

# **Occupational Musculoskeletal Disorders of the Arm and Hand**

Evidence of workplace factors in the development of hand osteoarthritis, nerve compression syndromes, Dupuytren's contracture, de Quervain's disease, trigger finger, hypothenar hammer syndrome and Kienbock's disease according to manual work and hand/arm vibration

A systematic review of the literature

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## Forord

Dette referencedokument er udarbejdet i henhold til de retningslinjer som Arbejds miljøforskningsfonden har beskrevet for udredningsprojektet "Arbejdsbetinget Sygdomme i Hånd og Underarm – En Systematisk Litteraturgennemgang", som blev udbudt i oktober 2009. Projektet er finansieret af Arbejds miljøforskningsfonden.

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Den videnskabelige bedømmelse af dokumentets kvalitet er gengivet i rapporten sammen med forfatternes bemærkninger hertil. Dokumentet er efterfølgende revideret af forfatterne i forhold til de fremkomne bemærkninger. Vi vil gerne rette en varm tak til de uafhængige fagfællebedømmere for deres omfattende kritik som på væsentlige punkter har medført en bedre rapport.

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Forfatterne

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## 1. Dansk Resumé

Gennem de sidste 30 år er der i den internationale litteratur kommet fokus på i hvilket omfang arbejdsrelateret overbelastning af bevægeapparatet medfører specifikke sygdomme. Der foreligger således omfattende dokumentation vedrørende visse lidelser, herunder hånd/arm vibrations syndrom og karpaltunnelsyndrom, men sammenhængen mellem arbejdsmæssig eksponering og udvikling af talrige andre lidelser er stadig uklar.

I denne rapport gives en systematisk oversigt over den aktuelle evidens for sammenhængen mellem erhvervseksponeringer og forekomsten af:

- Hånd osteoarthrose;
- Nerve-entrapment på underarmen (ulnaris, radialis og medianus, fraset karpaltunnelsyndrom);
- Dupuytren kontraktur;
- De Quervains tenosynovitis;
- Digitus saltans (springfinger);
- Hypothenar hammersyndrom; og
- Os lunatum malaci (Kienbocks sygdom).

Opgavens indhold og afgrænsning er anført af Arbejds miljøforskningsfondet, der har finansieret udarbejdelsen af dokumentet.

Der er foretaget en litteratursøgning i Medline (Pubmed 1966 – juli 2010) med anvendelse af følgende kriterier:

- 1) Original artikler hvor forekomsten af de relevante lidelser analyseres i forhold til arbejdsmæssige eksponeringer. Relevante deskriptive studier og rapporter blev også inkluderet mhp at understøtte baggrunds information og diskussion;
- 2) Artikler publiceret på engelsk;
- 3) Observationer på mennesker;
- 4) Full-tekst artikler.

Graden af evidens for årsagssammenhæng mellem sygdom og erhvervsrelaterede faktorer blev vurderet i henhold til kriterierne foreslået af Dansk Selskab for Arbejds- og Miljømedicin (side 11).

Til vurdering af graden af evidens for en årsagssammenhæng mellem eksponering og sygdom blev de arbejdsmæssige eksponeringer beskrevet i studierne kategoriseret i to kategorier hhv manuelt arbejde og eksponering for hånd/arm vibrationer.

### Hånd Osteoarthrose

Der blev i alt identificeret 28 studier som vedrører risiko for hånd osteoarthrose ved arbejdsmæssig eksponering, nemlig: 1 follow-up studie, 2 case-control studier, 18 tværsnitsstudier, og 7 kasuistikker. I 17 studier analyseredes risikoen i relation til biomekaniske faktorer og specifikke erhverv (manuelt arbejde), og i 4 studier risikoen ved eksponering for hånd/arm vibration. Vedrørende eksponering for manuelt arbejde fandt 12 studier en signifikant association til finger osteoarthrose, og 5 studier fandt ikke nogen association. Om eksponering for hånd/arm vibration, fandt 1 studie signifikant association til håndledsosteoarthrose, mens 3 studier ikke fandt nogen association.

På trods af at undersøgelserne vedrører vidt forskellige eksponeringer, er der ved en samlet vurdering fundet moderat evidens (++) for en årsagsmæssig sammenhæng mellem manuelt arbejde og risiko for finger osteoarthrose. Mens evidensen for en årsagsmæssig sammenhæng mellem eksponering for hånd/arm vibration og hånd osteoarthrose fandtes utilstrækkelig (0).

### Nerve-Entrapment på Underarmen

Der blev fundet 4 analytisk epidemiologiske studier (1 follow-up studie, 2 case-control studier, 1 tværsnitsstudie) og 27 deskriptive studier og kasuistikker. Tre af de analytiske studier omhandlede nervus ulnaris entrapment, og et studie omhandlede nervus radialis entrapment. Alle 4 studier fandt en positiv

association mellem biomekaniske faktorer og forekomst af nerve-entrapment syndrom. Hånd/arm vibration blev vurderet i 2 deskriptive studier.

Alle studier havde metodologiske mangler, således forekom der i tre studier selektion, information (inklusive recall bias) og / eller observatør bias. To af studierne havde kun inkluderet få cases, og i det eneste follow-up studie var den væsentligste arbejdsmæssig eksponering ikke klart defineret.

Den samlede evidens for en årsagsmæssig sammenhæng mellem nerve-entrapment på underarmen og manuelt arbejde er begrænset (+), mens evidensen for en kausal association med eksponering for hånd/arm vibration er utilstrækkelig (0).

### **Dupuytren Kontraktur**

Syv tværsnitstudier belyste forekomst af Dupuytren kontraktur (DK) i relation til arbejdsmæssige eksponeringer. Tre studier evaluerede manuelt arbejde, 3 studier eksponering for hånd/arm vibration, og 1 studie evaluerede begge eksponeringer. I forhold til eksponering for manuelt arbejde, fandt tre studier en positiv association med DK; mens 1 studie fandt ingen association blandt arbejdere i alder under 59 år, men negativ association blandt arbejdere i alder over 65 år. En positiv association mellem eksponering for hånd/arm vibration og DK blev fundet i 3 studier mens 1 studie ikke fandt nogen association. Alle studier havde væsentlige metodologiske mangler, herunder selektions- og informationsbias og manglende kontrol for andre personlige faktorer end alder og køn.

Den samlede evidens for en årsagsmæssig sammenhæng mellem DK og arbejdsmæssige eksponeringer er derfor begrænset (+).

### **De Quervain's Tenosynovitis**

I alt 9 tværsnitstudier og 1 follow-up studie omhandlede De Quervain's Tenosynovitis (dQT) i relation til erhvervs-mæssige eksponeringer. Alle studier analyserede manuelt arbejde som eksponering. I 6 af studierne blev der fundet en positiv association mellem dQT og de studerede; 1 studie fandt ikke nogen association; og 3 studier var udelukkende deskriptive.

Den samlede evidens for en årsagsmæssig sammenhæng mellem dQT og arbejdsmæssige eksponeringer er begrænset (+).

### **Springfinger**

Der blev fundet 1 follow-up studie, 5 tværsnitstudier, 2 kasuistikker og 1 serie med kirurgiske patienter, der omhandlede springfinger i relation til arbejdet. Fem studier analyserede ergonomiske faktorer ved manuelt arbejde, og et studie analyserede forekomsten i specifikke jobs. Fem studier fandt en positiv association mellem springfinger og de analyserede eksponeringer, og et studie fandt ikke nogen association.

Den samlede evidens for en årsagsmæssig sammenhæng mellem springfinger og arbejdsmæssige eksponeringer er fundet begrænset (+).

### **Hypothenar Hammersyndrom**

I alt 2 tværsnitstudier og 4 case-serier med flere end 10 patienter omhandlede arbejdsrelaterede risikofaktorer for hypothenar hammersyndrom (HHS). Det ene tværsnitstudie vedrørte hånd/arm vibration og det andet udsættelse for hyppig brug af den ulnare side af hånden som hammer. Begge studier samt alle kasuistikker præsenterede kliniske evidens for at repetitive trauma til den hypothenar område er associeret med udvikling af HHS. På den baggrund, er den kliniske evidens for en kausal association mellem HHS og repetitive hypothenar trauma stærk (+++), mens den epidemiologiske evidens er utilstrækkelig (0). Evidensen for en årsagsmæssig sammenhæng mellem hånd/arm vibration og HHS er utilstrækkelig (0).

### **Os lunatum malaci (Kienbocks sygdom)**

Der blev fundet 3 tværsnitstudier og 1 case serie om Kienbocks sygdom (KS) i relation til erhverv. De studerede eksponeringer omfattede manuelt arbejde (1 studie), sports aktiviteter (1 studie) og hånd/arm vibration (4 studier). To studier fandt en positiv association mellem KS og erhvervs-mæssig eksponering, og 2 studier var deskriptive, dvs. de præsenterede ingen analyser af eventuelle risiko faktorer for KS.

Den samlede evidens for en årsagsmæssig sammenhæng mellem KS og arbejdsmæssige eksponeringer er utilstrækkelig (0).

## 2. Overall Summary

Through the last 30 years the focus on occupational musculoskeletal disorders has been increasing in the international literature. There are extensive data on specific disorders, such as hand/arm vibration syndrome and carpal tunnel syndrome, but the causal relation between occupational exposures and the development of several others disorders is still unclear.

The aim of this document is to present a systematic critical literature review of the current evidence for a causal association between occupational exposures (specific manual work and exposure to hand/arm vibration) and the development of the following disorders:

- Hand osteoarthritis;
- Nerve compressive syndromes;
- Dupuytren contracture;
- De Quervain's disease;
- Trigger finger disorder;
- Hypothenar hammer syndrome;
- Kienbock's disease.

The relevant studies were identified through searches in the US National Library of Medicine (Pubmed 1966 – July 2010) according to the following inclusion criteria:

- 1) Original articles presenting one of the relevant health outcomes in relation to occupational exposures (manual work – including hand/arm vibration and sports when relevant). Descriptive studies and reports were included to support the background information and discussion when they specifically referred to occupational exposures;
- 2) Articles published in English;
- 3) Studies with humans;
- 4) Full text articles.

The level of evidence was evaluated based on a classification system established by The Scientific Committee of the Danish Society of Occupational and Environmental Medicine 2005, and used in other recent reviews (cf page 87).

The diverse occupational exposures assessed by the studies retrieved in this review were aggrouped in two categories – manual work and exposure to hand/arm vibration – which were used to present the overall evaluation of the level of evidence of a causal association with each of the disorders considered.

### Hand Osteoarthritis

The following studies presenting occupational factors in relation to hand osteoarthritis (OA) were retrieved: 1 follow-up study, 2 case-control studies, 18 cross-sectional studies, and 7 case-reports.

Seventeen of the epidemiological studies analyzed biomechanical factors and occupations in relation to hand OA (including the 2 case-control studies), and 4 studies analyzed exposure to hand / arm vibration (including the follow-up study).

Regarding exposure to biomechanical factors, 12 studies reported a significant association with hand OA (including 1 case-control study), and 5 studies did not report any significant associations (including 1 case-control study). When hand/arm vibration was the exposure analyzed, 1 cross-sectional study found a positive association with wrist OA, while 1 follow-up and 2 cross-sectional studies did not find any significant associations with hand and wrist OA.

The overall evidence level of a causal association between finger OA and manual work was considered moderate (++), while the level of evidence of a causal association between exposure to hand/arm vibration and hand OA is found insufficient (0).

### Nerve Compressive Syndromes

It was retrieved 4 analytic epidemiological studies (1 follow-up, 2 case-controls, 1 cross-sectional), 27 descriptive epidemiological studies and case reports.



Three of the analytic epidemiological studies addressed ulnar compression syndrome (1 follow-up, 1 case-control, 1 cross-sectional) and one radial compression syndrome (case-control). All four studies presented biomechanical factors as the occupational exposure, and found a positive association between the outcome and some or all the risk factors analyzed. Exposure to hand / arm vibration was studied by two descriptive studies, one analyzed cubital tunnel and thoracic outlet syndrome, and the other dysfunctions of ulnar, radial and median nerves.

The present level of evidence of a causal relation between nerve compressive syndromes and manual work is considered limited (+), while the level of evidence for a causal relation with exposure to hand/arm vibration is insufficient (0).

### **Dupuytren's Contracture**

We retrieved 7 cross-sectional studies providing data on risk of Dupuytren's contracture (DC) in relation to occupational exposures.

The exposure assessed in 3 studies regarded manual work, three studies evaluated exposure to hand/arm vibration, and 1 study evaluated both exposures. Regarding manual work, 3 studies found an association with DC; while 1 study found no association among workers younger than 65 years, but a negative association among workers older than 65 years. Regarding exposure to hand/arm vibration, a positive association was found by 3 studies, while one study found none association.

The level of evidence of a causal association between DC and manual work and exposure to hand/arm vibration is considered limited (+). That means, there is some epidemiological evidence on a positive relationship but it is not unlikely that this relationship could be explained by chance, bias, or confounding.

### **De Quervain's Disease**

We retrieved 9 cross-sectional studies and 1 follow-up study presenting occupational factors in relation to De Quervain's disease (dQD). The exposure assessed in all studies was manual work. A positive association between occupational exposures and dQD was found in 6 studies; one study found no associations; and 3 studies were exclusively descriptive.

The present level of evidence is considered limited (+) and further analytic controlled epidemiological studies are needed. De Quervain's disease do not differ in principle from tenosynovitis in other tendons (tendovaginitis, tenosynovitis). The evidence of a causal relationship between workloads and developing of dQD can therefore be equated with evidence for tendovaginitis in the other tendons in the wrist.

### **Trigger Finger Disorder**

We retrieved 1 follow-up study, 5 cross-sectional studies, 2 case reports and one surgical serie presenting occupational factors in relation to TF.

The exposure assessed in 5 studies regarded specific ergonomic factors in manual work, and specific occupations in one study. A positive association between occupational exposures and TF was found in 5 studies, and one study did not find any association.

The present level of evidence is considered limited (+) and further analytic controlled epidemiological studies are needed.

### **Hypothenar Hammer Syndrome**

We retrieved 2 cross-sectional studies, and 4 case series with more than 10 patients presenting occupational factors in relation to HHS. The exposures assessed in the epidemiological studies were hand / arm vibration and work with vehicle maintenance, which habitually require the use of the hand as a hammer. Both studies presented prevalence rates of HHS remarkably higher than expected rates from population samples. This consistent evidence is supported by a number of case reports / series.

Due to the high specificity of exposure and outcome, a plausible mechanism, and the fact that the disorder has seldom been reported in absence of hypothenar trauma, the clinical evidence for a causal relation between hypothenar repetitive trauma and ulnar artery anomaly in Guyons canal is considered strong (+++). The main uncertainty relates to limited knowledge on the prevalence of the condition in the general

population. Thus, the epidemiological evidence is insufficient (0). The evidence that hand-arm vibration may cause HHS is insufficient (0).

### **Kienbock's Disease**

We retrieved 3 cross-sectional studies and 1 case series presenting occupational factors in relation to KD.

The exposure assessed in the studies was: hand/arm vibration (in all 4 studies), manual work (1 study) and sport activities (1 study). A positive association between occupational exposures and KD was found in 2 studies, and 2 studies were descriptive, i.e. did not make any analyses on possible risk factors.

Given the very sparse literature on Kienbock's disease in relation to occupational exposures, the evidence of a causal association between KD and manual work or exposure to hand/arm vibration is insufficient (0). In other words, the available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

### 3. Introduction

Since the late 80's the concept of overuse syndromes and its synonyms, repetitive strain injury and cumulative trauma disorder, have been extensively discussed among occupational health practitioners. These terms characterize a wide variety of painful and chronic neuromusculoskeletal disorders of the neck and upper extremity.[1, 2] The reason why these disorders are so controversial is the fact that they do not conform to any identifiable anatomical or pathological pattern. In another words, there is no identifiable pathological basis to these entities. Besides, the signs and symptoms presented vary largely.[3] Already over 200 year ago, Ramazzini noticed that a considerable number of workers complained about painful disorders of the soft tissues. He assumed that one of the reasons for that could be due to "certain violent and irregular motions, and unnatural postures of the body, by reason of which, the natural structure of the vital machine is so impaired that serious diseases gradually develop therefrom." [4]

Today we have a better understanding of the human body and its biomechanical functions, and some specific disorders are now established occupational diseases, such white finger syndrome after prolonged exposure to hand / arm vibration. However, current knowledge on occupational disorders in the upper extremities is still limited. [5] As it was the case with Ramazzini, many physicians observed that a large part of the patients complaining of chronic painful disorders of the upper limb were manual workers. This observation led to the suspicion of a possible causal relation between occupational exposures and the development of musculoskeletal disorders. For instance, extensive discussions are found in the literature on overuse syndromes among musicians and sport practitioners.[5-7] There is a lack of studies elucidating whether these patients really develop disorders because of their exposure at work, or whether the occupational exposure just precipitate symptoms of disorders with others aetiological factors.

It is still not clear whether overuse syndromes are pathological entities by itself or a pre-stage of defined clinical diseases. Despite that, many reports in the literature present specific disorders as being the consequence of occupational overuse or strain.[1] This assertion is mainly seen for diseases, which are not so frequent in the population, presenting hereby a lack of epidemiological data.

The aim of the present review is to elucidate the current evidence for the relation between occupational exposures and the occurrence of hand osteoarthritis, nerve compressive syndromes of the arm and hand, Dupuytren contracture, de Quervain's disease, trigger finger, hypothenar hammer syndrome, and Kienbock's disease.

The evidence criteria applied for this review were recommended by The Danish Working Environment Research Fund by request of The Danish Working Environment Authority. The knowledge of this review is expected to benefit specialists in environmental medicine, professionals involved in rehabilitation – such as occupational therapists and physiotherapists –, authorities involved in occupational health issues, and persons in general who are engaged in occupational health.

#### 4. Methods and Inclusion Criteria

The relevant studies were identified through open searches and searches using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010) using the relevant searching keywords. Even though Pubmed database is open from 1966, it listed in some cases references prior to this date, which were included when relevant. The retrieved articles were first selected by title, then by abstract and finally by reading the full text articles. Further relevant articles were retrieved by consulting reference lists and reviews. Most of the articles dated from before 1966 were obtained this way. All the writers participated in the literature searching process.

The inclusion criteria for the retrieved articles were:

- 1) Original articles presenting one of the relevant health outcomes in relation to occupational exposures (manual work – including hand/arm vibration and sports when relevant). Descriptive studies and reports were included to support the background information and discussion when they specifically referred to occupational exposures;
- 2) Articles published in English;
- 3) Studies with humans;
- 4) Full text articles.

More details regarding specific searching keywords and the number of articles retrieved are described under the topic 'literature search' for each of the disorders presented.

The diverse occupational exposures assessed by the studies were for practical reasons aggrouped in two categories – manual work and exposure to hand/arm vibration – to present the overall evaluation of the level of evidence of a causal association with each of the disorders considered.

When the study did not provide any kind of risk estimate, the authors of this review calculated relative risk or the odds ratio (OR) based on the available data – whenever feasible.

The definition criteria for the health outcomes included in this review are presented in the table below:

Health outcome	Definition criteria
Hand / Finger / Wrist Osteoarthritis (specific joints: distal and proximal interphalangeal, metacarpophalangeal, carpometacarpal and carpal)	Clinical and radiographic (presence of joint-space narrowing and/or osteophytes and/or subcondrale cysts)
Nerve compressive syndromes	Clinical and electrophysiological (abnormal nerve conduction studies)
Dupuytren Contracture	Clinical (thickening with or without contractures of the palmar fascia)
De Quervain's Disease	Clinical (pain over the radial side of the wrist and/or with resisted thumb extension and/or resisted thumb abduction; and positive Finkelstein's test)
Trigger Finger Disorder	Clinical (catching or popping of digital movements with both flexion and extension at either the metacarpophalangeal or proximal interphalangeal joints)
Hypothenar Hammer Syndrom	Clinical and angiographic (vascular abnormalities of the ulnar artery at the wrist)
Kienbock's Disease	Clinical and radiographic (abnormalities of the lunate bone)

The level of evidence of a causal association between an exposure to a specific risk factor and a specific outcome was evaluated based on a classification system established by The Scientific Committee of the Danish Society of Occupational and Environmental Medicine (*DASAM*), which has been used in other recent reviews.[8, 9]

The following categories were used:

+++ strong evidence of a causal association

++	moderate evidence of a causal association
+	limited evidence of a causal association
0	insufficient evidence of a causal association
-	evidence suggesting lack of a causal association

**Description of categories:**

Strong evidence of a causal association (+++):

A causal relationship is *very likely*. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It can be ruled out with *reasonable* confidence that this relationship is explained by chance, bias or confounding.

Moderate evidence of a causal association (++):

A causal relationship is *likely*. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It cannot be ruled out with *reasonable confidence* that this relationship can be explained by chance, bias or confounding, although this is not a very likely explanation.

Limited evidence of a causal association (+):

A causal relationship is *possible*. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It is not unlikely that this relationship can be explained by chance, bias or confounding.

Insufficient evidence of a causal association (0):

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

Evidence suggesting lack of a causal association (-):

Several studies of sufficient quality, consistency and statistical power indicate that the specific risk factor is not causally related to the specific outcome.

**Comments:**

The classification does not include a category for which a causal relation is considered as established beyond any doubt.

The key criterion is the epidemiological evidence.

The likelihood that chance, bias and confounding may explain observed associations are criteria that encompass criteria such as consistency, number of 'high quality' studies and type of design. Biological plausibility and contributory information may add to the evidence of a causal association.

## 5. HAND OSTEOARTHRITIS

### 5.1 Introduction

Osteoarthritis (OA) can be characterized as progressive articular cartilage loss with concomitant changes in the bone underneath the cartilage. When it is extensive, the changes are visible on radiographs as joint-space narrowing, osteophytes, and subcondrale cysts.

Osteoarthritis is the most common form of arthritis affecting millions of people worldwide. The prevalence of radiographically diagnosed hand OA increases steadily with age. In the age group of 40 to 49 years, 10% of subjects are affected, whereas in subjects older than 70 years, the prevalence is 90% in women and 80% in men. [10] These numbers most likely overestimate the real clinical burden of hand OA. Mannoni et al for instance showed that the prevalence of symptomatic hand OA among subjects older than 65 years in Italy is only 15%. [11, 12] In the US the incidence of symptomatic radiographic hand OA is, according to Oliveria et al 1995, about 0,5% per year.[13]

Osteoarthritis of the hand is a major cause of impairment in performing activities of daily living. Thirty percent of all joints affected by OA are the joints of the hand.[14] The distal interphalangeal (DIP) joint demonstrates the highest OA prevalence overall. OA prevalence rates specific for second DIP, third proximal interphalangeal (PIP), and first carpometacarpal (CMC) joints have been reported at 35%, 18%, and 21%, respectively.[15] Women have a higher prevalence of symptomatic hand OA than do men.[16] The reason for that is still not clearly elucidated.[17]

Many people with pathologic and radiographic evidence of osteoarthritis have no symptoms[11]. From a clinical perspective, the most compelling definition of disease is one that combines the pathology of disease with pain that occurs with joint use.[18] The cause of pain in osteoarthritis is still unclear.[19, 20]

The aetiology of primary arthrosis is multi-factorial and age, gender, metabolic and genetic factors, nutrition and biomechanical factors (such as muscle weakness, joint laxity, joint injury and repetitive strain) have been studied as risk factors.[18, 21, 22]

The global frequency of OA is expected to increase with the progressive increase in life expectancy of the population. Considering that OA is the musculoskeletal disease with the highest number of known and suspected risk factors, it is to expect that modifying risk factors, when possible, may present opportunities for prevention of osteoarthritis-related pain and disability. With this in mind is the aim of this review to elucidate possible occupational risk factors for hand /finger / wrist OA (more specifically OA in the following joints: distal and proximal interphalangeal, first metacarpophalangeal, carpometacarpal and carpal) and hereby prevention perspectives.

<sup>1</sup>The American College Of Rheumatology (ACR) have established clinical criteria for symptomatic primary OA . They concluded that the clinical diagnosis of OA of the hand did not necessary require the present of typical radiographic changes.

The definition criteria for osteoarthritis applied for this review are clinical signs of OA and radiographic (presence of joint-space narrowing and/or osteophytes and/or subcondrale cysts) abnormalities confirmed osteoarthritis. The reason for using both clinical and radiographic criteria was to avoid including articles focusing more on symptoms suggesting osteoarthritis instead of the clearly diagnosed disorder.

### 5.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Osteoarthritis

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<sup>1</sup> Altman R, Alarcón G, Appelrouth D, *et al.* The American College Of Rheumatology criteria for the classification nad reporting of tha osteoarthritis of the hand. *Arthritis and Rheumatism, Vol.33, No.11*

- Finger
- Hand
- Occupational
- Hand-Arm Vibration Syndrome
- Hand Deformities, Acquired [Mesh]
- Hand Bones [Mesh]
- Hand Joints [Mesh]
- Finger Joint [Mesh]
- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]
- Occupational Health [Mesh]
- Occupational Groups [Mesh]
- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]

The diagnostic criteria for osteoarthritis should be based on clinical and radiological investigations.

The electronic search retrieved 864 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 62 articles, which were considered relevant. They are classified as follow: 34 articles regarding background information or reviews and 28 original articles. The latter includes 1 follow-up, 2 case-controls, 18 cross-sectional and 7 case-reports.

The studies are discussed below and resumed in the tables listed according to exposure to biomechanical factors or hand/arm vibration, and under each topic they are presented according to descending year of publication and alphabetic sequence both in the text and in the tables. The epidemiological studies regarding biomechanical occupational exposures (17 studies) are shown in table 1. Table 2 contains epidemiological studies regarding exposure to hand/arm vibration (4 studies) and table 3 presents case reports.

### 5.3 Biomechanical occupational exposures

From a longitudinal cohort study (The Clearwater Osteoarthritis Study), designed to identify the major risk factors for the development and progression of radiographic OA, Bernard et al 2010[23] carried out a cross-sectional study to assess the influence of different occupational exposures on risk of site-specific radiographic osteoarthritis of the knee, hand, foot, and cervical spine. The study sample consisted of 3436 men (1098) and women (2450) aged 40 years and older. Exposure was measured by a structured questionnaire. The occupational exposure evaluated for hand OA was jolting of the hands and legs. The reference group was those subjects who indicated that they performed their jobs "sitting most of the time". Only 6 % of the participants reported jolting of the hands and legs. The association between hand OA and jolting of the hands showed positive associations for women – OR = 1.82 (1.19-2.76) (adjusted for age and BMI). For men, there were no significant associations – OR = 0,93 (0,57-1,51).

The big sample size is a strength in this study, while a major limitation regards the exposure assessment. Jolting of hands was crudely assessed by self-reported information and was present only in about 6 percent of the population studied.

Fontana et al 2007[24] investigated the occupational risk factors for OA of the thumb-CMC joint among women. They designed a case-control study with 61 women requiring surgery for thumb-CMC OA (cases) compared with 120 women admitted in a department of orthopaedic surgery without signs of thumb-CMC OA (controls). A detailed structured interview was developed to elicit information about occupational factors. Occupational factors were based on a detailed history of job, coded to International Standard Classification of Occupations (ISCO-88). The different occupations were distinguished in four groups: manual occupations (those whose main task require the use of the hands); non-manual occupations; occupations assumed as

being at risk for CMC OA (occupations for which the main tasks require thumb use); and occupations not at risk. The occupational factors identified as risk factors were: 1) occupations presumed to be associated with increased risk for thumb-CMC OA – OR = 3.78 (95% CI, 1.20 – 11.92); 2) occupations involving repetitive thumb use (>20 movements per minute and/or thumb flexion/extension at least once per minute) – OR = 11.91 (95% CI, 3.65–38.86); and 3) jobs perceived by the subject having not enough rest breaks during a day – OR = 5.95 (95% CI, 1.66 –21.28).

The study has the strength that case and controls were adjusted for many different non-occupational factors, but the assessment of exposure was based on subjective and retrospective information. This predisposes to information bias, where affected individuals have the tendency to overestimate the exposures. Moreover, study size was limited and therefore only effects of highly prevalent occupational exposures can be detected.

In a cross-sectional study with 291 female dentists Solovieva et al 2006[25] evaluated whether the pattern of dental work tasks was associated with finger osteoarthritis. Three patterns emerged reflecting high, moderate, and mild task variation. They found that the dentists with a history of low task variation had a greater prevalence of osteoarthritis in the thumb, index, and middle fingers compared with dentists with high variation (OR 2.22; 95%CI 1.04-4.91).

One strength of this study is that the groups were adjusted for many different personal factors (age, family history of Heberden's nodes, BMI, specialization, number of years in clinical practice, daily use of computer, daily manual activities and smoking history), which reduces possible confounders. A few limitations of the study are that only women were included, the exposure was assessed retrospectively and there was no assessment of hand workload for the different work tasks.

Rossignol et al 2005 [26] investigated in a cross-sectional study with 2834 symptomatic patients the relation between thirty different occupations and five biomechanical stresses and the prevalence of OA of the knee, hip, and hand. Patients between the age of 20 and 80 years with osteoarthritis of the hip, knee or hand were recruited throughout France by their treating physician. Information about occupation and occupational stresses to joints were reported to the physicians. Patients had to have worked for one year or more during their lifetime and the occupations they held longest were reported. The biomechanical stresses evaluated were: 1) lift or carry heavy objects, 2) keep the affected joint in uncomfortable positions, 3) work in a vibrating vehicle or with vibrating tools, 4) repeat the same movements continuously and 5) work at a pace set by a machine. They found that repetition of movements continuously or working at machine pace were risk factors for developing hand OA among women, and that workers in construction, mechanics, clothing and food sectors had the highest proportion of osteoarthritis of the hands (48.0%) in the whole study population (36.2%) (p=0.01).

The discrimination of thirty different occupational groups gave the advantage of identifying the occupations with higher prevalence of OA, but the assessment of exposure to biochemical stresses was based just on subjective information, making recall and information bias possible.

In another cross-sectional study comparing 295 female dentists with 248 female teachers age 45-63 years Solovieva et al 2005 investigated the effect of mechanical stress on finger OA. The subjects were identified through the registers of the Finnish Dental Association and The Finnish Teachers' Trade Union. They found a pattern of involvement for moderately severe OA with clustering within the thumb, index and middle fingers among dentists and clustering within the ring and little fingers among teachers. On the other hand the prevalence of OA in any finger joint and also in any distal interphalangeal joint was higher among the teachers.[27]

One limitation in this study is that there was no specification of the hand load teachers were exposed to.

In a cross-sectional survey with over 3.000 subjects from the Mini-Finland Health Survey (which was the first national health examination survey in the world and represented the Finnish population over 30 years of age) Haara et al 2003[28] investigated finger joint OA and its associations with alleged risk factors and with life expectancy. The occupational biomechanical factors assessed were: 1) lifting or carrying heavy objects, 2) stooped, twisted, or otherwise awkward work postures, 3) vibration of the whole body or the use of vibrating equipment, 4) continuously repeated series of movements, and 5) paced work (working speed determined by a machine). The total number of these risk factors was designated "the sum index of physical stress at work". It was found a positive association between the maximal sum index of physical stress at work and OA in any



finger joint among women (OR=10,97 – 95% CI 1,25-95,90) but no association in men (OR=1,75 – 95% CI 0,78-3,91). The association was mainly due to close associations between workload and OA in PIP and MCP joints among women. No increasing risk from the minimal to maximal sum index of physical strain was found. The physical stress index showed a positive association (not statistically significant) to symmetrical DIP OA in either sex (OR=2,72– 95% CI 0,86-8,58 for men and OR=1,46 – 95% CI 0,33-6,51 for women). The group made a follow-up of mortality 14 years later to evaluate whether finger OA was a predictor of mortality.

Some strengths in this study are the big sample size and that the main outcome was finger osteoarthritis, while a weakness is retrospective self-reported exposure assessment.

Kessler et al 2003[29] investigated in a cross-sectional study including 693 patients scheduled for hip or knee replacement whether whether isolated OA of the first carpometacarpal joints and the interphalangeal joints differs in its aetiology, considering potential risk factors such as age, gender, body mass index, occupational history, OA in the hip or knee joints, hypertension and diabetes. Age showed an expected positive association with the occurrence of both interphalangeal OA (OR=1,11 – 95% CI 1,08-1,14) and carpometacarpal OA (OR=1,11 – 95% CI 1,08-1,15). Female gender showed a positive association with OA of the first CMC-joints (OR=1,8 – 95% CI 1,2-2,7) and a non-statistically significant association with interphalangeal OA (OR=1,3 – 95% CI 0,9-1,9). They did not find any association between heavy physical exertion at work place and OA of the first-CMC-joints (OR=0,7 – 95% CI 0,5-1,1) or IP-joints (OR=1,1 – 95% CI 0,7-1,6).

The main limitation of this article is that heavy physical exertion at work place was not specified, which makes the assessment of occupational exposure unclear.

Jones et al 2002[30] studied the association between sex and lifestyle factors and hand OA in a cross-sectional design with 522 participants. The lifestyle factors analyzed were smoking, occupation, sport participation and physical activity (the last three parameters regarded the current status and between the ages of 20 to 40 years). History of digit fracture and BMI were also included in the analysis. Each occupation received a score according to the degree of mechanical stress to hand joints (grade 0 = low impact or grade 1 = high impact). They found that high impact occupations did not show any statistically significant association to clinical or radiological hand OA (OR=1,3 – 95% CI 0,65-1,97 for Heberden's nodes; OR=1,29 – 95% CI 0,69-2,43 for DIP OA and OR=0,73 – 95% CI 0,4-1,33 for CMC disease). High impact physical activity or sport participation had no association with the prevalence or severity of hand OA either.

Some weaknesses of the study are that the recall of occupation was made subjectively and retrospectively, which allows information bias, and that the assessment of high or low impact occupations is not clearly detailed.

In a cross-sectional study Caspi et al 2001[31] investigated the frequency, severity and distribution of hand OA, and possible relation between these findings and the demographic, occupational, and medical data from 253 geriatric patients. Occupational history included details from the exact jobs and the hand requirements and strain involved, estimated later on a scale of 1 to 3 (occupational degree). The duration in years of occupation at each job was recorded. An occupational score was determined by summing the multiplication of the estimated hand occupational degree of each job (graded 1 to 3) by the duration of each job. The occupational scores resulted in a final classification into manual or non-manual work. The results showed that hand OA was prevalent in that elderly cohort, and that its severity was influenced by inherent traits such as age, female gender, ethnicity, and handedness. Occupational history did not show any correlation to the expression of hand OA.

The study has the limitations of a small number of participants with a high mean age (79 years), which do not reflect the age of the economic active population. Besides it is expectable to find a high prevalence of hand OA among all the participants given their old age. That can be the reason why it was not possible to find any relevant difference among the subjects regarding occupational history.

Nakamura et al 1993[32] investigated in a cross-sectional study the role of workload in the pathogenesis of OA of DIP-joints. They compared 482 female cooks considered to have primarily manual work with 298 female municipal employees. The group of cooks was further divided into two groups according to how many meals they prepared per working day. It was found statistically significant higher rates of DIP OA among the

cooks as follows: 13,5 and 5,9% contra 2,0% among municipal employees ( $P < 0,05$ ). Within the group of cooks they found that those who prepared more meals per working day presented higher rates of DIP OA when compared with those who prepared half as many meals per working day (13,5% contra 5,9%;  $P < 0,01$ ). The study presents the strength of comparing the same occupational group trying to make a differentiation only in workload. But the lack of precision regarding the description of the exposure besides the amount of meals prepared (for example regarding which specific cooking tasks and which kind of cleaning work was also performed by each group) constitutes a limitation of the study. It was not referred in the article how the occupational information was obtained, so a possible information bias should also be considered.

Lehto et al 1990[33] compared in a cross-sectional design 136 dentists with 940 controls from a population sample regarding the prevalence and distribution of hand OA. The results showed that the overall prevalence of hand OA was similar among dentists and controls (OR=1,3 – 95% CI 0,7-2,5 for male dentists and OR=0,6 – 95% CI 0,3-0,9 among female dentists). But the proportion of affected DIP-joints of all arthrotic joints of the hands was in both male and female dentists greater than that in controls, especially below the age 50 (0-60% among controls and 70-100% among dentists – statistical significance not informed).

Despite the small number of cases the study has some strengths. The specification of which joints presented OA in both groups made it possible to identify different patterns of involvement, and the choice of dentists, for whom the use of the precision grip is a well-established workload, made it possible to definite the exposure.

In a case-control study which compared skeletons of weavers and manual workers with non-manual workers performed by Waldron and Cox 1989[34] it was found none significant difference regarding the rates of hand OA. The limitation of this study was the small number of cases and controls (13 and 26 respectively) and the inaccuracy of the exposure's assessment given that occupational history was built up from post-mortem information.

Hadler et al 1978[35] compared in a cross-sectional study three groups of female textile workers – winders, burlers and spinners – ( $n=64$ ) who worked at the same rural mill regarding their workload and the pattern of hand OA involvement. A task description was made by a consulting industrial engineer and ergonomist, and a standard time-motion analysis was made available by the plant industrial engineer. Regarding task differences winding was the only task perceived as bymanual requiring considerable wrist motion and power grip and little fine finger motion or precision grip. For burling and spinning the workers used heavily and extensively precision grip with the first three fingers, while the 4<sup>th</sup> and 5<sup>th</sup> fingers were spared mainly in spinning. Range of motion and radiographic OA changes were analyzed for all workers. Symptoms were not taken into account in attempt to avoid their influence as a confounder. Regarding the findings of hand OA involvement they found significant differences between right and left hands with most of cases occurring in the right hand. Almost all the workers were right handed. It was also found that the winders were the only group with bilateral impairment of range of motion on the wrist. Burlers and spinners had significantly more OA changes in the 2<sup>nd</sup> and 3<sup>rd</sup> fingers than winders. And burlers had more clinical signs of OA in the 5<sup>th</sup> finger than spinners. So the found task differences corresponded to the pattern of usage at work.

Despite the small number of subjects, this study emphasises the importance of clearly specifying the outcomes and the different exposures.

In a cross-sectional study with 299 male foundry workers aged 35 years and over and 298 controls Lawrence et al 1966[36] investigated the prevalence of OA of hands, knee and hips and of disc degeneration of dorsal and lumbar spine, and correlated it with symptoms and loss of work due to disease. They found that foundry workers had significantly less OA of the DIP-joints than the controls (OR=0,64 – 95% CI 0,43-0,95). In none of the joints was there significantly more OA in the foundry workers.

The aim of this study was not specifically to investigate hand OA, and the focus of the discussion was disc degeneration in the lumbar spine and pain complaints related to exposure to radiant heat, which reduces the relevancy of the study to the this review.

Lawrence 1961[37] compared 345 cotton operatives with 345 controls regarding OA of hands and feet and disc degeneration of cervical, dorsal and lumbar spine. They found radiological evidence of OA more frequent in the DIP-, PIP- and in the 1-CMC-joints in the male cotton workers than in the controls (OR=1,9 –

95% CI 1,0-3,3; OR = 2,5 – 95% CI 1,1-5,7 and OR = 2,4 – 95% CI 1,2-5,0 respectively). In the MCP-joints the male cotton workers had much the same prevalence of OA as the controls but it was more severe (OR=1,1 – 95% CI 0,5-2,4). There were no significant differences between female cotton workers and controls. The authors divided the cotton workers in weavers, spinners and others in an attempt to identify, which function within a cotton mill would be associated with higher rates of OA, but there were insufficient male weavers for any statistical analysis and the results were not significant among women.

In a cross-sectional study with 380 participants from a population sample Kellgren and Lawrence 1958[38] investigated the prevalence of OA and pattern of joint involvement of the hands, feet, knees, hips, and of disc degeneration of cervical and lumbar spine. The occupations were divided in 74 miners, 18 cotton workers, 130 domestic workers and others, which were a miscellaneous group of different occupations. It was found that among male cotton workers, compared with the miscellaneous group of occupations, all the small joints of the hands appeared to be more frequently affected by radiological OA, but the number of cotton workers was too small for the observed differences to reach accepted levels of significance except for OA in the 1-CMC joints (OR=1,6 – 95% CI 1,6-13,2) and in the PIP-joints (OR=3,5 – 95% CI 1,1-11,0). The results were not statistically significant for female cotton workers. Among miners there was a suggestive trend of higher prevalence of OA of MCP joints but the results were not statistically significant either. Some limitations of this study were the small number of subjects and the lack of specification of the miscellaneous group, which was made up of small numbers of workers in a wide variety of not specified occupations.

The same group, i.e. Kellgren and Lawrence 1952[39] studied in a cross-sectional design degenerative joint diseases of hands, knees, and cervical and lumbar spine among 84 miners, 45 manual workers and 42 office workers. They found that hand OA occurred fairly equally among the miners and manual workers but were virtually absent in the office workers (OR= 8,2 – 95% CI 1,4-47,9 among miners and OR= 5,1– 95% CI 0,7-37,6 among manual workers compared to office workers).

The study focused on OA changes of spine and knees and commented the findings of hand OA very briefly. Besides that, the number of participants was small and hand OA was not further specified (fingers or wrist OA).

#### **5.4 Exposure to hand/arm vibration**

Four studies investigated whether there is a correlation between exposure to hand/arm vibration and development of hand or wrist OA.

Kivekas et al 1994[40] designed a seven-year follow-up study of white-finger symptoms and radiographic hand and wrist osteoarthritis in 213 lumberjacks and 140 referents. The subjects were first examined in 1978 regarding the prevalence of white-finger symptoms and translucencies in the wrist bones. Then in 1985 a follow-up study was performed to analyze changes in white-finger symptoms, the effect of these symptoms on the professional life of lumberjacks, and the relationship between hand/arm vibration and changes in hand and wrist bones. A questionnaire was answered by the subjects to determine work history, general state of health and symptoms. Clinical and radiographic examinations of wrist and hands were performed.

They found that in both groups there was a strong relationship between OA and age. After allowance for age, the prevalence of OA was not related to exposure time to hand/arm vibration among the lumberjacks (OR=1,3 – 95% CI 0,6-2,5).

Some strengths of this study are a long duration of exposure to hand/arm vibration (mean 19,7 years) and the differentiation between radiographically detectable translucencies (cysts and vacuoles) of the wrist and radiographic OA changes of hand and wrist. A limitation is that neither the exposure nor the outcome is further elucidated, for example regarding hours per day of exposure and which joints presented OA. ). The relatively young age of the subjects (18-54 years) can also be considered a limitation because it may underestimate an eventual risk factor for the developing of OA, given that this disorder is more frequent after the age of 50 years.

Bovenzi et al 1987[41] analyzed in a cross-sectional study bone and joint disorders in the upper extremities (wrist, elbow and shoulder) among 67 chipping/grinding operators and 46 manual workers not exposed to hand/arm vibration. The control group included workers performing manual tasks at the same foundry (mechanics, maintenance men). The found prevalence of wrist OA was 19,4% among the vibration-exposed

workers and 4,3% among controls ( $P < 0,025$ ;  $OR = 5,3$  – 95% CI 1,3-21,7). The prevalence of cysts in the metacarpal and carpal bones was almost the same in the two groups. Among the chipping and grinding operators a slight but not significant trend in the prevalence of skeletal abnormalities with increasing vibration exposure was observed.

One positive aspect of this study is the detailing of the exposure regarding vibration levels for the specific tools and exposure measurement by total hours of exposure.

Malchaire et al 1986[42] investigated bone and joint changes in the wrist and elbow in 82 workers exposed to hand/arm vibration to 75 age-matched controls in a cross-sectional design. The control group included manual workers from the same stone pits as the cases. All cases of wrist OA were found among subjects older than 45 years. It was found 13 cases of wrist OA among 48 wrists analyzed in the exposed group with, and 11 cases among 46 wrists in the control group. This finding was not statistically significant ( $OR = 1,09$  – 95% CI 0,4-2,6). Besides age, no other personal factors were taken into account.

The study did not specify which activities the control group of manual workers performed. This would be relevant to elucidate whether the control was exposed to factors suspected of contributing to the occurrence of wrist OA. This could maybe explain the lack of difference on the prevalence of wrist OA between the two groups.

Kumlin et al 1973[43] compared, in a cross-sectional study, radiological changes of carpal and metacarpal bones and phalanges between 35 lumberjacks and 35 controls not exposed to hand/arm vibration. The age-matched control group was selected at random from the radiological archives. They found no statistically significant differences regarding the prevalence of hand and wrist OA between the two groups ( $OR = 1,5$  – 95% CI 0,2-9,7).

### **5.5 Case reports**

It was found seven articles, which published case reports. Five of those regarded biochemical occupational exposures[44-48], and two reported exposure to hand/arm vibration.[49, 50] In most of the cases a pattern of involvement, which was proposed as associated to specific workloads was found.

**Table 5.6 – Epidemiological studies on hand osteoarthritis in relation to biomechanical occupational exposures**

OA = osteoarthritis; yrs = years; m = men; w = women; IP = interphalangeal joint; IP-thumb: interphalangeal joint of the thumb; PIP = proximal interphalangeal joint; DIP = distal interphalangeal joint; MCP = metacarpophalangeal joint; 1-CMC = first carpometacarpal joint; IC = intracarpal joints; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women; CI = confidence interval

Reference	Population	Design	Relevant exposure	Relevant outcome	Selected results - Risk estimate referred when possible (95% CI)
Bernard et al 2010 USA[23]	n=3436 (1098 m, 2450 w) Mean age: 63 yrs - m, 31 yrs - w	Cross-sectional	Jolting of the hands	Radiographic hand OA (DIP, PIP and 1-CMC)	ORm=0,93 (0,57-1,51) ORw=1,82 (1,19-2,76)  Adjusted for age and BMI
Fontana et al 2007 France[24]	n=181 women (61 cases, 120 controls) Mean age: 64 yrs (cases), 60 yrs (controls)	Case control	Occupations presumed to be associated with increased risk for CMC Repetitive thumb use (>20 movements per minute and/or thumb flexion / extension at least once per minute) Jobs perceived by subjects as having "Not enough rest breaks during a day".	Radiographic 1-CMC joint OA	Occupations at risk: OR=3,78 (1,20-11,92) Thumb use: OR=11,91 (3,65-38,86) "Not enough breaks": OR=5,95 (1,66-21,28)  Adjusted for age, smoking status, obesity, CMC OA family history, hysterectomy, parity and occasional jobs
Solovieva et al 2006 Finland[25]	n=291 female dentists Age: 45-63 yrs	Cross-sectional	Variation of work tasks: high (mixture of different tasks), moderate (½ restorative ½ surgical) and low (mainly restorative and endodontics)  Mean duration of dental practice: 26 years	Radiographic finger OA	Low task variation: OR= 2,22 (1,04-4,91) for OA in thumb, index and middle finger  Adjusted for age, family history of Heberden's nodes, BMI, specialization, number of years in clinical practice, daily use of computer, daily manual activities and smoking history
Rossignol et al 2005 France[26]	n=2834 (1615 m, 1219 w) Mean age: 61,8 yrs	Cross-sectional	Thirty different occupational groups + five different biomechanical	Radiographic (over 90% of the cases) or clinic hand OA	Repetition of movements continuously or working at machine

			stresses		pace: ORm=1,5 (0,9-2,5) ORw=3,6 (2,4-5,7)
Solovieva et al 2005 Finland[27]	n=543 (295 female dentists, 248 female teachers) Age: 45-63 yrs	Cross-sectional	Precise and repetitive movements among dentists	Radiographic finger OA (DIP, PIP, IP-thumb, MCP)	Patterns of joint involvement for moderately severe OA:  <b>Dentists:</b> OR=1.80 (1.16–2.80) for clustering within the thumb, index and middle fingers <b>Teachers:</b> OR= 9.75 (4.78–19.88) for clustering within the ring and little fingers  Adjusted for age
Haara et al 2003 Finland[28]	n=3595 (1560 m, 2035 w) Age: 35 - >75 yrs	Cross-sectional	Sum index of physical stress at work – based on the sum of five different exposures: lifting or carrying heavy objects stooped, twisted, or otherwise awkward work postures vibration of the whole body or the use of vibrating equipment continuously repeated series of movements paced work, working speed determined by a machine	Radiographic finger OA (DIP, PIP, MCP, CMC, IP-thumb)	For the maximal workload exposure: OA in any finger joint: ORm=1.75 (0.78-3.91) ORw=10.97 (1.25-95.90) <b>Symmetrical DIP OA:</b> ORm=2.72 (0.86-8.58) ORw=1.46 (0.33-6.51)  Adjusted for age, educational level, body mass index, and smoking
Kessler et al 2003 Germany[29]	n=639 (around 60% women) Age: 53-72 yrs	Cross-sectional	Heavy physical exertion at work place	Radiographic finger OA (1-CMC, IP)	For 1-CMC OA: OR=0,7 (0,5-1,1)  For IP-joints OA: OR=1,1 (0,7-1,6)
Jones et al 2002 Australia[30]	n=522 (174 m, 348 w) Mean age: 53 yrs (m), 57 yrs (w)	Cross-sectional	High impact occupations (those associated with high degree of mechanical stress to hand joints)	Clinical and radiographic finger OA (DIP- and CMC-joints)	For Heberden's nodes: OR=1,13 (0,65-1,97)  For DIP OA: OR=1,29 (0,69-2,43)  For CMC OA:

					OR=0,73 (0,4-1,33)  Adjusted for age, sex, age-sex interaction, BMI and family status
Caspi et al 2001 Israel[31]	n=253 (171 w, 82 m) Mean age: 79 yrs	Cross-sectional	Manual versus non-manual work	Clinical and radiographic finger OA (DIP, PIP, 1-CMC, MCP)	No significant correlation between occupational history and the clinical or radiologic OA of both hands in the whole group
Nakamura et al 1993 Japan[32]	n=780 (Cases: 482 female cooks; Controls: 298 female municipal employees) Age: 40-59 yrs	Cross-sectional	Elementary school cooks: 150-450 lunches daily Pre-school cooks: 30-80 lunches and snacks Municipal employees: cooked only at home	Clinic (Heberden's nodes) or radiographic DIP OA (radiographs from only 114 subjects)	Elementary school cooks: Heberden's nodes - OR=4,19 (2,4-7,31) <b>DIP OA - OR=7,57 (3,51-16,3)</b> Pre-school cooks: Heberden's nodes - OR=1,65 (0,83-3,26) <b>DIP OA - OR=3,02 (1,18-7,74)</b>
Lehto et al 1990 Finland[33]	n=1076 (136 dentists, 940 controls) Age: 33-69 yrs	Cross-sectional	Extensive use of precision grip for at least 10 years among dentists	Radiographic OA of fingers and wrist (DIP, PIP, IP, MCP, 1-CMC)	OA of all joints: ORm=1,3 (0,7-2,5) ORw=0,6 (0,3-0,9)  The proportion of arthrotic DIP joints of the total number of arthrotic joints of the hands was higher in dentists than in controls
Waldron and Cox 1989 UK[34]	n=39 male skeletons (13 cases, 26 controls) Mean age: 71,6 yrs (cases), 57,6 yrs (controls)	Case control	Weaver Manual Non-manual occupations	Pathologic signs of hand OA	No relation found between occupation and OA of hands, spine, shoulder or at any other site.
Hadler et al 1978 USA[35]	n=64 female textile workers (29 burlers, 16 winders, 19 spinners) Mean age: 52 yrs (burlers), 49 yrs (winders and spinners)	Cross-sectional	Highly repetitive, stereotyped and complex hand movements in spinning, burling or winding for at least 20 years	Radiographic finger and wrist OA	Task-related differences corresponding to the pattern of usage at work

Lawrence et al 1966 UK[36]	n=597 (299 male foundry workers, 298 male controls) Age: 35-74 yrs	Cross-sectional	Foundry work for at least 10 years	Radiographic finger and wrist OA	<b>DIP OA:</b> OR= 0,64 (0,43-0,95) <b>PIP OA:</b> OR= 1,53 (0,8-2,95) <b>MCP OA:</b> OR= 0,91 (0,56-1,47)  CMC and IC OA: OR= 0,73 (0,42-1,26)
Lawrence 1961 UK[37]	n=690 (345 cotton operatives, 345 controls) Age >45 yrs	Cross-sectional	Cotton workers (weavers, spinners and doublers, tenters and others)	Radiographic finger (DIP, PIP, MCP, 1-CMC) and wrist OA	DIP OA: ORm=1,9 (1,0-3,3) ORw=1,2 (0,7-1,9)  PIP OA: ORm=2,5 (1,1-5,7) ORw=1,3 (0,6-2,5)  MCP OA: ORm=1,1 (0,5-2,4) ORw=0,8 (0,3-1,9)  <b>1-CMC OA:</b> ORm=2,4 (1,2-5,0) ORw=1,4 (0,7-2,6)  Wrist OA: ORm=0,4 (0,1-1,1) ORw=0,8 (0,2-2,7)  Adjusted for age and sex
Kellgren and Lawrence 1958 UK[38]	n=380 (173 m, 207 w) Age: 55-64 yrs	Cross-sectional	Miners (only men), Cotton workers, Domestic (only women), Others	Radiographic hand (DIP, PIP, MCP, 1-CMC) and wrist OA	<b>Miners</b> <b>DIP</b> - OR=1,5 (0,6-3,5) <b>PIP</b> - OR=1,6 (0,7-4,0) <b>MCP</b> -OR=1,7 (0,8-3,8) <b>1-CMC</b> - OR=1,2 (0,5-2,8) <b>Wrist</b> - OR=1,1 (0,3-3,2)  <b>Cotton workers</b> <b>DIP</b> - ORm=2,3 (0,8-6,5) ORw=1,1 (0,4-2,9) <b>PIP</b> - ORm=3,5 (1,1-11,0) ORw=1,7 (0,6-4,6) <b>MCP</b> - ORm=2,3 (0,7-7,2)



					<p>ORw=0,5 (0,2-1,8)</p> <p><b>1-CMC</b> - ORm=4,6 (1,6-13,2)</p> <p>ORw=1,5 (0,5-4,0)</p> <p><b>Wrist</b> - ORm=1,3 (0,2-6,9)</p> <p>ORw=1,5 (0,1-15,8)</p> <p><b>Domestic</b></p> <p><b>DIP</b> - OR=0,8 (0,3-2,1)</p> <p><b>PIP</b> - OR=1,1 (0,4-2,7)</p> <p><b>MCP</b>-OR=0,6 (0,2-1,7)</p> <p><b>1-CMC</b> - OR=1,0 (0,4-2,5)</p> <p><b>Wrist</b> - OR=1,0 (0,1-9,0)</p>
Kellgren and Lawrence 1952 UK[39]	n=171 (84 male miners, 45 male manual workers, 42 male office workers) Age: 40-50 yrs	Cross-sectional	Miners Manual workers (blacksmiths, machinists, carpenters, painters and general labourers) Office workers (clerks and administrative staff)	Radiographic hand and wrist OA	<p><b>Miners:</b> OR= 8,2 (1,4-47,9)</p> <p>Manual workers: OR=5,1 (0,7-37,6)</p>

**Tabel 5.7 – Epidemiological studies on hand osteoarthritis in relation to exposure to hand/arm vibration**

OA = osteoarthritis; yrs = years; m = men; w = women; IP = interphalangeal joint; IP-thumb: interphalangeal joint of the thumb; PIP = proximal interphalangeal joint; DIP = distal interphalangeal joint; MCP = metacarpophalangeal joint; 1-CMC = first carpometacarpal joint; IC = intracarpal joints; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women; CI = confidence interval

	Population	Design	Relevant exposure	Relevant outcome	Selected results - Risk estimate referred when possible (95% CI)
Kivekas et al 1994 Finland[40]	n = 353 (213 male lumberjacks, 140 male controls) Age: 18-54 yrs	Follow-up	Work with old, heavy chain saws, whose vibration was poorly damped (mean exposure time 19,7 years)	Radiographic hand and wrist OA	1978: OR=0,8 (0,3-2,1) 1985: OR=1,3 (0,6-2,5)  Age adjusted
Bovenzi et al 1987 Italy[41]	n=113 (67male chipping / grinding operators, 46 male controls) Mean age: 39 yrs	Cross-sectional	Vibrating tools in chipping and grinding work (exposure time: 348-20160 hours)	Radiographic wrist OA	OR = 5,3 (1,3-21,7)  Age adjusted
Malchaire et al 1986 Belgium[42]	n=157 (82 male cases, 75 male controls) Age: 20-58 yrs	Cross-sectional	Work with pneumatic tools to quarry and slit granite blocks in stone pits on average 14,6 years around 1 hour per day	Radiographic wrist OA	OR=1,09 (0,4-2,6)
Kumlin et al 1973 Finland[43]	n=70 (35 male lumberjacks, 35 male controls) Age: 33-58 yrs	Cross-sectional	Work with chain saw (exposure time: 7-20 years)	Radiographic wrist and fingers OA	OR=1,5 (0,2-9,7)  Age adjusted

**Table 5.8 – Case reports on hand osteoarthritis in relation to occupational exposures**

OA = osteoarthritis; yrs = years; m = men; w = women; IP = interphalangeal joint; IP-thumb: interphalangeal joint of the thumb; PIP = proximal interphalangeal joint; DIP = distal interphalangeal joint; MCP = metacarpophalangeal joint; 1-CMC = first carpometacarpal joint; IC = intracarpal joints; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women

Reference	Population	Exposure	Results
Jensen and Sherson 2007 DK[44]	n=1 male industrial worker who made panels for folding doors Age: 44 yrs	Forceful and repetitive ulnar flexion of both first fingers for 9 years	Bilateral OA of 1-CMC joints
Poole 1993 UK[45]	n=3 female sewing machinists Age: 54-56 yrs	Paced, repetitive and stereotyped work	Case 1: severe DIP OA of the right index and middle fingers. Case 2 and 3: DIP OA of the right index, middle and ring fingers and sclerosis of the trapezioscapoid joint of right hand in case 3
Williams et al 1987 USA[46]	n=7 male manual workers Age: 51-72 yrs	Manual work demanding sustained gripping motions of both hands for more than 30 years (seven different occupations)	Bilateral MCP OA, most prominent in the second and third joints
Wilson and Stothard 1987 UK[47]	n=1 male armature winder Age: 55 yrs	Repetitive pressing down of coils into a slot using the thumbs for 8 years	Degenerative changes with hyperextension of the IP joints and flexion of MCP joints bilaterally, most prominent in the dominant hand
Fam and Kolin 1986 Canada[49]	n=1 male jackhammer operator Age: 62 yrs	Jackhammer operator in road construction for 27 years	Bilateral OA in second and third MCP and elbows. Minor OA changes in DIP, shoulder, knee and first MTP joint. No changes in the wrist.
Minuk et al 1982 USA[48]	n=1 female laboratory employee	Pipetting – flexion / extension movement of the first IP of the right hand about 20.000 times per hour	OA of right IP-thumb
Schumacher et al 1972 USA[50]	n=1 male jackhammer operator Age: 59 yrs	Construction worker and intermittently jackhammer operator for 30 years	Fusion of the carpal bones bilaterally but normal MCP and PIP, small osteophytes in the elbows, calcific tendonitis in right shoulder.

## 5.9 Discussion

### Design

The following studies presenting occupational factors in relation to hand OA were retrieved: 1 follow-up survey, 2 case-controls, 18 cross-sectional studies, and 7 case-reports.

The geographic distribution of the studies revealed seven studies from UK, six from Finland, three from France, one from Italy, one from Belgium, one from Denmark, one from Germany (in total of twenty European studies), five from USA, one from Canada, one from Israel, one from Australia and one from Japan.

Seventeen of the epidemiological studies analyzed biomechanical factors and occupations in relation to hand OA (including the 2 case-control studies), and 4 studies analyzed exposure to hand / arm vibration (including the follow-up study).

Regarding exposure to biomechanical factors, 12 studies reported a significant association with hand OA (including 1 case-control study), and 5 studies did not report any significant associations (including 1 case-control study). When hand/arm vibration was the exposure analyzed, 1 cross-sectional study found a positive association with wrist OA, while 1 follow-up and 2 cross-sectional studies did not find any significant associations with hand and wrist OA.

The retrieved original articles were most cross-sectional studies, which point out possible related factors, but do not elucidate causality.

The majority of the studies presenting comparisons between different groups did not include other characteristics than age and gender as possible confounders. None of the studies adjusted for polyarthrosis or obesity. It was retrieved only one follow-up study, which adjusted the groups only for age and did not have osteoarthritis as the main outcome.

### Diagnostic Criteria

The radiological definition of OA differs considerably among the studies because it was used different classification systems. The Kellgren and Lawrence system[51] was utilized by 11 studies; the atlas of radiographic features by Altman et al[52] was utilized by 3; a modification of Swanson's grading of osteoarthritis was used by Nakamura et al[32]; Malchaire et al described their own classification methods, and the classification criteria for radiographic OA was not mentioned in 4 studies. Waldron and Cox applied paleopathologic methods to diagnose OA, given that they studied skeletons. The criteria for the clinical definition of OA was not clearly specified or not even mentioned in most of the studies.

### Outcome

In six studies OA of the hand/finger/wrist was not the main outcome. Only very few studies informed whether finding of OA regarded the dominant or the non-dominant hand. Ten studies did not specify the outcome (which specific joints were affected), referring the outcome just as finger, hand or wrist OA.

### Patterns of involvement

Five of the epidemiological studies found particular patterns of finger OA involvement corresponding to the occupational workload exposure, suggesting a causal relation between specific workload exposures and the localization of osteoarthritis in the fingers.

Hadler et al[35] were the first group that published in 1978 results pointing out this possible causal relation. They found that the dominant hand was more affected than the non-dominant hand among winders, burlers and spinners. Besides, the pattern of involvement within the dominant hand was different for the three groups, corresponding three different patterns of usage during work. Their results are still widely referred by various authors of recent studies.

In a similar way Solovieva et al[25] evaluated whether the pattern of dental work tasks was associated with finger osteoarthritis. It was found greater prevalence of osteoarthritis in the thumb, index and middle fingers among the dentists with a history of low task variation than among dentists with high variation. The same group compared female dentists and teachers – occupations with different hand use –, and found different

patterns of involvement for moderately severe OA with clustering within the thumb, index and middle fingers among dentists, and clustering within the ring and little fingers among teachers. Remarkably they found also that the prevalence of OA in any finger joint and in any DIP joint was higher among the teachers compared with the dentists.[27] In a comparison of dentists and controls Lehto et al[33] found that the proportion of DIP OA of all arthrotic joints of the hands was in both male and female dentists greater than that in controls, especially below the age 50, while the prevalence of OA of all joints of the hands was very similar in both sexes of the controls and in female dentists with a tendency – though not statistically significant – to be higher in male dentists. It was pointed out that dentists extensively use precision grip, which probably overload mainly the DIP-joints.

Haara et al[28] found in a cross-sectional study of a population sample that history of physical workload was associated with OA in any finger joint among women, but it did not show any relation to symmetrical DIP OA in either sex.

Among the total of seven case reports, four of them presented peculiar patterns of finger OA involvement in the dominant hand that correspond to the occupational workload exposure, also suggesting a causal relation between specific work exposures and the development of finger OA.[44, 45, 47, 48]

So the question is whether symmetrical finger/hand/wrist OA has a different pathophysiology, and hereby risk factors, than OA presenting specific patterns of involvement. For example, could the development of interphalangeal OA be associated with performing fine repetitive movements? Or could the development of OA of the first carpometacarpal joint be associated with the repetitive use of power grip? These and other questions are expected to be answered by future controlled studies.

### **Exposure**

As in the case of outcomes, the exposures analyzed by the 21 epidemiological studies were very heterogeneous. Only four different exposures were reasonably comparable in 10 studies – dental work in 3 studies, hand/arm vibration in 4, cotton workers in 2 and miners in 2 (one study with both cotton workers and miners).

In some studies the exposure was not well defined and just referred as heavy physical exertion or heavy labor. The duration of exposure was not informed in various studies.

The exposure was called manual work in several studies, but the criteria for defining manual work varied widely. Some just applied the term to occupations generally known as manual, for example dentists, cooks, weavers, cotton workers, carpenters, painters, etc. Others used score classifications taking into account different biomechanical loads to evaluate whether a job could be called manual or not. Those classifications could for example be based on the articles author's opinion or on a consensus among rheumatologists and specialists in occupational medicine.

The choice of the study population was based on specific occupations in 8 studies. Those regarding dentists (three studies), cooks (one study), textile workers (one study) and cotton operatives (one study) based their choice on occupations requiring primarily hand/finger use. Foundry workers and miners were selected in two studies with the aim of investigate the prevalence of different forms of OA and of disc generative disease.

In almost all epidemiological studies the assessment of the exposure was based on subjective and retrospective information given by the workers, which presents the risk of recall and information bias. Only Hadler et al[35] used a task description based on extern observations from a consulting industrial engineer and ergonomist.

Regarding exposure to hand/arm vibration various studies suggest that wrist OA are not specific caused by vibration. Instead is likely to result from the strong dynamic and static joint loading (often in extreme positions of the joint) and repetitive movements typical for tool manipulation in any heavy labour. On the other hand exposure to vibration may induce additional articular load due to the increased need for joint stabilization and gripping forces.[53-55] Further investigations should take in account the great number of possible confounders and effect modifiers.

The fundamental reason why occupational exposure has been associated with OA is based on the theory affirming that the development of OA can be triggered by biomechanical factors producing joint overload.

Thus occupations promoting repetitive monotone movements would be the ideal model of joint overload predisposing to the development of OA. This pathophysiological theory is discussed below.

### **5.10 Pathophysiology**

The pathology of osteoarthritis involves the whole joint in a disease process that includes focal and progressive articular cartilage loss with concomitant changes in the bone underneath the cartilage, including development of marginal outgrowths, osteophytes, and increased thickness of the bony envelope (bony sclerosis). Soft-tissue structures in and around the joint are also affected. These structures include synovium, which may show modest inflammatory infiltrates; ligaments, which are often lax; and bridging muscle, which becomes weak.[18]

The association between intensive use of the same muscles or motions for a long duration promoting the development of hand OA, has been controversial.[30, 31, 56, 57] A beneficial effect of physical activity of moderate intensity on the strength of the muscles and ligaments has been suggested as a protective effect on joint OA. The results of the study by Rogers et al showed that moderate/high joint stress was associated with a reduced risk of hip/knee OA among women.[58]

On the other hand the findings of unusual patterns of involvement of hand OA among certain occupations, as discussed above, have supported the theory of biochemical stresses as aetiological factors.

This theory suggest that repetitive movements with relatively low muscle activity may not result in muscle tissue damage, whereas continuous overload of finger joints resulting from highly monotonous usage may lead to joint impairment.[25, 59]

The mechanism by which the possible deleterious effects of pressure and static positions are mediated to the joints might be a subtle interference with the nutrition of the articular cartilage. This probably requires pressure exerted on the cartilage by muscular contraction, given that arthrosis does not develop in paralyzed limbs despite of immobile positions, and that hands weakened by hemiplegia or peripheral nerve injury do not generate Heberden's nodes.[60, 61]

It is important to keep in focus that OA is a multi-factorial disease where non-mechanical factors as age, gender, metabolic and genetic factors and others mechanical factors as previous trauma play a role.

That is why some authors affirm that the development of OA depends on a generalized predisposition to the condition, and thus extern factors, as biomechanical stresses, more likely affects the localization of OA than the development of the disease itself. In another words a mechanical joint overload could accentuate a tendency toward development of OA in predisposed individuals, but will have little or none effect on those not predisposed.[62] But this assertion has not been elucidated yet, given various reports and studies showing the occurrence of OA among individuals without apparently predisposing factors.

For example Rossignol et al showed an early onset of OA among workers in heavy labour jobs, with almost 40% of patients reporting their first symptoms before the age of 50.[26] Lehto et al[33] also found higher prevalence of finger OA among dentists especially below the age 50 compared to controls from a population sample.

- **Osteoarthritis and gender**

In seven studies, the analyzed population included only men[34, 36, 39-43], and in five studies only women.[24, 25, 27, 32, 35] The articles, which studied only men, regarded occupations typically known for having male workers (grinding and chipping work, work with chain saws and pneumatic tools to quarry and slit granite blocks in stone pits, mining and metal industry). There is no clear reason why some studies included only female populations, given that the occupations analyzed are represented by both sexes (dentists, cotton workers, cooks and others)

Among the nine studies including men and women in the analyzed population[23, 26, 28-31, 33, 37, 38], two of them did not comment whether there was any difference in the prevalence or distribution of OA between these groups. In three studies the prevalence of OA was higher among women, where Rossignol et al found also that women presented higher prevalence of OA of multiple joints.[26, 29, 30] Only Lehto et al[33] reported higher prevalence of finger OA among male dentists compared with female dentists.

Three studies reported similar prevalence rates between men and women.[31, 37, 38] Though, more severe OA was found among women by Caspi et al, and higher prevalence of OA of multiple joints was found among women by Kellgren and Lawrence 58. None of these studies analyzed the reasons for the differences found between sexes.

It is relevant to investigate whether the differences in prevalence and distribution of hand OA among men and women could be explained by different biomechanical occupational exposures. It has been suggested for example that women preferably perform jobs requiring precision grip, and hereby are more exposed to overload of the DIP-joints. On the other hand it is not elucidated if men and women are exposed to different workloads within the same occupation. For example whether the stronger grip- and pinch-forces male dentists potentially exert, compared to female dentists, might be the reason why male dentists present higher prevalence of hand OA than female dentists as showed by Letho et al.[33]

### **5.11 Summary**

Osteoarthritis (OA) can be characterized as progressive articular cartilage loss with concomitant changes in the bone underneath the cartilage. It is the most common form of arthritis affecting millions of people worldwide. The prevalence of radiographically diagnosed hand OA increases steadily with age. Osteoarthritis of the hand is a major cause of impairment in performing activities of daily living. Thirty percent of all joints affected by OA are the joints of the hand.

The aetiology of primary arthrosis is multi-factorial and age, gender, metabolic and genetic factors, nutrition and biomechanical factors (such as muscle weakness, joint laxity, joint injury and repetitive strain) have been studied as risk factors.

The purpose of the present review was to evaluate the current evidence for causal relations between occupational exposures and the development of hand OA.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010).

The following studies presenting occupational factors in relation to hand OA were retrieved: 1 follow-up study, 2 case-control studies, 18 cross-sectional studies, and 7 case-reports.

Seventeen of the epidemiological studies analyzed biomechanical factors and occupations in relation to hand OA (including the 2 case-control studies), and 4 studies analyzed exposure to hand / arm vibration (including the follow-up study).

Regarding exposure to biomechanical factors, 12 studies – including four comprehensive large cross-sectional studies and one case-control study – reported a significant association with hand OA; while five studies – including a large comprehensive cross-sectional study – did not report any significant associations. When hand/arm vibration was the exposure analyzed, 1 cross-sectional study found a positive association with wrist OA, while 1 follow-up and 2 cross-sectional studies did not find any significant associations with hand and wrist OA.

Main limitations are crude or inadequate measures of exposure and large heterogeneity of analysed outcomes. Therefore it is hard to evaluate consistency across studies.

### **5.12 Conclusion**

We rate the overall evidence level of a causal association between finger OA and manual work as moderate (++) . A significant association between manual work and finger OA was found by 12 out of 17 independent studies including four large and comprehensive cross-sectional studies, where bias towards elevated risk seems less likely. A major concern in the cross-sectional studies is preferential drop-out of diseased workers among exposed, which will result in bias towards the null. Accordingly this type of bias may cause falsely negative studies and result in underestimation of risk in positive studies. Pronounced exposure misclassification is expected to cause bias in the same direction. On the other hand, retrospective collection of self-reported exposure information and inadequate confounding control may result in false positive findings. It is not possible in the single study or overall to evaluate the extent of these opposing types of bias.

The findings of specific clinical patterns of involvement of hand OA, which correlates to specific biomechanical workloads, provide a substantial support to the association.

On the other hand, we rated the level of evidence of a causal association between exposure to hand/arm vibration and hand OA as insufficient. The reason for that is the small number of studies on this issue (4 studies), with relatively few subjects analyzed, and with inconsistent results.

It is however undoubtedly that there is a lack of controlled studies with comprehensive and unbiased documentation of exposure as well as outcomes for both occupational exposures – manual work and hand/arm vibration.

It is a big challenge to elucidate the specific role of occupational exposures in the development of OA, given the large number of inherited and acquired factors, which have to be taken into account. But it is to expect that future controlled trials would make it possible.

Occupational joint overload of the hand is potentially an important aetiological factor contributing to the occurrence of OA in a sizeable segment of the population. Thus there is a need of further controlled studies focusing on precise exposures and well-defined populations.



## 6. NERVE COMPRESSION SYNDROMES

### 6.1 Introduction

Compression neuropathy refers to nerve damage from applied pressure of any source. Nerve compression syndromes of the upper extremity are characterized by compression of the ulnar, radial or median nerve along their course from the brachial plexus to the hand, resulting in clinical symptoms and/or electrophysiological changes.[63] [64] [65, 66] The term “entrapment” implies a mononeuropathy caused by pressure exerted by an anatomic or pathologic structure. All entrapment neuropathies are compression neuropathies, but not all compression neuropathies are caused by entrapment. A nerve may be compressed because of abnormal enlargement. A nerve of normal dimensions may be compressed from a narrowed space and the pressure can be externally or internally. The site of compression may be a static or dynamic structure, such as the pronator teres muscle. Compression neuropathies may develop acutely, as with tourniquet paralysis, or chronically. In the absence of trauma, the relation of the disorder to work or other activity has been suggested.[67] The present review aims to elucidate the available evidence of the association between occupational exposures and the development of nerve compressive syndromes, excluding carpal tunnel syndrome, given that this disorder has been reviewed prior in a similar paper.

### Ulnar nerve compressive syndromes

There are multiple potential areas of ulnar nerve entrapment or injury. The ulnar nerve passes between the medial border of the triceps and the intermuscular septum (arcade of Struthers) and may be compressed by the edge of the septum. The nerve passes posterior to the medial epicondyle and lies in the condylar groove. If the groove is shallow or the medial epicondyle is small, the ulnar nerve may sublux during elbow flexion, becoming hereby more vulnerable to trauma. Passing between the medial epicondyle and the olecranon the ulnar nerve enters the forearm between the heads of the flexor carpi ulnaris, which it innervates. The deep fascia forms a fibrous arcade that serve as the roof of a structures termed the cubital tunnel, which is another potential site of entrapment.[68] The ulnar nerve also innervates the medial head of flexor digitorum profundus muscle in the proximal forearm. The dorsal ulnar cutaneous sensory nerve arises from the ulnar trunk 5 – 6 cm proximal to the wrist and transmits sensation from the dorsoradial hand. In the palm, the ulnar nerve enters Guyon’s canal (the ulnar tunnel) between the pisiform and the hook of the hamate bones. Within the Guyon’s canal the superficial branch innervates the palmaris brevis muscle and supplies sensation to the fifth digit and the medial half of the fourth digit. The deep branch supplies the hypothenar muscles before exiting the ulnar tunnel to innervate the interossei, ulnar lumbricals, adductor pollicis, and deep head of flexor pollicis brevis muscles.

- **Ulnar neuropathy at the elbow (cubital tunnel syndrome)**

Ulnar neuropathy at the elbow (UNE) is the second most common upper extremity mononeuropathy, after only carpal tunnel syndrome.[55, 67] The mechanics of nerve injury likely include external compression, traction, or entrapment at the arcade of Struthers, condylar groove, or flexor carpi ulnaris. Space-occupying lesion, elbow deformity, arthritis, and peripheral neuropathy may predispose to UNE.[55, 69, 70]

Symptoms of UNE are commonly numbness and tingling in the little and ulnar half of the ring fingers, often accompanied by weakness of grip, particularly during activities for which torque is applied to a tool. Sensory involvement on the ulnar dorsal aspect of the hand also suggests UNE, as the dorsal cutaneous branch of the ulnar nerve originates proximal to the canal of Guyon. Atrophy of the ulnar intrinsic muscles of hand and clawing contracture of the ring and little fingers can be seen in advanced cases.[71] Important differential diagnoses for UNE are medial epicondylitis and nerve compressive syndromes from the neck or plexus brachialis.

Despite numerous reports describing the treatment of this disorder and its pathophysiology, its exact incidence and prevalence is still unknown. Mondelli et al 2005[72] reported an incidence of 24,7/100.000 person-year in a general population, and Descatha et[55] al found in a 3-year follow-up among industrial workers an estimated incidence of cubital tunnel syndrome of 0.8% per person-year. For a population exposed to repetitive and forceful movements, Pellieux et al 2001[73] estimated its annual incidence rate at 2.6%, based on claims for occupational diseases.

The prevalence of UNE reported in the literature varied from 2.8% among workers whose occupations required repetitive work to 6.8% in floor cleaners[55, 74]. Higher prevalence levels have been observed in

some studies or populations: 40% in a group of 69 musicians and 42.5% (subclinical ulnar nerve entrapment at the elbow) for 167 workers who used hand-operated vibrating tools.[75, 76]

Based mainly on surgical series, some risk factors have been identified. For example, male gender and fracture of the elbow predisposes the development of ulnar nerve compression at the elbow [77, 78]. However, most of the reported risk factors have not been the subject of epidemiological studies.[79]

- **Ulnar neuropathy at the wrist (Ulnar tunnel syndrome)**

Ulnar tunnel syndrome is compression of the ulnar nerve at the wrist (more specifically in the Guyon's canal) and may involve sensory or motor fibers or both. Shea and McClain[80] classified the ulnar tunnel syndrome into a pure motor, a pure sensory, or combined motor and sensory neuropathy.

The clinical presentation varies depending on the location of the lesion. Clinical findings that differentiate ulnar tunnel syndrome from UNE include normal sensation on the dorsum of the hand and normal strength of flexor carpi ulnaris and flexor digitorum profundus. Another important differential diagnose is carpal tunnel syndrome.

Ulnar compression at the wrist by ganglion cysts and other space-occupying lesions, tendovaginitis, occupational injuries, trauma, bicycling, and congenital anomalies has been described.

Modification of hand use with avoidance of pressure on the wrist or splinting is tried in cases in which no surgical lesion is found. [67, 81]

### **Median nerve compressive syndromes**

The most common form of all nerve entrapment syndromes is carpal tunnel syndrome, which consists in compression of the median nerve at the carpal tunnel at the wrist. According to Mysiew and Colacis 1991[82], median nerve compression is in more than 90% of these cases located at the carpal tunnel and less than 10% at the elbow level. This well-established syndrome is not included in this review that focus on more rare forms of entrapment of the median nerve known as pronator teres syndrome and anterior interosseous nerve entrapment.

Pronator teres syndrome consists in the compression of the median nerve in the forearm by or between the humeral and ulnar heads of the pronator teres muscle. [63, 67] The clinical manifestations include pain in the over the pronator muscle area worsened by forceful pronation, paresthesia of the 3 ½ radial fingers. The objective findings include weakness of flexor pollicis longus and the lateral thenar muscles with demonstrable atrophy in chronic cases. Usually there is no complaint of weakness of the grip or nocturnal exacerbation of pain or paresthesia, making a differential diagnose with carpal tunnel syndrome.

In the forearm the median nerve passes beneath the aponeurotic band of the biceps (lacertus fibrosus). The nerve enters the pronator teres muscle, where numerous fibrous bands may exist in the vicinity of the two heads of the muscle. The anterior interosseous nerve has its origin from the median nerve at this location. Leaving the pronator teres, the median nerve passes below the proximal edge of the flexor digitorum sublimis muscle. At the wrist the median nerve crosses into the palm through the carpal tunnel. The roof of this canal is the transverse ligament, and a concave arch of carpal bones constitutes the floor. [83]

Anterior interosseous nerve entrapment at the level of pronator teres or flexor digitorum sublimis muscles by fibrous bands, anomalies, or trauma (mainly fractures) also causes proximal forearm pain that increases with exercise. It may also occur spontaneously. Weakness of thumb and index flexion at the distal interphalangeal joints, demonstrated by abnormal pinch, is found in clinical examination. There is no sensory loss in the hand or weakness of the lateral thenar muscles, which differentiates this disorder from from pronator teres and carpal tunnel syndromes.

Neither the prevalence nor the incidence of pronator teres syndrome and of anterior interosseous nerve entrapment is known, given that the literature about these disorders presents only case reports and case series.

### **Radial nerve compressive syndromes**

Radial nerve compression is less common than median or ulnar nerve compression.

The main trunk of the radial nerve courses between the lateral and medial heads of the triceps then lies along the spiral groove of the humerus bone. The spiral groove is a potential site of radial nerve compression, known as high radial nerve compressive syndrome. Fractures of the humerus and external compression against the humerus in the spiral groove are the most common causes of high radial nerve compression. It may also result from compression by a tourniquet, from the use of crutches, and from allowing the arm of an anaesthetised patient to hang over the operation table. It may develop during sleep, especially when the patient is intoxicated ("saturday night palsy"). The nerve may also be damaged by deep intramuscular injection into the posterior or lateral aspects of the upper arm. Radial palsy after muscular effort is rare, but it has been reported.[84-87] The symptoms of high radial entrapment are characterized by loss of wrist and digital extension and sensory loss in the distribution of the superficial radial nerve. This can be clinically distinguished from posterior interosseous nerve entrapment, in which there is no sensory loss and no total loss of wrist extension.[88] Only case reports regarding high radial nerve entrapment are found in the literature, so its prevalence and incidence is still unknown, however it is considered a relatively rare entity.

After leaving the spiral groove in the humerus bone, the radial nerve runs anterior to the lateral epicondyle before supplying brachioradialis and extensor carpi radialis longus muscles. The main trunk then divides into a superficial sensory and terminal deep motor branch. The superficial sensory branch descends the radial aspect of the forearm and supplies the dorsal radial aspect of the hand. This trajectory is known as radial tunnel (from the radial head to the inferior border of the supinator muscle), therefore compression of the radial nerve at this site is by some authors called radial tunnel syndrome (RTS). The clinical manifestation of radial tunnel syndrome is forearm pain localized 3-5 cm distal to the lateral epicondyle worsened by resisted supination or middle finger extension. Paresis is not seen given that the entrapment affects the deep sensory branch of the radial nerve. The causes for RTS can be various including bands of fascia, the radial recurrent vessels, and the fibrous edge of the origin of the supinator that constitutes the Frohse arcade. Some observational studies of industrial workers or heavy manual workers suggested that some occupational factors, such as a cumulative trauma phenomenon, could predispose to RTS.[89-93] The main differential diagnosis is lateral epicondylitis. Very limited data is found regarding the prevalence of radial tunnel syndrome, mainly because of this entity is frequently confused with epicondylitis.[90] Werner [94] estimated the prevalence of RTS in 5% of cases of lateral epicondylitis (called by some authors by "resistant tennis elbow"). [93, 95]

The terminal motor branch of the radial nerve, the posterior interosseous nerve, passes through the supinator muscle and enters the extensor compartment where it supplies supinator, adductor pollicis longus, and all of the extensors of the forearm. The fibrous edge of the supinator, the arcade of Frohse, is a potential site of entrapment of the posterior interosseous nerve – condition known as posterior interosseous syndrome. Clinical manifestations include pain proximal in the forearm and weakness or paresis of the extensor muscles of the forearm. There is though normal function of the supinator and extensor carpi radialis longus muscles, which may lead to radial deviation of the wrist. There is no sensory loss. Surgery is indicated only if there is progression of motor loss or lack of response to activity modification and splinting.[67]

## 6.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Nerve compression syndromes
- Ulnar nerve
- Radial nerve
- Median nerve
- Pronator teres syndrome
- Occupational
- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]
- Occupational Health [Mesh]
- Occupational Groups [Mesh]

- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Hand-Arm Vibration Syndrome [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]
- NOT carpal tunnel syndrome [Mesh]

The diagnostic criteria for nerve compressive syndromes should be based on clinical and electrophysiological findings.

The electronic search retrieved 704 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 80 articles, which were considered relevant.

The articles presented the following designs: 49 reviews / background information, 4 analytic epidemiological studies (1 follow-up, 2 case-controls, 1 cross-sectionals), 27 other epidemiological studies and case reports. The studies are discussed below. Table 1 resumes the analytic epidemiologic studies. Tables 2, 3, and 4 present case reports and other epidemiological studies regarding ulnar, median and radial nerve compressive syndromes respectively. The studies are listed in the tables according to descending year of publication and alphabetic sequence.

### 6.3 Ulnar nerve compressive syndromes

- **Analytic epidemiological studies**

In a case-control study with 110 patients treated surgically for ulnar nerve compression at the elbow and 192 controls (patients with cervical or lumbar disc disease) Bartels and Verbeek 2007 [79] investigated the association between different risk factors and ulnar nerve compression at the elbow. The analyzed risk factors were gender, body mass index, smoking and alcohol consumption, occupation, level of education, previous fracture of or around the elbow, previous subluxation of the elbow joint, diabetes mellitus, hypothyroidism and hypertension. The only biomechanical occupational factor included was repetitive movement of arm during last job. Each occupation received a category number according to the British Standard Occupational Classification. The highest category numbers regarded heavy manual labour.

The number of the category was then multiplied by the length of time in years in that occupation and the sum of all these products was divided by the total time (in years) that a person had worked to indicate a categorical estimation of the total working history. Smoking (OR=2,94 95% CI 1,58-5,48), education level (OR=1,45 95% CI 1,16-1,81), total working experience (OR=1,25 95% CI 1,10-1,42) and heavy labour (OR=2,23 95% CI 1,31-3,80) were identified as risk factors for the development of ulnar nerve compression at the elbow. The fact that repetitive movement of the arm during work was not found as a risk factor (OR=1,1 95% CI 0,66-1,85) could be explained by a recall bias, where the patients could not precisely definite repetitive movements and recall the frequency of those.

The study is the first of its design, which analyzes different risk factors, including occupational history, in relation to nerve entrapment at the elbow. The main limitation of this study is the crude exposure assessment. Possible selection bias with exclusion of ulnar nerve compression with light symptoms, and incomplete survey response (87% of the cases and 74% of the controls) are other weaknesses that may be noticed.

Conlon and Rempel 2005 [96] designed a cross-sectional study with the aim of estimate the prevalence of mononeuropathy at the wrist among 202 engineers who use computers and identify associated risk factors. The evaluated outcomes were ulnar and median nerve entrapment at the wrist – the later being carpal tunnel syndrome. The analyzed factors age, gender, BMI, medication use, smoking status, physical activities, hours of computer use at work and private, typing speed, break time per day, duration of employment, and driving a car. The diagnoses were based on the presence of symptoms associated with abnormal electrophysiological studies. The prevalence of ulnar neuropathy at the wrist among

engineers was 1.8% (right hand), and 2.9% (left hand) – eight cases in total. The diagnoses ulnar neuropathy and carpal tunnel syndrome were considered together in the logistic regression analyses. Hours of computer use, BMI, and antihypertensive medication use revealed a positive association with the presence of the disorders (OR=6,53 95%CI 1,44-29,7; OR=1,11 95%CI 1,0-1,23; and OR=5,26 95%CI 1,28-21,8 respectively). Typing speed, driving hours per week, and total break time of 20 min per day present a negative association (OR=0,96 95%CI 0,93-0,98; OR=0,84 95%CI 0,73-0,96; and OR=0,57 95%CI 0,32-1,02 respectively). No analysis specifically for ulnar neuropathy was made.

The main strength of this study is the inclusion of several personal and occupational factors. But some limitations can be commented. The participants in the study presented higher rates of symptoms, comparing with the employees, who did not accept to participate in the study, resulting possible selection bias. And the self-reported assessment of exposure predisposed to information bias. Furthermore it is not explained in the study the reason for finding higher prevalence of neuropathy in the left hand compared to the right hand.

Descatha et al 2004[55] designed a 3-year-follow-up study with 598 workers from six different sectors to investigate the incidence of ulnar nerve entrapment at the elbow in repetitive work. The job sectors included were assembly line (packaging excluded), clothing and shoe industry (packaging excluded), food industry (packaging excluded), packaging and supermarket cashiering. The potential risk factors evaluated were: 1. Personal variables (age, gender, smoking, body mass index, leisure-time activities, presence of psychosomatic or depressive problems); 2. Occupational activity (sectors and number of years on the job); 3. Postures and biomechanical constraints (holding in position, turning and screwing, working with force, using elbows for support, holding a tool in position and using a vibrating tool); 4. Psychosocial work factors (job control and job satisfaction), and 5. Other work-related musculoskeletal disorders affecting the elbow or the ulnar nerve directly or indirectly. The found annual incidence was estimated at 0.8% per person-year, given that there were 15 new cases during the 3-year period. Holding a tool in position was the only biomechanical risk factor identified (OR=4.1, 95% CI 1.4–12.0). Obesity (OR=4.3, 95% CI 1.2–16.2) and the presence of medial epicondylitis, carpal tunnel syndrome, radial tunnel syndrome, and cervicobrachial neuralgia were also found as risk factors for ulnar nerve entrapment at the elbow. The associations with “holding a tool in position” and obesity were unchanged when the presence of other diagnoses was taken into account.

This is the first follow-up study investigating the incidence of ulnar nerve entrapment at the elbow in repetitive work. It is remarkable that a wide number of different potential risk factors were taken into account. But the study presents some limitations. Even though there were a large number of subjects in the study, the risk factors assessment was based on only 15 cases (new cases in the 3-year period). The diagnostic criteria for ulnar nerve entrapment at the elbow were exclusively clinical without confirmatory nerve conduction tests. The postures and biomechanical constraints had been self-assessed and many occupational health physicians were involved in the study, which may have induced information and observer bias. It was not clear what “holding in position” exactly involved, whether it should be an expression of static work for example.

- **Other epidemiological studies and case reports**

Hirata and Sakibara 2007 [97] performed sensory nerve conduction tests on 34 male workers diagnosed with hand/arm vibration syndrome compared to 23 controls. The aim of the study was to clarify the range of involvement for hand-arm vibration syndrome in the median, ulnar and radial nerves of the hand. Neuropathy types were classified by possible carpal tunnel syndrome (CTS), Guyon's syndrome and digital neuropathy. Guyon's syndrome was found in 26,5% of the cases versus 4,3% in the control group (P=0,03). Distal neuropathy of the radial nerve was found in 29,4% of the cases versus 4,3% in the control group (P=0,03). Multi focal neuropathy, defined in the study as a combination of CTS, Guyon's syndrome and digital neuropathy, was the most frequent disorder found in 52,9% of the cases and in 4,3% of the controls (P=0,000). They found no cases of cubital tunnel syndrome.

None analyses of the occupational exposures or of personal factors as possible confounders were made.

In a cross-sectional study with 21 male tennis players and 21 male controls, who did not perform any kind of regular sport activity, Colak et al 2004[98] analyzed the influence of regular and intense practice of an asymmetric sport such as tennis on nerves in the elbow region by nerve conduction studies. The groups were matched according to age, weight, height, and limb lengths. They found that the sensory and motor

conduction velocities of the radial nerve and the sensory conduction velocity of the ulnar nerve were significantly delayed in the dominant arms of tennis players compared with their non-dominant arms and normal subjects ( $P < 0,05$ ). There were no statistical differences in the latencies, conduction velocities, or amplitudes of the median motor and sensory nerves between controls and tennis players in either the dominant or non-dominant arms. None analyses of other potential risk factors between the groups were made.

This study is the first published analyzing asymptomatic tennis players with nerve conduction studies. Some limitations in the study can be cited. There was no information about whether other personal factors were taken into account as possible confounders, such as prior traumas and comorbidities. Although reaching statistical significance between the two groups, nerve conduction values for tennis players were within the normal range.

Ruess et al 2003[99] reported the findings of musculoskeletal disorders among 12 radiologists in relation to computer use in their work activities. Time working as staff, workday hours, and academic activities were recorded. Nonoccupational activities were also noted. An industrial hygienist evaluated the department work areas and staff offices. Three radiologists were diagnosed with cubital tunnel syndrome and one with carpal tunnel syndrome. Comparing these 4 cases with the others 8 radiologists, it was found that they had significantly greater workday hours ( $P < 0.05$ ) and performed more research ( $P < 0.003$ ) than the asymptomatic radiologists.

None analyses of the occupational exposures or of personal factors as possible confounders were made.

Patterson et al 2003 [100]described a cross-sectional study with 25 road or mountain bike riders before and after a 600-km bicycle ride with the aim of identify cases of ulnar and median nerve neuropathies at the wrist (the latter meaning carpal tunnel syndrome). The cases were determined based on symptoms and clinical examination, no electrophysiological tests were performed. Twenty-three of the 25 cyclists experienced either motor or sensory symptoms, or both. No statistical significant differences were found between the groups of road and mountain bike riders. No analyses on biomechanical exposures were made.

Kákósy 1994 [76]studied the prevalence of thoracic outlet syndrome and cubital tunnel syndrome among 167 workers exposed to hand/arm vibration. The occupations included motor sawyers, chipping and grinding workers, rock drill operators, grinders and operators of other vibrating tools. They found one of the referred compressive syndromes in 30% of the examined workers, while diffuse peripheral neuropathy was seen in 22%. Those results suggest that focal lesions of the peripheral nerve are more common than diffuse neuropathy.

None analyses of the occupational exposures or of personal factors as possible confounders were made.

It was retrieved 15 case reports on ulnar nerve entrapment at the wrist or at the elbow, which referred to the patients occupations. Those reports regarded the following activities: byciclism, kitchen chef, computer use, autovehicle driving, secretary job, rope fabric, video game playing, meat packing.

#### **6.4 Median nerve compressive syndromes**

- **Analytic epidemiological studies**

None was found.

- **Other epidemiological studies and case reports**

The results of Colak et al 2004[98], which are commented above included also median nerve neuropathy.

Stål et al 1998[101] performed a cross-sectional study with 30 female machine milkers in Sweden, who presented persistent symptoms (for a period of one year) from the upper extremity. They found a surprisingly high prevalence of pronator syndrome, 23 cases out of 30 examined individuals. The total sample of workers, where the cases were taken from was 201, resulting 11,4% of the workers presenting with pronator teres disorder. Given that the diagnostic criteria were symptoms and physical examination

the pertinent question is, whether it was made the correct diagnosis. Some ergonomic aspects of the machine milking work were discussed, but no assessment of exposures was made.

Only one case report on pronator teres syndrome referring the patients occupations was found. The reported activities were: heavy manual labor, baseball and musical instrument playing. [102]

## 6.5 Radial nerve compressive syndromes

- **Analytic epidemiological studies**

In a case-control study with 21 blue-collar workers previously diagnosed with radial tunnel syndrome and 21 controls (matched for gender, age and plant) Roquelaure et al 2000 [89] investigated occupational risk factors for radial tunnel syndrome. The workers were from three different plants, where television sets, shoes and automobile brakes were manufactured. The diagnosis of radial tunnel syndrome was established based on review of all employees' medical files. The cases were defined if the medical files included the following conditions: forearm pain along the radial nerve in front of the radial head, 3 to 5 cm distal to the lateral epicondyle; positive "middle finger test" (ie, pain elicited in the region of the common extensor origin by extension of the middle finger extended elbow) or positive "resisted forearm supination test"; positive results of a neurophysiological examination; or surgical release of the radial nerve. The assessed data were medical history (body mass index, hand dominance, smoking habits, alcohol consumption, use of analgesics, history of pregnancy, menopause, gynaecological surgery and oral contraceptives use), non-occupational activities (education level, marital situation, household chores, playing of musical instruments and physical exercise) and occupational activities (type of work, length of employment and duration of previous manual work). A job-site work analysis including type and posture of hand and elbow movements – e.g. repetitive, precise, forceful, static –, type of tools used, work cadence, and work hours and breaks was performed by direct observation by two specially trained assessors unaware of the medical status of the workers. It was found 3 occupational risk factors for radial tunnel syndrome (RTS). Exertion of force of over 1 kg more than 10 times per hour was the main biomechanical risk factor (OR=9.1, 95% CI 1.4-56.9). Prolonged static load applied to the hand during work (OR=5.9, 95% CI 1.2-29.9) and work posture with the elbow fully extended (OR=4.9, 95% CI 1.0-25.0) were also associated with RTS. Personal factors and activities, such as household chores, sport and leisure activities were not associated with RTS.

This is the only published article to date analysing occupational risk factors for RTS. The main strength of the study is the detailed objective exposure assessment. The main limitation is the small number of participants.

- **Other epidemiological studies and case reports**

The results of Colak et al 2004[98], which are commented under ulnar nerve compressive syndrome included also radial nerve neuropathy.

It was retrieved 5 case reports on radial nerve entrapment referring the patient's occupations. The reported activities were: heavy manual labor, tennis playing and kitchen chef.[84-87, 103]

**Table 6.6 – Analytic epidemiological studies on nerve compression syndromes in relation to occupational exposures**

yrs = years; m = men; w = women; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women; CI = confidence interval

Reference	Population	Design	Relevant exposure	Outcome	Diagnostic criteria	Selected results – risk estimate referred when possible (95% CI)
Bartels and Verbeek 2007 [79] Netherlands	n=302 (110 cases, 192 controls) Mean age: 50 yrs	Case-control	Total work experience Heavy manual work Repetitive movement of the arm during last job Lower or none education	Ulnar nerve compression at the elbow	Clinical and electrophysiological examination	Total work experience: OR=1,25 (1,10-1,42) Heavy manual work OR=2,23 (1,31-3,80) Repetitive movements: OR=1,1 (0,66-1,85) Lower or none education OR=1,45 (1,16-1,81)
Conlon and Rempel 2005[96] USA	n=202 engineers Mean age: 42 yrs	Cross-sectional	Hours of computer use Years of work with computer Typing speed Break time per day Driving a car	Ulnar nerve entrapment at the wrist and carpal tunnel syndrome	Questionnaire and electrophysiological examination	Hours of computer use: OR=6,53 (1,44-29,7)
Descatha et al 2004[55] France	n=598 workers (178 m, 420 w) Age: <30 - >50 yrs	Follow-up	holding in position turning and screwing working with force using elbows for support holding a tool in position repetitively using a vibrating tool)	Ulnar nerve entrapment at the elbow	Clinical examination	OR = 4.11 (1.38–12.23) for 3-year incidence statistically significant only for holding a tool in position repetitively.  Values for the others parameters not referred in the article
Roquelaure et al 2000[89]	n=42 workers (21	Case-control	exertion of force of >	Radial tunnel syndrome	Clinical and electrophysio-	Exertion of force:



France	cases, 21 controls) Age: 18-59 yrs		1kg more than 10 times per hour static work of the hand (pinching or squeezing objects or tools) working with the elbow fully extended		logical examination	OR=9,1 (1,4-56,9) Static work: OR=5,9 (1,2-29,9) Elbow extended: OR=4,9 (1,0-25,0)
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**Table 6.7 – Other epidemiological studies and case reports on ulnar nerve compressive syndromes in relation to occupational exposures**

yrs = years; m = men; w = women

Reference	Population	Exposure	Outcome	Diagnostic criteria
Krishnan et al 2009[103] Australia	n=1 male chef Age: 29 yrs	Whisking and chopping food for many hours	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Black et al 2007[104] USA	n=1 female bicyclist Age: 29 yrs	80-miles bike ride	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Hirata and Sakibara 2007[97] Japan	n=34 male workers diagnosed with hand/arm vibration	Work with vibrating tools for around 27 years	Guyon's syndrome, carpal tunnel syndrome, and digital neuropathy (involving ulnar, radial or median nerve)	Clinical and electrophysiological examination
Colak et al 2004[98] Turkey	n=42 men (21 tennis players, 21 controls) Mean age: 27 yrs	Regular and intense tennis practice	Ulnar, median and radial nerve entrapment at the elbow	Clinical and electrophysiological examination
Kalainov 2003[105] USA	n=1 male bicyclist Age: 41 yrs	One week-long mountain bicycling tour	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Liguori et al 2003 [106] Italy	n=5 computer users (1 woman, 4 men)	Compression of the proximal hypothenar eminence while using a computer mouse and keyboard for several months	Palmaris brevis spasm syndrome - lesion at the superficial branch of the ulnar nerve at the wrist	Clinical and electrophysiological examination
Patterson 2003 [100] USA	n=25 bicyclists (13 men, 12 women) Mean age: 33 yrs	600-km bicycle ride	Ulnar nerve compression at the wrist	Clinical examination
Ruess et al 2003[99] USA	n=12 radiologists	Computer use	Cubital tunnel syndrome and carpal tunnel syndrome	Clinical examination
Capitani and Beer 2002[107] Switzerland	n=3 male bicyclists Age: 38, 41, 49 yrs	Extension of the wrist with compression of the ulnar palm against the corner of the bicycles handlebar while cycling	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Kákósy 1994[76] Italy	n=167 workers exposed to hand/arm vibration	motor sawyers chipping and grinding workers rock drill operators grinders and operators of other vibrating tools	Thoracic outlet syndrome and cubital tunnel syndrome	Clinical and electrophysiological examination
Deleu 1992[108]	n=2 male computer users	Intermittently compression of the	Ulnar nerve compression distal to	Clinical and electrophysiological

Belgium	Age: 23, 34 yrs	region proximal to the wrist crease of while using a computer mouse for almost one year	the wrist	examination
Abdel-Salam et al 1991[109] UK	n=3 male vehicle drivers Age: 36, 44, 45 yrs	Resting on the elbow while driving	Ulnar nerve compression at the elbow	Clinical and electrophysiological examination
Davie et al 1991[110] UK	n=1 male computer user Age: 33 yrs	Pressure on the extended wrist and hypothenar eminence while using a computer mouse for several hours daily for five months	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Maimaris and Zadeh 1990[111] UK	n=2 male bicyclists Age: 24, 47 yrs	Cycling 120 and 80 miles	Ulnar nerve entrapment at the wrist	Clinical examination
Streib 1990 USA[112]	n=1 female secretary Age. 48 yrs	Writing or typing for several hours	Ulnar nerve compression at the wrist	Clinical and electrophysiological examination
Chew 1988 [113] New Zealand	n=1 male ropemaker Age: 24 yrs	Tightening up a rope and twinning it round the right forearm under considerable tension repeatedly for seven months	Ulnar nerve entrapment at the wrist	Not mentioned in the article
Friedland 1984 UK[114]	n= 1 male video game player Age: 28 yrs	Playing video-game 4-6 hours a day for 1 month	Ulnar nerve entrapment at the wrist	Clinical and electrophysiological examination
Streib and Sun 1984[115] USA	n=3 male meat packers Age: 24, 24, 39 yrs	Tight handgrip around the knife handle during deboning meat several hours per day	Ulnar nerve entrapment at the wrist	Clinical and electrophysiological examination
Noth et al 1980 Germany[116]	n=4 bicyclists (1 woman, 3 men) Age: 23, 24, 24, 26 yrs	Pressure on the ulnar side of the hand while cycling for several days	Ulnar nerve entrapment at the wrist	Clinical examination (electrophysiological studies in two cases)
Eckman 1975 USA[117]	n=3 bicyclists (data from only one case: male, 22 yrs)	Cycling 3000 miles in 30 days	Ulnar nerve entrapment at the wrist	Clinical and electrophysiological examination

**Table 6.8 – Other epidemiological studies and case reports on median nerve compressive syndromes in relation to occupational exposures**

yrs = years; m = men; w = women

<b>Reference</b>	<b>Population</b>	<b>Exposure</b>	<b>Outcome</b>	<b>Diagnostic criteria</b>
Stål et al 1998[101] Sweden	n=23 female machine milkers Mean age: 45 yrs	Holding a 2-3,5 kg milking cluster with dorsal flexed wrist, supinated forearm and few degrees flexed elbow repetitively while machine milking for around 20 years	Pronator teres syndrome (associated with ulnar nerve entrapment at the elbow in 2 cases and at the wrist   1 case)	Clinical examination
Morris and Peters[102] 1976 USA	n=7 male workers Age: 27-70 yrs	Heavy manual labour requiring forceful pronation and finger flexion (shoveler, woodworker, mechanic, baseball pitcher, fiddler, barber)	Pronator teres syndrome	Clinical and electrophysiological examination

**Table 6.9 – Other epidemiological studies and case reports on radial nerve compressive syndromes in relation to occupational exposures**

yrs = years; m = men; w = women

<b>Reference</b>	<b>Population</b>	<b>Exposure</b>	<b>Outcome</b>	<b>Diagnostic criteria</b>
Krishnan et al 2009 Australia[103]	n=1 female chef Age: 38 yrs	Whisking and chopping food for many hours	Radial tunnel syndrome	Clinical and electrophysiological examination
Prochaska et al 1993[86] USA	n=1 male tennis player	Intensive tennis training session for several hours.	High radial nerve entrapment	Clinical and electrophysiological examination
Streib 1992[85] USA	n=3 male workers Age: 38, 34, 27 yrs	Heavy continuous work with arm for many hours followed by a sudden forceful contraction and stretch of the arm muscles (lineman, factory worker, truck driver)	High radial nerve entrapment (associated with pronator teres syndrome in one case)	Clinical and electrophysiological examination
Mistunaga and Nakano 1988[84] USA	n=1 men Age: 20 years	Strenuous muscular activity (painting, lifting 50-pounds paint buckets repetitively, moving heavy wood and lifting and automobile motor and shell while painting the body)	High radial nerve palsy unilateral	Clinical and electrophysiological examination
Lotem et al 1971[87] Israel	n=3 male workers Age: 40, 45, 49 years	loading a truck with 50-kg pipes pushing a heavy container a few meters performing extension exercises of the elbow against weights	High radial nerve palsy unilateral	Clinical and electrophysiological examination

## 6.10 Discussion

### Design

The present review retrieved 4 analytic epidemiological studies – 1 follow-up, 2 case-controls and 1 cross-sectional. Information bias (from self-reported exposure assessment) and / or selection bias (incomplete survey response, selection based on symptoms, inclusion of suspected cases) were found in all studies. Given the relative rare incidence / prevalence of some nerve compression syndromes, the studies presented small number of participants. For example, the only follow-up study based their results in only 15 cases.

Not all epidemiological studies took personal factor into account as possible confounders.

The other studies included in this review were mainly descriptive epidemiological studies and case reports / series, which have a limited epidemiological relevance.

### Diagnostic criteria

Among the epidemiological studies two based the diagnoses of nerve compression syndromes only on the clinical examination, i.e. without confirming electrophysiological studies, including the only follow-up study.

The appropriate diagnose of nerve compression syndromes should be based on a complete assessment of symptoms, a detailed neurological clinical examination and on confirming electrophysiological studies. Well-established diagnostic criteria are essential to provide a possibility of comparison among different epidemiological studies.

### Outcome

Regarding the analytic epidemiological studies ulnar nerve entrapment at the elbow was the aim of two studies, ulnar nerve entrapment at the wrist (and carpal tunnel syndrome) of one, and radial tunnel syndrome of one. Most of the case reports / series regarded ulnar nerve entrapment at the wrist.

One case-control study and one case report were about radial tunnel syndrome. High radial entrapment was the issue of 4 case reports. Pronator teres syndrome was mentioned only in one cross-sectional study and one case report.

The diversity of outcomes makes a comparison among the studies impossible.

### Exposure

A large heterogeneity was observed in the assessment of exposure to physical risk factors. None of the included articles used the same definition to determine exposure to force, repetitiveness, hand–arm vibration or awkward posture. Besides, most of the studies used questionnaires or interviews only to determine magnitude, frequency or duration of exposure.

- **Biomechanical factors**

The association of nerve entrapment and occupational exposure is probably due to the fact that the proposed physiopathology is based on strain of the nerves. It is then to expect that occupations requiring repetitive movements, producing hereby motion and strain of the nerves, would result in higher prevalence of nerve entrapment, giving the opportunity to analyze those relative rare syndromes in larger samples.

There are several reports of apparently higher rates of nerve compression syndromes among certain occupations. For example regarding UNE, prevalence rates varied from 6.8% among floor cleaners [mondelli 06] to 40% in some group of musicians.[75] Lederman 2006[118] commented on his review of focal peripheral neuropathies in instrumental musicians that there is no sufficient evidence to suggest that instrumentalists are at higher risk of developing focal neuropathies than anyone else, although there are some specific disorders that appear to be related directly to the playing position or the manner in which the instrument is held[119].

Diverse exposures related to work activities has been suggested as possible risk factors for the development of nerve compression syndromes. As Bozentka [120] mentioned in his physiological study of this disorder, epidemiologic studies of occupational ulnar nerve entrapment at the elbow are rare. Most of the occupational studies are case reports in specific occupations or industrial sectors.[76, 100, 109, 121, 122] Most of them do not include an assessment of exposure to biomechanical factors.[55] Some studies though analyzed biomechanical factors.

A new danish (unpublished study) included 726 cases of patients diagnosed with ulnar neuropathy 2001-2007 and 1909 community referents. A job exposure matrix comprising 169 job groups with quantitative exposure estimates obtained by averaging five experts' ratings was constructed. Repetitive but not forceful work showed an odds ratio 1.3 95% CI 1.2-3.2; non-repetitive, but forceful work showed an odds ratio 1.9 95% CI 1.2-3.2; and repetitive and forceful work showed an odds ratio 2.0 95% CI 1.2-3.1. Results were adjusted for fractures, smoking, alcohol consumption, and BMI (Svendson SW et al., PREMUS 2010). These results support a causal relationship between work strain and ulnar neuropathy.

According to Roquelaure et al 2000[89], repetitive exertion of force, prolonged static load applied to the hand and work posture with full extension of the elbow (particularly with twisted posture of the forearm) were risk factors for the development of radial tunnel syndrome. This is in agreement with previous clinical studies showing the occurrence of RTS in manual workers performing repetitive tasks and forceful forearm pronation and elbow flexion or extension.[90, 92, 93]

In a review by Pilgian et al 2000[71] some work-related risk factors were mentioned and appeared to be common to cubital tunnel syndrome: repetitive and sudden elbow flexion, and repeated trauma or pressure to the elbow at the ulnar groove. However, no quantitative information from this review is available.[123]

In the results of the follow-up study of Descatha et al it was found that "holding a tool in position" was the main risk factor to the development of UNE. This biomechanical factor had not been mentioned in other studies on ulnar nerve entrapment at the elbow, but it was found in those that focused more on the role of vibration, than on the repetitive use of tools. In their study "exposure to vibrating tools" was restricted to hand-held tools, and "holding a tool in position" seemed to be more important for UNE than exposure to vibration issued from a sewing machine (which is met by almost all the workers in the clothing and shoe industries). The three incident cases in the shoe industry had to hold a tool in position, repeatedly, in addition to using a sewing machine. In bivariate analyses, there was also a positive association with "using elbows for support". Many authors have reported that elbow flexion and extension are involved in the occurrence of ulnar nerve entrapment at the elbow.[120, 124, 125] .

Colak et al[98] demonstrated that the sensory and motor conduction velocities of the radial and ulnar nerve were significantly delayed in the dominant arms of tennis players compared with their non-dominant arms and with control subjects. They suggest that repetitive motion and overload of wrist and elbow are the major factors contributing to these findings among tennis players.

Regarding pronator teres syndrome, Stål 1998[101] proposed that the concentration of muscle tension around the elbow during milking is probably considerable because the biceps and brachialis muscles are contracted in this working position and, furthermore, the pronator muscle is stretched. In this position, the median nerve could probably become entrapped.

The evidence for the associations mentioned above is primarily based on results presented in cross-sectional studies, therefore the causality of the reported associations between exposure and the occurrence of one of the specific disorders is debatable. Some of these mechanisms proposed above are supported by anatomic studies and are discussed below under physiopathology.

- **Hand/arm vibration**

The exposure to hand/arm vibration in relation to nerve compressive syndromes was the aim of two studies. The results of Kákósy[76], who study cubital tunnel and thoracic outlet syndromes, suggested that the neuropathy observed among exposed workers were more frequently focal (i.e. compressive syndromes) than diffuse. Hirata and Sakibara[97], who study dysfunctions of ulnar, radial and median nerves, found contrary results in their study, suggesting that diffuse neuropathy is the main effect of exposure to hand/arm vibration. This issue has been indirectly discussed in other reports, but at the moment there is no consensus on this issue.[126, 127] In another words, it is not clear whether the neurological alteration of hand/arm vibration syndrome are due to a direct effect of vibration on the nerves or to secondary nerve entrapment, caused by for example wrist or elbow deformities.

## 6.11 Pathophysiology

Nerves of the upper extremity have considerable mobility throughout their length, however their “tunnels” are narrow spaces in close relation to the surrounding tissues. Compression by adjacent structures may tether a nerve and restrict its mobility, thereby causing stretching in response to joint motion.[63]

Tension, motion, and friction are all known to be etiologic factors in compressive neuropathies, but their exact roles have not been elucidated. The effect of motion and tension on nerve conduction, blood flow, and histology has been studied in animal and human models.[69]

Wright et al 2001 [69] performed a biomechanical study with fresh-frozen transthoracic cadaveric specimens to establish the relationship between ulnar nerve excursion at the wrist and elbow and the movement of the shoulder, elbow, wrist, and fingers. Their results indicated that the ulnar nerve glides proximally and distally with upper extremity movement both at the wrist and elbow in the normal individual. They found that the ulnar nerve requires over 2 cm of unimpeded movement both at the elbow and wrist to perform full motions of the upper extremity involving the shoulder, elbow, wrist, and fingers. If this normal nerve excursion is obstructed, increased mechanical forces (strain) can occur across the portion of tethered nerve. This increase in strain may cause direct mechanical damage to the nerve or injury may result from ischemia, which likely occurs when a particular nerve experiences strain values more than 15%

These anatomical and physiological parameters are the base for the proposed theories about occupational exposure to repetitive motion and overload of wrist and elbow and the development of nerve compressive syndromes. Some theories are presented below. Those theories are mainly based on case series and descriptive epidemiological surveys, reason why they may be viewed critically.

Roles et al 1972[90] proposed that repeated forceful movements of the elbow (markedly pronation and extension of the elbow) tighten the fibrous edge of diverse muscles, which can become firm fibrous bands capable of marked nerve constriction. This process can cause a generalised rise in tissue tension with oedema of the paraneural tissue, resulting in focal ischaemia of the underlying nerve.

Regarding pronator teres syndrome, hypertrophy of the pronator muscle resulting from repeated pronation movements has been suggested as contributing to compression of the median nerve through this muscle. As the muscle repeatedly contracts, the flexor digitorum sublimis muscle's edge tautens, causing further trauma to the nerve.[128]

Given the superficial position of the ulnar nerve, it is vulnerable to external compression at the elbow and at the wrist. Examples of such situations have been seen among workers leaning on the elbows and compression of bicycle's handlebar during long rides. Various activities involving alternated supination-pronation motions and extension of the elbow have been implicated in the presence of ulnar nerve entrapment. [128]

In their study with tennis players Colak et al 2004[98] suggested that forceful repetitive movements of musculotendinous compartments of the forearm may cause fascial thickening, resulting in stretching or impingement of the surrounding nerve. Besides, as showed by clinical studies, the throwing motion and elbow flexion, which are repetitively performed by tennis players, increases cubital tunnel pressures around the elbow. Ulnar nerve traction and excursion occurs because the course of the nerve is behind the axis of rotation of the elbow (fact that could explain the absence of abnormality of the elbow joint itself and history of injury among patients suffering of UNE). This excursion and traction forces are further increased when the shoulder is placed in abduction and the wrist in extension, and in situations involving valgus forces, as in throwing.[69, 120]

It is important to keep in mind that nerve compression may also be produced by space-occupying lesions (such as tumors, cysts, inflammatory processes), systemic diseases, and by post-traumatic conditions. The mechanisms involved in those situations are discussed in other relevant papers.

- **Personal risk factors**

The role of demographic parameters such as age, gender and other personal risk factors in the development of nerve compressive syndromes is not totally elucidated.



Male gender has been suggested as predisposing to the development of ulnar nerve compression at the elbow.[77, 78] However, most of the reported risk factors have not been the subject of epidemiological studies.[79]

Smoking has been found as a risk factor for the development of ulnar nerve compression in some reports. The biological substrate for that is unclear and there is no evidence of a dose – response relationship. Nevertheless, it is possible that the effects of smoking on the microvasculature may reduce the likelihood of recovery in a damaged nerve. Alternatively, it may be postulated that the repetitive movement involved with smoking (flexing and extending the elbow) may predispose to nerve compression. However, smoking hand dominance is not correlated with the side on which surgery is performed, nor the amount of cigarettes smoked daily.[129]

Regular alcoholic consumption does not seem to be a risk factor as previously reported. [129] The association observed between obesity and ulnar nerve entrapment at the elbow, on the results of Descatha et al[55], can be explained by mechanisms similar to those involved in carpal tunnel syndrome, dealing with the increase of fat and edema in the cubital tunnel. The same study found an association between ulnar nerve entrapment at the elbow with other work-related musculoskeletal disorders, especially medial epicondylitis and carpal tunnel syndrome. This suggests that workers with one work-related musculoskeletal disorder have an increased risk for others, especially if there are common occupational risk factors involved.

Other causes for nerve compression suggested in the literature include hormonal alterations and systemic diseases, such as pregnancy, oral contraceptive ingestion, diabetes mellitus, and hypothyroidism. [130]

## **6.12 Summary**

Compression neuropathy refers to nerve damage from applied pressure of any source. Nerve compression syndromes of the upper extremity include compression of the ulnar, radial or median nerve along their course from the brachial plexus to the hand, resulting in clinical symptoms and/or electrophysiological changes. In the absence of trauma, the relation of the disorder to work or other activity has been suggested. The purpose of the present review was to evaluate the current evidence for a causal relation between occupational exposures and the development of nerve compressive syndromes, excluding carpal tunnel syndrome, given that disorder has been reviewed prior in a similar paper[8].

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). It was retrieved 4 analytic epidemiological studies (1 follow-up, 2 case-controls, 1 cross-sectional), 27 descriptive epidemiological studies and case reports.

Three of the analytic epidemiological studies addressed ulnar compression syndrome (1 follow-up, 1 case-control, 1 cross-sectional) and one radial compression syndrome (case-control). All four studies presented biomechanical factors as the occupational exposure, and found a positive association between the outcome and some or all the risk factors analyzed. Exposure to hand / arm vibration was studied by two descriptive studies, one analyzed cubital tunnel and outlet syndrome, and the other dysfunctions of ulnar, radial and median nerves.

## **6.13 Conclusion**

The present review aimed to present the current evidence for a possible association between occupational exposure and the development of ulnar, radial and median nerve compressive syndromes (excluded carpal tunnel syndrome). It was found a wide heterogeneity of case reports / series and descriptive studies, but only four analytic epidemiological studies, which presented different outcomes, diagnostic criteria and exposure assessments. All studies presented critical information and / or selection bias, which limit their epidemiological relevance. As a result the present level of evidence of a causal relation between nerve compressive syndromes and manual work is considered limited (+), while the level of evidence for a causal relation with exposure to hand/arm vibration is insufficient (0).

## 7. DUPUYTREN'S CONTRACTURE

### 7.1 Introduction

Dupuytren's contracture (DC) is characterized by thickening and contracture of fibrous bands of the palmar fascia (aponeurosis) resulting in progressive flexion of the fingers. First described by Guillaume Dupuytren, a French surgeon, in 1831 the disorder is also called Dupuytren's disease, *maladie de Dupuytren* and palmar fibromatosis.[131]

The condition is more frequent in males than females, and the prevalence increases with age, reaching 10-20% or higher among males, and 5% or higher among females in the 60<sup>th</sup> decade.[132, 133]The male / female ratio varies with age being of 8,4 in the age of 40-44 years and 2,7 in the age of 70-74 years. [133] Recent studies on the pathogenesis of DC suggested that the male predominance is related to the expression of androgen receptors in Dupuytren's fascia rather than genetics.[134]

Geographical differences have been reported, with the prevalence thought to be higher in places such as Scandinavia, the Netherlands, United Kingdom, and Australia than in Mediterranean areas, Africa, and the Orient; however, reports on DC in Japan have shown similar prevalences. [135] Most investigators today agree that genes only predispose the individual to the development of the disease rather than directly causing it. [134]

It is frequently bilateral; when unilateral, it has been more frequent in the right than left hand in some but not all series. In some cases changes similar to DC may be found in other parts of the body, including the feet (contracture plantar aponeurosis), the penis (Peyronie's disease), and knuckle changes on the extensor side of the hand (knuckle pads). [135]

The clinical picture includes nodules (which are usually central to the diagnosis), thickening or retraction of the skin, cords, and bands in the palmar side and, finally, joint contracture of the fingers. The ring finger has been most frequently affected in many series, followed by the little finger. The condition may be asymptomatic, even after contracture has developed, while others may complain of aching, tingling, or difficulty grasping objects; some eventually require surgery to the contracture for relief of symptoms or improved function. There is little confusion in recognizing advanced cases of DC, but the early signs challenge even the most experienced observer to distinguish between DK and the normal hand in which thick skin or prominent fascia are seen. [135]

Although one of the earliest references to the relation between DC and occupational activities dates back to its first description, its etiology remains unknown today and the role of occupational exposure is still debated.[136, 137]

Increased incidence of Dupuytren's disease has been seen in relation to alcohol abuse. Epilepsy / use of anti-convulsant drugs is also often linked to Dupuytren's disease, with the incidence in epileptics as high as 56 percent.[134] There are also links to diabetes mellitus and smoking.[138] The higher prevalence in diabetics is often believed to be related to the microangiopathy and increased collagen production that is present in these cases. It is interesting that diabetics also have increased rates of flexor tenosynovitis and carpal tunnel syndrome, other common "inflammatory" or "proliferative" processes in the hand.[137] Dupuytren's disease has been reported to be three times higher in smokers, which may be related to the microvascular changes in the hand that occur with smoking.[134, 138] Rheumatoid arthritis is the only condition that has been associated with a lower incidence of Dupuytren's disease.[137] The physiopathology of DC is further discussed below.

The aim of this review is to present the current evidence for a relationship between occupational exposures and the development of Dupuytren's contracture.

### 7.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Dupuytren contracture
- Dupuytren disease
- Occupational

- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]
- Occupational Health [Mesh]
- Occupational Groups [Mesh]
- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Hand-Arm Vibration Syndrome [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]

The diagnostic criteria for Dupuytren contracture were based on clinical findings of thickening with or without contractures of the palmar fascia.

The electronic search retrieved 982 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 24 articles, which were considered relevant.

The articles presented the following designs: 17 reviews / background information, and 7 cross-sectional studies. These studies are discussed below and presented in table 1. The studies are listed according to descending year of publication and alphabetic sequence both in the text and in the tables.

Lucas *et al* 2008[132] studied the relation between DC and personal factors and occupational exposure in a cross-sectional survey with 2.406 male civil servants employed at the Equipment Ministry in France in 1998. Less than 5% refused to be included in the study. Case subjects, that is, those diagnosed with Dupuytren's disease, were older on average than subjects with no signs of DC (50.7 years versus 44.8 years;  $P < 0.0001$ ).

Structured interview was used to obtain subjects' age and biomechanical exposure and medical history. The occupational biomechanical exposures included were: using a tool with handle, using a vibrating tool, manual handling, and repairing mechanical equipment. A score for each exposure was constructed to estimate the total duration of lifetime occupational exposure, expressed in months. The number of years worked was multiplied by an estimate of average annual frequency. The total exposure score was the sum of the four lifetime scores, one for each defined task. The occupational exposure was defined as low, intermediate, and high level of exposure. Diagnostic criteria for DC were clinical signs of thickening of the palmar fascia and/or flexion contracture in phalanx 2, 3, 4, or 5. Dupuytren's disease was diagnosed in 212 men (8.8%). The occupational exposure score was significantly higher in this group of cases than in the rest of the sample ( $P < 0.0001$ ). Occupational exposure was associated with DC (adjusted OR=2.20 95% CI 1.39–3.45 for the intermediate and 3.10 95% CI 1.99–4.84 for the high exposure groups), with adjustment for age, leisure physical activities, alcohol consumption ( $\geq 5$  servings per day), history of diabetes, epilepsy, hand trauma, and familial history of Dupuytren's disease.

The main strength of this study, which considerably enhances its relevancy for this review, are the analyses of occupational exposures together with most of the clearly established personal risk factors, and the attempt of making a quantitative assessment of manual occupational exposure. Some limitations are that the exposure assessment was based on questionnaire, and that smoking status was not taking into account. The reason for that is that the role of smoking habits in Dupuytren's disease was not clearly shown until after this study was designed.

Burke *et al* 2007[138] examined 97.537 male miners seeking compensation for hand/arm vibration syndrome with the aim of studying the effects of exposure to vibration, smoking, alcohol and diabetes on the prevalence of DC. All stages of the disease from thickening of the palmar fascia to established contractures being considered as cases of Dupuytren's disease. The assessment of exposure to hand/arm vibration was based on the claimant's answer of how many years during their employment in any industry they had been exposed to vibrating tools. The assessment simply related to the total years of exposure, without enquiry into the time during the shift when directly exposed to vibration or type of vibrating tool used. There was a statistically significant association with smoking, alcohol consumption and diabetes mellitus. It was found no

statistically significant correlation between years of exposure to vibration and the prevalence of DC (OR=1,00 95% CI 0,99-1,00; P=0,23). There was considerable collinearity between years of exposure and the linear and quadratic age variables, which is expected to have increased the standard error of years of exposure. However, the large sample size is likely to have compensated adequately for this effect.

The large sample size and the association of DC with personal factors in the analyses are strengths of this study. But the crude self-reported assessment of exposure to hand/arm vibration and the lack of information on how the quite large number of participants was enrolled (mainly whether there were many different examiners through a long period of time) constitute important limitations. A misclassification of the exposure could have happened given that miners perform in general manual work. So it is not possible to identify whether exposure to hand/arm vibration or manual work or both are the real potential risk factors to the development of DC. Including patients seeking compensation for a proposed occupational disease is a selection bias, which also may have predisposed to information bias.

Khan *et al* 2004[139] investigated the relationship between the incidence of DC and occupational social class among a survey population of 520.493 men in England and Wales. Social classes were defined as professional (1), managerial and technical (2), skilled non-manual (3N), skilled manual (3M), partly skilled (4), and unskilled (5). For men, classes 3M, 4 and 5 included predominantly manual occupations. The selection of DC cases was based on a national database using the International Statistical Classification of Diseases. It was found 169 new cases of DC recorded during a 12-month period (incidence of 34,3 per 100.000 men). The occupational social classes were grouped into “non-manual” (1, 2, and 3N) and “manual” (3M, 4, and 5) groups. The prevalence of Dupuytren’s disease in manual workers was similar to non-manual workers up to the age of 59 years. The cumulative incidence rates were found to be significantly higher in the non-manual than in the manual group beyond 65 years of age. No “P” values, odds ratio or confidence intervals were informed. This difference could not be explained by an eventual tendency for men from lower social classes to under-utilize primary health care, given that consultation rates per person with Dupuytren’s disease were actually higher in social class 5, and were no different for classes 3M and 4, than those for other social classes.

Some limitations in this study can be mentioned. There is no specification regarding biomechanical occupational exposures, and age was the only personal factor taken into account, which predisposes to a wide number of possible confounders.

Gudmundsson 2000[140] designed a cross-sectional study with 1297 men and 868 women from the Reykjavik study, which is a population-based prospective cohort study of randomly selected individuals born between 1907 and 1934 living in the Reykjavik and adjacent communes. The possible relation between the DC and clinical, social, and biochemical parameters were estimated with age-adjusted univariate logistic regression analysis. Participants who did not have signs of Dupuytren’s disease at the clinical evaluation compound the reference cohort. Participants were classified for 100 different occupations, but the study focused on manual workers (seamen, farmers, and laborer) and tradesmen (carpenters, blacksmiths, masons) and men in professions demanding higher education.

Among the 1297 men examined, 249 (19.2%) had definite signs of Dupuytren’s disease. The prevalence of the disease increased significantly with age from 7.2% in men aged 45–49 years to 39.5% among those 70–74 years old. The disease was much more rare among the 868 women. Only 38 (4.4%) had any signs of the disease of which most ( $n=31$ ) were 60 years or older. The left and right hands were equally often affected in both sexes.

Among the Dupuytren’s patients 15.3% (38/249) were manual workers compared to 8.6% (90/1048) of the reference cohort (OR = 1.66; 95% CI 1.08–2.53;  $P<0.02$ ). Furthermore, 14.5% (36/249) of the Dupuytren’s patients were tradesmen compared to 8.6% (90/1048) of the reference group (OR=1.83 95%CI 1.19–2.82;  $P<0.01$ ). Only 5.6% (14/249) of the Dupuytren’s patients had a university degree compared to 11.7% (123/1048) of the reference group (OR=0.55;  $P<0.05$ ). Comparison of manual workers and those with occupations demanding higher education shows that Dupuytren’s disease was almost three times more common among the manual workers (OR=2.95;  $P<0.002$ ).

Some limitations of this study are that the association of DC with work was not the main focus, and that there is no details about how the classification of the occupations was made.

In a cross-sectional study with 828 stone workers Bovenzi *et al* 1994[141] investigated the occurrence of disorders associated with hand/arm vibration syndrome. The group exposed to vibration included 145 quarry drillers who used rock breakers and rock drills, and 425 stonecarvers processing stone blocks in the mills. Of the stonecarvers, 188 used only rotary tools (angle grinders), and 237 used both rotary and percussive tools (angle grinders and light stone hammers). The remaining 258 stone workers formed the control group, which consisted of manual polishers and machine operators not exposed to hand transmitted vibration. The assessment of exposure included questionnaire answers (kind of vibration tools, hours of use / day, days / year and total years of use for each tool) and a workplace tool assessment (measurements of hand transmitted vibration during the most frequent work tasks) to determine the vibration levels.

The personal factors analyzed were age, history of musculoskeletal disorders (such as persistent pain of the shoulders, elbows, wrists, and hands, muscle weakness, weakness, and Dupuytren's contracture), leisure activities, previous muscle or tendon injuries, bone fractures, constitutional white finger, systemic diseases (diabetes, connective tissue diseases, cardiovascular, neurological, or joint disorders), regular medical treatment, smoking status, and alcohol consumption. No information about the diagnostic criteria for DC was given.

It was found 57 cases of DC among the workers exposed to hand/arm vibration, and 7 cases among the controls, resulting in OR=2,6 (95% CI 1,24-5,49). For the subgroups of exposed workers the following odds ratio were found: OR=2,58 (95% CI 1,07-6,2) for quarry drillers; OR=1,85 (95% CI 0,74-4,61) for stonecarvers using only rotary drills; and OR=3,23 (95% CI 1,44-7,23) for stonecarvers using both rotary and percussive tools.

For the occurrence of vibration induced white finger a dose-response relation with life-time vibration dose was found, and a similar trend was observed for DC, though the last was not statistically significant.

Some strengths of this study are worth mentioning. The exposure assessment was detailed, combining questionnaire with workplace assessment. Relevant personal risk factors, such as previous injuries, other musculoskeletal disorders and systemic diseases were taken into account to the analyses. Though the self-reported assessment of total years of exposure predisposed to information / recall bias.

Thomas and Clarke 1992[142] designed a cross-sectional study to investigate whether vibration induced white finger and Dupuytren's contracture were related. They assessed 500 claimants for vibration induced white finger, whose occupations were steel industry and shipbuilding (n=431), miners (n=10), construction / demolition (n=57) and others (n=2). An age-matched (50-85 years) control group was composed of 150 men consecutively admitted to a surgical department. All stages of DC were included, from single palmar nodule to advanced flexion contractures. Data on medical history and smoking habits were recorded, but there is no information whether the groups were controlled for those parameters. The assessment of exposure to vibrating tools was registered in total years of exposure based on questionnaire answers. It was found that the prevalence of DC among vibration-exposed workers was significantly higher compared to controls (19.9% and 10.7% respectively;  $P < 0,02 > 0,01$ ). No analyses for the specific occupations were made.

The main limitations of this study are that the groups were apparently not controlled for other personal factors than age, and that the assessment of exposure was self-reported. Besides, it seems that the control group (patients hospitalized at a surgical department) differs substantially from the cases (active working population), but this is not discussed in the study. The use of claimants seeking for compensation for their diseases predisposed a selection bias.

Bennet 1982[143] analyzed the occurrence of DC among 300 male workers in polyvinyl chloride manufacturing plants. Workers from a plant where bagging and packing were performed by hand (n=216) were compared to 84 workers from another plant where those activities were not performed. The groups were comparable regarding age, family history of DC, medical history, previous injuries, alcohol intake and smoking habits. The diagnosis of DC was graded as follow: presence of nodule but no contracture, minimal, moderate or severe contracture. It was found 16 cases of DC among the workers in the bagging and packing plant and one case among the controls (OR=6,6 95% CI 1,1-39,1).

There were no further analyses on personal risk factors or specific biomechanical exposures.

The main limitation in this study is the crude assessment of exposure, i.e. no specification of which biomechanical patterns the tasks of bagging and packing represented.

Mikkelsen 1978[144] studied, in a cross-sectional design, the influence of occupation and previous hand injuries on the occurrence of DC. The study sample was 901 individuals (647 men, 254 women) presenting DC among 15.950 citizens registered in an epidemiological study in a Norwegian town. It was recorded data on occupation, handedness and previous hand trauma. The occupations were divided into 4 groups: heavy manual work (lumberjacks, full time farmers, etc); medium heavy work (bricklayers, most of the mechanics); light manual work (dentists, most industrial workers); and non-manual work (clerks, vicars, etc). The hand injuries considered were fractures of hand or wrist, tendon injuries, lacerations, deep infections and burns leaving visible scars. There was no information about which diagnostic criteria were used.

Dupuytren's disease occurred in all type of occupations, but the prevalence increased with increasing degree of hard manual work. The odds ratio for DC among heavy manual work compared to light manual work was OR=1,6 (95% CI 1,2-2,2) for men, and OR=6,8 (95% CI 1,0-45,5) for women; and for heavy manual work compared to non-manual work was OR=3,0 (95% CI 2,2-4,2) for men, and OR=21,9 (95% CI 4,6-103,7) for women. The frequency of hand trauma was higher among men with DC when compared to the general population. For women this relation was not investigated. Considering that hand injury may occur more frequently among heavy manual workers, a new analysis was made without men with DC and previous hand trauma. The relationship between DC and heavy manual work was reduced, but not eliminated. The data from this analysis were not shown.

The limitation of this study is that no other personal factors than gender were taken into account as potential confounders.

Early 1962[145] investigated the occurrence of DC among 4881 men and 392 women at a large engineering works. The prevalence of DC among men varied from 1 in 1,000 for the age group 15-24 years, to 15% in those over 65 years. A separate analysis of office and manual workers showed no significant differences: 4% among office workers and 3,3% in manual workers (OR=0,81- 95% CI 0,49-1,36). Among women, who were mainly clerical workers, there was only one case of DC, which occurred in the group 45-54 years.

To elucidate whether occupation might affect the progress and severity of DC this factor was analyzed among non-manual, light manual and heavy manual workers. The highest proportion of mild cases occurred among light workers (96% of the cases were mild), while this proportion was very similar between non-manual (79%) and heavy manual workers (77%). This difference between light and heavy manual workers in the proportion of mild cases of DC ( $P=0,04$ ) may in part be due to the difference in the average length of history (9 and 12 years respectively) for those two groups.

An important limitation of this study is the lack of information about which kind of occupation was classified as manual (including light and heavy manual) and non-manual.

Hueston 1960[146] compared the prevalence of DC among 530 male employees of a large brewery and 550 male clerical workers (office workers). The age was divided in two categories:  $\leq 39$  years and 40-59 years. Of the brewery workers, approximately half worked handling bulk beer and the remainder handled bottled beer. There was no significant difference in the occurrence of DC among the two groups (OR=0,78 – 95% CI 0,52-1,16).

Interestingly the author analyzed also the relation between DC and manual inactivity (reflected by chronic bed patients) and found significant higher rates of DC among the chronic bed patients (OR=2,12 – 95% CI 1,43-3,15). A possible cause mentioned for that was association of DC with Sudeck's atrophy (a reflex sympathetic dystrophy syndrome which can occur following immobilisation), but this theory had not been further investigated.

Herzog 1951[147] investigated the prevalence of DC among 3.000 workmen and male clerks. All cases except four were found among workers aged over 40 years, as follows: 22 cases of DC among 503 steelworkers (4,3%), 22 cases among 451 miners (4,6%) and 19 cases among 480 clerks (3,75%). The odds ratio for DC was OR=1,17 (95% CI 0,62-2,21) among steelworkers, and OR=1,25 (95% CI 0,66-2,38) among miners compared to clerks. No other analyses were made.

**Table 7.3 – Epidemiological studies on Dupuytren’s disease in relation to occupational exposures.**

yrs = years; m = men; w = women; OR = odds ratio; ORm = odds ratio for men; ORw = odss ratio for women; CI = confidende interval

Reference	Population	Design	Relevant Exposure	Selected results – risk estimate referred when possible (95% CI)
Lucas et al 2008[132] France	n=2.406 male civil servants Mean age: 50 yrs	Cross-sectional	Low Intermediate High occupational score (based on exposure to manual work and hand/arm vibration)	Intermediate score: OR=2,20 (1,39-3,45) High score: OR=3,10 (1,99-4,84)  Adjusted for age, leisure physical activities, alcohol consumption, history of diabetes, epilepsy, hand trauma and familial history
Burke et al 2007[138] UK	n=97.537 miners Age: 25-99 yrs	Cross-sectional	Hand/arm vibration	OR=1,00 (0,99-1,00)  Adjusted for age, diabetes history, smoking status and alcohol consumption
Khan et al 2004 [139] UK	n=502.493 men Age: 40-84 yrs	Cross-sectional	Manual versus non-manual work	Cumulative incidence rates significantly higher among <u>non-manual</u> workers older than 65 years  Adjusted for age
Gudmundsson et al 2000[140] Iceland	n=2.165 (1297 men, 868 women) Age: 45-74 yrs	Cross-sectional	Manual workers (seamen, farmers, and laborer) Tradesmen (carpenters, blacksmiths, masons) Professions demanding higher education (university degree)	OR = 1.66 (1.08–2.53) for manual workers and OR=1.83 (1.19–2.82) for tradesmen comparing to the reference group  OR=2.95 (CI not informed; P<0.002) for manual workers comparing to professions demanding higher education  Adjusted for age
Bovenzi et al 1994[141] Italy	n=828 stone workers (570 cases, 258 controls) Mean age: 39 yrs	Cross-sectional	Hand/arm vibration	OR=2,6 (1,24-5,49)  Adjusted for age, smoking, alcohol consumption and upper limb injuries
Thomas and Clarke [142] 1992 UK	n=650 (500 cases, 150 controls) Age: 50-85 yrs	Cross-sectional	Hand/arm vibration	Higher prevalence of DC among vibration exposed workers  Adjusted for age
Bennet 1982[143] UK	n=300 male workers (216 cases, 84 controls) Age not informed	Cross-sectional	Manual bagging and packing work	OR=6,6 (1,1-39,1)  Adjusted for age, gender, family history of DC and medical history
Mikkelsen 1978[144]	n=901 workers (647 men, 254	Cross-sectional	Heavy manual work Medium heavy work	heavy manual work compared to light manual work:

Norway	women) Age: 20-89 years		Light manual work Non-manual work	OR <sub>m</sub> =1,6 (1,2-2,2) OR <sub>w</sub> =6,8 (1,0-45,5) heavy manual work compared to non-manual work: OR <sub>m</sub> =3,0 (2,2-4,2) OR <sub>w</sub> =21,9 (4,6-103,7)
Early 1962[145] UK	n=5273 workers (4881 men, 392 women) Age: 15-74 yrs	Cross-sectional	Manual work Office work	OR=0,81 (0,49-1,36) for manual work compared to office work (among men; analyses for women were not made)  Adjusted for age
Hueston 1960[146] Australia	n=1.080 male workers Age: <=39 – 59 yrs	Cross-sectional	Brewery workers Office workers	OR=0,78 (0,52-1,16)  Adjusted for age
Herzog 1951[147] UK	n=3.000 male workers Age: > 40 yrs	Cross-sectional	Steelworkers Miners Clerks	OR=1,17 (0,62-2,21) for steelworkers and OR=1,25 (0,66-2,38) for miners comparing to clerks  Age restriction; not stratification



## 7.4 Discussion

### Design

We retrieved 7 cross-sectional studies according to the selection criteria. Three of the studies did not control the analyses for other personal factors than age and gender. [139, 142, 144]

The sample size of the population study was larger than 10.000 individuals in 2 studies [138, 139], and below 1.000 subjects in 4 studies. [141-144] Selection and / or information bias were found in 4 studies. [132, 138, 141, 142]

A positive association between occupational exposures and DC was found in 5 studies; a negative association was found in one study; and one study did not find any association.

### Diagnostic criteria

The diagnosis of DC was based on clinical findings of thickening and / or contracture of fibrous bands of the palmar fascia in all studies.

### Outcome

Dupuytren's contracture was not the main outcome in one study. [141]

In 4 studies all stages of DC (from single palmar nodule to advanced flexion contractures) found in the clinical examination were considered as cases. [132, 138, 142, 143] None of these studies performed an inter observer control to validate the reproducibility of diagnosis. One study used codes for DC registered in a national database to select the cases.[139] There was no information about the diagnostic criteria for DC in 2 studies.[141, 144]

It is important to remind that distinguishing between DC and the normal hand with thick skin or prominent fascia can be a challenge. Lennox et al. [148] reported on the degree of clinical agreement between two orthopedic surgeons who independently examined 200 consecutive patients in geriatric wards in Aberdeen, Scotland. There was perfect agreement for observing flexion contractures ( $\kappa = 1.0$ ), while for skin tethering, palmar nodules, and knuckle pads there was good agreement ( $\kappa$  of 0.8, 0.7, and 0.7, respectively).

### Exposure

The exposure assessed in 4 studies regarded manual vs. non-manual work. The distinction between these groups was based on occupations in two studies; on social classes in one study; and on biomechanical exposures in one study.

Three studies evaluated exposure to hand/arm vibration in relation to the occurrence of DC. In all three studies, the total time of exposure was assessed based on self-reported data. In only one study objective measurements of the vibration levels of the tools used by the workers were performed.

Several studies used control groups who had manually forceful work, which in itself may be a risk factor for developing DC. This may lead to an underestimation of the combined effect of vibration and forceful work.

Manual work and use of vibrating tools have been suspected to have an association with DC since the first descriptions of this disorder by the French surgeon Guillaume Dupuytren.[131] Historical and surgical case series supported this assertion, and are the base for the exposures investigated in recent epidemiological studies.

## 7.5 Pathophysiology

Although the aetiology of Dupuytren's disease remains unknown, much has been uncovered about the associated cellular and connective tissue changes in DC.[136, 137] This disease is classified as a fibroproliferative disorder in a group that includes keloid scars. Fibroblast proliferation is a key feature of early Dupuytren's disease and manifests clinically as a nodule. In these early stages, Dupuytren's disease is histologically similar to fibrosarcoma.[149] As the disease progresses, proliferation fizzles out and connective tissue assembles, manifesting clinically as the cord. Parallels have been drawn between Dupuytren's disease and wound healing.[150] As well as cellular proliferation, both conditions are marked by collagen type III deposition.[151] Similarly, the myofibroblast, a contractile cell derived from fibroblast differentiation, is prominent in both granulation tissue, where it assists wound closure, and Dupuytren's tissue, where it may

be the engine behind contracture.[152] The healing wound is an environment rich in biologically active molecules that coordinate repair. Up-regulation of various growth factors and their receptors has also been shown in Dupuytren's tissue, including transforming growth factor  $\alpha$  and basic fibroblast growth factor.[134] What injurious events might precipitate a "wound healing" response in Dupuytren's disease is unknown, although hypoxia-induced free radicals and microtrauma of collagen fibres have been suggested as possible triggers. [136]

- **Occupational exposure**

Although one of the earliest references to an eventual causal relation between DC and occupational activities dates back to its first description, the role of occupational exposure is still debated. [136, 137] Two mechanisms whereby injury to the hand, wrist, or forearm – which may occur as a result of manual work – have been suggested as precipitating the onset of DC.[134]

Hyperextension injuries and falling on the outstretched hand result in microruptures in the palmar fascia that will trigger a repair process. In support of this theory is the study by Larson et al[153], who were able to reproduce these lesions in the palmar aponeurosis of the monkey as a result of partial rupture of the palmar fascia mechanically. Regarding manual work, it is not well elucidated which specific component in this kind of work that could trigger the development of DC. For example, whether microtraumas of the palmar fascia could arise from handling tools, or repetitive movements, or a combination of various factors.

The second theory of pathogenesis proposes a vascular mechanism and states that any trauma distal to the elbow is associated with ipsilateral hand swelling, vasomotor disturbance, and secondary ischemia of the palmar fascia. In support of this opinion is the study by Plewes[154] on industrial workers who developed Dupuytren's disease as a result of reflex sympathetic dystrophy after upper-limb injury.

Exposure to vibration at work has been suggested as an aetiological factor for DC based on the same mechanisms as explained above, i.e. by causing collagen fibre rupture or palmodigital ischaemia. [138] Palmodigital ischaemia may arise in the hand as part of the vascular component of hand / arm vibration syndrome. But it is important to keep in mind that work with vibrating tools requires in general biomechanical strains, which may contribute to the development of DC. But in praxis it is difficult to isolate vibration effects from biomechanical effects in work with vibrating tools.

- **Personal factors**

Various epidemiological studies have shown geographic variations in the occurrence of DC, which suggests a genetic predisposition. [134]

Most investigators agree that genes only predispose the individual to the development of the disease rather than directly causing it. In fact, the excessive collagen type III and fibrosis in Dupuytren's disease are known not to be caused by a genetic defect in collagen production but rather are secondary to an increase in fibroblast density.[155] Some studies have suggested that the male predominance in Dupuytren's disease is related to the expression of androgen receptors in Dupuytren's fascia rather than genetics.[156] More recently, however, there has been evidence that gene mutations may participate directly in the pathogenesis of Dupuytren's disease and the best example was shown by Bayat et al.[157] A study of 20 patients presenting Dupuytren's disease with a maternally transmitted inheritance pattern showed a mutation within the mitochondrial genome in 90% of patients. The defective mitochondria generate abnormally high levels of free radicals and have defective apoptotic mechanisms, and hence directly participate in the pathogenesis of the disease.

Smoking, diabetes and aging are factors that lead to microangiopathy and ischemia of the palmar fascia. Murrell et al[158] studied the palmar fascia from patients with Dupuytren's contracture and compared it with that from patients with carpal tunnel syndrome. The former showed markedly narrowed microvessels that were surrounded by thickened and laminated basal laminae. Ischemia results in two events occurring in the palmar fascia that result in the release of free radicals. As antioxidant enzyme activities decrease with age in fibroblasts, aging acts by both vascular and metabolic mechanisms.[157]

The release of free radicals has two main effects: proliferation of fibroblasts and production of cytokines. It is important to note that the level of free radical formation in Dupuytren's disease is relatively lower than other pathologic conditions such as ischemia–reperfusion injury.[134] Murrell et al showed that a low

concentration of free radicals stimulated fibroblast proliferation, resulting in a 6-fold and 40-fold increase in fibroblast density in the cord and nodular areas of Dupuytren's contracture, respectively, when compared with normal palmar fascia. [158] Furthermore, it is well known that as fibroblast density increases, collagen type III production is also relatively increased. [155]

Alcohol, which is a known predisposing factor in Dupuytren's disease, is associated with metabolic changes that result in increased release of free radicals and in increased products of lipid metabolism.[134]

Patients with Dupuytren's disease have also been noted to have raised serum lipids compared with controls.[136]

The use of phenobarbitone, commonly used to treat epilepsy, has also been associated with DC. This association could be the consequence of that phenobarbitone induces increased cholesterol metabolism, but this topic remains controversial.[159, 160]

There are various others complex interactions in the pathogenesis of Dupuytren's disease, which are still under study. Such interactions include metabolic, immunological and genetic processes.[134]

## **7.6 Summary**

Dupuytren's contracture (DC) is characterized by thickening and contracture of fibrous bands of the palmar fascia (aponeurosis) resulting in progressive flexion of the fingers. The condition is more frequent in males than females, and the prevalence increases with age, reaching 10-20% or higher among males, and 5% or higher among females in the 60<sup>th</sup> decade.

The purpose of the present review was to elucidate the current evidence for an association between occupational exposures and the development of DC.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). We retrieved 7 cross-sectional studies providing data on risk of DC in relation to occupational exposures.

The exposure assessed in 3 studies regarded manual work, three studies evaluated exposure to hand/arm vibration, and 1 study evaluated both exposures. Regarding manual work, 3 studies found an association with DC; while 1 study found no association among workers younger than 65 years, but a negative association among workers older than 65 years. Regarding exposure to hand/arm vibration, a positive association was found by 3 studies, while one study found none association.

## **7.7 Conclusion**

The current studies of the relationship between Dupuytren's disease and occupational exposures have failed to reach a consensus. Conclusions have varied depending on the populations surveyed, the type of work involved, the size of these populations, the diagnostic criteria for DC, and the possible confounders included. Therefore there is no enough data to enable meaningful comparisons to be made between the available studies. At the moment there is none controlled longitudinal study on this subject.

As a result, the level of evidence of a causal association between DC and manual work and exposure to hand/arm vibration is considered limited (+). That means, there is some epidemiological evidence on a positive relationship but it is not unlikely that this relationship could be explained by chance, bias, or confounding.

## 8. DE QUERVAIN'S DISEASE

### 8.1 Introduction

First described in 1895 by Dr. Fritz de Quervain[161], de Quervain's syndrome or disease, also called stenosing tenosynovitis of the first dorsal compartment on the styloid process of the radius, is characterized by thickening of the ligamentous structure covering the tendons in the first dorsal compartment of the wrist, more specifically of the retinacular sheath covering the abductor pollicis longus and extensor pollicis brevis muscles. Though often referred as stenosing tenosynovitis, histologic studies have shown that the pathologic changes are localized in the tendon sheath (tendovagina) and not the tenosynovium. So as in the case for trigger finger, the term tendovaginitis would be a more appropriate description.[162]

Despite the term tenosynovitis, evaluation of histological specimens presenting de Quervain's disease shows no inflammatory changes, rather a thickening and myxoid degeneration consistent with a chronic degenerative process.[163]

It affects primarily women between the ages of 35 and 55 years. [163]. One estimate is that de Quervain's is 6 times more common in women than in men.[164] A speculative rationale for this is that women have a greater styloid process angle of the radius, but scientific support for this theory is lacking.[165] De Quervain's tenosynovitis has also been reported in pregnant and lactating women, with a similar clinical presentation that is generally self limited.[164] Wolf et al 2009[164], which presented the largest population sample reported to date (n=11.332) on the epidemiology of de Quervain's disease, confirmed these previous findings – reported mainly by historical series and series including surgical patients – regarding gender and age differences. In their results women showed a significantly higher risk of developing de Quervain's disease comparing to men ( $P < 0.0001$ ), and age greater than 40 was also a significant risk factor for the development of dQD when compared to individuals under 20 years old ( $P < 0,0001$ ).

No racial differences had been observed, until Wolf et al 2009 found that the incidence of dQD among blacks was 1.3 per 1000 person-years compared to 0.8 among whites (adjusted rate ratio = 1,31 95% CI 1,21-1,42;  $P < 0,0001$  for blacks).

In around 30% of the population the APL and EPB tendons are divided by a septum. Patients with de Quervain's disease are more likely to have this anatomic variation, and it may play a role in the cause of this condition [1].

The incidence and prevalence of de Quervain's tenosynovitis is not well known. The primary sources of data on this disorder are derived from studies on upper extremity disorders in industry, including other diagnoses than dQD.[166, 167] There are only two epidemiological studies with population samples reporting on incidence/prevalence rates specifically for dQD. Wolf et al 2009 found an incidence rate of 0,94 per 1000 person-years, and Roquelaure et al 2006 found a prevalence rate of 0,7% among men and 2,1% among women.[164, 168]

The most recent descriptive epidemiological study regarding specifically about de Quervain's disease is that performed by Wolf et al 2009[164]. The results were based on a military databasis, including 11.332 cases of de Quervain's disease over a 8-years period. As the focus of the study was the analysis of personal factors (gender, age and race), none analysis of occupational exposure was performed.

The clinical presentation of de Quervain's tenosynovitis (dQD) is typical pain on the radial side of the thumb and wrist that may extend to the forearm. Impairment of the thumb function and thickening of the ligamentous structure covering the tendons in the first dorsal compartment of the wrist can also be found.

Conservative treatment with physiotherapy, local anesthetic and/or corticosteroid is the treatment of choice, followed by surgery. The effectiveness of the injection is probably related to the degree of ligamentous hypertrophy, ie, one would not expect a corticosteroid to have a major effect on a well-developed hypertrophic or fibrocartilaginous lesion. Immobilization does not appear to offer any therapeutic advantage.[163] However, high-quality randomized controlled trials examining the effectiveness of both the conservative and the surgical treatment of dQD are still lacking.[169]

There is a wide heterogeneity of historical case series and descriptive epidemiological studies empirically suggesting several potential risk factors to the developing of dQD associated to occupational exposures. The

aim of the present review is to elucidate the current epidemiological evidence of such a possible causal relationship.

## 8.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- De Quervain disease
- De Quervain tenosynovitis
- Occupational
- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]
- Occupational Health [Mesh]
- Occupational Groups [Mesh]
- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Hand-Arm Vibration Syndrome [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]

The diagnostic criteria for de Quervain's disease were based on clinical findings of pain over the radial side of the wrist and/or pain with resisted thumb extension and/or pain with resisted thumb abduction; and positive Finkelstein's test.

The electronic search retrieved 64 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) the following articles were considered relevant: 7 articles presenting background information / reviews, 1 follow-up study, 9 cross-sectional studies, and diverse historical case series.

The epidemiological studies are discussed below and presented in table 1, listed according to descending year of publication and alphabetic sequence.

## 8.3 Epidemiological studies

In a descriptive epidemiological study Roquelaure et al 2006[168] reported on the prevalence of upper-extremity musculoskeletal disorders (MSD) in the working population based on an epidemiological surveillance system in west-central France. This region represents around 5% of the French working population and is characterized by a large industrial sector. The surveillance system relies upon a regional network of occupational physicians and was designed to assess prevalence rates of musculoskeletal disorders and their risk factors in the working population. The study population included 2.685 workers (1.566 men, 1.119 women) at mean age of 38 years. The diagnoses assessed were rotator cuff syndrome, lateral epicondylitis, ulnar tunnel syndrome, de Quervain's disease, and flexor-extensor peritendinitis or tenosynovitis of the forearm-wrist region. Diagnostic criteria for dQD were: intermittent pain or tenderness localized over the radial side of the wrist; and positive Finkelstein's test and/or resisted thumb extension and/or resisted thumb abduction. Work exposure assessments were self-reported in a questionnaire including information on general job characteristics and tasks, work organization, and main risk factors for MSD of the upper limb and back. The latter was defined and quantified according to a criteria document for evaluating the work relatedness of the main upper extremity MSD published in 2001 by a group of European experts.[170] The occupational biomechanical risk factors considered were: high repetitiveness, high force, too little recovery time, high psychological demand, low social support, and specific extreme posture for the neck, shoulder, elbow and wrist. According to the criteria document, 4 exposure scores were computed for the neck, shoulders and arms, elbows and forearms, and wrists and hands. The scores took into account the general physical and nonphysical risk factors of MSDs. The scores were computed by adding together the

occurrence of the risk factors and a traffic light model was used to categorize the work exposures. [170] The level of exposure to risk factors of MSDs for each anatomic zone was classified as acceptable (green), moderate (yellow), or high (red).

Prevalence rates for dQD were 0,7% for men and 2,1% for women. The prevalence rate increased significantly with age for both sexes, even after adjusting for job seniority ( $P < 0,05$ ). The occupations with the highest prevalence rates of all diagnoses considered together were skilled and unskilled workers (particularly in industry and agriculture), and personal care employees for women; and public sector employees and skilled and unskilled workers (particularly industrial skilled workers, drivers, material handlers, and industrial unskilled workers) for men. The distribution of occupational risk factors of MSDs, medical conditions that could possibly increase the risk of MSDs (obesity, thyroid disorders, diabetes mellitus), and age in workers with >12 months of service were aggrouped according to the traffic light model of the work-relatedness of MSDs. The level of work exposure was high without any of the 3 medical conditions taken into account in the majority of cases (i.e., age < 50: 53% of men and 63% of women; and age > 50: 55% of men and 56% of women). No significant differences in these percentages were observed between men and women, regardless of age. A high job exposure coexisted with at least 1 of the medical conditions under review for 10% of men and 13% of women age < 50. The corresponding figures for men and women age > 50 were 12% and 5%, respectively. The level of work exposure was moderate without these medical conditions for 29% and 12% of men and women aged < 50, respectively; and 16% and 14% of men and women age > 50, respectively. In conclusion, according to the criteria document, a high percentage of MSD cases could be classified as probably work related (95% in men and 89% in women age < 50; and 87% in men and 69% in women age > 50). Fifty-nine percent of the workers were exposed to at least 2 risk factors for MSD of the wrist (which included dQD). The most exposed occupations were unskilled industrial workers and agricultural workers, followed by skilled workers and clerks.

Because the objective of the study was mainly to present descriptive results, no analyses on the relationships between MSD, individual characteristics, and work exposures were made. The data from this study could eventually serve to such analyses in the future.

Rossi et al 2005 [171] reported on 45 volleyball players (14 men, 31 women) with mean age at 24 years presenting dQD. The diagnosis of de Quervain disease was based on pain over the first extensor compartment, tenderness to palpation over the first extensor compartment, and a positive Finkelstein test. The cases were divided into two groups based on the severity of the symptoms and physical findings (mild or severe). It was found that the total training quantity (mean weekly training time multiplied by mean sports activity duration) in the group with more severe symptoms and physical findings was statistically significant higher than in the group with mild symptoms and clinical findings ( $P < 0,01$ ).

The study proposed that increased training time and consequent microtrauma associated with professional volleyball activity could increase the likelihood of de Quervain disease. But the design of the study did not elucidate whether more intensive training is a causal factor in the development of dQD or just a worsening factor for symptoms among individuals already presenting dQD.

Leclerc et al 2001[172] performed a 3-year follow-up study to determine the predictability of personal and occupational factors in the incidence of upper limb disorders in occupations requiring repetitive work. It was included 598 workers from five activity sectors: assembly line in the manufacture of small electrical appliances, motor vehicle accessories, or ski accessories (packaging excluded), clothing and shoe industry (packaging excluded), food industry (mainly, meat industry – packaging excluded), packaging (primarily in the food industry), supermarket cashiering. The age varied from  $\leq 29$  to  $\geq 50$  years. There were 178 men and 420 women. Three disorders were considered: carpal tunnel syndrome, lateral epicondylitis and wrist tendonitis (which included hand or wrist extensor peritendinitis or tenosynovitis, hand or wrist flexor peritendinitis or tenosynovitis, and De Quervain's disease). The diagnostic criteria for de Quervain's disease were pain on the radial side of the wrist, tender swelling, or pain produced by thumb extension, thumb abduction or the Finkelstein test. The potential risk factors analyzed were personal (age, gender, smoking status, BMI, somatic problems, depressive symptoms); occupational activity (sector and number of years on the job); biomechanical constraints (turn and screw, tighten with force, work with force (other than tighten), press with the hand, press with the elbow, hit, pull, push, hold in position); and psychosocial work factors (job control, job demand, support at work and satisfaction at work). The results for wrist tendonitis showed a prevalence of 11.2% and incidence of 5.7%. Gender, number of years on the job, and smoking were not associated with the incidence of any type of disorder. The only strong predictor of the incidence of wrist

tendinitis was the level of somatic problems at the beginning of the study (OR 3.78, 95% CI 1.63— 8.75). The only biomechanical risk factor associated with the incidence of wrist tendonitis was hitting repetitively, but the results were not statistically significant (OR=2,16 95% CI 0,84-5,56). A possible explanation for that could be that other biomechanical factors may have short-term effects that would have been seen if the interval between the exposure and incidence had been shorter than 3 years.

Some limitations of this study are observer bias (18 different observers); information bias (the assessment of repetitiveness of the tasks and use of vibrating tools were self-assessed; possible healthy worker effect (workers suffering from upper-limb disorders in repetitive work having no alternative to continuing to work in their jobs or in similar jobs); and that suspected diagnosis were also included as cases (not all the criteria met in the medical examination or diagnosis based on the description of symptoms that were no longer present at the time of the examination).

In a cross-sectional study with a population sample of 30.074 participants (corresponding to a statistically weighted population of 127 million) Tanaka et al 2001 [167] investigated the prevalence and risk factors of tendonitis and related disorders of the distal upper extremity among U.S. workers. The disorders included were tendonitis, synovitis, tenosynovitis, de Quervain's disease, epicondylitis, ganglion cyst, and trigger finger. Diagnostic criteria were not informed, given that the cases were selected based on their answers declaring that one of the included diagnoses was confirmed by a medical person within the preceding 12 months. The analyzed occupational risk factors were bend/twist of hands/wrist and use of hand-held vibrating tools. The personal factors analyzed were gender, age, race, BMI, smoking history, education and family income. There was no information about how many cases of dQD were found. For the analysis of adjusted odds ratios the diagnoses tendinitis, synovitis, tenosynovitis, de Quervain's disease, trigger finger, ganglion cyst, and epicondylitis were referred altogether as tendinitis and related disorders. Only female gender and bending/twisting of the hands/wrist were significantly associated with reporting of these disorders (OR=2,51 95% CI 1,68-3,74 and OR=2,56 95% CI 1,58-4,16 respectively).

The major strength of this study is the large national sample with a high response rate. Some limitations are the lack of information about which occupations were included; a limited assessment of exposure with only two parameters; and the possible recall bias for the exposure. Besides, because of the combination of de Quervain's disease with so many other upper extremity disorders makes an application of these results specifically to dQD difficult.

Ranney et al 1995 [173] examined 146 female workers in five industries considered demanding repetitive work activities (packaging, electronics, assembly, cashiers, sewing) for the presence of musculoskeletal disorders in the upper limbs. The assessment of repetitiveness of the jobs was based on the same method used by Armstrong et al 1987 presented below. All jobs were classified as highly repetitive.

The mean age of the workers was around 40 years. The health outcomes included were: upper limb neuritis; wrist and digit tendinitis and tenosynovitis (including de Quervain's disease); forearm and hand myalgia and epicondylitis; and neck / shoulder / arm myalgia and tendinitis. De Quervain's disease was diagnosed based on pain on the radial side of the wrist, tenderness over the first dorsal compartment, and a positive Finkelstein's test. Subjects with history of prior trauma to upper limb or systemic rheumatologic disorders were excluded. Musculoskeletal disorders of the upper limbs were found in 82 persons (56%), being 12 cases of dQD (8% of total, 15% of affected persons). Thus resulting in prevalence rate of 8,2%. Ten cases involved the right side (71%) and two cases were bilateral. According to industry category, there were no cases of dQD in the packaging, two in electronics, four in assembly, two in cashiers, and four in sewing. Relationships between ergonomic exposure factors and morbidity have not yet been published.

The main relevance of this article is to present such a relatively high prevalence of dQD among certain occupations. However, the lack of analyses regarding ergonomic factors in relation to specific diagnoses is a main limitation.

Moore and Garg 1994 [174] performed a retrospective cross-sectional study with 230 workers in a pork-processing plant. The aim of the study was to determine the prevalence of different distal upper extremity disorders and to investigate whether there was a relationship between occupational exposure factors and occurrence of such disorders. None personal factors, such as age and gender were taken into account, mainly because of the lack of demographic information. The included diagnoses were medial and lateral epicondylitis, trigger finger, de Quervain's disease, carpal tunnel syndrome, and non-specific hand/wrist pain.

The diagnostic criteria for dQD were pain and tenderness localized to the radial side of the wrist plus a positive Finkelstein's test. The exposure assessment was based on direct observations and videotapes of the various tasks performed at the plant. Forty-four jobs within eight production departments were analyzed resulting in 32 job categories. The exposure assessment methodology was semi-quantitative and included force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and exposure to cold temperature. Each job category was classified as hazardous or safe according to the predicted potential to cause upper-extremity disorders. This prediction was based primarily on the investigators' consideration of the exposure data plus their experience and judgment.

The hazardous categories required significantly greater strength and awkward wrist posture than the safe categories ( $P < 0,01$ ). One hundred and four cases of diagnosed conditions were found among the 14 hazardous categories and 4 cases among the 18 safe categories. There were 3 cases of de Quervain's disease (2 males and 1 female workers), resulting in a prevalence rate of 1,3% of the total sample analyzed. These workers performed three different jobs, which involved loading of the thumb combined with moderate wrist deviation but not necessarily use of pinch grasp.

The relative risk of developing epicondylitis and stenosing tenosynovitis (trigger finger and de Quervain's disease) altogether among workers in the hazardous jobs was found as  $RR = 19,4$  ( $P = 0,02$ ; 95% CI not informed) when compared with workers from the safe job categories.

The main strength of this study is the detailed and objective assessment of exposure identifying both job tasks and specific ergonomic factors. A remarkable limitation is the lack of demographic information on the participants, which results in the lack of an analysis for possible personal confounders. Because the study did not consider each diagnose separately, the application of the results specifically to de Quervain's disorder is limited.

Kurppa et al 1991 [175] performed a cross-sectional study on the incidence of tenosynovitis or peritendinitis in the hand and forearm and epicondylitis among workers in a meat-processing plant. Two cohorts were designed including 377 workers in strenuous manual jobs (152 men, 225 women) and 338 employees in manually non-strenuous work (141 men, 197 women). The mean age of two groups was similar (36 years). The cohorts were followed for a period of 31 months. The diagnostic criteria for tenosynovitis or peritendinitis in the hand and forearm were: swelling or crepitation and tenderness to palpation along the tendon, and pain at the tendon sheath, in the peritendinous area, or at the muscle-tendon junction during active movement of the tendon. De Quervain's disease was included in this group if this term was given by a physician in the medical files, even in the absence of a positive Finkelstein's test. The occupations considered as strenuous manual jobs were meatcutters, packers and sausage makers, while office workers, supervisors, and maintenance employees were included in the group of manually non-strenuous work. It was found 104 workers presenting tenosynovitis and peritendinitis. Eight of these workers received a diagnosis of dQD, but none of them presented positive Finkelstein's test (prevalence of 1,11% of the total sample). Ninety-eight workers out of the 104 cases belonged to the group of strenuous jobs. It was not informed which group the workers presenting dQD belonged to.

Incidence rates for tenosynovitis and peritendinitis, in rates per 100 person-years, were of less than 1% for employees in non-strenuous jobs (both men and women), and 11% among men and 21,4% among women in strenuous manual jobs.

The main limitations of this study are: observer bias (cases based on medical files by many different clinicians); inclusion of cases called dQD even without a positive Finkelstein's test; and the inclusion of dQD in the analyses together with other forms of tenosynovitis or peritendinitis in the hand and forearm not further specified.

Armstrong et al 1987 [176] studied the relationship between hand/wrist tendonitis with force, repetitiveness, and hand and wrist posture during work activities. A total of 652 workers were selected from the following occupational areas: electronics, sewing, appliance, bearing fabrication, bearing assembly, and investment molding plants. Age and sex distribution of the subjects were not informed. Hand and wrist tendonitis included de Quervain's disease, trigger finger, and "tendonitis/tenosynovitis". The diagnostic criteria for dQD were: pain in the anatomic snuffbox that might radiate up the forearm; no history of radial wrist fracture; symptoms that lasted more than 1 week or occurred more than 20 times in the last year; a physical examination that ruled out radial nerve entrapment; and a positive Finkelstein's test with a pain score  $\geq 4$



(range 1 to 8). The workers were distributed among four groups regarding occupational exposures: low force – low repetitiveness; high force – low repetitiveness; low force – high repetitiveness; and high force – high repetitiveness. High repetitive jobs were defined as those with a cycle time of less than 30 seconds or with more than 50% of the cycle time involved in performing the same motion pattern. Low repetitive jobs were those with a cycle time of more than 30 seconds and with less than 50% of the cycle time involved in performing the same kind of motion pattern. High force jobs were those with estimated average hand force requirements of more than 4 kg, and low force jobs, those with estimated average hand force requirements below 1 kg. Peak hand forces were estimated from the weight of tools and material and then verified by means of surface electromyography. It was found 16 cases of hand/wrist tendonitis.

The number of cases of dQD was not reported. The specific diagnoses were not evaluated separately. They found a statistically significant increased odds ratio for the prevalence of hand/wrist tendonitis among workers performing jobs characterized by high force – high repetitiveness when compared with the low force – low repetitiveness group (prevalence of 10,8% versus 0,6% respectively; OR=29,4; CI not informed;  $P<0,001$ ). This association was similar for both males and females. Although the overall prevalence was significantly higher in females (7,8%) than in males (1,7%), resulting in a job-adjusted odds ratio of 4.3. There were no associations with personal factors (use of birth control pills, hysterectomy, oophorectomy, recreational activities) or other work factors (exposure to hand/arm vibration and work posture). Work posture was evaluated by the percentage of work time spent in wrist flexion, ulnar deviation, wrist flexion and ulnar deviation, pinching, or pinching and wrist flexion.

The main strength of this study is the detailed assessment of work exposure. But some limitations can be named. The inclusion of other forms of tendonitis / tenosynovitis not further elucidated predisposed to overrepresentation of the cases, which limits the application of the results specifically to de Quervain's disease. The age of the workers is not informed and it is not clear whether the groups were adjusted for age. Even though the study sample is relatively large, the results are based on few cases found.

The method of assessment of force and repetitiveness used by Armstrong et al was prior described by Silverstein et al 1986[177] in a cross-sectional study of 574 workers from six different industrial sites regarding the occurrence of a miscellaneous of hand / wrist disorders. They also found significant positive associations between hand / wrist disorders and high force – high repetitive jobs. These associations were independent of age, sex, years on the specific job, and plant. The relevance of this study to the present review is very limited because the analyses for health outcomes included cases of tendonitis, tenosynovitis, de Quervain's disease, trigger finger, carpal tunnel syndrome, Guyon tunnel syndrome and digital neuritis all together.

Punnett et al 1985[178] compared in a cross-sectional study the prevalence of soft tissue disorders of the upper limbs among 162 female garment workers with that of 73 female hospital employees. Mean age was 43 years. The garment workers performed the following tasks: stitcher (sewing machine operator), finisher (sewing and trimming by hand), underpresser (ironing by hand), floor work (carrying work bundles), and others (shipping, operation of a fusing machine, etc). The first two tasks, which accounted for 86% of the workers, were considered highly repetitive, with low force to the wrist and fine finger motions. Finishers also used shoulder and elbow motions. Underpressers use somewhat more forceful shoulder, elbow, and wrist motions. The hospital employees presented the following jobs: nurses, laboratory technicians, therapists, laundry and food service workers, social service and administrative employees. Employees with jobs requiring four or more hours of typing per day were excluded. The disorders analyzed were carpal tunnel syndrome, de Quervain's disease, and degeneration of the thumb carpo-metacarpal joint.

The diagnostic criteria for dQD were persistent pain over the thumb joint and positive Finkelstein's test. Thirteen cases of dQD among the garment workers and two cases among the hospital employees were found. Resulting in prevalence rates of 8,0% among garment workers and 2,7% among hospital employees, and OR = 3,0 (95% CI 0,73-13,1).

There was no comparison of ergonomic factors to the health outcomes and no other results presented regarding de Quervain's disease.

Luopajarvi et al 197[179] reported the prevalence of tenosynovitis and other injuries of the upper extremity among 152 female assembly-line packers in a food processing factory and 133 female retail shop assistants (excluding cashiers). The mean age was 39 years. Various disorders of the neck, shoulder, elbow and hands

were included. Workers presenting prior trauma to the hand, rheumatoid arthritis and neurological disease were excluded. The “muscle-tendon syndrome” in the forearm and hand was called tenosynovitis when it was located at the tendon sheath area of the dorsal or palmar side of the wrist, and peritendinitis when it involved structures higher up in the forearm. Tenosynovitis was divided in flexor and extensor tenosynovitis (the latter included carpal extensors and tendons of the thumb).

The assessment of exposure for the assembly-line packers was performed by a group comprising a foreman, a worker, a labor safety officer, and an occupational physiotherapist. The work movements were videotaped and evaluated by a work study engineer and a physician. Most of tasks were considered highly repetitive (up to 25.000 cycles per workday), and requiring static muscle work, awkward positions of the fingers and wrist and lifting the average of 5.000 kg daily. The shop assistants' was considered physically light.

The prevalence of extensor tenosynovitis was 44% (67 cases) among packers and 6% (8 cases) among shop assistants, resulting in OR = 12,31 (95% CI 6,2-24,2). The packers had extensor tenosynovitis significantly more often than flexor tenosynovitis (44% vs 18%; P<0,001). The workload of assembly-line packing and shop work were described and contrasted, but no statistical analyses were performed.

#### **8.4 Historical case reports and case series**

In a case serie with 100 patients Kay 2000[180] discussed critically the perception of most of the historical series that dQD is a causative factor in the development of dQD. After reporting the medical and working status of the patients, they recommended that “clinicians furnishing forensic medical reports on patients with de Quervain's disease should address the question of causation very carefully”, given that “there is no scientific evidence that can be validated to show that work is causative of the pathologic changes”. No relationship analyses were made.

It was found several historical case series (from 1920 to 1960) including dQD together with other forms of tendonitis and tenosynovitis, and case reports with less than 10 patients. In most of them the authors assumed that occupational factors might be involved in the aetiology of these disorders, and some suggest possible pathophysiologic mechanisms, but those assertions are mainly based on their personal opinions or professional experience. Diverse occupations and exposures are cited in those series, such as pinch gripping in ulnar deviation, and activities requiring thumb use – buffing a machine, fitting rubber rings on a pipe, typewriting, piano-playing, sewing, knitting, weaving, cutting, shifting gear while mountain biking, playing video game, and turning control wheels in a colonoscope.[163, 165, 180-183]

**Table 8.5 – Epidemiological studies on de Quervain’s disease in relation to occupational exposures**

yrs = years; m = men; w = women; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women; CI = confidence interval

Reference	Population	Design	Exposure	Outcome	Diagnostic criteria for de Quervain’s disease	Selected results – risk estimate referred when possible (95% CI)
Roquelaure et al 2006[168] France	n=2.685 workers (1.566 m, 1.119 w) Mean age: 38 yrs	Cross-sectional	High repetitiveness, high force, too little recovery time, high psychological demand, low social support, and specific extreme posture for the neck, shoulder, elbow and wrist	Rotator cuff syndrome, lateral epicondylitis, ulnar tunnel syndrome, de Quervain’s disease, and flexor-extensor peritendinitis or tenosynovitis of the forearm-wrist region	Pain over the radial side of the wrist and/or pain with resisted thumb extension and/or resisted thumb abduction; and positive Finkelstein’s test	Prevalence rates for dQD: 0,7% <sub>m</sub> , 2,1% <sub>w</sub> Prevalence rate increased significantly with age for both sexes, even after adjusting for job seniority (P<0,05)
Rossi et al 2005[171] Italy	n=45 volleyball players Mean age: 24 yrs	Cross-sectional	Total training quantity (mean weekly training time multiplied by mean sports activity duration)	De Quervain’s disease	Pain and tenderness to palpation over the first extensor compartment, and positive Finkelstein test	Total training quantity in the group with more severe symptoms and physical findings higher than in the group with mild symptoms and clinical findings (P< 0,01)
Leclerc et al 2001[172] France	n=598 industrial workers (178 m, 420 w) Age: <= 29 to >=50 yrs	Follow-up	occupational activity biomechanical constraints (turn and screw, tighten with force, work with force, press with the hand, press with the elbow, hit, pull, push, hold in position psychosocial work factors (job control, job demand,	Carpal tunnel syndrome, lateral epicondylitis and wrist tendonitis (included hand or wrist extensor peritendinitis or tenosynovitis, hand or wrist flexor peritendinitis or tenosynovitis, and De Quervain’s disease).	Pain on the radial side of the wrist, tender swelling; or pain produced by thumb extension, thumb abduction or by the Finkelstein’s test	Relation between wrist tendinitis and level of somatic problems at the beginning of the study (only strong predictor of the incidence): OR=3.78 (1.63- 8.75) Wrist tendinitis and hitting repetitively:

			support at work and satisfaction at work)			OR=2,16 (0,84-5,56)
Tanaka et al 2001[167] USA	n=30.074 (14.647 m, 15.427 w) Age: 18 - >65 yrs	Cross-sectional	bend/twist of hands/wrist use of hand-held vibrating tools	Tendinitis and related disorders (included tendinitis, synovitis, tenosynovitis, de Quervain's disease, and epicondylitis)	Not informed	Bend/twist of the hands: OR=2,56 (1,58-4,16) Hand vibration: OR=1,54 (0,93-2,55)  Adjusted for gender, age, race, BMI, smoking history, education and family income
Ranney et al 1995[173] Canada	n=146 female workers Mean age: 40 yrs	Cross-sectional	5 industries (packaging, electronics, assembly, cashiers, sewing), where all jobs were classified as highly repetitive	Upper limb neuritis; wrist and digit tendinitis and tenosynovitis (including de Quervain's disease); forearm and hand myalgia and epicondylitis; and neck / shoulder / arm myalgia and tendinitis	Pain on the radial side of the wrist, tenderness over the first dorsal compartment, and positive Finkelstein's test	Prevalence rate of dQD=8,2%
Moore and Garg 1994 [174] USA	n=230 workers in a pork-processing plant Age and gender not informed	Cross-sectional	Hazardous versus safe jobs (based on force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and exposure to cold temperature)	Epicondylitis and stenosing tenosynovitis (trigger finger and de Quervain's disease together)	Pain and tenderness on the radial side of the wrist and positive Finkelstein's test	Relative risk for the three disorders together in the hazardous jobs vs. the safe jobs: RR=19,4 (P=0,02; 95% CI not informed)
Kurppa 1991 [171]	n=715 workers in a meat-processing plant (377 cases, 338 controls) Median age: 36 yrs	Cross-sectional	Strenuous manual jobs (meatcutters, packers and sausage makers) versus non-manual jobs (office workers, supervisors, and	Tenosynovitis or peritendinitis in the hand and forearm (including de Quervain's disease)	Swelling or crepitation and tenderness along a tendon; and pain at the tendon sheath, in the peritendinous area, or at the muscle-	Incidence of tenosynovitis and peritendinitis (per 100 person-years): 11% <sub>m</sub> , 21,4% <sub>w</sub> in manual jobs; < 1% in non-manual jobs

			maintenance employees)		tendon junction during motion	(for both men and women)
Armstrong et al 1987[176] USA	n=652 workers Age and gender distribution not informed	Cross-sectional	Force and repetitiveness hand posture and exposure to hand/arm vibration (occupational areas: electronics, sewing, appliance, bearing fabrication, bearing assembly, and investment molding plants)	Hand/wrist tendinitis (including de Quervain's disease, trigger finger and "tendinitis/tendosynovitis" altogether)	Pain in the anatomic snuffbox, and positive Finkelstein's test	OR for hand/wrist tendinitis = 29,4 (P<0,001) when jobs presenting high force – high repetitiveness were compared to the low force – low repetitiveness group
Punnett et al 1985[178] USA	n=235 female workers (162 cases - garment workers, 73 controls - hospital employees) Mean age: 43 yrs	Cross-sectional	Garment work: stitcher (sewing machine operator), finisher (sewing and trimming by hand), underpresser (ironing by hand), floor work (carrying work bundles), and others (shipping, operation of a fusing machine, etc)	Carpal tunnel syndrome, de Quervain's disease, and degeneration of the thumb carpo-metacarpal joint	Persistent pain over the thumb joint and positive Finkelstein's test	Prevalence rates of dQD: 8,0% among garment workers, 2,7% among hospital employees OR = 3,0 (0,73-13,1)
Luopajarvi et al 1979[179] Finland	n=285 female workers (152 cases, 133 controls) Mean age: 39 yrs	Cross-sectional	Highly repetitive work requiring static muscle work, awkward positions of the fingers and wrist, and lifting the average of 5.000 kg daily	Various disorders of the neck, shoulder, elbow and hands, including flexor and extensor tenosynovitis (the latter included carpal extensors and tendons of the thumb)	Not informed	Prevalence of extensor tenosynovitis: 44% among cases, 6% among controls OR = 12,31 (6,2-24,2)

## 8.6 Discussion

### Design

The majority of the published studies on de Quervain's disease are case series related to the surgical treatment of the condition. As a result, there have been a wide heterogeneity of opinions and observations on the aetiology, pathology and treatment of dQD. In addition, surgical series are limited to almost exclusively patients that failed to respond to conservative treatment, and the ascertainment of cases by the practitioners predisposes to selection bias. The number of studies including control or comparison groups is small. For those reasons, the opinions expressed in many of these articles must be viewed critically.

The present review described 8 cross-sectional studies and one follow-up survey. Regarding the cross-sectional studies, most of their results are descriptive and they present limitations. The study of Leclerc et al[172] presents the advantages of being a follow-up study including diverse personal factors and occupational exposures. But the inclusion of suspected diagnosis in the same group as confirmed cases (not all the criteria met in the medical examination or diagnosis based on the description of symptoms that were no longer present at the time of the examination) predisposes to an overestimation of the number of cases.

The study of Tanaka et al[167] is relevant mainly because of the big sample size, but the lack of information regarding which occupations were included, and the analysis of only 2 biomechanical exposures limit the application of their results for the relation between dQD and occupational and biomechanical exposures. Both studies, of Leclerc et al[172] and Tanaka et al[167], present possible selection and information/recall biases.

The studies of Moore and Garg[174] and Armstrong et al[176] presented objective assessments of the occupational and biomechanical exposures, but the lack of demographic information from the participants did not allow a control for possible personal confounders.

### Diagnostic criteria

Seven epidemiological studies consider pain in the radial side of the wrist together with a positive Finkelstein's test as diagnostic for dQD. And in two studies the diagnostic criteria for dQD were not informed.

Roquelaure et al 2006[168] presented the first study applying the recommendations of the criteria document for evaluating the work relatedness of the main upper extremity musculoskeletal disorders (MSD) published in 2001 by a group of European experts.[170] This document proposed a standardization of the surveillance of MSD in the European Union, which would allow more accurate comparisons of prevalence rates between economic sectors and occupations. The classifications suggested by this document are one of the most exhaustive found in the literature, but to date the diagnostic value of the consensus has not been assessed. However, the disorder and physical examination signs definitions are close to those of the Health and Safety Executive consensus group[184] and of the Southampton examination protocol diagnostic criteria, which demonstrated good diagnostic properties.[185, 186] The physical examination procedures, particularly the diagnostic criteria charts and the clinical guide using photographs of clinical tests, were judged positively by the occupational physicians and were considered easy to apply in an occupational health setting to standardize the physical examination of any workers included in MSD surveillance programs.

### Outcome

All the epidemiological studies but one[171] did not present de Quervain's disease as the main outcome. And in most of them the analyses were made to dQD together with various different diagnoses. Besides, most of them present a large number of non-specific hand/wrist disorders. It is unclear how to place these disorders into context. Some question whether those disorders are precursors to the development of the more specific disorders.[174]

### Exposure

The biomechanical occupational exposures contributing to the development of dQD are not known. But several factors observed within job activities requiring thumb use have been speculatively suggested as risk factors, based on the apparently overweight of workers from manual occupations in several case series.

For example, found Kurppa et al[175] in a meat processing factory an annual incidence of tenosynovitis or peritendinitis of less than 1% for employees in nonstrenuous jobs, while the rates were 25,3% for female

packers, 16,8% for female sausage makers, and 12,5% for male meatcutters. In investigations of a miscellaneous of distal upper extremity disorders, Moore and Garg[174] reported a prevalence of 2,9% among workers in a pork processing plant and Leclerc et al[172] found prevalence rates of 11,2% and incidence of 5,7% among occupations requiring repetitive work. Compared to incidence and prevalence rates found in population samples of under 1%, these results rise speculations about a possible causal relationship between the development of hand/wrist disorders (de Quervain's disease included) and occupational exposures. [164, 167, 168] Other results stimulating these speculations are reports on the developing of dQD among relatively young individuals within a certain occupation, for whom age is not an expect risk factor. As an example the results of Rossi et al[171] reporting volleyball players with mean age of 24 years presenting dQD can be cited.

These clinical observations resulted in three proposed theories of pathogenesis in the context of hand usage, including static compression, repeated compression and trauma. The role of force exertion by the thumb has not been evaluated isolated, only in association with compression. Those physiopathologic theories are discussed below.

Among the epidemiological studies selected in this review only two of them studied specific biomechanical factors in association with hand/wrist musculoskeletal disorders. Armstrong et al [176] analyzed force exertion, repetition, and posture (wrist flexion, ulnar deviation and pinching). Force exertion and repetition, but not posture, were associated with the prevalence of hand and wrist tendinitis (de Quervain's disease, trigger finger, and tendonitis/tendosynovitis). Moore and Garg[174] analyzed force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and exposure to cold temperature in order to classify different job tasks in "hazardous" or "safe" within a pork-processing plant in association with distal upper extremity disorders (medial and lateral epicondylitis, trigger finger, de Quervain's disease, carpal tunnel syndrome, and non-specific hand/wrist pain). They found that workers in the "hazardous" jobs were at higher risk of developing the referred disorders, but they did not analyze the biomechanical parameters individually.

## 8.7 Pathophysiology

At the present moment the role of personal factors in the developing of dQD, such as age, gender, race, BMI, and anatomical variations, has not been thoroughly explored.[164, 180] Three different theories of pathogenesis of de Quervain's disease involving trauma and hand usage are proposed[163], which are discussed below.

- **Static compression**

Observations by clinicians suggest that dQD is related to repeated, prolonged, or unaccustomed exertions that involve the thumb in combination with non-neutral wrist of thumb postures. Thumb exertions are associated with tensile loading of the abductor pollicis longus (APL) and extensor pollicis brevis (EPB). Postural deviation of the wrist or carpometacarpal joint of the thumb makes the APL or EPB turn a corner at the extensor retinaculum. These factors in combination create a compressive force between the tendons and the distal end of the retinaculum. The retinaculum may respond to this compressive stimulus with functional hypertrophy or fibrocartilaginous metaplasia. The fibrocartilaginous changes in the retinaculum and the granulomatous changes on the surface of the tendon (secondary to collagen fibril disruption) are consistent with compression being the critical mechanism. In this model isolated observation of posture or isolated assessment of applied force with the thumb would be insufficient for estimation of compressive force on the extensor retinaculum. The duration of compression is more important than the repetition of compressions, e.g., one prolonged exertion at relatively moderate levels of compressive load could be more significant than a serie of brief and intermittent exertions at the same or higher levels of compressive load.

- **Repeated compression**

This theory relies on the same biomechanical argument as the static compression theory, except that the number of episodes of loading during a period of activity is considered more critical than the accumulated duration of loading.

- **Acute trauma ("One-Hit")**

A single episode of acute trauma involving the first dorsal compartment, such as a contusion, has been reported to be related to up to 25% of cases of dQD.[160] It is important to notice though that not all

episodes of such trauma necessarily lead to dQD and that qualitative and quantitative descriptions of such stimuli are lacking. The proposed aetiology begins with a single episode of blunt trauma directly over the region of the first dorsal compartment. Three subsequent pathways appear plausible.

The first pathway involves disruption of the collagen fibers within the extensor retinaculum, followed by a repair response that leads to thickening of the retinaculum and stenosis of the fibro-osseous canal.

The second pathway involves disruption of collagen fibers within the tendon(s) of the APL or EPB, followed by a repair response that leads to a nodular lesion on the tendon. This nodular lesion leads to a "relative" stenosis of the fibro-osseous canal, even though the extensor retinaculum is otherwise unaffected. The third pathway involves hemorrhage and edema in the general region, which increases compressive or shear forces between the otherwise normal APL or EPB tendons and the extensor retinaculum. Because there is little information upon which to base this theory of physiopathology, the proposed mechanism should be considered quite tentative.

If the proposed models for the pathogenesis of De Quervain's tenosynovitis are validated, they might also serve as a starting point for models of pathogenesis for stenosing tenosynovitis at other locations in the body, such as trigger finger and other forms of stenosing tenosynovitis of the upper-extremity.

## **8.8 Summary**

De Quervain's disease (dQD), also called stenosing tenosynovitis of the first dorsal compartment on the styloid process of the radius, is characterized by thickening of the ligamentous structure covering the tendons in the first dorsal compartment of the wrist, more specifically of the retinacular sheath covering the abductor pollicis longus and extensor pollicis brevis muscles. It affects primarily women between the ages of 35 and 55 years.

There is a wide heterogeneity of historical case series and descriptive epidemiological studies suggesting several occupational risk factors for the developing of dQD. The aim of the present review is to elucidate the current evidence for an association between occupational exposures and the development of dQD.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010).

We retrieved 9 cross-sectional studies and 1 follow-up study presenting occupational factors in relation to dQD. The exposure assessed in all studies was manual work. A positive association between occupational exposures and dQD was found in 6 studies; one study found no associations; and 3 studies were exclusively descriptive.

## **8.9 Conclusion**

The current knowledge base for de Quervain's disease is generally limited to historical case series and cross-sectional epidemiological studies. As a result no definitive conclusions about the relationship between de Quervain's disease and personal factors or hand use are possible at the present moment. The present level of evidence is considered limited (+) and further analytic controlled epidemiological studies are needed. De Quervain's disease do not differ in principle from tenosynovitis in other tendons (tendovaginitis, tenosynovitis). The evidence of a causal relationship between workloads and developing of dQD can therefore be equated with evidence for tendovaginitis in the other tendons in the wrist.



## 9. TRIGGER FINGER

### 9.1 Introduction

First described by Notta in 1850[187], trigger finger disorder is characterized by thickening and narrowing of the fingers flexor tendon retinacular sheath. Though often referred as stenosing tenosynovitis, histologic studies have shown that the pathologic changes are localized in the tendon sheath (tendovagina) and not the tenosynovium. So the term tendovaginitis has been proposed as more appropriate description of trigger finger.[162]

The term trigger finger (TF) refers to the painful popping or clicking sound elicited by flexion and extension of the involved finger.

The lifetime risk for developing trigger finger was estimated by Strom around 2%, but increases up to 10% in diabetics.[188] It occurs more frequently in the ages between 50 – 60 years and is up to six times more common among women than men.[187, 189] The reason for this age and sex predilection is not entirely clear.

The first annular pulley at the metacarpal head is by far the most often affected pulley in trigger finger, though cases of triggering have been reported at the second and third annular pulleys, as well as at the palmar aponeurosis.[187] The ring finger is most commonly affected, followed by the thumb (trigger thumb), long, index and small fingers in patients with multiple trigger digits. [187, 189] Unless other is referred, the term trigger finger in this paper refers to the pathology involving all fingers, including triggering of the thumb.

Other than a difference in localization, the pathology of flexor tendon entrapment of the digits is essentially identical to tendon entrapment at the first dorsal compartment (de Quervain's tenosynovitis).[189]

The A1 pulley of the tendon sheath is thick and fibrous, thus comprising the cross-sectional area of the fibro-osseous canal. Histologically, the A1 pulleys and, in some cases, the adjacent surfaces of the flexor tendons demonstrate findings consistent with fibrocartilagenous metaplasia, degenerative changes and proliferation of fibrous tissue. The absence of inflammatory changes was noted by several authors.[189]

The initial clinical manifestation is usually a painless clicking with digital movement. Further development can cause painful catching or popping with both flexion and extension, occurring at either the metacarpophalangeal or proximal interphalangeal joints.

Trigger finger can be attributed to many different conditions including diabetes mellitus, rheumatoid arthritis, sesamoid bones, tumor, anatomical variations, rheumatoid arthritis, and thyroid disease.[189] No relation to pregnancy has been reported.[189] Race differences have not been established but some descriptive epidemiological studies have reported different prevalences among blacks.[167, 189]

The association of TF with occupational exposures has been controversial. The aim of the present review is to elucidate the current epidemiological evidence for this association.

### 9.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Trigger Finger
- Occupational
- Hand-Arm Vibration Syndrome
- Occupational Exposure
- Occupational Medicine
- Occupational Diseases
- Occupational Health
- Occupational Groups
- Occupational Accidents

- Industry
- Employment
- Occupations
- Disorders of Environmental Origin
- Environmental Exposure

The diagnostic criteria for trigger finger were based on clinical findings of catching or popping of digital movements with both flexion and extension at either the metacarpophalangeal or proximal interphalangeal joints.

The electronic search retrieved 111 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 18 articles, which were considered relevant. They are classified as follow: 10 regarding background information or reviews, 1 follow-up, 5 cross-sectional studies, 2 case reports and one surgical serie.

The epidemiological studies are discussed below and shown in table 1, listed according to descending year of publication and alphabetic sequence.

### 9.3 Epidemiological studies

In a cross-sectional study with a population sample of 30.074 participants (corresponding to a statistically weighted population of 127 million) Tanaka et al 2001[167] investigated the prevalence and risk factors of tendinitis and related disorders of the distal upper extremity among U.S. workers. There were 14.647 men and 15.427 women. The younger age included was 18 years, and the older age was just referred as >65 years. The disorders included were tendinitis, synovitis, tenosynovitis, de Quervain's disease, epicondylitis, ganglion cyst, and trigger finger. Diagnostic criteria were not informed, given that the cases were selected based on their answers declaring that one of the included diagnoses was confirmed by a medical person within the preceding 12 months. The analyzed occupational risk factors were bend/twist of hands/wrist and use of hand-held vibrating tools. The personal factors analyzed were gender, age, race, BMI, smoking history, education and family income. It was found only 4 cases of trigger finger, corresponding to a prevalence of 0,02 %. For the analysis of adjusted odds ratios the diagnoses tendinitis, synovitis, tenosynovitis, de Quervain's disease, trigger finger, ganglion cyst, and epicondylitis were referred altogether as tendinitis and related disorders. Only female gender and bending/twisting of the hands/wrist were significantly associated with these disorders (OR=2,51 95% CI 1,68-3,74 and OR=2,56 95% CI 1,58-4,16 respectively).

The major strength of this study is the large national sample with a high response rate and minimum of selection bias. Some limitations are the lack of information about which occupations were included; a limited assessment of exposure with only two parameters; and the possible recall bias for the exposure. Besides, because of the combination of trigger finger with so many other upper extremity disorders makes an application of these results specifically to trigger finger difficult.

Trezies et al 1998[190] investigated whether there were differences regarding the distribution of occupations among individuals presenting with trigger finger when compared to a population sample. It was included 177 cases of trigger finger treated at an orthopaedic surgery department, whose occupations were compared with the occupational data for the same county collected in the 1991 Census. Thirty-three cases were excluded because of a history of diabetes, rheumatoid arthritis or thyroid disease, resulting in 144 patients (61 men and 83 women). The mean age was 60 years. The occupations were distributed in four categories: unemployed / housewife / retired; office work; light manual work, and heavy manual work. No further information about the control group was given. Thirteen patients (9%) had prior trauma to the fingers, and 21 patients (15%) used vibrating tools at the work. For all four occupational classes, the data from the population sample fell within the 95% confidence limits of the trigger finger patients, indicating that the distribution of occupations in the two populations was not significantly different.

This is the first study comparing the distribution of occupations among trigger fingers patients with a population sample. The inclusion of surgical patients creates a bias, which may not represents the occupational profile of individuals with TF, given that a large part of the cases may not search medical assistance for mild symptoms, and that a considerable percentage of those who search treatment respond to conservative measures.

Gorsche et al 1998[191] analyzed the prevalence and incidence of trigger finger in a meat-packing plant. All employees performed tasks in separate departments designed for skinning, sawing, gutting, trimming, bagging, boxing, and loading beef products. Average age was 32 years. First, a cross-sectional study was performed with 665 workers to determine the prevalence of trigger finger in this plant. There were 572 men (86%) and 93 women (14%). The diagnostic criteria for trigger finger were: history of pain along the digit flexor tendon, and locking of the affected digit; and presence of palpable nodule at the distal palmar crease of the affected digit, and / or evidence of locking of the affected digit at the physical examination. Data on comorbidities, alcohol consumption, pregnancy, and prior hand surgery were recorded. Type and position of hand-held tool used, dominant hand, length of employment, and job description within the plant was also recorded by interview. The found prevalence of trigger finger was of 14% (93 cases). The prevalence was independent of age ( $P=0,71$ ). Among the prevalence group, 80 workers (86%) used a hand tool showing a relative risk of 1,9 ( $P=0,02$ ; 95% CI 1,1-3,8). This relative risk was unaffected by the hand position used to hold the hook or knife. Thirteen workers (14%) had multiple digits affected by TF in the left hand, 20 (21%) had multiple digits affected in the right hand, and 11 (12%) had bilateral involvement. The third and fourth digits were involved in 85% of cases.

Subsequently the group designed a follow-up study with 454 workers from the same sample without trigger finger, which were distributed in two cohorts, either tool users or non-tool users. The aim was to investigate the relationship between hand-tool use and the development of trigger finger. Criteria for tool use involved performing a job that required the application of a hand-held device to complete the task (ie, knife, hook).

The median period of the two follow-up intervals was 255 days. It was found 43 cases of TF among the tool use group and 3 cases in the non-tool use, resulting in person-year incidence rates of 12,4% and 2,6%, for a relative risk of 4,7 (95% CI 1,5-23,9;  $P<0,02$ ). Other biomechanical parameters were not evaluated. Multiple digit involvement in the left and right hands were 19,5 and 8,7%, respectively, and 13% were bilateral. The third and fourth digits were the most often affected in both left and right hands (94,7 and 78,1% respectively).

This is the first follow-up study associating TF with work activities. It is remarkable that, controversially to prior data, age and gender were not associated with prevalence or incidence of TF in this study. This could possibly be due to the overrepresentation of male workers in the study sample and the young age of the participants.

The main limitations of the study are the subjective assessment of occupational exposures and the high employee turnover in the plant (almost one-third of the workers examined at initial testing in the incidence study failed to make the second of two follow-up visits).

Moore and Garg 1994[174] performed a retrospective cross-sectional study with 230 workers in a pork-processing plant. The aim of the study was to determine the prevalence of different distal upper extremity disorders, and to investigate whether there was a relationship between occupational exposure factors and occurrence of such disorders. Personal factors, such as age and comorbidities were not taken into account, because of the lack of demographic information. The distribution of gender was not informed. The included diagnoses were medial and lateral epicondylitis, trigger finger, de Quervain's disease, carpal tunnel syndrome, and non-specific hand/wrist pain. The diagnostic criteria for trigger finger were subjective sensation of locking or impaired extension of the affected digit combined with either objective demonstration of triggering or palpation of a nodule along the flexor tendon that would be consistent with stenosis at the A1 pulley.

The exposure assessment was based on direct observations and videotapes of the various tasks performed at the plant, and included force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and cold temperature. Forty-four jobs within eight production departments were analyzed resulting in 32 job categories. Each job category was classified as hazardous or safe according to the predicted potential to cause upper-extremity disorders. This prediction was based primarily on the investigators' consideration of the exposure data plus their experience and judgment.

The hazardous categories required significantly greater strength and awkward wrist posture than the safe categories ( $P<0,01$ ). One hundred and four cases of diagnosed conditions were found among the 14 hazardous categories and 4 cases among the 18 safe categories. It was found 14 cases of trigger finger (9

men, 5 women), resulting in a prevalence rate of 6,0%. All cases of TF among males occurred in Wizard Knife operators and affected only the fourth and fifth digits of the right hand.

The relative risk of developing epicondylitis and stenosing tenosynovitis (trigger finger and de Quervain's disease) altogether among workers in the hazardous jobs was found as RR=19,4 (P=0,02; 95% CI not informed) when compared with workers from the safe job categories.

The main strength of this study is the detailed and objective assessment of exposure identifying both job tasks and specific ergonomic factors in relation to specific upper extremity disorders. A remarkable limitation is the lack of demographic information on the participants, which results in the lack of an analysis for possible personal confounders. Because the study did not consider each diagnosis separately, the application of the results specifically to trigger finger disorder is limited. However, as in the case of the study of Gorsche et al, the findings of such high prevalence of TF within a specific occupation requires attention and further analyses.

Armstrong et al 1987[176] studied the relationship between hand/wrist tendinitis with force, repetitiveness, and hand and wrist posture during work activities. A total of 652 workers were selected from the following occupational areas: electronics, sewing, appliance, bearing fabrication, bearing assembly, and investment molding plants. Age and sex distribution of the subjects were not informed. Hand and wrist tendinitis included de Quervain's disease, trigger finger, and "tendinitis/tenosynovitis". The diagnostic criteria for TF were: history of locking of the finger in extension or flexion; presence of a palpable nodule at the base of the digit, and locking of the digit in flexion or extension at the physical examination.

The workers were distributed among four groups regarding occupational exposures: low force – low repetitiveness; high force – low repetitiveness; low force – high repetitiveness; and high force – high repetitiveness. High repetitive jobs were defined as those with a cycle time of less than 30 seconds or with more than 50% of the cycle time involved in performing the same motion pattern. Low repetitive jobs were those with a cycle time of more than 30 seconds and with less than 50% of the cycle time involved in performing the same kind of motion pattern. High force jobs were those with estimated average hand force requirements of more than 4 kg, and low force jobs, those with estimated average hand force requirements below 1 kg. Peak hand forces were estimated from the weight of tools and material and then verified by means of surface electromyography.

It was found 16 cases of hand/wrist tendinitis. The specific diagnoses were not evaluated separately. They found a statistically significant increased odds ratio for the prevalence of hand/wrist tendinitis among workers performing jobs characterized by high force – high repetitiveness when compared with the low force – low repetitiveness group (prevalence of 10,8% versus 0,6% respectively; OR=29,4; CI not informed; P<0,001). This association was similar for both males and females. Although the overall prevalence was significantly higher in females (7,8%) than in males (1,7%), resulting in a job-adjusted odds ratio of 4.3. There were no associations with personal factors (use of birth control pills, hysterectomy, oophorectomy, recreational activities) or other work factors (exposure to hand/arm vibration and work posture). Work posture was evaluated by the percentage of work time spent in wrist flexion, ulnar deviation, wrist flexion and ulnar deviation, pinching, or pinching and wrist flexion.

The main strength of this study is the detailed assessment of work exposure. But some limitations can be named. The inclusion of other forms of tendonitis / tenosynovitis not further elucidated predisposed to overrepresentation of the cases, which limits the application of the results specifically to trigger finger disorder. The age of the workers is not informed and it is not clear whether the groups were adjusted for age. Even though the study sample is relatively large, the results are based on few cases found.

The method of assessment of force and repetitiveness used by Armstrong et al was prior described by Silverstein et al 1986[177] in a cross-sectional study of 574 workers from six different industrial sites regarding the occurrence of a miscellaneous of hand / wrist disorders. They also found significant positive associations between hand / wrist disorders and high force – high repetitive jobs. These associations were independent of age, sex, years on the specific job, and plant. The relevance of this study to the present review is very limited because the analyses for health outcomes included cases of tendonitis, tenosynovitis, de Quervain's disease, trigger finger, carpal tunnel syndrome, Guyon tunnel syndrome and digital neuritis all together.

#### **9.4 Case reports and series**

Lapidus and Fenton 1952[192] reported a surgical serie with 369 patients operated for trigger finger. There were 92 males (25%) and 277 females (75%). The average age was 46 years. Regarding the occupations of the patients, the largest groups were represented by housewives (n=162), sewing machine operators (n=34), needle workers (n=32) and clerks (n=27).

It was found two case reports on trigger finger in relation to occupational exposures. Rayan and Facs 1990[193] reported two cases of trigger finger in female bowlers, who had practiced this sport frequently for several months in one case and for approximately 20 years in another. And Ross 1978[194] described one case of TF in a regarded a caulker/burner, where the cause of TF was assumed to be trauma on the hand from a pneumatic metal chipper for one week; and a second case in a kitchen assistant, where the cause of TF was presumed to be unaccustomed trauma by the handle of a pelling knife during peeling vegetables for several consecutive hours for five weeks.

**Tabel 9.5 – Epidemiological studies on trigger finger in association with occupational exposures**

yrs = years; m = men; w = women; RR = relative risk; OR = odds ratio; CI = confidence interval

Reference	Population	Design	Exposure	Health outcome	Results - risk estimate referred when possible (95% CI)
Tanaka et al 2001[167] USA	n=30.074 (14.647 men, 15.427 women) Age: 18 - >65 yrs	Cross-sectional	bend/twist of hands/wrist use of hand-held vibrating tools	Tendinitis, synovitis, tenosynovitis, de Quervain's disease, epicondylitis, ganglion cyst, and trigger finger	OR for all health outcomes <u>together</u> : bend/twist of hands: OR=2,56 (1,58-4,16) hand vibration: OR=1,54 (0,93-2,55)  Adjusted for race, age, gender, BMI, education, income and smoking status
Gorsche et al 1998[191] Canada	n=665 workers in a meat-packing plant Mean age: 32 yrs	Cross-sectional	Use of a hand tool (knife, hook) for skinning, sawing, gutting, trimming, bagging, boxing, and loading beef products	Trigger finger	RR = 1,9 (1,1-3,8)
Gorsche et al 1998[191] Canada	n=454 workers in a meat-packing plant Mean age: 32 yrs	Follow-up	Use of a hand tool versus non-tool use	Trigger finger	RR = 4,7 (1,5-23,9)
Treziev et al 1998[190] UK	n=178 surgical patients (61 m, 83 w) Mean age: 60 yrs	Cross-sectional	unemployed/ housewife / retired office work light manual work heavy manual work	Trigger finger	No differences in distribution of occupations between patients with trigger finger and individuals from population sample
Moore and Garg 1994[174] USA	n=230 workers in a pork processing plant Age and gender not informed	Cross-sectional	Hazardous vs. safe job categories (based on force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and cold temperature)	Medial and lateral epicondylitis, trigger finger, de Quervain's disease, carpal tunnel syndrome, and non-specific hand/wrist pain	RR for epicondylitis, trigger finger and de Quervain's disease <u>altogether</u> = 19,4 (P=0,02; 95% CI not informed) among workers in the hazardous jobs
Armstrong et al 1987[176] USA	n=652 workers Age and gender distribution not informed	Cross-sectional	Force and repetitiveness Hand posture and hand / arm vibration  (occupational areas: electronics, sewing, appliance, bearing fabrication, bearing	Hand/wrist tendinitis (including de Quervain's disease, trigger finger, and "tendinitis / tenosynovitis" altogether)	OR for hand/wrist tendinitis = 29,4 (P<0,001) when jobs presenting high force – high repetitiveness were compared to the low force – low repetitiveness group

			assembly, and investment molding plants)		
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## 9.6 Discussion

### Design

There are only two epidemiological studies in the published literature that focused on trigger finger in an occupational context. The one is a cross-sectional study of the occupational distribution of surgical patients [190], and the other a cross-sectional survey followed by a follow-up study of employees at a meat-packing plant.[191] Both studies presented selection bias and had a relatively low number of participants. Besides, the study including a follow-up survey made a subjective assessment of the occupational exposures.

Three other cross-sectional studies did not present TF as the main health outcome, and three case reports / series assumed work activities to have contributed to the development of TF. The only study that presented an objective assessment of occupational exposures did not take personal factors into account in the final statistic analyses.[174]

### Diagnostic criteria

In three of the studies the case definition for TF was based on history of locking of the fingers, and presence of palpable nodules of the palmar tendons or locking of the digits on the physical examination.[174, 176] In one study the population studied was surgical patients[190], and in one study the diagnosis of TF was based on the subjects' answers declaring that this disorder was confirmed by a medical person.[167]

### Outcome

Currently there are only two studies in the published literature presented trigger finger as the main health outcome in relation to occupational exposures.[190, 191] The others studies included in this review considered trigger finger together with other disorders of the upper extremity such as de Quervain's disease and other forms of tendinitis, tenosynovitis and unspecific hand/wrist disorders.

### Exposure

The exposures evaluated in four studies were the following ergonomic factors: bend /twist of hands, and use of hand-held vibrating tools by Tanaka et al; use of hand-held tool (knife, hook) by Gorsche et al; force, wrist posture, type of grasp, speed of work, localized mechanical compression, vibration, time measurements and cold temperature by Moore and Garg; and force, repetitiveness, hand posture and exposure to hand / arm vibration by Armstrong et al. Trezies et al evaluated different occupations as the main exposure.

The fact that prevalence rates of TF as high as 6% and 14% were found within meat processing plants [174, 191], compared to rates of around 2% in the population [188], suggest that those occupations may expose the workers somehow to factors contributing to the development of TF. These findings require undoubtedly further investigations.

A major challenge in defining exposures potentially associated with the development of TF is the lack of standardized methods for evaluating the generic potential risk factors, such as force, posture, repetition, etc.

Moore and Garg proposed "The strain index" as a job analysis methodology for prediction of risk for distal upper extremity disorders in 1995.[195] Similar methods might serve as inspiration to overcome this challenge in future studies.

## 9.7 Pathophysiology

At the present moment the role of personal factors in the developing of TF, such as age, gender, race, rheumatologic disorders, and anatomical variations, has not been thoroughly explored.(kay 2000, wolf 09)

Similarly to the proposed physiopathology to de Quervain's disease there are currently three theories describing plausible mechanisms for the development of flexor tendon entrapment of the digits in the context of acute trauma and hand usage. [189]

- **Static compression**

Some clinicians have suggested that TF may be related to repeated, prolonged, or unaccustomed exertions. Gripping, pinching, or pressing with the fingers involve exertions that require tensile loading of the flexor tendons of the digits. Flexion of the metacarpophalangeal joint makes the flexor tendons turn a corner at the A1 pulley. Tensile loading of the tendons in combination with their turning a corner creates a compressive force between the tendons and the A1 pulley. The A1 pulley may respond to this



compressive stimulus with functional hypertrophy, fibrocartilagenous metaplasia, or both. The fibrocartilagenous changes in the pulley and granulomatous changes on the surface of the tendon (secondary to collagen fibril disruption) are consistent with compression being the critical mechanism.

Biomechanical studies of this proposed mechanism have shown that the duration of compression is more important than the number (repetition) of compressions. For example one prolonged exertion at relatively moderate levels of compression could be more significant than a series of brief and intermittent exertions at the same or higher levels of compression.

- **Repeated compression**

This theory relies on the same biomechanical argument as the static compression theory, except the number of episodes of loading during a period of activity is considered more critical than the accumulated duration of loading.

- **Acute trauma**

A single episode of acute trauma does not seem to be as common an aetiological factor for flexor tendon entrapment of the digits compared with de Quervain's tenosynovitis. At this time, no model of pathogenesis for this mechanism is proposed. It is to be expected, however, that such a model might be similar to the one proposed for de Quervain's disease.

If the proposed models for the pathogenesis of De Quervain's tenosynovitis and trigger finger are validated, and confirmed being the same, these and other forms of stenosing tenosynovitis might be investigated together and eventually treated under the same conditions.

## **9.8 Summary**

Trigger finger (TF) disorder is characterized by thickening and narrowing of the fingers flexor tendon retinacular sheath. The term trigger finger refers to the painful popping or clicking sound elicited by flexion and extension of the involved finger.

The lifetime risk for developing trigger finger was estimated around 2%, but increases up to 10% in diabetics. It occurs more frequently in the ages between 50 – 60 years and is more common among women than men. The reason for this age and sex predilection is not entirely clear.

The purpose of the present review was to elucidate the current evidence for an association between occupational exposures and the development of TF.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010).

We retrieved 1 follow-up study, 5 cross-sectional studies, 2 case reports and one surgical series presenting occupational factors in relation to TF.

The exposure assessed in 5 studies regarded specific ergonomic factors in manual work, and specific occupations in one study. A positive association between occupational exposures and TF was found in 5 studies, and one study did not find any association.

## **9.9 Conclusion**

The current knowledge base to understanding the causes for trigger finger is primarily limited to observations by clinicians and few descriptive results from epidemiological studies of workers within specific occupations. As a result no definitive conclusions about the relationship between trigger finger disorder and occupational exposures are possible at the present moment. The present level of evidence is considered limited (+) and further analytic controlled epidemiological studies are needed.

## 10. HYPOTHENAR HAMMER SYNDROME

### 10.1 Introduction

First reported by Van Rosen [196] in 1934, hypothenar hammer syndrome (HHS) is characterized by digital ischemia as a result of ulnar artery thrombosis. Conn and colleagues, in 1970, coined the term hypothenar hammer syndrome (HHS) for the post-traumatic digital ischemia. [197] Some authors consider it as an uncommon form of secondary Raynaud phenomenon, given that the initial clinical presentation of HHS is most commonly Raynaud phenomenon. [198]

Although considered a rare disorder, HHS may have a greater prevalence than the literature reports (fewer than 200 cases), as subjects with HHS may be asymptomatic. In previous studies of patients exhibiting Raynaud phenomenon, prevalence rates of around 1% were reported.[198, 199] However, among 79 mechanics who were usual hypothenar hammerers (automobile repairmen), Little and Ferguson found a 14% prevalence of asymptomatic ulnar artery occlusion.[200]

HHS is most commonly seen in males younger than 50 years of age.[198, 201] It occurs mainly in manual workers who experienced repeated trauma to the palm of the hand. Reports on various specific jobs are found, such as mason, painter, trucker driver, carpenter, metal worker, factory worker, roofer, and others. [198, 199, 202-206] The age and gender specific prevalence in population-based samples is unknown.

HHS it may also be a result of a single acute blunt trauma to the palm of the hand, as seen in around 10% of the cases in some reports.[198, 207-209]

A large number of sport activities have also been described to be associated with HHS. These include tennis, squash, golf, mountain biking, motorcycling, baseball, volleyball, handball, hockey, badminton, Frisbee, karate, and aikido.[197, 199, 202, 204, 210-217]

Because of the anatomic configuration of the Guyon canal, the ulnar artery is particularly vulnerable to mechanical injury due to its entrapment between a hammer (external force) and an anvil (the hamate bone). In patients with HHS, the hook of the hamate bone indeed strikes the superficial palmar branch of the ulnar artery in the Guyon space, leading to the development of 1) an aneurysmal dilatation of the ulnar artery with secondary downstream embolization; and / or 2) a local segmental occlusion of the ulnar artery [199, 202-204, 206, 218] Pathologic examination of resected artery has revealed intimal hyperplasia along with fragmentation of the internal elastic lamina and luminal occlusion by organized thrombi with or without aneurysm formation. Other histologic findings have included hemorrhage into the media and fibrosis of the vessel wall within the media and/or adventitia. [198] The reason that some patients had aneurysm and others had thrombosis is unclear. Van Rosen suggested that damage to the intima would result in thrombosis, whereas damage to the media would produce aneurysm.

Hypothenar hammer syndrome was recognized from its first descriptions as an occupational disease occurring mainly in subjects who use the hypothenar part of the hand as a hammer to pound, punch, push, strike, or twist objects. [198, 200, 206]

Clinical manifestations related to HHS are more often reported in the dominant hand (75%), which is exposed to repetitive trauma of the palmar ulnar artery.[198] When the non-dominant hand is involved, it is relevant to define whether this is the hand used for hammering.

The initial clinical presentation of HHS is most commonly Raynaud phenomenon, affecting the index, the long, and the ring fingers.[198, 199, 202, 204, 206] Other signs of HHS include ischemia and necrosis of the ulnar fingers, paresthesia and painful numbness in the fourth-fifth fingers, and neurologic symptoms. [198, 202-204, 209, 219]

Clinical characteristics distinguishing Raynaud phenomenon related to HHS from primary Raynaud phenomenon have been identified by Spencer-Green et al, specifically: 1) male predominance; 2) occupational history of repetitive hand/wrist trauma; 3) asymmetric distribution; 4) absence of the hyperemic phase; 5) diminished ulnar pulses; and 6) digital ulcers in areas supplied by affected vessel.[218]

Doppler examination, angiography (considered the gold standard test), multidetector computed tomography angiography, and magnetic resonance angiography (MRA) are the diagnostic methods performed for HHS. [198]

The aim of the present review is to elucidate the current epidemiological evidence for a causal relationship between occupational exposures and the development of hypothenar hammer syndrome.

## 10.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Hypothenar hammer syndrome
- Occupational
- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]
- Occupational Health [Mesh]
- Occupational Groups [Mesh]
- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Hand-Arm Vibration Syndrome [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]

The diagnostic criteria for hypothenar hammer syndrome were based on clinical and angiographic findings.

The electronic search in Pubmed retrieved 146 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 45 articles, which were considered relevant.

The articles presented the following designs: 39 reviews / background information, 2 cross-sectional studies, and 4 case series with more than 10 patients. We found 27 case reports presenting less than 10 patients, which are cited as background information under the discussion session.

The selected articles are discussed below and showed in table 1, listed according to descending year of publication and alphabetic sequence.

Marie *et al* 2007[198] reported on 47 patients diagnosed with HHS in their department among 4148 patients, who had been evaluated for Raynaud phenomenon in the period from 1990 to 2006. The aim of the study was to determine the prevalence of HHS in patients with Raynaud phenomenon and to assess the short- and long-term outcome of the patients presenting HHS. The diagnosis of HHS was based on the combination of the 3 following criteria: 1) thrombosis or aneurysm of the palmar ulnar artery on arteriography; 2) repetitive episodes of trauma resulting from the use of the hypothenar side of the hand as a hammer in either work or recreational activities, as well as acute palmar/wrist trauma; and 3) other causes of Raynaud phenomenon had been excluded—that is, primary Raynaud phenomenon, Raynaud phenomenon associated with underlying connective tissue diseases (mainly systemic sclerosis), vasculitis, thromboangiitis obliterans, atherosclerosis with subsequent thrombosis, arterial emboli from a cardiac source, as well as thoracic outlet syndrome, carpal tunnel syndrome, and hand/arm vibration syndrome. Sex, age, previous medical history of cardiovascular predisposing factors, and both occupational and recreational exposure to repetitive trauma of the palmar ulnar artery, as well as acute hand/wrist injuries were recorded.

The found prevalence of HHS among patients presenting Raynaud phenomenon was 1.13% (47 cases out of 4148 patients). There were 44 men and 3 women. The mean age was 42 years (range 30-62 years). Raynaud phenomenon was unilateral in 41 patients. Forty-three patients (93,6%) had occupational or

recreational exposure to repetitive palmar trauma, as follows: factory worker, mason, carpenter, metal worker, automobile mechanic, roofer, woodman, gardener, truck driver, wood carver, professional karate teacher, and aikido athlete practitioner. The mean duration of occupational exposure to repetitive palmar trauma at HHS diagnosis was 21 years. In 3 patients (6.4%), the onset of HHS symptoms could be clearly related to a single direct injury to the hypothenar area, which had occurred during the 6 months before HHS diagnosis. Most of the patients had concomitant comorbidities known to exacerbate HHS, including smoking (in 82.9% of the cases), dyslipidemia (14.9%) and arterial hypertension (17%). No patient had underlying connective tissue disease.

Only 2 patients, exhibiting digital necrosis and multiple digital artery occlusions, underwent reconstructive surgery, while 45 patients received conservative treatment. The median length of follow-up was 15.9 months. Thirteen patients (27.7%) exhibited clinical recurrences of HHS; the median time of HHS recurrence onset was 11 months. Outcome of HHS relapse was favorable with conservative measures in all cases. This is currently the study with the largest series of patients presenting HHS.

Ferris *et al* 2000[204] found 21 cases of HHS among 1300 subjects treated in a university clinical research center study of hand ischemia from 1971 to 1998. The prevalence of HHS on this population was hereby 1,61%. The diagnosis of HHS was based on angiographic findings. All patients were men on age 25-60 years (mean 42 years). All patients had occupations with exposure to repetitive palmar trauma within following activities: mechanic, equipment operator, industrial worker, woodworker, construction worker, electrician, steel worker, carpenter, miner, machinist, factory worker, and roofer. Sixteen patients (76%) were smokers. No patient had a history of previous hand injury, earlier Raynaud's syndrome, or connective tissue disorder. Three patients had abnormal serology results, consisting of lupus inhibitor in one patient, rheumatoid factor in one patient, and antinuclear antibody in one patient. Bilateral upper-extremity angiography was performed in 13 patients. Palmar ulnar artery abnormalities in the asymptomatic and the symptomatic hand were revealed by means of 12 of the 13 bilateral angiograms. The reason why bilateral angiograms were not performed in all 21 patients is not informed. Given the striking occurrence of bilateral abnormalities in patients with unilateral symptoms, Ferris and his colleagues proposed that patients with HHS might have a preexisting palmar ulnar artery fibrodysplasia, predisposing to the development of this disorder when the subjects are exposed to repetitive palmar trauma. This assertion is further discussed below.

Kaji *et al* 1993[220] investigated, in a cross-sectional study, the occurrence of HHS among 330 workers exposed to hand / arm vibration. Primary Raynaud's disease, obstructive arterial diseases, and connective tissue disorders were ruled out. Arteriography was performed in all workers. To hundred and ninety-three workers were diagnosed with "vibration disease", which is not further elucidated. Among those it was found 24 cases of HHS (23 men and 1 woman) on age 43 – 66 years (mean 55 years), resulting in a prevalence rate of 7,3% among vibration exposed workers. The right hand was involved in 53% of cases, the left in 25% and both in 22%. The occupations of the cases were coal miners and rock drillers, forestry workers, carpenter, worker of concrete plant and iron founder. The mean duration of vibration exposure was 19,4 years. Twenty-one of the cases were smokers. No other personal factors were registered. No further analyses on the occupational exposure were made.

Vayssairat *et al* 1987[199] reported on 17 cases of HHS diagnosed in their department of vascular diseases in the period between 1979 and 1985, resulting on prevalence rate of 1,7%. In 12 cases the symptoms were unilateral. There were 16 men and 1 woman on age 30-56 years (mean 40 years). The diagnostic criteria were: presence of thrombosis or aneurysm of the ulnar artery proved by arteriography, regular occupational or recreational use of the hand as a hammer, and exclusion of other diseases. The occupations of the cases were: metal worker, brick layer, printer, tailor, professional karate practitioners, and sculptress. The mean duration of exposure was 15 years. Fifteen patients were smokers.

Little and Ferguson 1972[200] studied 127 male mechanics from two maintenance shops with the aim of investigate the prevalence of HHS. The mean age was 38 years. Duration of employment, smoking status, symptoms, and working habits (with emphasis on the use of the hand as hammer) were recorded. Allen's test was performed with all workers and if it suggested artery insufficiency, Doppler examination was performed. Seventy-nine workers (62%) admitted using the palm of their hand as a hammer one or more times a day. Among those, 11 (14% of the 79 cases, and 8,6% of all workers) showed evidence of HHS in the dominant hand, with bilateral findings in 2 cases. All cases presented mild symptoms (cold sensitivity and intermittent paresthesia or color change), and had therefore never sought medical help. There was no case of HHS among the rest of the workers (48 men) who did not use their hands as a hammer at work ( $P < 0,004$ ).

There was no difference between the ages and length of employment of the hammerers and the non-hammerers. However, among the hammerers the mean age of subjects with HHS was significantly greater than the subjects with patent ulnar artery (49 vs. 36 years;  $P < 0,01$ ). Two young workers (21 and 27 years old) presenting HHS reported history of familiar Raynaud's phenomena and prior severe hand trauma respectively. The mean duration of employment for the cases of HHS

This study showed that the prevalence of sub-clinical ulnar artery occlusion can be high in certain settings, which induced the authors to propose, that workers in industries where the hand is used to hammer, push or squeeze strongly should be regularly screened for ulnar artery insufficiency with Allen's test. This suggestion has been supported by other authors since. [200]

Conn *et al* 1970[197] described 11 cases of HHS, which were part of a group of 39 patients with severe upper extremity ischemia treated at their department on the period 1966-1970, resulting on a prevalence rate of 28,2%. The diagnosis of HHS was based on angiography. All patients were men on age 28-63 years, and used the palm of the hand as a hammer either at work or at play. The specific work activities were not informed. Ten cases were unilateral affecting the dominant hand. None of the cases had evidence of generalized occlusive vascular disease. No other personal factors were registered.

**Table 10.3 – Cross- sectional studies and case series presenting more than 10 patients with hypothenar hammer syndrome**

HHS = hypothenar hammer syndrome; yrs = years; m = men; w = women; OR = odds ratio; ORm = odds ratio for men; ORw = odds ratio for women; CI = confidence interval

Reference	Population	Design	Exposure	Diagnostic criteria	Selected results – risk estimate referred when possible (95% CI)
Marie et al 2007[198] France	n=47 (44 m, 3 w) Age: 30-62 yrs	Case serie	Repetitive palmar trauma (n=44): factory worker, mason, carpenter, metal worker, automobile mechanic, roofer, woodman, gardener, truck driver, wood carver, professional karate teacher, aikido practioner Acute palmar trauma (n=3)	Arteriography	Prevalence of HHS among patients presenting Raynaud phenomenon: 1.13%
Ferris et al 2000[204] USA	n=21m Age: 25-60 yrs	Case serie	Mechanic, equipment operator, industrial worker, woodworker, construction worker, electrician, steel worker, carpenter, miner, machinist, factory worker, and roofer	Arteriography	Prevalence of HHS among patients with hand ischemia: 1,61%
Kaji et al 1993[220] Japan	n=330 workers Age: 43-66 yrs	Cross-sectional	Hand / arm vibration Occupations: coal miners and rock drillers, forestry workers, carpenter, worker of concrete plant and iron founder. Mean duration of exposure: 19,4 yrs	Arteriography	Prevalence of HHS among vibration exposed workers: 7,3%
Vayssairat 1987[199] France	N=17 (16 m, 1 w) Age: 30-56 yrs	Case serie	Metal worker, brick layer, printer, tailer, professional karate practitioners, and sculptress. Mean duration of exposure: 15 yrs	Arteriography	Prevalence of HHS among patients treated for vascular diseases: 1,7%
Little and Ferguson 1972[200] Australia	N=127 male mechanics Mean age: 38 yrs	Cross-sectional	Hammering of the hand to strike spanners and levers that will not yield to ordinary pressures. Mean duration of exposure: 29 yrs	Allen's test and Doppler examination	14% of the workers who used the palm of the hand as a hammer presented HHS
Conn et al 1970[197] USA	N=11 men Age: 28-63 years	Case serie	Use of the palm of the hand as a hammer either at work or at play (specific activities not mentioned)	Arteriography	Prevalence of HHS among patients with severe upper extremity ischemia: 28,2%

## 10.4 Discussion

### Design

The present review revealed that there are no epidemiological analytic studies on hypothenar hammer syndrome. The retrieved articles included 2 cross-sectional studies and 4 case series with more than 10 patients. The cross-sectional studies evaluated different exposures, which limit comparisons between the results. In all reports and studies no analyses for possible confounders, such as personal risk factors for vascular diseases, were made.

### Diagnostic criteria

Arteriography, which is considered the gold standard test for diagnosing HHS, was the diagnostic tool used by all the articles presented in this review. The Allen's test may be used as a screening tool.[220, 221] Jarvis *et al*[221] reported the 5 seconds cut-off as having a diagnostic accuracy of 79,6% (sensitivity of 75.8% and specificity of 81.7%), and the 6 seconds conventional cut-off as having a diagnostic accuracy of 78,5% (sensitivity of 54.5% and specificity of 91.7%).

### Exposure

Since its first reports by Van Rosen[196], HHS has been linked to occupational or recreational exposure to repeated trauma to the hypothenar region of the hand. While most of the case series found in the literature report prevalence rates of under 2% among patients treated in departments for vascular diseases, rates of up to 14% have been found among certain occupations.[200, 220] Various occupations involving any kind of trauma to the hypothenar area are reported, such as mason, painter, trucker driver, carpenter, metal worker, factory worker, roofer, among others.[198, 199, 202-206]

Sport practioners are also described among patients presenting HHS. There are reports on tennis, squash, golf, mountain biking, motorcycling, baseball, volleyball, handball, hockey, badminton, Frisbee, karate, and aikido. [197, 199, 202, 204, 210-217]

One single direct trauma to the hypothenar area has been reported associated with HHS, which is found in around 10% of the cases in some reports.[198, 207-209]

## 10.5 Pathophysiology

### • Repetitive trauma

The vulnerability of the ulnar artery to blunt trauma in manual workers who use the palm of their hands as a hammer is explained by its unique anatomic course. After exiting the Guyon's canal, being bounded dorsally and superficially by ligamentary structures and laterally by the pisiform and hamate bone, the superficial branch of the ulnar artery runs on the surface of the hypothenar muscles until terminating in the superficial palmar arch covered by the palmar aponeurosis. Along this 2–3-cm-long segment distal to Guyon's canal, the artery is protected only by soft tissue and skin, so that it is prone to trauma, since the hook of the hamate serves as an eminent counterpart. Even single injuries, but most repetitive traumas in terms of punching and pounding, will cause a lesion of the vessel wall. Affection of the intima could lead to thrombosis, whereas chronic damage to the media will be followed by the formation of aneurysms, both characterizing HHS. Both circumstances may promote embolic events leading to digital ischemia.[219]

But in contrast to the large number of working individuals being exposed, the prevalence of HHS is comparatively low. Therefore trauma alone does not seem to be the cause for the development of HHS.

An underlying vascular pathology, making the ulnar artery particularly susceptible to traumatic injury, has been discussed as a predisposing factor to HHS, among subjects exposed to repetitive trauma to the hypothenar region. This possibility was first suggested in a case report by Hammond *et al* 1993[222], in which they identified a patient with onset unilateral finger ischemia and a clinical history consistent with HHS. A thrombosed palmar ulnar artery was revealed by means of angiography. This patient had a known irregular ectatic ulnar artery, which was discovered during upper-extremity angiography performed for unrelated reasons 2 years earlier.

More specifically fibromuscular dysplasia has been suggested as the underlying abnormality of the ulnar artery in HHS.

Vayssairat *et al* [199] found angiographic patterns characteristic of fibromuscular dysplasia (alternating areas of stenosis and ectasia – “corkscrew” configuration), in the affected palmar ulnar arteries of 17 workers exposed to hammering of the hand.

Khatri *et al* [223] identified fibromuscular dysplasia of the ulnar artery distal to the wrist in a 20-year-old male college student who had recent-onset unilateral finger and hand ischemia without history of repetitive hand trauma.

And finally Ferris *et al* 2000 [204] reported on palmar ulnar artery abnormalities both in the asymptomatic hand and the symptomatic hand among 12 out of the 13 subjects, who had been undergone bilateral angiograms. Among their total sample of 21 patients, 19 were surgically treated and histologic results were available from 18 patients. Hyperplastic proliferation of the intima or media and disruption of the internal elastic lamina without inflammation, which are well characterized histologic findings of fibromuscular dysplasia, were present in all patients. [223]

Based on these findings and previous reports Ferris *et al* proposed that fibromuscular dysplasia of the palmar ulnar artery exists in patients presenting with HHS, making the artery more prone to form intraluminal thrombus from repetitive striking of the palm. [204]

But many questions must be answered before it can be conclusively stated that HHS results when preexisting ulnar artery FMD is subject to repetitive palmar trauma. These include: the prevalence of asymptomatic ulnar artery FMD in the population; the degree to which the asymptomatic hand of patients with FMD is also subject to trauma; why the big majority of patients reported with HHS are men, considering the general preponderance of women in FMD patient series; and whether subjects with HHS and FMD of the hands also have the later at other, more frequently reported sites. [204]

Another possible explanation to the relatively rare occurrence of HHS comparing to the large number of workers exposed to repetitive trauma to the hand, may be sub-clinical disease. This assumption is supported by the results of Little and Ferguson. They reported a 14% prevalence (11 out of 79) of sub-clinical HHS by using a combination of Allen’s testing and Doppler examination among workers who were usual hypothenar hammerers. [200] No radiographic or histologic studies were available.

However, none of the proposed aetiologies for HHS has been investigated in controlled epidemiological studies.

If the theory of the existence of underlying vascular abnormalities in HHS is proven correct, screening for such abnormalities of workers in jobs involving repetitive trauma of the hypothenar area might be necessary to prevent eventual digital ischemia, and its serious complications among predisposed individuals.

- **Hand/arm vibration**

Hypothenar hammer syndrome (HHS) and vibration-induced white finger (VWF) syndrome show both similarities and differences. This distinction is necessary to provide an appropriate approach especially concerning management and prognosis of these disorders. There is common agreement on that routine screening of ulnar artery patency by means of Allen’s test is essential on evaluating patients with VWF, but given that this test can be false negative in up to 25% of patients, angiographic studies may be required in doubtful cases. [219]

While the responsible pathologic process in VWF have been extensively studied and defined as a multifactorial disturbance of neural and hemostatic vasoregulatory components, the role of vibration exposure in HHS is not well established.

Reports on cases of arterial thrombosis in workers with hand / arm vibration syndrome suggest that vibration may contribute to the development of thrombosis seen in HHS. Noël *et al* 1998 [224] reported for instance one case of bilateral proximal ulnar artery occlusion in a worker exposed to hand / arm vibration for many years. Cases of isolated digital vessel thrombi without ulnar involvement in vibration-exposed workers have also been seen. [225, 226] And Usui *et al* 1990 [227] found that the diameter of the ulnar artery in the hand was smaller than the radial artery in over 70% of 454 vibration exposed workers.



Thompson and House 2006[225] proposed that resonance phenomena transmitted to the hamulus of the hamate and to the pisiform bone, associated with force applied to a tool against this region are the key to the development of thrombosis of the ulnar artery. This phenomenon might be attributed to activation of the coagulation cascade by vibration-induced shear stress damage to the vascular endothelium, but the literature does not provide much insight in this regard.[225]

- **Personal factors**

The personal factors mentioned in the literature in relation to HHS are the well known risk factors for vascular diseases, such as smoking, diabetes, arterial hypertension, hypercholesterolemia, and rheumatologic disorders.[198, 204] But none of these factors has been investigated specific in association with HHS in controlled epidemiological studies.

## **10.6 Summary**

Hypothenar hammer syndrome (HHS) is characterized by digital ischemia as a result of ulnar artery thrombosis. Hypothenar hammer syndrome was recognized from its first descriptions as an occupational disease occurring mainly in subjects who use the hypothenar part of the hand as a hammer to pound, punch, push, strike, or twist objects.

Although considered a rare disorder, HHS may have a greater prevalence than the literature indicates, as subjects with HHS may be asymptomatic or the nature of symptomatic cases may remain undetected. In previous studies of patients exhibiting Raynaud phenomenon, prevalence rates of around 1% were reported. It is most commonly seen in males younger than 50 years of age.

The purpose of the present review was to elucidate the current evidence for an association between occupational exposures and the development of HHS.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010).

We retrieved 2 cross-sectional studies, and 4 case series with more than 10 patients presenting occupational factors in relation to HHS. The exposures assessed in the epidemiological studies were hand / arm vibration and work with vehicle maintenance, which habitually require the use of the hand as a hammer. Both studies presented prevalence rates of HHS remarkably higher than expected rates from population samples. This consistent evidence is supported by a number of case reports / series.

## **10.7 Conclusion**

Thrombosis of the ulnar artery in Guyons canal is a rare highly specific disorder of the hand which, according to two cross-sectional studies and several case-series, seems to be almost exclusively linked to repetitive trauma of the hypothenar region by occupational or sport activity. Due to the high specificity of exposure and outcome, a plausible mechanism, and the fact that the disorder has seldom been reported in absence of hypothenar trauma, the clinical evidence for a causal relation between hypothenar repetitive trauma and ulnar artery anomaly in Guyons canal is considered strong (+++). The main uncertainty relates to limited knowledge on the prevalence of the condition in the general population. Thus, the epidemiological evidence is insufficient (0). The evidence that hand-arm vibration may cause HHS is insufficient (0).

## 11. KIENBOCK'S DISEASE

### 11.1 Introduction

Robert Kienböck, an Austrian radiologist, provided the first description of avascular necrosis of the lunate.[228] In 1910 he described an isolated disease of the lunate associated with secondary changes in the other carpal bones. Therefore necrosis of the lunate bone is commonly known as Kienbock's disease (KD), but it can also be found as lunate malacia, lunatomalacia and aseptic necrosis of the lunate bone in the literature. This process was believed by Kienböck to be a result of trauma. He believed that repeated sprains, contusions or subluxations lead to ligaments and vascular injury, resulting in loss of blood supply to the lunate. Acute fracture or trauma as an etiology has been implicated in many series as many patients report a history of injury preceding the exacerbation of symptoms. There are diverse reports on the presence of fracture lines in KD. However, it remains unclear whether these fractures are the cause of the result of a vascular necrosis.[229]

Ulnar variance (the height relationship between the radius and the ulna at the distal radioulnar and radiocarpal joints), which affects the distribution of force across the wrist, has long been discussed in the aetiology of KD. In 1928, Hultén, in an evaluation of 23 Swedish patients with Kienböck's disease, noted that 78% had an ulnar negative variance (the ulna is shorter than the radius), compared with only 23% of the general population.[230] This study led to a longstanding belief in an association between ulnar negative variance and avascular necrosis of the lunate. Though more recent studies evaluating patients of Asian ethnicity have shown that Kienböck's disease can occur in patients with ulnar neutral (equal lengths of ulna and radius) and ulnar positive variance (ulna longer than radius).[231]

Although mechanical, anatomic, and systemic mechanisms have all been implicated in the development of the disease process, no specific etiologic mechanism has been identified. It is most likely that a complex interrelationship between multiple factors contribute to the disease process.[232, 233] More details on the present theories about the development of KD are discussed below under the topic physiopathology.

It occurs most commonly in young adult men (age 20–40) and is rare in children, although some case reports have documented pediatric involvement.[234] It is rarely bilateral. [232, 235] Patients affected with Kienböck's disease typically present with pain and weakness in the wrist. Symptoms may be present a variable amount of time before presentation, although patients will often complain of longstanding symptoms that are progressive. For this reason, the natural history of this condition is not well known. The pain can be described from just mild and occasional to severe and debilitating. The clinical examination reveals localized dorsal wrist swelling about the lunate, likely due to synovitis, which is painful on palpation. Decreased range of motion, with loss of flexion and extension of the wrist joint, and loss of grip strength, is usually seen at the time of carpal collapse. There is typically pain at the end range of motion, particularly with extension. Forearm rotation is typically preserved. Radiographic evaluation can reveal isolated changes in the proximal aspect of the lunate, with eventual collapse and fragmentation.[229, 236]

The aim of this review is to present the current evidence for a relationship between occupational exposures and the development of Kienbock's disease.

### 11.2 Literature search

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010). The following searching keywords were combined using the relevant operators 'and' / 'or':

- Lunate malacia
- Kienbock's disease
- Osteonecrosis [Mesh]
- Lunate Bone [Mesh]
- Occupational
- Occupational Exposure [Mesh]
- Occupational Medicine [Mesh]
- Occupational Diseases [Mesh]

- Occupational Health [Mesh]
- Occupational Groups [Mesh]
- Occupational Accidents [Mesh]
- Industry [Mesh]
- Employment [Mesh]
- Hand-Arm Vibration Syndrome [Mesh]
- Occupations [Mesh]
- Disorders of Environmental Origin [Mesh]
- Environmental Exposure [Mesh]

The diagnostic criteria for Kienbock's disease were based on clinical and radiographic findings of abnormalities of the lunate bone.

The electronic search retrieved 213 articles. After selecting the articles as described under the topic 'methods and inclusion criteria' (on the introduction of this review) there were 13 articles, which were considered relevant.

The articles presented the following designs: 9 reviews / background information, 3 cross-sectional studies and 1 case serie mentioning KD in association with occupational exposure. The epidemiological studies are discussed below and presented in table 1, listed according to descending year of publication and alphabetic sequence.

Nakamura et al 1991[237] reported on 92 patients diagnosed with Kienbock's disease in their department in the period 1973-1987. They compared 10 patients, who were engaged in sports activities, with 82 manual laborers regarding age and sex distribution, radiographic and clinical findings, and symptoms. The sports practiced by the patients were: fencing, gymnastics, volleyball, tennis, karate, aikido, handball, and kung-fu. The occupations of the manual workers included carpentry, transport of heavy objects, use of pneumatic wrench, spot welding, and electrical work.

No differences regarding sex distribution, stage of the disease, range of motion in the wrist, grip strength, or radiographic findings were found. Sports active patients had a significant shorter period of insult prior to the onset of symptoms (mean of 5 years versus 9 years;  $P < 0,05$ ). Sport practitioners were younger than manual laborers (mean of 18 years versus 34 years;  $P < 0,001$ ), but younger people participate in more strenuous sports, so this difference probably did not reflect fundamental differences in KD between the groups.

This is the first report published in English proposing an association between KD and sports. The main weakness of this study is the lack of control for others possible confounders, such as comorbidities among the population studied.

Malchaire et al 1986[42] analyzed in a cross-sectional study bone and joint changes in wrist and elbow and their association with hand/arm vibration exposure. The study included 82 subjects exposed to pneumatic tools in quarrying and slitting granite blocks in stone pits, and a control group of 75 manual workers from the same environment who never been particularly exposed to hand/arm vibration. The mean age of the subjects was 34 years. The two groups were adjusted for age with roughly 50% of the workers being less than 30 years old and 30% more than 45 years old. The mean exposure time to vibration was 14 years. There was one case of KD in the control group (subgroup of 30-45 years old), and 11 cases in the exposed group (4 cases in the subgroup of 30-45 years, and 7 in the subgroup older than 45 years). This difference was significant only for the older age subgroup ( $P < 0,01$ ). There was no information about other personal factors, such as the presence of comorbidities and prior hand trauma. A possible correlation between exposure to hand/arm vibration and the development of bone disorders was discussed only for osteoarthritis and bone cysts.

The main limitation of this study is that Kienbock's disease was not considered a main outcome, but the difference found in the prevalence of KD was markedly significant. Some important biases to mention are that the radiographs were not read blindly, and half of the subjects studied were younger than 30 years, which could have limited finding more cases of KD.

Härkönen et al 1984[238] performed a cross-sectional study with 279 lumberjacks and 178 controls to analyze the occurrence of symptoms of vibration syndrome and radiographic findings of the wrists. The mean age in both groups was around 34 years (150 subjects were younger than 35 years) and the mean

duration of exposure to vibration among lumberjacks was 10 years. The study cited that among lumberjacks three workers presented lunatic necrosis, and that they had a history of wrist strain, but this exposure was not further elucidated. There were no cases of KD among controls. The main outcomes in the study were white finger symptoms and bone cysts radiographically detected, so statistical analyses were performed only for these diagnoses. The findings of lunatic necrosis were not discussed in the article

Similarly to the article presented above, the main limitation of this study is that Kienbock's disease was not considered a main outcome, so there were no statistical analyses regarding this diagnose.

Meilä et al 1963[239] presented a cross-sectional study of 852 workers exposed to hand/arm vibration who had taken radiographs of the hands at their departments through a period of 10 years. They found 7 cases of osteonecrosis of the lunate bone, i.e. a proportion of 0,82%. Three cases were detected among 338 workers from the metallurgic industry (use of pneumatic hammers), and 4 cases among 514 miners (use of rock and drill hammers). All patients denied prior traumas. None analyses of the exposures were made, and there was no information about other personal factors, such as the presence of comorbidities and age.

**Table 11.3 – Articles presenting Kienbock’s disease in relation to occupational exposure**

KD = Kienbock’s disease; yrs = years; m = men; w = women; OR = odds ratio; CI = confidence interval

Reference	Population	Design	Exposure	Selected results – risk estimate referred when possible (95% CI)
Nakamura et al 1991[237] Japan	n=92 cases of KD (10 sport practitioners, 82 manual workers) Mean age: 18 yrs for sports practitioners and 34 for manual workers	Cross-sectional	Sports: fencing, gymnastics, volleyball, tennis, karate, aikido, handball, kung-fu Manual work: carpentry, transport of heavy objects, use of pneumatic wrench, spot welding, electrical work	No statistical significant differences regarding sex distribution, stage of the disease, range of motion in the wrist, grip strength, or radiographic findings between the two groups.  Sport active patients had a significant shorter period of insult prior to the onset of symptoms (mean of 5 yrs versus 9 yrs; P<0,05)
Malchaire et al 1986[42] Belgium	n=157 workers (82 exposed, 75 controls) Mean age: 34 yrs	Cross-sectional	Hand/arm vibration (quarrying and slitting granite blocks in stone pits) Mean exposure: 14 yrs	11 cases of KD among workers exposed to hand/arm vibration versus 1 case among controls (P<0,01)
Härkönen et al 1984[240] Finland	n=457 (279 lumberjacks, 178 controls) Mean age: 34 yrs	Cross-sectional	Hand/arm vibration Mean exposure time: 10 yrs	Three cases of KD among the workers exposed to hand/arm vibration and none among controls
Meilă et al 1963[239] Romania	n=852 male workers Age not informed	Cross-sectional	Hand/arm vibration (use of pneumatic hammers in metallurgic industry and use of rock and drill hammers in mining)	Prevalence of 0,82% among miners and workers from metallurgic industry

## 11.4 Discussion

### Design

Only 3 cross-sectional studies and 1 case serie presenting Kienbock's disease as a health outcome in relation to occupational exposures were found. A positive association between occupational exposures and KD was found in 2 studies, and 2 studies were descriptive, i.e. did not make any analyses on possible risk factors.

The major part of literature published on this disorder is surgical series.

### Outcome

Two of the cross-sectional studies did not present KD as the main health outcome investigated.

### Exposure

The occupational exposures mentioned in relation to KD by the few studies found to this review are hand/arm vibration (reported in all 4 studies), manual work (not further specified – 1 study) and sports resulting repeated hand impact (1 study). The choice of such exposures is based on the mechanical theory for the development of KD, which is discussed below.

## 11.5 Pathophysiology

The lunate articulates proximally with the radius and with the triangular fibrocartilage (TFC). The thickness of the TFC is proportional to the negative ulnar variance: the shorter the ulna, the thicker the TFC. [241] Distally, in approximately one-third of the wrists, the lunate articulates only with the capitate bone. In the other cases, a second distal joint surface is present articulating with the hamate.[242] Lee 1963 [243] found that 26% of lunates had an arterial supply from either the palmar or the dorsal non-articular surfaces alone, by means of a single major vessel, 8% had palmar and dorsal vessels without intra-osseous anastomoses, and the remainder had a similar arrangement but with anastomoses.

Other authors reported that in between 7% and 20% of normal lunates only palmar vessels vascularised the whole bone, placing the lunate at risk of traumatic interruption of its vascular supply.[244] Pichler and Putz [245] studied the venous drainage of the carpal bones. They observed the existence of delicate periosteal dorsal and palmar venous plexuses, which were smaller for the lunate owing to its semicircular shape.

Although the precise aetiology of Kienbock's disease is not known, histological studies have shown that osteonecrosis is the factor leading to lunate fragmentation and collapse. There are currently two theories on the primary factor leading to osteonecrosis, one proposing vascular events as the main aetiological factor, and other proposing mechanical factors.

The vascular theory assumes that the loss of blood supply may be the consequence of primary circulatory problems. As noted above, a proportion of normal lunates are at risk of interruption of their vascular supply. Jensen 1993 and Schiltenswold et al 1996 measured high intra-osseous pressures in the lunate of patients with Kienbock's disease. In particular it was found that dorsiflexion of the wrist markedly increased the pressure, sometimes to above the systolic pressure. They also measured the intra-osseous pressure in normal lunates and found higher pressures than in the neighbouring capitate. These observations suggest that necrosis of the lunate might be the consequence of impaired venous outflow, and the last may occur secondary to systemic and/or local factors.[245-247]

Examples of such factors are conditions in which there is a tendency to hypercoagulability, decreased arterial inflow, or increased venous congestion.[233] Systemic corticosteroid use, sickle cell disease, cerebral palsy (with a consequent abnormally flexed wrist), and septic emboli have all been associated with osteonecrosis, although there is no defined correlation between these conditions and lunate osteonecrosis.[232]

According to the mechanical theory, necrosis of the trabeculae of the lunate is the consequence of progressive collapse of the bone under excessive loads, causing repeated microfractures or a major trauma. There would be a 'nutcracker' effect between the capitate and the relatively rigid radius on the radial side, and the relatively elastic TFC on the ulnar side. [248] Some lunates may be predisposed to collapse because of their particular anatomy causing an uneven internal distribution of the bone stresses. The initial lesion

might be a fracture caused by minor trauma. Interruption of the intra-osseous vessels may cause localised trabecular necrosis.[243] The anatomical factors that would create a significant risk are disputed in the literature. Since the initial observations of Hultén 1928 [230], many authors, but not all, have found a statistical relationship between negative ulnar variance and KD. (Schuind) This possible relation seems to vary geographically around the world. In East Asia, KD has been reported among patients with positive ulnar variance, a very rare observation in Caucasians.[232] Other anatomical factors that could play a role, are uncovering of the lunate by the distal radius, the shape of the lunate, the existence of a midcarpal facet on the lunate to articulate with the hamate, and the radial inclination of the distal radius.[241]. In favour of the mechanical theory is the fact that many patients recall initial trauma to the wrist, occasionally with an identifiable fracture line or even with scapholunate dissociation.[248, 249]

Theoretically both theories would be applicable in the setting of occupational exposures. For example activities requiring abnormally flexed wrist and / or predisposing to minor trauma at the wrist could be involved in vascular complications and microfractures of the lunate bone respectively. But none of these theories has been tested in epidemiological controlled studies in relation to work activities.

## **11.6 Summary**

Kienbock's disease (KD) is characterized by avascular necrosis of the lunate bone with secondary changes in the other carpal bones. It occurs most commonly in young adult men (age 20–40) and is rare in children, although some case reports have documented pediatric involvement. It is rarely bilateral. Although mechanical, anatomic, and systemic mechanisms have all been implicated in the development of the disease process, no specific etiologic mechanism has been identified.

The purpose of the present review was to elucidate the current evidence for an association between occupational exposures and the development of KD.

The relevant studies were identified through open searches and search using Medical Subject Headings (MESH-terms) in the US National Library of Medicine (Pubmed 1966 – July 2010).

We retrieved 3 cross-sectional studies and 1 case serie presenting occupational factors in relation to KD.

The exposure assessed in the studies was: hand/arm vibration (in all 4 studies), manual work (1 study) and sport activities (1 study). A positive association between occupational exposures and KD was found in 2 studies, and 2 studies were descriptive, i.e. did not make any analyses on possible risk factors.

## **11.7 Conclusion**

Given the very sparse literature on Kienbock's disease in relation to occupational exposures, the evidence of a causal association between KD and manual work or exposure to hand/arm vibration is insufficient (0). In another words, the available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

## 12. Overall Evaluation

Disorder	Level of evidence of causal relation to occupational exposures
Hand Osteoarthritis	Manual work: moderate (++) Hand/arm vibration: insufficient (0)
Nerve Compression Syndromes	Manual work: limited (+) Hand/arm vibration: insufficient (0)
Dupuytren Contracture	Manual work: limited (+) Hand/arm vibration: limited (+)
De Quervain's Disease	Manual work: limited (+)
Trigger Finger	Manual work: limited (+)
Hypothenar Hammer Syndrome	Repetitive trauma to the hypothenar region: * Clinical evidence: strong (+++) * Epidemiological evidence: insufficient (0) Hand/arm vibration: insufficient (0)
Kienbock's Disease	Manual work: insufficient (0) Hand/arm vibration: insufficient (0)



### 13. Videnskabelig bedømmelse

Denne rapport er videnskabelige bedømt af uafhængige reviewers. Deres kommentarer er efterfulgt af forfatterens bemærkninger hertil. Professor Anders Fuglsang Frederiksen, overlæge dr.med Sigurd Mikkelsen og professor Stengaard-Pedersen har endvidere foreslået en række sproglige korrektioner som vi har fulgt uden at referere disse her.

#### **Professor, overlæge, dr.med. Anders Fuglsang Frederiksen (AFF), Neurofysiologisk afdeling, Århus Sygehus**

**AFF.** "Til at graduere graden af evidens er benyttet kriterier foreslået af Dansk Selskab for Arbejds- og Miljømedicin. Man har ikke diskuteret hvorfor disse kriterier er valgt frem for andre evidensgraderinger for klinisk praksis. Er de benyttede kriterier evalueret, eller er de bedre til de valgte patientgrupper?"

***Forfatterne:** De anvendte kriterier er en modificeret version af kriterierne som anvendes af International Agency for Research on Cancer (IARC) og er ikke valgt specifikt til dette review, men er af Dansk Selskab for Arbejds- og Miljømedicin (DASAM) vurderet som relevant ved vurdering af årsagsmæssige sammenhænge indenfor Arbejdsmedicin. Kriterierne er baseret på de generelle principper for kausal interferens i epidemiologien.*

**AFF.** "Forfatterne har grundigt og meget konsistent gennemgået evidensen for sammenhæng mellem de forskellige sygdomme og arbejdsrelateret overbelastning af bevægeapparatet delt op i manuelt arbejde og hånd/arm vibration. I diskussionsafsnittet eller i introduktionen savner jeg en overvejelse over et differentialdiagnostisk problem, nemlig "Myofascial pain symptoms arising from muscle trigger points – tender points with referred pain" (ref. f.eks. Qerama et al. 2009), som kan spille en rolle ved diagnostik af nerve entrapment, hvis der ikke er foretaget neurofysiologisk bekræftelse af diagnosen, men også for enkelte af de andre lidelser."

***Forfatterne:** De valgte diagnostiske kriterier for nerve entrapment inkluderer både kliniske og neurofysiologiske tegn på nervepåvirkning for at undgå nævnte problematik. Diskussionen er kort opdateret som foreslået.*

#### **Professor, overlæge dr.med. Niels Sæe Nielsen (NSN), Ortopædkirurgisk afdeling, Gentofte Sygehus**

**NSN.** "In the past 30 years there has been growing awareness among health professionals dealing with Occupational Musculoskeletal Disorders or work-related diseases. The literature shows that the problems are found worldwide and lot of questions have been recognized for centuries. This systematic critical literature review focused on the current evidence for the relation between occupational exposures and occurrence of seven pathological conditions of the arm and hand. Two of the conditions are rare or underdiagnosed – hypothenar hammer syndrome and Kienbock's Disease in proportion to the five other conditions, which are very often seen in the clinic. The critical review shows that only the osteoarthritis and the hypothenar hammer syndrome has a moderate to strong level of evidence regarding to manual work and occupational exposures. This review is in great demand and would be of great help to understand these work-related conditions together with a treatment strategy."

#### **Overlæge dr.med. Sigurd Mikkelsen (SM), Afdeling for Arbejds- og Miljømedicin, Bispebjerg Hospital**

**SM.** "Jeg er af forfatterne blevet bedt om at kommentere afsnittet om Dupuytren's kontraktur, idet jeg for en del år siden har beskæftiget mig med dette område. Jeg har nærlæst afsnittet om Dupuytren's kontraktur, og Summary og Conclusion for Hand Osteoarthritis. Resten er kun kursorisk læst og er ikke kommenteret særskilt. Litteraturgennemgangen er samlet set meget velstruktureret og systematisk. Jeg har følgende kritiske bemærkninger/forslag til forbedringer:

## Litteratursøgning

Selve litteratursøgningen er beskrevet ved søgeord og MESH-termer (men ikke hvilke operators ('and' / 'or'/'not')). Søgningen kunne beskrives nøjagtigt som den er foretaget ved at tage en kopi af søgningen fra Pubmed. Det er ikke beskrevet, hvordan man kom fra et meget stort antal artikler til de få, der er valgt som relevante i litteraturgennemgangen. Er der læst titel og abstract på alle referencer? Eller er de først kasseret på titel, herefter på abstract og herefter på gennemlæsning? Man kunne evt. redegøre for antallet i hver gruppe. Hvilken procedure er fulgt, hvis der har været tvivl om, hvorvidt en artikel skulle indgå eller ikke indgå i den videre udvælgelse? Har der været nogen valideringsprocedure (fx ved at en eller flere andre fra forfattergruppen har læst et antal titler, et antal abstracts, og et antal artikler med henblik på om de skal indgå i næste trin)?

Litteratursøgningen går tilbage til 1966, inddrager kun engelsk litteratur, og der søges kun i Pubmed. Det er ikke oplyst, om der indhentes andre artikler end de, der findes ved litteratursøgningen, fx relevante artikler der indgår i andre reviews eller fra de referencer, der medtages i litteraturgennemgangen. Det er velkendt, at litteratursøgning i en enkelt database sjældent finder alle relevante artikler. Der er også lavet epidemiologiske undersøgelser før 1966, og de øvrige store europæiske lande er først for alvor begyndt at publicere på engelsk de sidste ca. 30 år. Disse begrænsninger synes jeg man er nødt til at skrive lidt om og diskutere, om det kan have medført at vigtige artikler ikke er medtaget."

**Forfatterne:** *Vi finder kritikken relevant. Der er dog inkluderet litteratur fra før 1966, som i nogle tilfælde er fremkommet ved søgning på Pubmed, men som i hovedparten af tilfældene er indhentet fra reference lister og reviews. Søgningssystematik er nu præciseret under afsnittet 'Methods and Inclusion Criteria' og under 'Literature Search' for hver lidelse.*

**SM.** "Til litteraturen vedr. Dupuytren's kontraktur har jeg følgende kommentarer (referencerne kan findes i de artikler, der er refereret og i Liss og Stock's oversigtsartikel fra 1996):

Skoog's gamle undersøgelser tror jeg indeholdt en tværnsnitsundersøgelse af skovarbejdere, men om der var en kontrolgruppe husker jeg ikke, så den reference skal måske/måske ikke med. Men hvorfor er undersøgelserne af Early(1962), Herzog (1951), Hueston (1960), Landgrot (1975), Patri (1982) og Cocco (1987), der er nævnt i Liss og Stock's oversigtsartikel fra 1996 ikke med i gennemgangen? Nogle af artiklerne er fra før 1966, men det er så ikke helt konsekvent, når Lawrence og Kellgrens undersøgelser fra 1958-1966 har fundet vej til afsnittet om osteoarthrose. Der er også en relevant befolkningsundersøgelse fra Island (Gudmundsson (2000)), der er nævnt i undersøgelsen af Lucas (2008), og en interessant artikel om bjergklatring og DC (Logan AJ et al, Br J Sports Med 2005, 39:639-44) som jeg tilfældigt faldt over. I den refererede litteratur er der ud over ovenstående flere andre referencer, som måske/måske ikke er relevante. Dupuytren's kontraktur er en gammel og velkendt lidelse, som arbejdsmedicinere i hele Europa har interesseret sig for siden den blev beskrevet af Dupuytren, så der kunne måske være relevante undersøgelser på andre europæiske sprog, og måske længere tilbage i tiden end 1966. Dupuytren's kontraktur har i mange år været en anerkendt erhvervs sygdom i Tyskland (jeg ved ikke om den stadig er)."

**Forfatterne:** *Artiklerne fra Early 1962, Herzog 1951, Hueston 1960 og Gudmundsson 2000 er inkluderet i nærværende opdaterede udgave af rapporten. Artiklerne fra Landgrot 1975, Patri 1982, Cocco 1987 er ikke inkluderet fordi de er skrevet på andre sprog end engelsk. Artiklen fra Logan 2005 er ikke inkluderet fordi deres cases of Dupuytren kontraktur var baseret på svar fra spørgeskema, og de diagnostiske kriterier anvendt for selektion af studier vedrørende Dupuytren kontraktur til denne review var baseret på klinisk diagnose. Litteraturopdateringen har ikke medført ændring i vores vægtning af den samlede evidens.*

**SM.** "Det er svært at se, hvilke undersøgelser, der lægges mest/mindst vægt på i den samlede vurdering. Kvaliteteten af de enkelte studier vurderes ved at fremhæve styrker og svagheder, og det er fint, men det er ikke let at få et billede af, hvad de reelt betyder for tolkningen i den efterfølgende opsummering i diskussionen. Og jeg er heller ikke for alle studierne helt enig i de styrker og svagheder, der fremhæves, men det er til dels subjektivt, hvad man mener om det. Fx mener jeg, at Bennet-studiet er meget svagt, næsten at sidestille med en case-story, der er hypotesegenererende. Studiet af Lucas er et rigtig godt studie, meget bedre end de øvrige, men det står der ingen steder. Mikkelsens befolkningsundersøgelse og Gudmundssons befolkningsundersøgelse (den sidste er ikke med i gennemgangen) er også gode. De peger alle på en sammenhæng. Angivelsen af "strengths and limitations" for Lucas' og Mikkelsen's studier er rigtige, - men hvilken vægt skal de tillægges? Hvor sandsynligt er det, at de påviste sammenhænge skyldes confounding, bias eller tilfældigheder? Studiet af Burke et al. er materiale- og metodemæssigt meget uklart

beskrevet. Det meget store antal personer må være rekrutteret over en lang årrække og dermed er der helt sikkert en masse støj betinget af mange undersøgere og formentlig metodeskift undervejs, men det skriver de intet om, - de beskriver det tværtimod som om der er styr på det hele, men det er der næppe. Det er muligt, at deres undersøgelse ikke peger på vibrationer som årsag til DC, men den siger ikke noget om fysisk manuel belastning som årsag. Thomas og Clarke's studie er efter min mening klart biased på grund af en kontrolgruppe, som slet ikke ligner case-gruppen, - det fremgår også af, at man finder en OR på 6.6. Det har ikke noget med den virkelige verden at gøre. Studiet bør tælle meget lidt i den samlede vurdering. Hvad med Kahn-studiet? Er det et godt studie i den her sammenhæng? - det har styrker og svagheder, men hvor stor vægt skal man lægge på undersøgelsens resultater? Er bjergklatrer studiet af Logan et al (se ovenfor) relevant i sammenhængen? Det er sådanne vægtninger og begrundelsen herfor jeg savner i diskussionen. Som diskussionen er nu er det mest en "optællings"-diskussion, - selv om gennemgangen også skal have kredit for, at der nogle steder er gode ansatser til vægtninger. Ovenstående gælder ikke kun afsnittet om Dupuytren's kontraktur. Det er også svært i Hand Osteoarthritis afsnittet at se anden begrundelse for at vurdere evidensen som moderat end at der er 12 positive studier ud af 17 studier, der finder en signifikant sammenhæng. Jeg har ikke gennemgået disse 17 studier, men nogen bør helt sikkert tillægges større vægt end andre i den samlede vurdering. Man skulle måske også overveje at opdele udfaldet i fingerarthroser og mellemhånds og håndledsarthroser."

**Forfatterne:** *Vurderingen af litteraturen er ikke baseret på en omfattende systematisk gennemgang af alle tænkelige former for bias i de enkelte undersøgelser. De styrker og svagheder som er fremhævet for hvert studie er udtryk for en vurdering af hvad vi har fundet væsentligt ved vurdering af årsagssammenhæng mellem arbejde og lidelse. I et opdateret diskussions afsnit har vi mere eksplicit vægtet den samlede evidens frem for at drøfte de enkelte undersøgelser, især fordi i de allerfleste tilfælde var undersøgelserne meget forskelligartede og derfor ikke sammenlignelige.*

**SM.** "Jeg savner en diskussion af, om man kan adskille vibrations-belastning fra "almindelig" fysisk håndbelastning. Det tror jeg ikke man kan (Bovenzi prøver (måske), men angiver ikke den mekaniske håndbelastning for kontrolgruppen eller for de tre vibrations-udsatte grupper). Så vibrationsudsættelse kan være en proxy for relevant manuel belastning, især hvis der arbejdes med tunge værktøjer (mejsler, motorsave mv). Men det er jo langt fra sikkert, at mål for vibrationsudsættelse er en god indikator for den manuelle belastning.

Man kan selvfølgelig ønske sig målinger, der mere nøjagtigt angiver belastningen af hulhånden, direkte og indirekte. Men jeg synes det er "overkill" og lidt akademisk at kalde det en svaghed ved disse studier, at der ikke foreligger sådanne målinger. Der er ikke nogen simpel løsning på at få repræsentative og objektive biomekaniske mål for kraftpåvirkningen af hulhånden. Det er heller ikke let at forestille sig en prospektiv undersøgelse af incidensen af Dupuytren's kontraktur, der er en lidelse, der udvikler sig gradvist og med meget usikker diagnostik de første mange år (gælder også osteoarthritis). Så det er to kritikpunkter, som jeg ikke synes man skal anvende som målestok for de undersøgelser, der er publiceret. Man kan tage det med i diskussionen. Jeg mener man må nøjes med en vurdering af, om man synes det beskrevne manuelle arbejde indebærer en betydeligt større håndbelastning end kontrolgruppens belastning."

**Forfatterne:** *Diskussionen om adskillelse af vibrationseffekter og biomekaniske belastninger er opdateret på basis af ovennævnte bemærkninger som vi tilslutter os.*

**SM.** "Det er efter min mening ikke særlig sandsynligt, at bedre confounderkontrol ville ændre ret meget på tolkningen af studierne. En undtagelse er måske socioøkonomisk status i de tilfælde hvor eksponeringen kun er målt som manuelt arbejde vs non-manuelt arbejde, men her vil justering for socioøkonomisk status måske være overjustering. Jeg synes derfor ikke, at man "bare" skal sige, at det er en svaghed, at der ikke er kontrolleret for en eller flere faktorer, men at man i stedet skal sige, at der er ikke kontrolleret for a, b, c ...etc., men at det ikke er sandsynligt at resultatet ville være anderledes hvis man havde kontrolleret for disse faktorer, eller det modsatte, hvis man mener det."

**Forfatterne:** *Vi er enige i at manglende confounderkontrol af velkendte determinanter for Dupuytren's kontraktur som arvelighed, alkohol og tobaks forbrug, diabetes og brug af fenobarbital næppe spiller nogen større rolle i praksis og ikke er den væsentligste mangel ved vurdering af evidensen.*

**SM.** "Patofysiologi-afsnittet i diskussionen kunne med fordel gøres en del kortere med fokus på de to hovedteorier for mekanismer relateret til mikrotraumer og cirkulationsforstyrrelser."

**Forfatterne:** *Vi har fulgt forslaget og forkortet dette afsnit.*

**SM.** "Sproget er gennemgående godt, men der er alligevel en del steder, hvor det er uklart, hvad der menes, så jeg tror det vil være gavnligt med en sproglig revision."

**Forfatterne:** *Der er foretaget en sproglig af foreliggende udgave.*

**Professor, overlæge dr.med. Kristian Stengaard-Pedersen (KSP), Reumatologisk Afdeling, Århus Hospital**

### **KSP. "General Comments**

#### **Title**

Normally soft tissue refers to muscles, tendons etc. Thus, it is unnecessary to use both the words musculoskeletal and soft tissue disorders. Words as 'workplace factors' or 'work relatedness' might be better than the sentence '.....to manual work and hand/arm vibration', it can also be discussed how systematic the selection of articles are and we suggest: 'A systematic critical literature review' should be changed to: 'A critical literature review' and the title could be changed to: Musculoskeletal Disorders of the Arm and Hand – Evidence of workplace factors in the development of hand osteoarthritis, nerve compression syndromes, Dupuytren's contracture, de Quervain's disease, trigger finger, hypothenar hammer syndrome and Kienbock's disease – A critical literature review"

**Forfatterne:** *titlen er ændret i henhold til ovenstående frasen at vi bibeholder ordene 'Occupational' og 'A systematic literature review' med henblik på at fremhæve at rapporten vedrører arbejdsrelaterede lidelser ligesom der efter vores opfattelse er foretaget en systematisk litteratursøgning. Dette fremstod umiddelbart ikke tydelig beskrevet, men efter revisionen af rapporten, er metoden /systematikken ved literatursøgningen nærmere beskrevet.*

#### **KSP. "Purpose:**

The review examines the epidemiological evidence, which associate musculoskeletal disorders (MSDs) of the upper extremity with exposure to physical factors at work. Understanding these associations and relate them to disease aetiology is critical to identify workplace exposures, which can be reduced or prevented. This could be emphasized even more by mentioning the persons who will benefit from reading the document: 1) Specialists in environmental medicine, 2) occupational and physiotherapists, 3) persons involved in re-education/rehabilitation to new jobs etc."

**Forfatterne:** *ovenstående forslag er inkluderet under introduktionsafsnit.*

**KSP.** "A short introduction, which reviews all the common causes of pain and decreased function of the hand and arm, is missing. Why is tendinitis (rotator cuff, golf or tennis elbow etc) as well as tenosynovitis (biceps, flexor and extensor tendons to the fingers etc.) not mentioned. Regional myofascial syndromes are not mentioned in the review. The most common type of arm pain from the cervical spine and more seldom diseases as polymyalgia rheumatica, arthritis, vasculitis etc. as well as pain that irradiates from the thorax should be mentioned. I suggest that the common causes of arm pain and decreased functions are mentioned by their diagnosis, one or two recent references and detailed motivation or reasons to chose only certain diseases of which some are very seldom."

**Forfatterne:** *Vi finder kritikken meget relevant. De hånd-arm lidelser som rapporten omfatter har i alt væsentligt været bestemt af projektudbyder, som ikke i udbudsmaterialet har begrundet, hvorfor man ønsker en vurdering af netop disse lidelser. Vi formoder at blandt de ovenfor nævnte sygdomme ikke er medtaget fordi der foreligger nyere litteraturgennemgange i den internationale litteratur. Disse forhold er anført i forordet.*

**KSP. "Medline literature search and selection of articles**

It is not possible to see how the different search words were combined to extract the certain number of articles and therefore, it will not be possible for other researchers to control the process. This could easily be explained in a table. After the search in Medline the authors have selected articles by the following criteria: original articles, articles published in English, observations in humans, and full text articles, however, this is not a sufficient explanation how 864 articles from the electronic search in PubMed after the selection process were reduced to 62 articles (page 12). It is necessary with clear selection criteria that allows researchers to follow the authors selection of articles on which this document is based."

*Forfatterne: Søgningssystematik er blevet nærmere præciseret under afsnit 'Methods and Inclusion Criteria' og under 'Literature Search' for hver lidelse.*

**KSP. "General aspects on tables**

For each study/reference the authors have the following headlines: population, design, relevant exposure, outcome, diagnostic criteria, and selected results that are relevant, but I miss a column with comments, which has the main strength and limitations of the study."

*Forfatterne: De relevante svagheder og styrker for hver enkelt studie er angivet i teksten og er udeladt af tabellerne for at skabe bedre overblik.*

**KSP. "Summary and conclusion of each chapter**

The summary is a repetition of what already has been mentioned in the introduction and it could easily be left out.

*Forfatterne: Formålet med afsnittene 'summary' er at præsentere et hurtigt overblik over hver enkel lidelse, som vi ønsker at bibeholde aht læsere som undlader at læse alle afsnittene.*

**KSP. "Key reference**

US Department of Health and Human Services (Public Health Service, Centres for Disease Control and Prevention, National Institute for Occupational Safety and Health) has published: Musculoskeletal Disorders and Workplace Factors - A Critical Review of Epidemiologic Evidence for Work-Related Musculoskeletal Disorders of the Neck, Upper Extremity, and Low Back. US Department of Health and Human Services (NIOSH), Cincinnati, USA, 1997 (Ed Bernard BD), <http://www.cdc.gov/niosh/docs/97-141/pdfs/97-141.pdf>. Although from 1997, there is much inspiration for the document in this reference, in terms of electronic research and selection criteria for the articles, analysis of the selected articles, and preparation of tables, and to summarize the main results into educational tables."

*Forfatterne: Vi er bekendt med denne væsentlige reference.*

**KSP. "Headlines/line spacing of introduction**

The chapter named introduction is divided in small segments by line spacing. However, it was not always easy to follow the definition/characterization of the disease, epidemiology, clinical manifestations, aetiology and pathogenesis, work factors known to influence disease development and progression, and finally the objective of this study. Pathophysiology is a large section under discussion, but the topic has only sporadically been dealt with in the introduction section, which is surprising. In general the section summary could be left out as it is only a repetition of what already has been mentioned earlier in the chapter. The conclusions might be even sharper and a few lines under the heading future aspects would more clearly show the authors suggestions for future research."

*Forfatterne: Introduktions afsnit er indelt i definition, epidemiologi, klinisk præsentation kortfattet ætiologi / kendte risiko faktorer. Vi har valgt at reddegøre mere omfattende for ætiologi og patofysiologi under diskussions afsnit fordi, for de fleste lidelser, er disse ikke veletableret endnu. Rapportens hovedformål er forklaret under den fælles introduktion, hvorfor man, under hver afsnit, blot angiver at formålet med review er at afklare den epidemiologiske evidens for en mulig årsagssammenhæng mellem den pågældende lidelse og arbejde.*

## **KSP. "Specific comments**

### **Hand osteoarthritis**

"The ACR Criteria for Osteoarthritis should be used and cited in the introduction."

**Forfatterne:** *Vi er enige i at disse burde nævnes, og der er nu refereret til dem i indledningen . ACR's (American College of Rheumatology) kriterier for hånd osteoarthrose er udelukkende klinisk. Man finder ikke at det er nødvendigt med røngtnologiske forandringer for at kunne stille diagnosen. Da studierne generelt har anvendt meget forskellige kliniske inklusionskriterier, har vi valgt at inkludere artikler, hvor såvel kliniske fund som radiologiske forandringer indgår.*

**KSP.** "A little uneducational rattling off analysis of the most important selected articles, but the analysis is alright and it is positive to end with strength and limitations of each study. How are the seven case reports mentioned a part of the analysis and not among the many discarded articles?"

**Forfatterne:** *Som nævnt i det opdaterede afsnit om metode og inklusionskriterier er literaturgennemgangen baseret på kontrollerede undersøgelser med estimering af risiko for anførte lidelse som funktion af arbejdsmæssige risikofaktorer. Deskriptive studier og case serier, som specifikt omhandlede arbejdsmæssige eksponeringer, blev inkluderet for at støtte baggrundsinformation og diskussion.*

**KSP.** "Under the section Diagnostic Criteria I miss a reference to the ACR Criteria/definition of osteoarthritis (clinical, biochemical, radiological) and also that there is no good agreement between radiological osteoarthritis and pain/decreased function. Further, what should the consequences be of the not clearly specifying diagnostic criteria as well as the degree of pain and disablement in the studies?"

**Forfatterne:** *Der henvises venligst til kommentar ovenfor. Under introduktionsafsnittet for osteoarthrose er det angivet at der ikke findes god korelation mellem radiografisk verificeret osteoarthrose og symptomer. Grunden til at studier som alene vedrører symptomer på osteoarthrose ikke er inkluderet er anført i introduktionsafsnittet for osteoarthrose.*

### **KSP. "Nerve Compression Syndromes**

A figure, which shows the location of the different nerve compression syndromes and their frequency would be helpful or it could be shown in a table,"

**Forfatterne:** *Vi har forsøgt at præsentere det overskueligt i teksten.*

**KSP.** "I miss a discussion of the methods including the electronic research and selection criteria, hereunder possible selection bias in this study."

**Forfatterne:** *Vi tillader os at henvise til svar vedrørende systematikken ved litteratursøgning ovenfor under de øvrige reviewere.*

### **KSP. "Dupuytren's Contracture**

The methods of this document including electronic search results and selection criteria should be easy to follow and possible selection criteria should be discussed here."

**Forfatterne:** *Se venligst ovenfor.*

### **KSP. "De Quervain's Disease**

A discussion of the methods with focus on a possible selection bias is missing."

**Forfatterne:** *Se venligst ovenfor.*

### **KSP. "Trigger Finger**

The single selected studies are analysed briefly and their strengths and limitations finally emphasized. Except for the overlap of the text in the tables it is a clear 'results' chapter. How can the two case reports on be more important than the many discarded articles?"

**Forfatterne:** *Vi er enige i at case-reports repræsenterer svag evidens for årgssammenhæng men hvor der kun findes meget sparsomme studier med stærkere designs er enkelte case-studier medtaget.*

**KSP.** "Electronic research and selection criteria, which is the basis for this critical review, should be discussed. The authors should account for possible selection bias."

**Forfatterne:** Vi henviser venligst til bemærkninger om litteratursøgningen ovenfor.

**KSP. "Hypothenar Hammer Syndrome**

Why was such a seldom condition selected instead of more common conditions e.g. tendinitis and tendovaginitis?"

**Forfatterne:** Som nævnt under den introduktionsafsnittet er indholdet i denne rapport anført af Arbejds miljø forsknings fondet, der har finansieret udarbejdelsen af dokumentet.

**KSP.** "The electronic search and selection criteria in the section 'methods' should be appropriately discussed."

**Forfatterne:** Vi henviser venligst til bemærkninger om litteratursøgningen ovenfor.

**KSP. "Kienbock's Disease**

The electronic search and selection criteria should be appropriately discussed."

**Forfatterne:** Vi henviser venligst til bemærkninger om litteratursøgningen ovenfor.

**KSP. "References**

The reference list has not been checked in details."

**Forfatterne:** Tak. Vi har opdateret referencelisten.

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