EDITORIAL
DIABETES MELLITUS AND THE RHEUMATOLOGIST

RHEUMATOLOGISTS have long accepted that diabetes predisposes to septic arthritis and is also the commonest cause of neuropathic joints outside lepromatous regions. The diabetic atherosclerotic plaque and capillary basement membrane thickening are both disorders of connective tissue matrix and it is therefore not surprising that interstitial connective tissues such as skeleton, joints and periarticular structures are also affected. These disorders fall into two groups. Firstly, there are those characterized by reduced bone density: insulin is a bone growth factor and mild osteoporosis commonly occurs before insulin-dependent diabetes is treated. It is caused by a failure of new bone formation rather than increased resorption [1, 2]. Secondly, there are disorders of inappropriate connective tissue deposition.

Most attention has focused on the second category and two reports in this issue explore these associations [3, 4]. Lundbaeck [5] described hand stiffness in young diabetics in 1957 and this was subsequently termed 'diabetic hand syndrome', 'limited joint mobility' or 'cheiroarthropathy'. The clinical signs of thick, tight waxy skin, joint restriction and tenosynoviosclerosis (rather than tenosynovitis) are reminiscent of scleroderma. Perhaps 'diabetic collagenosis' is a preferable term. Skin thickening occurs over the dorsal of the hands [6–8], and in one report was found proximal to the metacarpophalangeal joints and over the toes [8]. Another feature of diabetic collagenosis is joint restriction. The prevalence of distal upper limb joint limitation is 8–50% [2, 4, 8] and large joints may also be affected [8, 9]. Recent reports have shown that non-insulin-dependent diabetics (NIDD) may be as affected as juvenile-onset insulin-dependent patients (IDD). Forty-five per cent of adult NIDD had limited joint mobility, although 86% were receiving insulin [10]! The Newcastle group have described this in 52% of adults with NIDD [4]. Most authors have reported no relationship between joint restriction and sex, insulin dosage or quality of control as measured by glycosylated haemoglobin (Hb A1C). In contrast, most reports emphasize that joint restriction is related to disease duration [4, 6, 9] and microangiopathy [3, 4, 6, 9]. A defective microcirculation may indeed link scleroderma to diabetic collagenosis and perhaps the study of diabetic nailfold capillaries may prove as useful as their examination in scleroderma.

Fibrous thickening of flexor tendon sheaths is also critical [8, 11]. The Middlesex Hospital group, perhaps illogically, chose to exclude such patients from their study group and also excluded patients with Dupuytren's contracture [3]. Noble et al. [12] recognized mild tethering of skin and knuckle pads as features of Dupuytren's as defined by the presence of contractile myofibroblasts. Most physicians would hesitate before drawing clinical distinctions between dermal sclerosis, joint capsular thickening, flexor tenosynoviosclerosis and mild Dupuytren's contracture. These may share a single pathogenesis in diabetes. Myofibroblasts have been reported in the nodules of Ledderhose's disease of the plantar fascia [13] and in penile tissue in Peyronie's disease [14], both of which are, more common in diabetes. Carpal tunnel syndrome also complicates the diabetic hand [15] but Fisher et al. [3] have not confirmed the association between diabetic joint contracture and carpal tunnel syndrome previously reported [16]. This is surprising as median nerve delay in diabetes is probably caused by fibrous compression. The Middlesex Hospital group did not perform nerve conduction studies on all their patients and further data are awaited.
The two reports in this issue disagree about the association of collagenosis of the distal ('cheiroarthropathy') with the proximal limb ('adhesive capsulitis'). Pal et al. [4] found that of 21 diabetics who had shoulder capsulitis, 12 also had 'cheiroarthropathy'. However, they could not confirm a significant difference between the prevalence of shoulder capsulitis in patients with and without limited joint mobility. Fisher et al. [3] by careful matching with diabetics who had no hand involvement have demonstrated an association of shoulder capsulitis with distal involvement. It is likely that diabetic capsulitis differs fundamentally from the idiopathic form. The diabetic shoulder may be less painful, respond less well to treatment and last longer. This view would be compatible with the histological report of diabetic shoulder capsular tissue which found microangiopathy and fibrosis identical to that of Dupuytren's disease [17]. In contrast, many cases of idiopathic capsulitis have true inflammatory features [18]. Shoulder capsulitis, an attenuated form of shoulder–hand syndrome, has also been considered an example of algodystrophy [2]. Diabetes predisposes to all forms of this expanding disease category [19] and 'forefoot osteolysis' occurs almost exclusively in diabetes [20].

Associations between diabetes and commoner rheumatological diseases have been proposed. The link with pyrophosphate arthropathy has not been confirmed [21] and a recent review concluded that non-obese diabetics run no greater risk of gout [2]. Since both diabetes and RA share HLA-DR associations, their coexistence is not surprising although this has been disputed [22]. Osteoarthritis may be commoner and more severe in diabetics [10, 23]. Insulin stimulates cartilage and proteoglycan biosynthesis but in diabetics there is depressed cartilage growth and reduced formation of proteoglycans and high molecular weight aggregates [2, 24]. There is an increased incidence of ankylosing hyperostosis, hyperostosis frontalis interna and osteitis condensans illi in diabetes and it is possible that they are mediated by somatomedins, stimulated by increased growth hormone [25]. These growth factors may also be important in diabetic collagenosis.

The molecular basis of diabetic collagenosis is unclear. It could result from increased synthesis or reduced degradation of collagen. Diabetic skin fibroblasts synthesize more collagen in vitro [26]. Hyperglycaemia increases glycosylation of collagen and keratin which may make diabetic collagen more resistant to degradation. Its decreased solubility in acetic acid suggests increased intermolecular cross-linking [7]. The stimulation in diabetes of lysyl oxidase activity, a critical enzyme in collagen cross-link formation [27], may be more important than increased glycosylation which may inhibit the cross-linking and maturation of collagen fibres [28].

Tight control of blood glucose may reduce skin thickness and improve joint mobility [11]. A novel, less obvious therapeutic avenue has been suggested. Cyclo-oxygenase inhibitors prevent an increase in the thermal rupture time of diabetic rat tail collagen (a measure of collagen stability) and could, in theory, be useful in the treatment of diabetic collagenosis [29].

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