The detection of pathological foot changes and the inspection of the patient’s footwear and stockings can also be undertaken by chiropodists following the appropriate training.
The treatment of an ingrowing toenail (unguis incarnatus), which is traditionally done surgically for example by means of wedge excision (Emmert-plasty) can according to a more recent study be successfully treated conservatively by means of packing, pressure relief and, where necessary, antibiotics. Surgical operations on the diabetic foot are associated with an increased risk of development of gangrene. In the USA and Great Britain well-trained foot care specialists (podiatrists or chiropodists) have taken over a large part of the management of diabetic foot patients. Similarly in Denmark the amputation rates were reduced by 30% between 1981 and 1989 as a result of the further training of 450 chiropodists for the qualified treatment of diabetics. In contrast, in Germany in 1994 the Federation of German Physicians and Insurance Funds (BdÄK) excluded medical foot care from compulsory reimbursement by the regulatory health insurance funds. This procedure was justified on the grounds firstly that foot care is a general measure of body care and hygiene and thus not a compulsory service of the health insurance funds, and secondly on the grounds of the inadequate quality of medical foot care, without defining this further. According to a ruling of the Düsseldorf County Court of 1997, not to exempt patients with foot diseases (e.g. with diabetic foot syndrome) from this regulation is illegal and hence void.

It is true that medical foot care in Germany has not been legally regulated to date. Schools of podology with a structured, two-year training course have been set up in several German cities. Also, the establishment by the German Diabetes Society (DDG) for a transitional period of a syllabus for qualification as a DDG chiropodist should provide qualified foot care for diabetics throughout the whole of Germany as soon as possible.

It has recently been demonstrated that such regular treatment not only reduces the risk of relapse, but also substantially decreases treatment costs for foot problems. Fifty-one patients (48 of whom had a previous foot ulcer) received foot care treatment at monthly intervals from a specially trained and qualified nurse working in co-operation with a diabetes outpatient unit. The relapse rate was reduced to 8% per year with the simultaneous provision of protective shoes. Instead of 30 patients admitted the previous year,
Pressure points with bruising on the back of the feet following the use of diabetes adapted insoles with insufficiently deep footwear: the consequence of superficial knowledge in the patient and therapist

hospitalisation due to foot problems occurred in only 7 patients. Before the introduction of professional foot care, 30% of patients had performed their foot care themselves, half of whom had occasionally injured themselves in the process. The costs generated by foot problems were reduced by 80% as a result of this measure.

It seems particularly unlikely in elderly people that self-administered foot care can prevent the occurrence of foot injuries. In a study of diabetics over 75-years-old, only 14% were able to inspect the sole of their own feet and more than 50% had problems with nail care.

The regular implementation of professional foot care for this age group in particular will definitely have a more effective preventive result than thorough training of the patients.
Provision of adapted footwear for diabetics

Between 28%\textsuperscript{78} and 55%\textsuperscript{79} of all foot lesions in diabetics are related to footwear. In principle, shoes serve the same purposes in diabetics and non-diabetics: they are worn for pleasure and for reasons of fashion, but what is least firmly established in people’s minds is that they serve to protect the feet. Some people also use (or misuse) shoes to hide changes in the foot. Medical functionality is therefore only one of a number of aspects of footwear. To reduce the importance of shoes to this purely functional aspect or even to the subsidiary aspect of the protection of the diabetic foot against any form of trauma is often difficult for the patient to understand and causes the carer difficulties in dealing with these patients\textsuperscript{220}.

It is only in recent years that there has been increasing recognition of the importance of suitable footwear for diabetics. There are now results of clinical case control studies on the prevention of relapse of foot ulcer comparing industrially produced shoes, off-the-shelf shoes (cost of about 200 EUR per pair) and customised orthopaedic shoes (850 EUR per pair)\textsuperscript{221, 222, 223, 224, 225}. According to these studies, the relapse rate as a result of stage-specific shoe provision can be reduced to about 25% after one year and approximately 40% after two years.

This effect is even more apparent from an analysis of the prevention of shoe-related relapses following an initial lesion due to footwear. From this viewpoint, protective footwear saves 86% of patients from a relapse if the shoes are worn sufficiently long every day over a period.

Off-the-shelf, diabetes-adapted protective shoe with sole stiffening, a rocker sole and raised toe room (Buratto company)
of two years. The occasional wearing of normal shoes (27%), an incongruity between foot shape and customised shoe in the presence of gross deformities (27%) and hard toecaps are the reasons for further lesions despite specialist shoe provision.

The basic features of diabetes-adapted footwear date back to the work of Tovey in 1984. He suggested a low heel to prevent increased pressure on the forefoot, a broad forefoot without stiffness in the toe area and sufficient space to be able to take an elastic insole are among the basic characteristics. In addition, high-quality soft leather should be used for the uppers and internal stitches should be avoided. To reduce plantar pressure, a sole stiffening plate with a rocker sole are among the design features of suitable protective shoes for diabetics. There is a 40–50% reduction in pressure in the sole area with such shoes which have appropriate multilayered insoles compared to normal shoes (60% reduction of pressure as compared to walking bare foot). Specially padded stockings can also reduce the pressure load by up to 30%, as well as reducing the effect of shear forces. Sufficiently deep running shoes are considered by some authors to be the minimal acceptable option in the absence of deformities until the permanent protective shoe is finished or if the patient refuses specialist shoe provision. This type of provision reduces the plantar pressure load by 30–45%.

The fact that relapses cannot be avoided in a quarter of patients annually is due to various reasons. Firstly, patient acceptance of diabetes-adapted footwear is low at 22%–63%. Although not all patients approved the appearance of their customised orthopaedic shoes, 51 out of 85 foot outpatients were wearing their customised shoes at a random inspection. Patients who displayed a higher degree of compliance were older and more frequently had previous amputations than the less compliant patients. Patient participation in the design of the shoes and a broader range in terms of shapes and colours would possibly increase the frequency with which such footwear was worn. More intensive information, directed at patients with shoe-related lesions, the
provision of a sufficient number of suitable pairs of shoes and the additional prescription of slippers could also contribute to reducing relapses. Twenty-two percent of patients with foot ulcers in a Southern German diabetes clinic\textsuperscript{79} and a similar percentage of patients in our own outpatient foot department were not prescribed protective shoes in 1994 and 1995\textsuperscript{78}. Regular inspection of the shoes and insoles, particularly in the period after the prescription, and the consistent improvement of deficiencies are essential for quality assurance and avoidance of ulcers.

A further obstacle to the widespread use of therapeutic footwear became apparent in an American study. Only 6\% of all doctors who were informed about the possibility of prescribing protective footwear with reimbursement by insurance companies prescribed such shoes in the following three years (one in 10 orthopaedic surgeons, one in 21 internists and only one in 53 general practitioners or family doctors). Fiftynine percent of the patients provided with footwear had a previous history of foot ulcer in this study and 25\% of patients had previous amputation\textsuperscript{236}. 

Blueprint of a slightly altered diabetic foot: by positioning their own shoes over the top, the patient was able to see the incongruity between shoe size and foot size
Compared with studies of the benefit of specialised shoe provision in the prevention of relapses, the data on shoe provision for prophylaxis in patients without previous foot injuries is less extensive. In a German study over a 2-year period, only one in 21 patients without a previous foot lesion suffered a foot injury following the provision of protective shoes\textsuperscript{226}, and two out of 49 patients in another study\textsuperscript{237}. Predictors of the occurrence of foot lesions in this patient group are the purchase of new shoes in the six months prior to the occurrence of the ulcer and wearing the wrong size of shoes\textsuperscript{238}. In 80% of patients from a diabetic population, among whom 27% had already suffered a foot ulcer, the feet were never measured when buying shoes\textsuperscript{212}. Recent studies on the subject have shown that the feet of diabetics with neuropathy match the normal size in terms of length.

In terms of width, the normal shoe width G is too narrow for 65 - 95% of patients. Even the next width up, extra G (extra large), was inadequate for 44%--84% of patients\textsuperscript{239}. According to another study, only about 20% of diabetic patients were able to use normal footwear, and only to a limited extent. About 60% of patients were able to wear off-the-shelf protective shoes, while for 22% of male diabetics and 13% of female diabetics, a proper fit was only possible with hand-made customised shoes\textsuperscript{240}. Although clinically tested off-the-shelf protective shoes are currently specifically excluded from compulsory benefits from the health insurance funds, a large proportion of patients could be supplied cheaply.
with such footwear to match the stage of their condition. Only patients with gross deformities or who have already undergone amputations of part of the foot require the more expensive hand-made customised footwear. The value of computer-assisted foot pressure measurement procedures in the production and follow-up of specialised shoe provision for diabetics cannot be conclusively established at the present time.
Footwear provision for the diabetic foot – Classification by risk groups

Ia: Diabetes mellitus without PNP/AOD*:
Off-the-shelf shoe

Ib: As above, with foot deformity:
Orthopaedic inserts, shoe devices

IIa: Diabetes mellitus with PNP/AOD:
Suitable off-the-shelf protective shoe

Minimal criteria for a shoe of this kind include sufficient toe room, sufficient width, no stitches in front part of shoe, soft leather, removable insole with soft cushioning and reduction of pressure points by at least 30% in the metatarsal region. No hard toe caps. The efficacy of off-the-shelf protective shoes – with or without individually designed insoles – needs to be demonstrated in studies.

IIb: As above with foot deformity:
Off-the-shelf protective shoe where appropriate; in the event of specific foot deformities, shoe devices and/or individual diabetes-specific insoles, possibly custom-made shoes

Inspection of insoles and regular renewal

III. Foot as II and status following ulcer:
Shoe provision as for II.

IV. Foot as II and high grade deformity or osteoarthropathy:
Custom-made shoes, orthoses, inner shoes

V. Status following partial foot amputations:
As IV, plus toe and forefoot replacement prostheses.

The effectiveness of custom-made shoes with individually designed insoles needs to be demonstrated in studies since at present there is no standardisation of materials and design of custom-made shoes for the diabetic foot.

VI. Footwear provision in acute ulcers, etc.:
Various relief shoes and pressure-relieving orthoses are used here in plantar ulcers and bandage shoes in non-plantar ulcers.

The effectiveness of the various pressure-relieving and therapeutic shoes also needs to be demonstrated in studies.

Erich Gromotka, orthopaedic shoemaker
Georg Seeßle, orthopaedic shoemaker
Jürgen Stumpf, orthopaedic shoemaker
Karl Türk, orthopaedic shoemaker
Dr. Bettina Born
Dr. Christoph Metzger
Dr. Maximilian Spraul

Working party
„Quality criteria and evaluation of shoe provision for the diabetic foot“

* PNP = Polyneuropathy
AOD = Arterial Occlusive Disease
Structures for screening, treatment and aftercare of patients with diabetic foot syndrome

The financial burden and the human suffering caused by diabetic foot syndrome need not be accepted as inevitable. Numerous studies in the past few years have shown that more than 50% of all amputations in diabetics are avoidable if the following procedures are applied systematically:

- Regular inspection of feet and footwear of diabetics at each visit to the doctor
- Preventive foot care and shoe provision in high-risk patients and additional education
- Use of multifactorial and multidisciplinary treatment concepts in the case of foot lesions
- Early diagnosis and appropriate treatment of peripheral circulatory disorders in diabetics
- On-going aftercare of patients with previous foot ulcerations or prior amputations
- Strict adherence to defined indications for amputation and establishment of amputation registers

The management of Diabetic Foot Syndrome in non-specialist German hospitals at the beginning of the 1990s unfortunately revealed a different, somewhat gloomier picture. Almost 50% of the foot lesions treated there culminated in an amputation and every second amputation was a major amputation. In patients with an arterial occlusive disease only, the rate of major amputations was 56%. In patients with combined neurological and ischaemic findings, the amputation rate was 38%, and in patients with purely neuropathic foot lesions, 27% of treatments ended in amputation. Inappropriate conservative treatment concepts and complete ignorance of vascular surgical treatment options were the reasons for the frightening amputation statistics in the study quoted. If patients in whom an indication was established for minor or major amputation were transferred to a specialist centre (mostly on their own initiative), 83% of impending limb amputations and 79% of scheduled foot amputations were avoided as a result of the exploitation of all the therapeutic options.
The fact that things could be different had been impressively demonstrated many years ago: In the 1970s Davidson in Atlanta had demonstrated the possibilities of reducing amputations in diabetics through a team concept with risk screening, education and systematic aftercare of the patient. The amputation figures halved between 1973 and 1980 after the introduction of these measures (from 13.3 to 6.7 amputations/1000 patients/year). A total of 555 amputations were avoided over this period. Similar figures were reported in the following years from Switzerland, England, Scandanavia, Italy and Germany. The healing rates for diabetic foot lesions reported from such centres were 72% to 80% in ischaemic lesions and 86% to 95% in neuropathically infected foot ulcers. Between 1994 and 1998 in our own outpatient diabetic foot department at the Marienkrankenhaus, (Soest/Germany) major amputations were entirely avoided in purely neuropathically induced foot lesions. In purely ischaemic lesions a 40% reduction in all types of amputation was obtained.

The establishment of outpatient diabetic foot departments in specialised clinics, however, not only results in a marked reduction in the number of amputations necessary and consequently an improvement in the quality of life of those affected, but also produces considerable cost savings. The need for inpatient treatment can be reduced from on average about 40 days to approximately 20 days through the possibility of follow-up outpatient care, i.e. it can be shortened by about three weeks. Inpatient hospital treatment can even be totally avoided in a high proportion of purely neuropathically related lesions.

The leg preservation rate with the maximum exploitation of vascular surgical possibilities (43% crural and 12% pedal vascular reconstructions) for patients with critical limb ischaemia is 85% after two years and almost as high for patients with neuropathic lesions complicated by a serious infection. If vascular reconstruction is not possible in patients with ischaemic lesions, the limb preservation rate is reduced to 17% after two years.
Not only have these outpatient diabetic foot departments demonstrated their value in terms of improved prognosis for manifest foot lesions, but also their efficacy in the prevention of lesions in previously ulcer-free high-risk patients is now documented. Over a three-year period, patients who did not receive regular care from an outpatient foot department suffered a foot ulcer 24 times more often than patients who received constant attention from such a department. A lack of patient compliance (in this case defined as a failure to attend less than half the arranged appointments) increased the probability of ulcer 54-fold and the risk of amputation 20-fold for the whole population, including patients with previous foot lesions251.

Patients with diabetic foot syndrome remain high-risk patients throughout their life. Despite structured aftercare, about a third of patients suffer a first relapse within one year of the healing of an initial lesion78,37, while after two years the figures are between 40% and 50% of patients78,79,37. After five years seven out of ten patients have suffered a recurrence of the lesion37. In previously amputated patients the annual relapse risk is reported as 85%252. If such patients are not continuously treated by a specialist establishment after the healing of a foot injury, their risk of amputation in the event of a relapse is almost 70%. If they continue to be treated by an outpatient foot department, this risk falls to about 20%253. In one of our own studies in 30 patients who suffered a relapse despite receiving care from an outpatient diabetic foot department, amputations were completely avoided after a second lesion. The need for hospitalisation in association with a recurrent lesion regressed to 7%, compared to 73% with the first lesion, and the duration of healing was reduced from 64 to 29 days254.

Structured care therefore shows a positive effect on the avoidance of foot lesions in high risk patients, the course manifest foot injuries take, and the prognosis in case of recurrence.
## Levels of care for the support of patients with diabetic foot syndrome (modified by Reike)

<table>
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<tr>
<th>Target group</th>
<th>Activity</th>
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| **Medical foot care practice (Chiropodist/DDG, German Diabetes Society)** | Patients at risk of foot lesions | Atraumatic removal of callosities  
Skin and nail care  
Advice to patients |
| **General practitioner** | All diabetics  
Patients at risk of foot lesions | Primary/secondary prevention  
Metabolic control/advice |
| **Practitioner with specialisation in diabetes** | Patients with a healed foot lesion | Screening of risk patients  
Clinical follow-up examination and diagnosis. Basic instrumental examination. Footwear inspection. Where appropriate, microbiology and structured local wound treatment in Wagner stage 1 (possibly 2) |
| **Outpatient diabetic foot clinic (hospital based)** | Diabetics with Wagner stage 2 and 3 foot lesions  
Diabetics with foot lesions and wound healing disorders  
Diabetics with osteoarthropathy (acute/chronic Charcot's foot) | Neurological, angiological and radiological diagnosis. Microbiological diagnosis. Interaction with other specialist disciplines. Structured local wound management, where necessary with establishment of a treatment plan for GP care. Co-operation with orthopaedic technician and orthopaedic shoemaker. Referral to outpatient care services. Education of (high-) risk patients. |
| **DFS inpatient unit** | Diabetics with foot lesions and wound healing disorders  
Diabetics with critical ischaemia  
In order to allow successful specialist treatment of patients with diabetic foot lesions at an early stage, all the existing centres must co-operate to streamline treatment. In a current Swedish study, there was an interval of between 31 and 189 days between the first presentation of a foot injury at the general practitioner’s and the institution of care by an outpatient foot department. Antibiotic treatment was instituted in a primary care setting in 44% of patients, but additional measures, such as pressure relief, were implemented in only 8% of cases\textsuperscript{255}. In our own prospective study, the interval between the occurrence of the lesion and the first presentation at the outpatient diabetic foot department in 153 patients without any prior information about the procedure to be followed in the event of foot problems was on average 71 days. However in 62 patients with previous education or contact with the outpatient foot department for a previous lesion, the interval was 13 days. The corresponding amputation rates were 24% and 10%, respectively\textsuperscript{256}.

The role of the family doctor might be:
1. The identification of patients at risk of foot lesions
2. The provision of basic information to these patients
3. The implementation of preventive measures
4. The regular inspection of foot status

Minor foot lesions can be managed in a diabetes clinic and, in emergency cases, in specialised outpatient diabetic foot departments. The complete diagnosis and treatment of more complex foot lesions should also be undertaken there, with the involvement of diabetologists, surgeons, vascular surgeons, chiropodists, orthopaedic shoemakers and interventional radiologists. Emergency facilities and the presence of a special foot unit with appropriately trained staff should be among the features of such specialised establishments. Problem-centred interdisciplinary visits can further improve the efficiency of such establishments.
Successful co-operation in a network of this kind requires seamless transitions (frequently complicated by the strict separation of outpatient and inpatient structures in Germany), the absence of fear of contact and the presence and implementation of guidelines which are valid for all participants. A consensus paper in this respect on the diagnosis and treatment of the diabetic foot was published for the first time in May 1999 by the International Working Group on the Diabetic Foot.

**The diabetic foot: a global problem**

The prevalence of diabetes world-wide, which affected approximately 135 million patients in 1996, is predicted to grow to 300 million patients by the year 2025 on the basis of increasing life expectancy throughout the world, the change in dietary habits and the increase in the proportion of obese patients. In particular, countries with little or no infrastructure and no standards of foot care, will experience the most dramatic increases in type 2 diabetics. Thus, in the year 2025 India is predicted to have 57 million diabetics and China 38 million. In Central and Southern African countries, the number is estimated to grow from 3 million at present to 8 million, representing an increase of 185%. Although the pathogenesis of diabetic foot problems is probably the same everywhere in the world, the clinical manifestations and the problems observed differ according to local conditions and sociocultural features between the distinct countries and the various geographic regions.

In Western European countries, the distribution of risk conditions (arterial occlusive disease and diabetic sensorimotor neuropathy) is very similar to that found internationally. Also the treatment results essentially reveal no differences between Central European and North American centres. The conditions in other parts of the world are quite different as a result of specific epidemiological factors and the features of the relevant healthcare systems.
In Eastern Europe, specialist centres for the treatment of the diabetic foot are rare. In many places amputation is still considered the standard. As a result of twinning programmes with Western European countries, structural improvements are gradually occurring in certain regions. In South America, where the prevalence of diabetes is more than 6%, the establishment of institutions has so far only been observed in Costa Rica, Mexico and Brazil. In some North African countries more than 10% of the population are diabetics, up to 12% of patients with foot ulcerations are found among hospital inpatients and 7% of diabetics have had previous amputation. In Australia programmes involving foot care in diabetics have already been implemented countrywide. In some tropical countries, the co-existence of diabetes mellitus and leprosy has resulted in a particularly high occurrence of patients with a potential risk of occurrence of foot lesions. In addition, a relatively high proportion of foot

Manifestations of diabetic foot syndrome in India:

a) Callus formation on the dorsum of the foot in a Moslem diabetic patient – a result of the typical kneeling praying position with crossed feet

b) Burn in the area of the rear of the foot as a result of placing the naked foot on the hot exhaust pipe of a motorbike (both pictures were kindly provided by Dr. V. Viswanathan, Chennai, India)
(and hand) infections is found here in diabetics without the conventional risk conditions, such as arterial occlusive disease and diabetic neuropathy\textsuperscript{260,261}.

On the basis of our own study (613 patients), the following essential differences were observed in the presenting conditions of diabetic foot syndrome between an industrial country (Germany) and two developing countries (Tanzania and India). In developing countries there is a far smaller proportion of patients with arterial occlusive disease, because abuse of nicotine is less common. The patients are much younger and the duration of diabetes is shorter. Shoe-related lesions were found in the developing countries in only 5 to 6\% of cases, as opposed to 27\% in the industrial nations. The presence of a diabetic neuropathy in patients with diabetic foot syndrome, however, was equally high in both populations, at about 80\%\textsuperscript{262}.

The situation in some African countries is characterised by the high proportion of illiteracy among foot patients and the more difficult conditions for the provision of information and education. In some cultural environments amputation of a limb is considered to be more serious than the loss of one's own life\textsuperscript{261}. This explains the high proportion of self-discharges by patients before the end of treatment from hospitals, especially in view of a more than 50\% amputation rate. Unusual manifestations due to specific sociocultural conditions characterise the picture of the diabetic foot in India. In a country in which 30\% of people live below the poverty line, wearing shoes tends to be the exception rather than the rule. Infections of fissures resulting from walking barefoot are among the causes of diabetic foot problems in India, as are burns from the hot cobble stones of the Hindu temples where the faithful are strictly forbidden to wear shoes and pressure sites in the ankle region because of the particular praying position of the Moslems\textsuperscript{263}. Rat bites of the toes of neuropathic patients\textsuperscript{264} are among the unusual presenting forms of diabetic foot syndrome in India, as well as infections from tropical worms.
Summary and prospects

More than half of all limb amputations are carried out in patients with diabetes mellitus. In more than 70% of cases, amputation is preceded by a foot ulcer progressing to deep gangrenous infection. Most of these ulcers are caused by minor trauma, frequently as a result of poorly fitting footwear or inadequate foot care. Sensorimotor diabetic neuropathy or a peripheral arterial occlusive disease of varying severity are in most cases present as risk conditions predisposing to injury.

The continuous registration of amputations (amputation registers, e.g. the Danish amputation register, North Rhine Chamber of Physicians Diabetology/Surgery Quality Assurance) can help to reduce amputation rates in diabetics\textsuperscript{265}. The DCCT study\textsuperscript{6} has shown that intensive treatment of type 1 diabetics and optimised blood sugar control can reduce the probability of diabetic neuropathy occurring by 50%. However, as long as the avoidance of secondary micro-angiopathic complications remains a goal for a majority of diabetics, the early identification of risk conditions, the avoidance of lesions in high risk patients and the structured treatment and aftercare of ulcer patients (and previous amputees) must be made a priority.

Key preconditions for improving the prognosis of diabetics with foot lesions are:
1. Regular screening of diabetics for impaired nerve function and inadequate circulation
2. Problem-centred patient education
3. Regular foot care and the supply of protective footwear to those affected
4. Structured and team-based care of patients with active ulcerations

The specific recording of individual causes of injury and integration of these findings in the risk-centred education and aftercare of patients and relatives may help to reduce the emergence of recurrent lesions and hence the risk of amputation still further\textsuperscript{78,266}. 
The implementation of prevention and treatment strategies has been shown to help avoid more than 50% of amputations in diabetics.

According to Swedish estimates, halving the amputation rate would reduce the costs of treatment of diabetic foot problems by about 20 to 40\%\textsuperscript{267}.

Although in the new millennium new treatment options may facilitate the treatment of diabetic foot lesions, the continuing construction of suitable treatment establishments and their regional networking certainly cannot be replaced. Extensive and structured treatment and aftercare of patients with diabetic foot syndrome in specialised and quality assured institutions is necessary to implement the requirements of the St. Vincent Declaration. The key to success for the development of appropriate infrastructures to allow the creation of foot teams for problem patients lies in obtaining the necessary contribution from insurance companies, as well as early registration and targeted care of high risk patients.

In view of the enormous expenditure on amputations in diabetics and the comparatively low costs of preventive measures in diabetic foot syndrome, it may be assumed that such efforts will be associated with a favourable cost-benefit ratio.

Extensive knowledge alone remains ineffective. To contribute to successful treatment, this knowledge must be applied. In the form of behavioural changes in patients and also in the professional groups treating them within the healthcare system. It is not the hope of new treatment procedures, but simply the consistent application of what is known, established and already possible that in the future will result in amputations becoming an exception and not the rule in patients with diabetic foot syndrome.
Definitions and explanations

**Amputation**
Resection of a part of a limb

**Arterial occlusive disease**
Presence of clinical signs such as the absence of foot pulses, previous history of intermittent claudication, rest pain and/or abnormalities in non-invasive examinations indicating impaired or insufficient circulation

**Cellulitis**
Presence of swelling, redness and heat as evidence of an inflammatory reaction, irrespective of origin

**Charcot’s deformity**
Resulting from Charcot’s disease or arthritis; also neuropathic arthritis - it is a rapid progressive degeneration in a joint which lacks position sense and protective pain

**Chopart amputation**
Amputation through the talo-navicular joint

**Deep infection**
Presence of evidence of an abscess, septic arthritis or osteomyelitis

**Débridement**
Removal of dead tissue

**Deep ulcer**
Lesion affecting the whole thickness of the skin and extending to the subcutis, possibly involving muscles, tendons, bones and joints at the same time

**Diabetic foot syndrome**
Infection, ulceration and/or destruction of deep tissue associated with neurological abnormalities and various degrees of severity of arterial circulatory disorders of the lower extremity

**Diabetic neuropathy**
Presence of signs and/or symptoms of disorders of peripheral nerve function in patients with diabetes mellitus after the exclusion of other causes
Foot deformity
Structural changes in the foot, such as the presence of hammer toes, claw toes, hallux valgus, prominent metatarsals and conditions due to neuro-osteoarthropathy, as well as surgery on the foot and amputations

Foot lesion
Blisters, erosion, cut or ulcer on the foot

Gangrene
Progressive necrosis of the skin and deeper structures (muscles, tendons, bones or joints) indicating irreversible destruction, in which healing cannot be obtained without the loss of part of the extremity

Infection
Penetration and proliferation of micro-organisms in body tissue, which may be clinically insignificant or may result in local cell death, as a result of toxins, intracellular microbial proliferation or an immune response

Intermittent claudication
Pain in the foot, thigh or calf which is increased on walking and relieved on stopping, associated with evidence of an arterial occlusive disease

Major amputation
Any amputation above the ankle joint

Minor amputation
Amputation at the level of the ankle joint or lower

Necrosis
Dead tissue, either dry or moist, regardless of the tissue affected

Neuro-osteoarthropathy
Non-infectious destruction of the bone or joints associated with a neuropathy

Neutropenia
Relative or absolute decrease in the number of neutrophilic leucocytes in the blood

Osteomyelitis
Infection of the bone with involvement of the bone marrow
**Pirogoff amputation**
The calcaneum is cut across so that the posterior 2 cm remain in the heel flap and this is attached to the lower end of the tibia, making a longer stump than in the Syme’s amputation.

**Polymicrobial**
Infections with more than one organism causing damage

**Pressure relief**
Relief of load-bearing areas of the foot through the systematic use of crutches, wheelchairs, partial foot relief shoes or other orthopaedic devices

**Protective footwear**
Footwear of proven benefit in the prevention of ulcerations

**Superficial infection**
Infection of the skin without involvement of muscles, tendons, bones or joints

**Superficial ulcer**
Lesion affecting the whole thickness of the skin without extending to the subcutis

**Syme’s amputation**
The original level of amputation was through the ankle joint with the medial and lateral malleolus trimmed. The amputation has been modified to divide the tibia and fibula 1 cm above the joint line. In an emergency the patient is able to stand and walk without the prosthesis.
Abbreviations:

<table>
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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>ABI Ankle Brachial Index</td>
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<td>ADA American Diabetes Association</td>
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<td>AOD Arterial Occlusive Disease</td>
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<td>ATR Achilles Tendon Reflex</td>
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<td>bFGF b-Fibroblast Growth Factor</td>
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<td>BMT Biochemical Wound Therapy</td>
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<td>CNS Central Nervous System</td>
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<td>CSII Continuous Subcutaneous Insulin Infusion</td>
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<td>CT Conventional Insulin Therapy</td>
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<td>CVA Cerebral Vascular Accident</td>
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<td>DCCT Diabetes Control and Complication Trial</td>
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<td>DDG Deutsche Diabetes Gesellschaft (German Diabetic Association)</td>
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<tr>
<td>DFS Diabetic Foot Syndrome</td>
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<td>DNOAP Diabetic Neuropathic Osteoarthropathy</td>
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<td>DSA Digital Subtraction Angiography</td>
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<td>ESR Erythrocyte Sedimentation Rate</td>
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<td>EUR Euro</td>
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<td>GAD Glutamic Acid Decarboxylase</td>
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<td>GCSF Granulocytes Stimulating Factor</td>
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<td>GDM Gestational Diabetes Mellitus</td>
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<tr>
<td>HbA1c Haemoglobin Receptor A1 c</td>
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<tr>
<td>HBO Hyperbaric Oxygen</td>
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<tr>
<td>ICA Islet Cell Antibodies</td>
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<tr>
<td>ICT Intensified Conventional Insulin Therapy</td>
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<td>MRI Magnetic Resonance Imaging</td>
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<td>PDGF Platelet Derived Growth Factor</td>
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<td>PNP Polyneuropathy</td>
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<tr>
<td>PNS Peripheral Nervous System</td>
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<td>PTA Percutaneous Transluminal Angioplasty</td>
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<tr>
<td>rhPDGF Recombinant Platelet Derived Growth Factor</td>
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<tr>
<td>TCPO₂ Transcutaneous Partial Oxygen Pressure</td>
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<tr>
<td>TGFβ Tissue Growth Factor β</td>
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<tr>
<td>UKPDS United Kindom Prospective Diabetes Study</td>
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<td>V Volt</td>
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<td>WHO World Health Organisation</td>
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Proposed further reading


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