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diabetic patients aged 15 - 50 years
A population-based study
ABSTRACT

FOOT LESIONS IN DIABETIC PATIENTS AGED 15-50 YEARS. A POPULATION-BASED STUDY.

Bengt Borssén, Departments of Orthopaedics and Medicine, University of Umeå, S-90185 Umeå.

Foot problems are not only the most common but in general also the most severe of the diabetic complications. The age group 15-50 yrs in this study was chosen because these patients were considered to be at their most active age and were felt to require optimal foot function. 380 patients (96 %) participated, 78 % with Type 1, 20 % Type 2 and 1 % with secondary diabetes mellitus (DM) and 100 healthy controls. Only six patients had signs of peripheral ischaemia but half of the patients had deformities such as fallen forefoot arches and hammer toes. With sensory thresholds and clinical signs it was demonstrated that age, duration of DM and tall stature are major risk factors for diabetic neuropathy. Gender differences depend on differences in height. Dorsiflexion of the toes against resistance was used to test the function and volume of m.extensor digitorum brevis. When compared with measurements of sensory thresholds for vibration, perception and pain, it was found to be a valuable test for screening of distal motor neuropathy. To prevent worsening of foot deformities 266 patients with Type 1 DM were followed for 3 years. Those with the most pronounced deformities were fitted with custom-made insoles and had repeated examinations. Improvement was more common in patients with insoles compared to patients without insoles. Bone mineral density (BMD) was measured in nine patients with osteopathy in their feet and 18 controls. BMD was lower in L2-L3, but not in the proximal femur, implying osteopenia being a possible risk factor for distal osteopathy. Plaster cast treatment was used in 33 diabetic patients with severe foot ulcers who were selected because previous conservative treatment had been unsuccessful and they had been judged unsuitable for vascular surgery. The lesions healed in 19 patients. In conclusion, the main findings demonstrate the need for an increased awareness of early preventive foot care in young and middle-aged diabetic patients.

Key words: Diabetes mellitus Foot deformities Sensory threshold M. extensor digitorum brevis
Det va´ som det va´
tills det blev som det blev
Det blir som det blir
när det är som det är

Det är som det är
tills det blir som det blir
Faran är att det blir som det var

Alf Henriksson
Och i sitt trettionionde regeringsår fick Asa en sjukdom i sina fötter, och sjukdomen blev övermåttan svår;
men oaktat sin sjukdom sökte han inte HERREN, utan allenast läkares hjälp.

2 Krön 16:12
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Bengt Borssén

Umeå 1996
ABSTRACT

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To prevent worsening of foot deformities 266 patients with Type 1 DM were followed for 3 years. Those with the most pronounced deformities were fitted with custom-made insoles and had repeated examinations. Improvement was more common in patients with insoles compared to patients without insoles.

Bone mineral density (BMD) was measured in nine patients with osteopathy in their feet and 18 controls. BMD was lower in L2-L3, but not in the proximal femur, implying osteopenia being a possible risk factor for distal osteopathy.

Plaster cast treatment was used in 33 diabetic patients with severe foot ulcers who were selected because previous conservative treatment had been unsuccessful and they had been judged unsuitable for vascular surgery. The lesions healed in 19 patients.

In conclusion, the main findings demonstrate the need for an increased awareness of early preventive foot care in young and middle-aged diabetic patients.

Key words: Diabetes mellitus Foot deformities Sensory threshold M. extensor digitorum brevis
LIST OF ORIGINAL PAPERS

This thesis is based on the following papers which will be referred to by their Roman numerals;


Definitions and assessments

Arterial insufficiency was defined as an ankle/arm systolic blood pressure index below 0.9.

Body mass index (BMI) was defined as body weight (kg) times height (m)^2.

Bone mineral density (BMD) was measured by dual photon x-ray absorptiometry (Lunar DPX-L).

Callosities was defined as localized hyperkeratosis, usually over a bony prominence on the sole of the foot.

Claudication was defined after a history was taken according to the protocol suggested by Rose et al. 1

Cutaneous sensory impairment was assessed by a monofilament test.2,3

Diabetes mellitus (DM) was classified as either Type 1 or Type 2 on clinical grounds.4 Where classification was difficult, a glucagon-stimulated C-peptide level 5 was measured to distinguish between Type 1 and Type 2 DM. All patients had a treated DM prior to entering the study.

Dry feet were diagnosed if the patient history revealed loss of perspiration that could be confirmed on examination.

Extensor digitorum brevis (EDB) muscle is the short toe extensor which extends the proximal phalanx of the four medial toes. The muscle belly is localized on the proximal and lateral aspect of the dorsum of the foot.

Fissures were defined as lesions of the sole of the foot localized to the cuticular layer of the epidermis.

Forefoot arch describes the transverse convexity towards the dorsum of the foot at the transverse line of the metatarsal heads (arcus pedis transversalis). For the assessment of degree of loss of the forefoot arch a semiquantitative scale ranging from normal, slight, moderate to marked was devised. Moderate indicated a flat fore foot, and marked loss described a forefoot arch which is convex towards the sole of the foot.
Hammer toes describes an extension in the metatarso-phalangeal (MTP) joint and a subsequent flexion in the proximal interphalangeal (PIP) joint. A semiquantitative grading was used; normal, slight indicating a slight hyperextension in the MTP joint, moderate an obvious hyperextension, and marked an additional clawing in the distal IP joint.

Healing was defined as full epithelial coverage and no sign left of a local soft tissue reaction.

Major amputation refers to all levels from the ankle joint and above.

Melin’s shin spots are small, light brown, circumscribed atrophic lesions on the mid or lower leg. They are seldom larger than 10 mm in diameter.

Necrobiosis lipoidica diabeticorum usually found on the mid to lower leg, are defined as having a characteristic translucent, brownish-red periphery with central atrophic yellow areas with prominent telangiectasis.

Osteopathy is a skeletal condition that clinically in its early form starts as an oedematous, erythematous foot with increased skin temperature. X-rays show progressing involvement of especially the metaphyses with fragmentation and hypertrophic periosteal reaction, joint narrowing and finally subluxation and dislocation. Joint involvement is a secondary phenomenon.

Pubertal age was assumed to be 13 years when assessing the importance of development of diabetes before or after puberty in relation to height in Type 1 DM.

Purpura was defined as the presence of numerous petechiae or somewhat larger cutaneous haemorrhages in patients in whom other causes of purpura had been excluded.

Range of motion of the ankle joint was measured according to Lindsjö et al.

Sensory thresholds were measured with two different modalities to assess the vibration threshold, and the thresholds for perception and pain.
Smoking was quantified in pack years, defined as the number of packs of 20 cigarettes smoked daily, multiplied by the duration of smoking in years.

Ulceration was defined as a full-thickness penetrating lesion of the skin.

Yellow toenails refers to smooth nails of yellow or yellowish-green colour that are often somewhat thickened. (Patients with nail lesions caused by psoriasis or onchomycosis were excluded).
Introduction

Successful treatment of foot lesions is dependent on some kind of intervention and preferably prophylactically. It is important, especially in times of limited financial resources, to have access to epidemiological data in order to direct our resources towards these groups of patients where they are best needed. It should be pointed out that epidemiological studies in DM have shown the value of screening for pre-symptomatic complications such as retinopathy and proteinuria and the effect of early treatment for the prevention of visual impairment or renal failure. It is also important that the clinician has access to simple and reliable methods that are easy to use in the ordinary clinical situation.

Background

The isolation of the hormone insulin in 1921 made treatment possible for people stricken with Type 1 DM (insulin dependent diabetes mellitus). These patients once often faced death within one year after diagnosis. Today Type 1 DM is suspected to arise from an autoimmune reaction directed specifically towards the B-cells of the islets of Langerhans, and genetic abnormalities, which increase the propensity to develop DM. The disease appears overt when at least 80% of the B-cells are destroyed.

In Type 2 DM (non-insulin dependent diabetes mellitus) the etiology is more obscure and probably more diversified. The patients produce varying quantities of insulin, but a decreased insulin release function through insulin resistance seems to be the main causal reason. In Type 2 DM as well as in about half of the patients of Type 1 DM there is a genetic predisposition although unlike Type 1 DM, life style factors have a known impact on the etiology of Type 2 DM. It has even been claimed that in some environments Type 2 DM has been a prerequisite for the maintenance of life itself.

Neither insulin treatment, nor oral antidiabetic drugs or dietary restrictions can usually fully normalize the metabolic dysfunction well enough to prevent the patients from the well-known complications of DM - nephropathy, retinopathy, neuropathy and foot lesions.
Epidemiology

With introduction of insulin treatment there was an increasing prevalence of DM. The total prevalence in a Swedish municipality is reported to be 3.5 %. There is an even more pronounced increase of DM with age. In elderly Caucasians the figure approaches 20%, and substantially higher in specific ethnic populations, in Pima Indians in particular, the prevalence reaches 50% or more. Since duration of DM as well as high age have a high impact on the complication rate, the increasing prevalence of DM, especially in the elderly, must be considered a potential problem to individuals and health care systems in the years to come.

Biochemical basis of complications

Empirically as well as from numerous investigations the same conclusion has been drawn: - high levels of blood glucose for long time is a prerequisite of diabetic vascular or neurological complications. In a superabundance of glucose non-enzymatic glycosylation processes form early reversible glycosylation products of which the best known is haemoglobin A1c. These early glycosylation products may undergo a slow complex series of chemical rearrangements that react with long-lived proteins or lipoproteins forming irreversible advanced glycosylation endproducts (AGE). The transformation rate of AGE:s is proportional to degree and time during which the hyperglycaemia persists. The AGE:s accumulate in the tissues and have increasingly been recognized as factors in the pathogenesis of diabetic complications. Within the vessel wall AGE:s are thought to accumulate continually, irreversibly bound to vessel wall proteins. The endothelial AGE complexes induce oxidant stress which increases the vascular permeability, activates cytokines eventually leading to the atherosclerotic process. The atherosclerotic process is enforced and aggravated in patients with hypertension and elevated hydrostatic pressure. The development of diabetic neuropathy is suggested to occur in the hyperglycaemic patient by excessive intracellular accumulation of sorbitol and its ramifications leading to both axonal degeneration and demyelination. The formation of AGE:s binding to nerve cell wall components may also be of importance.

Pathophysiology of diabetic foot complications

Diabetic foot complications signify lesions in general secondary to macro- and microangiopy and neuropathy such as gangrene, ulcers, deformities, atrophy of soft tissues, increased skin fragility.
The contributory intrinsic factors that lead to diabetic foot complications have traditionally been considered to be vascular disease, peripheral neuropathy and infection. There is, however, no convincing evidence that infection is a primary cause of ulceration.\textsuperscript{30} It seems more likely that the bacteriae are spongers after the initial ulceration has occurred. Pecoraro et al.\textsuperscript{31} defined three main groups of diabetic patients with high probability for foot lesions and subsequent amputation: 1) patients with polyneuropathy without evidence of vascular disease; 2) patients with polyneuropathy and vascular disease; and 3) patients with vascular disease without evidence of polyneuropathy. Of importance are also changes secondary to DM that jeopardize normal foot biomechanics; altered postural control and gait;\textsuperscript{32} limited joint mobility (LJM),\textsuperscript{33} a condition that is thought to be caused by AEG:s accumulating on collagen\textsuperscript{34} thereby decreasing its elasticity which results in stiffness of the connective tissues and a subsequent reduction of range of motion.\textsuperscript{35,36,37} Finally, osteopathy, an enigmatic condition which shows more or less pronounced breakdown of the toe or foot skeleton and may lead to deteriorated foot architecture and function.\textsuperscript{38}

It has been stated that there is a high incidence of atherosclerotic peripheral vascular disease (PVD) in the lower leg\textsuperscript{39} as well as peripheral neuropathy\textsuperscript{40} in DM. Although PVD is an important contributory factor in the pathogenesis of foot ulceration and subsequent major amputation, less than 15\% of foot ulcers are judged to be of a purely ischaemic nature.\textsuperscript{41,42,43,44} Usually it is a combination of one or more of the factors mentioned above and an intrinsic or extrinsic trauma that leads to tissue breakdown and ulceration.\textsuperscript{45} Peripheral neuropathy prevalence rates are reported as ranging from 13 to 54\% with a median value of 32\%.\textsuperscript{46} As the onset of these secondary manifestations of DM is insidious and many diabetic patients never experience any symptoms, it is important to recognize that the absence of symptoms must never be interpreted as a healthy foot. The identification of the "foot at risk" must rely on careful examination. Much attention should also be given to multiple risk factor intervention like weight reduction, cessation of smoking and treatment of hypertension and peripheral oedema.
Diabetic foot complications give rise to considerable morbidity and expense. It has been stated that these complications have the greatest socio-economic impact of all DM complications. At least 15% of all diabetic patients are estimated to be affected during their lifetime; 5 - 20% of all diabetic in-patients have a lower extremity ulcer condition and resulting in a longer hospital stay. The estimated annual incidence of foot ulcers is 3 - 5.6% and the prevalence 4.4 - 10%. The results of prospective research on diabetic foot lesions indicate that peripheral neuropathy, long duration of DM and high foot pressure appear most importantly related to these lesions. To be able to deal with these patients more successfully we have to increase our knowledge of epidemiology and the chain of events. Thereby we can achieve the goals of the S:t Vincent declaration as presented by the World Health Organisation and the International Diabetic Federation in 1989, i.e. decreasing the number of major amputations caused by gangrene by half in a five years' period. This is an important task also in view of the fact that the diabetic population account for 40 - 70% of all major lower leg amputations and that foot ulcers preced the amputation in 54 - 84% of all diabetic patients. Several studies have reported that a programme for preventive foot care and treatment of lesions reduces the rate of major amputations. Furthermore it has been pointed out that even from an economic point of view it is beneficial to treat diabetic foot lesions rather than to perform an amputation. The humanitarian aspect is obvious.
Aims

The present studies are mainly based on a standardized foot examination of a population-based group of diabetic patients aged 15-50 years.

The aims of the present studies were:

To assess the epidemiology of foot lesions in younger diabetic patients.

To study the prevalence of diabetic neuropathy and its relation to age, duration of DM, height and smoking.

To evaluate the extensor digitorum brevis (EDB) muscle test as a predictor of motor-neuropathy in DM.

To evaluate the effect of education and moulded insoles as means of preventive treatment for forefoot deformities in DM.

To evaluate the presence of a generalized osteoporosis as a contributing cause in the development of osteopathy in diabetic patients.

To evaluate total contact plaster cast treatment for soft tissue lesions in the diabetic foot.
Patients and participation

Study I - V

All identified diabetic individuals (n=395) in Umeå county (population 118 500) aged 15 - 50 years were invited to participate in a standardized foot examination. The subjects were identified through our hospitals out-patient and in-patient registers or through all primary care centres. To make the patient material as complete as possible, all prescriptions for anti diabetic drugs were collected during a 6-months period at all pharmacies in the county. Anti- diabetic drugs are available in Sweden on prescription and are only dispensed for a maximum of 3 months use.

The age group 15 - 50 years was chosen because these patients were considered to be at their most active age and were felt to require optimal foot function. Further, this group of patients was of manageable size and well suited for repeated follow-up examinations and longitudinal studies.

One hundred healthy persons, mainly hospital personnel, aged 15-50 years were enrolled as control subjects. Their foot deformities were treated as in the diabetic group.

( I )

All together 395 diabetic patients aged 15 - 50 years were identified and 380 (96%) of them took part, of whom 298 (78%) had Type 1 DM, 77 (20%) had Type 2 diabetes. Twenty Type 2 diabetic patients were insulin treated, 18 were treated with oral anti-diabetic drugs and 39 by diet alone. Two of the Type 1 diabetic patients were being followed up in primary care, 19 at the Department of Pediatrics and 277 at the Department of Medicine. Forty-seven of the patients with Type 2 DM were being followed up in primary care, while 30 attended the Department of Medicine.

Fifteen diabetic patients (5 women) chose not to participate. Ten had Type 1 DM, 4 Type 2, and 1 had secondary diabetes due to a verified pancreatitis.

At the index examination five patients (1%) were found to have secondary DM due to verified chronic pancreatitis and subsequently excluded from the analyses, leaving 375 diabetic individuals (78% Type 1) for analysis.
These studies are based on the examination of 370 (94%) out of 395 identified diabetic patients aged 15 - 50 years within Umeå county described in (I). Besides the 20 patients excluded from analysis in (I), another 5 patients were excluded since their measurements turned out to be incomplete. Out of the 370 patients remaining for analysis, 293 (79%) were Type 1 DM.

This study is a three years follow up of the Type 1 diabetic patients from our original cohort described in (I). At the index examination all participating individuals were educated in suitable foot care and foot wear. Patients with the most pronounced deformities were provided with custom-made insoles. These patients were re-examined after fitting and with further visits to the chiropodist’s clinic if necessary. Out of 298 patients with Type 1 DM participating at the index examination 266 (89%) attended the three year follow up, as did 64 / 100 (64%) of the control subjects. During the observation period five patients with Type 1 DM (age 32 - 52 years) had died; three patients in myocardial infarction and none of the controls was deceased. The primary reason for the large number of drop-outs in the control group was that they had moved to other parts of the country.

Nine patients from our original group of diabetic patients aged 15 - 50 years were found by clinical examination to have obvious foot changes that radiologically could be confirmed as skeletal lesions of osteopathic type. Four patients had pronounced lesions, five patients had lesions of a more limited type. No patient could recall any history of trauma.

A control group of 18 diabetic individuals was obtained by selectively pairing as closely as possible each patient with a distal skeletal lesion with two individuals without any signs or history of foot problems. Pairing criteria were gender, age and duration of diabetes. When a choice of controls was available, we always selected the one with longest duration of DM.
Study VI
This study is based on thirty-three consecutive diabetic patients, of whom 29 had Type 2 DM, with soft tissue lesions of different gradings according to Wagner, who were treated with casts when their initial conventional treatment (elimination of peripheral oedema, strict metabolic control, cessation of smoking, no weight bearing and local wound care) had failed. They had also been judged unsuitable for vascular surgery by a vascular surgeon.
Methods

Each patient was examined in a standardized clinical set up. A medical history was taken and verified against hospital records.

Threshold for vibration (VT) was determined according to the method described by Goldberg and Lindblom. The hand held vibrometer (Somedic, Stockholm, Sweden) uses its own weight as a constantly monitored pressure, and it measures the tissue displacement in um. By increasing the stimulus from zero to the point where vibratory sensation is first perceived, the vibration perception threshold (VPT), and then decreasing the stimulus from an easily perceived level to the point where the sensation disappears, the vibration disappearance threshold (VDT), are determined. The vibration threshold (VT) is then calculated from the formula VT = (VPT + VDT) / 2.

Thresholds for cutaneous perception and pain were measured according to transcutaneous electrical stimulation sensimetry. A constant current electrical stimulator, (ISSAL 1412, ISSAL Medical Products, Skellefteå, Sweden) was used. It has a bipolar saline soaked felt electrode that delivers a 0.2 ms square pulse with a frequency of 100 Hz. The intensity is digitally readable within 0.1 - 60.0 mA. The threshold for perception (Pe) was defined as the lowest intensity at which the subject felt any sensation (usually a tingling). After increasing the intensity, the subject felt a growing unpleasant prickling sensation, and the intensity at which this was hardly bearable was defined as the pain threshold (Pa). The vibration thresholds were measured on the subjects dominant side at the medial malleolus and on the dorsal aspect of the big toe, while perception and pain thresholds were measured above the proximal end of the first metatarsal and on the dorsum of the digit number one. Three determinations were made at each point and the means calculated.

The EDB muscle test. The EDB-muscle, innervated by the deep peroneal nerve, aids the long digital extensor in extending the four medial toes. The subject was requested to maximally forced dorsiflexion of the toes against the investigators resistance. This makes the muscle belly optically visible and palpable. A semiquantitative scale was created and the muscle volume was classified as normal, reduced or absent. A barely perceptible muscle was classified as reduced.

A pre-trial training period was organized to facilitate the standardization of our examination technique and assessment.
Measurement of range of motion - ROM (capacity of dorsal extension) of the ankle joint under load according to Lindsjö et al. was undertaken with the patient leaning forward with most of the bodyweight on the examined foot. Maximum dorsal extension with the sole of the foot flat to the surface was measured with a protractor. Calculations were made on one side only. A range of at least 20 ° dorsal extension is considered normal.

Cutaneous sensory loss was quantified by the Semmes-Weinstein monofilaments, (Research Design Inc; Huston, Tx, USA) using three different filaments representing 4.17 , 5.07 and 6.10 log(0.1mg) force respectively. The filaments were randomly applied on eight standardized sites on the sole of the foot. The borderline value for protective sensation in the feet is 5.07 log(0.1 mg) force and consequently a sensation level at 6.10 log(0.1mg)force means loss of protective sensibility.

Bone mineral density - BMD of the lumbar spine (L2 - L3, lateral projection) and proximal femur was measured by Lunar DPX-L dual photon x-ray absorptiometry; (Lunar Corp. Madison, Wi, USA) a technique that uses two filtered separate x-ray energies, and the BMD is calculated from the differences in absorption in the tissues.

Plaster cast treatment

The cast was applied as a lower leg cast including the whole foot but leaving the toes free. The cast was windowed over the present lesion if necessary, allowing inspection, local treatment and control for progression. All patients subjected to plaster cast treatment were admitted for the first 24 - 48 h treatment to optimize medication of diabetes and concomittant disorders (e.g. heart failure). Patients with severe foot lesions and / or severe pain were often treated as in-patients for a longer period. The first cast was changed within 1 week for assessment. If patient and wound conditions permitted, the patients were treated on an out-patient basis with cast changing intervals extended to 3 - 4 weeks. The patients were allowed full weight baring. Antibiotics were administered only when there was a prominent reaction of the soft tissues surrounding the present lesion. Local treatment was limited to dry absorbing dressings. The patients were followed to end point being healing or major amputation.
Ethical aspects

All patients and control subjects had given their informed consent to take part in the studies. The studies were approved by the local Hospital Ethical Committee.
Main results

Epidemiology of foot lesions (I)

The physical examination revealed a significantly increased prevalence of signs of dry feet, yellow toe nails and Melin's shin spots in diabetic patients compared to control subjects (I - Table 1). Furthermore, the prevalence of these three signs increased significantly with duration of DM in the Type 1 DM patients. Signs of altered forefoot arch and hammer toes were more common in diabetic patients but callosities were not. Deterioration of forefoot arch, prevalence of hammer toes and callosities as well as signs of dry feet, yellow toe nails and Melin's shin spots increased with age in patients with Type 1 DM compared to patients Type 2 DM and control subjects.

Six patients had a systolic ankle pressure index below 0.9. Three of these (2 men) had longstanding Type 1 diabetes and had undergone below-knee amputation because of gangrene. Two were smokers and the sixth patient was an ex-smoker. One of the male amputees had claudication in his remaining leg. Three other patients (2 men), all of whom were smokers, had claudication; 1 had Type 1 DM and 2 had Type 2 DM. During the study period of one and a half years, all amputees had signs of severe macrovascular disease: 1 suffered a myocardial infarction, 1 suffered a thrombotic stroke, and 2 underwent amputation of their second leg. One of the patients with claudication died from myocardial infarction.

Within the group of Type 1 diabetic patients there were significant differences in thresholds for vibration, perception and pain between patients with and without signs of dry feet, hammer toes and loss of forefoot arch. These differences were not seen within the Type 2 diabetic patients or control subjects.

Concerning foot lesions, with the exception of necrobiosis, found in 9 Type 1 diabetic women and Melin's shin spots more common in men, there were no differences according to gender.

Sensory thresholds for vibration, perception and pain (II)

In the 293 Type 1 diabetic patients as well as in the 77 Type 2 diabetic patients there were significantly elevated mean sensory thresholds compared to control subjects. In Type 1 diabetic patients significant correlation was found between elevated
sensory thresholds and age, duration of DM and height but not for smoking. In Type 2 diabetic patients there was a significant correlation between sensory thresholds and height whereas in control subjects correlations were seen between sensory thresholds and both height and weight. Most sensory thresholds were significantly higher in men compared to women, the differences disappeared, however, after normalizing for height. Furthermore height was inversely correlated to duration of DM and men with Type 1 DM diagnosed prior to the age of 13 were significantly shorter than those whose Type 1 DM was diagnosed after 13 years of age.

**Extensor digitorum brevis test in diabetic neuropathy (III)**

In both Type 1 and Type 2 diabetic patients reduced or absent EDB was found significantly more often than in control subjects. Thresholds for vibration, perception and pain were all higher in patients with reduced or absent EDB, and there was a stepwise increase in sensory thresholds in both Type 1 and Type 2 diabetic patients as well as control subjects with increasing EDB muscle loss, although not statistically significant in Type 2 patients and control subjects.

In the 293 Type 1 diabetic patients, loss of EDB muscle was significantly correlated with clinical signs of dry feet and foot ulcers but not with fallen forefoot arch, hammer toes, fissures or callosities. Further, reduced or absent EDB-muscle correlated to age, shorter stature, duration of DM, smoking, Melin’s shin spots purpura and yellow toenails.

**Preventive treatment of foot deformities in diabetic patients (IV)**

Forty-three per cent of the patients had normal fore-foot arches at the index examination, whereas 31% were found to have normal fore foot arches at the follow up three years later. Patients with normal fore foot arches were younger, had shorter duration of DM and lower sensory thresholds for vibration compared to patients with reduced or absent arches. Compared to controls, however, patients judged to have normal arches at the index examination frequently had clinical signs of neuropathy such as dry feet, pathological EDB-test and significantly increased sensory thresholds for vibration.
Deterioration of the fore foot arches was associated with increased sensory thresholds for perception, pain and vibration. During the observation period there was an improvement of deformities in some patients and it was significantly more pronounced in patients fitted with molded insoles. The mean range of motion (extension) in loaded ankle correlated negatively with diabetes duration, VT and EDB-test. In six out of ten patients (2%) with ROM-extension less than 20° no other cause than DM could be found.

Three patients had been submitted to major amputation during the observation period.

Is osteoporosis a complementary cause in the development of diabetic osteopathy? (V)

The bone mineral density, BMD, of the lumbar spine (L2 - L3, lateral projection) was significantly lower in patients with osteopathy compared to their paired controls. In the proximal femur, however, no differences were found.

According to the EDB test and the Semmes-Weinstein monofilament test, the EDB muscle was significantly reduced as was the cutaneous sensibility in patients with osteopathic skeletal lesions. When defining loss of protective sensibility as a minimum stimulus force of 6.10 log(0.1 mg) in at least 5 out of 8 sites on the sole of the foot there was a significant difference as 6/9 of patients with osteopathy compared to 3/18 control patients had lost protective sensibility.

Plaster casts in the management of advanced ischaemic and neuropathic diabetic foot lesions. (VI)

Out of 33 patients treated with casts, four died before healing, one was withdrawn because of non compliance and 1 had not healed before the end of the study leaving 27 patients for assessment. Of these 27 patients, eight were subsequently referred to amputation, and they significantly distinguished themselves from the healed patients by a lower ankle / arm index, more local pain and their soft tissue lesions (ulcers) more often located to the toes. A discriminant analysis applied revealed that local pain, degree of severity of lesion, low ankle / arm index and site of lesion (toe) respectively were the most evident risk factors for major amputation.

The soft tissue lesions (ulcers) healed in more than half (58%) of the patients.
Casting treatment was well tolerated irrespectively of degree of lesion and did not deteriorate any ulceration. Windowed casts have been criticized for causing increased pressure round the edges of the window, and tend to decrease the total contact necessary for good healing. We found no such problems. One major complication occurred in one patient who developed a deep venous thrombosis that was diagnosed two days after the plaster cast treatment was completed.

A control group was established consisting of 40 consecutive diabetic out-patients with "fresh" foot lesions seen at the chiropody clinic at the department of medicine for the first time. They were judged to be unsuitable for casting treatment mostly because severe cardiovascular disease. These patients were followed parallel with the intervention group. Ten control patients had unhealed their lesions at the end of the study.
General discussion

The epidemiology of foot lesions

It seems from our investigations as if clinically noticeable foot changes appear early in the course of the diabetic disease. No previous studies have, however, reported findings from a standardized population-based foot examination in a large series of diabetic individuals and subsequently there is a lack of historical data. By limiting this study to diabetic patients 15 - 50 years we have reduced the likelihood of finding advanced lesions. On the other hand we have created possibilities to study and report on future events of this well defined group of diabetic patients. A further advantage of a population-based study is that the results can be generalized. This would not have been the case if the study had been performed in a selected group of patients.

The prevalence of ulcers, here only seen in patients with Type 1 DM, was 3% and 10% had a history of ulcers. Previous studies report on a higher prevalence; in Stockholm 4.4%; in UK ranging from 5.3% to 7.4%. The lower prevalence in our group of patients could probably be attributed to the lower mean age of our patients. Our main findings were that foot deformities are common in patients with both Type 1 and Type 2 DM at younger ages. Compared to control subjects there was in the Type 1 diabetic group a significantly elevated prevalence of yellow toenails, Melin’s shin spots and dry feet. These changes are ascribed to DM and were subsequently found to increase with duration of DM but also with age. The Melin’s shin spots were in accordance with previous investigations twice as frequent in men than in women, and they were as well as yellow toenails seen early in the course of the disease although the finding of yellow toenails previously has been related to elderly diabetic patients. It has been reported that it may be possible to diagnose DM in elderly people only by inspection of the lower legs. The finding of these lesions in younger people not known to be diabetic should also arouse the suspicion that they have DM or are at risk for developing DM.

Foot changes of a more structural type as fallen forefoot arch and hammer toes were found to increase with age but not by duration of DM within the group of Type 1 diabetic patients. In Type 2 diabetic patients, however, there were no significant increases with either age or duration of DM. This is probably depending on the fact that they despite high mean age, had a significantly shorter
duration of their DM. The control subjects had more structural lesions than we had expected, maybe indicating that there is normal wear in all feet. The youth of the patients probably explains the small number of patients with frank macroangiopathy \((n=6)\) as we \(^7^5\) and others \(^7^6\) have shown that patients' mean age at presentation with diabetic ulceration is about 68 years. Except for Melin's shin spots there was only one difference according to gender; necrobiosis diabeticorum was only seen in women with Type 1 DM.

**Sensory thresholds**

Significantly increased sensory thresholds indicating neuropathy were seen in Type 1 diabetic patients with dry feet, fallen forefoot arches and hammer toes compared to both Type 2 diabetic patients and control subjects. The lack of any association of altered sensory thresholds to Type 2 diabetic patients together with the weak association of some of the variables in Type 1 diabetic patients, suggests that neuropathy is not the only cause of these changes. Except for a poor but possible correlation between clinical signs and neurophysiological findings there could be extrinsic factors to explain structural changes such as poor footwear and hosiery. Structural changes together with neuropathy, however, increase the risk for ulceration,\(^5^9,^7^7\) and further follow-ups of this group of diabetic patients may help us to better understand the process and explain the importance of the factors involved.

Another "extrinsic" factor of interest for the development of complications in diabetes is smoking. This has been shown previously \(^7^8\) as well as in our study (II) to be significantly associated with clinically defined neuropathy in Type 1 diabetic patients using linear regression. With multiple regression analysis smoking turned out to be of no significant importance in Type 1 diabetic patients compared with age, duration of DM and height. This could be due to differences in definition of smoking, methods of evaluation of neuropathy but also that our patients were younger with probably shorter time of exposition. The observed difference between men and women could be explained as previously described, by the fact that men have a taller stature. This has been ascribed to increased neuron length.\(^7^9\) Gender differences in our study disappeared when sensory thresholds were normalized for height, supporting this suggestion. Thus height rather than gender appears to be the important factor. Our conclusion is that age, duration of DM and tall stature, respectively, appear to be major risk factors for diabetic neuropathy, while smoking only is of minor importance.
Diabetic patients whose DM is diagnosed before puberty have been found to be of shorter stature.80 This was confirmed in our study (II) in male diabetic patients. In female diabetic patients, however, this was not the case which could in part depend on that the chosen age level for puberty was to high. Even after the introduction of insulin therapy, diabetic patients whose DM was diagnosed before the growth-spurt years tend to be shorter, findings similar to our own. This may be the result of poor metabolic control during the growth spurt and decreased anabolic effect due to the lack of insulin.

The EDB muscle test

The patients and clinicians always benefit from diagnostic tools that are easy to use. The EDB muscle is, at least in younger and middle-aged patients well suited for clinical evaluation. Weakness and atrophy of the short toe extensors has been found to be an early motor manifestation in patients with amyloidosis and neuropathy as shown by EMG.81 Nevertheless, it has been said that the EDB test has no value as a clinical indicator for peripheral neuromuscular disease, as it is unspecific and highly variable in the normal population, but no studies have been performed to confirm this. However, one study has compared the EDB test with the results of EMG examination. Unselected patients who were referred for routine measurement of nerve conduction showed a highly significant reduction in conduction velocity in legs when the EDB muscle could not be palpated, while the conduction values in patients with a palpable EDB muscle were close to those observed in normal subjects. Thus it was stated that the lack of palpable EDB muscle is a predictor of peroneal disease.82

In our study (III) it was shown that there was a highly significant relationship between reduction in EDB muscle volume and signs of neuropathy as measured by the sensory thresholds for vibration, perception and pain. While it is easy to differentiate a normal EDB muscle from an absent one, our definition of reduced EDB muscle as barely perceptible could be open to subjective bias. This is not corroborated as the independent results of sensory threshold measurements showed a significant difference between reduced and normal EDB muscle volume. This means, as far as our interpretation concerns, that when screening for motor neuropathy in diabetic patients the clinicians can use the EDB muscle test as performed in our study. One should, however, look for side differences as the diabetic neuropathy is supposed to be of a bilateral and symmetric nature.
In the present study diabetic foot lesions such as dry feet, Melin's shin spots, purpura and yellow toenails were significantly associated with an absent EDB muscle.

We were, however, unable to demonstrate an association between impaired EDB muscle and foot lesions such as fall of forefoot arch or hammer toes. This may be due to the fact that these lesions also may be an effect of other factors, in addition to diabetic neuropathy, such as external pressure from ill fitting shoewear or trauma.

The finding that an impaired EDB muscle correlated to a shorter stature is probably due to that these patients have a longer duration of their DM.

Hence we believe that the finding of a symmetrically reduced or absent EDB muscle on both feet in the diabetic patient can be interpreted as a sign of neuropathy, and this finding may be used as a piece in the complex jigsaw puzzle of establishing the "foot at risk".

**Preventive treatment**

At the three years follow-up (IV) a significant improvement was demonstrated in a group of 67 patients who were supplied with moulded insoles, repeated education and foot examinations. They were selected to be the patients with the most pronounced foot deformities. Almost all patients wished to continue to use their insoles and follow-up examinations. Consequently it seems as if moulded insoles and education combined with follow-ups have the potential of improving foot deformities such as hammer toes and fallen forefoot arches.

High forefoot pressure usually accompanies an abnormal structure of the foot and has been reported to be associated with peripheral neuropathy and accordingly an important risk factor for plantar ulceration in diabetic patients. Furthermore, high degrees of fallen forefoot arches, hammer toes and impaired EDB muscle were significantly associated with increased sensory thresholds for vibration, perception and pain suggesting that neuropathy is an important factor in the ethiology of these lesions. Hence, systematic education of diabetic patients and personnel working with diabetic patients is recommended. Foot examinations and education ought to start early in the course of DM.

It was also noted that the test of ankle mobility showed a significantly reduced range of motion (ROM) in Type 1 diabetic patients compared to control subjects. The differences of ROM,
It was also noted that the test of ankle mobility \(^9\) showed a significantly reduced range of motion (ROM) in Type 1 diabetic patients compared to control subjects. The differences of ROM, however, in almost all individuals values were within the normal range of 20\(^0\). \(^9\) The noted difference could be due to the limited joint mobility (LJM) - syndrome \(^3\) although when evaluating its effects on the diabetic foot one would appreciate to have the means to measure reduction in elasticity of the mid and fore foot. To date, however, we have no applicable method to do this. The empiric impression of its necessity is clear.

**Osteopathy and osteoporosis**

The diabetic osteopathy, often called neuroarthropathy, is an enigmatic condition, that presents with an onset similar to a septic condition with a swollen hot and red foot. It should be regarded as a disease of the skeleton and not of the joints. It usually begins at the metaphyseal or periarticular part of the bones of the diabetic foot.\(^7\)\(^8\) It also has a different location and clinical picture than originally described by Charcot.\(^8\) The term neuroarthropathy (Charcot) is thus a misnomer.

The diagnosis is readily made on x-ray. It is essential to eliminate the diagnosis of infection. In a series of 1001 diabetic patients in Liverpool \(^8\) osteopathy occurred in 0.4%. When screening for radiographic bone and joint abnormalities Cavanagh and co-workers \(^8\) found that 16% of the patients exhibited characteristic osteopathic changes. They also refer to reports where the figure is given as 7 and 37%. In our series, the prevalence was estimated to be 0.2% which is a lower figure than presented in earlier studies. This is probably due to the low mean age of our patient group but also because the initial diagnosis was made strictly on patient history and physical examination.

In a previous report on a consecutive series of 162 diabetic patients with foot ulcerations, 48 (30%) of the patients had osteopathy \(^8\) of which 20 also had osteoporosis. In total, osteoporosis was found in 23 patients. This led us to our basic thought of a generalised skeletal fragility due to osteoporosis as a complementary cause of the osteopathy. It was supported as we found (V) a low BMD in the lumbar spine (L2 - L3) in patients with osteopathy. Suominen and co-workers \(^8\) have shown a close relationship in BMD between the lumbar spine and the os calcis. Young et al.\(^8\) however, did not find any axial osteoporosis but a
reduced BMD in the lower extremities of their 12 diabetic patients. Interestingly, Rawesh and coworkers found an overall reduction within three months of 23% in bone density in the feet of three diabetic patients developing osteopathy. This reduction of BMD is so great that it could not be explained by the mechanical fragmentation of the skeleton which is supposed to occur in the Charcot joints proper. It rather supports the theory of a complex organic cause of the condition including localized skeletal resorption. In our series as well as in the series of Young et al. there was a marked neuropathy of an unspecific nature which is in contrast to Stevens et al. who found support for a selective kind of neuropathy in a group of diabetic patients with what they called neuroarthropathy. Although the diabetic osteopathy is insufficiently defined, there is no empiric support for this theory and it has not been confirmed elsewhere. The background of this condition is still unclear but the findings of osteoporosis and osteolysis should be investigated further.

Plaster cast treatment

It has long been known that mechanical factors play a critical role in the aetiology of neuropathic foot ulceration. These so called trophic or mechanically induced soft tissue lesions have been blamed on insensitivity to pain from repeated traumas because of neuropathy. There are, however, other effects of neuropathy that should be accounted for; the development of A-V shunts and capillary ischaemia implying an inability to regulate or restore capillary blood flow after local ischaemia due to localised pressure. The most frequent localisation of a neuropathic soft tissue lesion is on the sole of the foot. It is usually a fairly "clean" lesion surrounded by yellowish hyperkeratosis. This hyperkeratosis or callus has been shown to act as a foreign body and increase local pressure significantly. The patient history often reveals a long standing ulcer without tendency to heal but causes limited pain and problems. When, however, load is relieved by means of e.g. total contact casting and protection secured, these lesions will heal uneventfully within 2 months.

This is in accordance with our own series of plaster cast treatment (VI) where all patients with plantar lesions (n=10) healed but 50% of the patients with what was classified as dysvascular lesions of the toes did not heal and subsequently referred to lower leg amputation.

It has been argued that complete plaster casts should be used only in the treatment of ulcers of Wagner's grade 1 and 2. This would
The beneficial effects of the total contact plaster cast seem to be connected with immobilisation, reduction and distribution of walking pressure, prevention from trauma or chafe and reduction of oedema. Although we have not shown that plaster cast treatment shortens the healing time, we think that it probably does, at least for plantar ulcers. Furthermore, it offers full weight bearing and the opportunity of treatment on an out-patient basis. One should, however, look carefully for signs that can be used as predictors for an unsuccessful outcome and according to the present study (VI), above all ischaemic pain, a sign of imminent amputation, and follow the treatment accordingly. There were few complications of plaster cast treatment in our study despite the advanced age of our patients and the severity of their lesions and subsequently this treatment can be used in patients even with severe soft tissue lesions.
General summary

The present study permits the following observations and conclusions:

Foot lesions are common in young and middle-aged patients with both Type 1 and Type 2 DM. In patients with Type 1 DM, structural changes such as fallen forefoot arches and hammer toes increase with age only while skin changes increase with age as well as with duration of DM. In Type 2 diabetic patients there is no significant increase of foot lesions with age or duration of DM. Control subjects had more foot lesions than anticipated. It seems as if, besides the effects of DM, there is "normal" wear in all feet.

There is a significant association between elevated sensory thresholds and long duration of DM, age and height but not with smoking in patients with Type 1 DM. In patients with Type 2 DM sensory thresholds are associated only with height. The observed difference between men and women, with significantly higher thresholds for men, was eliminated when normalized for height. Thus age, duration of DM and tall stature appear to be major risk factors for neuropathy in diabetic patients. The EDB muscle test is easy to perform and may be used to screen for diabetic motor neuropathy, as it is significantly correlated to elevated sensory thresholds and foot lesions which are significantly related to DM.

Significant improvement of forefoot deformities was demonstrated at a three years follow-up in patients fitted with custom made insoles in combination with education although these patients were older and had longer duration of DM. Plantar ulcers did not occur in patients with moulded insoles. Forefoot deformities are common and appear early in the course of DM. Moulded insoles seem to be an effective mode of treatment, early treatment is advocated. Education and moulded insoles can be used as an armamentum to prevent worsening of forefoot deformities in young and middle-aged patients with DM.

Generalized osteoporosis may be an additional risk factor for diabetic osteopathy. Patients with osteopathy, had a significant
Total contact plaster cast can be used as an efficient method for treatment of soft tissue lesions in the diabetic foot irrespective of location and was demonstrated to be applicable also in patients with lesions of Wagner grade 3 and 4.
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