definition of occupational kneeling and squatting has varied between studies, but relative risks have often been two or higher.

It seems likely that the hazard arises from unusual mechanical stresses on the joint, and it is notable that the same occupational activities have also been linked with degenerative tears of the menisci. In addition, some occupations such as professional footballers carry a risk of acute meniscal injury which may later lead to osteoarthritis.

The challenge now is to translate these epidemiological observations into effective policies for the prevention of disease. In most developed countries, the requirement for heavy physical work has declined over recent decades as a consequence of increasing mechanisation. However, there are still many jobs that involve kneeling or squatting. Often, as for example in the construction industry, the work environment is difficult to control and the hazardous tasks cannot easily be eliminated or substituted. Knee pads may be used to reduce discomfort and protect against pre-patellar bursitis, but as yet we have no evidence that they reduce the risk of osteoarthritis.

Another approach might be to identify individuals who are at unusually high risk from kneeling because of the concomitant presence of other risk factors. For example, in a recent case-control study, the interaction of occupational kneeling with obesity was approximately multiplicative. It follows that the absolute reduction in risk from avoidance of obesity would be greater in workers who have to kneel in their jobs. Where the combination of occupational kneeling with other risk factors leads to exceptionally high risk, there may even be a case for selectively excluding such individuals from certain jobs.

Physiology of endothelial cell – Friday 15 June, 16.00-17.30/South Hall

SP0087 TISSUE ENGINEERING AND STEM CELL BIOLOGY: DEVELOPMENT OF BONES, JOINTS AND SYNOVIUM

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Skeletal morphogenesis begins in structures called limb buds 4 1/2 weeks after gestation. The limb buds, comprised of mesodermal cells, form at discreet locations beneath a layer of ectoderm. The initial stimuli for limb development are still vague, but FGF-8 and possibly retinoic acid are important. By week 5 the limb primordium begins to bulge from the body wall. Despite the bud's simple structure it contains enough information to guide its development, for if transplanted to another site or cultured *in vitro* it will become a limb. At the apex of the bud is a thickened ectoderm (apical ectodermal ridge) and experiments have shown that continuous interactions between the AER and underlying mesoderm promote the initiation phase, outgrowth phase, and subsequent skeletal morphogenesis. The limb develops along three axis's; proximodistal (base of limb to digits); anteroposterior (digits 1 to 5); dorsoventral (top of hand/foot to palm/sole). Each is under the influence of "morphogens" made in discreet signalling centres.

Abstract SP0087 Table 1

Axis	Signalling Centre	Molecular signals
Proximodistal	Apical ectodermal ridge (AER)	FGF-2, 4, 8
Anteroposterior	Zone of polarising activity (ZPA)	Sonic hedgehog
Dorsoventral	Dorsal ectoderm	Wnt-7a (dorsal)
	Ventral ectoderm	En-1 (ventral)

Skeletal elements of the limbs first appear in a core of mesenchymal cells, then in cartilage (weeks 5 1/2 to 6 1/2), and finally in bone (6 to 8 weeks). The condensed cells that form the pre-cartilage express bone morphogenetic proteins (BMP-2 and -4). As development continues they are restricted to cells that will become periosteum or perichondrium.

In contrast, BMP-6 is only expressed in maturing cartilage within limbs. Another signalling molecule, Indian hedgehog, found in the same location is thought to induce the BMP-6 expression.

Joint formation is a late feature in limb differentiation. Around week 6, between condensations in the precartilage, there develop transverse bands of tightly packed, flat mesenchymal cells, called interzones. At this time, growth/differentiation factor-5, a member of the BMP family, is expressed in the condensed cells. The interzone consists of two regions of high cell density surrounding a region of low cell density. The former will become articular cartilage, while the latter disappears through apoptosis leaving behind a cavity. At the periphery of each interzone are mesenchymal cells and blood vessels. These arise from the primordial perichondrium and will become the future synovium and joint capsule.

The synovium consists of an incomplete lining (the intima) sitting on a vascularized matrix. After birth two cell types can be identified. One (the type A synoviocyte) arises in the bone marrow, passes into the circulation and enters the joint as a monocyte, but during its progression into the intima acquires attributes of a tissue macrophage (including the CD68 phenotype). The other lining cell is a specialised fibroblast, similar to bone marrow stromal cells that supports hematopoiesis (type B – fibroblast-like synoviocyte). However, these only acquire VCAM-1 and the typical FLS phenotype after birth.

The shafts of long bones (diaphysis) are completely ossified at birth, but the ends of the bones (epiphysis) are still cartilaginous. Only later, when secondary centres of ossification develop does this segment gradually become bone. Even then, however, a layer of cartilage persists between the epiphysis and the growing end of the diaphysis. In man chondrocyte proliferation continues in this growth plate for about twenty years and not until epiphyseal fusion does bone growth cease.

SP0089 CELL-BASED TECHNOLOGIES IN JOINT REPAIR

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Tissue engineering is a field of Biomedicine that is rapidly growing, and is critically driven by scientific advances in the areas of developmental and cell biology, material sciences and biochemistry/polymer chemistry. Regeneration of skeletal tissues, including joint surface repair, skin repair, and treatment of CNS disorders are among the most promising areas, and are closest to