CHAPTER 1

REVIEW OF LITERATURE
1.1 Diabetes Mellitus

Type 1 diabetes mellitus (T1DM), formerly known as insulin dependent diabetes mellitus commonly occurs in children or young adults. In Australia 40,000 people have T1DM, 7,000 of whom are under the age of 25 years (Diabetes Australia, 1996). The latest epidemiological research indicates that the incidence of T1DM, in children up to 14 years old increased at an average rate of 3.2% annually between 1990 and 1996 in New South Wales, Australia (Craig et al, 2000). A Swiss study also found that the incidence of T1DM in children under the age of 5 years increased significantly between 1991 and 1999 (Schoenle et al, 2001).

People with T1DM suffer from an absolute lack of insulin, such that insulin therapy is essential to maintain life (Palmer and Lenmark, 1990; Carter, 1992). Insulin was discovered by Banting and Best in 1921 and was a landmark breakthrough in the treatment of T1DM. Its introduction meant that ineffective treatments such as thyroid extract could be abandoned but patients involved in the first trials of insulin had conservative and inflexible treatment regimes imposed upon them. They were expected to spend months hospitalised while meticulous monitoring of calorie intake and glucose excretion was carried out, then plan their lives around dietary and insulin injection rules (Tattersall, 1995). It was not until 1923 that Dr. Robin Lawrence found that adapting the treatment to the patient was the most effective way to control diabetes (Tattersall, 1995).

Since these early days many advances have been made in treatment, care and monitoring of people with diabetes in an effort to achieve normoglycaemia and to minimize the complications of the disease. The development of short and long acting insulins, home glucose monitoring equipment, urinalysis, retinal photography, retinal laser therapy are just some of the advances made.
Although these developments in treatment and care of people with diabetes have improved their lifestyle, many researchers continue to concentrate their efforts on investigating aetiological factors and methods of identifying individuals at risk of developing T1DM. Some have found that the onset of T1DM has been associated with viral infections while others have investigated genetic or immunological factors (Yoon et al, 1979; Dobersen et al, 1980; Craighead, 1981; Albin and Rifkin, 1982). In the early 1990’s, a radioimmunoassay was developed which measures anti-GAD, glutamic acid decarboxylase antibodies (Rowley et al, 1992). These antibodies have been found in approximately 80% of newly diagnosed T1DM cases (Atkinson and Maclaren, 1994). Such investigations may provide a means of identifying individuals at risk and allow intervention when appropriate (Diabetes Australia, 1996).

Type 2, or non-insulin dependent, diabetes mellitus (T2DM) is far more common than type 1. In 1985 Glatthaar et al found that approximately 160,000 Australian adults had NIDDM but in 2001 the number of people affected was estimated at one million (Diabetes Australia). The reason for this massive increase is unknown, but may be due to increased longevity, obesity and inactivity of the general population (Diabetes Australia, 1996).

Type 2 DM is due to a dysfunction in insulin production or insulin resistance (Reaven, 1988; Bodansky, 1989). Heredity and lifestyle factors including obesity, low activity levels and stress has been found to have a profound influence on disease onset (Diabetes Australia, 1996). Treatment consists of diet control and if necessary the use of oral hypoglycaemic agents. In some instances insulin may also be needed to achieve normoglycaemia.

For both T1DM and T2DM, improvements in treatment regimens have led to greater longevity, which increases the likelihood of individuals developing long-term
complications. Early detection of diabetes complications and intervention are therefore becoming more important.

The most serious complications of diabetes are: visual impairment and blindness resulting from retinopathy or cataracts, renal failure resulting from persistent microalbuminuria and hypertension, and gangrene and lower limb amputations in association with diabetic neuropathy and/or ischaemia.

This study will concentrate on the evaluation of structural and functional changes in the lower limb of young people with T1DM. Relationships between retinopathy, nephropathy, neuropathy and lower limb complications will be examined. These tests are routinely undertaken in the screening clinic but, because of the youth of the subjects and therefore the unlikely event of finding clinically significant vascular disease, ischaemic changes in the lower limb were not examined and will generally not be discussed.

1.2 Complications of diabetes affecting the lower limb

The DCCT (1993) demonstrated beyond doubt that systemic complications of T1DM could be greatly reduced by adhering to intensification of therapy, which included a rigid regime of either external insulin pump therapy or, three or more insulin injections a day, guided by frequent blood-glucose monitoring. Microvascular complications of diabetes were reduced by 35% to 70% and macrovascular disease by 41% using intensive therapy. However nine years following the publication of this study systemic complications of T1DM are still a major concern for individuals with diabetes, and those who treat people with diabetes.

Possibly the most serious of the lower limb complications of T1DM is diabetic neuropathy. When associated with structural and functional changes caused
by diabetes, the resultant lower limb complications of the disease can be catastrophic to the sufferer. Many structural and functional abnormalities known to predispose adults with diabetes to foot problems have been investigated. A summary of these abnormalities and their presence in young people with T1DM is shown in table 1.1.

1.2.1 Diabetic Neuropathy

The term neuropathy is derived from the Greek neuron meaning a nerve and -patheia meaning suffering or disease. John Rollo first noted involvement of the nervous system in DM in 1798, by describing the presence of pain and paraesthesia. For many years the high incidence of neurological abnormalities in patients with DM led to the belief that DM resulted from lesions of the nervous system. It was not until 1864 that Marchal de Calvi postulated that the reverse may be true, that diabetes may be the cause and not the result of the changes found in the nervous system (Martin, 1953).

Extensive investigations into the effects of diabetic neuropathy followed. Mononeuropathy of the cranial nerves was first described by Althaus in 1866, loss of deep tendon reflexes by Bouchard in 1884, acute painful neuropathy by Althaus in 1885 and autonomic neuropathy by Rundles in 1945 (Martin, 1953; Clements and Bell, 1982). Indeed, this phenomenon attracts much interest today.

It is now apparent that nerve changes can occur very quickly following the onset of T1DM. Reduced nerve conduction velocity can be detected in most diabetic patients (Clements and Bell, 1982; Zimmerman, 1987; Boulton, 1991; Hyllienmark et al, 1995). However only about one third to one half of all diabetic patients will develop clinically significant signs of neuropathy (Pirame, 1978; Cefalu, 1990).
Table 1.1

Documented risk factors for the development of foot problems in adults and adolescents with DM

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Author, year</th>
<th>n</th>
<th>Age (years)</th>
<th>Duration (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LJM Subtalar joint</td>
<td>Delbridge et al, 1988</td>
<td>62</td>
<td>59 ± 3.2</td>
<td>9.9 ± 1.6</td>
</tr>
<tr>
<td></td>
<td>Meuller et al, 1989</td>
<td>46</td>
<td>60 ± 11.3</td>
<td>16 ± 8</td>
</tr>
<tr>
<td>Adolescent study</td>
<td>Duffin et al, 1999</td>
<td>302</td>
<td>14.6 (11-20)</td>
<td>6.2 [4-10]</td>
</tr>
<tr>
<td>LJM 1st MTP joint</td>
<td>Delbridge et al, 1988</td>
<td>62</td>
<td>59 ± 3.2</td>
<td>9.9 ± 1.6</td>
</tr>
<tr>
<td></td>
<td>Bevan &amp; Bowker, 1999</td>
<td>42</td>
<td>62 (29-85)</td>
<td>13.3 ± 12.3</td>
</tr>
<tr>
<td>Adolescent study</td>
<td>Duffin et al, 1999</td>
<td>302</td>
<td>14.6 (11-20)</td>
<td>6.2 [4-10]</td>
</tr>
<tr>
<td>LJM Ankle joint</td>
<td>Simmons et al, 1997</td>
<td>48</td>
<td>57 ± 10.6</td>
<td>15 ± 9.6</td>
</tr>
<tr>
<td></td>
<td>Meuller et al, 1989</td>
<td>46</td>
<td>60 ± 11.3</td>
<td>16 ± 8</td>
</tr>
<tr>
<td>Adolescent study</td>
<td>Rosenbloom et al, 1981</td>
<td>309</td>
<td>Range 1-28</td>
<td>Not stated</td>
</tr>
<tr>
<td>Digital contraction</td>
<td>Edmonds et al, 1986</td>
<td>239</td>
<td>64.1 (21-92)</td>
<td>15.7 ± 12.6</td>
</tr>
<tr>
<td>Adolescent study</td>
<td>Duffin et al, 1999</td>
<td>302</td>
<td>14.6 (11-20)</td>
<td>6.2 [4-10]</td>
</tr>
<tr>
<td>Plantar callus</td>
<td>Bevan &amp; Bowker, 1999</td>
<td>42</td>
<td>62 (29-85)</td>
<td>13.3 ± 12.3</td>
</tr>
<tr>
<td></td>
<td>Young et al, 1992</td>
<td>17</td>
<td>58 (39-88)</td>
<td>17.9 (2-30)</td>
</tr>
<tr>
<td>Not previously assessed in adolescents with diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High plantar pressure</td>
<td>Veves et al, 1992</td>
<td>86</td>
<td>53 (17-77)</td>
<td>17.1 (1-36)</td>
</tr>
<tr>
<td></td>
<td>Boulton et al, 1987</td>
<td>44</td>
<td>52 (24-69)</td>
<td>Not stated</td>
</tr>
<tr>
<td>Not previously assessed in adolescents with diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High pressure time integrals</td>
<td>Birke et al, 1995</td>
<td>58</td>
<td>55.7 ± 12.7</td>
<td>17.3 ± 11.8</td>
</tr>
<tr>
<td>Not previously assessed in adolescents with diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plantar soft tissue changes</td>
<td>Delbridge et al, 1985</td>
<td>30</td>
<td>57.8 ± 18.1</td>
<td>Not stated</td>
</tr>
<tr>
<td></td>
<td>Abouaesa et al, 2001</td>
<td>157</td>
<td>61.2 ± 10.2</td>
<td>16.4 ± 10.3</td>
</tr>
<tr>
<td>Not previously assessed in adolescents with diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plantar aponeurosis changes</td>
<td>Suggested, not assessed</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Kidd and Kidd, 1993</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Not previously assessed in adolescents with diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory nerve changes</td>
<td>Veves, 1994</td>
<td>469</td>
<td>54 (17-85)</td>
<td>12.4 (0-60)</td>
</tr>
<tr>
<td></td>
<td>Boulton et al, 1987</td>
<td>44</td>
<td>52 (24-69)</td>
<td>Not stated</td>
</tr>
<tr>
<td>Adolescent study</td>
<td>Donaghue et al, 1996</td>
<td>102</td>
<td>14.5 (10-18)</td>
<td>6.8 (1.3-15)</td>
</tr>
</tbody>
</table>

Data is shown as mean ± SD or (range)., median [interquartile range], N/A not assessed. Unshaded = investigations in adults, Shaded = investigations in adolescents.
Controversy has surrounded both metabolic and vascular theories on the mechanism by which nerve damage occurs in diabetic patients. One metabolic theory of the pathogenesis of diabetic neuropathy links hyperglycaemia to nerve damage and implicates the depletion of nerve myo-inositol (Greene et al, 1990). Chronic hyperglycaemia results in increased activity in the Sorbitol (Polyol) pathway (see figure 1.1) which reduces the levels of nicotinamide-adenine dinucleotide phosphate (NADPH), glutathione and myo-inositol (Brownlee et al, 1984; Brownlee et al, 1986). The decreased levels of myo-inositol are thought to affect intracellular signaling, reducing nerve conduction velocity and eventually causing irreversible axonal damage (Cavanagh et al, 1993).

Figure 1.1
The Sorbitol (polyol) Pathway
(Adapted from Boulton, 1991)

\[ \text{Glucose} + \text{NADPH} + \text{H}^+ \xrightarrow{\text{Aldose Reductase}} \text{Sorbitol} + \text{NADP} \]

\[ \text{Sorbitol} + \text{NAD} \xrightarrow{\text{Dehydrogenase}} \text{D- Fructose} + \text{NADH} + \text{H}^+ \]

Another metabolic process implicated is glycation of protein (Brownlee et al, 1984; Brownlee et al, 1988). This process involves the attachment of glucose to various proteins in nerves resulting in altered function. The contribution of this process to the eventual development of diabetic neuropathy is still unclear, but the
mechanism involved in the glycation of haemoglobin and collagen in other complications of DM has been investigated in some detail and will be elucidated in 1.2.3 (nonenzymatic glycation).

The vascular theory of the pathogenesis of diabetic neuropathy suggests that alteration in the microcirculation of the nerves causes ischaemia and nerve damage. Supporting this theory, Williams et al (1980) demonstrated that subjects with diabetes have abnormalities in the circulation of the epineurium, a dense connective tissue sheath surrounding the nerve trunk (Gray, 1984). They also found that they had increased vascular resistance of the connective tissue which penetrates between individual nerve fibres, the endoneurium (Gray, 1984), resulting in endoneurial hypoxia in these same subjects. Both the epineurium and endoneurium serve as access planes for the peripheral nerve vasculature (Gray, 1984) and the anomalies demonstrated by Williams and colleagues have been cited as important considerations in the pathogenesis of diabetic neuropathy (Boulton, 1991).

In the past, exponents of the metabolic and vascular theories of the pathogenesis of diabetic neuropathy have followed separate paths, but there is now some convergence. It appears that the aetiology of diabetic neuropathy has both a metabolic and a vascular component which eventually leads to axon loss (Boulton, 1991; Cavanagh et al, 1993) and segmental demyelination (Brown and Asbury, 1984). Axonal loss, measured by decreased fibre density, has been a major finding of several studies of subjects with diabetic neuropathy but abnormalities in Schwann cells, epineurial cells and endoneurial vasculature have also been described (Brown and Asbury, 1984; Dyck, 1987; Greene et al, 1990).

Diabetic neuropathy can be divided broadly into two groups, mononeuropathies and the more common polyneuropathies. Sensorimotor
neuropathy is a distal symmetrical peripheral polyneuropathy, which occurs first in the toes and then progresses proximally (Cavanagh, 1993; Boulton, 1996). Clinically the subject presents with reduced or absent thermal and vibration sensation and diminution of pinprick sensation (Heimans et al, 1987; Zimmerman, 1987; Young et al, 1994; Boulton, 1996). There may also be a loss of proprioception and absence of ankle reflexes, which are features of large fibre sensory neuropathy (Clements and Bell, 1982; Low, 1987; Tesfaye et al, 1996). The onset is insidious and usually occurs 10-15 years after the development of diabetes (Pirart, 1978). Numbness and paraesthesia are often the first symptoms of sensory neuropathy but symptoms may intensify resulting in pain in the lower limbs, particularly at night. Some subjects develop a ‘painful-painless’ foot, which manifests as painful symptoms combined with reduced or absent sensation (Boulton, 1996).

Motor neuropathy almost invariably accompanies sensory loss (Clements and Bell, 1982) and causes atrophy and wasting of distal muscles (Low, 1987; Cavanagh et al, 1993; Boulton, 1996). The intrinsic muscles in the feet may be affected resulting in an imbalance of the flexors and extensors of the toes causing clawing of the digits and prominence of the metatarsal heads (Clements and Bell, 1982; Boulton, 1996). In some cases muscular weakness may also affect the anterior leg and thigh musculature (Banks, 1989) leading to a loss of strength in the flexors of the foot and subsequent footdrop (Clements and Bell, 1982).

Other clinical features of motor neuropathy have been investigated by Cavanagh et al (1993) who provided the first quantitative evidence that control of gait and posture is a clinically significant problem in the neuropathic diabetic patient. Although not fully understood, somatosensory function deficit associated with distal peripheral neuropathy, may be an extremely important feature of diabetic neuropathy
and be related to the increased injury rate described by Cavanagh’s group. Mechanoreceptors located in joint capsules, ligaments, tendons, muscles and skin relay information to the somatosensory system to help provide postural and gait control in a variety of situations (Cavanagh et al, 1993). Somatosensory function deficit may interfere with the afferent information from these receptors regarding body segment orientation, resulting in increased sway, poor postural control and the occurrence of falls in the diabetic population.

Autonomic neuropathy may also be present in the lower limbs. It may affect the sympathetic nerve fibres to pedal sweat glands, causing reduced sweating, leaving skin dry and prone to cracking and fissuring (Clements and Bell, 1982; Boulton, 1996). The skin under the foot affected by autonomic neuropathy is far more likely to develop callus and open fissures, both of which may lead to ulceration in the insensate foot.

Another serious manifestation of autonomic neuropathy is the de-nervation of the sympathetic vasculature leading to sympathetic neuropathy. Changes in sympathetic nerve function may lead to arteriovenous (AV) shunting and subsequent bone resorption (Stevens et al, 1992). AV shunting results in increased blood flow and a warm insensitive foot, while bone resorption weakens the bony structures of the foot. For diabetic subjects with this form of neuropathy, even minor trauma poses the risk of bone disorganisation leading to severe foot deformities, such as Charcot’s arthropathy (Stevens et al, 1992).
1.2.2 Limited Joint Mobility (LJM)

The strong link between diabetic neuropathy and plantar ulceration has been well documented, yet not all individuals with neuropathy develop ulcerations. This quandary has resulted in more in-depth investigations into the aetiology of plantar ulcers. Many investigators now believe that joint limitation in the feet increases plantar pressure, which in turn leads to tissue breakdown and ulceration (Delbridge et al, 1988; Mueller et al, 1989; Cavanagh et al, 1991; Fernando et al, 1991; Cavanagh and Ulbrect, 1994).

Masson (1992), in his study of plantar pressures, found that high plantar pressures in subjects with neuropathy were relatively uncommon when joint mobility was within normal range. He also found that subjects with LJM had the highest mean forefoot pressures and the most forefoot ulcerations. This confirmed the findings of Cavanagh et al (1991) and Fernando et al (1991) which established the primary determinant of high plantar pressures to be LJM and neuropathy was a secondary phenomenon. Cavanagh and Ulbrect (1994) again measured the plantar pressures of diabetic subjects and concluded that joint limitations in the foot altered the mechanics of gait and contributed to high plantar pressures and ulceration. However the significance of LJM, as a serious complication in itself has not been investigated in young people with diabetes.

LJM in adults with diabetes was first documented by Lundbaek (1957) who described stiff hands in patients with TIDM as a type of “vascular disease of the hands”. Patients with this condition displayed thick, tight, waxy skin and because it was initially only noted in the hands it was referred to as cheiroarthropathy, from the Greek cheir meaning hand, arthron meaning a joint and -patheia meaning suffering or disease.
Grgic et al (1976) were the first to note this phenomena in children with diabetes. Since Lundbeck and Grgic’s early description of cheiroarthropathy, this same joint limitation has been noted in many other areas of the body, including the lower limb, and the name of the condition changed to the more appropriate, ‘limited joint mobility’. Rosenbloom et al (1981) quantified the degree of joint involvement using a number of tests to evaluate range of motion of various joints.

Following these early observations the relationship between DM and LJM has been evaluated extensively in medical literature (Campbell et al, 1984; Buckingham et al, 1984; Beacon et al, 1985; Mueller et al, 1989; Clarke et al, 1990; Young et al, 1993; Spencer, 1994). Its prevalence in young people with T1DM has been reported to range from 7% to 42% (Clarke et al, 1990; Pickup and Williams, 1991). Studied primarily for its role as an indicator of microvascular changes in T1DM, its importance as a potentially damaging complication in itself has been ignored.

LJM in children with DM involves thickening of the skin and periarticular connective tissue (Rosenbloom et al, 1981; Rosenbloom et al, 1983; Rosenbloom, 1984; Shinabarger, 1987). Radiographic examination of a child with LJM shows no osseous changes (Rosenbloom, 1984); in fact the joint limitation occurs due to changes in soft tissue, not bone (Shinabarger, 1987). The skin of some young people affected by LJM has been described as feeling thick, tight and waxy, and flexion contractures of the fingers may be present (Grgic et al, 1976; Rosenbloom et al, 1981). The significance of these skin changes in the upper-body has remained elusive. In more severe cases of LJM growth retardation, delayed sexual maturation and microvascular complications have been documented (Rosenbloom et al, 1981; Tubiana-Rufi et al, 1991; Brik et al, 1991).
The consequences of LJM, particularly in the feet of people with DM make it important to identify as early as possible. Close monitoring of foot function, intervention when necessary (see 1.3.4), and improved glycaemic control (see 1.2.3) may prevent serious foot pathology occurring, but care must be taken to avoid confusion with other conditions, which mimic its symptomology. To assist with the differential diagnoses of LJM, Rosenbloom et al (1984) described various other pathologies which effect the hands in a similar manner to LJM and the candidate (1996) described those effecting the lower limbs (see table 1.2).
**Table 1.2**

Differential diagnosis of LJM in young people with DM
(Adapted from Duffin *et al*, 1996 after Rosenbloom *et al*, 1984)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Usual Joints involved</th>
<th>Pain</th>
<th>Muscle</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dupuytren contracture</td>
<td>3rd &amp; 4th MCP, PIP</td>
<td>No</td>
<td>Normal</td>
<td>Thickened palmar fascia, never found in the young.</td>
</tr>
<tr>
<td>Flexor tenosynovitis</td>
<td>1st, 3rd, 4th MCP, PIP</td>
<td>Yes</td>
<td>Normal</td>
<td>About 1/3rd associated with diabetes-typically asymmetric</td>
</tr>
<tr>
<td>Carpal tunnel</td>
<td>All fingers equally</td>
<td>Yes</td>
<td>Palmar Atrophy</td>
<td>Paraesthesia- decreased nerve conduction velocity.</td>
</tr>
<tr>
<td>Reflex sympathetic dystrophy</td>
<td>May affect any area</td>
<td>Severe</td>
<td>Atrophy</td>
<td>Demineralisation on x-ray-severe pain when using the hands</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>May affect any area</td>
<td>May be severe</td>
<td>Normal</td>
<td>Typical radiographic changes</td>
</tr>
<tr>
<td>Tarsal coalition</td>
<td>ST, Midtarsal</td>
<td>In some cases</td>
<td>Normal</td>
<td>Osseous / cartilaginous may require MRI for diagnosis</td>
</tr>
<tr>
<td>Ankle equinus</td>
<td>Ankle</td>
<td>In some cases</td>
<td>May be calf tightness</td>
<td>Radiographic evaluation for osseous, muscle testing for gastroc/soleus forms.</td>
</tr>
<tr>
<td>Hallux limitus</td>
<td>1st MTP</td>
<td>In some cases</td>
<td>Normal</td>
<td>Usually in older subjects - radiographic evaluation</td>
</tr>
<tr>
<td>Limited joint mobility</td>
<td>PIP, MCP, ST Ankle, Wrist, MTP, Elbow</td>
<td>No</td>
<td>Normal</td>
<td>Pain, neurological findings or other disability only if associated other conditions</td>
</tr>
</tbody>
</table>

PIP - proximal interphalangeal joints. MCP - metacarpophalangeal joints. MTP - metatarsophalangeal joints. ST - subtalar joint.
1.2.3 Non-enzymatic glycation / pathogenesis

A great deal of research has been directed towards determining the pathogenesis of complications of diabetes (see 1.2.1) but as yet no conclusive evidence has been documented (Brownlee et al, 1984; Lyons and Kennedy, 1985; Vlassara et al, 1986; Larkin et al, 1988). A widely held view is that there is an abnormal chemical interaction between glucose and protein leading to their attachment to one another without the aid of enzymes, a process referred to as non-enzymatic glycation (Vlassara et al, 1986). Comprehensive reviews of this process implicate its role in diabetic complications in the retinal capillaries, renal tissues, cardiovascular system, nervous system and soft tissues of the body (Paul and Bailey, 1996; King and Brownlee, 1996). In soft tissues such as skin, tendons, ligaments and joint capsules, it appears to result in thickening and reduced flexibility of tissues leading to limited joint mobility (see 1.2.2).

There are two distinct types of nonenzymatic glycation products. The first occurs with proteins that have a short half-life (days to weeks), such as serum albumin and apoproteins. These react with glucose to form Schiff base and, within a few weeks a chemical rearrangement occurs forming the Amadori product (figure 1.2).

**Figure 1.2**

Proteins with a half-life of days to weeks
(Adapted from Vlassara et al, 1986)

<table>
<thead>
<tr>
<th>K1</th>
<th>K2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose + NH2 protein</td>
<td>&gt; Schiff base</td>
</tr>
</tbody>
</table>

K1 – first reaction, K2 – chemical rearrangement
Arrows show the direction of the reactions
Tissue samples from subjects with diabetes have been found to have two to three times the concentration of Amadori products of non-diabetic tissue. At this level nonenzymatic glycation is reversible.

The second reaction occurs in proteins which turn over at a much slower rate (weeks to years), such as those found in collagen, elastin and myelin. In this process an advanced glycated endproduct (AGE) is derived slowly from the Amadori products (figure 1.3).

**Figure 1.3**

Long-lived structural proteins
(Adapted from Vlassara *et al*, 1986)

```
<table>
<thead>
<tr>
<th>Glucose + NH2 protein</th>
<th>K1</th>
<th>K2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; Schiff base</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; Amadori Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
```

**K1** – first reaction, **K2** – chemical rearrangement
Arrows show the direction of the reactions

These end-products will continue to accumulate for the life of the protein causing cross-linking between protein molecules and their derivatives (Banks and McGlamry, 1989; Vlassara *et al*, 1986). Cross-linking can progress despite return to normoglycaemia because these glycated proteins have the ability to trap and cross-link soluble proteins, even when glucose is not available (Vlassara, 1986). At this level of glycation the process is irreversible. As this eventually leads to significant alterations of structure and function of the affected tissue (Delbridge *et al*, 1985; Reeve *et al*, 1985) early detection and remediation before cross-linking occurs is important.
Vlassara considered that the duration of hyperglycaemia was critical to the progression of nonenzymatic glycation. Therefore young people with T1DM must be considered to be at greatest risk of developing complication from this process, as they are likely to have the longest duration of diabetes. The early diagnosis of complications such as LJM and retinal damage, resulting from nonenzymatic glycation in young people with T1DM, gives the opportunity to improve glycaemic control and possibly halt this process.

1.2.3.1 Differential diagnosis of nonenzymatic glycation

Skin and soft tissues changes resulting from nonenzymatic glycation may mimic other pathologies. For instance scleredema diabeticorum, like nonenzymatic glycation causes alteration of the dermal collagen. It results in thickening of the dermis to the extent that dermal tissue replaces sub-cutaneous fat (Goodfield and Millard, 1988). However unlike nonenzymatic glycation, sclerederma diabeticorum is confined to the face, neck and shoulders and may be related to a systemic streptococcal infection (Cantwell and Kelso, 1980). Scleredema diabeticorum is also extremely rare and unlikely to occur in children.

Progressive systemic sclerosis or Scleroderma, although showing similar skin changes to nonenzymatic glycation (Brik et al, 1991), has several features which make its differential diagnosis in children relatively simple. The associated systemic manifestations of Scleroderma such as Raynaud’s phenomenon, calcinosis and visceral sclerosis are not caused by nonenzymatic glycation.

Other pathologies, which affect the thickness of the skin such as “stiff-hand syndrome” and Dupuytren’s Contracture, are confined to the hands and are rarely seen in children. In fact any skin condition which is painful, paraesthetic or results in
swelling or muscular atrophy can be discounted as being the result of nonenzymatic glycation as these symptoms have never been reported in the literature.

A theory put forward by Kidd and Kidd, in 1993 suggests the plantar aponeurosis may also be affected by nonenzymatic glycation. Therefore pathologies of the plantar aponeurosis such as plantar fasciitis and plantar fibromatosis may also be confused with nonenzymatic glycation. Plantar fasciitis results in thickening of the plantar aponeurosis (Cardinal et al, 1996; Wall et al, 1993). However plantar fasciitis is often painful and results from repeated mechanical microtrauma (DeMaio et al, 1993). In plantar fasciitis, pain can be elicited by palpation of the insertion of the fascia into the medial calcaneal tubercle (Bordelon, 1983); nonenzymatic glycation is not painful.

Plantar fibromatosis also involves thickening of the plantar fascia and is obvious in the central area of this structure. This condition takes the form of nodules rather than general thickening of the fascia. Nodules are not a feature of tissue affected by nonenzymatic glycation.

1.3 Force and pressure

Recent technological advances have meant that conclusions drawn from subjective and observational information regarding the formation of foot ulcers in people with diabetes can now be quantified.

High plantar pressure, although anecdotally implicated in the development of neuropathic ulceration, has now been scientifically investigated in some detail (Veves et al, 1992; Young et al, 1992; Caputo et al, 1994; Katoulis et al, 1996; Stess et al, 1997). High pressure / time integrals have also been implicated in the development of skin ulceration (Fuller, 1996). In the insensate foot, excessive
external pressures for long periods result in the breakdown of the epithelium and eventually cause ulceration (Kosiak, 1959; Bauman et al., 1963).

Although neuropathy is an essential part, high plantar pressures are now known to be a major determinant for the development of neuropathic ulcers in adults with diabetes (Cavanagh and Ulbrect, 1994; Veves et al., 1992; Masson, 1992; Cavanagh et al., 1991; Fernando et al., 1991). Indeed, in a prospective study on the incidence of foot ulceration in diabetic patients with high plantar pressures, Veves et al. (1992) confirmed that elevated plantar pressures are strongly predictive of subsequent ulceration especially in the presence of neuropathy. Furthermore, no patient with normal foot pressures developed a plantar ulcer.

Having confirmed the importance of high plantar pressures, the question of their aetiology has also recently been addressed, with LJM of the ST and MTP joints being implicated (Boulton, 1990; Fernando et al., 1991; Cavanagh et al., 1991; Masson, 1992; Veves et al., 1992; Cavanagh and Ulbrect, 1994).

An array of terms is used to describe plantar pressures including force, stress and shear; hence considerable confusion exists over the use of this terminology. In an attempt to eliminate this confusion, Cavanagh et al. (1992) has suggested that when discussing plantar pressure, the term force be confined to describing net force measured by a force platform and that the term stress be analogous with pressure. Although this definition simplifies the usage of the terms force and pressure it really does not explain the differences.

Force represents the action of one body on another and possesses quantity, magnitude and direction (Beer and Johnston, 1988). According to Newton's 2nd law, force is equal to mass times acceleration; \( F = MA \). Thus, when evaluating force acting beneath the foot during gait, if the weight and cadence of a subject remain
constant, force will be a constant. The word pressure comes from the Latin *pressura*, meaning a force steadily exerted upon or against a body by another in contact with it. Pressure is equal to force divided by area; \( P = \frac{F}{A} \). Any alterations in pressure are the consequence of a redistribution of force, or a change in the area over which that force is being distributed, again provided that weight and cadence are constant. Therefore if force is distributed over a large area, pressure will be lower than if the same force is distributed over a small area.

To define the term ‘shear’ we must look more closely at direction. Whereas ‘pressure’ or ‘stress’ act perpendicular to the supporting surface, shear is a strain caused by pressure upon a body in which the layers of its substance move in approximately parallel planes (Cavanagh *et al*, 1992). Shear stress has been strongly suspected of contributing to the development of plantar ulcers in the diabetic foot (Lord, 1981; Delbridge *et al*, 1985; Brand, 1988). However little progress has been made in measuring this type of pressure since Tappin *et al* constructed an in-shoe shear stress transducer in 1980 (Cavanagh *et al*, 1992). Cobb and Claremont (1995) describe recent developments in shear stress transducer, and at an international conference in Brisbane in 1998, Novel introduced the prototype of a shear-sensing mat, which they hoped would be available commercially by 2003. The introduction of such equipment will undoubtedly further increase our understanding of the intricacies of human locomotion and the development of plantar ulcers in people with diabetes.

For over a century various investigators have devised methods of measuring the distribution of pressure beneath the foot. Carlet (1872) and Marey (1873) used specially designed shoes with air sacks in the soles, in an attempt to measure dynamic foot pressures (Alexander *et al*, 1990). Beely in 1882 tried to assess plantar
pressure by standing subjects in a sack filled with Plaster of Paris (Lord, 1981). Subsequently an impressive array of methods of gathering information about plantar pressures has been devised. Devices such as the Harris and Beath footprinting mat (Harris, 1947), Pedobarograph (Chodera, 1960) and modified Pedobaragraph (Grieve and Rashdi, 1984) produce a printed image or indentation on aluminium foil. These impressions provide an indication of both the pressure exerted in various areas beneath the foot and differential pressure between these areas. These relatively simple devices have been demonstrated to be effective in both clinical and research environments (Hughes et al, 1987), but the analysis of the data gathered is both laborious and time consuming.

Recently the advent of computer technology has allowed the development of sophisticated devices such as walkway force and pressure plates. The most widely used force plates are the Kistler (Kistler Instruments Ltd., Whiteoaks, The Grove, Hartley Wintney, Hants, UK.) and Musgrave (Preston Communications Ltd, Castle St, Llangollen, North Wales). More recently, the Emed (Novel gmbh, Beichstrasse 8, 8000 Munchen 40, Germany) pressure plates system has also been extensively used.

1.3.1 Force plates

The Kistler force plate uses piczoelectric crystals, which generate an electric charge when deformed. The charge between the faces of a crystal is proportional to a specific compressive force and can be measured using a suitable amplifier (Lord, 1981). This device has been evaluated by several authors and has been found to be highly accurate (Lord, 1981; Bobbert and Schamhardt, 1990). Bobbert and Schamhardt found that the maximum variation between measured total force and actual total force was 1.6%. However a major drawback with this instrument is the
need for it to be permanently fitted into a walkway, on a concrete support. Making its use in research confined to purpose built research facilities.

1.3.2 Pressure plates

The Musgrave system uses force sensitive resistive film to produce information about the vertical pressures being applied to its surface over a period of time (Barnett, 1996). The force sensing resistors are arranged in a matrix formation (Schaff, 1993) within a thin plastic film. The sensors use semi-conductive carbon ink applied between two layers of mylar (plastic) which are covered with conductive silver based ink. When pressure is applied to the sensors the contact area between the carbon and silver layers is increased and resistance is decreased (Mortlock, 1990 cited in Barnett, 1996). The output from the sensors is then relayed to a computer, which manipulates the data providing visual and numeric evaluation of various aspects of pressure analysis. The system can be used in a single or double plate set up and should also be set into a walkway. The accuracy and repeatability of this device has also been found to be high (Bennett and Duplock, 1994; Ledoux et al, 1995; Barnett, 1996). Ledoux et al found a 3.51% error between the actual pressure values and the measured pressure values using this device.

The Emed system is a capacitance mat transducer system (McPoil and Cornwall, 1992). A capacitor consists of two conducting plates separated by an insulating layer. When pressure is applied, the separation between the two plates is reduced increasing the capacitance, which is the ratio of electric charge to a resulting potential (Cavanagh et al, 1992). Like the Kistler and Musgrave systems the plate should ideally be set into a walkway. The accuracy of the Emed has been assessed and has been found to be acceptable for most variables (Hughes et al 1991; Quaney,
1995). Hughes et al used the coefficient of reliability to assess the Emeg and found that a reliability coefficient of 0.759 was achieved using a single foot measurement and 0.904 when the mean of three foot falls were used.

Although all three systems have been found to be accurate and repeatable, the data obtained is not readily transposable between systems. The differences in the number of sensors, sampling rate and data generated by the instruments are the main reasons for this variability. Unfortunately this makes comparisons between studies using different equipment extremely difficult. This fact also holds true for many other devices, which have been described and evaluated in detail by Lord (1981), Alexander et al (1990) and Cavanagh et al (1992).

1.3.3 In-shoe devices

Further advances in plantar pressure measurement include, notably, in-shoe electronic devices such as the Electrodynograph (EDG-Langer Corporation, Deer Park, NY, USA), F-Scan (Tekscan, Inc., Boston, MA, USA) and Pedar (Novel gmbh, Beichstrasse 8, 8000 Munchen 40, Germany). These systems are used to analyse plantar force and pressure under various conditions, within a shoe. Simple hosiery, cushioning protective insoles or even thermoplastic orthoses can now be evaluated.

The development of in-shoe devices to accurately measure plantar pressures has been more problematical than the development of walkway plates. The warm, moist and sometimes contoured environment inside a shoe and the need for flexible transducer cables has increased the incidence of error and device failure (Cavanagh et al, 1992).

One of the earliest computer assisted in-shoe force measurement devices, the Electrodynograph (EDG) was introduced in the early 1980’s (Langer et al, 1984
cited in Cavanagh et al., 1992). It uses force sensing resistors to gather data about the forces acting beneath the foot. The transducers are relatively inexpensive but their fragility requires them to be replaced frequently. The EDG relies on the correct placement of ‘discrete’ transducers over various anatomically defined areas on the plantar surface of the foot (Cavanagh et al., 1992). The individual transducers are attached to a lead, which is connected to a data collection unit. Although the sensors are extremely thin, their very presence in the shoe could act as a foreign body and concerns have been raised about the possibility of sensor migration resulting from shear stress (Kernozek et al., 1996) which may limit the value of the data gathered.

The F-scan insole also uses force sensing resistors but instead of individual discrete units, this device uses a matrix of 960 individual sensor points in an extremely thin disposable insole (Brown et al., 1996). The F-scan uses two printed circuits separated by a conductive ink layer. Force applied to the insole changes the composition of the ink layer, which results in an alteration in the output of the resistors (Cavanagh et al., 1992). Although having the advantage of being unobtrusive within a shoe, their reliability is in some doubt (Cavanagh et al., 1992; McPoil et al., 1995; Brown et al., 1996; Nicolopoulos et al., 2000). McPoil et al. found during static testing that the average error, when comparing known to measured pressure, ranged from 4% at low pressure (5 N/cm²) to 24% at higher pressure (50 N/cm²). They also found, during dynamic testing, that over two separate testing sessions the reliability of the F-scan was extremely poor. The ICC (2,1) values were too low to be calculated.

The Pedar system, based on a barefoot measurement mat developed by Nicol and Hennig in 1978 (Cobb and Claremont, 1995), uses a range of insoles of various sizes. The number of flexible capacitance transducers in each insole is either 80 or 99
depending on its size. While being superficially similar to the F-scan, the Pedar system differs in several key areas. The Pedar insoles are much thicker (2.2mm) than the paper thin insoles of the F-scan. They are also expensive, about AU$2,500 per pair and clearly not disposable. However there are some benefits in using capacitance transducers over the force sensing resistor system used in the F-scan. In particular the sensors in the Pedar insoles can be individually calibrated (Graf, 1993). Although they cannot be cut to fit perfectly into various sized shoes, a variety of insole sizes are available to fit most common foot sizes; currently the largest will fit a men’s size 11½ shoe.

The reliability of the Pedar insoles appears to be superior to the F-scan. McPoiil et al (1995) found during static testing that the average error, when comparing known to measured pressure, ranged from 16% at low pressure (5 N/cm²) to 0.8% at higher pressure (50 N/cm²). They also found, during dynamic testing over two separate testing sessions, the reliability of the Pedar system was high with an ICC (2,1) value of 0.84.

1.3.4 Reducing high pressure

The reduction of abnormally high plantar pressure is vital to protect the insensate foot from ulceration or re-ulceration (Dellon, 1992; Kato et al, 1996; Lavery et al, 1996). Various treatment modalities aimed at reducing pressure have been investigated.

High levels of pressure reduction have been reported using total contact casting, removable walking casts and pressure relieving footwear (Lavery et al, 1996). The cumbersome nature of these treatment modalities means they are usually
reserved for diabetic patients with severe acute problems, or with plantar ulcerations that have not responded to simpler treatments.

1.3.4.1 Cushioning

The use of cushioning at contact points between the foot and shoe of subjects with diabetic neuropathy may be appropriate (Caputo et al, 1994). Boulton et al (1984) successfully used a visco-elastic polymer material to reduce the plantar pressure of diabetic subjects with a history of neuropathic foot ulceration. McPoil and Cornwall (1992) found that Spenco (Spenco Medical Corp, Waco TX), Viscolas (PAL Health Technologies, Pekin, IL.) and PPT (PPT Professional Technology, Inc., Deer Park, NY.) significantly reduced peak pressures in both the plantar metatarsal and plantar calcaneal areas of the foot. Pollard et al (1983) tested Plastazote (BXL Plastics Ltd, Croydon, Hertfordshire, England) and reported a reduction in vertical force using this material.

The shock absorbing and energy return characteristics of various cushioning materials have also been tested with PPT and Viscolas showing the best performance (Pratt et al, 1986; Lewis et al, 1991).

1.3.4.2 Orthoses

Thermoplastic orthoses fabricated from non-weightbearing plaster casts have also been found to be beneficial in the treatment of the diabetic foot. Albert and Rinoie (1994) found that custom made thermoplastic orthoses reduced plantar pressure in subjects with diabetes who displayed abnormal subtalar joint pronation. They found that orthoses reduced pressure on the medial side of the foot and increased total contact area. They suggested that by redistributing pressure on the

Colagiuri et al, 1995 suggested that custom thermoplastic orthoses could reduce the chance of ulceration on the neuropathic foot by reducing the formation of callus. Although they did not assess the plantar pressure of the subjects, they suggested that the reduction in plantar callus was the result of a reduction in peak pressure at the site of callosities.

1.4 Joint examinations

Limited joint mobility of the ankle, subtalar and 1st metatarsophalangeal joints of adults with DM has been found to be associated with neuropathic ulceration (Mueller et al, 1989, Delbridge et al, 1988). A previous study of adolescents with T1DM, evaluated the ROM of the ST, 1st MTP joints of the feet and IP joints of the fingers and toes. This study found that LJM in the feet was associated with retinopathy and elevated AER and LJM in the hands was associated with retinopathy (Duffin, 1996). Rosenbloom et al, (1981) examined the ankle joint, in combination with the IP joint of the hands and other joints in the upper body of young people with T1DM, to evaluate the relationship between LJM and microvascular disease. In Rosenbloom’s study the IP joints of the hands and ankle joints were not examined in isolation, but when grouped with other joints affected by LJM, demonstrated an association with microvascular disease. A possible link between plantar ulceration and LJM of the ST, 1st MTP and ankle joints in adults, highlighted by Mueller and Delbridge, and the association between microvascular disease and LJM of the IP joints of the hands prompted the inclusion of these joints in the current study.
1.4.1 The Ankle (talocrural) joint

The minimum range of ankle dorsiflexion required for normal gait ranges from $5^\circ$ to $10^\circ$ past the $90^\circ$ ankle position (Perry, 1974; Root et al, 1977; McCrea, 1985; Subotnick, 1989; Cusick, 1990). If this minimum ROM is not available as the knee extends, prior to heel lift, an early heel lift may result. This leads to early transference of weightbearing forces to the forefoot as seen in figure 1.4 (Root, 1977). Given that most neuropathic ulcers occur under the forefoot (Sincore et al, 1987), early transference of weightbearing forces to the forefoot is of particular importance for the function of the diabetic foot (Mueller et al, 1989).

Figure 1.4

Early transference of weightbearing force to forefoot due to restricted ankle dorsiflexion
(adapted from Root et al, 1977 pp 272)
The osseous structures of the ankle joint consist of the distal end of the tibial shaft and medial malleolus, distal end of the fibular shaft and lateral malleolus, and the trochlear surface of the talus. The joint capsule is thin and weak anteriorly and posteriorly to accommodate flexion and extension but, as with all hinge joints, it is strengthened medially and laterally by capsular ligaments (Palastanga, 1989; Sarrafin, 1993). Medial stability is achieved by the deltoid ligament which attaches to the medial malleolus proximally and the talus, calcaneus and navicular distally. Laterally the joint is stabilised by the anterior and posterior talofibular ligaments and the calcaneofibular ligament. Anterior and posterior ankle joint stability is aided by the anterior and posterior ligaments which are actually localised thickenings of the joint capsule (Palastanga, 1989). A detailed diagrammatic representation of the anatomical structures of the ankle joint is given in figure 1.5.

Although the ankle joint is classified as a hinge joint, its axis is oblique to the coronal plane running in a posteriolateral direction. The axis is inclined in the transverse, frontal and sagittal planes (Inman and Mann, 1973; Oatis, 1988). This allows the joint to function with triplanar motion causing a small amount of pronation and abduction during dorsiflexion and a small amount of supination and adduction during plantarflexion (Palastanga, 1989). While recognising that the concept of a fixed joint axis is simplistic, it is still useful to explain the general direction of joint motion.

The average range of the ankle joint dorsiflexion is 20° (Kapanji, 1985; Palastanga et al, 1989) but the minimum range of dorsiflexion required for normal ambulation may be only 10° (Root et al, 1977; Valmassy, 1981; Subotnick, 1989).
1.4.2 The subtalar (talocalcaneal) joint

Delbridge et al (1988) suggested a causal link between LJM and neuropathic ulceration of the foot, but conceded that the neuropathic ulcers being assessed may have been in part due to unrelated factors such as unknown trauma or undetected abnormalities in gait or foot structure. This work on adult diabetic feet prompted the
previous study on adolescents with diabetes, which revealed that 35% of diabetic subjects evaluated for subtalar (ST) joint LJM had limited motion when compared to non-diabetic controls (Duffin, 1996). Although this does not demonstrate a causal link between LJM of the STJ and neuropathic ulceration, it does suggest that the restricted motion found in the Delbridge subjects was the direct result of diabetes and not extraneous factors.

The ST joint consists of the concave facet of the undersurface of the body of the talus and the convex upper portion of the posterior calcaneus surface (Palastanga, 1989; Sarrafian, 1993). Anteriorly the talus articulates with the navicular, and the calcaneus articulates with the navicular and cuboid. The subtalar joint is a synovial joint surrounded by a thin fibrous capsule, which is thickened medially, laterally and posteriorly by talocalcaneal ligaments. The anterior and posterior portions of the interosseous talocalcaneal ligament of the ST joint lay directly below the long axis of the leg and are essential in maintaining joint stability during rest and activity (Palastanga, 1989). The stability of the ST joint also relies upon the medial and lateral ligaments of the ankle joint, which hold the talus securely between the leg and the calcaneus. A detailed diagrammatic representation of the anatomical structures of the subtalar joint is given in figure 1.6.

The ST joint allows the foot to adapt to rotatory forces acting above and below the joint (Cusick, 1990). Motion of the joint occurs in all three body planes in the directions of inversion and eversion. Inversion consists of supination, adduction and plantarflexion while eversion involves pronation, abduction and dorsiflexion (Palastanga, 1989; Sarrafian, 1993). The motion of the ST joint allows the foot to adapt to uneven terrain and because of its interconnection with the midtarsal joint it
also aids in the stability and the maintenance of the arches of the foot (Inman et al., 1981; Cusick, 1990).

Figure 1.6

Anatomy of the Subtalar Joint
(Adapted from Palastanga et al, 1989 page 553)
1.4.3 The 1st Metatarsophalangeal (MTP) joint

In a previous study LJM of the 1st MTP joint was examined in adolescents with diabetes and was found in 18% of subjects tested (Duffin, 1996). Those with LJM at this joint had a weightbearing ROM below 57°. Root et al (1977) and Hopson et al (1995) suggested that the minimum range of 1st MTP joint dorsiflexion needed during gait is 65° (figure 1.7). Hopson et al (1995), when discussing the function of the 1st MTP joint, stated that restriction of dorsiflexion significantly impairs foot function during gait. Although the exact details of this dysfunction remain elusive, restricted motion of the 1st MTP joint results in an early transference of pressure to the hallux.

The 1st MTP joint is a synovial condyloid joint which consists of the head of the 1st metatarsal and the base of the proximal phalanx (Palastanga, 1989). The joint is enclosed by a joint capsule, which is reinforced by plantar and collateral ligaments. Joint stability is assisted dorsally by the extensor hallucis longus and brevis tendons and plantarly by the flexor hallucis longus and brevis tendons (Palastanga, 1989). A detailed diagrammatic representation of the anatomical structures of the 1st MTP joint is given in figure 1.8.

The 1st MTP joint functions primarily as a hinge joint, allowing dorsiflexion and plantarflexion but the joint structure also allows a smaller degree of abduction, adduction and circumduction. It acts as the final transmitter of weight-bearing force during propulsion (Cusick, 1990). Dorsiflexion of the 1st MTP joint is essential to allow the smooth transference of body weight from the rearfoot to the forefoot (Dananberg, 1986). However the motions of plantarflexion, abduction and adduction available to this joint seem to be of little importance during gait (Root et al, 1977). It is likely that these accessory motions were of greater importance earlier in evolution.
Figure 1.7

Minimum range of 1st MTP joint motion required during final propulsion
(Adapted from Root et al, 1977 pp 58)
Figure 1.8

Anatomy of the 1st Metatarsophalangeal Joint
(Adapted from Palastanga et al, 1989 pp 573 & DuVries, 1978, pp 245)
1.4.4 The Interphalangeal (IP) joints of the fingers and toes

Testing for LJM of the IP joints of the hands is simple to perform clinically, making it a valuable test for all investigators. In a previous study LJM of the IP joints was strongly associated with longer duration of diabetes, higher lifetime HbA$_{1c}$ and microvascular disease (Duffin et al, 1999). It was included in the current study to determine if this simple test could also be used as an indicator of high plantar pressures, soft tissue changes and LJM in joints of the foot. Flexion deformities of the toes (hammer toes) have not been found to be significantly more common in young people with T1DM (Duffin et al, 1999) but have been associated with ulceration on the mature diabetic foot (Edmonds et al, 1986). This association makes the early detection of this abnormality extremely important.

The IP joints are comprised of the articular surfaces of the head of the more proximal phalanx and the base of the more distal phalanx. The collateral and palmar ligaments in the fingers and collateral and plantar ligaments in the toes strengthen the joint capsules. The joints are further stabilised by the flexor and extensor tendons (Gray, 1980; Palastanga, 1989). Detailed diagrammatic representations of the anatomical structures of the IP joints of the fingers and toes are given in figure 1.9.

In both the fingers and toes, motion is assessed from a fully extended position. Motion occurs primarily in the sagittal plane and consists of flexion only. The fully extended position of each joint places the connecting phalanges at 180 degrees (Kapandji, 1985).

The primary function of the IP joints is to facilitate gripping movements of the hands (Palastanga, 1989).
Figure 1.9

Anatomy of the Interphalangeal Joints of the Fingers and Toes
(Adapted from Palastanga et al, 1989 pp 263 & 575)

The Finger

Extensor digitorum
Extensor expansion

Third palmer interosseous
Flexor digitorum profundus

Third lumbrical
Flexor digitorum superficialis

The Toe

Extensor digitorum longus

Dorsal interosseous
Lumbrical

Extensor digitorum longus

Dorsal interosseous
Flexor digitorum longus
Lumbrical
Flexor digitorum brevis
1.5 Joint measurement

1.5.1 Goniometry

Many methods have been described to measure joint motion. Most use some variety of ‘angle-finder’ with which to quantify joint motion, a process known as goniometry (eg. Grk. Gonia = angle, metron = measure). Goniometry is used as a means of determining partial or total range of motion (ROM) or position of a joint within its range (Norkin and White, 1985). Highly sophisticated methods of measuring joint position and range have been devised, such as the flexible electrogoniometer (Nicol, 1989), high-speed cinematography (Gajdosik and Bohannon, 1987), and various radiographic measurements (Spencer, 1994). The manual universal goniometer remains the most widely used instrument in clinical practice because it is readily available and inexpensive (Gajdosik and Bohannon, 1987).

Goniometers may be used in measuring both passive motion and active motion. Passive motion is assessed by the examiner moving the joint through its whole excursion without the assistance of the subject. Active motion is assessed by the subject moving the joint through its total range without the aid of the examiner. Passive ROM is slightly greater than active because each joint has a small amount of motion not under voluntary control, which allows joints to absorb extrinsic forces (Norkin and White, 1985). Assessing active ROM can give a false impression of the true motion available at a joint as it is determined by the subject’s ability to move the joint, not the true ROM possible (Norkin and White, 1985). Assessing passive motion provides a more accurate picture of the integrity of the articulating surfaces and the extensibility of the joint capsule, ligaments and muscles (Norkin and White, 1985).
1.5.1.1 Measuring the Ankle Joint

The method for measuring ankle joint motion described by Root et al (1971) and Meuller et al (1989) relies on the accurate placement of a tractograph or protractor over a bisection line marked on the lateral lower 1/3rd of the fibula. The method for determining the position of this line was not defined, but from diagrammatic representation it appears to be established by bisecting the proximal and distal ends of the fibula then marking a line on the lateral side of the leg (see figure 1.10).

Figure 1.10

Root method of measuring ankle joint dorsiflexion
(adapted from Root, 1971 pp 95)

(Protractor crosses the foot in the lateral arch, around the base of the 5th metatarsal giving a falsely high measurement of ankle flexion)

Drawing a bisection line on the lateral side of the leg is problematical due to the uneven surface and skin movement. It is also necessary to align the protractor or tractograph with this bisection line. Finally if a protractor were used in place of a
tractograph the measurement of ankle flexion would be falsely high. On a large foot the plantar surface would not intersect the instrument at the head of the 5th metatarsal but closer to its base (see figure 1.10). Cusick (1990) offers an alternative technique, that of estimating ankle dorsiflexion thus eliminating the complication of identifying and marking bony landmarks, but this method is only useful as a simple clinical indicator of ankle restriction.

1.5.1.2 Measuring the Subtalar Joint

A plethora of instruments have been designed and used by various investigators for the evaluation of ST joint motion such as the electrogoniometer, the digital biometer, pluri-meter, K-square and tractograph (Kurtzweil, 1968; Kaye and Sorto, 1979; Gerhardt, 1982, Anthony, 1992; Phillip and Lidtke, 1992; Bevans, 1993; Menz, 1993). The majority of these were designed with the sole purpose of separately evaluating the movements of inversion and eversion.

Clinically, the measurement technique devised and published by Root et al (1971) has been widely used to evaluate the amount of inversion and eversion of the ST joint, separately. It involves bisecting the posterior aspect of the calcaneus in both fully inverted and everted positions, and bisecting the posterior lower 1/3rd of the leg. The bisection lines on the posterior aspect of the calcaneus then appear as a ‘V’ or ‘Y’ shape with the apex of these shapes being located distally. (see figure 1.11)

Error due to the location, skin movement and marking of the bisection of the calcaneus is increased with this method, and compounded once more due to difficulty in marking bisection lines while holding the calcaneus initially in an inverted then in an everted position. Further error arises from the difficulty in locating the bisection of the posterior leg.
Figure 1.11

Root technique for measuring subtalar joint motion
(adapted from Root, 1971 pp 47)
The accuracy of devices such as the electrogoniometer, digital biometer, pluri-meter and K-square have been well documented (cited in Menz, 1993). When used to evaluate the ST joint all have the same fundamental problem as the Root method; the accuracy of locating the bisection of the calcaneus. These devices also have the added disadvantage of poor availability and high cost making them impractical to use in a clinical setting.

1.5.1.3 Measuring the 1st Metatarsophalangeal Joint

The tractograph has been used for measurement of 1st MTP joint dorsiflexion (Norkin and White, 1987) and is both simple and inexpensive. The method suggested by Norkin and White requires the placement of a tractograph over the dorsal skin surface of the 1st MTP joint, with the fulcrum directly over the joint itself. This method reduces the chance of some measurement error by avoiding marking bony landmarks on the skin. However, the possibility of a dorsiflexed distal phalanx interfering with the ability of the examiner to place the instrument in full contact with the entire length of the hallux, made this method unsuitable (see plate 2.6 in materials and methods).

Bevans (1993) used an electrogoniometer to evaluate 1st MTP joint dorsiflexion. This device requires the accurate placement of two end blocks over the bisection of the 1st metatarsal and proximal phalange. The end blocks are connected by an element, which measures the displacement between them and gives a digital readout of the motion occurring between the blocks. Although the reliability of this instrument was high, Bevans reported that the attachment of the end blocks to subjects was found to be quite difficult. Nicol (1989) also examined this device, stating that electrogoniometry has the same inherent problems as standard
goniometry, with the addition of the difficulties involved in placement of the end blocks. Although reasonable accuracy can be expected from this instrument with practiced use its high cost and inconvenience make it impractical in a clinical setting.

Radiographic evaluation of joint ROM has the advantage of easier determination of bony landmarks allowing metatarsal and phalanx marking without the complicating factor of skin movement, which has been found to cause inaccuracies in joint motion analysis (Elveru et al, 1988). However variability in measurements may occur even with this method due to inconsistencies in positioning the subject and equipment, orientation for x-ray, parallax error, or from inaccuracies in the determination of correct bony landmarks and correct placement of measuring instruments (Wright and Feinstein, 1992).

1.5.1.4 Measuring the Interphalangeal Joint of the Fingers and Toes

No instrumentation has been used for measuring the extensibility of the IP joints of the fingers or toes. Active extension of the fingers has been examined using the 'prayer sign' (plate 1.1), first described by Rosenbloom et al in 1981. They suggested that if the prayer sign was positive the examiner should confirm limitation by attempting to extend passively the IP joints. Passive extension of the fingers and toes has been assessed by the examiner holding the finger or toes and attempting to achieve a position of 180° of extension (Duffin et al, 1999), (plate 1.2).
Plate 1.1

Test for active extension of the IP joints of the hands
(the prayer sign)

Plate 1.2

Test for passive extension of the IP joints of the hands
1.6 Soft tissue examination

1.6.1 The Plantar Aponeurosis

The plantar aponeurosis is rich in collagen, in conjunction with the plantar ligaments it helps maintain the longitudinal arch of the foot (Hicks, 1954; Palastanga et al., 1989; Sarrafian, 1993). If non-enzymatic glycation of collagen affects the plantar aponeurosis, alterations in elasticity and arch height may result. Kidd and Kidd (1993) suggested that these changes may lead to the formation of a cavoid foot type with resultant plantarflexion of the metatarsal heads and digital contraction. As the plantar metatarsal area and the digits are common areas for the development of neuropathic ulcers (Walters et al., 1992; Edmond et al., 1986), further investigation of this area of the foot is warranted.

The plantar aponeurosis inserts anteriorly into the proximal phalanx of each of the five toes and posteriorly into the calcaneus. It is composed of collagen fibres aligned predominantly in a longitudinal manner except in its anterior portion where it splits and transverse fibres bind the five slips together (Palastanga, 1989; Sarrafian, 1993). The central section of the aponeurosis is stronger and thicker than the medial and lateral portions. The medial, central and lateral sections of the aponeurosis all become thinner as they proceed distally.

At its distal insertions the aponeurosis also inserts superficially into the dermis of the plantar metatarsal area of the foot where it aids in the stability of the skin by limiting motion. The distal sections of the aponeurosis also project vertical fibres, which pervade the four fat pads underlying the five metatarsophalangeal joints, again functioning to stabilise these structures. The superficial, proximal section of the aponeurosis also inserts into the dermis and adipose tissues aiding in the stability of these structures during locomotion (Gray, 1980; Sarrafian, 1993).
These fine but collectively strong strands of collagen fibres which pervade the dermis and adipose tissue in the plantar calcaneal and plantar metatarsal areas are adapted to the prevailing impact and shear stresses which occur during gait. They tether the skin and limit the displacement of fat, augmenting the resilient cushioning effect essential in these areas. A detailed diagrammatic representation of the anatomical structures of the plantar aponeurosis is given in figure 1.12.

During propulsion when the proximal phalanges dorsiflex, the aponeurosis tightens causing what is known as the ‘windlass’ effect (figure 1.13). The tightening of the aponeurosis results in a raising of the longitudinal arches of the foot (Hicks, 1954; Palastanga, 1989; Sarrafian, 1993).
Figure 1.12
The Plantar Aponeurosis
(Adapted from Henkel, 1913 in Sarrafian 1993, pp142)
The Windlass Effect
(Adapted from Hicks, 1954 in Sarrafian 1993, p557)

The initial length $L_1$ of the foot diminishes to $L_2$ and the initial height of the arch $H_1$ increases to $H_2$. 

[Diagram of the Windlass Effect with labels $L_1$, $H_1$, $L_2$, and $H_2$.]
1.6.2 The Skin

The skin on the foot has to undergo many stresses during daily activities to protect the individual from mechanical trauma such as friction, impact pressure and shear (Edwards and Marks, 1995).

The epidermis is the outer layer of tissue surrounding the body. It is differentiated into various layers, the stratum corneum and lucidum are the outer most layers with the strata granulosum, spinosum and basale being directly below (Gray, 1984; Palastanga, 1989). The entire epidermal layer is strongly attached to the dermis by a complex peg and socket arrangement which serves to anchor the two layers and prevent the epidermis being stripped off the surface of the dermis by shearing forces (Gray, 1984).

The dermis is a tough, flexible and highly elastic layer composed of the deeper reticular and more superficial papillary layers. These layers consist of felted connective tissue with varying numbers of blood vessels, lymphatic vessels and nerves. The dermis is very thick in the palms of the hands and soles of the feet and tends to be thicker posteriorly and laterally (Gray, 1984). A detailed diagrammatic representation of the anatomical structures of the skin is given in figure 1.14.

The skin is a specialised boundary lamina, which acts as the interface between the body and its environment. It minimises the traumatic effects of mechanical, chemical, thermal and photic environmental stresses and also acts as a barrier to invasion by microorganisms. The complex neurovascular system in the skin regulates heat exchange with the environment and enables the skin to act as the major sensory surface of the body (Gray, 1984).
1.7 Evaluating soft tissues of the foot

Skin changes in diabetes are similar to those that occur in Scleroderma (Brik et al, 1991) and in the aging process (Goodfield and Millard, 1988). In essence these changes cause a loss of elastic fibres, clumping of residual elastic tissue (Braveman and Yen, 1984), a loss of anchoring fibrils in the basement membrane of the epidermis and thickening of the dermis (Dowd et al, 1986). Taken together these predispose the affected area to injury from minor trauma (Dowd et al, 1986).
The effects of diabetes on the skin of the upper and lower limbs have been investigated using ultrasound and punch biopsies in adults (Lyons and Kennedy, 1985; Vishwanath et al, 1986; Huntley and Walter, 1990; Forst et al, 1994). Plantar keratin changes (Delbridge et al, 1985) and alterations in plantar fat pad thickness have been observed (Gooding et al, 1986; Abouaesha et al, 2001) but plantar skin thickening has not been examined.

In young people with T1DM skin thickening has been observed but not examined quantitatively (Rosenbloom et al, 1981; Rosenbloom et al, 1983; Rosenbloom, 1984). In these subjects pinching or tenting of the skin on the dorsum of the hand has been used to detect skin thickening. However reduced tenting of the skin may indicate a loss in elasticity or an increase in subcutaneous adipose tissue rather than an increase in skin thickness. Pathology analyses of skin scrapings and punch biopsies is probably the most effective method of detecting micro changes to the skin but because of their potential to scar, they are not suitable for evaluation of plantar skin, especially in young people.

Techniques to evaluate the thickness of the plantar aponeurosis have relied on the use of ultrasonography (Wall et al, 1993; Cardinal et al, 1996, Groshar et al, 2000). These studies used the hyperechoic nature of the plantar aponeurosis and the almost isoechoic fat pad of the heel to evaluate thickening of the aponeurosis. Wall et al (1993) and Cardinal et al’s (1996) investigations of the aponeurosis were concerned with evaluating changes in the proximal insertion of the aponeurosis due to the effects of plantar fasciitis. These changes did not extend further than 2.8 cm distal of the calcaneal tubercle (Wall et al, 1993). Therefore, if we assume that non-enzymatic glycation would effect the entire structure of the aponeurosis,
measurements should be made more than 2.8cm distal of the calcaneal tubercle to avoid assessing aponeurotic thickening resulting from plantar fasciitis.

Diagnostic ultrasound has not been widely used for the evaluation of foot structures but it is not invasive, expensive or time consuming making it the preferred medium for examining the plantar aponeurosis and plantar skin of people with T1DM.

1.7.1 Ultrasound

The term ultrasound comes from the Latin *ultra* meaning beyond the normal and *sonus* meaning to give out sound. Spallanzani, in 1794, first postulated the existence of sound which could not be perceived by the human ear after noticing that bats flying in the dark were able to avoid obstacles (Azimi, 1976). The importance of his observation remained obscure for almost a century.

In 1880 Pierre and Jacques Curie discovered the piezoelectric effect, ie. that mechanical pressure applied to a quartz crystal produces an electric charge. In 1881 they found that an oscillating electrical potential applied across a quartz crystal caused vibrations in the crystal which produced sound waves inaudible to the human ear. It was this work that laid the foundations for the development of the ultrasonic transducer which is used for the transmission and collection of ultrasound energy (Azimi, 1976).

Early medical interest in ultrasound was directed towards its therapeutic applications, which only require a transmitter. Industry on the other hand, was more interested in using it to detect inconsistencies within solid objects, utilising ultrasound for its diagnostic properties. This required the use of a transmitter and a means of detecting the ultrasound echo which had been generated. Initially this was
chieved by placing transducers on either side of an object with the second transducer collecting sound waves which had passed through the object. In 1944 lloyd Firestone developed the ‘reflectorscope’. This device used the same transducer to generate pulsed ultrasound and also picked up returning echoes (Eisenberg, 1992). he introduction of medical diagnostic ultrasound followed several years afterirestone’s work and required the collaboration between the medical, military and industrial fraternities (Goldberg and Kimmelmann, 1988).

The Dussik brothers (1947) of Austria were the first to successfully apply ultrasound to medical diagnosis. However some of the more significant breakthroughs in diagnostic ultrasound are attributed to Dr. J. Wild and an engineer named J. Reid. In 1952 these men developed a hand-held scanner and used an aqueous jelly to allow sonic contact, instead of the immersion baths and water tanks, which had been employed by other investigators. They were also the first to introduce a two-dimensional static scanning system called ‘B-mode’ or brightness mode (see 1.7.1.1).

Diagnostic ultrasound continued to evolve during the 1960’s but in the early 970’s the introduction of analog and digital scan converters greatly improved the quality of the image produced. These converters were capable of recording and displaying images, which revealed subtle changes in tissue. Improvements in scan converters and the development of real-time scanning have made ultrasonography a valuable diagnostic tool which is now used in many areas of medicine (Eisenberg, 1992).
1.7.1.1 Ultrasonic display modes and scan converter

The choice of display mode selected for diagnostic ultrasound depends upon the information required for the investigation being undertaken (Smith, 1996). The A or amplitude mode, in which the amplitude of the ultrasonic echo is displayed along a vertical axis of a graph and the distance into the subject is shown along the horizontal axis, is the simplest display system (figure 1.15). This mode of ultrasound production is recommended for anatomical structures such as the eye and mid-brain (Goldstein, 1993; Smith, 1996).

Figure 1.15
A-mode display
(Adapted from Goldstein pp 9)

Amplitude mode displays the amplitude of the received echoes at the depth of their respective reflectors.
The M or motion mode adds to the information gained during ultrasonic investigation by providing information about the velocity and amplitude of the echo. A vertical line of this graphic representation indicates the distance into the subject, and amplitudes of the echo are shown by variations in brightness. This vertical sweep across the display at a constant velocity (Goldstein, 1993). The first echo displayed as a straight line, the slope of the following trace lines gives an approximate measure of the velocity at which the echo is moving towards or away from the transducer (figure 1.16). The M-mode display is most useful in cardiac cases (Smith, 1996).

**Figure 1.16**

M-mode display

(Adapted from Goldstein pp. 9)
Doppler, like M-mode, is used in detecting moving structures but gives information about direction, it also has the added advantage of audio analysis (Smith, 1996). The motion of the target, relative to the stationary transducer, causes a change in the frequency of the received echoes. To assess whether the target is moving away from or towards the transducer the equation;

\[ f_{eff} = \frac{Cf_o}{C \pm V_s} \]

is used where \( f_{eff} \) is the effective or received frequency, \( C \) is the acoustic velocity, \( f_o \) is the transmitted frequency and \( V_s \) is the velocity of the source. If the target is moving towards the receiver, the sign will be negative if away from the receiver the sign will be positive (Goldstein, 1993). This form of diagnostic ultrasound is primarily used in the assessment of blood flow (Smith, 1996).

The B or brightness mode produces an image of the structures being examined in two dimensions. The echo data is represented as spots on a cathode ray tube (CRT). The image is displayed in a grey scale, where the amplitude of the echo is represented in various shades of grey (figure 1.17). The brightness of the spots on the screen is proportional to the amplitude of the echo received (Goldstein, 1993).

**Figure 1.17**

B-mode image

(Adapted from Goldstein pp 9)

The brightness of the spot on the screen is proportional to the echo amplitude.
The scan converter is the means by which the echo data is converted into broadcast television format. Analog and digital scan converters have been used for this process but the analog converter has been made obsolete by the less expensive and more reliable digital system (Goldstein et al, 1974).

To convert the scanned data the amplitudes of the received echoes are quantified into pixels or picture elements that can be represented numerically. These numbers represent various shades of grey in the image. The translation of these various pixels into corresponding brightness levels is called grey scale mapping (Smith, 1996). After the conversion of the echo has been accomplished, the cross-sectional image is then projected onto the screen in real time. The ability to display a scanned area in real time allows the examiner to move the transducer until the desired area for examination is found.

1.7.1.2 Echo Reflection

Echoes occur as sound waves meet with various structures; i.e. bone, fat, fascia, muscle or any other soft tissues or organs. The amount of echo reflection will depend on the acoustic impedance of the tissue being examined (Chivers and Parry, 1978). The acoustic impedance of water is very low ($4 \times 10^{-4}$), it will not impede the transmission of sound waves to any great extent and therefore the reflection will be low. On the other hand bone has a very high acoustic impedance (7.80) and will reflect a larger percentage of the sound waves transmitted (table 1.3).

The manner in which various body tissues appear on the ultrasound screen is described as its echogenic appearance. Structures which appear as dark areas on the screen are described as being hypoechoic, those appearing as bright areas are referred
to as being hyperechoic. Tissues, which appear the same, are called isoechoic (Fornage and Rifkin, 1988).

**Table 1.3**

Acoustic impedance of various body components  
(Adapted from Goldstein, 93 pp 3)

<table>
<thead>
<tr>
<th>Body component</th>
<th>Acoustic impedance ($10^5$ Rayls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0.0004</td>
</tr>
<tr>
<td>Water</td>
<td>1.48</td>
</tr>
<tr>
<td>Fat</td>
<td>1.38</td>
</tr>
<tr>
<td>Soft tissue (average)</td>
<td>1.63</td>
</tr>
<tr>
<td>Muscle</td>
<td>1.70</td>
</tr>
<tr>
<td>Bone</td>
<td>7.80</td>
</tr>
</tbody>
</table>

At the point where two different soft tissues join a phenomenon known as *specular* reflection occurs. This occurs at the interface of any soft tissues and appears as a line. This is because the sound waves being transmitted through the first soft tissue propagate into the second, which in turn reflect sound waves back into the first. The strength of the specular reflection depends on the ratio of the two acoustic impedances at the boundary (Goldstein, 1993). This aspect of ultrasonic imaging is of great assistance when examining structures such as the skin or plantar aponeurosis. A distinct line appears at the interface of the surrounding tissue making procedures such as measuring relatively simple.
1.8 The Gait Cycle

Gait is the term used to describe the manner, in which an individual steps or walks (Funk and Wagnall, 1974). In humans it is a bipedal form of locomotion resulting in a forward translation of the body (Sarrafian, 1993). Gait requires the participation of the entire body in a synchronous transference of body mass from one supporting foot to the other. The cycle of events which occur to achieve forward motion begin as one heel contacts the ground and ends as the same heel contacts the ground at the next step. When analysing lower limb motion during the gait cycle a number of variables must be recognised and considered.

The movement of the lower limb has been described in the literature using a variety of terms for the phases and sub-phases of the gait cycle (Inman et al, 1981; Palastanga, 1989; Sarrafian, 1993). For the purposes of this study the gait cycle will be divided into two main phases, the stance and swing phases (Inman et al, 1981; Sarrafian, 1993). The stance phase consists of movement of the foot from heel strike, through mid-stance to the propulsive phase (figure 1.18). Heel strike commences the instant the heel contacts the supporting surface (Palastanga, 1989). Then, as full weight is taken by the rearfoot, the ST joint moves in the direction of eversion until the forefoot contacts the ground (DuVries, 1978). The motion of ST joint eversion also causes the leg to internally rotate during this phase of the gait cycle (DuVries, 1978; Inman et al, 1981). The end of heel strike, and the commencement of mid-stance occurs as the metatarsals and toes contact the ground. During mid-stance the centre of the body passes over the weightbearing foot and the ipsilateral foot is in swing phase. The heel inverts during early mid-stance and the leg externally rotates initiating ST joint supination which causes a structural rearrangement of the midfoot. This transforms the foot into a rigid lever allowing efficient transference of weight
from the rearfoot to the forefoot in preparation for the final phase, propulsion (DuVries, 1978).

The end of mid-stance and the beginning of the propulsive phase occur as the heel is lifted from the ground and weight is transferred to the forefoot. The foot continues to invert during the early part of the propulsive phase and actively plantarflexes (Palastanga, 1989). As the metatarsophalangeal joints are forced into a hyperextended position (DuVries, 1978; Sarrafian, 1993) the plantar aponeurosis is tightened by the windlass mechanism, described by Hicks in 1954. This causes a relative shortening of the inner longitudinal arch, passively inverting the foot (DuVries, 1978). Weight continues to be transmitted distally to the toes where digital extension is rapidly followed by flexor contraction of the lesser toes, then of the hallux (Palastanga, 1989). The inversion force, which has dominated the mid-stance and propulsive phases of gait, is now replaced by a medial shift in weight. Force is transferred from the lateral side of the foot to the medial side in preparation for full load bearing by the ipsilateral foot which has now moved from heel strike to early mid-stance. Propulsion, having accelerated the foot to this point, ends and the swing phase begins at the instant the toes leave the ground (Sarrafian, 1993).

The foot is initially in a plantarflexed position as it enters swing phase. In order for the toes to clear the ground during mid-swing, the ankle must dorsiflex and the toes extend (Palastanga, 1989). This movement continues while the foot decelerates in preparation for the next heel strike and thus the gait cycle is complete (Sarrafian, 1993) (Figure 1.19)
**Figure 1.18**

The Stance Phase of Gait
(Adapted from Sarrafian, 1993, page 574)

*Stance phase commences at the instant the heel contacts the ground and ends at the instant the toes leave the ground.*

<table>
<thead>
<tr>
<th>HEEL STRIKE</th>
<th>FOOT FLAT</th>
<th>HEEL RAISE</th>
<th>PUSH OFF</th>
<th>TOE OFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heel Strike</td>
<td>Mid Stance</td>
<td>Propulsion</td>
<td>Propulsion</td>
<td>Propulsion</td>
</tr>
</tbody>
</table>

**Figure 1.19**

The Swing Phase of Gait
(Adapted from Sarrafian, 1993, page 574)

*Swing phase commences at the instant the toes leave the ground and ends at the instant the heel strike the ground.*

<table>
<thead>
<tr>
<th>TOE OFF</th>
<th>*SWING PHASE</th>
<th>HEEL STRIKE</th>
</tr>
</thead>
<tbody>
<tr>
<td>END OF STANCE</td>
<td>TOE CLEARANCE</td>
<td>DECELERATION</td>
</tr>
</tbody>
</table>
Other aspects of gait, which must be considered, are stride length, cadence, base and angle of gait. Stride length (figure 1.20) is the linear distance traveled during one gait cycle (Perry, 1974). Variations in stride length may alter load on the forefoot, for example a long stride length causes an increased load due to the elongation of the propulsive phase of gait (Root et al, 1977). ‘Cadence’ refers to the speed at which a subject walks. Changes in cadence can result in changes in the forces and pressures being exerted beneath the foot during gait. The significance of this aspect of gait will be discussed in detail in chapter 2, section 2.3.

The ‘base’ of gait (figure 1.21) is the distance between the line of progression of one foot compared to the other (Rogers, 1988). In early studies (Murray et al, 1966; Inman, 1981) changes in the base of gait or ‘stride width’ were observed with changes in walking speed. As speed increases, slight increases in the base of gait also occur (Inman et al, 1981). This increase in the base of gait may lead to slight increases in the lateral shear forces acting on the foot (Inman et al, 1981) but the effect is difficult to detect without appropriate shear sensing equipment.

The ‘angle’ of gait (figures 1.21 & 1.22) is determined by measuring the angle formed between the bisection of the foot and the line of progression of body motion (Inman et al, 1981). The average angle of gait, around 15°, is determined by joint alignments from the lumbosacral area to the MTP joints and structural features of the femur, tibia, fibula and talus (Cusick, 1990). Changes in the angle of gait, resulting from rotational changes in the lower limb, have a direct effect on the function of the subtalar joint. If the limb is internally rotated the foot will assume an intoeed posture and the ST joint will evert. If externally rotated the foot will outtoe and the ST joint will invert (Sarrafian, 1993). Motions of inversion and eversion of
the ST joint result in redistribution of weightbearing forces laterally or medially respectively (Cusick, 1990).

**Figure 1.20**

Stride Length  
(Adapted from Sarrafian, 1993 page 571)

One stride length is the distance from the heel strike of one foot to the next heel strike of the same foot.
Figure 1.21

Base of gait or 'stride width'
Angle of gait or 'foot angle'
(Adapted from Murray et al, 1964, page 335)

The stride wide or base of gait is calculated as the distance between successive points of foot-to-floor contact of alternate feet.

Figure 1.22

Angle of gait
(Adapted from Inman, 1981 page 15)

External rotation of limb will result in out-toe gait

Internal rotation of limb will result in in-toe gait

Viewed from above

The angle of gait is determined by joint alignments from the lumbosacral area to the MTP joint.
1.9 Conclusions

Our current understanding of the processes involved in the development of diabetes and its lower limb complications has increased enormously in the last century. We know that if rigid control of blood glucose levels is maintained that systemic complications can be greatly reduced. However the complexities of the disease process is obviously still not fully understood. Even with what we now consider excellent control, complications from diabetes are inevitable for many sufferers.

The knowledge base presently available indicates that early detection of lower limb complications of diabetes is vital to prevent progression to amputation. However in adolescents with T1DM lower limb complications have in the most part been ignored. This is understandable in one way, adolescents with diabetes do not exhibit neuropathic or vascular ulceration and amputations in these individuals are unheard of. But our knowledge base tells us that the building blocks of these lesions are detectable before serious foot problems are evident and that early intervention can indeed save limbs and lives. The following four experiments will hopefully give a greater understand of the complexities involved in lower limb complications of diabetes and present a solid case for early assessment of structural and functional changes in the feet of young people with T1DM.
CHAPTER 2

MATERIALS AND METHODS

This chapter describes the subject selection, equipment, methods used to collect data for the experiments and repeatability studies. This thesis is divided into four main areas of investigation. The first group of experiments was designed to evaluate joint range of motion of diabetic subjects compared to controls. The second was designed to assess plantar pressures in these two groups. The third assesses the efficacy of various interventions used to reduce high plantar pressures. The fourth and final experiment evaluated non-invasive methods of determining any soft tissue changes caused by diabetes.

The subjects for all four experiments were drawn from the initial study group; thus the general subject selection and exclusion criteria apply to the entire study. Subject selection and exclusion criteria, which are peculiar to individual experiments, will be discussed in turn. Finally consideration of the repeatability of the testing procedures, error and accuracy of the experiments and justification of the statistical analyses is discussed.
2.1 Selection of subjects

To determine the appropriate number of subjects required for evaluation a power analysis was performed. As many of the approximations used for power analysis came from studies on adults, this figure was quadrupled for the diabetic subjects. There is a dearth of information on foot complications in young people with T1DM but it was assumed that, if present, they would be less severe than in adults so a larger number of subjects would be needed to detect any abnormality.

The study group consisted of 216 young people with Type 1 diabetes mellitus (113 females and 103 males) who were volunteers from the Diabetes Complication Assessment Clinic at The Children Hospital at Westmead, New South Wales, Australia. Admittance to the full complications screening program in the hospital required the diabetic subjects to have had diabetes for a minimum of two years. The median age was 15.3 years (interquartile range [IQR]: 13.5 to 16.8 years). The median diabetes duration was 6 years (IQR: 3.9 – 10.2 years). As footwear and pressure sensing insoles were to be used, subject inclusion in the study also required that appropriate footwear sizes and / or pressure sensing insoles were available. Those with foot size less than five or greater than eleven and a half could not be included in the pressure testing study.

The control group consisted of 57 non-diabetic subjects (30 females and 27 males) with a median age was 15.6 years (IQR: 13.8 to 16.4 years). All were drawn from the general population or from friends of the diabetic group. The control subjects were matched with the diabetic subjects for age and gender and were unrelated to those with diabetes or to each other.
2.1.1 Exclusion criteria

Control and diabetic subjects with any known form of arthritis or joint disease at the time of assessment were not included in the study as these diseases may have affected joint motion and pressure analysis. Subjects with acutely painful conditions which may have affected joint motion or gait were also excluded from the study. To prevent genetic bias no more than one member of a nuclear family was included in the control group.

2.2 Materials and methods – limited joint mobility

All subjects were assessed for joint ROM at the hospital in the same 12’ x 12’ examination room, which was kept at a constant temperature, 22°C, by central air-conditioning. The room was distanced from any noisy distractions, to avoid the subjects becoming tense during the examination. Each subject was asked to bring shorts and loose fitting clothing to avoid having trousers or long skirts rolled or held up by the subject during the assessment.

2.2.1 Joint selection

The criteria used to determine which joints were evaluated are detailed in Chapter One, Section 1.4.

2.2.1.1 Ankle joint measurement

**Equipment:** A purpose built long-armed goniometer was used for measuring ankle dorsiflexion. The main shaft of the goniometer is 600mm long with a groove cut into the back surface, allowing the attachment of an engineering protractor, which can slide the length of the shaft. The engineering protractor has a circular area
in its centre divided into 360, one-degree intervals. The protractor is movable and the circular centre indicates the angle formed between the shaft and the base of the protractor.

Method: Ankle joint flexion was measured with the subject lying prone on the examination table. The lateral malleoli and fibular head were marked. The long-arm of the goniometer was placed over these marks and the base of the goniometer was aligned with the lateral side of the plantar surface of the foot. Measurements were taken with the knee extended then flexed (plates 2.1 & 2.2)

2.2.1.2 Subtalar joint measurement

Equipment: A tractograph was used to evaluate the ST joint; it has two arms which extend to 180 degrees. Each arm is 15cm long and the fulcrum of the instrument is located at the centre of the measuring face where a metal pin is situated. When the instrument is closed, the measuring face reads zero degrees (plate 2.3).

Method: The posterior leg (line A-A) and calcaneus (line B-B) were bisected using a fine marking pen (plate 2.4). The tractograph was aligned with these marks, its fulcrum over the ankle joint. The rearfoot was fully inverted, then everted and total range of motion (ROM) was noted. This method is described by Delbridge et al. in 1988 and Duffin, 1996.
Plate 2.1
Ankle joint measurement (knee extended)

Plate 2.2
Ankle joint measurement (knee flexed)
Plate 2.3
Tractograph

Plate 2.4
Marking the leg and foot for ST joint measurements
2.2.1.3  **1st Metatarsophalangeal joint measurement**

**Equipment:** An orthopaedic evaluation device (OED) was used for evaluation of 1st MTP joint extension. It has a transparent rectangular back plate, which is attached to a protractor. The base line of the protractor is aligned with the base line of the back plate. The protractor may be moved through 360 degrees. The fulcrum of the OED is a metal pin, which sits in the centre of the base line (plate 2.5).

**Method:** The proximal phalanx of the hallux was marked with a fine-point marker (plate 2.6). First MTP joint extension was measured during weightbearing by placing an orthopaedic evaluation device (OED) on a supporting surface with its fulcrum directly over the 1st MTP joint. The hallux was then dorsiflexed passively to resistance and joint extension was measured (Duffin et al, 1999) (plate 2.6).

2.2.1.4  **Interphalangeal joint measurement of the Fingers and Toes**

**Method:** The examiner evaluated passive extension of the IP joints of the fingers and toes by grasping the proximal and distal phalanx and attempting to extend each digit. The number of digits unable to fully extend (180°) was noted (plate 1.2, page 44).

2.2.1.5  **Other examinations**

Retinopathy was assessed by stereoscopic fundus photography of seven standard fields and graded according to a modification of the Airlie House method (Klein et al, 1989). Body mass index (BMI) was assessed by dividing the subjects weight (kg) by the height squared (meter).
Plate 2.5

Orthopaedic Evaluation Device

Plate 2.6

1st MTP joint measurement
Glycated haemoglobin (GHB) was measured by colorimetric analysis of whole blood \(^{25}\) until February 1994, when the laboratory changed to measuring HbA\(_{1c}\) by the diamat assay high performance liquid chromatography assay (Biorad Laboratories, Hercules, CA, USA). For this study the colorimetric values were converted to HbA\(_{1c}\) using the following equation: HbA\(_{1c}\) (\%) = 1.9088 + 0.0043 \times GHB (pmol HMF mg Hb\(^{-1}\)). For each adolescent a ‘lifetime’ HbA\(_{1c}\) was calculated by taking the median of all previous HbA\(_{1c}\) assessments. The median number of HbA\(_{1c}\) assessments was 12 [IQR: 7 - 19] and the median lifetime glycated haemoglobin was 8.6% [IQR: 7.8 - 9.3%]. The non-diabetic range HbA\(_{1c}\) is 4-6%.

The mean albumin excretion rate (AER) was calculated from three consecutive timed overnight urine collections. Albumin was measured by radioimmunoassay (Pharmacia, Ryde, Australia). Elevated AER was defined as 7.5 \(\mu\)g min\(^{-1}\) or above, which is the 95th centile for Australian schoolchildren (Couper \textit{et al}, 1994).

Early changes in peripheral nerve function were assessed by determining the thermal threshold for heat and cold at the left wrist and left foot (Thermal Threshold Tester, Medelec Ltd, Old Woking, Surrey, UK), and the vibration threshold at the left medial malleolus and left great toe (Biothesiometer, Biomedical Instrument Co., Newbury, Ohio, USA). Reference ranges have been established in our population and were undertaken to detect early sensory nerve change, not clinical neuropathy (Donaghue \textit{et al}, 1993). Early sensory nerve changes were defined as any reading outside the 97.5th centile reference for non-diabetic subjects.

The examiner of joint motion was not blinded to whether the adolescents had diabetes but was blinded as to which subjects had microvascular complications. The
examiners testing for microvascular complications of diabetes were blinded as to which subjects had LJMs.

2.2.2 Definitions of limited joint mobility

The data analysis defined here pertains to evaluations undertaken in chapter 3. The first data evaluation (3A) defined LJM using critical values obtained in a previous study (Duffin et al, 1996). The critical values to define limited joint mobility at the subtalar joint was a mean total ROM of less than 25.3° and at the 1st MTP joint a mean dorsiflexion of less than 57.3°.

The second data evaluation defined LJM as less than two standard deviations below the mean for the control group and/or the inability to fully extend the IP joints of the fingers or toes. Some variation was noted between the left and right sides so the most affected side, that showing the lowest ROM was used for evaluation. The second evaluation was undertaken to allow comparisons with other examinations discussed in later chapters of this study.

2.3 Materials and methods - pressure analysis

2.3.1 Equipment

The Pedar in-shoe pressure measurement system was chosen for this study (plate 2.7). Selection of a system to evaluate plantar pressure depends upon the objectives of the study being undertaken. Force and pressure plates have been widely used and have several advantages over in-shoe devices (McPoil and Cornwall, 1992; Bennett, 1993; Birke et al, 1995; Barnett, 1996). They have a greater number of sensors per given area, a higher sampling rate and do not suffer potential interference
from footwear acting as a hostile environment for sensors; ie heat, moisture and contours. However force and pressure plates do have one obvious disadvantage in that they cannot measure pressure being exerted within footwear. In-shoe devices allow the assessment of the therapeutic value of various types of insoles and footwear.

In 1992, McPoil and Cornwall evaluated the pressure reducing effects of various cushioning materials by placing different sheets of material on top of an Emed SF pressure plate. When discussing the investigative protocol the authors felt that future studies should be conducted in-shoe, thereby considering the foot-shoe interface as it is possible that the manner in which the insole material behaves under loading could be altered when the material is placed inside the shoe (McPoil and Cornwall, 1992). Cavanagh (1992) also felt that monitoring the interface between the shoe and the foot was extremely important. He suggested that in modern society a great deal of time is spent in footwear, and assessing foot pressures in their most common environment is of much greater significance than barefoot evaluation.

Only in-shoe devices can be used when evaluating the effects of various orthotic devices upon plantar pressure. The contoured interface between the foot and orthosis cannot be assessed with a force or pressure plate but the introduction of in-shoe pressure analysis has enabled evaluation of the potential therapeutic value of such devices (Novick et al, 1993; Kato et al, 1996).

Several other advantages are gained when an in-shoe pressure measurement system is chosen over a force or pressure plate; the device may be utilized in a variety of situations, the subject need not ‘target’ a plate on a walkway and data from multiple steps can be gathered at one time. Notwithstanding, these gains require the
examiner to be much more attentive to variables which may be introduced during in-
shoe pressure evaluation; these are considered later in this chapter.

The technical data distributed with the Pedar systems states that the accuracy
of the equipment is better than 5% at temperatures between 10° to 40° C and the
measurement frequency is 10,000 sensors per second. The sampling frequency is 50
Hz (Kemozek et al, 1996).

2.3.2 Method

All subjects were fitted with the Pedar data collection equipment and were
asked to walk along a 10 metre long and 2.5 metre wide walkway (plate 2.8). Clark’s® ‘Detroit’ extra-depth footwear and nylon hosiery were supplied by the
examiner. Before data collection commenced subjects were given sufficient time to
become acclimatised to the equipment and method. Usually two passes over the
walkway were needed and the subjects were unaware of when data collection
commenced or ceased.

The examiner did not dictate the speed at which the subjects walked but
contact time was analysed to evaluate any significant speed variation between tests
and between those tested. To determine whether this was a valid method for
detecting changes in walking speed a pilot study was undertaken the results of which
are described in section 2.7.

The presence of callus was determined visually. The amount of callus was not
graded due to the highly subjective nature of grading. When detected its position on
the foot was noted.
Plate 2.7

Pedar data collection unit

Plate 2.8

Subject fitted with Pedar data collection unit
2.3.3 Data analysis

The data analysis defined here pertains to evaluation undertaken in chapters 4 and 5. A suite of data was collected from the mid-four steps of each of the left and right footfalls. These files were converted to Emed format using the Pedar Emed link program then averaged for the left and right foot separately using the Novel-ortho 08.7 average program. The standard 5-masks in the Novel-ortho 08.7 automask program was used to determine whether callused areas corresponded to areas of highest pressure and highest pressure time integrals.

2.3.4 Definition of high plantar pressure

High peak pressure and high pressure / time integrals were defined as greater than two standard deviations above the mean for the controls as suggested by Cavanagh and Ulbrecht in 1994. Only the foot displaying the highest peak pressure or highest pressure time integral was used for further evaluation. As some variability between the left and right foot was noted, using the mean of both would have eliminated subjects with only one foot at risk.

2.4 Materials and methods – interventions

2.4.1 Subject selection and exclusion criteria exclusive to this section

Twenty-two (9 male, 13 female) diabetic subjects showing high peak pressure and forty-one diabetic subjects (18 male, 23 female) with plantar callus were examined. Seventeen in each group volunteered to be fitted with various interventions. Twenty-three diabetic subjects who had used orthoses for 12 months and 67 diabetic subjects who had used no intervention over the same period returned for re-evaluation. No non-diabetic controls were used in this section of the study.
2.4.2 Equipment

2.4.2.1 Cushioning

Three millimeter thick PPT was used (PPT Professional Technology, Inc., Deer Park, NY.). PPT is an open-cell polyurethane protective material, which increases the plantar loading area resulting in a reduction in plantar pressures (McPoil and Cornwall, 1992). It also has shock absorbing and energy return characteristics superior to many other cushioning materials (Pratt et al, 1986; Lewis et al, 1991; Novick et al, 1993).

2.4.2.2 Non-weightbearing Casting

Non-weightbearing casting was used to achieve a neutral or congruent alignment of the foot structures (Cusick, 1990) which can be transferred to an orthosis. The neutral position of the joints of the foot has been referred to as “..the anatomical position..” (Palastanga, 1989) and the “..rectus..” position (McCrea, 1985). Non-weightbearing subtalar neutral casts were taken using the suspension casting technique originally described by Root et al (1971) (Ross and Jones, 1982). The posterior calcaneal section of the cast was bisected to determine the amount of forefoot posting required. Intrinsic forefoot posting was the only cast modification (Plate 2.9).

2.4.2.3 Custom orthoses

The term orthoses can refer to a wide range of insoles and although some authors refer to devices used as industry standard custom-fabricated orthotics (Albert and Rinoie, 1994) there does not appear to be a standard device. The word orthoses can include anything from an ethyl-vinyl-acetate appliance to rigid or even 75°
inverted devices. In the current study the completed device aimed at maintaining the rearfoot in a position perpendicular to the supporting surface as suggested by Valmassey (cited in Cusick, 1990). Semi-rigid orthoses fabricated from low-density polyethylene (LDPE) were used. Intrinsic forefoot posting was added to bring the rearfoot into a position perpendicular to the supporting surface. A zero degree LDPE rearfoot post was added to all devices. The heel cupping was 20mm high. The most distal edge of the appliance finished immediately behind the metatarsal heads (Plate 2.10).

2.4.3 Methods

All non-weightbearing plaster of Paris neutral position casts were taken as soon as possible following the initial, non-intervention examination. Orthoses were fabricated for both feet of each individual included in this section of the study. The orthoses were fitted approximately one week after casting. Subjects were asked to wear the orthoses daily but to adjust at their own comfort level. The average period of acclimatisation was 10 days. All subjects fitted with orthoses were re-examined after their acclimatisation period. As changes in non-intervention pressures may have occurred due to the time lapse subjects were re-examined with no-intervention. All subjects fitted with orthoses were then examined with 3mm PPT alone, orthoses alone and 3mm PPT placed under the orthoses. To avoid a period effect, interventions were assessed in random order. All subjects were examined using the same area and method used for their initial examination.
Plate 2.9
Non-weightbearing, neutral position plaster cast

Plate 2.10
Custom orthosis fabricated from low density polyethylene
All subjects, those with and without orthoses, who attended a 12 month follow-up examination had non-intervention pressures re-examined. These pressures were compared to their initial non-intervention pressure tests.

2.4.4 Data analysis

All diabetic subjects showing HPP, whether on one or both feet were included in the interventional phase of the study. Only the foot showing the highest peak pressure was evaluated. Most of those with callus had bilateral problems but again only the foot with the highest peak pressure was further evaluated.

2.5 Materials and method - soft tissue examination

2.5.1 Subject selection and exclusion criteria exclusive to this experiment

Subjects with plantar callus under the 1st MTP joint were not included in the ultrasonic assessment of skin thickness as the callus would give a false reading. It was not considered necessary to exclude these subjects from measurement of the plantar aponeurosis as deeper structures were being evaluated.

2.5.2 Equipment

The ultrasound machine used in the current study was an ACUSON 128 grey scale imager (1220 Charleston Rd., Mountain View, CA 94039 U.S.A.) which consisted of a transmitter, receiver, display and scan converter (plate 2.11). These components are basic to most diagnostic ultrasound machines (Goldstein, 1993). A linear-array, 7-megahertz (Mhz) high-resolution transducer was selected.

To evaluate any association between thickness of the plantar aponeurosis, foot size and arch height a Branie® foot measuring device was utilised (plate 2.12).
2.5.2.1 Ultrasound equipment selection criteria

The clarity and reliability of ultrasound imaging and measurements depend upon the selection of the appropriate transducer frequency, display unit and functions. Selection of an appropriate transducer frequency depends upon the nature and depth of the area being examined. The examiner must consider the ‘dead zone’, ultrasonic wave attenuation and the proportion of the transmitted acoustic beam which is absorbed or scattered (Goldstein, 1993; Smith, 1996).

The ‘dead zone’ is defined as the distance from the transducer front face to the first identifiable echo and occurs as a result of transducer ringing and reverberations at the transducer/patient interface (Smith, 1996). In order to reduce the depth of the ‘dead zone’ the frequency of the transducer needs to be increased.

Ultrasonic wave attenuation, which refers to the loss of strength of acoustic waves as they travel through tissue, also needs to be considered. Higher frequency sound waves, 7-12 Mhz, are more severely attenuated than low frequency waves, under 5Mhz (Goldstein, 1993). So while the selection of a higher frequency would reduce the dead zone, it would be more severely attenuated.

Soft tissues absorb and scatter only a small proportion of the transmitted acoustic beam whereas bone absorbs a much larger proportion of ultrasonic waves reducing refraction greatly and giving a poorer ultrasonic image (Goldstein, 1993).
Plate 2.11

ACUSON 128 grey scale imager

Plate 2.12

Branic foot measuring device

Sliding guide for arch length evaluation
In the current study the depth of the ‘dead zone’ needed to be as small as possible because of the superficial nature of the tissues examined but the image needed to be clear enough for measurement. The lowest of the higher frequency transducers (7 Mhz) was chosen because the higher frequency transducers reduce the dead zone but lower frequencies decrease sound wave attenuation and improve the clarity of the image.

The display unit of the ultrasound machine houses a broadcast TV or cathode ray tube (CRT), the face of which is a two dimensional surface. The echo data is displayed on the screen as a two-dimensional image. The display mode used in the current study was the B-Mode or brightness mode in which the brightness of the CRT spot represents the amplitude of the echo received. The B-Mode image presents a set of cross-sectional image lines of the area scanned in a grey scale (Goldstein, 1993).

The keyboard of the ultrasound unit has several features allowing the operator to manipulate the image on the screen. In the current study two of these features, the freeze frame and calipers were needed to assist in evaluating the image. The freeze frame option allowed a single frame to be held on the screen when an appropriate image was presented. This permitted the operator to use the caliper option to measure the thickness of the tissues being examined. To activate the calipers the first caliper button was pressed and the caliper could then be moved over the screen to the appropriate position, with the aid of a positioning ball similar in function to a computer mouse. The second caliper button was then pressed and the second caliper was moved into position. The machine calculates the distance between the two caliper points and displayed the measurement at the bottom of the screen. A store
button was then pressed and the image chosen was filed in the hospital main frame computer.

2.5.2.2 Precautions - The biological effects of ultrasound

Ultrasound investigations release energy into the tissues being examined. It must therefore be accepted that some risk of injury or damage to the tissues may be possible (Kremkau, 1993).

Studies of the biological effect of diagnostic ultrasound on cells have thus far given varied results regarding harmful side effects. In 1982, Liebeskind et al reported alterations in the motility patterns of fibroblasts however M. Miller et al (1990) were unable to corroborate these results. In 1989, D. Miller et al demonstrated strand breaks in DNA when human leukocytes cells were exposed to various frequencies of ultrasound. Notwithstanding The American Institute of Ultrasound in Medicine (AIUM) concluded that because the studies had been in vitro, that the results obtained may not pertain to the in vivo situation and their clinical significance should be viewed with caution (AIUM, 1988). In general it appears that exposure to diagnostic ultrasound does not constitute any risk of a permanent nature to cells (Kremkau, 1993).

Tissue hyperthermia resulting from exposure to ultrasound is another area which has been examined as a potential risk factor, with a rise in temperature greater than 1°C being considered significant (AIUM, 1988). Fetal tissue seems to be at greatest risk of damage from over heating with Miller and Ziskin (1989) listing 79 biological consequences of hyperthermia in tests on animals including abortion, developmental abnormalities, skeletal deformities and cardiovascular abnormalities.
However research in this area has concluded that at frequencies between 2 and 10 MHz, tissues will not rise significantly above the 1° threshold (AIUM, 1988).

The final risk factor which must be considered when ultrasound is used is that of cavitation, the production and dynamics of bubbles in a liquid. Flynn (1982) found that cavities in tissue occurred with continuous, high-intensity ultrasound waves. The oscillation of these bubbles may cause them to collapse leading to the production of shock waves, light emission and extremely high temperatures (Kremkau, 1993). The AIUM (1988) investigated the cavitation mechanism and concluded that it was not possible, with the data available, to determine threshold pressure amplitudes at which acoustic cavitation will occur in mammals.

Other investigations of the risk factors of diagnostic ultrasound indicate that, at the frequency used in the current study, adverse biological effects should occur rarely, if at all (Kremkau, 1993). However a conservative approach was adopted in the current study, commensurate with obtaining a satisfactory image, by using the shortest time possible for each image acquisition.

2.5.3 Methods

2.5.3.1 Foot and arch length measurement

The left and right foot and arch lengths were measured using a Branic device. When the foot rests in the device the foot length was measured using the horizontal lines on the base of the machine. Arch length was assessed by moving a concave knob on the Branic device (see plate 2.12) until it rests beside the medial side of the 1st MTP joint. The Branic assigns a numeric value to foot and arch length; on average a foot size 8 should have an arch length 8. The foot length to arch length ratio (foot/arch ratio) was determined by dividing the foot length by the arch length.
If the arch length measurement is equal to the foot length the foot/arch ratio was 1. A low arched foot has a longer arch length therefore the foot/arch ratio is less than 1. A high arched foot has a shorter arch length therefore the foot/arch ratio is greater than 1.

2.5.3.2 Skin and Plantar Aponeurosis measurements

Skin thickness was evaluated by placing the centre of a wide 7-megahertz transducer parallel to the skin under the 1st MTP joint. It is important to avoid compression of the skin, so the transducer was placed lightly over the area being examined and care was taken to avoid the transducer coming into contact with the skin. The area of measurement was determined by visualisation of the apex of the curve of the skin over the base of the 1st metatarsal.

Plantar aponeurosis thickness was assessed while the subjects lie prone on the examination table. A line was drawn from the longitudinal bisection of the calcaneus to the 2nd/3rd intermetatarsal space. This line was measured, then bisected, and a second line was drawn at 90° to the first at the bisection point (plate 2.13). The wide 7-megahertz transducer was also used for plantar aponeurosis measurements. It was placed longitudinally over the centre of the foot at least 3cm from the insertion of the aponeurosis into the calcaneus. During both skin and aponeurosis measurements the transducer was placed parallel to the area being examined, placing the beam perpendicular to the structures being examined.

When a clear image was visible, it was frozen on the screen. Calipers were used to spot the superior and inferior margins of the skin and aponeurosis and the measurement was recorded. All images were stored on the hospital computer and examined by the radiologist and for future reference. Examples of skin and plantar aponeurosis measurements are shown in figure 2.14 and 2.15.
2.5.4 Definition of soft tissue abnormalities

The data analysis defined here pertains to evaluations undertaken in chapter 6. To enable comparisons with previous experiments only the foot with the thickest plantar aponeurosis or skin was used for further evaluation. Thickening of the plantar aponeurosis or skin was defined as greater than 2 standard deviations above the mean for the controls.

Plate 2.13

Foot markings for plantar aponeurosis evaluations
Plate 2.14

Plantar skin measurement

Arrows indicate superior and inferior limits of skin

Plate 2.15

Plantar aponeurosis measurement

Arrows indicate superior and inferior limits of aponeurosis
2.6 Consideration of error

2.6.1 Examination of joint mobility

The relative merits and problems associated with using goniometers when evaluating joint range of motion have been discussed in chapter 1, section 1.5. Potential sources of error identified were taken into consideration when designing the measurement protocols and will be discussed.

The accuracy and appropriateness of the dimensions of the instruments used for joint evaluation have been identified as contributing to their reliability and repeatability (Stratford et al, 1984). The long-armed goniometer was specifically designed to allow various leg lengths to be easily accommodated during the measurement of ankle dorsiflexion. The accuracy of the instruments used in the current study was determined before their inclusion. The tractograph, OED and long-armed goniometer were calibrated against known angles, between 0 and 180 degrees. Plus or minus one degree was considered acceptable (Nicol, 1989).

Many authors have found that intra-examiner error is much lower than inter-examiner error (Stratford et al, 1984; Diamond et al, 1989; Nicol, 1989; Bovens et al, 1990; Wright and Feinstein, 1992). Some have also concluded that the expertise of the examiner considerably improved reliability (Diamond et al, 1989; Wright and Feinstein, 1992). All joint measurement techniques in the current study were practiced before data collection to ensure proficiency. Inter-examiner error was not an issue in this study as all data was collected by the candidate.

There is some debate over the accuracy of using the mean of multiple measures rather than a single measurement to determine joint motion. Some examiners maintain that using the mean of multiple measurements of the same joint improves accuracy (Low, 1976; Nicol, 1987; Griffiths, 1988; Himes, 1989). Others
used single measurements of each joint ROM as they considered this to be as reliable as the mean of multiple measurements (Boone et al., 1978; Rothstein, 1983; Elveru et al., 1988). In the current study single measurements were used to evaluate the joint ROM. This was determined to be the best course of action as repeated measurements may have had the effect of mobilising the joints, an undesirable side-effect when limitation of joint motion was being evaluated.

Marker thickness has also been identified as a source of error when using skin markings to assist in the evaluation of joint motion (Kaye and Sorto, 1979). The ST, 1st MTP and ankle joint measurements all required lines to be drawn for accurate placement of the instrument. A 0.5mm fine-point marker was used in all tests in the current study in an attempt to minimize error.

Subject anxiety may also effect the results obtained in studies measuring joint motion. If the subjects are not at ease in their surroundings (Wright and Feinstein, 1992) or have not been fully advised of the techniques that will be employed during the examination, they may not relax sufficiently for the examiner to obtain accurate readings. This problem was overcome to some extent in the current study, as each subject was fully informed of testing procedures employed and was examined in comfortable surroundings, distanced from noisy distractions.

Strenuous activity may increase joint ROM and is therefore a potential source of error. This was controlled by each of the subjects being examined after midday and having undergone a series of non-strenuous examinations for 2 to 4 hours prior to their joint tests.

Unfortunately some other factors influencing the reliability of goniometric measurements are not as easily overcome as those outlined above. Variability in the location of bony landmarks, placement of skin markings and the subjective
determination of patient positioning have been suggested as sources of inaccuracies in goniometric measurement (Salter, 1955; Nicol, 1989). The ST joint motion has been highlighted as particularly subject to error of this type.

Reliability studies of the tractograph as an evaluation tool for measurement of ST joint inversion and eversion have been found to vary from poor (Boone, et al, 1978), to moderate (Elveru, 1988), to good (Diamond et al, 1989). In each of these studies the main objective has been to quantify inversion and eversion separately. In the current study these two aspects of coronal plane motion were not separated, only total ROM was assessed. This meant that some of the errors associated with this testing procedure were eliminated. The accurate determination of bony landmarks and positioning of bisection was not of importance when measuring the ST joint ROM in the current study, as the initial angular placement of the bisection lines drawn on the subject was of no consequence. If the ST joint was slightly inverted or everted when measurement was commenced, the end results of the total ROM remained constant.

However this factor did not influence the reliability of the 1st MTP and ankle joint measurement, as total ROM was not evaluated in these joints. Although care was taken to minimize the effects of these complicating factors by careful positioning and determinations of the landmarks being used, these variables cannot be dismissed in this study.

Variability in the force applied by the examiner when determining passive joint ROM has also been found to greatly alter joint measurements (Amis and Miller, 1982, Nicol, 1989). A device called the dynamometer has been designed to control force being applied when determining joint motion (Bohannon and Lieber, 1986 - cited in Spencer, 1994) but this instrument was not available to the examiner and
error due to variation in force cannot be ignored. In the current study the ability to use the examination techniques in a clinical setting was considered a priority. As dynamometers are not readily available to clinicians, its use was deemed to be inappropriate.

2.6.2 Examination of plantar pressure

The potential problems involved in collecting plantar pressure data have, to some extent, been addressed in section 2.6.1 but other confounding aspects will now be discussed.

Young in 1998, suggested that the walkway should be long enough to allow 7-8 steps and the width should be 1.5 to 2.0 meters. According to Young and Novel’s criteria the length and width of the walkway in which the subjects were examined was ample for the purpose. It was carpeted with a low pile carpet, a covering, which has been found to be acceptable for data collection (Novel, Pedar manual).

Standardized, Clark’s® ‘Detroit’ extra-depth school shoes were used for all examinations to eliminate variables such as shoe instability, in-built cushioning and wear and tear from previous usage (Cook et al, 1985). These shoes were chosen because they have a reinforced heel counter to improve stability and durability, and they do not have a cushioning sole. Following recommendations set out in the Pedar manual, hosiery was standardized by using thin nylon stockings during all tests.

Pressure exerted beneath the foot, even under perfect conditions, exhibit considerable variability (Cavanagh et al, 1992). The number of footfalls required to obtain a repeatable and reliable average of the subjects gait has been suggested as being between 3 and 6 (Young, 1998). In the current study the mid-four footfalls
were used for the examination of each subject. Pilot study results (see 2.7.1) showed that this was an acceptable number of steps to achieve a repeatable outcome.

The speed at which a subject walks during testing has been shown to alter foot pressure measurements significantly (Kernozek et al, 1996). In the current study, free walking was used but the contact time during each test was evaluated to determine if any significant changes in plantar pressure might have resulted from changes in speed. The results of the pilot study (see 2.7.1) allowed this method of speed analysis to be used with confidence.

The lesser number of sensors and lower frequency of data collection of the Pedar (sampling rate, 50Hz) may have lead to some inaccuracies but the nature of the study made use of a platform device impractical.

### 2.6.3 Examination of interventions

Apart from the sources of error already discussed in sections 2.6.1 and 2.6.2, the complicating factor of contoured orthoses need to be considered in this section of the study. As force and pressure measuring plates and insoles are only able to measure vertical impact on sensors, the contours of the orthoses may interfere with the integrity and magnitude of pressure being displayed. Schaff (1993) points out that Pedar insoles are not highly flexible in three dimensions and therefore lack the ability to mould to the contours of an orthotic device. However as the testing method was identical in all evaluations comparative analysis should provide repeatable and reliable data.

The neutral casting of patients for the fabrication of orthoses is widely used. The techniques described for neutral casting (Root et al, 1971; Valmassey, 1979; Ross and Jones, 1982; McCrea, 1985) and the evaluation procedures for determining
the 'neutrality' of a cast (Ross and Jones, 1982) is extremely subjective. Regardless of the care taken minor variations in position and therefore cast morphology may result but many of the aspects of casting inaccuracy can be monitored by the examiner (Ross and Jones, 1982).

Variations may also have occurred during the fabrication of the thermoplastic orthoses. Inadvertently inverting or everting the device to some degree may have influenced the function of the device. Valmassey (1984) and Cusick (1990) suggest that a congruent alignment in children be achieved by maintaining the calcaneus in a position vertical to the supporting surface although this may not necessarily indicate a true neutral foot position. This method of orthoses manufacture was adopted in this study but inadvertently altering the rearfoot alignment as a result of unintentional deviation from the protocol may have changed foot function and altered the pressure readings obtained. Incorrectly locating the flexion points of the 1st and 5th MTP joints may also have resulted in the finished orthoses being too short or too long. To minimize inter-operator error all devices were constructed personally.

Finally the time lapse and effect of adjusting to orthoses may have effected the non-intervention pressure measurements vs. intervention measurements so all subjects fitted with orthoses had all four measurements undertaken at the same session.

2.6.4 Examination of soft tissue

The same machine was utilised for all ultrasonic images thus between-machine variance was not an issue. Factors outlined in experiment no. 1 such as patient apprehension, inter-tester variability, single verses multiple measurements,
correct location of landmarks and correct placement of instrumentation also pertain to this experiment.

Although not an ultrasonographer, the examiner had twelve months training in the protocol used and was proficient in the use of the equipment before data collection commenced. To assess the correct use of the equipment, in particular the accuracy of placement of the calipers used for measuring the soft tissues, all ultrasound tests were examined and measurements verified by the Associate Professor of Radiology at The Children’s Hospital at Westmead.

It was found, through initial experimentation, that during skin examinations accuracy was improved by placing the transducer head approximately 3mm from the skin surface. Distances greater than this tended to distort the image on the screen and made visualisation of the skin layers more difficult. It was also found that with repeated use the coupling gel became more liquid, distorting the image so new gel was used for each evaluation. As the transducer was not in contact with the skin surface during measurement of the skin thickness, it was important not to use the proximal or distal edges of the transducer. If the centre of the transducer was not directly over the 1st MTP joint the image was distorted and the measurement suffered accordingly.

The final areas identified as a possible source of error were related to the actions of the subject during the examination. If the subject was moving at all or talking to the examiner the accuracy of the measurements declined so all subjects were asked to remain still and quiet during the examination.
2.7 Further considerations of examination methods

2.7.1 Accuracy of examination methods

To examine the repeatability of the methods used to evaluate joint motion, plantar pressure and soft tissue changes various pilot studies were undertaken.

The repeatability of the methods used for the evaluation of ST, 1st MTP and ankle joint motion, was assessed by examining four subjects (2 diabetic and 2 non-diabetic adolescents) once a week over a ten week period. The methods used were identical to those described earlier in this chapter. The various instruments were operated with the measurement shielded from the operator to avoid expectation bias (Stratford et al, 1984).

The examinations were not performed by repeated examinations during the same session because it was likely that the actual examination process would mobilise the joints being tested, giving greater ROM readings as testing progressed. The coefficient of variation for the ST joint measurements was 5.2%, for the 1st MTP joint was 4.2% and for the ankle joint was 5.8%. The intraclass correlation coefficients (ICC 3,1) for ST joint measurement was 0.90, the 1st MTP joint was 0.81 and the ankle joint 0.89 with the knee flexed and 0.88 knee extended.

The repeatability of the method used for pressure analysis was evaluated by assessing 8 non-diabetic adolescents five times each over two testing sessions. The results of intraclass correlation coefficients (ICC, 3,1) were evaluated for the various areas of the foot examined (Table 2.1).
Table 2.1

Intraclass correlation coefficients values for the repeatability of examinations using the Novel Pedar

<table>
<thead>
<tr>
<th>Area of foot examined</th>
<th>Peak Pressure</th>
<th>Pressure time integrals</th>
<th>Contact time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full foot</td>
<td>0.92</td>
<td>0.84</td>
<td>0.93</td>
</tr>
<tr>
<td>Plantar metatarsal</td>
<td>0.82</td>
<td>0.88</td>
<td>N/A</td>
</tr>
<tr>
<td>Plantar hallux</td>
<td>0.73</td>
<td>0.74</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A = not assessed

To assess the relationship between walking speed and contact time five subjects were tested two times each on a treadmill at 2.5km/hr, 3.0 km/hr, 3.8 km/hr, 5km/hr and 7.5km/hr. The results of this study showed that a broadly linear inverse relationship exists between speed and contact time \( r = -0.98 \). As speed increases contact time decreases (Figure 2.1).

Figure 2.1

Relationship of Contact time to speed

The x axis represents varying increments in speed –
0% = 2.5k/hr, 20% = 3.0k/hr, 50% = 3.8k/hr, 100% = 5k/hr, 200% = 7.5k/hr
To evaluate the repeatability of the Branic measurement protocol, a pilot study was undertaken which examined six subjects on five occasions. The ICC (3,1) values for the foot length was 0.96 and for the foot/arch ratio was 0.92.

To assess test-retest variability of ultrasonic measurements four subjects were measured, ten times in the same session. To avoid expectation bias the measurements obtained were shielded from the examiner until all measurements were completed and stored on computer. The ICC value for the skin measurement was 0.92, for the aponeurosis was 0.89.

The evaluation criteria suggested by Portney and Watkins in 1993, states that intraclass correlation coefficient values above 0.75 show good reliability. The only tests which showed values below 0.75 were pressure measurements under the hallux and these values were very close to the values recommended by Portney and Watkins.

2.7.2 Potential side effects from examinations

Joint motion and pressure analysis examination, do not display any potential side effects. The only examination, which may have significant side effects, was ultrasound. The potential problems to subjects being evaluated with this modality have been considered in some detail in section 2.5.2.2 of this chapter.

2.7.3 Ethical issues

All subjects or their parents, when appropriate, gave informed consent before any examinations were undertaken. Subjects had the relevance of all procedures fully explained. Any abnormalities detected were explained to both diabetic and control
subjects and appropriate advice was given as to treatment options. When orthoses were suggested the cost of the appliances was borne by the candidate.

All data collected was stored on either the main computer at The Children’s Hospital at Westmead or on the candidate’s portable computer. Data was only available by password, to those involved in the study. No data was shared with any external organization.

2.8 Statistical evaluations

The SAS software package (SAS Institute, Cary, NC, USA) was used to analyse the data for all studies in this thesis. The significance level was determined as $P \leq 0.05$. The two sample Student’s $t$-test was used to compare continuous variables between the diabetic and control groups when the distribution of data was normal. The Wilcoxon’s rank sum test was used otherwise. The Chi-square test was used to test associations between categorical data. Diabetic subjects were screened to evaluate the sensitivity and specificity of LJM as an indicator of microvascular complications of diabetes.

The formula used for testing sensitivity is; $\frac{a}{a + c}$, for specificity is; $\frac{d}{b + d}$, where $a$ is the number of subjects with a true positive result, $b$ is the number with a false positive result, $c$ is the number with a false negative result and $d$ those with a true negative result.

Interventions were analysed using a one-way repeated measures analysis of variance (ANOVA). ANOVA’s were performed on measurements from the three interventions and non-intervention condition, then with the three interventions alone. A post hoc comparison with Bonferroni’s adjustment was used to determine differences among the intervention means. The 12 month follow-up measurements
for diabetic subjects with and without orthoses was evaluated using the paired \( t \)-test when the distribution of data was normal or the Wilcoxon signed-ranks test otherwise. Non-intervention peak pressure, pressure time integrals and contact times were evaluated during the 12 month follow-up.

Logistic regression was undertaken on all of the variables evaluated. Continuous data were stratified into four equal quartiles to evaluate correlations between increasing abnormality and microvascular complications of diabetes. Multivariate logistic regression was used to evaluate associations between plantar aponeurosis thickness, foot size and gender.

2.8.1 Consideration of statistical methods

Various forms of statistical analyses were utilized to determine variations between the diabetic and non-diabetic control groups and also to evaluate intra-group variations. In the latter case the experimental subjects were diabetic subjects displaying an abnormality and the control group consisted of diabetic subjects without this abnormality. The central tendency of data was calculated to investigate its spread and distribution. This procedure involves determining the dispersion of scores gathered i.e. whether the distribution is normal, forming a simple bell curve or skewed to the left or right. It was undertaken to allow further appropriate statistical analysis.

The two sample Student’s \( t \)-test and paired \( t \)-tests were used for the initial analyses when the distribution of data was normal, parametric. These are robust testing methods which evaluate the mean of the sample scores. This reflects the average score, the standard deviation and the variability of score around the mean. The SAS statistics package automatically analyses \( t \)-tests with both pooled and
separate standard deviation estimates and indicates the F-ratio and \( p \) values for each
test. The F-ratio calculates the variance between group means relative to the variance
within the groups. If the F-ratio is greater than 1.0, the between-groups variance is
high and the null hypothesis is rejected, the variation is significant. The pooled
standard deviation score were used for all tests.

If the data distribution was not normal, non-parametric, the Wilcoxon’s rank
sum test or Wilcoxon signed-ranks tests were applied. These tests have similar
applications to the \( t \)-test but instead of using the mean and standard deviation for
calculations they use the median and interquartile range. The median (50\(^{\text{th}}\) percentile)
is the score at which 50\% of the scores fall above and 50\% below. The interquartile
range indicates the difference between the 25 percentile and 75 percentiles in a
distribution. Non-parametric analysis is useful when population normality and
homogeneity are questionable. This testing procedure applies a ranking of each score
from smallest to largest with the smallest score being assigned the rank of 1 and the
largest \( n \), tied scores are given the same rank. Therefore the sum of the ranks for the
two groups being examined should be equal if no variation is present. The
Wilcoxon’s rank sum test assumes that the two groups being examined are from the
same population and significant values indicate differences between the groups.

An analysis of categorical data was undertaken using the Chi square statistic.
This method of analysis uses actual numbers of persons, objects or events in specific
categories. Ranks or percentages cannot be used with this form of analysis. The
significance of any variation between groups is analysed using critical values of \( \chi^2 \)
and a \( p \) value is determined.

Sensitivity and specificity testing were undertaken to determine the validity
of using screening tests to accurately assess the presence or absence of other
conditions. The sensitivity of a screening method tests its ability to obtain a true positive. The specificity of a screening method tests its ability to obtain a true negative. That is, a test is more sensitive when it is able to identify a large number of persons who have that condition. Conversely a screening method is more specific when it accurately identifies subjects who do not have that condition. Unfortunately there is usually some trade-off when examining sensitivity and specificity. Rendering a screening method more sensitive, will often make it less specific. In the current study it would be more desirable to have a simple screening test for microvascular complications of diabetes which has high sensitivity. Results are rated between 0.00 and 1.00; the closer to 1.00, the higher the sensitivity and specificity.

Variations between interventions used in this thesis were analysed using a one-way repeated measures analysis of variance (ANOVA). This form of analysis is used for parametric data in place of repeated t-tests. to avoid generating a type 1 error, that is rejecting the null hypothesis when in fact no statistical variation between treatments is evident. This form of analysis is useful when repeated experiments are performed on the same subjects. In repeated measures design all subjects must be tested under the same conditions. The ANOVA results are given in the form of F-ratio and P value and reflect variability between the examination states. However ANOVA testing does not indicate significant variations between individual intervention means. To allow analyses of this aspect of the study post hoc testing with Bonferroni's adjustment was used. This testing procedure enables multiple comparisons of paired data to be achieved by essentially reducing the α (alpha) value by the number of tests being undertaken. For example if four tests are undertaken with a desired overall probability of 0.05 each individual comparison would require a
significance value of 0.013 (0.05 / 4). The post hoc testing with Bonferroni’s adjustment again reduces the chance of generating a type I error.

Stratification was undertaken to ‘partition’ continuous data into four subsets. Using this method of evaluation subject characteristics were divided into quartiles, ranging from the least affected to the most affected. This allows the examination of each subset against complication outcomes. Stratification can increase the precision of data analysis when the stratified variable is closely related to the variable of experimental interest. This technique also allows the examiner to explore any trends within data, for example a relationship between increasing skin thickness and sensory neuropathy.

Logistic regression is a form of multiple regression analysis, used to examine dichotomous variables. It is useful when the examiner wishes to establish the risk of getting a disease under given conditions. Logistic regression yields a value between 0 and 1, which represents the odds of getting a disease. This coefficient is then converted to an odds ratio which represents how the odds of getting a disease will change with a one unit change in the exposure variable. An odds ratio of 10 indicates that for every one unit change in the exposure variable, the odds of getting a disease increases 10 times.

Multivariate logistic regression analyses the relationship between one dependent variable and a set of predictor variables. Using this method the relative importance of one predictor variable can be examined against another. This method of statistical examination can be used to determine the importance of one predictor variable after allowing for the influence of other predictor variables.

Intraclass correlation coefficients were performed to determine the reliability of the testing methods used in this thesis. Historically correlation coefficients have
been widely used to evaluate test-retest reliability but these scores are more an indicator of correlation rather than reliability. From a clinical perspective it is often the repeatability of the measurement, which is of greater importance. The intraclass correlation coefficient (ICC) is a reliability coefficient, which uses analysis of variance to estimate variance. There are six different equations used in ICC calculations used for evaluating both inter and intra rater reliability. In this study ICC (3,1) was used. The first number in parentheses designates the model used (either 1, 2 or 3), the second number indicates whether each evaluation was a single measurement (1) or the mean of several measurements (\(k\)), where \(k\) indicates the number of measurements. Models 1 and 2 are used for multiple raters evaluating inter-rater reliability. Model 3 is used to evaluate repeated measures of a single rater and was considered the most appropriate for this study. This ICC model uses a repeated measures analysis of variance design and reliability rating of 0.00 to 1.00 are given. Values closer to 1.00 represent stronger reliability.
CHAPTER 3

LIMITED JOINT MOBILITY IN YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS

Two hundred and sixteen young people with T1DM and 57 non-diabetic controls had subtalar, 1st MTP, ankle, finger and toe mobility assessed using goniometry.

Chapter 3A

Comparison of the current study with Duffin et al study, 1999.

The aims of this section are:

i) To investigate the presence of joint motion in young people with T1DM compared to non-diabetic controls.

ii) Using the definition for LJM described by Duffin et al in 1999, Appendix 1 (critical values were used); compare findings from the current study to those found in 1999.

iii) To examine the relationship between LJM and microvascular complications of DM using critical values for LJM defined in 1999.

Chapter 3B

Defining LJM as two standard deviations below the control mean

The aims of this section are:

i) To redefine LJM, establishing a uniform method of statistical evaluations between this and subsequent chapters in this thesis.

ii) To evaluate the relationship between LJM and microvascular complications of DM using 2 SD below control mean to define LJM.

iii) To determine if a simple single joint test could be used to detect subjects with complications of diabetes.
3.1 Characteristics and joint mobility of diabetic subjects vs. non-diabetic controls in the current study

The comparison of joint motion in the diabetic and control subjects in the current study is shown in table 3.1. There was no significant difference in age or gender between diabetic and control subjects. Ankle flexion, with the knee extended, was the only joint which did not show significantly less motion in the diabetic subjects. The range of motion in all other joints was significantly lower in diabetic subjects compared to non-diabetic controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n = 57)</th>
<th>Diabetes (n = 216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - years</td>
<td>15.6 [13.8 - 16.4]</td>
<td>15.3 [13.5 - 16.8]</td>
</tr>
<tr>
<td>Gender - male : female</td>
<td>27 : 30</td>
<td>103 : 113</td>
</tr>
<tr>
<td>Subtalar joint - ROM</td>
<td>30° [28-34]</td>
<td>28° [25-31] *</td>
</tr>
<tr>
<td>1st MTP joint - ROM</td>
<td>72° [70-76]</td>
<td>67° [60-72] *</td>
</tr>
<tr>
<td>Ankle flexion (knee extended)</td>
<td>100° [96-103]</td>
<td>99° [96-102]</td>
</tr>
<tr>
<td>Ankle flexion (knee flexed)</td>
<td>115° [113-121]</td>
<td>113° [108-119] †</td>
</tr>
<tr>
<td>Finger LJM (% affected)</td>
<td>0%</td>
<td>13% †</td>
</tr>
<tr>
<td>Toe LJM (% affected)</td>
<td>10%</td>
<td>22% †</td>
</tr>
</tbody>
</table>

The results are given as median [interquartile range]. **Bold** indicates significant difference between diabetic and control subjects, *P < 0.01, †P < 0.05
Comparison of the current study with Duffin *et al*, 1999.


The data for the Duffin *et al*, 1999 study were collected between 1990 and 1996. The paper can be found in Appendix 1. The data for the current study were collected between 1996 and 2001. There was no significant difference in age, gender or joint range of motion of the diabetic subjects examined in the two studies except for toe LJM which was significantly more common in the current study (*P* = 0.01). Data from the two studies is shown in Table 3.2. The ankle joint was not assessed in the 1999 study and the hip joint was not assessed in the current study.

Table 3.2

Characteristics of diabetic subjects - current study vs. 1999 study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Current study Diabetes (n = 216)</th>
<th>1999 study Diabetes (n = 302)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - years</td>
<td>15.3 [13.5 – 16.8]</td>
<td>14.6 [13.4 – 16.4]</td>
</tr>
<tr>
<td>Gender - <em>male : female</em></td>
<td>103 : 113</td>
<td>144 : 158</td>
</tr>
<tr>
<td>Duration - <em>years</em></td>
<td>6.0 [3.9 – 10.2]</td>
<td>6.2 [4.0 – 9.8]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - <em>%</em></td>
<td>8.6</td>
<td>8.4</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; MTP joint - <em>ROM</em></td>
<td>67° [60 - 72]</td>
<td>67° [60 – 73]</td>
</tr>
<tr>
<td>Finger LJM (<strong>% affected</strong>)</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td>Toe LJM (<strong>% affected</strong>)</td>
<td><strong>22%</strong></td>
<td>14%</td>
</tr>
</tbody>
</table>

The results are given as mean (SD) or median [interquartile range]. **Bold** indicates significant difference between diabetic subjects from the current and 1999 study, *P* = 0.01
3A.2 Comparisons of age, gender and joint motion of non-diabetic control subjects in the current study and Duffin et al, 1999

There was no significant difference in gender or joint range of motion of the control subjects examined in the two studies. Age was the only characteristic, which showed any significant difference between the two groups. Control subjects in the current study were significantly older than those in the 1999 study ($P = 0.01$). Data from the two studies are shown in Table 3.3.

**Table 3.3**

Characteristics of control subjects - current study vs. 1999 study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Current study Controls ($n = 57$)</th>
<th>1999 study Controls ($n = 51$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age - years</strong></td>
<td>15.6 [13.8 - 16.4]$^*$</td>
<td>13.9 [12.2 - 16.1]</td>
</tr>
<tr>
<td>Gender - <em>male : female</em></td>
<td>27 : 30</td>
<td>23 : 28</td>
</tr>
<tr>
<td>Subtalar joint - ROM</td>
<td>30° [28 - 34]</td>
<td>31° [28 - 35]</td>
</tr>
<tr>
<td>1st MTP joint - ROM</td>
<td>72° [70 - 76]</td>
<td>73° [67 - 78]</td>
</tr>
<tr>
<td>Finger LJМ (% affected)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Toe LJМ (% affected)</td>
<td>10%</td>
<td>8%</td>
</tr>
</tbody>
</table>

The results are given as mean (SD) or median [interquartile range]
Bold indicates significant difference between the control subjects from the current and 1999 study, $*P = 0.01$. 
3A.3 Comparison of diabetic subjects affected by LJM in the current study and Duffin et al., 1999

To allow comparisons with the 1999 study, critical values established in 1999 were used. The critical values for LJM in the 1999 study were defined as less than the fifth percentile reference for controls in that study. In the current study twenty-one percent of diabetic subjects had a ST joint range of motion less than or equal to 25.3°. They were predominantly male and had diabetes for a significantly longer period than those with ST joint motion greater than 25.3° ($P < 0.05$). In the 1999 study thirty-five percent had ST joint motion less than 25.3°. They were predominantly male and were more likely to have retinopathy and elevated AER ($P < 0.03$). Significantly fewer subjects had less than 25.3° of ST motion in the current study when compared to the 1999 study ($P < 0.001$).

In the current study sixteen percent of diabetic subjects had a 1st MTP joint range of motion less than or equal to 57.3°. They were predominantly male ($P < 0.05$) and were significantly older than those with 1st MTP joint motion greater than 57.3° ($P < 0.01$). In the 1999 study eighteen percent had 1st MTP joint motion less than 57.3°. They were older and more likely to have retinopathy and elevated AER ($P < 0.01$).

In the current and 1999 studies thirteen percent of diabetic subjects had finger LJM. In the current study those with finger LJM had higher HbA$_{1c}$ levels and were more likely to have retinopathy than those without ($P < 0.05$). In the 1999 study those with finger LJM were older, had longer duration of diabetes, higher HbA$_{1c}$, retinopathy, elevated AER than those without finger LJM ($P < 0.05$). In the current study twenty-two percent of diabetic subjects had toe LJM, they were older than
those without toe LJM ($P < 0.05$). In the 1999 study fourteen percent had toe LJM and no significant associations were found ($P > 0.05$). The only association with microvascular complications of diabetes found in the current study cohort was with finger LJM and retinopathy ($P < 0.05$). Significantly more subjects had toe LJM in the current study when compared to the 1999 study ($P = 0.01$) (Table 3.4).

Table 3.4

Comparison of percentage of diabetic subjects affected by LJM and significant associations with other characteristics - current study vs. 1999 study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Current study ($n = 216$)</th>
<th>Significant associations</th>
<th>1999 study ($n = 302$)</th>
<th>Significant associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtalar joint - % affected $&lt; 25.3^\circ$</td>
<td>21% $^1$</td>
<td>Male, longer duration</td>
<td>35%</td>
<td>Male, retinopathy, AER &gt; 7.5</td>
</tr>
<tr>
<td>1st MTP joint - % affected $&lt; 57.3^\circ$</td>
<td>16%</td>
<td>Male, older</td>
<td>18%</td>
<td>Older, retinopathy, AER &gt; 7.5</td>
</tr>
<tr>
<td>Finger LJM - % affected $&lt; 180^\circ$</td>
<td>13%</td>
<td>Higher HbA1c, retinopathy</td>
<td>13%</td>
<td>Older, longer duration, higher HbA1c, retinopathy, AER &gt;7.5</td>
</tr>
<tr>
<td>Toe LJM - % affected $&lt; 180^\circ$</td>
<td>22% $^*$</td>
<td>Older</td>
<td>14%</td>
<td>No associations found</td>
</tr>
</tbody>
</table>

**Bold** indicates significant difference between the percentage of subjects affected by LJM in the current study compared to the 1999 study. $^* P = 0.01$, $^1 P < 0.001$
3A.4 Comparison of diabetic subjects affected by microvascular complications in the current study and Duffin et al, 1999

In the current study background retinopathy was present in 28% of the diabetic subjects tested, elevated AER in 26%. In the 1999 study 34% had background retinopathy and 44% elevated AER. A reduction in both complications was noted in the current study compared to the 1999 study, although this only reached a statistically significant level for those with elevated AER ($P = 0.001$) (Table 3.5).

<table>
<thead>
<tr>
<th>Microvascular complication</th>
<th>Current study Diabetes ($n = 216$)</th>
<th>1999 study Diabetes ($n = 302$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinopathy (% affected)</td>
<td>58 / 208 (28%)</td>
<td>61 / 237 (34%)</td>
</tr>
<tr>
<td>AER &gt; 7.5 (% affected)</td>
<td><strong>51 / 193 (26%)</strong> *</td>
<td>97 / 198 (44%)</td>
</tr>
</tbody>
</table>

**Bold** indicates significant difference in diabetic subjects with microvascular complications of DM in the current and 1999 studies. * $P = 0.001$

3A.5 Discussion

The overall comparisons of median range of joint motion of the diabetic subjects compared to non-diabetic controls in the current study showed that joint motion was significantly reduced in diabetic subjects at the ankle joint (knee flexed), ST joint, 1st MTP joint, fingers and toes.
Ankle joint motion was not assessed in the previous study (Duffin et al., 1999) but the diabetic and control median range of joint motion at ST joint, 1st MTP joint and fingers in the current study were almost identical to those obtained in 1999 study. The only test which showed any significant change between the current and the earlier study was toe LJMs, which was present in 14% of those tested in 1999 and 22% in the current study. Hammer and claw toe deformities, the inability to fully extend the toes, seen in the diabetic subjects tested is potentially a very serious problem. Up to 25% of all neuropathic ulcers in adults with diabetes occur as a result of hammer and claw toes being irritated by footwear (Edmonds et al., 1986). The clinical implications of this finding will be discussed in the final chapter.

Using critical values established in the 1999 study the percentage of diabetic subjects affected with LJMs at the 1st MTP joint and fingers was almost identical in the current study when compared to the previous study. However a significantly lower percentage of diabetic subjects were affected at the ST joint in the current study (35% in 1999 vs. 21% current). Associations found between LJMs of the ST and 1st MTP joints and retinopathy and elevated AER in the earlier study were not replicated in the current study even though data evaluation methods were identical. In the current study LJMs of the fingers was the only test which showed an association to retinopathy, none showed a direct association with elevated AER.

Several factors need to be considered in order to understand the variations between the two studies. First it needs to be noted that it was not only the correlation between joint motion and microvascular complications that changed in the current study but the percentage of subjects displaying microvascular complications was lower as was the percentage of diabetic subjects with LJMs at the ST joint. Background retinopathy was found in 34% of adolescents in 1999 and 28% in the
current study. Elevated AER was significantly lower; 44% of adolescents tested in the 1999 study showed this abnormality and 27% in the current study.

The two studies have encompassed a period of over 12 years. In this time examiners of retinal and renal complications have changed and this may have lead to some variation in these results. However, the same examiner assessed LJM at the ST joint and the number of subjects affected was significantly lower than in the previous study. These differences may be due to normal variation between the two groups tested, unintentional variations in examination technique or hopefully, improved management of diabetes.

The reduced number of diabetic subjects with elevated AER, retinopathy and LJM at the ST joint may reflect the success of regular complications screening clinics. The subjects’ diabetes duration (6.2 years, previous vs. 6.0 years, current) and mean HbA1c (8.4%, previous vs. 8.6%, current) in both studies were very similar and the subjects in the current study were marginally older (median 14.6 years, 1999 vs. 15.3 years, current). As complications of diabetes are often associated with increasing age one would expect the percentage of subjects with retinal, renal and joint complications to increase rather than decrease. Notwithstanding, whatever the reasons for the variations between the two studies the reduced number of diabetic subjects who presented with complications of diabetes must have had a great impact on the association between LJM and retinopathy, and particularly LJM and elevated AER.

The only abnormality found more frequently was LJM in the toes. In the current study 22% of diabetic subjects were unable to extend all the toes to 180° while only 14% were effected in the previous study. This variation may be explained by the small difference in the age of the subjects tested in the two studies. The median age of the diabetic adolescents in the 1999 study was 14.6 years (IQR: 13.4 – 16.4).
In the current study the median age was 15.6 years (IQR: 13.8 – 16.4 years). As this abnormality is related to increasing age the slightly older subjects in the current study would be more likely to have developed it.

3A.6 Conclusions

Some variations between the previous and current study were noted but the overall comparisons between the two studies showed close similarities. The two control groups only showed a significant variation in the age of the subjects tested. Median joint motion in these two groups showed no significant variations. The two diabetic groups only showed a significant difference in the number of subjects affected with toe LJM. Median joint motion in the two diabetic groups showed no significant variations.

The close similarities in the median joint ROM between two control groups and between the two diabetic groups indicate that the testing methods did not vary greatly over the period between the two studies. This gave the examiner confidence in the examination techniques used.
3B Defining LJM as 2 standard deviations below the control mean

3B.1 Comparisons of diabetic subjects with and without LJM

Using two standard deviations below the control mean for the determination of LJM in subjects with diabetes, LJM was found in 9% at the ST joint, 30% at the 1\textsuperscript{st} MTP joint, and 4% at the ankle joint with the knee flexed. Inability to extend the fingers passively was present in 13% of diabetic subjects but in none of the controls. The inability to extend the toes passively (hammer or claw toe deformity) was present in 22% of the diabetic subjects and 10% of controls.

Potential associations with retinopathy, elevated AER and early sensory nerve change were examined in the five joints, which had significantly reduced ROM compared to the controls (tables 3.6, 3.7, 3.8, 3.9, 3.10).

Only ankle joint LJM showed a predominance of females ($P = 0.04$). All other tests for LJM in young people with diabetes showed a predominance of males, although this only reached significant levels in those effected at the ST and 1\textsuperscript{st} MTP joints ($P < 0.01$). Diabetic subjects with LJM at the 1\textsuperscript{st} MTP joint and / or the toes were significantly older than those without ($P \leq 0.05$). Those with LJM at the 1\textsuperscript{st} MTP joint also had diabetes for a significantly longer period than those without LJM at this joint ($P \leq 0.05$). Limited joint mobility in the fingers was associated with higher HbA$_{1c}$ levels ($P \leq 0.05$).

The only joints, which showed any association between LJM and microvascular changes, were the STJ and fingers. The ST joint showed an association between LJM and sensory nerve abnormality ($P \leq 0.05$) and finger LJM was associated with retinopathy ($P \leq 0.05$).
Diabetic subjects with limited joint mobility in one foot joint were likely to also have LJM in other foot joints assessed. Subtalar joint LJM was significantly associated with LJM at the 1st MTP joint and toes ($P < 0.02$). Limited joint mobility in the fingers was only significantly associated with LJM in the toes ($P = 0.01$). Subjects with LJM in the fingers were also more likely to have LJM in other foot joints but this association did not reach significant levels.
Table 3.6

Characteristics of diabetic subjects with LJM ( < 22°) at the subtalar joint

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM (n = 196)</td>
</tr>
<tr>
<td>Gender - M : F</td>
<td>87 : 109</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.3 [13–17]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 [7.9–9.1]</td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.0 [3.8–10]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>27 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 μg/min</td>
<td>28 %</td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>38 %</td>
</tr>
<tr>
<td>1st MTP joint LJM</td>
<td>28 %</td>
</tr>
<tr>
<td>Ankle joint LJM</td>
<td>5 %</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>20 %</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>12 %</td>
</tr>
</tbody>
</table>

The results are given as percentage affected or median [interquartile range]. **Bold** indicates significant differences between diabetic subjects with LJM at the ST joint and those without. * P ≤ 0.01, † P < 0.05
Table 3.7

Characteristics of diabetic subjects with LJM ( < 60°) at the 1st MTP joint

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM</td>
</tr>
<tr>
<td></td>
<td>(n = 151)</td>
</tr>
<tr>
<td>Gender (M : F)</td>
<td>63 : 88</td>
</tr>
<tr>
<td>Age - years</td>
<td>15 [13–16]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 [8.0–9.1]</td>
</tr>
<tr>
<td>Duration - years</td>
<td>5.6 [3.8–9.2]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>25 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>29 %</td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>32 %</td>
</tr>
<tr>
<td>Subtalar joint LJM</td>
<td>6 %</td>
</tr>
<tr>
<td>Ankle joint LJM</td>
<td>5 %</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>19 %</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>10 %</td>
</tr>
</tbody>
</table>

The results are given as percentage affected or median [interquartile range]. **Bold** indicates significant differences between diabetic subjects with LJM at the 1st MTP joint and those without, * \(P \leq 0.01\), † \(P < 0.05\)
Table 3.8

Characteristics of diabetic subjects with LJM ( < 180° of extension) in the fingers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM</td>
</tr>
<tr>
<td></td>
<td>(n = 184)</td>
</tr>
<tr>
<td>Gender - M : F</td>
<td>86 : 98</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.0 [14–17]</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.5 [20–25]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.3 [7.9–9.0]</td>
</tr>
<tr>
<td>Duration - years</td>
<td>5.9 [3.8–9.7]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>24 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 μg/min</td>
<td>25 %</td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>40 %</td>
</tr>
<tr>
<td>Subtalar joint LJM</td>
<td>8 %</td>
</tr>
<tr>
<td>1st MTP joint LJM</td>
<td>29 %</td>
</tr>
<tr>
<td>Ankle joint LJM</td>
<td>4 %</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>20 %</td>
</tr>
</tbody>
</table>

The results are given as percentage affected or median [interquartile range]. **Bold** indicates significant differences between diabetic subjects with LJM in the fingers and those without, *P ≤ 0.01, † P < 0.05.
Table 3.9

Characteristics of diabetic subjects with LJM ( < 180° of extension) in the toes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM (n = 167)</td>
</tr>
<tr>
<td>Gender - M : F</td>
<td>75 : 92</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.2 [14–17]</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.7 [20–25]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 [7.9–9.1]</td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.1 [3.9–10.0]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>25 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>27 %</td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>38 %</td>
</tr>
<tr>
<td>Subtalar joint LJM</td>
<td>7 %</td>
</tr>
<tr>
<td>1st MTP joint LJM</td>
<td>28 %</td>
</tr>
<tr>
<td>Ankle joint LJM</td>
<td>4 %</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>10 %</td>
</tr>
</tbody>
</table>

The results are given as percentage affected or median [interquartile range]. **Bold** indicates significant differences between diabetic subjects with LJM in the toes and those without, *P = 0.01, †P = 0.05
Table 3.10

Characteristics of diabetic subjects with LJM (\(< 100.5^\circ\)) at the ankle joint (knee flexed)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM ((n = 207))</td>
<td>with LJM ((n = 9))</td>
<td></td>
</tr>
<tr>
<td>Gender - (M : F)</td>
<td>102 : 105</td>
<td>1 : 8 (P = 0.04)</td>
<td></td>
</tr>
<tr>
<td>Age - years</td>
<td>15 [14-17]</td>
<td>17 [15-18]</td>
<td></td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.4 [7.8-8.1]</td>
<td>8.9 [8.2-9.0]</td>
<td></td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.0 [3.8-10.2]</td>
<td>6.9 [5.3-10.3]</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>27 %</td>
<td>50 %</td>
<td></td>
</tr>
<tr>
<td>AER (\geq 7.5 \mu g/\text{min})</td>
<td>27 %</td>
<td>25 %</td>
<td></td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>40 %</td>
<td>44 %</td>
<td></td>
</tr>
<tr>
<td>Subtalar joint LJM</td>
<td>10 %</td>
<td>0 %</td>
<td></td>
</tr>
<tr>
<td>1st MTP joint LJM</td>
<td>31 %</td>
<td>11 %</td>
<td></td>
</tr>
<tr>
<td>Toe LJM</td>
<td>22 %</td>
<td>33 %</td>
<td></td>
</tr>
<tr>
<td>Finger LJM</td>
<td>13 %</td>
<td>0 %</td>
<td></td>
</tr>
</tbody>
</table>

The results are given as percentage affected or median [interquartile range]. **Bold** indicates significant differences between diabetic subjects with LJM at the ankle joint (knee flexed) and those without, \(P = 0.04\).
3B.2 Diabetic subjects with LJM at both the ST and 1st MTP joints.

Eleven of the 216 diabetic subjects displayed LJM at both the ST and 1st MTP joints. None of the non-diabetic controls had limitations at both these joints. The diabetic subjects with limited motion at both these joints were predominantly male, had higher body mass index and were more likely to have restricted extension of the interphalangeal joints in the hands. No significant associations with age, HbA1c, duration, microvascular complications or toe LJM were found (Table 3.11).

3B.3 Associations between various microvascular complications of DM

Background retinopathy was present in twenty-eight percent of diabetic subjects tested, elevated AER in twenty-seven percent and sensory nerve abnormality in thirty-two percent. These microvascular abnormalities were evaluated in young people with diabetes to assess any associations between these complications (Tables 3.12, 3.13 and 3.14). There was an association between retinopathy and elevated AER in the group of diabetic subjects assessed ($\chi^2$ 4.35, $P = 0.04$) but no association was found between either of these abnormalities and abnormal nerve function ($P > 0.05$).
### Table 3.11

Characteristics of diabetic subjects with LJM at both the ST and 1st MTP joints

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without LJM</td>
<td>with LJM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 205)</td>
<td>(n = 11)</td>
<td></td>
</tr>
<tr>
<td>Gender - (M : F)</td>
<td>93 : 112</td>
<td>10 : 1*</td>
<td></td>
</tr>
<tr>
<td>Age - years</td>
<td>15.3 [14 – 17]</td>
<td>16.6 [14 – 19]</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.5 [20 – 25]</td>
<td>26 [23-27]†</td>
<td></td>
</tr>
<tr>
<td>Lifetime HbA1c - %</td>
<td>8.51 (± 0.96)</td>
<td>8.22 (± 0.85)</td>
<td></td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.0 [3.8 –10.2]</td>
<td>9.2 [5.3 – 2.1]</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>27 %</td>
<td>45 %</td>
<td></td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>27 %</td>
<td>18 %</td>
<td></td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>39 %</td>
<td>64 %</td>
<td></td>
</tr>
<tr>
<td>Toe LJM</td>
<td>21 %</td>
<td>45 %</td>
<td></td>
</tr>
<tr>
<td>Finger LJM</td>
<td>12 %</td>
<td>36 %†</td>
<td></td>
</tr>
</tbody>
</table>

The results are given as percentage affected, mean (± SD) or median [interquartile range]

**Bold** indicates significant differences between diabetic subjects with LJM at both the ST and 1st MTP joints and those without,

\* \(P = 0.003\), † \(P = 0.03\)
**Table 3.12**  
Association between elevated AER and retinopathy

<table>
<thead>
<tr>
<th></th>
<th>Retinopathy</th>
<th>No retinopathy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AER ≥ 7.5 μg/min</td>
<td>20 (40%)</td>
<td>30 (60%)</td>
<td>50</td>
</tr>
<tr>
<td>AER &lt; 7.5 μg/min</td>
<td>34 (24%)</td>
<td>105 (76%)</td>
<td>139</td>
</tr>
</tbody>
</table>

**X² = 4.35,  P = 0.04**  
Significant association found

---

**Table 3.13**  
Association between abnormal nerve test and retinopathy

<table>
<thead>
<tr>
<th></th>
<th>Retinopathy</th>
<th>No retinopathy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve abnormality</td>
<td>23 (28%)</td>
<td>60 (72%)</td>
<td>83</td>
</tr>
<tr>
<td>No nerve abnormality</td>
<td>32 (26%)</td>
<td>91 (74%)</td>
<td>123</td>
</tr>
</tbody>
</table>

**X² = 0.07,  P = 0.8**  
No significant association found

---

**Table 3.14**  
Association between abnormal nerve test and elevated AER

<table>
<thead>
<tr>
<th></th>
<th>AER ≥ 7.5 μg/min</th>
<th>AER &lt; 7.5 μg/min</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve abnormality</td>
<td>20 (26%)</td>
<td>56 (74%)</td>
<td>76</td>
</tr>
<tr>
<td>No nerve abnormality</td>
<td>31 (27%)</td>
<td>84 (73%)</td>
<td>115</td>
</tr>
</tbody>
</table>

**X² = 0.01,  P = 0.9**  
No significant association found
3B.4 Sensitivity and specificity of joint tests

The sensitivity and specificity of LJM of the ST, 1st MTP and inability to fully extend the fingers were assessed to determine whether any of these tests could be used in isolation to detect LJM in the other joints or microvascular complications of diabetes.

The sensitivity (ability of LJM at the ST joint to detect a true positive result) was 0.17 for the 1st MTP joint, 0.19 for the inability to extend the fingers, 0.11 for retinopathy, 0.08 for elevated AER, 0.16 for neuropathy. The specificity (ability of LJM at the ST joint to detect a true negative result) was 0.94 for the 1st MTP joint, 0.92 for the inability to passively extend the fingers, 0.91 for retinopathy, 0.89 for elevated AER, 0.94 for neuropathy.

The sensitivity (ability of LJM at the 1st MTP joint to detect a true positive result) was 0.55 for the subtalar joint, 0.44 for the inability to extend the fingers, 0.39 for retinopathy, 0.27 for elevated AER, 0.28 for neuropathy. The specificity (ability of LJM at the 1st MTP joint to detect a true negative result) was 0.72 for the subtalar joint, 0.71 for the inability to passively extend the fingers, 0.72 for retinopathy, 0.66 for elevated AER, 0.70 for neuropathy.

The sensitivity (ability of LJM in the fingers to detect a true positive result) was 0.25 for the subtalar joint, 0.18 for the 1st MTP joint, 0.22 for retinopathy, 0.14 for elevated AER, 0.14 for neuropathy. The specificity (ability of LJM in the fingers to detect a true negative result) was 0.88 for the subtalar joint, 0.90 for the 1st MTP joint, 0.90 for retinopathy, 0.88 for elevated AER, 0.89 for neuropathy.
3B.5 Discussion

The primary aims of this section were to examine the relationship between LJM and microvascular disease after establishing a uniform method of statistical evaluation of LJM which could be used for comparisons of anomalies investigated in subsequent examinations in this thesis. This part of the study also evaluated the efficacy of using a single joint test to detect other complications of diabetes. To fulfill these aims LJM at the ankle, subtalar and 1st MTP joints were defined as 2SD above the mean for the controls of the current study (most affected side only). The definitions of dichotomous variables (LJM at the fingers and toes) remain constant as examinations results were either normal or abnormal.

Using this definition LJM was present in up to 30% of the diabetic subjects tested. Diabetic subjects with LJM were more likely to have sensory nerve abnormalities when compared to those without but this only reached significant levels in subjects with LJM at the ST joints and fingers. Some of the findings in the current study followed those in the 1999 study; in that diabetic subjects affected by LJM were predominantly male and were older than those without LJM. Associations with duration and HbA1c levels also mirrored the earlier study. However associations with retinopathy and elevated found in previous study were not replicated in the current study.

Except for the ankle joint, LJM was more common in males. This was particularly apparent with subjects affected at either the ST or 1st MTP joints. When both these joints were affected in one individual the ratio of males to females was 10 to 1. Although the number of subjects with both joints affected was small there appears to be a strong association between LJM in the foot and male gender. The male predominance of lower limb complications in young people with diabetes has
been found in a previous study (Duffin et al., 1999), but this same trend does not seem to be associated with ankle and upper body LJM (Rosenbloom et al., 1981; Rosenbloom et al., 1983). Male predominance of lower limb amputations has also been shown in many studies of adults with DM (Deeochanawong et al., 1992; Group, 2000; Benotmane et al., 2000; Muhlhauser et al., 2000; Oyibo et al., 2001). In fact in the Wisconsin epidemiological study in 1999 males with T1DM diagnosed under the age of 30 years were more than 5 times more likely to have a lower limb amputation than females (Moss, et al., 1999).

The reason for the increased number of male adolescents affected by lower limb complications of diabetes is unclear but several factors may be playing a part. Hormonal variations between male and female are probably the most obvious reason for the differences found but poorer compliance, different occupations and recreational activities may also play a role in earlier onset of lower limb complications in males. These factors have not been investigated to determine any relationship between the early onset of lower limb complications of diabetes and higher incidence of lower limb amputations in males with diabetes but further investigations in this area are required.

The increased number of females with LJM at the ankle joint may be attributed to the variation in footwear between males and females. Teenage girls tend to wear high heels which may cause contraction of both the gastrocnemius and soleus muscles. Shortening of these muscles reduces flexion at the ankle joint and when combined with non-enzymatic glycation of the soft tissues around the joint may have been the reason for the higher percentage of females being affected by ankle joint LJM.
In comparison to control subjects, diabetic subjects had significantly lower motion at the ankle joint when the knee was flexed but not when the knee was extended. In order to understand this one should note the differing anatomical structures influencing ankle joint motion in these two positions. Ankle joint motion is limited by muscular and tendonous structures when the knee is extended, in particular the gastrocnemius. The gastrocnemius is a powerful limiter of ankle motion. If the knee is extended this muscle is fully engaged and reduced ankle flexion may indicate tightness of the gastrocnemius and Achilles tendon rather than true LJM. When the knee is flexed ankle flexion is limited by capsular and ligamentous structures, in combination with the soleus. The soleus is a much less powerful limiter of ankle flexion than the gastrocnemius making this measurement a more useful indicator of the presence of LJM. However the number of subjects with LJM at the ankle joint when the knee was flexed was very low reinforcing the notion that LJM effects small joints before larger (Duffin et al, 1999).

The sensitivity for tests of LJM at the ST joint, 1st MTP joint and finger extension was poor. None of these tests could be relied upon to successfully detect LJM at other joints, retinopathy, elevated AER or sensory nerve abnormalities. From the results of this study it would appear that LJM in the foot is a poor tool for assessing the likelihood of other systemic complications of diabetes. There are many factors affecting the mobility of the foot not the least of which is the starting ROM of various joints. Without the complications of diabetes, the minimum range of ST joint motion found in the non-diabetic population in this study was 24°. A diabetic subject with this ROM before developing diabetes would be incorrectly categorised as having LJM. In contrast the highest range of ST joint motion recorded for the non-diabetic subjects was 43°. A diabetic subject with this high ROM before developing diabetes,
Id have a 40% drop in subtalar motion and still not be categorised as being affected by LJM. Clearly using any generalised cutoff point in joint ROM in the foot to determine which subjects are affected by complications of diabetes cannot be relied on. It would be preferable to do progressive evaluations of joint motion to detect changes in joint ROM. The diabetic subjects would then act as their own control and since with continuing reductions in motion could be safely categorised as having M. However to determine at what point a significant reduction in joint motion has occurred in diabetic subjects, non-diabetic subjects would need to be evaluated over several years to assess any normal variations in joint ROM.

The great variation in joint ROM in non-diabetic subjects must surely make an assessment of LJM in the foot a very poor indicator of other microvascular complications of diabetes. This is particularly true when we compare microvascular complications such as retinopathy, elevated AER and nerve abnormalities with one another. The relationships between these more universally accepted markers of diabetes complications were moderate to very poor. In fact the only two microvascular complications which showed any association were retinopathy and elevated AER and this association was marginal.

The specificity of testing for LJM at the ST joint and passive extension of the fingers was quite high. Those who do not have LJM at these joints are unlikely to have LJM at other joints or microvascular complications of diabetes. While these tests are not useful for determining who has LJM or microvascular complications there is around a 90% probability that they will successfully exclude those who have not. Though both these tests are useful in determining which subjects are not likely to have other complications of diabetes, testing passive finger extension is undoubtedly the most simple to perform clinically. The testing of LJM at the 1st MTP joint was the
least specific of the three testing procedures and is not a useful screening tool for complications of diabetes.

3B.6 Conclusions

Limited joint mobility was found in the feet and hands of young people with diabetes and was more common in males. When present in the foot it does not show a significant association with microvascular complications of diabetes. Although not associated with microvascular complications of diabetes previous research on adults with DM has found that it affects foot function, in particular it increases plantar pressure. This aspect of LJM will be further investigated in the next chapter.
CHAPTER 4

PLANTAR PRESSURE, PRESSURE TIME INTEGRALS AND PLANTAR CALLUS IN YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS

Two hundred and sixteen young people with T1DM and 57 non-diabetic controls were assessed for peak pressure, pressure time integrals and contact time using the Pedar in-shoe pressure measuring device and were visually examined for plantar callus.

The aims of this section of the study are:

i) To determine if young people with T1DM have higher peak pressure (PP), higher pressure / time integrals (P/TI) and exhibit plantar callus more frequently than their non-diabetic counterparts.

ii) To evaluate any relationships between high PP, high P/TI, LJM and plantar callus.

iii) To examine any relationship between high PP, high P/TI and callus with microvascular complications of DM and demographic variables.
4.1 Plantar pressure of diabetic subjects vs. controls

The median peak pressure for the entire diabetic group was 400 KPa and for the controls was 420 KPa. The median pressure-time integrals for the entire diabetic group was 534 KPa/sec and for the controls 533 KPa/sec. The median contact time for the entire diabetic group was 3670 milliseconds and for the controls was 3680 milliseconds. No significant difference was found between the two groups for PP, P/TI or contact time (Table 4.1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pressure - KPa</td>
<td>420 [370-500]</td>
<td>400 [34-49]</td>
</tr>
<tr>
<td>Pressure/time integral - KPa/sec</td>
<td>533 [457-604]</td>
<td>534 [463-635]</td>
</tr>
<tr>
<td>Contact time - Milliseconds</td>
<td>3680 [3280-4160]</td>
<td>3670 [3260-4200]</td>
</tr>
</tbody>
</table>

The results are given as median [interquartile range]. No significant differences were found between the diabetic and control subjects. KPa = Kilopascals
4.1.1 High peak pressure

The mean of both feet of the controls was used to derive high PP but some variations between the left and right feet were found. Some subjects had HPP on one foot but normal pressure on the other. Using the mean of both may have eliminated some subjects with unilateral anomalies. Therefore only the most affected side was used for further evaluation. Twenty-two of diabetic subjects and 6 controls showed high peak pressure on at least one foot. Two standard deviation above the mean PP for the controls equated to 590 KPa. The proportion of subjects with HPP on at least one foot in the diabetic and control groups was the same. Diabetic subjects with HPP had a higher body mass index than diabetic subjects without HPP ($p < 0.001$). There was no significant difference in gender, age, duration of diabetes, retinopathy, elevated AER, sensory nerve abnormalities or HbA1c between diabetic subjects with or without HPP (Table 4.2a).

Diabetic subjects with HPP had significantly higher P/TI than diabetic subjects without HPP ($p < 0.001$). Motion at the 1º MTP joint was significantly reduced in both diabetic ($p = 0.05$) and control ($p = 0.01$) subjects with HPP when compared to their respective subjects without HPP. There was no significant difference in any of the pressure or joint variables tested when diabetic subjects with HPP were compared to controls with HPP or when diabetic subjects without HPP were compared to controls without HPP (Table 4.2b).
Table 4.2a

Characteristics of diabetic subjects with and without HPP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without HPP (n=194)</td>
<td>with HPP (n=22)</td>
<td></td>
</tr>
<tr>
<td>Gender M:F</td>
<td>94:100</td>
<td>9:13</td>
<td></td>
</tr>
<tr>
<td>Age - years</td>
<td>15.2 [13.5-16.7]</td>
<td>15.9 [15.1-17.8]</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.3 [20.0-24.7]</td>
<td><strong>25.9 [23.9 - 27]</strong> *</td>
<td></td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 (0.9)</td>
<td>8.4 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.0 [3.9 - 10.3]</td>
<td>6.3 [3.3 -10.2]</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>28 %</td>
<td>32 %</td>
<td></td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>26 %</td>
<td>30 %</td>
<td></td>
</tr>
<tr>
<td>Nerve abnormality:</td>
<td>33 %</td>
<td>24 %</td>
<td></td>
</tr>
</tbody>
</table>

*Bold indicates significant differences between diabetic subjects with HPP compared to diabetic subjects without. The results are given as percentage affected, mean (± SD), median [interquartile range] *P < 0.001
Table 4.2b

Pressure and joint variables of diabetic subject with and without HPP and of controls with and without HPP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without HPP</td>
<td>with HPP</td>
</tr>
<tr>
<td></td>
<td>(n=194)</td>
<td>(n=22)</td>
</tr>
<tr>
<td>P/TT - KPa/sec</td>
<td>521 (112)</td>
<td>701 (184)*</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>70° [61-74]</td>
<td>65° [56-69]*</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>20%</td>
<td>14%</td>
</tr>
</tbody>
</table>

Bold indicates significant differences between diabetic subjects with HPP compared to diabetic subjects without, or control subjects with HPP compared to controls without. Only finger and toe LJM showed significant differences between diabetic subjects with HPP compared to controls with HPP. Only finger and toe LJM showed significant differences between diabetic subjects without HPP and controls without HPP. The results are given as percentage affected, mean (± SD), median [interquartile range]. *\( P < 0.001\), †\( P = 0.01\), *\( P = 0.05\)
Pedar analysis of the diabetic subjects with HPP, localised the highest peak pressure to the plantar hallux area (16 subjects) or the plantar metatarsal area (6 subjects). Differences in both ST and 1st MTP joint motion were found when subjects with HPP in one area, were compared to those with HPP in the other. Those with HPP under the hallux had significantly lower 1st MTP joint motion ($P = 0.03$), while those with HPP under the metatarsal heads showed a tendency to lower ST joint motion (Table 4.3).

### Table 4.3

Joint motion of diabetic subjects with highest peak pressure under the hallux compared to highest peak pressure under the metatarsal heads

<table>
<thead>
<tr>
<th>Joint tested</th>
<th>HPP in PHA ($n=16$)</th>
<th>HPP in PMA ($n=6$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtalar joint</td>
<td>30.6° (6.5)</td>
<td>26.7° (2.9)</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td><strong>60.9° (9.6)</strong>*</td>
<td>70.5° (6.2)</td>
</tr>
</tbody>
</table>

PHA = plantar hallux area, PMA = plantar metatarsal area

**Bold** indicates significant difference between diabetic subjects with HPP in the PHA compared to diabetic subjects with HPP in the PMA.

The results are given as mean (± SD) *$P = 0.03$
4.1.2 High pressure time integrals

Thirteen young people with diabetes and one control had high P/TI on at least one foot. The small number of controls affected meant that only the diabetic subjects could be further evaluated. Two standard deviations above the mean P/TI for the controls equated to 750 KPa/sec. Motion at the ST or 1st MTP joint was not significantly different in diabetic subjects with or without high P/TI. Those with high P/TI had higher peak pressure and longer contact time compared to those without \( P = 0.0001 \). Diabetic subjects with high P/TI were also more likely to have sensory nerve abnormalities than those without \( P = 0.03 \). There was no significant difference in gender, age, duration of diabetes, retinopathy, elevated AER, or HbA1c between diabetic subjects with or without high P/TI (Table 4.4).
Table 4.4

Comparison of diabetic subjects with and without high P/TI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without High P/TI</td>
</tr>
<tr>
<td></td>
<td>(n=203)</td>
</tr>
<tr>
<td>Gender M:F</td>
<td>96 : 107</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.3 [14 - 17]</td>
</tr>
<tr>
<td>Av. Lifetime HbA1c - %</td>
<td>8.5 (0.9)</td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.0 [4 - 10]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>29 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 μg/min</td>
<td>25 %</td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>30 %</td>
</tr>
<tr>
<td>Peak pressure - KPa</td>
<td>380 [330 - 460]</td>
</tr>
<tr>
<td>Contact time - Milliseconds</td>
<td>3640 [3220-4120]</td>
</tr>
<tr>
<td>Subtalar joint</td>
<td>29.8° (5.3)</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>69° [61 - 74]</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>11 %</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>19 %</td>
</tr>
</tbody>
</table>

**Bold** indicates significant differences between diabetic subjects with high pressure time integrals and diabetic subjects without. The results are given as percentage affected, mean (± SD), median [interquartile range], * P = 0.0001, † P = 0.03
4.1.3 Plantar callus

Forty-one (19%) diabetic subjects and 12 (21%) controls had plantar callus. There was no significant difference in the percentage of subjects with callus between those with diabetes and the non-diabetic controls. Diabetic subjects with callus were significantly older and were more likely to have retinopathy and sensory nerve abnormalities than those without but no difference in gender, duration of diabetes or HbA1c was found (Table 4.5a).

The median PP for the diabetic group with callus was significantly higher than those without callus \((P < 0.001)\), this was only marginally true for the controls \((P = 0.04)\). The mean P/TT for the diabetic and control group with callus was also higher than their non-callused counterparts but this only reached significant levels in the diabetic subjects \((P < 0.001)\). Subjects with plantar callus had a longer contact time than those without but again this was only statistically significant in the diabetic subjects \((P < 0.05)\). Joint motion at the ST or 1st MTP joint was not significantly different in either the diabetic or control group with plantar callus although both showed a tendency toward lower motion at the 1st MTP joint (Table 4.5b).

In the diabetic subjects callus was found under the metatarsal heads in 31 subjects, under the hallux in 11 subjects and under the heel in 5 subjects. Some were affected in more than one area. Highest peak pressure corresponded to the callused area in 18 of the 41 cases. Highest P/TT corresponded to the callused area in 26 of the 41 cases.
Table 4.5a

Characteristics of diabetic subjects with and without plantar callus

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without callus (n=175)</td>
</tr>
<tr>
<td>Gender M:F</td>
<td>85 : 90</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.0 [13.3-16.4]</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.1 [19.9-24.6]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 (0.9)</td>
</tr>
<tr>
<td>Duration - years</td>
<td>5.8 [3.8-9.5]</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>25 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>26 %</td>
</tr>
<tr>
<td>Nerve abnormality:</td>
<td>29 %</td>
</tr>
</tbody>
</table>

**Bold** indicates significant differences between diabetic subjects with callus compared to diabetic subjects without. The results are given as percentage affected, mean (± SD), median [interquartile range]*\(P < 0.001\), †\(P < 0.05\)
Table 4.5b

Pressure and joint variables of diabetic subject with and without plantar callus and of controls with and without plantar callus

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without callus (n=175)</td>
<td>with callus (n=41)</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>69° [61-73]</td>
<td>66° [60-75]</td>
</tr>
<tr>
<td>Finger LJM</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Toe LJM</td>
<td>17%</td>
<td>28%</td>
</tr>
</tbody>
</table>

**Bold** indicates significant differences between diabetic subjects with callus compared to diabetic subjects without, or control subjects with callus compared to controls without. Only finger and toe LJM showed significant differences between diabetic subjects with plantar callus compared to controls with plantar callus. Only finger and toe LJM showed significant differences between diabetic subjects without plantar callus and controls without plantar callus. The results are given as percentage affected, mean (± SD), median [interquartile range], *P < 0.001, † P = 0.05
4.1.4 Plantar callus and HPP

Nine diabetic subjects and two controls had both plantar callus and HPP. There was no significant difference in the percentage of subjects affected between the diabetic and control groups. The small number of control subjects affected meant that only the diabetic subjects were further evaluated.

Diabetic subjects with both HPP and callus were significantly older, had a higher body mass index and had diabetes for a longer period \((P = 0.01)\). Those with HPP and callus also had much higher pressure time integrals \((731 \text{ vs. } 531 \text{ KPa/sec})\) than those without this combination of anomalies \((P < 0.0005)\). Gender and lifetime HbA1c was not significantly different between the two groups. Subjects with plantar callus and HPP were not more likely to have retinopathy, elevated AER or sensory nerve abnormalities than those without.
### Table 4.6

Comparison of diabetic subjects with and without high peak pressure and plantar callus in combination

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without HPP and callus (n=207)</td>
<td>with HPP and callus (n=9)</td>
<td></td>
</tr>
<tr>
<td>Gender M : F</td>
<td>99 : 108</td>
<td>4 : 5</td>
<td></td>
</tr>
<tr>
<td>Age - years</td>
<td>15.2 [13-17]</td>
<td>17.8 [16-19]</td>
<td></td>
</tr>
<tr>
<td>Av. Lifetime HbA1c - %</td>
<td>8.5 (1.0)</td>
<td>8.6 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Duration - years</td>
<td>5.9 [4-10]</td>
<td>12.5 [9-14]</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>27 %</td>
<td>56 %</td>
<td></td>
</tr>
<tr>
<td>AER ≥ 7.5 µg/min</td>
<td>26 %</td>
<td>38 %</td>
<td></td>
</tr>
<tr>
<td>Nerve abnormality</td>
<td>32 %</td>
<td>38 %</td>
<td></td>
</tr>
<tr>
<td>P/TI - KPa/sec</td>
<td>531 (125)</td>
<td>731 (160)</td>
<td></td>
</tr>
<tr>
<td>Contact time - Milliseconds</td>
<td>3660 [3260-4134]</td>
<td>3680 [3260-4680]</td>
<td></td>
</tr>
<tr>
<td>Subtalar joint</td>
<td>30 [26-33]</td>
<td>28 [24-31]</td>
<td></td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>69 [60-73]</td>
<td>65 [61-68]</td>
<td></td>
</tr>
</tbody>
</table>

**Bold** indicates significant differences between diabetic subjects with and without high peak pressure and plantar callus. The results are given as percentage affected, mean (± SD), median [interquartile range].

* $P < 0.0005$, † $P = 0.01$
4.2 Discussion

This section of the study found that high PP, high P/TI and plantar callus were not more common in young people with diabetes than controls. This similarity between the non-diabetic and diabetic subjects mirrors a previous study by Bevans and Bowker (1999). Although using much older subjects they also found that the number of subjects with plantar callus was the same in the diabetic and non-diabetic population. Comparisons with controls and diabetic subjects in the current study indicate that high peak pressure, high pressure time integrals and plantar callus are not complications of diabetes, but studies on adults with diabetes have shown beyond doubt that they indeed complicate diabetes. Bevans and Boker undertook extensive mechanical evaluations to determine the cause of plantar callus and found that deformity and reduced motion at the subtalar, 1st MTP and ankle joints play an important role in the formation of plantar callus in both diabetic and non-diabetic subjects. With the added diabetic complication of LJM, young people with diabetes who have plantar callus, high plantar pressure or high pressure time integrals must be at greater risk of developing foot problems.

The results of this section also support the hypothesis of Delbridge et al, 1988 that LJM of the foot alters the ‘dynamics of gait’ leading to HPP. In the current study both young people with diabetes and controls had significantly reduced motion at the 1st MTP joint associated with high plantar pressure. It is likely that reduced motion at the 1st MTP joint causes a more rapid transference of pressure to the hallux during the propulsive phase of gait. This notion is reinforced by the relationship between HPP in different areas of the foot and limited joint mobility. Diabetic subjects with HPP under the hallux area had significantly less motion at the 1st MTP joint than those with HPP
under the metatarsal heads. In contrast those with HPP under the metatarsal heads had less motion at the ST joint than those with HPP under the hallux.

Diabetic subjects with HPP also had significantly higher BMI than those without HPP. This is an expected finding when we examine the relationship between body mass and foot size. An increase in body mass without a similar increase in foot area must lead to an increase in force and pressure. This is explained by combining force and pressure equations; pressure = mass x acceleration / area, but the association between HPP and BMI was not further examined in this section of the study.

Diabetic subjects with plantar callus showed a significant association with retinopathy and neuropathy. It is likely that this is the result of the shared pathogenesis between nerve changes and retinopathy, that is non-enzymatic glycation. But the common link between callus and these microvascular changes remains elusive. Diabetic and control subjects with callus also had significantly higher plantar pressure than those without callus, but much lower than respective groups with HPP. The peak pressure for diabetic subjects with callus was 190 KPa lower than diabetic subjects with HPP, and only 10 KPa above the median range for the entire diabetic group. It is likely that plantar callus in these younger people has not developed sufficiently to act as a foreign body, which would increase peak pressure, but diabetic and control subjects with callus already show very high P/TTI. There was little difference in P/TTI between diabetic subjects with HPP (701 KPa/sec) and those with callus (628 Kpa/sec). The P/TTI for diabetic subjects with HPP and / or callus tended to be higher than their respective counterparts without HPP but diabetic subjects without HPP or callus had almost identical peak pressure to their respective controls. The significance
of these associations will be further discussed in combination with findings on neuropathy.

The diabetic subjects with the combination of HPP and plantar callus had greater age, body mass index and duration of diabetes. Whilst BMI was associated with HPP and plantar callus was associated with older age, duration of diabetes was much longer in those with both anomalies (Table 4.6). The longer duration of diabetes in this group may be merely the result of these subjects being older than those without this combination of anomalies. High PP and callus showed a significant association with higher PTI’s individually. It is logical that those with both anomalies would also display this association.

High P/TT’s indicate that pressure is being exerted for a longer period of time and are important in evaluating predisposition to skin ulceration in subjects with diabetes (Fuller, 1996). The diabetic subjects with callus had high P/TT, longer contact time (slower cadence) and were more likely to have sensory nerve abnormalities. Indeed, subjects with high P/TT and / or plantar callus were the only groups who displayed significantly longer contact time and sensory nerve abnormalities. It may be that the slower cadence, significantly longer contact time, and higher P/TT’s displayed in some of the young people with diabetes are the result of these early motor nerve changes but only EMG studies could confirm this. It may also be that the slower cadence simply increases the time peak pressures are being exerted. Regardless of the reasons for these gait changes, the combination of plantar callus, high PP, high P/TT and sensory nerve abnormalities must place these subjects at great risk of plantar ulceration later in life.

Clements and Bell in 1982, in a review article on diabetic neuropathy, stated that muscular weakness in the lower limb almost invariably accompanies sensory
changes and may be unilateral. Muscular changes due to diabetic neuropathy can be seen in the foot as an obvious imbalance between the digital flexors and extensors. This muscular imbalance follows atrophy of the interosseous muscles of the feet and results in clawing of the digits. These muscular changes are definitely not limited to adults with diabetes as we can see in plate 4.1 which shows these features on a 14 year old boy.

**Plate 4.1**

Flexion of digits and intrinsic muscle wasting

Investigation of the peak pressure and pressure time integrals on the area of the foot which corresponded to area of callus revealed that the P/TI was highest in the callused area in 63% of cases while PP was highest in the callused area in only 44% of cases. This finding and the very high P/TI found in those with callus suggest that high P/TI's are more closely related to callus formation than high peak pressure and warrants further investigation. However shear was not examined in these individuals.
a component of pressure widely suspected of having a strong influence on callus formation.

The clinical implications of the finding in this chapter will be discussed further in chapter eight.

4.3 Conclusions

High plantar pressure was associated with 1st MTP joint LJ M and higher BMI. High pressure time integrals was associated with sensory nerve abnormalities and longer contact time. Plantar callus was associated with older age, sensory nerve abnormalities, high P/TI and longer contact time.

High plantar pressure, high pressure time integrals and plantar callus were no more common in young people with diabetes than non-diabetic controls. However research on adults with diabetes indicates that these anomalies place individuals with diabetes at greater risk of developing plantar ulcerations. These non-diabetic complications can therefore be seen in a similar light to ill-fitting footwear, in that although ill-fitting footwear is not a complication of diabetes its effect on the neuropathic foot can be devastating and should be rectified as soon as possible. Methods to reduce HPP high P/TI and callus are investigated in the following chapter.
CHAPTER 5

MONITORING INTERVENTIONS IN YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS WHO DISPLAY HIGH PLANTAR PRESSURE, HIGH PRESSURE TIME INTEGRALS OR PLANTAR CALLUS

Seventeen young people with diabetes who displayed high plantar pressure and seventeen who displayed plantar callus were monitored using PPT cushioning, custom thermoplastic orthoses and a combination of both. Twenty-three subjects who had used orthoses for 12 months and 67 who had not, were monitored for changes in peak pressure and pressure time integrals over the 12 month period.

The aims of this section of the study are:

i) To monitor the effect of three interventions (cushioning, custom thermoplastic orthoses or a combination of the two) on PP and PTI.

ii) To determine if peak pressure and pressure/time integrals could be significantly reduced in subjects with high PP and/or plantar callus.

iii) To investigate unobtrusive methods of reducing high plantar pressure, pressure time integrals and callus in young people with diabetes.

iv) To monitor the long term (12 months) effect of orthoses on peak pressure and pressure time integrals.
5.1 Monitoring interventions

5.1.1 High peak pressure - interventions

Subjects with HPP showed significant reductions in PP and P/TL using the three interventions (cushioning, orthoses or the combination of both) when compared to the no intervention condition. Significant differences were also found for PP and P/TL when the three interventions were compared to each other. No significant difference in contact time was found. Post hoc analyses showed a significant reduction in PP with cushioning alone and the combination (both cushioning and orthoses) compared to the no intervention condition ($P < 0.01$) but orthoses alone was borderline ($P = 0.058$). All three interventions significantly reduced P/TL compared to no intervention ($P < 0.01$).

- Cushioning vs. orthoses – no significant difference for PP or P/TL ($P > 0.05$).
- Combination vs. orthoses - significantly reduced PP ($P < 0.01$) and P/TL ($P < 0.05$).
- Combination vs. cushioning – significantly reduced P/TL ($P < 0.01$).

The change in peak pressure using the three interventions ranged from an increase of 9% to a decrease of 63%. The change in pressure time integrals ranged from an increase of 10% to a decrease of 54% (Table 5.1a).

Evaluation of individual responses to various interventions showed that PPT alone did not achieve a high level (greater than 50%) reduction in peak pressure or pressure time integrals. Orthoses alone were more likely to achieve a higher level of pressure reduction but were also more likely to have achieved only a minimal effect (less than 5%). The combination of PPT and orthoses showed the best individual responses, with subjects achieving the highest level of pressure and pressure time integral reductions and the least number of subjects with less than 5% reduction (Table 5.1b).
Table 5.1a

Results of interventions for diabetic subjects with high peak pressure (n=17).

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Intervention</th>
<th>PPT cushioning</th>
<th>Custom Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Peak pressure</td>
<td>629 (14)</td>
<td>502 (104)</td>
<td>539 (130)</td>
<td>434 (140)</td>
</tr>
<tr>
<td>- KPa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range of change in PP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- %</td>
<td>+2 to -42</td>
<td>+9 to -51</td>
<td>+5 to -63</td>
<td></td>
</tr>
<tr>
<td>† Pressure/time</td>
<td>692 (107)</td>
<td>554 (106)</td>
<td>548 (100)</td>
<td>469 (109)</td>
</tr>
<tr>
<td>- KPa/sec</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range of change in P/TTI</td>
<td>-6 to -27</td>
<td>+10 to -50</td>
<td>-2 to -54</td>
<td></td>
</tr>
<tr>
<td>- %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact time</td>
<td>3655 (496)</td>
<td>3629 (598)</td>
<td>3812 (578)</td>
<td>3721 (593)</td>
</tr>
<tr>
<td>- Milliseconds</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The results are given as mean (± SD) or percentage change; + (increase), - (decrease)
ANOVA - all four measurements *PP (F=14.02; P<0.001), †P/TTI (F=38.27, P<0.001)
Bold indicates significant differences compared to no intervention, p <0.05.
ANOVA – for three interventions *PP (F=4.57; P=0.01), †P/TTI (F=15.63; P < 0.001)
No significant difference in PP or P/TTI between PPT and orthoses alone (P > 0.05).
Significant reduction in PP between orthoses alone compared to both in combination (P < 0.01) and significant reduction in P/TTI between both in combination compared to orthoses alone (P < 0.05) and PPT alone (P < 0.01).
Table 5.1b

Individual responses to interventions - number of diabetic subjects with <5%, 5-25%, 26-50% and >50% reduction in PP and P/TI

<table>
<thead>
<tr>
<th>Change in peak pressure</th>
<th>PPT cushioning</th>
<th>Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5% reduction or increase</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>5% to 25% reduction</td>
<td>7</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>26% to 50% reduction</td>
<td>6</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>&gt;50% reduction</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change in pressure time integrals</th>
<th>PPT cushioning</th>
<th>Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5% reduction or increase</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>5% to 25% reduction</td>
<td>12</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>26% to 50% reduction</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>&gt;50% reduction</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
5.1.2 Plantar callus – interventions

Diabetic subject with plantar callus showed significant reductions in PP and P/TI when the three interventions were compared to the no intervention condition. Significant differences were also found for PP and P/TI when the three interventions were compared to each other. No significant difference in contact time was found. Post hoc analyses showed a significant reduction in peak pressure with cushioning alone ($P < 0.01$), orthoses alone ($P = 0.05$) and the combination of cushioning and orthoses ($P < 0.01$) compared to the no intervention condition. A significant reduction in P/TI was found using all three interventions compared to no intervention ($P < 0.01$).

- Cushioning vs. orthoses – no significant difference for PP or P/TI. ($P > 0.05$).
- Combination vs. orthoses - significantly reduced PP ($P<0.05$) and P/TI ($P<0.01$).
- Combination vs. cushioning – no significant difference for PP or P/TI ($P < 0.01$).

The change in peak pressure using the three interventions ranged from an increase of 13% to a decrease of 60%. The change in pressure time integrals ranged from an increase of 11% to a decrease of 54% (Table 5.2a).

Evaluation of individual responses to various interventions again showed that PPT alone did not achieve a high level (greater than 50%) reduction in peak pressure or pressure time integrals but was the least likely to achieve less than 5% reduction in PP or P/TI. Orthoses alone were again more likely to achieve a higher level of pressure reduction but were also more likely to have achieved less than 5% reductions. The combination of PPT and orthoses once more showed the best individual responses with subjects achieving the highest level of pressure and pressure time integral reductions. However in this case a larger number of subjects displayed less than 5% reduction than with PPT alone (Table 5.2b).
Table 5.2a

Results of interventions for diabetic subjects with plantar callus ($n=17$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>No intervention</th>
<th>PPT</th>
<th>Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pressure - KPa</td>
<td>524 (106)</td>
<td>410 (93)</td>
<td>431 (147)</td>
<td>379 (126)</td>
</tr>
<tr>
<td>Range of change in PP - %</td>
<td>0 to -42</td>
<td>+13 to -46</td>
<td>+2 to -60</td>
<td></td>
</tr>
<tr>
<td>Pressure/time - KPa/sec</td>
<td>660 (117)</td>
<td>534 (112)</td>
<td>507 (119)</td>
<td>457 (106)</td>
</tr>
<tr>
<td>Range of change in P/TI - %</td>
<td>-6 to -27</td>
<td>+11 to -50</td>
<td>-2 to -54</td>
<td></td>
</tr>
<tr>
<td>Contact time - Milliseconds</td>
<td>3921 (614)</td>
<td>3854 (636)</td>
<td>3755 (679)</td>
<td>3700 (636)</td>
</tr>
</tbody>
</table>

The results are given as mean ($\pm$ SD) or percentage change; + (increase), - (decrease)
ANOVA - all four measurements *PP ($F=16.12$; $P<0.001$), †P/TI ($F=45.34$, $P<0.001$)
Bold indicates significant differences compared to no intervention, $P \leq 0.05$.  
ANOVA – for three interventions * PP ($F=4.78$; $P=0.02$), †P/TI †($F=14.33$; $P<0.001$)  
No significant difference in PP or P/TI was found comparing PPT and orthoses alone ($P > 0.05$). Significant reductions in PP and P/TI were found between orthoses alone compared to both in combination ($P < 0.05$).
**Table 5.2b**

Individual responses to interventions - number of diabetic subjects with <5%, 5-25%, 26-50% and >50% reduction in PP and P/TI

<table>
<thead>
<tr>
<th>Change in peak pressure</th>
<th>PPT cushioning</th>
<th>Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5% reduction or increase</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>5% to 25% reduction</td>
<td>8</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>26% to 50% reduction</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>&gt;50% reduction</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change in pressure time integrals</th>
<th>PPT cushioning</th>
<th>Orthoses</th>
<th>PPT &amp; Orthoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5% reduction or increase</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5% to 25% reduction</td>
<td>14</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>26% to 50% reduction</td>
<td>3</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>&gt;50% reduction</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
Twelve-month follow up of diabetic subject with and without orthoses

Twenty-three diabetic subjects who had used orthoses for twelve months and seven who had not were evaluated for changes in PP and P/TI. No intervention pressures, pressure time integrals and contact time were reassessed and were to initial measurements taken twelve months earlier. The twelve-month follow up of diabetic subjects tested showed that a significant reduction in peak pressure occurred with subjects fitted with orthoses over this period ($P = 0.0003$). Though reductions also occurred in pressure time integrals and contact time, in those fitted with orthoses, these changes did not reach statistical significance. Those diabetic subjects not fitted with orthoses showed a minor reduction in peak pressure and a minor increase in pressure time integrals and contact time but none of the changes in this group showed any statistical variation over the 12 month period (Table 5.3a).

The individual changes in PP and P/TI in diabetic subjects who had used orthoses for 12 month and diabetic subjects who had not were evaluated. Fifty percent of those who had used orthoses and forty-nine percent of those who not, had less than 5% reduction (or an increase) in PP over the 12 month period. Forty percent of those who had used orthoses and fifteen percent of those who had showed a reduction in PP greater than 26%. Thirty-five percent of those who had orthoses and sixty-one percent of those who had not, showed less than 5% action (or an increase) in P/TI. Thirty-five percent of those who used orthoses and percent of those who had not, showed greater than 26% reduction in P/TI over the month period (Table 5.3b).
Table 5.3a

Changes in peak pressure, pressure time integrals and contact time over 12 month period for diabetic subjects with and without orthoses

<table>
<thead>
<tr>
<th>Variable</th>
<th>With orthoses ($n = 23$)</th>
<th>Without orthoses ($n = 67$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pressure - KPa</td>
<td>-120 *</td>
<td>-16</td>
</tr>
<tr>
<td>Range of change in PP - %</td>
<td>+ 41 to -35</td>
<td>+ 74 to -50</td>
</tr>
<tr>
<td>Pressure/time - KPa/sec</td>
<td>-72</td>
<td>+ 0.5</td>
</tr>
<tr>
<td>Range of change in P/TI - %</td>
<td>+ 41 to -35</td>
<td>+ 69 to -34</td>
</tr>
<tr>
<td>Contact time - Milliseconds</td>
<td>-20</td>
<td>+110</td>
</tr>
</tbody>
</table>

The results are given as mean change (KPa) for PP, median change (KPa/sec) for P/TI and median change (milliseconds) contact time. Range of change was evaluated by percentage change from initial no intervention measurements to no intervention measurements after 12 months.

**Bold** indicates significant difference compared to initial evaluation (± orthoses), *$p = 0.0003$.*
Table 5.3b

Individual responses after 12 months - number of diabetic subjects with <5%, 5-25%, 26-50% and >50% reduction in PP and P/TI

<table>
<thead>
<tr>
<th>Change in peak pressure</th>
<th>With orthoses for 12 months (n = 23)</th>
<th>Without orthoses (n = 67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5% reduction or increase</td>
<td>7 (30%)</td>
<td>33 (49%)</td>
</tr>
<tr>
<td>5% to 25% reduction</td>
<td>7 (30%)</td>
<td>24 (36%)</td>
</tr>
<tr>
<td>26% to 50% reduction</td>
<td>8 (35%)</td>
<td>10 (15%)</td>
</tr>
<tr>
<td>&gt;50% reduction</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

| Change in pressure time integrals|                                       |                           |
|----------------------------------|                                       |                           |
| <5% reduction or increase        | 8 (35%)                              | 41 (61%)                  |
| 5% to 25% reduction              | 7 (30%)                              | 22 (33%)                  |
| 26% to 50% reduction             | 8 (35%)                              | 4 (6%)                    |
| >50% reduction                   | 0 (0%)                               | 0 (0%)                    |

Results are given as number of subjects (percentage of entire group assessed)

Six of the twenty-three diabetic subjects who had used custom orthoses for 12 months, had plantar callus at the initial examination, two did not have plantar callus after 12 months. Seven of the sixty-seven diabetic subjects who had not used orthoses had plantar callus at the initial examination; all seven still had plantar callus after 12 months.
5.2 Discussion

Many investigators have tested various pressure-reducing modalities (Boulton et al, 1984; McPoil and Cornwall, 1992; Albert and Rinoie, 1994; Colagiuri et al, 1995; Kato et al, 1996, Raspovic et al, 2000) but none have made direct comparisons between cushioning and custom orthoses. This section of the study found that using a simple 3mm flat PPT cushioning insole (20% reduction) or custom orthoses (15% reduction) could reduce peak pressure. However the most effective way of reducing peak pressure (27%) was placing 3mm of cushioning under the custom orthoses. This is a curious result as the cushioning was placed under the orthoses. It would appear that combining cushioning and orthoses either enhances the effect of the cushioning by redistributing pressure away from extremely high pressure areas or enhances the effect of the orthoses by simply padding the plantar metatarsal and plantar digital areas of the foot during the propulsive phase of gait, or both.

Whatever the rationale for the pressure reduction, not all subjects tested with these interventions responded in the same manner. The subject specific and unsystematic responses to interventions found in the current study have also been noted previously (Stacoff et al, 2000), although Stacoff et al examined changes in bony alignment not plantar pressure. The percentage change in peak pressure ranged from an increase in PP of 9% to a decrease of 63%. The use of cushioning, orthoses or both cannot guarantee a reduction in PP in a clinical setting. Some subjects actually recorded an increase in peak pressure when using one or other of these interventions, but if they did not respond to one they did to another. These variations may be due to test / retest variability but the use of any one modality should be considered a starting point. Monitoring individuals with pressure analysis equipment should produce the best clinical results.
Close scrutiny of the P/TI responses to treatment for those with HPP reveals a slightly different picture. The percentage change in P/TI using various modalities ranged from an increase in P/TI of 10% to a decrease of 54%. In fact only one subject in each group had an increase in P/TI using any of the interventions. If the aim is to reduce P/TI any of these modalities can be used with a greater degree of confidence than if the aim is to reduce PP. The results for the diabetic subjects with plantar callus were much the same as those with HPP.

Subjects with diabetes tested 12 months after their initial evaluation showed some most interesting changes. Those who had been using orthoses had a significant reduction in their non-intervention peak pressures over the 12 month period. While those who had not used orthoses showed no significant change in the same period. Pressure time integrals for those using orthoses also reduced but did not reach statistical significance. Pressure time integrals for those who did not use orthoses were virtually unchanged. The variations between those with and without orthoses indicate that some functional changes are occurring in the group who used orthoses, at least on a temporary basis. It may be that the orthoses cause changes in the muscle activation system or it may be changes in joint capsule and ligamentous structures. Whatever the mechanism of change the mean reduction in peak pressures of 120 KPa, median reduction in pressure time integrals of 72 KPa/sec and elimination of plantar callus in two subjects must be seen as a positive change.

Cushioning and orthoses both reduced peak pressure in young people with diabetes but the variability in their efficacy indicates that care should be taken when prescribing either of these modalities. Cushioning, which is simple to prescribe and inexpensive may have disadvantages. The ‘sensory-attenuation hypothesis’, when applied to people with diabetes, suggests that placing cushioning under the foot may
in fact increase weight-bearing on the metatarsal heads and detrimentally alter foot morphology in diabetic subjects who have not yet developed or are in the early stages of developing sensory neuropathy (Payne, 2000). This notion is quite controversial and further investigation is needed before giving it credence. However if it is demonstrated to be correct, then care would need to be taken in assessing whether the use of cushioning could increase instability and sensory neuropathy in susceptible individuals.

Tests on adults with diabetes have shown that the use of custom orthoses can be very effective at reducing HPP (Albert and Rinoie, 1994) but in some cases modifications to these devices are needed to effect reductions. In the current study neutral foot position orthoses were used in all cases and no modifications were made to the appliances. Without the aid of quantification, obtained using equipment such as the Pedar, the type of modification needed to guarantee a reduction in peak pressure is extremely difficult for clinicians to determine. This study found unmodified custom devices, in the majority of cases, could be relied upon to reduce PP. Once again, care needs to be taken when prescribing these devices to subjects with diabetic neuropathy. During the initial adjustment time subjects should be closely monitored for abnormally high pressure spots and sharp edges.

The examinations of various treatment modalities were all undertaken at the individuals’ self-regulated pace/gait. Some studies indicate that speed should be regulated when examining the effects of one intervention against another (McPoil and Cornwall, 1992; Kernozek et al, 1996), though this method does have some intrinsic problems. To successfully dictate walking speed, subjects must use a treadmill or have their walking pace timed, both of which interfere substantially with the subjects’ normal walking pattern. Some changes in the gait pattern will occur
even under ideal conditions (Cavanagh et al., 1992). To dictate speed ignores one of these normal changes and may give an inaccurate message of the effects of various interventions. That is, just because an intervention is efficacious at a regulated pace, does not mean it will necessarily be so during normal gait. Dictating speed may also disguise some of the effects of various interventions, such as increasing or decreasing subjects’ speed.

If the subjects’ mass (in this case body mass) and the area (in this case foot size) remains unaltered, then the only factor which will increase or decrease pressure (other than the intervention used or postural instability) is the speed at which the subject walks. This is a direct consequence of the two equations: \( F = MA \) (\( F = \) force, \( M = \) mass and \( A = \) acceleration) and \( P = F/a \) (\( P = \) pressure, \( F = \) force and \( a = \) area). The time the foot is in contact with the ground will vary with speed, so assessing contact time should give a good indication of variations in subjects’ walking speed during consecutive examinations. This method of speed assessment was tested and reported in Section 2.7.1.

The changes in contact time during examinations of various modalities demonstrated that in most cases subjects walked slightly faster, though this was not statistically significant. Subjects involved in the 12-month follow-up assessment also showed minor variations in contact time. Those who had used orthoses walked slightly faster than those who had not. Thus, theoretically, the reductions in PP and P/TI found in this study would have been more significant, had speed been regulated.
5.3 Conclusions

The examination of various pressure-reducing modalities in this section of the study was undertaken to determine if any of these modalities could be relied upon to unobtrusively reduce peak pressure and pressure time integrals. The overwhelming message regarding this aspect of the study is that generalities, even when statistical relevance is found, cannot be relied upon to determine the most effective type of intervention for all patients. Reliance should not be placed upon any one modality for uniform pressure reduction across the entire population. This finding emphasizes the importance of assessment using pressure analysis equipment as an integral component of the clinical decision making process when managing young people with diabetes.
CHAPTER 6

PLANTAR SKIN AND PLANTAR APONEUROSIS CHANGES IN YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS

Two hundred and sixteen young people with diabetes and 57 non-diabetic controls were examined for changes in thickness of the skin on the plantar surface of the foot and plantar aponeurosis using diagnostic ultrasound.

Specific aims of this section of the study are:

i) To determine if young people with T1DM exhibit any variations in the thickness of their skin on the plantar surface of the foot and plantar aponeurosis when compared to their non-diabetic counterparts.

ii) To examine any relationship between soft tissue thickening in young people with T1DM and foot size, arch height, PP, P/H, TTM, microvascular complications and demographic information.
6.1 Skin and plantar aponeurosis changes due to DM

The thickness of the skin on the plantar surface of the foot and plantar aponeurosis of diabetic subjects was compared to non-diabetic controls (Table 6.1). A significant difference in plantar aponeurosis thickness was noted ($P < 0.01$) when diabetic subjects were compared to non-diabetic controls but no significant difference in skin thickness was found. Although the median plantar aponeurosis thickness in the diabetic subjects was only $1/10^{th}$ of a mm thicker, the interquartile range varied considerably from the non-diabetic controls. The range of plantar aponeurosis thickness measured in the control groups was 1.1mm to 1.9mm, in the diabetic group 1.1mm to 2.6mm (Figure 6.1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls $n = 57$</th>
<th>Diabetic $n = 216$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin thickness (mm)</td>
<td>1.0 (0.1)</td>
<td>1.0 (0.1)</td>
</tr>
<tr>
<td>Aponeurosis thickness (mm)</td>
<td>1.5 [1.3-1.5]</td>
<td>1.6 [1.5-1.8]*</td>
</tr>
</tbody>
</table>

**Bold** indicates significant difference between diabetic and control subjects. The results are given as mean ($\pm$ SD) or median [interquartile range] $*P < 0.01$
Sixty-seven (32%) diabetic subjects had plantar aponeurosis thickness > 2 SD above the control mean (>1.7mm). Nine (4%) diabetic subjects had skin thickness > 2 SD above the control mean (>1.2mm). Univariate analysis of diabetic subjects showed that those with thickened plantar aponeurosis were predominantly male ($P < 0.01$), had significantly less motion at the ST joint ($P < 0.01$) and had larger feet ($P < 0.01$) than those without thickened plantar aponeurosis. With further statistical analysis the relationship between foot size and plantar aponeurosis thickness was found to be tenuous.

The percentage of diabetic subjects with retinopathy, elevated AER and neuropathy was greater in diabetic subjects with thickened plantar aponeurosis than those without but no statistically significant associations were found. The foot / arch length ratio showed no variation between diabetic subjects with or without thickened plantar aponeurosis. Nor was there any significant difference in age, body mass index,
HbA₁c, duration of diabetes, peak pressure, pressure time integrals or 1st MTP joint motion (Table 6.3).

Those with thickened skin showed no significant association with any of the variables tested but peak pressure and pressure time integrals were higher and contact time was longer in this group (Table 6.4).

To examine any association between foot size and plantar aponeurosis thickness both the control and diabetic groups were assessed. Using Pearson’s correlation coefficient, no correlation between these variables was found in either the control ($r = 0.044$) or diabetic ($r = 0.147$) groups (Figures 6.2 and 6.3).

Further evaluations of associations between gender, foot size and plantar aponeurosis thickening were undertaken using multivariate logistic regression. Both male gender and foot size were significant in predicting plantar aponeurosis thickening by univariate analysis but foot size was not significant after adjusting for gender. Males were nearly three times more likely to have thickened plantar aponeurosis (OR 2.99 [CI: 1.63 – 5.47]), $P = 0.0004$. 
Table 6.2

Comparison of diabetic subjects with and without thickened plantar aponeurosis (PA)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects without PA thickened (n=146)</th>
<th>Diabetic subjects with PA thickened (n=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>58 : 89</td>
<td>44 : 23 *</td>
</tr>
<tr>
<td>Age - years</td>
<td>15.4 [13.5-16.9]</td>
<td>15.2 [13.8-16.3]</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.5 [20.0-25.0]</td>
<td>22.8 [20.9-26.2]</td>
</tr>
<tr>
<td>Foot length</td>
<td>7.0 [6.0-8.5]</td>
<td>8.0 [7.0-10.0] *</td>
</tr>
<tr>
<td>Arch/foot ratio</td>
<td>0.9 [0.87-0.96]</td>
<td>0.9 [0.88-1.0]</td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.5 (0.96)</td>
<td>8.6 (0.93)</td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.3 [3.8-9.7]</td>
<td>5.8 [3.9-10.7]</td>
</tr>
<tr>
<td>Retinopathy - % affected</td>
<td>25 %</td>
<td>33 %</td>
</tr>
<tr>
<td>AER ≥ 7.5 μg/min - % affected</td>
<td>27 %</td>
<td>29 %</td>
</tr>
<tr>
<td>Nerve abnormality - % affected</td>
<td>36 %</td>
<td>47 %</td>
</tr>
<tr>
<td>Peak pressure - KPa</td>
<td>390 [330 – 460]</td>
<td>390 [320 – 480]</td>
</tr>
<tr>
<td>Pressure/time integrals - KPa/sec</td>
<td>533 [460 – 620]</td>
<td>537 [480 – 670]</td>
</tr>
<tr>
<td>Contact time - milliseconds</td>
<td>3640 [3220-4134]</td>
<td>3700 [3260-4368]</td>
</tr>
<tr>
<td>ST joint</td>
<td>30.6° (5.4)</td>
<td>28.0° (4.6)*</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>67.8° (9.9)</td>
<td>66.3° (8.9)</td>
</tr>
</tbody>
</table>

Significant differences between diabetic subjects with and without PA thickening are shown in **bold**.

Results are given as percentage affected, mean ± SD and median [interquartile range].

* P < 0.01
Table 6.3
Comparison of diabetic subjects with and without thickened skin

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic subjects</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without skin thickened ($n=204$)</td>
<td>with skin thickened ($n=9$)</td>
<td></td>
</tr>
<tr>
<td>Gender M : F</td>
<td>97 : 107</td>
<td>4 : 5</td>
<td></td>
</tr>
<tr>
<td>Age - years</td>
<td>15.4 [13.5-16.8]</td>
<td>15.1 [13.6-15.8]</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.7 [20.3-25.1]</td>
<td>21.3 [18.9-25.3]</td>
<td></td>
</tr>
<tr>
<td>Foot length</td>
<td>7.5 [6.3-9.0]</td>
<td>6.5 [5.5-8.30]</td>
<td></td>
</tr>
<tr>
<td>Arch/foot ratio</td>
<td>0.9 [0.88-0.96]</td>
<td>0.9 [0.86-0.98]</td>
<td></td>
</tr>
<tr>
<td>Av. lifetime HbA1c - %</td>
<td>8.51 (0.94)</td>
<td>8.56 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Duration - years</td>
<td>6.1 [3.9-10.3]</td>
<td>5.0 [4.3-7.6]</td>
<td></td>
</tr>
<tr>
<td>Retinopathy - % affected</td>
<td>28 %</td>
<td>11 %</td>
<td></td>
</tr>
<tr>
<td>AER ≥ 7.5 μg/min - %</td>
<td>27 %</td>
<td>33 %</td>
<td></td>
</tr>
<tr>
<td>Nerve abnormality - %</td>
<td>39%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Peak pressure - KPa</td>
<td>390 [330 - 470]</td>
<td>460 [380 - 550]</td>
<td></td>
</tr>
<tr>
<td>Pressure/time integrals - KPa/sec</td>
<td>533 [460 - 630]</td>
<td>668 [480 - 710]</td>
<td></td>
</tr>
<tr>
<td>Contact time - milliseconds</td>
<td>3660 [3250-4193]</td>
<td>3980 [3180-4368]</td>
<td></td>
</tr>
<tr>
<td>ST joint</td>
<td>29.9° (5.3)</td>
<td>27.0° (4.7)</td>
<td></td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>67.2° (9.8)</td>
<td>70.8° (4.5)</td>
<td></td>
</tr>
</tbody>
</table>

No significant differences were found between diabetic subjects with and without skin thickening.
Results are given as percentage affected, mean (± SD) and median [interquartile range]
Figure 6.2
Plantar aponeurosis thickness vs. foot size (controls).
Thickest aponeurosis 1.9mm ($r = 0.044$)

Figure 6.3
Plantar aponeurosis thickness vs. foot size (diabetes).
Thickest aponeurosis 2.6mm ($r = 0.147$)
6.2 Discussion

Thirty-two percent of the young people tested with diabetes showed significant thickening of the plantar aponeurosis when compared to the non-diabetic controls. However, the plantar skin of the diabetic subjects was not significantly thicker than the controls. The similarity in thickness of the skin of subjects with diabetes when compared to non-diabetic controls is in direct contrast to various other studies of skin in other areas of the body.

Thickening of the skin of young people with diabetes has been widely reported in the literature (Rosenbloom et al., 1981; Rosenbloom et al., 1983; Rosenbloom, 1984; Shinabarger, 1987). In adults with diabetes, skin thickening has been found in various areas of the body (Forst et al., 1994; Huntley et al., 1990) and a reduction in general plantar tissue thickness (skin and adipose tissue) has been noted on the plantar surface of the foot (Abouaesha et al., 2001). In young people with DM, this phenomenon has, in the most part, been examined qualitatively rather than quantitatively. Simple pinching or tenting of the skin has been widely used for skin thickness evaluation, but this method may indicate a loss in skin elasticity or an increase in subcutaneous adipose tissue, not necessarily an increase in skin thickness. It is also notable that skin thickness, alone, has not been examined on the plantar surface of the foot. The majority of examinations have been undertaken on the dorsum of the hand or foot. Those, which have examined the plantar surface of the foot, have primarily examined the fat pad rather than the skin (Gooding et al., 1986; Brink, 1995; Abouaesha et al., 2001). This is an interesting fact when the skin most at risk of trauma in diabetes is on the plantar surface of the foot.

It is accurate to say that the skin of some young people with diabetes appears thick, tight, and waxy but this current quantitative study found that the plantar skin of
these individuals is, in fact, no thicker than the non-diabetic population. Only a small percentage (4%) of the diabetic subjects tested displayed skin thickness greater than two standard deviations above the mean for the controls and this abnormality did not follow the patterns of other experiments undertaken in previous chapters. None of the evaluations indicated that skin thickening was associated with diabetes but interestingly those with thicker skin had higher peak pressure, pressure time integrals and longer contact time than those without. Again no significant relationship was found with any of these abnormalities but these results are similar to those found for young people with plantar callus (section 4.2.3). It may be that this early thickening is the result of mechanical stress on the tissue similar to that occurring in plantar callus formation rather than a complication of diabetes but none of the subject with thick skin presented with callus under the 1st MTP joint.

Some studies on adults have looked at skin changes in diabetes on a microscopic level (Braverman et al, 1984; Buckingham et al, 1984; Delbridge et al, 1985; Lyons and Kennedy, 1985). Microscopic analysis has found that skin changes are primarily associated with cross-linking of collagen due to non-enzymatic glycation. These analyses have shown clearly that skin changes do occur in adults with diabetes. Forst et al (1994) and Huntley and Walter (1990) used diagnostic ultrasound to evaluate skin thickness in adults but could find no correlation between skin thickness on the dorsum of the foot and diabetes complication.

Although skin thickening does not seem to be evident in young people with diabetes the thickness of the plantar aponeurosis does appear to be affected. The large number of diabetic subjects found with this abnormality indicates that soft tissue changes are occurring. The subjects displaying this change were predominantly male, as were diabetic subjects with abnormalities discussed in previous chapters, and they
had significantly larger feet. Statistically significant associations between plantar aponeurosis thickening and microvascular complications of diabetes were not demonstrated in this section of the study, although retinopathy, elevated AER and abnormal sensory nerve tests were more common in diabetic subjects with thickened aponeurosis.

The fact that diabetic subjects with thickened plantar aponeurosis have larger feet is likely the result of the great predominance of males being affected by this complication of diabetes. Comparisons of foot size to plantar aponeurosis thickness in both the non-diabetic controls and diabetic subjects showed that these two variables do not display any relationship. That is to say, the relationship between foot size and plantar aponeurosis thickness in the diabetic subjects was not purely a matter of the larger the foot the thicker the plantar aponeurosis. Males were nearly 3 times more likely to have thickened plantar aponeurosis than females. The relationship between male gender and lower limb complications has been discussed in chapter 3.

The arch/foot ratio was used to determine whether subjects with thickened plantar aponeurosis had higher arches compared to those without this abnormality. This study found that there was no association between these variables. The notion put forward by Kidd and Kidd, 1993 suggested that non-enzymatic glycation of the plantar aponeurosis may increase arch height by plantarflexing the metatarsals. This process would then lead to increased pressure in the plantar metatarsal area. This notion was not reinforced by the findings of this study. Those with thickened plantar aponeurosis did not have higher arches, higher peak pressure or higher pressure time integrals when compared to diabetic subjects without plantar aponeurosis thickening.

A study by Melling et al, (1999) of the palmar aponeurosis may shed some light on the results for the plantar aponeurosis. The palmar and plantar aponeuroses
are anatomically similar tissues, so we can assume that they will respond in the same way to biochemical changes due to diabetes. They found that there was marked thickening of the palmar aponeurosis of diabetic subject when compared to non-diabetic controls but the viscoelastic properties of this tissue were not significantly different in diabetic subjects. It follows that although the plantar aponeurosis is thickened in young people with diabetes, it has not lost its elasticity. Extrapolating further from the Melling’s findings, the plantar aponeurosis thickening is likely due to non-enzymatic glycation of collagen.

The evaluations undertaken to this point indicate that thickening of the plantar aponeurosis does not seem to be altering the mechanical function of the foot in a manner which interferes with its efficiency. However the individuals examined are quite young and the greater significance of this finding may emerge at a later time.

The association between ST joint LJM and thickening of the plantar aponeurosis is likely due to a shared pathogenesis between the two conditions, non-enzymatic glycation. First MTP joint motion was also lower for those with thickened plantar aponeurosis but this did not reach a statistically significant level.

6.3 Conclusions

The plantar skin of subjects with diabetes was not significantly thicker than non-diabetic controls. The plantar aponeurosis was significantly thicker in diabetic subjects. Significant associations were found between thickening of the plantar aponeurosis and male gender and between thickening of the aponeurosis and reduced ST joint motion. Young diabetic subjects with thickened plantar aponeurosis do not appear to have any alteration in foot function resulting for this abnormality.
CHAPTER 7

STRATIFIED ANALYSES OF YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS

Two hundred and sixteen young people with T1DM were stratified into four groups in order to evaluate relationships between microvascular change resulting from diabetes and joint abnormalities discussed in chapter 3, pressure changes discussed in chapter 4 and soft tissue abnormalities discussed in chapter 6. HbA1c was compared to continuous variables using Pearson correlation coefficient.

The aims of this section of the study are:

i) To stratify continuous variables into four groups by severity of abnormality, to determine whether various levels of abnormality were significantly more associated with microvascular complications of diabetes such as retinopathy, elevated AER and sensory nerve abnormalities.

ii) To examine any relationship between mild, moderate and severe abnormalities and other variables tested in previous chapters of this thesis.

iii) To determine any correlation between HbA1c and other continuous variables.
7.1 Stratification process

Continuous variables for diabetic subjects were stratified into four groups; group one consisted of subjects with no abnormalities, group two mild abnormalities, group three moderate abnormalities and group four severe abnormalities (Table 7.1). Finger and toe LJM were also evaluated, although these variables were dichotomous (normal or abnormal). Logistic regression was used to assess whether the stratified variables correlated with microvascular complication of diabetes; retinopathy, elevated AER and early sensory nerve changes. Correlation coefficients were used to examine relationships between continuous variables and HbA1c.

The continuous predictors considered for HbA1c, retinopathy and elevated AER were subtalar and 1st MTP joint motion, skin and plantar aponeurosis thickening. Peak pressure, pressure time integrals and contact time were also stratified and considered for sensory nerve changes.

In each case subjects in group two, three and four were evaluated against those in group one.
Table 7.1

Stratification of abnormalities in diabetic subjects based on joint motion, soft tissue change and increased pressure ($n = 216$)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not abnormal 1st group</th>
<th>Mild 2nd group</th>
<th>Moderate 3rd group</th>
<th>Severe 4th group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtalar joint -</td>
<td>34 – 48</td>
<td>30 – 33</td>
<td>26 – 29</td>
<td>17 - 25</td>
</tr>
<tr>
<td>Degrees</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st MTP joint -</td>
<td>75 – 95</td>
<td>67 – 74</td>
<td>62 – 66</td>
<td>40 - 61</td>
</tr>
<tr>
<td>Degrees</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plantar aponeurosis</td>
<td>0 – 1.49</td>
<td>1.5 – 1.59</td>
<td>1.6 – 1.79</td>
<td>1.8 – 2.5</td>
</tr>
<tr>
<td>Millimeters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin -</td>
<td>0 – .99</td>
<td>1 – 1</td>
<td>1.01 – 1.1</td>
<td>1.11 – 1.6</td>
</tr>
<tr>
<td>Millimeters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure time -</td>
<td>270 – 462</td>
<td>463 – 533</td>
<td>534 – 634</td>
<td>635 – 1002</td>
</tr>
<tr>
<td>KPa/sec</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact time -</td>
<td>2120 – 3249</td>
<td>3250 – 3659</td>
<td>3660 – 4192</td>
<td>4193 - 5000</td>
</tr>
<tr>
<td>Milliseconds</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The range of motion, soft tissue thickness, PP, P/TI or contact time shown, defines the four groups of diabetic subjects. Non-diabetic data is not included.
7.1.1 Retinopathy

Compared to group 1, there was no statistically significant association between retinopathy and any of the continuous variables examined in groups 2, 3 or 4. Limited joint mobility in the fingers was the only dichotomous variable found to predict retinopathy (OR 2.32 [CI: 1.14, 4.73]).

7.1.2 Elevated AER

Compared to group one there was no statistically significant association between elevated AER and any of the continuous variables examined in groups 2, 3 or 4. The dichotomous variables tested also showed no significant association with elevated AER.

7.1.3 Sensory nerve changes

Higher pressure time integrals were associated with sensory nerve changes. Subjects in groups 3 were significantly more likely to have sensory nerve changes when compared to those in group one (OR 2.39 [CI: 1.05, 5.41]). Those in groups 2 and 4 were borderline but did not show a significant association with sensory nerve changes (Table 7.2).

Subjects in groups 2 and 4 who had longer contact time than those in group 1, were significantly more likely to have sensory nerve changes, (O.R. 2.85 [C.I. 1.24, 6.53]) for group two, (O.R 3.32 [C.I. 1.45, 7.61]) for group four. Contact time in group 3 was not significantly associated with sensory nerve changes. Other continuous or dichotomous variables examined showed no significant association with sensory nerve changes.

The odds ratios and confidence intervals for groups 2, 3 and 4 were assessed against group one to determine if a trend of increasing association with sensory nerve
changes occurred with increasing pressure time integrals and contact time. No obvious trend was demonstrated (Table 7.2).

### Table 7.2

Odds ratios for abnormal sensory nerve tests as a function of increasing P/II and contact time

<table>
<thead>
<tr>
<th>Group comparison</th>
<th>Pressure time integrals</th>
<th>Contact time</th>
</tr>
</thead>
<tbody>
<tr>
<td>2(^{nd}) group vs. 1(^{st})</td>
<td>2.23 (0.99, 5.03)</td>
<td>2.85 (1.24, 6.53)*</td>
</tr>
<tr>
<td>3(^{rd}) group vs. 1st</td>
<td>2.39 (1.05, 5.41) †</td>
<td>1.76 (0.77, 4.04)</td>
</tr>
<tr>
<td>4(^{th}) group vs. 1st</td>
<td>2.14 (0.94, 4.84)</td>
<td>3.32 (1.45, 7.61) ‡</td>
</tr>
</tbody>
</table>

Odds Ratio (95% confidence intervals), † *P* < 0.04, * P = 0.01, ‡ *P* = 0.005

**Bold** indicates significant difference between the groups examined for diabetic subjects only. No trend was found.

#### 7.1.4 HbA\(_{1c}\) levels

Examination of correlation coefficients of continuous variables showed that ST joint ROM had a negative correlation with HbA\(_{1c}\) (*r* = -0.15). The lower the range of ST joint motion the higher the HbA\(_{1c}\) level. No other correlations were found between continuous variables. Finger LJM was the only dichotomous variable to show an association with higher HbA\(_{1c}\) (Chapter 3, Table 3.8).
7.2 Discussion

Associations with retinopathy were the same as found with previous analyses in chapter 3, the only abnormality associated with retinopathy was LJM in the fingers. This is a dichotomous variable and could not be further stratified. Subjects with this abnormality were more than twice as likely to have retinal change. The reason for the association is likely to be their shared pathogenesis, non-enzymatic glycation. This association was noted in a previous study (Duffin et al, 1999). The odds ratio for retinopathy for those with finger LJM in the current study being 2.32 increased risk association with retinopathy was similar to that found in the 1999 study which showed a 2.53 increased risk association with retinopathy. This test is a very simple and must be the most reliable method for predicting retinopathy in young people with diabetes.

No association with continuous or dichotomous variables and AER was found in the current study. These findings are in contrast to the findings of the Duffin et al, study in 1999 which found that subjects with LJM at the ST and 1st MTP joints were more than twice as likely to have elevated AER. The reason for the variations between the two studies has been discussed in Chapter 3.

The correlation found between higher HbA1c levels and reducing ST joint motion was weak. Earlier analyses in this study and the results of the 1999 study found no association between LJM in the foot and higher HbA1c, so there is little evidence to suggest a true association between these two abnormalities.

One of the most interesting findings in this section of the study is the association between pressure time integrals, contact time and early sensory nerve changes. Those in groups 3 with moderately high pressure time integrals were more than twice as likely to have sensory nerve changes compared to subjects in group one
with no abnormality. Previous analysis of subjects with high pressure time integrals in chapter 4 also showed associations between these variables. Those with high P/TI were significantly more likely to have early sensory nerve and had significantly longer contact time that diabetic subjects without high P/TI.

For contact time those in groups 2 and 4 were significantly more likely to have sensory nerve changes. Those with the slowest gait (group 4) were over three times more likely to have sensory nerve changes compared to subjects with the fastest gait (group 1).

A causal link between early sensory nerve changes and early motor nerve changes causing a slowing of gait has already been considered in the discussion section in chapter 4. However it is also possible that gait changes are causing early changes to sensory nerves. Sensory nerve ends are well protected from damage from pressure by pacinian corpuscles (Loewenstein and Rathkamp, 1958) but it may be that extended periods of low level elevated pressure has an effect on the function of sensory nerves in the feet.

Current empirical evidence offers no directional component to this association. However anecdotally, if tight fitting footwear is used for long periods, superficial sensory nerves react by causing pins and needles or even numbness to the effected area. This effect in subjects with diabetes may be increased due to non-enzymatic glycation of superficial nerves, resulting in more permanent changes in nerve function when long periods of pressure are exerted. That is, there is no reason to assume that nerve changes are resulting in gait changes, any more than gait changes are resulting in nerve change but further investigation is warranted.

None of the evaluations undertaken in this section showed any trends between increasing abnormalities and microvascular complications of diabetes. It
may be that foot abnormalities in people with diabetes are not merely the effect of diabetes but occur in conjunction with undetected mechanical abnormalities. This would explain the poor correlation between foot abnormalities detected in this study and other microvascular complications of diabetes. These same undetected mechanical abnormalities may be causing early changes in sensory nerves in young people with diabetes.

Long term monitoring of these young people should clarify any relationship between foot and microvascular abnormalities.

7.3 Conclusions

Using stratification, the only examinations undertaken in this study which showed any association with microvascular complications were pressure time integrals and sensory nerve changes and contact time and sensory nerve changes. Of the dichotomous variables the only association noted was between finger LJM and retinopathy. The only examinations which showed any association with HbA1c levels was subtalar joint motion. A weak correlation between reducing ST joint motion and increasing HbA1c levels was found.
CHAPTER 8

SUMMARY, CONCLUSIONS, CLINICAL IMPLICATION AND FUTURE DIRECTION OF RESEARCH

This chapter summarises the main findings of this thesis and draws conclusions from discussions in previous chapters. The clinical implications of findings and future direction of research into foot problems in young people with T1DM are presented.
8.1 Summary

Structural and functional abnormalities of the foot which may predispose young people with Type 1 diabetes mellitus to serious foot problems as adults were examined. Table 8.1 shows a simple breakdown of the risk factors examined in this thesis, whether they are known to be related to foot problems in adults with DM and their presence in the young people examined in this study. Limited joint mobility of the fingers was also found more commonly in young people with diabetes (13% of those with diabetes but not found in controls)

<table>
<thead>
<tr>
<th>Risk factors examined</th>
<th>Known to be related to foot problems in adults</th>
<th>Found in young people with diabetes</th>
<th>Proportion of young people with DM affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>LJM Subtalar joint</td>
<td>Yes</td>
<td>Yes</td>
<td>9 %</td>
</tr>
<tr>
<td>LJM 1st MTP joint</td>
<td>Yes</td>
<td>Yes</td>
<td>30 %</td>
</tr>
<tr>
<td>LJM ankle joint</td>
<td>Yes</td>
<td>Yes</td>
<td>4 %</td>
</tr>
<tr>
<td>Digital contraction</td>
<td>Yes</td>
<td>Yes</td>
<td>22 %</td>
</tr>
<tr>
<td>Plantar callus</td>
<td>Yes</td>
<td>Yes *</td>
<td>19 %</td>
</tr>
<tr>
<td>High plantar pressure</td>
<td>Yes</td>
<td>Yes *</td>
<td>10 %</td>
</tr>
<tr>
<td>High pressure time integrals</td>
<td>Yes</td>
<td>Yes *</td>
<td>6 %</td>
</tr>
<tr>
<td>Plantar skin thickening</td>
<td>Not examined</td>
<td>No *</td>
<td>4 %</td>
</tr>
<tr>
<td>Plantar aponeurosis thickening</td>
<td>Not examined</td>
<td>Yes</td>
<td>32 %</td>
</tr>
<tr>
<td>Sensory nerve changes</td>
<td>Yes Clinical neuropathy</td>
<td>Yes Early changes</td>
<td>32 %</td>
</tr>
</tbody>
</table>

* Plantar callus, high peak pressure, high pressure time integrals and thickened skin were no more common in subjects with T1DM than non-diabetic controls.
Significant risk factors for young people with diabetes were associated with male gender, age, duration and microvascular complications of diabetes. Table 8.2 gives a breakdown of these associations.

This study found two distinct groups of anomalies in young people with diabetes; those which are found more commonly in young people with diabetes (shaded - table 8.2) and those which are not more common in young people with diabetes but which are indeed complicated by diabetes (unshaded - table 8.2).
Table 8.2

Risk factors for foot pathology and statistically significant associations with other variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gender</th>
<th>Age</th>
<th>BMI</th>
<th>Duration of DM</th>
<th>Retinopathy</th>
<th>Elevated AER</th>
<th>Nerve changes</th>
<th>Higher HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>LJM ST Joint</td>
<td>Male</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
</tr>
<tr>
<td>LJM Ankle joint</td>
<td>Female</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>LJM 1st MTP joint</td>
<td>Male</td>
<td>Yes</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>LJM Finger</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>LJM Toe</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Thick Plantar Aponeurosis</td>
<td>Male</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>High Peak Pressure</td>
<td>*</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>High Pressure Time Integrals</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
</tr>
<tr>
<td>Plantar Callus</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>Yes</td>
<td>*</td>
</tr>
</tbody>
</table>

* = no significant association found.
- shaded = abnormalities detected in the current study which were significantly more common in subjects with diabetes than non-diabetic controls
- unshaded = anomalies detected in the current study which were not significantly more common in subjects with diabetes than non-diabetic controls
8.1.1 Complications of diabetes

All subjects found to have diabetic foot complications (except ankle joint LJM) were predominantly male although LJM in the toes did not reach a statistically significant level. Older age was only significantly associated with LJM at the 1st metatarsophalangeal joint and toes. Again looking at foot complications only LJM at the subtalar joint was associated with microvascular changes due to diabetes and only LJM at the 1st metatarsophalangeal joint was associated with longer duration of diabetes.

Limited joint mobility in the hands was associated with retinopathy, higher HbA1c levels and toe LJM. None of the diabetes complications was associated with elevated AER. Thickening of the plantar aponeurosis has never been assessed in adults or young people with diabetes but it was the most commonly found foot complication of diabetes. It was not associated with any of the microvascular complication of diabetes but it was more common in males and was associated with foot size and LJM at the ST joint.

Limited joint mobility in one foot joint was frequently associated with LJM in other foot joints. Subtalar joint limitation was associated with 1st MTP joint and toe limitation. Finger LJM was associated with toe LJM but not subtalar and 1st MTP joint limitation.

8.1.2 Anomalies found which may be complicated by diabetes

High peak pressure, high pressure time integrals and plantar callus were not more commonly found in young people with diabetes when compared to non-diabetic controls. These anomalies cannot be considered to be the result of diabetes but have been found to be complicated by diabetes in studies on adults.
High peak pressure was not associated with any microvascular complications of diabetes but was associated with higher body mass index. This anomaly was also associated with high pressure time integrals and LJM at the 1st MTP joints. The control subjects with HPP also had significantly reduced motion at the 1st MTP joints implying that reduced joint motion at this joint increases peak pressure. Finding reduced motion at the first MTP joint in diabetic subjects with HPP under the hallux reinforced this inference.

Diabetic subjects with plantar callus and high pressure time integrals showed some similarities. Both groups were significantly associated with early sensory nerve changes, HPP and longer contact time. Although not complications of diabetes these early changes in sensory nerves place these individuals into a category requiring careful long term monitoring. Progression to clinically significant sensory neuropathy would place these individuals at great risk of future foot problems such as ulceration and amputation.

### 8.1.3 Monitoring interventions

Simple cushioning, custom orthoses and the combination of these two interventions significantly reduced both peak pressure and pressure time integrals. During a twelve month follow-up of individuals with diabetes who had been using custom orthoses, peak pressure was significantly reduced even after the devices had been removed. After twelve months pressure had not significantly changed in the group not fitted with orthoses.
8.2 Conclusions

Many factors known to predispose adults with diabetes to foot problems are present in young people with diabetes. Thickening of the plantar aponeurosis and limited joint mobility at the ankle (knee flexed), ST, 1st MTP and interphalangeal joints of the fingers and toes were significantly more common in young people with diabetes when compared to non-diabetic controls.

Anomalies such as high plantar pressure, high pressure time integrals and the presence of plantar callus, although known to predispose individuals with diabetes to foot problems do not appear to be direct complications of diabetes. The number of diabetic subjects affected with these anomalies was no greater in the diabetic subjects when compared to the controls. However this finding should not diminish the importance of detecting these problems in young diabetic subjects. Significant associations were found between complications of diabetes such as LJM and sensory nerve changes, and normal variants such as plantar callus and plantar pressure. The effects that diabetic complications have on these normal variants may compromise the future foot health of affected individuals and both diabetic and non-diabetic anomalies should be considered together.

In subjects with direct complications of diabetes several features stand out. Except for ankle LJM, males were more commonly affected by diabetic complications in all of the foot structures examined, significantly so at the ST joint, 1st MTP joint and plantar aponeurosis. The male predominance of lower limb complications in adolescents with diabetes, particularly LJM, was also found in a previous study (Duffin et al, 1999) but this trend is not mirrored in upper body LJM (Rosenbloom et al, 1981; Rosenbloom et al, 1983).
The reason for the increased number of young male subjects being affected by foot complications of diabetes is unclear. No evidence has been forthcoming to point to any one determinant but hormonal variations between male and female, poorer compliance and different occupations and recreational activities may all play a role.

In contrast males were not more commonly affected with HPP, high P/TT and plantar callus, an interesting finding which again supports the view that these anomalies are not direct complications of diabetes. However diabetic foot complications such as LJM at the 1st MTP can complicate both HPP and plantar callus. Both diabetic and non-diabetic subjects with HPP showed significantly reduced motion at the 1st MTP joints when compared to their counterpart without HPP. This same trend occurred in both diabetic and non-diabetic subjects with plantar callus although not reaching statistically significant levels in either group.

If we take these findings one step further and assume that LJM is a progressive complication of diabetes, then the reducing range of 1st MTP joint motion available will result in increasing PP, P/TT and callus formation. So normal variants in younger people with diabetes, which are not the direct result of diabetes, are affected by specific complications of diabetes and place individuals at greater risk of future foot problems.

It is also likely that HPP, high P/TT and callus are the result of some undetected mechanical abnormality in susceptible individuals. Factors not assessed in this study such as mechanical, soft tissue, and functional abnormalities and bony deformity suggested by Delbridge et al, (1988) and Meuller et al (1989) may all play a role in increasing plantar pressures.
One of the more interesting significant findings in those with high P/TI and callus, was the association between these anomalies, increased contact time (slower cadence) and early signs of peripheral nerve abnormalities. Plantar callus and high pressure time integrals in young people with diabetes showed a significant association with sensory nerve changes. Slower cadence was associated with plantar callus formation in both diabetic and non-diabetic subjects, although only significantly so in the diabetic group. The interrelationship of these variables raises the question whether changes in sensory and motor nerve function are having an effect on foot function or visa versa. Slower cadence may be the body’s way of reducing pressure over high pressure areas. Indeed slower cadence has been shown to reduce peak pressure (Hughes et al, 1991). However a reduction in gait speed could also result in an increase in the time pressure is being exerted. This could lower peak pressure and increase pressure time integrals. The relationship between the area affected by callus and highest P/TI is closer than the relationship between callus and high PP, reinforcing this theory. Sixty three percent of diabetic subjects showed highest P/TI in callused areas compared to 44% with highest PP in callused areas.

The complexities of the processes involved in high peak pressure, high pressure time integrals and formation of plantar callus are not yet clear but this study indicates that the processes are not simple.

The effect of increased BMI was also investigated in the current study in subjects with diabetes. This feature was only significantly associated with HPP and plantar callus. Diabetic subjects with high pressure time integrals also had higher BMI but this did not reach significant levels.

The use of cushioning and orthoses have been suggested as being vital to the protection of the diabetic foot (Albert and Rinoie, 1994; Caputo et al, 1994) but the
findings of this study indicate that the use of these modalities must be prudent. If diabetic subjects did not have a reduction in PP using one intervention they did with another. In fact, some individuals had an increase in PP using cushioning, some had an increase using orthoses and some had an increase using both. Mean and median values can indicate the most likely response to intervention but each individual must be carefully monitored.

The obvious complexities of diabetic foot problems have a profound effect on the structure and function of the foot. Individual needs are best monitored using equipment such as the Novel Pedar. However this equipment is expensive and not readily available to individual clinicians, so appropriate screening of foot structure and function should be an integral part of early intervention programmes aimed at young people with T1DM.

8.3 Clinical implications of findings

The high number of diabetic subjects being affected with LJM in the toes (hammer and claw toe deformity) indicates that up to 22% need immediate advice regarding appropriate footwear. Mobilisation techniques of the affected interphalangeal joints of the feet, although not yet proven to be successful, should also be considered when the toes are contracted as LJM affects the soft tissues surrounding the joints rather than the osseous structures (Shinabarger, 1987; Meuller et al, 1989). If the toes remain in a flexed position, flexor contractions and damage at the interphalangeal joints may occur resulting in fixed contractures of the digits, increasing the risk of irritation from footwear.

The assessment of foot joint motion as an indicator of microvascular complications of diabetes is not recommended. However limitation of passive finger
extension should be considered as a screening tool for diabetic subjects who have not yet demonstrated LJM in the feet or microvascular complications of diabetes. There is a 90% chance that a subject will not have other complications of diabetes when this abnormality is not present. This test is also a more useful screening tool because it is not found in the non-diabetic population.

The early nerve changes displayed by a significant number of diabetic subjects with plantar callus and high pressure time integrals make these individuals at greater risk of developing foot problems. The early detection of nerve changes gives the clinician the opportunity to encourage tighter glycaemic control measures and may prevent the development of significant sensory and motor nerve changes (DCCT, 1993). In fact all those young people detected with HPP, high P/TI or callus should also be targeted to improve their long-term glycaemic control. This may reduce the likelihood of other complications of diabetes, such as LJM, ever developing.

In adults with diabetes, plantar callus has been implicated in the development of neuropathic ulceration (Veeses et al, 1992; Caputo et al, 1994; Katoulis et al, 1996). Sage et al (2001) found that callus formation preceded diabetic ulceration in 82% of cases studied and that frequent debridement of hyperkeratotic tissue reduced the chance of more serious ulceration. The removal of plantar callus in adults has also been shown to significantly reduce plantar pressure (Young et al, 1992). In young people with diabetes appropriate treatment should include a recommendation that affected individuals attend a podiatrist for regular callus removal. This encourages good foot-care behaviour and immediately reduces peak pressure (Young et al, 1992).
The intervention study found that various modalities could successfully reduce pressure on the plantar surface of the foot. Effective use of appropriate pressure reducing modalities has direct and obvious financial implications for ulcer prevention in adults, and for reduction in lower limb amputations. The studies described in chapters three, four and six show that some young people with diabetes already have abnormalities, which may predispose them to plantar ulceration. The study described in chapter five found that PP and P/PI could effectively be reduced with various interventions. This does not mean that all young people with diabetes who have high plantar pressure, high pressure time integrals or plantar callus should be subjected to long term use of orthoses or cushioning. However appropriate treatment when one or more of these abnormalities are associated with early neuropathic change may prevent plantar ulceration ever occurring for these individuals.

This study has addressed both investigations of complication in the diabetic foot of young people and simple methods available to reduce the progression to serious foot problems. Early assessment and intervention when necessary gives the clinician the opportunity to change the future of younger people affected by T1DM. The flowchart found in the introduction of this thesis could be restructured. The gray areas showing a reduced chance of progression to amputation for these younger individuals and the red areas indicate the best opportunities for intervention (Figure 8.1).
Table 8.1
Pathways for prevention of, or progression to amputation in young people with T1DM

- Limited joint mobility in the foot
- Callus formation
- Foot deformities (incl. Hammer toes)
- Plantar soft tissue changes

- Gait changes
- High plantar pressure and high pressure time integrals
- Shoe pressure on dorsal, medial and lateral soft tissues

- Intervention and pressure reduction
- Sensory neuropathy and/or vascular insufficiency

- Intervention and pressure reduction
8.4 Future directions of research

This study has illuminated several factors regarding the structure and function of the young diabetic foot and has given direction to further evaluations of this under researched area.

Plantar aponeurosis thickness and joint mobility in the foot of young people with diabetes should be evaluated over several years to determine whether continuing increases in plantar aponeurosis thickness and reductions in joint mobility are associated with microvascular complications of DM and increasing plantar pressure measurements. This would shed more light on the relationship between these variables and may produce a relatively simple marker for those at risk of future foot pathology.

The continued monitoring of interventions in young people with diabetes may also be of great advantage. The supply of simple devices to reduce pressure and plantar callus in these young people may have a profound effect on the future of at risk individuals. These evaluations should not only include orthoses but cushioning and the combination of both interventions. The Pedar equipment allows us to determine the best intervention for pressure and pressure time reductions in individual cases.

A greater knowledge of the candidate genes, which promote foot complications in diabetes, may also permit a greater understanding of the complexities of foot problems. Genetic factors have been implicated in the development of retinopathy and nephropathy. The DCCT Research Group in 1997, indicated that improved glycaemic control could modify the effect of genetic influences.
APPENDIX No. 1
Limited joint mobility in the hands and feet of adolescents with Type 1 diabetes mellitus

A. C. Duffin*,†, K. C. Donaghe†*, M. Potter*, A. McInnes*, A. K. F. Chant, J. King†, N. J. Howard† and M. Silink†*

*University of Brighton, Brighton, UK
†Royal Alexandra Hospital for Children, Westmead, NSW, Australia
‡University of Sydney, NSW, Australia

Received 17 July 1998; accepted 1 October 1998

Abstract

Aims Limited joint mobility (LJM) in the foot has not been assessed in adolescents with Type 1 diabetes mellitus (DM) but is associated with neuropathic ulceration in adults. This study was designed to determine the presence of LJM in adolescents with Type 1 DM and its association with microvascular disease.

Methods The hands, feet and hips were examined in 302 diabetic adolescents and 51 non-diabetic controls (aged 11.5–20 years). LJM was defined as less than the fifth percent reference for controls.

Results Reduced motion was found in 35% of diabetic adolescents at the subtalar (ST) joint, 18% at the first metatarsophalangeal (MTP) joint, 26% at the fifth metacarpophalangeal (MCP) joint and 13% had limited passive extension of the interphalangeal (IP) joints of the hands. Limited passive IP joint extension of the hands was not present in the controls. Limited active IP joint extension, a positive ‘prayer sign’, occurred in 35% of diabetic adolescents and 14% of controls. Diabetic adolescents showing LJM in any of these areas, except the prayer sign, were more likely to have retinopathy (odds ratio 2.53, CI: 1.53–4.18). Those with LJM in the foot were more likely to have albumin excretion rates > 7.5 μg/min (OR 2.06, CI: 1.16–3.68).

Conclusion LJM in the feet of adolescents with Type 1 DM is associated with microvascular disease and is a useful routine clinical measure.


Keywords adolescents, limited joint mobility, foot, microvascular complications; prayer sign, Type 1 diabetes mellitus,

Abbreviations GHB, glycated haemoglobin; HPLC, high performance liquid chromatography; IP, interphalangeal; IQR, interquartile range; LJM, limited joint mobility; MCP, metacarpophalangeal; MTP, metatarsophalangeal; OED, orthopaedic evaluation device; OR, odds ratio; ROM, range of motion; ST, subtalar

Correspondence to: Anthony Duffin, 6-8 Hannah Street, Suite 29, Beecroft, NSW 2119, Australia. E-mail acduffin@cyber.net.au

©1999 British Diabetic Association. Diabetic Medicine, 16, 125–130
Introduction

Limited joint mobility (LJM) in children with Type 1 diabetes mellitus (DM) is associated with retinopathy, nephropathy and neuropathy [1-4]. Rosenbloom et al. found that LJM in children was associated with a fourfold increased risk of microvascular complications compared to those without LJM [4]. The pathogenesis of LJM is probably the non-enzymatic glycation of collagen [5], resulting in thickening of skin, tendons, ligaments and joint capsules, reducing tissue flexibility.

To date LJM in adolescents has not been considered a potentially serious complication in itself [6] though it has been found in the cervical and thoracolumbar spine, wrist, elbow, ankle and the metacarpophalangeal joints [3]. We know that, in adults with diabetes, LJM in the foot alters the dynamics of gait causing high plantar pressures which ultimately lead to plantar ulceration [7-9] but to date the feet of young people with diabetes have not been assessed.

This is the first study to examine extensively joint mobility in the feet of adolescents with diabetes. The secondary aim of this study was to examine the relationship between microvascular disease and LJM of commonly affected joints to determine which joint tests, if used alone, were the best indicators of microvascular complications of diabetes.

Patients and methods

The study group of 302 adolescents with Type 1 DM (144 males and 158 females) were volunteers from the Diabetes Complications Assessment Clinic at the Royal Alexandra Hospital for Children. The median age of the subjects was 14.6 years (range: 11.7-20.2 years), the median diabetes duration was 6.2 years (interquartile range (IQR): 4.0-9.8 years). None were prepubertal. The control group consisted of 51 non-diabetic adolescents (23 males and 28 females) with a median age of 13.9 years (range: 11.6-20.2 years), who were unrelated to those with diabetes or to each other.

 Adolescents or their parents (where appropriate) gave informed consent and the study was approved by the ethics committee of The Royal Alexandra Hospital for Children. All measurements were taken by the same examiner (ACD), a podiatrist. To avoid potential mobilization of affected joints by the examination itself, each joint was measured only once. No significant variation was noted between the left and right side. The mean range of motion (ROM) for the two sides was calculated. LJM was defined as less than the fifth percentile reference limit for the controls and/or the inability to fully extend the IP joints of the fingers or toes.

Test-retest variability was assessed by measuring four subjects weekly over 10 weeks. The coefficients of variation were all less than 10%. The examiner was not blinded to whether the adolescents had diabetes or not, but he was blinded as to which patients had microvascular complications.

Total rotation at the hip joint was measured in both an extended and a flexed position, using a goniometer [10,11]. The total range of inversion/eversion of the subtalar (ST) joint was measured using a tractograph [7,12]. First metatarsophalangeal (MTP) joint extension was measured weightbearing, by placing the base of an orthopaedic evaluation device (OED) on a supporting surface and its fulcrum directly over the first MTP joint. The proximal phalanx was dorsiflexed passively to resistance and joint extension was measured. Percentage contraction of the second, third and fourth toes was calculated by measuring the length of the toes in a relaxed, then passively extended position. The inability to extend the toes passively to 180° was also recorded.

Passive extension of the fifth metatarsophalangeal (MCP) joint was assessed by placing an OED against the lateral side of the fifth metacarpal and extending the proximal phalanx to resistance. Passive extension of the interphalangeal (IP) joints was evaluated by the examiner grasping the proximal and distal phalanges and attempting to extend each finger 180 degrees. Active extension of the IP joints was assessed by asking the adolescent to approximate the palmar surfaces of the ‘prayer sign’ [3].

Retinopathy was assessed by stereoscopic fundus photography of seven standard fields and graded according to a modification of the Airlie House method [13]. The examiners were blinded as to which subjects had LJM.

Glycated haemoglobin (GHb) was measured by colorimetric analysis of whole blood [14] until February 1994, when the laboratory changed to measuring HbA1c by the dianiamid high performance liquid chromatography (HPLC) assay (BioRad Laboratories, Hercules, CA). For this study the colorimetric values were converted to HbA1c using the following equation: (GHb) = 1.9088 + 0.0043 X GHb (pmol HMF mg/Hb). For each adolescent a ‘lifetime’ HbA1c was calculated by taking the median of all previous HbA1c assessments. The median number of HbA1c assessments was 14 (IQR: 8-23) and the median lifetime glycated haemoglobin was 8.4% (IQR: 7.8-9%). The nondiabetic range of HbA1c was 4-6%.

The mean albumin excretion rate (AER) was calculated from three consecutive timed overnight urine collections. Albumin was measured by radioimmunoassay (Pharmacia, Ryde, Australia). Elevated AER was defined as greater than 7.5 μg/min, which is the 95th centile for Australian schoolchildren [15]. The examiner was blinded as to which subject had LJM.

Statistical analysis

The SAS software package (SAS Institute, Cary, NC) was used to analyse the data. The significance level was determined as 0.05. The two sample Student’s t-test was used to compare continuous variables between the diabetic and control groups when the distribution of data was normal, the Wilcoxon’s

© 1999 British Diabetic Association. Diabetic Medicine, 16, 125-130
Table 1 Comparison of joint motion: controls vs. diabetic subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n=51)</th>
<th>Diabetic adolescents (n=302)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint range of motion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip rotation (flexed)</td>
<td>93° (±10)</td>
<td>92° (±10)</td>
</tr>
<tr>
<td>Hip rotation (extended)</td>
<td>88° (±9)</td>
<td>85° (±10)</td>
</tr>
<tr>
<td>Subtalar joint</td>
<td>31° (±4)</td>
<td>27° (±5)†</td>
</tr>
<tr>
<td>1st MTP joint</td>
<td>73° (±9)</td>
<td>66° (±10)†</td>
</tr>
<tr>
<td>5th MCP joint</td>
<td>78° (±5)</td>
<td>70° (±11)†</td>
</tr>
<tr>
<td>Percentage of subjects unable to fully extend digits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prayer sign</td>
<td>14%</td>
<td>35%*</td>
</tr>
<tr>
<td>Passive finger extension</td>
<td>0%</td>
<td>13%*</td>
</tr>
<tr>
<td>Passive toe extension</td>
<td>8%</td>
<td>14%</td>
</tr>
<tr>
<td>Percentage contraction of toes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd toe contracture</td>
<td>5.0% [2.4–7.0]</td>
<td>4.0% [1.4–6.8]</td>
</tr>
<tr>
<td>3rd toe contracture</td>
<td>5.4% [1.8–8.8]</td>
<td>5.4% [2.7–8.6]</td>
</tr>
<tr>
<td>4th toe contracture</td>
<td>7.4% [3.4–10]</td>
<td>7.5% [4.0–10.5]</td>
</tr>
</tbody>
</table>

The results are given as mean (± SD) or median [interquartile range]. *P < 0.05, †P < 0.005, ‡P < 0.0005.

The chi-squared test was used otherwise. The chi-squared test was used to test associations between categorical data. Univariate logistic regression was used to evaluate potential relationships of LJM with retinopathy, elevated AER, height, weight, gender, duration (years) and HbA1c (%). Multivariate logistic regression was used to determine significant factors after allowing for other covariates.

**Results**

The comparisons of joint motion in the diabetic and control subjects is shown in Table 1. In those with diabetes, reduced ROM was found in 35% at the ST, 18% at the first MTP and 26% at the fifth MCP joints. The prayer sign was present in 35% of diabetic adolescents and 14% of controls. Inability to extend the fingers passively was present in 13% of diabetic adolescents but in none of the controls. The ROM of the hip joint was not significantly lower in the diabetic subjects. Although not statistically more common, the inability to passively extend the toes to 180° (hammer or claw toe deformity) was more prevalent in the diabetic group (14% vs. 8%).

Potential associations with microvascular complications were examined in the five joints which had significantly reduced ROM compared to the controls.

Background retinopathy was present in 34% and elevated AER in 44%. Longer duration, in years, was associated with retinopathy (odds ratio (OR) 1.25 (CI: 1.16–1.35)) and elevated AER (OR 1.15 (CI: 1.06–1.26)). Higher lifetime HbA1c in percent (OR 1.27 (CI: 1.01–1.61)) increased the risk for retinopathy but not for elevated AER (Figs 1 and 2). Subjects with LJM at the ST, first MTP and fifth MCP joints or those unable to extend their fingers passively were more likely to have retinopathy (OR 2.53 (CI: 1.53–4.18)). Those with LJM at the ST or first MTP joints in the foot were more likely to have AER > 7.5 μg/min (OR 2.06 (CI: 1.16–3.68)). LJM in the foot was a significant factor for elevated AER by itself but not after adjusting for age, duration and weight. Associations of individual joint limitations and microvascular complications are shown in Figs 1 and 2.
Using multivariate logistic regression, reduced ROM at the first MTP joint was the only test which remained significantly associated with retinopathy after adjusting for other covariates (OR 2.47 [CI 1.26-4.84]). Age and duration of diabetes continued to be significantly related to both LJM at the first MTP joint and retinopathy. Reduced ROM at any of the joints tested did not remain significantly associated with raised AER after allowing for other covariates.

LJM was associated with older age, longer duration and higher lifetime HbA1c (Table 2). Diabetic adolescents with LJM were predominantly male: at the ST joint, 46 females had LJM and 60 males (P = 0.05) and at the fifth MCP joint, 27 females and 49 males (P = 0.001).

A positive prayer sign was not associated with retinopathy or elevated AER. However, adolescents with a positive prayer sign were more likely to have LJM in the other four joints: for the ST joint (P = 0.001), for the first MTP joint (P = 0.02), for the fifth MCP joint (P = 0.001) and for inability to extend the fingers passively (P = 0.001). The sensitivity (ability of the prayer sign to detect the true positive result) was 0.48 for the ST joint, 0.49 for the first MTP joint, 0.68 for the fifth MCP joint and 0.95 for passive finger extension. The specificity (ability of the prayer sign to detect the true negative result) was 0.73 for the ST joint, 0.68 for the first MTP joint, 0.77 for the fifth MCP joint and 0.74 for passive finger extension.

**Discussion**

Limited joint mobility was common in the feet as well as hands of adolescents with Type 1 DM. This study confirms the association between LJM and microvascular complications in childhood diabetes found by others, despite differences in examination techniques [2,3,4]. Retinopathy was associated with LJM at the subtalar, first MTP, fifth MCP joints and restricted passive finger extension. Elevated AER was associated with limitation of the subtalar and first MTP joints.

Longer diabetes duration was a risk factor for both LJM and microvascular complications. Higher HbA1c was a risk factor for retinopathy and LJM but not elevated AER. After allowing for...
for other covariates, only LJ M at the first MTP joint remained significantly associated with retinopathy.

The pathogenesis shared between LJ M and microvascular complications is likely to be the altered function of collagen in the soft tissue surrounding the joints and in the mesangium and basement membrane, causing increased joint stiffness and increased vascular permeability. In support of this hypothesis, modifications in cross-linking of collagen at the glomerulus have been seen in experimental animal diabetes [16] and in extensor tendons in human diabetes [17].

Diabetic adolescents detected with LJ M in the foot are potentially at risk of developing serious foot problems as adults for the following reasons. The unimpaired function of the ST and first MTP joints is important to the efficient transference of forces during gait [12,18]. Reduced motion at these joints has been associated with increased plantar pressures. In the presence of neuropathy, high plantar pressures are relatively uncommon if ROM is normal, but if joint mobility is limited, forefoot pressures are high [19]. In a prospective study, elevated plantar pressures were strongly predictive of subsequent ulceration. In fact ulceration did not occur in subjects with normal foot pressures [20].

The inability to extend the toes fully, hammer and claw toe deformities, found in diabetic adolescents is potentially a more serious problem than in nondiabetic adolescents. Up to 25% of all neuropathic ulcers in adults with diabetes occur as a result of hammer and claw toes being irritated by footwear [21].

Prevention of future foot disorders in adolescents with diabetes should be considered a priority. As LJ M affects the soft tissues surrounding the joints rather than the osseous structures [18,22], mobilization techniques may prevent some of the pathomechanical changes that LJ M can cause. Mobilization of the joints of the feet should be considered if the toes are contracted or when limitation of motion is found in the subtalar or first MTP joints.

The ‘prayer sign’ was not significantly associated with either microvascular complication, although it was a common finding in the diabetic group. If approximation of the palmar surfaces of the hands was incomplete (the test now commonly called the ‘prayer sign’), Rosenbloom et al. [3] recommended that passive extension be used to confirm the limitation. Subsequently the ‘prayer sign’ has been suggested as a useful screening test for limited joint mobility in the clinical setting [6]. The results of this study confirm an association with the prayer sign and LJ M in other joints. However the sensitivity and specificity of this test as an indicator of other joint limitations was poor. Positive prayer sign was found in 14% of nondiabetic controls, similar to a previous report [23].

The results of the current study show that testing the ST and first MTP joints are good indicators of retinopathy and elevated AER and that passive extension of the fingers is a good screening test for retinopathy. Assessment of passive finger extension is simple to perform in a clinical setting, and although only a small percentage of adolescents showed this feature of LJ M (13%), they had nearly three times the risk of retinopathy compared with the group without this limitation. Furthermore the inability to extend the fingers passively did not occur in the control group.

Longitudinal studies are needed to examine the potential benefits of mobilization on LJ M and to ascertain whether the joint limitations found in these diabetic adolescents persist into adulthood. Evaluation of plantar pressures in young people with diabetes may also assist in determining which subjects may be at greater risk of developing future foot problems.

References
7 Cavanagh PR, Fernando DJS, Masson EA, Veves A, Boulton AJM. Limited joint mobility (LJM) and loss of vibration sensation are predictors of elevated plantar pressure in diabetes (Abstract). Diabetes 1991; 40 (Suppl 1): S13A.


**Cavanagh PR, Fernando DJS, Masson EA, Veves A, Boulton AJM.** (1991) Limited joint mobility (LJM) and loss of vibration sensation are predictors of elevated plantar pressure in diabetes. *Diabetes*, 40 (suppl 1): 513A.


Inman VT. (1973) *Biomechanics of the foot and ankle* St. Louis, C.V. Mosby: 3-22.


Menz H. (1993) *A comparison of the inter- and intra-tester reliability of the angle finder and rearfoot biometer in the measurement of neutral calcaneal stance position (NCSP) and resting calcaneal stance position (RCSP)* Thesis for B.Sc (Hons) Degree LaTrobe University: 18-46.


Rundles RW. (1945) Medicine 24, III.


STRUCTURAL AND FUNCTIONAL CHANGES IN THE FEET OF YOUNG PEOPLE WITH TYPE 1 DIABETES MELLITUS

By

ANTHONY C. DUFFIN

Doctor of Philosophy

2002

University of Western Sydney

© AC Duffin, April 2002
“Coming events cast their shadow before”

Thomas Campbell
PLEASE NOTE

The greatest amount of care has been taken while scanning this thesis,

and the best possible result has been obtained.
Statement of Authentication

The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in whole or in part, for a degree at this or any other institution.

Anthony Cecil Duffin
ETHICAL APPROVAL

All studies described in this thesis were approved by the Ethics Committee of The University of Western Sydney and the Ethics Committee of The Children’s Hospital at Westmead. All subjects, or their parents when appropriate, gave written informed consent for the examinations undertaken.
ACKNOWLEDGEMENTS

I would firstly like to thank my supervisors Dr. Robert Kidd and Dr. Kim Donaghue. Without the support of these two outstanding individuals this thesis would not have been completed. I think myself lucky to have had two such devoted mentors and friends to assist me in this arduous task.

I would also like to especially thank Dr. Albert Lam for making available ultrasonic equipment for use in this project. Not only did Dr. Lam allow me to use the equipment but he also gave freely of his time to ensure that the protocol used was appropriate and that I was well tutored in the use of the equipment.

I am very grateful to the staff of the Ray Williams Institute of Endocrinology and the Medical Imaging Department of The Children’s Hospital at Westmead. All the staff in these two departments have given me invaluable advice and friendship in the 17 years I have been associated with the hospital and especially during the time I have been undertaking this Ph.D. In particular I wish to thank Mr. Albert Chan for his advice and assistance with data and statistical evaluation, Ms. Mandy Crocker, Ms. Janine Cusumano, Ms. Lucy Cutler and Dr. Jan Fairchild whose data on other microvascular complications of diabetes I used in conjunction with my own data. Their hard work allowed me to investigate the broader significance of my findings.

Another group of people whose assistance and friendship has been greatly valued during this project is the staff and students of The University of Western Sydney, Macarthur. Without the financial and academic support of the School of Podiatry I would have been unable to undertake this thesis. I would particularly like to thank Diana
Palin (final year Podiatry student) for giving up her free time to assist me in data collection for almost a year. Her help and enthusiasm made the immense task of data collection much more enjoyable.

Possibly the most important group to thank are the adolescents who were the subjects of the studies described in this thesis. In many cases these people traveled great distances and gave much of their free time to assist in pilot studies and follow up treatment evaluations. This was particularly true in the case of the control subjects whose only reward was the hope that their contribution may in some way help to fathom the complexities of a widespread and potentially devastating disease. To them, their parents and friends, I extend my heartfelt thanks.

This work was financially supported by Clark’s Footwear Australia, the Australian Podiatry Association (N.S.W.) membership and the Diabetes Podiatry Group (N.S.W.). These organisations were extremely supportive throughout the project and I thank them.

Finally, I wish to acknowledge the unwavering support of my family over the period of this project. My children, James and Lyndal, gave up my company for many nights and weekends (sometimes thankfully) and helped when possible by being photographic models and guinea-pigs for various experimental measuring techniques. Above all I give my love and thanks to my wife, Denise. Denise has given me all the support and assistance any partner could ask for. She has been invaluable to the editing of this thesis, and has remained enthusiastic throughout my Ph.D. candidature. Thank you, Denise for the many, many hours of our life you have given up to enable me to complete this thesis.
# TABLE OF CONTENTS

Table of Contents

List of Tables

List of Figures and Illustrations

List of Plates

List of Abbreviations

Definitions

Abstract

Introduction

Hypotheses to be tested

Aims and Overview of this Thesis

## Chapter One

**Review of Literature**

1.1 Diabetes Mellitus

1.2 Complications of Diabetes Mellitus affecting the lower limb

1.2.1 Diabetic Neuropathy

1.2.2 Limited Joint Mobility (LJM)

1.2.3 Non-enzymatic glycation / pathogenesis

1.2.3.1 Differential diagnoses of non-enzymatic glycation

1.3 Force and pressure

1.3.1 Force plates

1.3.2 Pressure plates

1.3.3 In-shoe devices

1.3.4 Reducing high pressure
1.3.4.1 Cushioning 26
1.3.4.2 Orthoses 26
1.4 Joint examinations 27
  1.4.1 The ankle (talocrural) joint 28
  1.4.2 The subtalar (talocalcaneal) joint 30
  1.4.3 The 1st metatarsophalangeal (MTP) joint 33
  1.4.4 The interphalangeal (IP) joints of the fingers and toes 36
1.5 Joint measurement 38
  1.5.1 Goniometry 38
    1.5.1.1 Measuring the ankle joint 39
    1.5.1.2 Measuring the subtalar joint 40
    1.5.1.3 Measuring the 1st metatarsophalangeal joint 42
    1.5.1.4 Measuring the interphalangeal joint of the fingers and toes 43
1.6 Soft tissue examination 45
  1.6.1 The plantar aponeurosis 45
  1.6.2 The skin 49
1.7 Evaluating soft tissue of the foot 50
  1.7.1 Ultrasound 52
    1.7.1.1 Ultrasonic display modes and scan converter 54
    1.7.1.2 Echo reflection 57
1.8 The gait cycle 59
1.9 Conclusions 65
Chapter Two

Materials and methods

2.1 Selection of subjects

2.1.1 Exclusion criteria

2.2 Materials and method – Limited joint mobility

2.2.1 Joint selection

2.2.1.1 Ankle joint measurement

2.2.1.2 Subtalar joint measurement

2.2.1.3 1st metatarsophalangeal joint measurement

2.2.1.4 Interphalangeal joint measurement of the fingers and toes

2.2.1.5 Other examinations

2.2.2 Definitions of limited joint mobility

2.3 Materials and method – Pressure analysis

2.3.1 Equipment

2.3.2 Method

2.3.3 Data analysis

2.3.4 Definition of high plantar pressure

2.4 Materials and method – Interventions

2.4.1 Subject selection and exclusion criteria exclusive to this section

2.4.2 Equipment

2.4.2.1 Cushioning

2.4.2.2 Non-weightbearing casting

2.4.2.3 Custom orthoses

2.4.3 Methods
2.4.4 Data analysis

2.5 **Materials and method – Soft tissue examination**

2.5.1 Subject selection and exclusion criteria exclusive to this section

2.5.2 Equipment

2.5.2.1 Ultrasound equipment selection criteria

2.5.2.2 Precautions - The biological effects of ultrasound

2.5.3 Methods

2.5.3.1 Foot and arch length measurement

2.5.3.2 Skin and plantar aponeurosis measurements

2.5.4 Definition of soft tissue abnormalities

2.6 **Consideration of error**

2.6.1 Examination of joint mobility

2.6.2 Examination of plantar pressure

2.6.3 Examination of interventions

2.6.4 Examination of soft tissues

2.7 **Further consideration of examination methods**

2.7.1 Accuracy of examination methods

2.7.2 Potential side effects from examinations

2.7.3 Ethical issues

2.8 **Statistical evaluations**

2.8.1 Consideration of statistical methods
Chapter Three

Limited joint mobility in young people with Type 1 Diabetes Mellitus

Specific aims of this section of the study

3.1 Characteristics and joint mobility of diabetic subjects vs. non-diabetic controls in the current study

3A Comparison of the current study with Duffin et al, 1999

3A.1 Comparison of age, gender and joint motion of diabetic subjects in the current study and Duffin et al, 1999

3A.2 Comparison of age, gender and joint motion of non-diabetic control subjects in the current study and Duffin et al, 1999

3A.3 Comparison of diabetic subjects affected by LJM in the current study and Duffin et al, 1999

3A.4 Comparison of diabetic subjects affected by microvascular complications in the current study and Duffin et al, 1999

3A.5 Discussion

3A.6 Conclusions

3B Defining LJM as 2 standard deviations below the control mean

3B.1 Comparison of diabetic subjects with and without LJM

3B.2 Diabetic subjects with LJM at both the ST and 1st MTP joints

3B.3 Associations between various microvascular complications of DM

3B.4 Sensitivity and specificity of joints tests

3B.5 Discussion

3B.6 Conclusions
Chapter Four

Plantar pressure, pressure time integrals and plantar callus in young people with Type 1 Diabetes Mellitus

Specific aims of this section of the study

4.1 Plantar pressure of diabetic subjects vs. controls
   4.1.1 High peak pressure
   4.1.2 High pressure time integrals
   4.1.3 Plantar callus
   4.1.4 Plantar callus and HPP

4.2 Discussion

4.3 Conclusions

Chapter Five

Monitoring interventions in young people with Type 1 diabetes mellitus who display high plantar pressure, high pressure time integrals or plantar callus

Specific aims of this section of the study

5.1 Monitoring interventions
   5.1.1 High peak pressure – interventions
   5.1.2 Plantar callus – interventions
   5.1.3 Twelve-month follow up of diabetic subjects with and without orthoses

5.2 Discussion

5.3 Conclusions
Chapter Six

*Plantar skin and plantar aponeurosis changes in young people with Type 1 Diabetes Mellitus*  
167

Specific aims of this section of the study  
167

6.1 Skin and plantar aponeurosis changes due to DM  
168

6.2 Discussion  
174

6.3 Conclusions  
177

Chapter Seven

*Stratified analyses of young people with Type 1 diabetes mellitus*  
178

Specific aims of this section of the study  
178

7.1 Stratification process  
179

7.1.1 Retinopathy  
181

7.1.2 Elevated AER  
181

7.1.3 Sensory nerve changes  
181

7.1.4 HbA1c levels  
183

7.2 Discussion  
183

7.3 Conclusions  
185

Chapter Eight

*Summary, conclusions, clinical implications and future direction of research*  
186

8.1 Summary  
187

8.1.1 Complications of diabetes  
190

8.1.2 Anomalies found which may be complicated by diabetes  
190

8.1.3 Monitoring interventions  
191

8.2 Conclusions  
192
Chapter Nine

References

Appendix No. 1 - Published paper –
# LIST OF TABLES

<p>| Table 1.1 | Documented risk factors for the development of foot problems in adults and adolescents with DM | 6 |
| Table 1.2 | Differential diagnoses of LJM in young people with DM | 14 |
| Table 1.3 | Acoustic impedance of various body components | 58 |
| Table 2.1 | Intraclass correlation coefficients values for the repeatability of examinations using the Novel Pedar | 100 |
| Table 3.1 | Comparison of control and subjects with diabetes in the current study | 109 |
| Table 3.2 | Characteristics of diabetic subjects – current study vs. 1999 study | 110 |
| Table 3.3 | Characteristics of control subjects – current study vs. 1999 study | 111 |
| Table 3.4 | Comparison of percentage of diabetic subjects affected by LJM and significant associations with other characteristics – current study vs. 1999 study | 113 |
| Table 3.5 | Percentage of diabetic subjects affected by microvascular complications of diabetes – current study vs. 1999 study | 114 |
| Table 3.6 | Characteristics of diabetic subjects with LJM (&lt;22°) at the subtalar joint | 120 |
| Table 3.7 | Characteristics of diabetic subjects with LJM (&lt;60°) at the 1st MTP joint | 121 |
| Table 3.8 | Characteristics of diabetic subjects with LJM (&lt;180° of extension) in the fingers | 122 |
| Table 3.9 | Characteristics of diabetic subjects with LJM (&lt;180° of extension) in the toes | 123 |
| Table 3.10 | Characteristics of diabetic subjects with LJM (&lt;100.5°) at the ankle joint (knee flexed) | 124 |
| Table 3.11 | Characteristics of diabetic subjects with LJM at both the ST and 1st MTP joints | 126 |
| Table 3.12 | Association between elevated AER and retinopathy | 127 |
| Table 3.13 | Association between abnormal nerve test and retinopathy | 127 |
| Table 3.14 | Association between abnormal nerve test and elevated AER | 127 |
| Table 4.1 | Comparison of peak pressure, pressure/time integrals and contact time controls and diabetic subjects | 135 |
| Table 4.2a | Characteristics of diabetic subjects with and without HPP | 137 |
| Table 4.2b | Pressure and joint variables of diabetic subjects with and without HPP and of controls with and without HPP | 138 |
| Table 4.3 | Joint motion of diabetic subjects with highest plantar pressure under the hallux compared to highest plantar pressure under the metatarsal heads | 139 |
| Table 4.4 | Comparison of diabetic subjects with and without high P/TI | 141 |
| Table 4.5a | Characteristics of diabetic subjects with and without plantar callus | 143 |
| Table 4.5b | Pressure and joint variables of diabetic subjects with and without plantar callus and of controls with and without plantar callus | 144 |
| Table 4.6 | Comparison of diabetic subjects with high peak pressure and plantar callus in combination | 146 |
| Table 5.1a | Results of interventions for diabetic subjects with high peak pressure | 154 |
| Table 5.1b | Individual responses to interventions - number of diabetic subjects with &lt;5%, 5-25%, 26-50% and &gt;50% reduction in PP and P/TI | 155 |
| Table 5.2a | Results of interventions for diabetic subjects with plantar callus | 157 |
| Table 5.2b | Individual responses to interventions - number of diabetic subjects with &lt;5%, 5-25%, 26-50% and &gt;50% reduction in PP and P/TI | 158 |
| Table 5.3a | Changes in peak pressure, pressure time integrals and contact time over 12 month period for diabetic subjects with and without orthoses | 160 |
| Table 5.3b | Individual responses after 12 months - number of diabetic subjects with &lt;5%, 5-25%, 26-50% and &gt;50% reduction in PP and P/TI | 161 |
| Table 6.1 | Comparison of skin and aponeurosis thickness controls vs. diabetic subjects | 168 |
| Table 6.2 | Comparison of diabetic subjects with and without thickened plantar aponeurosis | 171 |
| Table 6.3 | Comparison of diabetic subjects with and without thickened skin | 172 |
| Table 7.1 | Stratification of abnormalities in diabetic subjects based on joint motion, soft tissue changes and increased pressure | 180 |
| Table 7.2 | Odds ratio for abnormal sensory nerve tests as a function of increasing P/TI and contact time | 182 |
| Table 8.1 | Known risk factors for development of foot problems in adults with DM and their presence in young people with DM | 187 |
| Table 8.2 | Risk factors for foot pathology and statistically significant associations with other variables | 189 |</p>
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1.1</td>
<td>The Sorbitol (polyol) Pathway</td>
<td>7</td>
</tr>
<tr>
<td>Figure 1.2</td>
<td>Proteins with a half-life of days to weeks</td>
<td>15</td>
</tr>
<tr>
<td>Figure 1.3</td>
<td>Long-lived structural proteins</td>
<td>16</td>
</tr>
<tr>
<td>Figure 1.4</td>
<td>Early transference of weightbearing force to the forefoot due to restricted ankle flexion</td>
<td>28</td>
</tr>
<tr>
<td>Figure 1.5</td>
<td>Anatomy of the ankle joint</td>
<td>30</td>
</tr>
<tr>
<td>Figure 1.6</td>
<td>Anatomy of the subtalar joint</td>
<td>32</td>
</tr>
<tr>
<td>Figure 1.7</td>
<td>Minimum range of 1st MTP joint motion required during final propulsion</td>
<td>34</td>
</tr>
<tr>
<td>Figure 1.8</td>
<td>Anatomy of the 1st metatarsophalangeal joint</td>
<td>35</td>
</tr>
<tr>
<td>Figure 1.9</td>
<td>Anatomy of the interphalangeal joints of the fingers and toes</td>
<td>37</td>
</tr>
<tr>
<td>Figure 1.10</td>
<td>Root method of measuring ankle joint dorsiflexion</td>
<td>39</td>
</tr>
<tr>
<td>Figure 1.11</td>
<td>Root method of measuring subtalar joint motion</td>
<td>41</td>
</tr>
<tr>
<td>Figure 1.12</td>
<td>The plantar aponeurosis</td>
<td>47</td>
</tr>
<tr>
<td>Figure 1.13</td>
<td>The Windlass effect</td>
<td>48</td>
</tr>
<tr>
<td>Figure 1.14</td>
<td>The skin</td>
<td>50</td>
</tr>
<tr>
<td>Figure 1.15</td>
<td>A-mode display</td>
<td>54</td>
</tr>
<tr>
<td>Figure 1.16</td>
<td>M-mode display</td>
<td>55</td>
</tr>
<tr>
<td>Figure 1.17</td>
<td>B-mode image</td>
<td>56</td>
</tr>
<tr>
<td>Figure 1.18</td>
<td>The stance phase of gait</td>
<td>61</td>
</tr>
<tr>
<td>Figure 1.19</td>
<td>The swing phase of gait</td>
<td>61</td>
</tr>
<tr>
<td>Figure 1.20</td>
<td>Stride length</td>
<td>63</td>
</tr>
<tr>
<td>Figure 1.21</td>
<td>Base of gait or ‘stride width’, Angle of gait or ‘foot angle’</td>
<td>64</td>
</tr>
<tr>
<td>Figure 1.22</td>
<td>Angle of gait</td>
<td>64</td>
</tr>
<tr>
<td>Figure 2.1</td>
<td>Relationship of contact time to speed</td>
<td>100</td>
</tr>
<tr>
<td>Figure 6.1</td>
<td>Range of thickness of plantar aponeurosis</td>
<td>169</td>
</tr>
<tr>
<td>Figure 6.2</td>
<td>Plantar aponeurosis thickness vs. foot size (controls)</td>
<td>173</td>
</tr>
<tr>
<td>Figure 6.3</td>
<td>Plantar aponeurosis thickness vs. foot size (diabetes)</td>
<td>173</td>
</tr>
<tr>
<td>Figure 8.1</td>
<td>Pathways for prevention of, or progression to, amputations in young people with TIDM</td>
<td>198</td>
</tr>
<tr>
<td>Plate</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>1.1</td>
<td>Test for active extension of the IP joints of the hands (the prayer sign)</td>
<td>44</td>
</tr>
<tr>
<td>1.2</td>
<td>Test for passive extension of the IP joints of the hands</td>
<td>44</td>
</tr>
<tr>
<td>2.1</td>
<td>Ankle joint measurement – knee extended</td>
<td>70</td>
</tr>
<tr>
<td>2.2</td>
<td>Ankle joint measurement – knee flexed</td>
<td>70</td>
</tr>
<tr>
<td>2.3</td>
<td>Tractograph</td>
<td>71</td>
</tr>
<tr>
<td>2.4</td>
<td>Marking the leg and foot for ST joint measurements</td>
<td>71</td>
</tr>
<tr>
<td>2.5</td>
<td>Orthopaedic evaluation device (OED)</td>
<td>73</td>
</tr>
<tr>
<td>2.6</td>
<td>1st MTP joint measurement</td>
<td>73</td>
</tr>
<tr>
<td>2.7</td>
<td>Pedar data collection unit</td>
<td>78</td>
</tr>
<tr>
<td>2.8</td>
<td>Subject fitted with Pedar data collection unit</td>
<td>78</td>
</tr>
<tr>
<td>2.9</td>
<td>Non-weightbearing, neutral position plaster cast</td>
<td>82</td>
</tr>
<tr>
<td>2.10</td>
<td>Custom orthosis fabricated from low density polyethylene</td>
<td>82</td>
</tr>
<tr>
<td>2.11</td>
<td>ACUSON 128 grey scale imager</td>
<td>85</td>
</tr>
<tr>
<td>2.12</td>
<td>Branic foot measuring device</td>
<td>85</td>
</tr>
<tr>
<td>2.13</td>
<td>Foot markings for plantar aponeurosis evaluations</td>
<td>90</td>
</tr>
<tr>
<td>2.14</td>
<td>Plantar skin measurement</td>
<td>91</td>
</tr>
<tr>
<td>2.15</td>
<td>Plantar aponeurosis measurement</td>
<td>91</td>
</tr>
<tr>
<td>4.1</td>
<td>Flexion of digits and intrinsic muscle wasting</td>
<td>150</td>
</tr>
</tbody>
</table>
**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AER</td>
<td>Albumin excretion rate</td>
</tr>
<tr>
<td>AGE</td>
<td>Advanced glycated endproduct</td>
</tr>
<tr>
<td>AIUM</td>
<td>American Institute of Ultrasound Medicine</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>AV</td>
<td>Arteriovenous</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>C</td>
<td>Celsius</td>
</tr>
<tr>
<td>CI</td>
<td>95% confidence intervals for odds ratio</td>
</tr>
<tr>
<td>CRT</td>
<td>Cathode ray tube</td>
</tr>
<tr>
<td>DCCT</td>
<td>Diabetes Control and Complications Trial</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>EDG</td>
<td>Electrodynagraph</td>
</tr>
<tr>
<td>GHb</td>
<td>Glycated haemoglobin</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Glycated haemoglobin measurement</td>
</tr>
<tr>
<td>HPP</td>
<td>High peak pressure</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
</tr>
<tr>
<td>ICC</td>
<td>Interclass correlation coefficient</td>
</tr>
<tr>
<td>IP</td>
<td>Interphalangeal</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>Kg</td>
<td>Kilogram</td>
</tr>
<tr>
<td>Km/hr</td>
<td>Kilometers per hour</td>
</tr>
<tr>
<td>KPa</td>
<td>Kilopascals</td>
</tr>
<tr>
<td>KPa/sec</td>
<td>Kilopascals per second</td>
</tr>
<tr>
<td>LDPE</td>
<td>Low density polyethylene</td>
</tr>
<tr>
<td>LJM</td>
<td>Limited joint mobility</td>
</tr>
<tr>
<td>MCP</td>
<td>Metacarpophalangeal</td>
</tr>
<tr>
<td>Mhz</td>
<td>Megahertz</td>
</tr>
<tr>
<td>MTP</td>
<td>Metatarsophalangeal</td>
</tr>
<tr>
<td>N</td>
<td>Newtons</td>
</tr>
<tr>
<td>NADPH</td>
<td>Nicotinamide-adenine dinucleotide phosphate</td>
</tr>
<tr>
<td>N/A</td>
<td>Not assessed</td>
</tr>
<tr>
<td>OED</td>
<td>Orthopaedic evaluation device</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PCA</td>
<td>Plantar calcaneal area</td>
</tr>
<tr>
<td>PHA</td>
<td>Plantar hallux area</td>
</tr>
<tr>
<td>PIP</td>
<td>Proximal interphalangeal joint</td>
</tr>
<tr>
<td>PMA</td>
<td>Plantar metatarsal area</td>
</tr>
<tr>
<td>PP</td>
<td>Peak pressure</td>
</tr>
<tr>
<td>PPT</td>
<td>An open cell polyurethane cushioning material</td>
</tr>
<tr>
<td>PT/I</td>
<td>Pressure time integrals</td>
</tr>
<tr>
<td>ROM</td>
<td>Range of motion</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>ST</td>
<td>Subtalar</td>
</tr>
<tr>
<td>T1DM</td>
<td>Type 1 diabetes mellitus</td>
</tr>
<tr>
<td>T2DM</td>
<td>Type 1 diabetes mellitus</td>
</tr>
</tbody>
</table>
DEFINITIONS

AER $\geq 7.5$ $\mu$g/min  Mean albumin excretion rate greater than or equal to 7.5 $\mu$g/min (95th centile for Australian children)

Eversion  A complex triplane motion involving pronation, abduction and dorsiflexion

Force  The action of one body on another. It possesses quantity, magnitude and direction; force is equal to mass times acceleration, $F = MA$

Inversion  A complex triplane motion involving supination, adduction and plantarflexion

Pressure  A force steadily exerted upon or against another in contact with it; pressure is equal to force divided by area, $P = F/a$

Retinopathy  Presence of any microaneurysm or haemorrhage in either eye
ABSTRACT

Diabetes can affect the structure and function of the foot, resulting in severe limitation of mobility and reduction of life expectancy. The early warning signs of foot problems in adults with diabetes have been investigated and treatments evaluated, but few studies have examined the feet of young people with diabetes. Early warning signs of foot problems include limited joint mobility (LJM), soft tissue changes, high plantar pressure (HPP), high pressure time integrals (P/TI) and plantar callus. These abnormalities were examined in 216 young people with diabetes and 57 controls.

The fingers, toes, ankle, subtalar (ST) and 1st metatarsophalangeal (MTP) joints showed reduced motion and the plantar aponeurosis was thicker in diabetic subjects. Skin thickness was the same for diabetic and control subjects. Limited joint mobility in the feet was more common in males and older subjects. Subtalar and finger LJM was associated with early sensory nerve changes and finger LJM was associated with retinopathy and higher HbA1c. Thicker plantar aponeurosis was associated with male gender and larger feet.

High peak pressure, high P/TI and callus were no more common in diabetic subjects than controls. However high P/TI and callus were associated with early sensory nerve changes in young people with diabetes. Diabetic subjects with callus were significantly older than those without callus. Those with HPP had higher body mass index and less motion at the 1st MTP joints than those without HPP. Although plantar callus, HPP and high P/TI were no more common in young people with diabetes these anomalies may be complicated by diabetes.

Cushioning, custom orthoses or both in combination significantly reduced peak pressure and P/TI’s in diabetic subjects. Young people with diabetes who had
worn orthoses for twelve-months had significantly lower peak pressure than those who had not, even when the orthoses were removed.
INTRODUCTION

Fifty percent of people with diabetes will develop diabetic neuropathy within 25 years of disease onset (Diabetes in Australia, 1996). Many of these people will develop plantar neuropathic ulcerations which, when further complicated by infection and/or vascular insufficiency, can result in gangrene and amputation. Diabetes related foot problems account for half of all non-traumatic lower limb amputations in the USA (ADA, 1993).

For many years distal symmetric polyneuropathy was accepted as the primary determinant of neuropathic ulcerations, but in recent years the development of these lesions has been investigated from new perspectives. Delbridge et al (1988) and Mueller et al (1989) were among the first to question why only some and not all people with diabetic neuropathy develop plantar ulcers. They investigated the relationship between limited joint mobility (LJM) and neuropathic ulcerations on the feet of adults with diabetes and concluded that limited motion at the subtalar joint interfered with the foot's ability to absorb shock and transfer forces efficiently during the midstance and propulsive phases of the gait cycle. Investigations into the development of neuropathic ulcers continued from this time and it is now generally accepted that LJM alters the dynamics of gait, causing high plantar pressures which lead to ulceration on the neuropathic foot (Cavanagh et al, 1991; Fernando et al, 1991; Masson, 1992; Cavanagh and Ulbrect, 1994).

Plantar callus, which acts in a manner analogous to a foreign body, has also been shown to increase plantar pressure in adults with DM and has been implicated in the development of neuropathic ulcers (Young et al, 1992; Veves et al, 1992; Katoulis et al, 1996). In 1992, Young et al confirmed the relationship between plantar
callus and high plantar pressure by removing callosity and thereby reducing plantar pressure by up to 26%.

In 1995, Kidd and Kidd suggested another possible complicating factor in the development of neuropathic ulcers. Non-enzymatic glycation of collagen could tighten the plantar aponeurosis leading to the formation of a cavoid foot type with resultant plantarflexion of the metatarsal heads.

The plantar metatarsal area and the digits are common areas for the development of neuropathic ulcers (Edmonds et al, 1986; Walters et al, 1992). As the plantar aponeurosis is rich in collagen (Palastanga et al, 1989; Sarrafian, 1993) it is susceptible to non-enzymatic glycation of its collagenous component and may be affected by the complications of diabetes. It has not previously been examined.

Upper body skin changes in subjects with diabetes have also been demonstrated in recent years. Alterations in skin structure and function resulting from diabetes are similar to those that occur in Scleroderma and in the aging process (Goodfield and Millard, 1988; Brik et al, 1991). The skin on the plantar surface of the foot has to undergo many stresses during daily activities. It protects individuals from mechanical trauma (Edwards and Marks, 1995), so early recognition of pathological changes in plantar skin is extremely important.

All the scientific investigations into structural and functional changes in the feet of people with diabetes have focused on mature subjects with a view to discovering predisposing factors in the development of serious foot problems. It is expected that early intervention will increase mobility and reduce mortality for ‘at risk’ individuals. This study has focused on young people with diabetes, with a view to discovering if these same predisposing factors are present and discernible and thus treatable at an earlier age.
Until recently the presence of LJM in young people with diabetes has only been used as an indicator of other systemic complications of the disease and has not been seen as a potentially pathological complication in itself. Indeed, research into LJM in young people with diabetes did not extend more distally than the ankle joint (Rosenbloom et al., 1981; Rosenbloom et al., 1983; Rosenbloom, 1984; Shinabarger, 1987; Tubiana-Rufi et al., 1991; Brik et al., 1991). In 1996 it was then found that the subtalar and 1st metatarsophalangeal joints of the foot were also affected by LJM in a large percentage of adolescents with diabetes (Duffin et al., 1996). However this work raised more questions than it answered, and it is these questions which are the subject of this study.

Limited joint mobility is present in the feet of young people with diabetes. Is it associated with increased plantar pressure? Skin changes have been found in young people with diabetes. Are these changes evident on plantar skin, which is most at risk from trauma in people with diabetes? Does diabetes change the structure and function of the plantar aponeurosis as suggested by Kidd and Kidd? If so do these changes lead to potentially pathological mechanical changes in foot function? Callus increases plantar pressure and risk of plantar ulceration. Do young people with diabetes have plantar callus? Are structural and functional changes in the feet of young people with diabetes associated with microvascular changes?

The early diagnoses and treatment of diabetic foot problems is crucial in reducing morbidity and mortality in the diabetic population. Having developed diabetes at an early age, young people with diabetes are at great risk of developing complications of this disease during their lifetime. The early recognition of foot abnormalities in young people with diabetes must be considered extremely important.
Prevention of, or progression to, amputation

The progression to lower limb amputation in people with diabetes mellitus may follow several pathways. In many cases these pathways can be interrupted and prevention of amputation is possible. The following flow-chart describes the processes involved in the progression to lower limb amputation in subjects with diabetes mellitus and suggests the stages at which interventions may arrest or at least postpone further tissue breakdown and amputation.
Pathways for prevention of, or progression to, amputation in people with DM

- Limited joint mobility in the foot
- Callus formation
- Foot deformities (incl. Hammer toes)
- Plantar soft tissue changes

- Gait changes
- High plantar pressure and high pressure time integrals
- Shoe pressure on dorsal, medial and lateral soft tissues

- Intervention and pressure reduction
- Sensory neuropathy and / or vascular insufficiency
- Intervention and pressure reduction

- Intervention and tissue repair
- Soft tissue breakdown and ulceration

- Infection / gangrene

- Partial foot amputation
- Lower limb amputation
HYPOTHESES AND AIMS OF THIS THESIS

Hypotheses to be tested

1) That plantar callus and LJM of the subtalar, 1st metatarsophalangeal and ankle joints are present in the feet of young people with type 1 diabetes mellitus and are associated with microvascular complications of diabetes, soft tissue changes and increased plantar pressures during gait.

2) That cushioning materials, firm orthoses and the combination of both can reduce plantar pressures and pressure time integrals in adolescents with diabetes.

3) That young people with diabetes have thickening of the plantar aponeurosis and skin which is associated with microvascular complications, LJM in the foot and high plantar pressures.

4) That a simple single joint test may be used to indicate which young people with diabetes have microvascular disease, LJM, high plantar pressures, and thickening of the plantar aponeurosis and skin.
Aims of this thesis

The aims of this thesis are described below. The specific aims of each study are described at the beginning of each chapter.

1) To examine the feet of young people with diabetes for structural and functional abnormalities known to predispose adults with diabetes to serious long-term foot problems.

2) To determine whether in-shoe interventions could reduce plantar pressures and pressure time integrals in young people with diabetes.

3) To identify a simple testing procedure that could be used to detect pathomechanical and microvascular changes in young people with diabetes.

Overview of this thesis

Chapter one provides historical background material and a framework needed to understand the examinations undertaken. Chapter two describes the materials and methods used in this study. Chapter three examines the joint motion of subjects with diabetes compared to non-diabetic controls. Chapter four examines plantar pressure and plantar callus in subjects with diabetes compared to non-diabetic controls. Chapter five investigates interventions which may be used to reduce high plantar pressure and plantar callus. Chapter six assesses soft tissue thickness of subjects with diabetes compared to non-diabetic controls. Chapter seven investigates the interaction of any abnormalities found in young people with diabetes. Chapter eight summarises and concludes the thesis and suggests the clinical implication of findings and the direction of future research in this area.