Key reference database project
ACC Internal Review
Draft 19 March 2013

Causation of knee pathologies/ injuries

Part A

Meniscal tears
Meniscal tears - their relationship to osteoarthritis
Association of knee alignment and knee pathology
Chondral injuries and edema post trauma
Insufficiency fracture
Chondrocalcinosis and gout: their effect on the knee joint
Ganglion cysts

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Summary

In this report (Part A) definitions, causation and other factors related to various knee injuries and disease are reviewed to answer a wide range of questions. The body of this report concentrates on the literature post 2009 as much of the earlier literature was covered in a previous report published in 2010 that investigated the evidence for degeneration and trauma as causes of meniscal tearing\(^1\). A summary of the 2010 report can be found in Appendix 1.

The Summary here is extensive as it is structured to answer specific questions and includes information from this report and the 2010 report.

Part B of the report concentrates on the more clinical aspects of knee trauma/disease including diagnosis, imaging and treatment.

Meniscal tears

1. What are the different types of meniscal tear and what causes them?

   Key references - Anderson\(^2,3\) for terminology, Englund\(^4\) for a general background review

   The terminology of meniscal tears has been standardised (page 16). Horizontal, complex and flap tears are often considered to be of degenerate origin whereas vertical tears are usually of traumatic origin. They can be associated with anterior cruciate ligament (ACL) tears.

   The evidence that horizontal, flap and complex tears are often of degenerate origin and that vertical tears are predominantly traumatic comes from the following –

   - There is high quality evidence from a cohort study\(^5\) that prevalence of meniscal tears and meniscal degeneration increases strongly with age; in ambulatory subjects 50 to 90 years of age over 40% of the tears found were horizontal tears and 37% complex, suggesting that these types are most typically associated with age and are of degenerative origin.
   - Histological studies in cadavers which show that horizontal tears and flap tears are characteristically found in the menisci of older subjects\(^6,7\).
   - Direct observation at surgery showed that complex, flap and horizontal tears were found more commonly in the older population and followed a more degenerative pattern\(^8\).
   - A clear association of peripheral, vertical tears with ACL injuries\(^9,10\) which therefore suggests a traumatic origin for these types of tears.
   - Occurrence of tears in symptomatic and asymptomatic knees: the prevalence of tears has been compared in the traumatically injured knee with that in the contralateral uninjured knee\(^11\). The prevalence of horizontal and flap tears did not differ between symptomatic and asymptomatic knees whereas vertical and complex tears were found mainly in the symptomatic knees. In a similar study it was found...
that recent trauma was associated with the presence of radial, longitudinal and complex meniscal tears, and not with horizontal\textsuperscript{12}.

- Body mass index (BMI): there is good evidence from one community based cohort study and one case-control study that prevalence of tears is strongly associated with BMI\textsuperscript{5,13}.
  More recent studies have supported the link between obesity and meniscal damage\textsuperscript{14,15}.

- Association with osteoarthritis (OA). There is excellent evidence from a variety of studies that degenerate menisci and degenerative tears, particularly horizontal tears and complex tears, are more strongly associated with the presence of OA than other tears. In one study the percentage of horizontal tears increased from 18.4\% where no OA was present to 61.5\% for grade 3 OA\textsuperscript{7}. Tears are so common in the elderly with moderate OA that some consider it to be pointless to conduct an MRI to prove their presence (in one study 91\% of such subjects had meniscal tears\textsuperscript{16}).

It is concluded that the body of evidence outlined above makes a compelling case for a dichotomous classification of tears into those predominately of a degenerative origin (horizontal and flap, and to a lesser extent complex) and those of predominately traumatic (longitudinal-vertical) origin. This classification is not absolute and it must be accepted that there are many gray areas.

2. Are horizontal cleavage tears of the menisci considered degenerative in nature? (literature after 2009).

Horizontal tears are the archetypal degenerative tear. The evidence for this is as outlined in question 1. Newer research has linked horizontal tears to the development of OA and this provides further evidence that in general, horizontal tears are mostly degenerative in nature.

- Crema\textsuperscript{17} studying a cohort of community-based women found a significant relationship between single tears, most of which were horizontal, and cartilage loss measured two years later in the central medial femur.

- Based on research which studied the relationship between meniscal tears and meniscal position, Allen\textsuperscript{18} has hypothesized that ‘complex tears, meniscal maceration, intrameniscal cysts and degenerative horizontal tears which lead to meniscal extrusion, predispose to more rapid, progressive OA’.

3. What is the prevalence of asymptomatic meniscal tears in normal knees?

Key reference - Englund\textsuperscript{5}

There is high quality evidence from the Framingham cohort, (50 – 90 years of age) that meniscal tears and meniscal degeneration as determined by MRI increase with age. Overall prevalence of meniscal damage was 35\% and 31\% for meniscal tears. The great majority of these tears were degenerative (horizontal, flap, complex and tears in a degenerated meniscus). The prevalence of a meniscal tear or of meniscal destruction in the right knee as detected on MRI ranged from 19\% among women 50 to 59 years of age to 56\% among men 70 to 90 years of age.
In another Framingham study, in those who had no detectable OA by radiography (mean age 62, 29% had knee pain) it was shown by MRI that prevalence of meniscal lesions rose from 17% in those aged 50-59 to 36% in those over 69.

Meniscal tears and their relationship to OA

Key reference - Englund

4. What relationship does the morphology of meniscal tears have to osteoarthritis (OA) of the knee?

5. What is the strength of any association between osteoarthritis and meniscal tears (including prevalence/incidence of meniscal tears in population with OA knees)? Do specific tear types or configurations of meniscal pathology have an increased/decreased association with osteoarthritis?

In general the prevalence of degenerative tears especially horizontal tears is strongly associated with OA. There are multiple lines of evidence that meniscal tearing and meniscal degeneration are strongly related to the development of OA. The evidence for this is as follows:

**Strength of the association of tears (in general) with OA**

Bhattacharyya et al reported a case-control study on the clinical importance of meniscal tears as detected by MRI to the presence or absence of symptoms of OA. They found that medial or lateral meniscal tears were a very common finding in older asymptomatic subjects (prevalence 76%) but were more common in the patients with symptomatic osteoarthritis (91%).

**Association of OA with particular types of tear**

There is good evidence that particular types of tear are more strongly associated with OA than others.

Noble in his histological case series studies has shown that the coincidence of horizontal cleavage lesion and osteoarthritis is frequent. The percentage of horizontal tears increased from 18.4% where no OA was present to 61.5% for grade 3 OA.

Englund et al in a cohort study investigated the link between the development of hand OA and knee OA in a group of patients who had undergone a meniscectomy 20 years earlier. They found that those who developed hand OA had a higher incidence of degenerative types of meniscal tears (flap, horizontal, complex and tears in a meniscus with degenerative changes) 20 years earlier than did patients who did not develop hand OA (47% of those who developed hand OA had meniscal degeneracy compared to 26% who did not develop hand OA). Furthermore, the subjects who had a degenerative meniscus had developed radiographic knee OA more frequently 20 years later than had patients with non-degenerate tears both in the index knee and in the contralateral knee. They suggested that a degenerative tear may be regarded as an early signal of susceptibility to osteoarthritic disease.

As outlined in question 2, Crema studying a cohort of community-based women found a significant relationship between single tears, most of which were horizontal, and cartilage loss measured two years later in the central medial femur.
Studies in Turkish\textsuperscript{21} and Asian\textsuperscript{22,23} populations have found that radial tears of the root of the medial posterior horn are associated with OA, chondral lesions, obesity and meniscal extrusion. According to Ozkoc\textsuperscript{21} radial tears may have a traumatic or degenerative origin.

**Association with severity of tearing**
Englund\textsuperscript{24} found in older subjects that those with minor tears were 3 times more likely to develop OA over 30 months than those without; those with severe tears were 7.9 times more likely to do so.

**Association with progression of OA**
There is excellent evidence from prospective cohort studies that those with meniscal tears at baseline will in the following years be more likely to go on and develop radiographically detectable OA as well as symptomatic OA. Englund\textsuperscript{24} found in older subjects (50 - 79 years), followed for 30 months, that meniscal damage (any tear, maceration or destruction) at baseline was more frequent in those who developed symptomatic OA than for control knees (those who did not develop OA) (54\% v. 18\%); those with any meniscal damage at baseline were 5.7 times more likely to develop OA than those without. It was concluded that a meniscal tear in middle aged to older subjects was a potent risk factor for the development of OA.

**Risk factors for fast cartilage loss**
Roemer\textsuperscript{25} in a high quality cohort study showed in subjects of mean age 61 years and with a low radiographic score at baseline that over the following 30 months, BMI, meniscal tears and extrusion were risk factors for fast cartilage loss.

**Association of knee alignment with knee pathology**

6. What is the effect of the knee alignment (varus/valgus) in the development of knee pathology (meniscal tears/ degenerative/OA change)?

Hunter in a 2009 review believed it was clear that malalignment was a critical determinant of OA disease progression\textsuperscript{26}; varus alignment increased risk of OA progression medially and valgus alignment increased risk laterally.

A large cohort study has also found evidence that varus alignment was a risk factor for incident cartilage damage in the medial compartment\textsuperscript{27}. Valgus was not associated with incident damage.

In a cohort of middle aged to older American subjects\textsuperscript{15} without meniscal pathology at baseline, varus alignment was associated with an approximately 100\% increased risk of development of meniscal pathology at 30 month follow up. And others consider that meniscal and other structural changes are likely to lead to further malalignment\textsuperscript{28}.

It is concluded that malalignment increases risk of cartilage damage, meniscal pathology and OA progression. There is some evidence that varus malalignment increases risk of initiation of OA as well. In general it seems that varus alignment impacts medially, valgus laterally.
Chondral injuries and edema post trauma

7. Some literature around chondral injuries post trauma in the weight-bearing surface of the knee joint (medial/ lateral femoral condyle).

**Epidemiology of chondral defects**

A systematic review of eleven studies has been made to determine the prevalence of chondral defects in the knees of athletes. The mean overall prevalence of full thickness focal chondral defects was 36%; 35% of defects were located on the femoral condyles, 37% in the patellofemoral joint and 25% on the tibial plateaus. Of those studies that classified defects on the femoral condyle, 68% were medial and 32% lateral. Of those with patellofemoral defects, 64% were patella and 36% trochlea. 59% of asymptomatic athletes (basketball players or endurance runners) had a full thickness defect.

In the general population the prevalence of full thickness articular cartilage defects as determined at arthroscopy was around 16%. In those aged under 40 years without any other concurrent knee pathology, prevalence was 5%.

Participants in a large, community-based study in Framingham who had no detectable OA by radiography (mean age 62, 29% had knee pain) were subsequently shown to have a high prevalence of lesions typical of OA in the tibiofemoral joint when examined by MRI. Prevalence of any lesion was 89%. Osteophytes were found in 74%, cartilage damage in 69%, bone marrow lesions in 52% and meniscal lesions in 24%. Prevalence of meniscal lesions rose from 17% in those aged 50-59 to 36% in those over 69. The authors concluded that most middle aged to older subjects show lesions typical of OA. This suggests that in older people a high proportion of the population may have MRI detectable knee lesions in the absence of recent or any acute trauma.

It is concluded that chondral defects after injury are extremely common in athletes and MRI detectable chondral damage is common in older community-living subjects with no radiographically detectable OA.

**Cartilage loss in relation to meniscal lesions**

Research is showing that meniscal lesions do not necessarily have a global impact on development of chondral lesions.

- Chang et al investigated the subregional impact of a meniscal tear on cartilage loss over two years. They found that cartilage loss was not spatially uniform across the tibial and femoral cartilage surfaces and some of the impact of a meniscal tear occurred locally. For example, medial posterior horn tears were specifically associated with posterior tibial subregion cartilage loss and other subregions were not affected.

- A case series analysis has reported that medial meniscus tears were most commonly observed arthroscopically in association with medial femoral condyle lesions while lateral tears were most commonly associated with lateral tibial plateau lesions.

- These findings were reinforced by Huetink who reported that after 10 years of follow up the characteristic finding of OA development after a medial meniscus tear was diffuse medial cartilage loss and after lateral meniscus tears, focal lateral cartilage loss. After ACL rupture OA was seen mostly medially but also laterally.
MRI of 17 subjects with traumatic knee injury has shown that after a mean time of 9.1 years at follow up, of those who developed cartilage loss, in each case the loss was seen adjacent to the subregions where meniscal damage and/or osteochondral damage had occurred.

**Cartilage loss post ACL rupture**

Cartilage loss post ACL rupture is more global. A Swedish study investigated the presence of OA in knees of subjects who had experienced ACL ruptures either 12 years earlier (57 women) or 14 years earlier (120 men). All subjects had been injured playing soccer. Structural changes in the ACL injured group were evenly distributed between medial and lateral compartments and there was a relatively even distribution between osteophytes on the tibia and femur. In the non traumatic group structural changes were largely located medially. The authors concluded that there was a global effect on degeneration of cartilage after ACL injury.

8. What are bone marrow edema, bone bruising, bone marrow lesions and subchondral edema? What are the differences?

**Key reference – Roemer** (covers definitions and imaging)

**Definitions**

Post-traumatic bone bruises are thought to be a result of fractures of the medullary trabecula which are usually neither seen radiologically nor at arthroscopy; in OA the bone marrow edema-like signal is secondary to bone marrow necrosis, fibrosis and trabecular abnormalities with only minimal edema.

Roemer suggests that it is appropriate to use the term ‘bone marrow lesions (BML)’ for a range of subchondral MRI signal alterations and to add the specific type of lesion being discussed (e.g. traumatic BML without associated fracture; idiopathic, non-traumatic BML). Roemer presents a useful table (page 1120) that provides a basis for distinguishing various lesions and thereby defining them. For example, ‘traumatic bone marrow lesions’ are described there as ‘bone contusion/bone bruise; they have the typical appearance of a diffuse, epi- or epi-metaphyseal lesion without other associated imaging findings; their location depends on injury mechanism; the history includes adequate direct or indirect trauma, the lesion is seen immediately after trauma; they are typically seen in young active and elderly patients; they often have other associated ligamentary/meniscal injuries; and the lesion itself usually resolves within two years’.

The term bone bruise/contusion seems to be reserved for a bone marrow lesion/edema where there is a clear history of acute injury to which it may be attributed. Typically a bone bruise resulting from trauma would be expected to be found in non-cystic areas.

Roemer’s table provides the basis for differential diagnosis of the various bone marrow lesions. Further notes on diagnosis of bone bruise, methods of distinguishing their etiology and their relation to mechanism of injury are provided in Part B of this report.

**Epidemiology of bone marrow lesions/edema and natural history**

In a case series study of subjects referred for suspected meniscal tears (mean age 42.7 years), edema-like bone marrow abnormalities were found in 36% of symptomatic knees compared to 3% in the contralateral, asymptomatic knee.
A Tasmanian, community-based cohort study\textsuperscript{38} (mean age 63) has reported that 43\% of subjects had bone marrow lesions at baseline. Over 2.7 years 25\% of lesions decreased in size, 24\% increased and 7\% developed a new lesion. A change in size of the bone marrow lesions was associated with changes in pain in those without established radiographic OA.

Bone marrow edema and other knee lesions were commonly found pre-season in asymptomatic basketball players\textsuperscript{39}. This and other studies have lead Lin\textsuperscript{36} to conclude that the presence of bone marrow edema-like signals in athletes must be interpreted with caution as they may be pre-existing and transitory.

The osteochondral impact over time of edema/bone bruising due to trauma appears to be variable: Koster\textsuperscript{40} found that, at one year post trauma in a younger cohort, 23\% showed an increase in the grade of OA which was strongly linked to the presence of edema post-injury. In contrast Roemer\textsuperscript{41} concluded that, after a minimum of 2 years post-trauma, bone marrow edema had disappeared in the majority of patients. It is quite clear though that knee injury is itself a potent risk factor for the development of OA\textsuperscript{42}.

It is concluded that the term bone marrow lesion is the preferred terminology but additional information is required for interpretation. Such lesions are very common in the community and in some cases may be transitory. Their presence need not necessarily be indicative of recent acute trauma as they are also associated with a wide range of other conditions.

**Insufficiency fracture**

9. What is the cause of insufficiency fracturing in the knee? What role if any does trauma play?

Key references – Kattapuram\textsuperscript{43}, Roemer\textsuperscript{35} for definitions and imaging diagnosis.

**Introduction**

Stress fractures have been defined\textsuperscript{44} as ‘fatigue fractures’ which occur when abnormal stress is applied to bone that has normal elasticity, whilst ‘insufficiency fractures’ occur when the stress of normal daily living is applied to bone with deficient elastic resistance.

According to Kattapuram et al\textsuperscript{43} the pathology originally known as idiopathic or spontaneous osteonecrosis of the knee (SONK) might now be more appropriately described as subchondral insufficiency fracture. In their view the evidence suggests that it is an acute fracture that occurs as a result of chronic stress or minor trauma to a weakened subchondral bone plate. Typically it is seen in older, female patients without a history of trauma and the osteonecrosis involves the distal femur, proximal tibia and one or both condyles or plateaus.

Roemer\textsuperscript{35} provides a range of definitions together with MRI characteristics –

- Insufficiency fractures are a type of stress fracture that occurs in bone unable to withstand the stresses of daily living and are observed in situations where bone
mineral content is reduced. They are not the result of physical activity or preceding trauma.

- Repetitive microtrauma/overuse. Stress-related bone marrow lesions can be observed without any existing degenerative or traumatic changes.

- SONK most often affects the weight-bearing surface of the medial femoral condyle and typically occurs in elderly female patients who present with severe medial joint pain unrelated to trauma.

**Epidemiology**

The prevalence of SONK in older patients has been determined in a prospective cohort study of subjects presenting with initial meniscal symptoms without a history of trauma. Overall prevalence of SONK of the medial femoral condyle was 3.4% for those over 50 years of age and 9.4% in those over 65 years. In 5.7% of patients initially diagnosed with SONK the lesion was transient.

**Pathogenesis**

There is no consensus in the literature as to causation of insufficiency fracture and little evidence to suggest that insufficiency fracture is not a subset of a range of SONK-like pathologies with multiple etiologies. It has been suggested that SONK may arise from a primary vascular incident or a subchondral stress fracture, both of which may lead to an elevation of intraosseous pressure and subsequent osteonecrosis. Kattapurum has suggested that possible causation has been linked to meniscal lesions which may induce stresses that lead to ischaemic necrosis of the femoral condyle.

Osteoporosis and osteopenia are commonly found in patients with osteonecrosis of the knee but this is not seen in all patients.

It is concluded that insufficiency fracture is likely to be part of a spectrum of disorders which have an uncertain etiology. In some cases insufficiency fracture is associated with meniscal lesions, osteoporosis and osteopenia, but this is not always the case.

**Distinguishing insufficiency fracture of traumatic origin from non-traumatic causations**

Insufficiency fracture may be distinguished from subchondral fractures accompanying trauma, as with trauma there are usually signs of other traumatic meniscal and ligament injuries.

Kattapuram has also proposed that lesions are likely to be due to an acute injury when they are characterised by MRI as having a linear component in the subchondral bone, a substantial region of edema and tend to occur in the weight bearing portions of the knee, typically the medial femoral condyle. Lesions without a linear component or significant edema were distributed in all locations: they were associated with articular cartilage defects and were considered to be due to subacute or chronic processes associated with OA.
Chondrocalcinosis and gout: their effect on the knee joint

10. What effect does chondrocalcinosis/ calcium pyrophosphate deposition (CPPD) have on the menisci and joint surfaces?

Key references - Richette\textsuperscript{49}, Filippucci\textsuperscript{50} for ultrasound findings associated with calcium pyrophosphate disease, Zhang\textsuperscript{51, 52} for EULAR recommendations on terminology, diagnosis and management

Introduction

Calcium pyrophosphate deposition disease (CPPD) is a generic term referring to calcification within the cartilage usually due to calcium pyrophosphate deposition\textsuperscript{53}. Chondrocalcinosis (CC) refers to radiographic calcification of the articular, fibro or hyaline cartilage; pyrophosphate arthropathy refers to structural abnormalities of the bone and cartilage associated with CPPD\textsuperscript{49}.

Crude prevalence of CPPD in a British community was 7% and the main risk factors were age and OA. There was no gender effect on prevalence and CPPD was bilateral in 72% of cases\textsuperscript{49}. CPPD has strong associations with a range of clinical conditions including hyperparathyroidism, gout and hemachromatosis\textsuperscript{54}.

Clinical presentation

The knee is the most common site for CPPD\textsuperscript{51}. EULAR proposes four clinical presentations as follows -

- Asymptomatic: CC is frequently asymptomatic and an incidental finding in older subjects\textsuperscript{49}.
- OA with CPPD: joint shows changes of OA and CPPD present.
- Acute calcium pyrophosphate crystal arthritis (replaces the term pseudogout): acute onset, self limiting synovitis with CPPD\textsuperscript{51}. The acute onset of severe joint pain, swelling and tenderness that reaches a maximum at 6-24 hours with overlying erythema is highly suggestive of this condition but not specific.
- Chronic CPP crystal inflammatory arthritis: chronic inflammatory arthritis associated with CPPD\textsuperscript{51}.

Association with OA

OA and CC induced arthropathy have pathological profiles that are indistinct from each other and the effect that each has on the pathogenesis of the other is not clear\textsuperscript{49}, but people with OA are three times more likely to have CPPD\textsuperscript{51}. CPPD in knees with OA may associate with more inflammatory features and more rapid progression than in knees without CPPD but the associations are marginal and not useful for diagnosis\textsuperscript{51}. CPPD may associate with an atypical distribution of OA: OA with CPPD may occur less in such joints as the elbow and radiocarpal joints and show more patellofemoral compartment involvement\textsuperscript{51}. 
Association with meniscal tearing

In a case series of over 1000 knee arthroscopy cases (mean age 67) it was found that 74.1% of those with CC had meniscal tears compared to a prevalence of 28.7% in those without CC (there was a low level of trauma related events in the series). Relative risk of tears in knees with CC was 2.58 compared to those without CC. The authors concluded that CC was a strong predictor of meniscal tearing.

Association with trauma

CC has been reported to occur after joint trauma, typically in younger subjects and unilaterally without evidence of other disease. The knee joint was involved in 13 of 18 subjects in a case series; 9/13 had undergone a meniscectomy and the remaining four appeared to have meniscal tears. Another study found CC to be more common in post-meniscectomy/post-injury knees than in the contralateral, unoperated knee.

Arthropathy

Pathological abnormalities have been described in CPPD in 85 men and women with an average age of 74 years. Arthropathy was commonly observed in the knees as well as other joints and resembled OA with joint space narrowing, subchondral eburnation and cyst formation. Calcification of knee fibrocartilage was seen in nearly all affected knees and of hyaline cartilage in about half of the cases. CPPD differed from degenerative disease in the following respects:

- The arthropathy was not only observed in weight bearing articulations such as the knee and hip but also at sites not commonly affected by OA such as the wrist, elbow and glenohumeral joint.
- The intra-articular distribution of abnormalities was unusual and in the knee featured the patellofemoral compartment.
- Subchondral cyst formation was prominent. At X-ray cysts appeared frequently and were often large.
- CPPD was frequently severe and progressive with extensive subchondral bony collapse and fragmentation resulting in numerous intra-articular bodies.
- Osteophyte formation was variable.

An ultrasound assessment of knees with CPPD, presumably with less advanced disease than in the above study (median age 66; median duration of disease 6 years), has reported that 37.1% of knees also had joint effusion, 64.2% showed intra-cartilaginous hyperechoic spots in the hyaline cartilage of the femoral condyles, 77.1% had meniscal calcification, 7.8% had had enthesal thickening of the quadriceps tendon, 7.1% showed hyperechoic spots in the patellar tendon, 9.3% enthesal thickening of the patellar tendon and 27.1% a popliteal cyst in the gastrocnemius-semimembranous bursa.

Natural history

A prospective study has followed 64 patients (mean age at initial visit 66 years) initially presenting with CC and/or CPPD crystals in the synovial fluid. In 91% of subjects the knee was the major joint involved. Over 4.6 years, symptoms worsened in 27%,
remained the same in 33% and improved in 41%. 27% developed symptoms in new joints. Arthropathy (described as joint space narrowing with subchondral bone reaction, osteophytes, loss of cortical integrity, cyst formation and CC) worsened in 16%, often with an increase in osteophyte formation with bone remodelling. In 50% arthropathy remained unchanged. The authors concluded that CPPD is not necessarily progressive and those presenting with acute attacks alone do well.

Conclusion

It is concluded that CPPD has strong associations with age and OA but is probably not strongly associated with the progression of OA: these conclusions are supported by a systematic review. In advanced disease the arthropathy may be severe. CPPD may occur unilaterally in association with knee injury or following meniscal surgery.

11. What effect does gout have on the menisci and joint surfaces of the knee?

The overall prevalence of gout is around 0.7% to 1.4% in men and 0.5% to 0.6% in women. In people older than 65, prevalence is 4.4% to 5.2% in men and 1.8% to 2.0% in women. In males prevalence reaches a maximum in the fifth decade.

Incidence and prevalence parallel that of hyperuricemia, which is closely associated with increased risk of developing gout. It has been shown in a cross-sectional study that gout at individual joint sites (including the knee) is positively associated with clinically assessed OA at that site. The authors hypothesised that OA may predispose to deposition of urate crystals but there appears to be a lack of evidence for this conclusion.

An ultrasound assessment of knees with gout (median age, 59; median duration of disease 6 years) has reported that 35% of knees also had joint effusion, 16% synovial hypertrophy and 41.6% had enhancement of the superficial margin of the hyaline cartilage of the femoral condyles; none had calcification of the menisci.

Ganglion cysts

12. What is the cause of ganglion cyst in the knee joint?

Key reference - McCarthy

McCarthy describes ganglion cysts as benign cystic masses with a dense fibrous connective tissue capsule containing a viscous mucous rich in mucopolysaccharides. They may include a main body, pseudopodia and small capsular cysts communicating with the main body.

The incidence of intra-articular cysts or ganglia varies between 0.6% and 2% as seen at arthroscopy in symptomatic knees. Krudwig et al have reported on a retrospective case series of nearly 8000 knees investigated by arthroscopy where 85 ganglion cysts were found: 58% originated from the ACL, 19% from the posterior cruciate ligament (PCL), 14% from the anterior menisci, 4% from the posterior menisci, 4% in the infrapatellar fat pad, and one each from the medial plica and the subchondral bone.

Krudwig et al reported that 11% of those with ganglion cysts in their case series were symptomatic due to the cyst's presence and that none of these cysts were associated with
concomitant intra-articular lesions. In the remaining 89% symptoms were attributed to degenerative diseases and all such knees demonstrated signs of meniscal and/or patellofemoral pathologies.

McCarthy\textsuperscript{62} has outlined a number of theories for causation including -

- Most commonly it is believed that ganglion cysts result from mucoid cystic degeneration in a collagenous structure in areas under stress such as the joint capsule and tendon. Consistent with this theory is that ganglion cysts are often located in areas under stress and cells of the ganglion lining are able to secrete substances rich in mucopolysaccharides.
- Primary cellular hyperplasia with mucin secretion and secondary cystic degeneration of connective tissue.
- Development from proliferating pluripotential mesenchymal cells.
- Ganglia arise from displaced synovial remnants that have arisen during embryogenesis.

There appears to be no clear evidence or consensus to support one theory over another. Trauma has been reported as being implicated in the pathogenesis of ganglion cysts -

- In Krudwig's series\textsuperscript{64} many of the 85 cases with ganglion cysts reported a history of repeated minor trauma, 'usually without a single episode of serious injury'.
- In those with posterior cruciate ligament ganglion cysts, 40% had a history of trauma\textsuperscript{65}
- In other case series of subjects with intra-articular cysts, an injury was reported prior to the onset of symptoms in 38%, 45% and 67% of cases\textsuperscript{63}. 

Causation of knee pathologies/ injuries

Part A

Introduction

In 2010 a review on the causation of meniscal tears was prepared\(^1\) which outlined the evidence that certain types of tears (horizontal and flap) were most commonly of degenerative origin and longitudinal-vertical tears were most commonly related to acute traumatic events especially anterior cruciate ligament injuries. A summary of this report is included in Appendix One along with key references.

In this follow-up report the causation and related issues of various knee injuries and diseases are reviewed covering the questions set out in the Summary and reviewing in the main the literature post 2009 as much of the earlier literature was covered in the 2010 report. For convenience the report has been broken down into two parts: Part A dealing with definitions, causation and related subjects and Part B with the more clinical aspects.

Meniscal tear terminology

Key reference - Anderson\(^2\,^3\)

The International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine (ISAKOS) has an agreed terminology for classification of meniscal tears and quality of meniscal tissue as follows\(^3\) (Fig 1) -

Tear shape:
- Longitudinal-vertical: extension is a bucket handle tear
- Horizontal
- Radial
- Horizontal flap
- Vertical flap
- Complex (2 or more tear patterns).

Quality of Tissue:
- Non-degenerative
- Degenerative
- Undetermined
ISAKOS discourages the use of the terms acute, subacute and chronic in preference to the time from onset of symptoms. Classifications for tear depth, location, radial location etc. are also given in Anderson.

The ISAKOS Committee also uses the term 'degenerative tear' and suggests that they have characteristics that include cavitation, multiple tear patterns, softening of meniscal tissue, fibrillation and other degenerative changes.

**Traumatic meniscal tears**

*Key reference - Englund*

The archetypal traumatic meniscal tear is the longitudinal - vertical tear and it occurs acutely in association with knee twisting and sports injuries. The meniscus splits vertically and in line with the circumferential collagen fibres parallel to the meniscal periphery (Fig 1) resulting in a longitudinal tear. Such tears are often associated with ACL injury.

**Degenerative meniscal tears**

The main degenerative meniscal tears are horizontal and flap. Complex tears are also often included in this category. The evidence that they are degenerative comes mainly from their association with age and OA.
**Meniscal anatomy/ histology**

**Key reference - Englund**

The matrix of the meniscus is about 75% collagen fibres, mostly type 1, which superficially are orientated radially but in the deep layer are arranged circumferentially following the meniscal periphery. The radial fibres are woven between the circumferential fibres which helps distribute the load stresses. According to Anderson, the changing pattern of tears with aging probably reflects the changes that occur in collagen fibre orientation with aging and intrasubstance degeneration.

In the menisci of those with OA there is a severe loss of collagen especially in the middle and deep zones compared to those in controls, suggesting that the menisci are actively affected by the disease process of OA.

**Recent research and studies not included in 2010 report**

Meniscal tears and osteoarthritis (OA)

**Key reference - Englund**

1. **Prevalence of knee lesions**

Participants in a large, community-based study in Framingham, who had no detectable OA by radiography (mean age 62, 29% had knee pain) were subsequently shown to have a high prevalence of lesions typical of OA in the tibiofemoral joint when examined by MRI. Prevalence of any lesion was 89%. Osteophytes were found in 74%, cartilage damage in 69%, bone marrow lesions in 52%, and meniscal lesions in 24%. Prevalence of meniscal lesions rose from 17% in those aged 50-59 to 36% in those over 69. The authors concluded that most middle aged to older subjects show lesions typical of OA. This suggests that in older subjects a high proportion of the population have MRI detectable knee lesions.

2. **Localised impact of meniscal tears on chondral lesions**

Research is showing that meniscal lesions do not necessarily have a global impact on development of chondral lesions.

- Chang et al investigated the subregional impact of a meniscal tear on cartilage loss over two years. They found that cartilage loss was not spatially uniform across the tibial and femoral cartilage surfaces and some of the impact of a meniscal tear occurred locally. For example medial posterior horn tears were specifically associated with posterior tibial subregion cartilage loss and other subregions were not affected.

- A case series analysis has reported that medial meniscus tears were most commonly observed arthroscopically with medial femoral lesions while lateral tears were most commonly associated with lateral tibial plateau lesions.

- These findings were reinforced by Huetink who reported that after 10 years of follow up the characteristic finding of OA development after a medial meniscus tear was diffuse medial cartilage loss and after lateral meniscus tears, focal lateral cartilage loss. After ACL rupture OA was seen mostly medially but also laterally.
• MRI of 17 subjects with traumatic knee injury has shown that after a mean time of 9.1 years at follow up, of those who developed cartilage loss, in each case the loss was seen adjacent to the subregions where meniscal damage and/or osteochondral damage had occurred.

• See also Crema study below (4).

3. Development of OA in ACL ruptured knees

Key reference - Sward

A Swedish study investigated the presence of OA in knees of subjects who had experienced ACL ruptures either 12 years earlier (57 women) or 14 years earlier (120 men). All subjects had been injured playing soccer. The presence of OA was compared with the knees of 155 subjects with non-traumatic knee pain. Stark but not absolute differences in the location of OA were found between the two groups. Structural changes in the ACL injured group were evenly distributed between medial and lateral compartments and there was a relatively even distribution between osteophytes on the tibia and femur. In the non traumatic group structural changes were largely located medially. The authors concluded that there was a global effect on degeneration of cartilage after ACL injury. The increased development of OA in the lateral compartment after ACL injury compared to that in subjects with intact ACLs has been confirmed in an American study. This study and others referred to in this paper indicate that ACL injuries result in long term pathology in the medial compartment and also laterally.

A smaller American cohort study has reported that chondral degradation may occur longer term after ACL injury in compartments unaffected by the initial bone bruise. Regardless of whether or not subjects received reconstructive surgery, 7 to 11 years after injury, risk of cartilage loss for the lateral femoral condyle was 50 times baseline, 30 times for the patella and 19 times for the medial femoral condyle.

4. Is the development of OA linked to specific tears types?

Crema et al studying a cohort of community-based women found a significant relationship between single tears, most of which were horizontal, and cartilage loss measured two years later in the central medial femur. They concluded that horizontal tears may alter the function of the medial meniscus and lead to regional cartilage loss; the degenerative tears could be an early sign of degeneration of the medial compartment including the underlying articular cartilage.

Studies in Turkish and Asian populations have found that radial tears of the root of the medial posterior horn are associated with OA, chondral lesions, obesity and meniscal extrusion. According to Ozkoc radial tears may have a traumatic or degenerative origin.

Intrameniscal signal changes not regarded as tears do not appear to be a risk factor for subsequent cartilage loss nor for subsequent development of tears over one year.

Based on their research Allen et al have hypothesized that ‘complex tears, meniscal maceration, intrameniscal cysts and degenerative horizontal tears which lead to meniscal extrusion, predispose to more rapid, progressive OA’.

It is concluded then that there is some evidence that horizontal tears are linked to the development of OA and possibly complex and radial tears as well.
5. Risk factors for OA

In a multicentre US study five or more bony enlargements in the finger joints increased risk of knee meniscal pathology by about 60% over 30 months of follow up. The authors concluded that their data supported the hypothesis that meniscal tissue is affected by degenerative processes possibly related to an early stage generalised OA process. Similarly a Norwegian based cohort study has reported that hand joint space narrowing is associated with reduced knee cartilage thickness medially, and hand osteophytes are associated with radiographic knee OA. These and other papers provide good evidence that OA often has a significant systemic component and development of knee OA is not always an anatomically isolated process.

Additional studies on the impact of obesity on prevalence of meniscal and cartilage lesions

A cohort study has reported that in middle aged subjects without baseline OA there was a higher prevalence and severity of meniscus and cartilage lesions in those with a raised BMI; there was also significantly increased cartilage lesion progression over 36 months of follow up in those with a raised BMI. A second cohort study found that obesity as measured by a BMI greater than or equal to 30 was a risk factor for development of meniscal extrusion at 30 month follow up, but not for meniscal lesions. Such obesity increased risk of medial meniscal pathology by about 50% over that seen in those with a BMI of 25 or less.

Impact of knee alignment on knee pathology

Key references – Hunter, Sharma

Hip, knee and ankle alignment contribute to the load distribution across the knee. The load bearing axis is represented by a line drawn from the mid femoral head to the mid ankle. In a varus knee this line passes medially indicating increased force on the medial compartment and in valgus it passes laterally indicating increased load there.

A literature review has concluded that of ten studies, nine demonstrated a significant association between alignment and OA.

Hunter in a 2009 review believed it was clear that malalignment was a critical determinant of OA disease progression; varus alignment increased risk of OA progression medially and valgus alignment increased risk laterally.

At that time it was claimed that it was less clear whether the observed malalignment was a cause or a consequence of worsening disease but it was considered that in many knees it was probably both. Englund considered that the role of malalignment in OA disease initiation remained controversial.

A large cohort study has found evidence though that varus alignment was a risk factor for incident cartilage damage in the medial compartment and this was considered to provide further evidence of a link between varus alignment and initial development of OA.

In another study it was shown that varus alignment was associated with an approximately 100% increased risk of development of meniscal pathology at 30 month follow up in a cohort of middle aged to older American subjects. And others consider that meniscal and other structural changes are likely to lead to further malalignment.
It is concluded that malalignment increases risk of cartilage damage, meniscal pathology and OA progression. There is some evidence that malalignment increases risk of initiation of OA as well. In general it seems that varus alignment impacts medially, valgus laterally.

Chondral injuries

Key reference - Flanigan

Epidemiology

A systematic review of eleven studies has been made to determine the prevalence of chondral defects in the knees of athletes (931 subjects, average age 33 [aged range 26 – 47], 79% male). All knees were evaluated at arthroscopy and/or by MRI. The mean overall prevalence of full thickness focal chondral defects was 36%: 883 defects in 335 subjects. 35% of defects were located on the femoral condyles, 37% in the patellofemoral joint and 25% on the tibial plateaus. Of those studies that classified defects on the femoral condyle, 68% were medial and 32% lateral. Of those with patellofemoral defects, 64% were patellar and 36% trochlear. 59% of asymptomatic athletes (basketball players or endurance runners) had a full thickness defect.

In the general population the prevalence of full thickness articular cartilage defects as determined at arthroscopy was around 16%. In those aged under 40 years without any other concurrent knee pathology prevalence was 5%.

A larger case series study included in the systematic review discussed above (320 subjects, 38% female, mean age 29 [age range 13 – 56], 79% sports trauma, 13% household or traffic accidents, 79% had complete rupture of ACL) has reported on degenerative joint disease following acute presentation. Mild cartilage lesions were evenly distributed over all joint surfaces. Deep defects of cartilage seen as erosions at arthroscopy (grade 3) or focal total loss of cartilage (grade 4) were seen most commonly on the strongly curved surfaces of the patella and condyle.

In a very large Polish case series of over 25,000 knee arthroscopies in subjects of average age 39 years (but predominantly younger) it was found that 60% of subjects had chondral lesions. In 58% of cases the onset of symptoms was due to a traumatic and non-contact origin usually associated with activities of daily living or sports participation. 67% of cases were classified as localized focal osteochondral or chondral lesions and 29% classified as OA.

Other studies have shown that chondral injuries were found in 37% to 57% of those with meniscal injuries and in those with ACL injuries, chondral damage was found in about 16% to 24% of cases.

Risk factors for cartilage loss

Key reference - Roemer

High BMI, presence of meniscal tears and meniscal extrusion are among the factors closely associated with fast cartilage loss over 30 months. It is also reported that subchondral bone changes are an early consequence of meniscal extrusion and meniscal extrusion is a predictor of increases in subchondral bone lesions.
Bone marrow lesions/edema of the knee

Key reference – Roemer\textsuperscript{35} (covers definitions and imaging)

Definitions

Post-traumatic bone bruises are thought to be a result of fractures of the medullary trabecula which are usually seen neither radiologically nor at arthroscopy; in OA the bone marrow edema-like signal is secondary to bone marrow necrosis, fibrosis and trabecular abnormalities with only minimal edema\textsuperscript{36}.

Roemer\textsuperscript{35} suggests that it is appropriate to use the term ‘bone marrow lesions (BML)’ for a range of subchondral MRI signal alterations and to add the specific type of lesion being discussed (e.g. traumatic BML without associated fracture; idiopathic, non-traumatic BML). Roemer presents a useful table (page 1120\textsuperscript{35}) that provides a basis for distinguishing various lesions and thereby defining them. For example ‘traumatic bone marrow lesions’ are described there as ‘bone contusion/bone bruise; they have the typical appearance of a diffuse, epi- or epi-metaphyseal lesion without other associated imaging findings; their location depends on injury mechanism; the history includes adequate direct or indirect trauma, the lesion is seen immediately after trauma; they are typically seen in young active and elderly patients; they often have other associated ligamentary/meniscal injuries; and the lesion itself usually resolves within two years’.

The term bone bruise/contusion seems to be reserved for a bone marrow lesion/edema where there is a clear history of acute injury to which it may be attributed. Typically a bone bruise resulting from trauma would be expected to be found in non-cystic areas\textsuperscript{37}.

Roemer’s table provides the basis for differential diagnosis of the various bone marrow lesions. Further notes on diagnosis of bone bruise, methods of distinguishing its etiology and the relation of injury mechanism to location of bruise are provided in Part B of this report.

Epidemiology of bone marrow lesions/edema and natural history

In a case series study\textsuperscript{11} of subjects referred for suspected meniscal tears (mean age 42.7 years) edema-like bone marrow abnormalities were found in 36% of symptomatic knees compared to 3% in the contralateral, asymptomatic knee.

A Tasmanian community-based cohort study\textsuperscript{38} (mean age 63) has reported that 43% of subjects had bone marrow lesions at baseline. Over 2.7 years 25% of lesions decreased in size, 24% increased and 7% developed a new lesion. A change in size of the bone marrow lesions was associated with changes in pain in those without established radiographic OA.

A small study\textsuperscript{39} of 17 asymptomatic varsity basketball players has shown that pre-season MRI imaging reveals a high percentage of knee lesions: 41% had bone marrow edema, 35% had joint effusion, 24% showed signals in the patellar tendon and 41% had abnormal cartilage signal or focal abnormality. This and other studies have lead Lin\textsuperscript{36} to conclude that the presence of bone marrow edema-like signals in athletes must be interpreted with caution as they may be pre-existing and transitory.

The osteochondral impact over time of edema/bone bruising due to trauma appears to be variable: Koster\textsuperscript{40} found that, at one year post-trauma in a younger cohort, 23% showed an increase in the grade of OA which was strongly linked to the presence of edema post-injury. In contrast Roemer\textsuperscript{41} concluded that, after a minimum of 2 years post-trauma, bone marrow edema
had disappeared in the majority of patients and more severe articular surface injuries such as subchondral bone impaction or chondral/osteochondral fractures had healed without obvious sequelae. It is quite clear though that knee injury is itself a potent risk factor for the development of OA.

It is concluded that the term bone marrow lesion is the preferred terminology but additional information is required for interpretation. Such lesions are very common in the community and in some cases may be transitory. Their presence need not necessarily be indicative of recent acute trauma as they are also associated with a wide range of other conditions.

Insufficiency fracture of the knee

Key references – Kattapuram, Roemer for definitions and imaging diagnosis.

Introduction

Stress fractures have been defined as ‘fatigue fractures’ which occur when abnormal stress is applied to bone that has normal elasticity, whilst ‘insufficiency fractures’ occur when the stress of normal daily living is applied to bone with deficient elastic resistance.

According to Kattapuram et al the pathology originally known as idiopathic or spontaneous osteonecrosis of the knee (SONK) might now be more appropriately described as subchondral insufficiency fracture. In their view the evidence suggests that it is an acute fracture that occurs as a result of chronic stress or minor trauma to a weakened subchondral bone plate. Typically it is seen in older, female patients without a history of trauma and the osteonecrosis involves the distal femur, proximal tibia and one or both condyles or plateaus.

Roemer provides a range of definitions together with MRI characteristics –

- Insufficiency fractures are a type of stress fracture that occurs in bone unable to withstand the stresses of daily living and are observed in situations where bone mineral content is reduced. They are not the result of physical activity or preceding trauma.

- Repetitive microtrauma/overuse. Stress-related bone marrow lesions can be observed without any existing degenerative or traumatic changes.

- SONK most often affects the weight-bearing surface of the medial femoral condyle and typically occurs in elderly female patients who present with severe medial joint pain unrelated to trauma.

Epidemiology

The prevalence of SONK in elderly patients has been determined in a prospective cohort study of subjects presenting with initial meniscal symptoms without a history of trauma. Overall prevalence of SONK of the medial femoral condyle was 3.4% for those over 50 years of age and 9.4% in those over 65 years. In 5.7% of patients initially diagnosed with SONK the lesion was transient.

Pathogenesis

There is no consensus in the literature as to causation of insufficiency fracture and little evidence to suggest that insufficiency fracture is not a subset of a range of SONK-like
pathologies with multiple etiologies. It has been suggested that SONK may arise from a primary vascular incident or a subchondral stress fracture, both of which may lead to an elevation of intraosseous pressure and subsequent osteonecrosis. The vascular theory proposes that the microcirculation is disturbed through unknown factors and results in edema.

Evidence from a small study suggests that the early histological features of SONK are subchondral fracture and repair processes. The authors suggested that osteonecrosis is a later development. These findings are supported by similar reports.

Kattapurum et al have suggested that possible causation has been linked to meniscal lesions which may induce stresses that lead to ischaemic necrosis of the femoral condyle. In one small case series 80% of those with SONK had posterior meniscal root tears. The authors suggested that their findings supported the hypothesis that the tears increased pressure on the femoral condyle predisposing to subchondral fracture.

Osteoporosis and osteopenia are commonly found in patients with osteonecrosis of the knee but this is not seen in all patients.

It is not uncommon in the literature to read that insufficiency fracture was linked to a traumatic causation. What appears to be meant by this is that typically there is an absence of a history of acute injury and the fracture has arisen from activities more associated with daily living or minor incidents. The fracture results from weakened subchondral bone due to medial meniscus tears, cartilage thinning, osteoarthritis and/or osteoporosis.

It is concluded that insufficiency fracture is likely to be part of a spectrum of disorders which have an uncertain etiology. In some cases insufficiency fracture is associated with meniscal lesions, osteoporosis and osteopenia, but this is not always the case.

Distinguishing insufficiency fracture of traumatic origin from non-traumatic causations

Insufficiency fracture may be distinguished from subchondral fractures accompanying trauma, as with trauma there are usually signs of other traumatic meniscal and ligament injuries.

Kattapuram et al have also proposed that lesions are likely to be due to an acute injury when they are characterised by MRI as having a linear component in the subchondral bone, a substantial region of edema and tend to occur in the weight bearing portions of the knee, typically the medial femoral condyle. Lesions without a linear component or significant edema were distributed in all locations: they were associated with articular cartilage defects and were considered to be due to subacute or chronic processes associated with OA.

Insufficiency fracture is usually distinguishable from secondary osteonecrosis (Table 1).

<table>
<thead>
<tr>
<th>Category</th>
<th>Insufficiency fracture</th>
<th>Secondary osteonecrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Sudden and severe pain which persists at rest</td>
<td>Often insidious onset of mild pain</td>
</tr>
<tr>
<td>Predisposing factors</td>
<td></td>
<td>Corticosteroid use, rheumatoid arthritis, alcohol consumption, sickle cell disease etc.</td>
</tr>
</tbody>
</table>
Lesion size and location | Usually unilateral involving the medial femoral condyle | Bilateral occurrence common (30-80%). Lateral condyle affected 60% of time. May involve simultaneously knees, hips and shoulders
---|---|---
Histopathological appearance | Involves a small area of the subchondral bone | Lesion is larger
| Other distinguishing factors are also present
Age/Gender | Mostly in older females | May occur at any age, no gender bias

### Calcium pyrophosphate crystal deposition disease

**Key references** - Richette⁴⁹, Filippucci⁵⁰ for ultrasound findings associated with calcium pyrophosphate disease, Zhang⁵¹ ⁵² for EULAR recommendations on terminology, diagnosis and management

### Introduction

Calcium pyrophosphate deposition disease (CPPD) is a generic term referring to calcification within the cartilage usually due to calcium pyrophosphate deposition⁵³. Chondrocalcinosis (CC) refers to radiographic calcification of the articular fibro or hyaline cartilage; pyrophosphate arthropathy refers to structural abnormalities of the bone and cartilage associated with CPPD⁴⁹. CPPD may be classified as sporadic, hereditary or secondary⁸². Sporadic forms usually occur in middle aged to older subjects with no gender bias. Hereditary forms have a female predominance and may occur at a relatively early age. Hereditary forms may present as a severe arthropathy⁸².

Crude prevalence of CPPD in a British community was 7% and the main risk factors were age and OA. There was no gender effect on prevalence and CPPD was bilateral in 72% of cases⁴⁹. CPPD has strong associations with a range of clinical conditions including hyperparathyroidism, gout and hemachromatosis⁵⁶.

A cadaver study (mean age 50) has concluded that calcification of knee cartilage occurs before evidence of cartilage breakdown appears and that calcification is primarily an effect of aging⁸³.

Zhang⁵³ in a British study has concluded that chondrocalcinosis (CC) does not have a major genetic predisposition except in isolated cases.

### Clinical presentation

The knee is the most common site for CPPD⁵¹. EULAR proposes four clinical presentations as follows -

- **Asymptomatic**: CC is frequently asymptomatic and an incidental finding in older subjects⁴⁹.
- **OA with CPPD**: joint shows changes of OA and CPPD present.
Acute calcium pyrophosphate crystal arthritis (replaces the term pseudogout): acute onset, self-limiting synovitis with CPPD. The acute onset of severe joint pain, swelling and tenderness that reaches a maximum at 6-24 hours with overlying erythema is highly suggestive of this condition but not specific.

Chronic CPP crystal inflammatory arthritis: chronic inflammatory arthritis associated with CPPD.

In patients younger than 55 years a primary metabolic disorder or a familial predisposition should be considered.

NB. Ultrasound may be more useful for diagnosis of CPPD than conventional radiography.

Association with meniscal tearing

In an American case series of over 1000 knee arthroscopy cases (mean age 67) it was found that 74.1% of those with CC had meniscal tears compared to a prevalence of 28.7% in those without CC (there was a low level of trauma-related events in the series). Relative risk of tears in knees with CC was 2.58 compared to those without CC. The authors concluded that CC was a strong predictor of meniscal tearing.

Association with OA

OA and CC induced arthropathy have pathological profiles that are indistinct from each other and the effect that each has on the pathogenesis of the other is not clear. People with OA are three times more likely to have CPPD. Some possible distinguishing features that may be present are:

- CPPD in knees with OA may associate with more inflammatory features and more rapid progression than in knees without CPPD but the associations are marginal and not useful for diagnosis.

- CPPD may associate with an atypical distribution of OA: OA with CPPD may occur less in such joints as the elbow and radiocarpal joints and show more patellofemoral compartment involvement.

- Radiographs in joints with OA and CPPD may show prominent cyst and osteophyte formation.

- In primary OA of the knee the medial compartment is more commonly involved whereas with CPPD the lateral compartment is more likely to be affected.

Association with trauma

CC has been reported to occur after joint trauma, typically in younger subjects and unilaterally without evidence of other disease. The knee joint was involved in 13 of 18 subjects in a case series; 9/13 had undergone a meniscectomy and the remaining four appeared to have meniscal tears. Another study found CC to be more common in post-meniscectomy/post-injury knees than in the contralateral, unoperated knee.
Arthropathy

Pathological abnormalities have been described in CPPD\textsuperscript{58} in 85 men and women with an average age of 74 years. Arthropathy was commonly observed in the knees as well as other joints and resembled OA with joint space narrowing, subchondral eburnation and cyst formation. Calcification of knee fibrocartilage was seen in nearly all affected knees and of hyaline cartilage in about half of the cases. CPPD differed from degenerative disease in the following respects –

- The arthropathy was not only observed in weight bearing articulations such as the knee and hip but also at sites not commonly affected by OA such as the wrist, elbow and glenohumeral joint.

- The intra-articular distribution of abnormalities was unusual and in the knee featured the patellofemoral compartment.

- Subchondral cyst formation was prominent. At X-ray cysts appeared frequently and were often large (subchondral cysts are said to be the hallmark of the condition\textsuperscript{85}).

- CPPD was frequently severe and progressive with extensive subchondral bony collapse and fragmentation resulting in numerous intra-articular bodies.

- Osteophyte formation was variable.

An ultrasound assessment of knees with CPPD\textsuperscript{50}, presumably with less advanced disease than in the above study (median age 66; median duration of disease 6 years), has reported that 37.1% of knees also had joint effusion, 64.2% showed intra-cartilaginous hyperechoic spots in the hyaline cartilage of the femoral condyles, 77.1% had meniscal calcification, 7.8% had had entheseal thickening of the quadriceps tendon, 7.1% showed hyperechoic spots in the patellar tendon, 9.3% entheseal thickening of the patellar tendon and 27.1% a popliteal cyst in the gastrocnemius-semimembranous bursa.

Natural history

A prospective study\textsuperscript{59} has followed 64 patients (mean age at initial visit 66 years) initially presenting with CC and/or CPPD crystals in the synovial fluid. In 91% of subjects the knee was the major joint involved. Over 4.6 years, symptoms worsened in 27%, remained the same in 33% and improved in 41%. 27% developed symptoms in new joints. Arthropathy (described as joint space narrowing with subchondral bone reaction, osteophytes, loss of cortical integrity, cyst formation and CC) worsened in 16%, often with an increase in osteophyte formation with bone remodelling. In 50% arthropathy remained unchanged. The authors concluded that CPPD is not necessarily progressive and those presenting with acute attacks alone do well.

Effect of chondrocalcinosis on MRI imaging of knee menisci

Sensitivity and specificity to detect meniscal tears is significantly decreased in the presence of chondrocalcinosis\textsuperscript{86} and there are case reports that suggest that chondrocalcinosis can mimic a meniscal tear\textsuperscript{87,88}.
Clinical management and imaging

Evidence based recommendations for treatments have been prepared by EULAR\textsuperscript{52}. Conventional radiology has a sensitivity for CC as low as 39%\textsuperscript{62}. The test of choice is synovial fluid examination\textsuperscript{62}.

Conclusion

It is concluded that CCPD has strong associations with age and OA but is probably not strongly associated with the progression of OA: these conclusions are supported by a systematic review\textsuperscript{49}. In advanced disease the arthropathy may be severe. CC may occur unilaterally in association with knee injury or following meniscal surgery.

Gout: effect on joint surfaces of the knee

The overall prevalence of gout is around 0.7% to 1.4% in men and 0.5% to 0.6% in women. In people older than 65, prevalence in men is 4.4% to 5.2% in men and 1.8% to 2.0% in women. In males, prevalence reaches a maximum in the fifth decade\textsuperscript{60}.

Incidence and prevalence parallel those of hyperuricemia, which is closely associated with increased risk of developing gout\textsuperscript{60}. Evidence has been presented that prevalence and incidence is increasing with time. New Zealand studies suggest that gout once unknown in Maori now has a higher incidence than in New Zealand Europeans and in both ethnicities prevalence has increased over the years\textsuperscript{89}.

It has been shown in a cross-sectional study that gout at individual joint sites, including the knee, is positively associated with clinically assessed OA at that site\textsuperscript{61}. The authors hypothesised that OA may predispose to deposition of urate crystals but there appears to be a lack of evidence for this conclusion.

Acute attacks with rapid development of severe pain, swelling and tenderness that reaches a maximum at 6-12 hours especially with overlying erythema is highly suggestive of crystal formation but is not specific for gout\textsuperscript{90}. EULAR have published evidence based recommendations for treatment of gout\textsuperscript{91}.

An ultrasound assessment of knees with gout\textsuperscript{50} (median age 59; median duration of disease 6 years) has reported that 35% of knees also had joint effusion, 16% synovial hypertrophy, 41.6% had enhancement of the superficial margin of the hyaline cartilage of the femoral condyles, none had calcification of the menisci, 13.3% had entheseal thickening of the quadriceps tendon, 13.3% showed an intra-tendinous power Doppler signal in the quadriceps tendon, 11.6% had entheseal thickening of the patellar tendon, and 10% showed an intra-tendinous power Doppler signal in the patellar tendon.

Subcutaneous or extra-articular tophi are reported to appear at an average of 11.6 years (range 3 - 42 years) after the first attack of gout\textsuperscript{92}. A study from Taiwan\textsuperscript{92} (mean age 46 years; mean duration of current episode 7.3 months) has shown that in those with tophaceous gout, location of tophi were found by MRI in the infrapatellar fat pad and anterior joint recess (87%), the lateral rim of the lateral femoral condyle (popliteal groove) (78%), the intercondylar fossae (69%) and the tibial eminence (31%). Bone erosions were found at the lateral rim of the lateral femoral condyle (35%), roof of the condylar notch (30%) and tibial eminence (22%).
Ganglion cysts, especially their causation

**Key reference - McCarthy**

McCarthy et al describe ganglion cysts as benign cystic masses with a dense fibrous connective tissue capsule containing a viscous mucous rich in mucopolysaccharides. They may include a main body, pseudopodia and small capsular cysts communicating with the main body.

The incidence of intra-articular cysts and ganglia varies between 0.6% and 2% as seen at arthroscopy in symptomatic knees. Krudwig has reported on a retrospective case series of nearly 8000 knees investigated by arthroscopy where 85 ganglion cysts were found; 58% originated from the ACL, 19% from the PCL, 14% from the anterior menisci, 4% from the posterior menisci, 4% in the infrapatellar fat pad, and one each from the medial plica and the subchondral bone.

Intra-articular ganglia have a M/F ratio of 3:1. Rarely the peroneal nerve is affected by a ganglion cyst and footdrop may result.

Ganglion cysts are not readily differentiated from synovial cysts: unlike ganglion cysts, synovial cysts have a cyst wall lined with synovial cells and derive from synovial tissue.

A case series by Krudwig et al reported that 11% of subjects with ganglion cysts were symptomatic due to the cyst’s presence and that none of these cysts were associated with concomitant intra-articular lesions. In the remaining 89%, symptoms were attributed to degenerative diseases and all such knees demonstrated signs of meniscal and/or patellofemoral pathologies.

McCarthy has outlined a number of theories for cyst causation, including –

- Most commonly it is believed that ganglion cysts result from mucoid cystic degeneration in a collagenous structure in areas under stress such as the joint capsule and tendon. Consistent with this theory is the fact that ganglion cysts are often located in areas under stress, and cells of the ganglion lining are able to secrete substances rich in mucopolysaccharides.
- Primary cellular hyperplasia with mucin secretion and secondary cystic degeneration of connective tissue.
- Development from proliferating pluripotent mesenchymal cells.
- Ganglia arise from displaced synovial remnants that have arisen during embryogenesis.

There appears to be no clear evidence or consensus to support one theory over another.

Trauma has been reported as being implicated in the pathogenesis of ganglion cysts –

- In Krudwig’s series, many of the 85 cases with ganglion cysts reported a history of repeated minor trauma, ‘usually without a single episode of serious injury’
- In those with posterior cruciate ligament ganglion cysts, 40% had a history of trauma.
- In other case series of subjects with intra-articular cysts, an injury was reported prior to the onset of symptoms in 38%, 45% and 67% of cases.
Epidemiology of knee injuries and knee pathology – some recent papers and ACC data

Key reference - Gage

A huge study based on American Emergency Department data of 6.6 million knee injuries presenting over 10 years has reported. Data was broken down by injury type, gender, age and activity. The study identified an emerging issue of increasing knee injury rates among adults and seniors.

In middle aged to older subjects with risk factors for OA but asymptomatic, the prevalence of knee lesions has been shown to be extremely high. This large American cohort study reported on the prevalence of knee lesions in asymptomatic 45 to 55 year olds who were regarded as at risk for development of OA (risk factors included some knee symptoms in the last 12 months, history of knee surgery and injury, family history of total knee replacement and Heberden nodes); meniscal lesions were found in 47% of subjects, cartilage lesions in 74.6%, bone marrow edema in 40.3% and ligament lesions in 17%. Prevalence was related to degree of physical activity.

ACC volumes for knee surgery over the last three financial years are shown in Table 2. Surgical volumes fell sharply between 2009/10 and 2010/2011 but less so in the 2011/2012 year.

**ACC Knee surgery volumes 2010 - 2012**

<table>
<thead>
<tr>
<th>Service Item</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>KNE50 - Knee Arthroscopic Surgery - Simple</td>
<td>7,819</td>
<td>6,071</td>
<td>5,763</td>
</tr>
<tr>
<td>KNE51 - Knee Arthroscopy Proceed To Open Surgery - Simple</td>
<td>78</td>
<td>67</td>
<td>43</td>
</tr>
<tr>
<td>KNE60 - Knee Arthroscopic Surgery - Complex 1</td>
<td>543</td>
<td>529</td>
<td>473</td>
</tr>
<tr>
<td>KNE61 - Knee Arthroscopy - Proceed To Open Surgery - Complex 1</td>
<td>44</td>
<td>42</td>
<td>25</td>
</tr>
<tr>
<td>KNE70 - Knee Arthroscopic Surgery - Complex 2</td>
<td>45</td>
<td>39</td>
<td>20</td>
</tr>
<tr>
<td>KNE71 - Knee Arthroscopy - Proceed To Open Surgery - Complex 2</td>
<td>12</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>KNE80 - Knee ACL Reconstruction - 1</td>
<td>2,372</td>
<td>Data no longer collected</td>
<td></td>
</tr>
<tr>
<td>KNE90 - Knee ACL Reconstruction - 2</td>
<td>480</td>
<td>Data no longer collected</td>
<td></td>
</tr>
<tr>
<td>Totals excluding KNE80 and 90</td>
<td>8,541</td>
<td>6,783</td>
<td>6,336</td>
</tr>
</tbody>
</table>
Appendix 1. Summary of the 2010 report ‘Causation Review - Meniscal Tears’ with key references

An earlier ACC Research report has reviewed the evidence that certain meniscal tears (especially horizontal, flap and complex) are degenerative in nature and several lines of evidence for the classification of tears into traumatic and degenerative types were reviewed. The summarised evidence from that report is set out below.

1. Age

Key reference - Englund

There is high quality evidence from a cohort study which shows that prevalence of meniscal tears and meniscal degeneration increase in frequency with age; Englund’s Framingham data on community living subjects 50 to 90 years of age suggest that about one third of knees in those over 50 years have degenerate tears. The prevalence of meniscal tears increased with age ranging from 19% in women aged 50 – 59 to over 50% in men aged 70 – 90 years. In addition 10% of the population had partial or complete destruction of the meniscus, pathology closely related to the presence of OA. 40% of the tears were horizontal and 37% complex suggesting that these types are most typically degenerative.

This evidence is supported by –

- Histological studies in cadavers which show that horizontal tears and flap tears are characteristically found in the menisci of older subjects

- Direct observation at surgery where complex, flap and horizontal tears were found more commonly in the older population and followed a more degenerative pattern

2. ACL injuries

Key references – Keene, Tandogan

There is good evidence, consistent across a range of case series studies, that 70% to 90% of tears associated with acute ACL injuries are peripheral, longitudinal tears suggesting a traumatic origin for this type of tear. The percentage of degenerative tears found (flap and horizontal tears) is small. Most commonly ACL tears are in the medial compartment, but they occur laterally as well.

3. Occurrence of tears in symptomatic and asymptomatic knees

Key references - Boks, Zanetti

Zanetti has compared the prevalence of tears in the traumatically injured knee to that in the uninjured knee. The prevalence of horizontal and flap tears did not differ between symptomatic and asymptomatic knees whereas vertical and complex tears were found mainly in the symptomatic knees. This provides further evidence then that degenerate tears occur with high frequency bilaterally and are not usually the result of acute trauma.

In a similar study it was found that recent trauma was associated with the presence of radial, longitudinal and complex meniscal tears, and not with horizontal.
4. Body mass index

Key references - Ford\textsuperscript{13}, Englund\textsuperscript{5}

There is good evidence from one community based cohort study and one case-control study that prevalence of tears is strongly associated with BMI\textsuperscript{5 \textbf{13}}. Both studies were on middle aged to older subjects. In the cohort study of Englund the tears refer mostly to horizontal and complex tears. Ford found that the age-adjusted odds ratios for likelihood of meniscal surgery among those with a BMI of $\geq 40.00$ was 15.0 for men, and 25.1 for women. All odds ratios with a BMI equal to or over 27.5 for men and 25 for women were statistically significantly elevated over the control BMI category of 20.00 to 22.49.

5. Osteoarthritis (OA)

Key reference - Noble\textsuperscript{7}

There is excellent evidence from a variety of studies that degenerate menisci and degenerative tears, particularly horizontal tears and complex tears, are more strongly associated with the presence of OA than other tears. In one study the percentage of horizontal tears increased from 18.4\% where no OA was present to 61.5\% for grade 3 OA\textsuperscript{7}. Tears are so common in the elderly with moderate OA it has been suggested that it is pointless to conduct an MRI to prove their presence (in this reference, 91\% of such subjects had meniscal tears)\textsuperscript{16}.

Englund et al\textsuperscript{20} in a cohort study investigated the link between the development of hand OA and knee OA in a group of patients who had undergone a meniscectomy 20 years earlier. They found that those who developed hand OA had a higher incidence of degenerative types of meniscal tears (flap, horizontal, complex and tears in a meniscus with degenerative changes) 20 years earlier than did patients who did not develop hand OA (47\% of those who developed hand OA had meniscal degeneracy compared to 26\% who did not develop hand OA). Furthermore, the subjects who had a degenerative meniscus developed radiographic knee OA more frequently 20 years later than had patients with non-degenerate tears both in the index knee and in the contralateral knee. They suggested that a degenerative tear may be regarded as an early signal of susceptibility to osteoarthritic disease.

There is some evidence from a retrospective cross-sectional study that flap and other degenerative tears were associated with the development of more advanced OA changes than other types\textsuperscript{96}. Case series studies generally support this view. For example, complex and horizontal tears were more highly associated with an increased incidence and severity of cartilage degeneration compared with other types of meniscal tears\textsuperscript{97}.

Conclusions from the 2010 paper

It was concluded that the body of evidence outlined above makes a compelling case for a dichotomous classification of tears into those predominately of a degenerative origin (horizontal and flap) and those of predominately traumatic origin (longitudinal-vertical). This classification is not absolute; degenerate tears may have a traumatic component, and younger, active subjects will present with tears that would be categorised as degenerate in older subjects. It must be accepted that there are many gray areas.
References


70. Crema MD, Hunter DJ, Roemer FW, Li L, Marra MD, Nogueira-Barbosa MH, et al. The relationship between prevalent medial meniscal intrasubstance signal changes and
incident medial meniscal tears in women over a 1-year period assessed with 3.0 T MRI. Skeletal Radiol 2011;40(8):1017-23.


95. Stehling C, Lane NE, Nevitt MC, Lynch J, McCulloch CE, Link TM. Subjects with higher physical activity levels have more severe focal knee lesions diagnosed with 3T MRI: analysis of a non-symptomatic cohort of the osteoarthritis initiative. Osteoarthritis Cartilage 2010;18(6):776-86.