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RESEARCH PAPER

The Use of Palaeopathological or Historical Data to Investigate the Causation of Disease

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This paper describes how palaeopathological or historical data can be used to investigate the comparative importance of internal or external causes of diseases that may affect bone. Two examples of the method are given: osteoarthritis of the costo-vertebral and costo-transverse joints of the spine, and the infectious disease, osteomyelitis. In the former case we suggest that the palaeopathological data support the view that internal factors are much the most important, since the characteristics of the disease are similar in skeletons widely separated in time and space. In the latter case, in which historical medical data have been used, it seems probable that the decrease in the prevalence of the disease in recent times has been due primarlly to external factors, particularly improvements in hygiene and diet. We hope that these findings will stimulate others to apply this methodology to other pathological considtions affecting the skeleton.

Introduction

Most diseases are caused by varying combinations of intrinsic and extrinsic (internal and external) factors, the former including age, sex and genetic make-up, and the latter such things as diet, activity, and personal habits. The relationship between them has been most extensively studied in relation to infectious diseases such as measles, malaria, and cholera (Koelle & Pascual 2004). Determining which factor is of most significance in a particular case can be important in a public health context as it is generally easier to control external factors when devising strategies for disease control.

One of the most interesting aspects of palaeopathology is the study of changes in the epidemiology of diseases, again with a view to determining which factors – internal or external – might have contributed most to any that are noted. This can be achieved, for example, by determining either the prevalence or distribution of a disease in assemblages that are widely separated in time or space, or by comparing the epidemiology of the disease in an archaeological assemblage with that in a modern comparison. In each case it will be known that the individuals within the assemblages are likely to have varied considerably in their life-styles, habits, and activities. Thus if the features of the

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disease are the same in each of the separated groups, it would seem reasonable to conclude that internal, rather than external factors are the more important in its causation. Conversely, if the characteristics of the disease differ substantially, further investigation could be undertaken to determine which of the external factors might have contributed substantially to its causation.

This paper reports two examples of this methodology here, the first concerning a specific type of osteoarthritis (OA), and the second the infectious disease osteomyelitis. These diseases have been chosen because there are good comparative data from populations widely separated in time and space. Other diseases have been more widely studied in the palaeopathological and historical literature but in many cases it is not possible to derive the epidemiological data required for comparative purposes, either because none is given in sufficient detail, or the methods by which prevalences have been calculated are either in error, or not explained sufficiently clearly to ensure that they make for valid comparisons with data presented here. It is hoped that this paper may stimulate further research in this area and if the approach is successful, the results could inform strategies to control aspects of modern disease.

Osteoarthritis of the costo-vertebral and costo-transverse joints

Osteoarthritis (OA) is a disease of the synovial (freely moving) joints and is the most common disease seen in skeletal assemblages. It is an age-related degenerative joint disease resulting from a breakdown of articular cartilage in synovial joints such as the costo-vertebral (CV) and costo-transverse (CT) joints (Arden & Nevitt 2006; Garner, Alshameeri & Khanduja 2013). There are several known precipitants of osteoarthritis: internal factors such as age, sex, obesity and genetic predisposition; external factors include movement (and by implication activity or occupation), and trauma. There are also some other disease that predispose to osteoarthritis but they are relatively uncommon compared to other factors (Felson *et al.* 2000).

The costo-vertebral and costo-transverse joints connect the ribs to the thoracic vertebrae. The anatomy of the CV joints is somewhat complicated. The head of each of the twelve ribs articulates with the body of the adjacent vertebrae. The second to tenth ribs articulate with their own vertebral body but also with the one above, forming superior and inferior synovial joints separated by a ligament that arises from the V-shaped head of the rib and inserts into the intervertebral disc. Ribs one, eleven and twelve form only a single joint with their corresponding vertebra and, by convention, these are referred to as superior joints. Thus there are twelve superior and nine inferior CV joints on each side. Only the first ten ribs form a costo-transverse (CT) joint between the neck of the rib and the transverse process of the corresponding vertebra. In total, therefore, there are 62 separate joints in this complex.

Materials and Methods

Skeletons were examined from three Medieval Nubian sites: 3-J-18, located at the fourth cataract of the Nile, and Soba East and Gabati which are much further south. The sites all date to approximately AD 500 – 1500, and were excavated by the British Museum and the Sudan Archaeological Research Society. All the material is stored in the British Museum.

The entry criteria for the study were that skeletons had to be fully adult with intact spines and enough of the remainder of the skeleton to permit age and sex estimations using standard anthropological techniques. Age and sex estimates were based on the pelvis whenever possible, due to the comparative accuracy of these methods and the excellent preservation of the pelvis in most of the specimens. Sex was estimated using pelvic morphology, including the width and shape of the sciatic notch and shape of the subpubic region. Age was estimated using both the pubic symphysis method and auricular surface methods as outlined in Buikstra and Ubelaker (1994).

A total of 78 skeletons was selected. Each of the CV and CT joints was carefully examined macroscopically and OA was diagnosed in the presence of eburnation, or if eburnation was not present, if two of the following four features were noted: marginal osteophyte, new bone on the joint surface, pitting on the joint surface, or alteration in the joint contour (Waldron 2009). The prevalence of OA at each anatomical site was calculated, using the number of affected joints as the numerator and the total number of joints (normal + diseased) as the denominator; 95% confidence intervals (95%CI) were also calculated.

Results

There were small difference in prevalence between the right and left sides, and between males and females, but these were not statistically significant (that is, the 95%CI did not overlap ($p > 0.05$)). Nor were there statistically significant differences between skeletons from the three archaeological sites, which were then considered together in further analyses. The distribution of OA in the upper CV joints for all skeletons is shown in **Figure 1**. The only significant difference in prevalence was in the age categories – young adults versus old adults – where, as expected, the old adults had a higher prevalence of OA (**Figures 2** and **3**). However, it was notable that both age categories had the same distribution of OA of

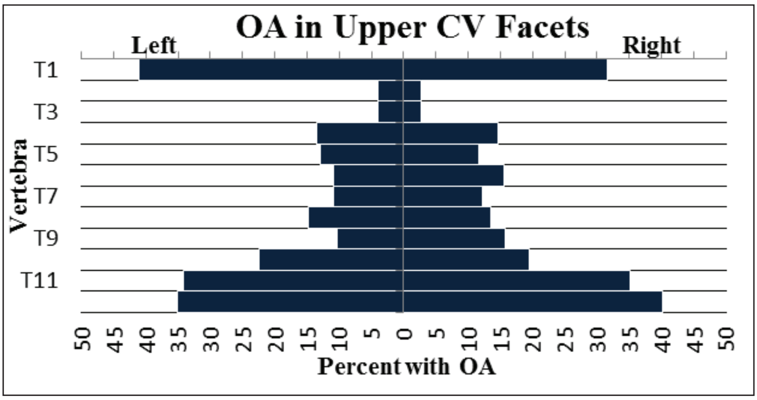

Figure 1: Prevalence of OA in superior CV joints for all skeletons combined.

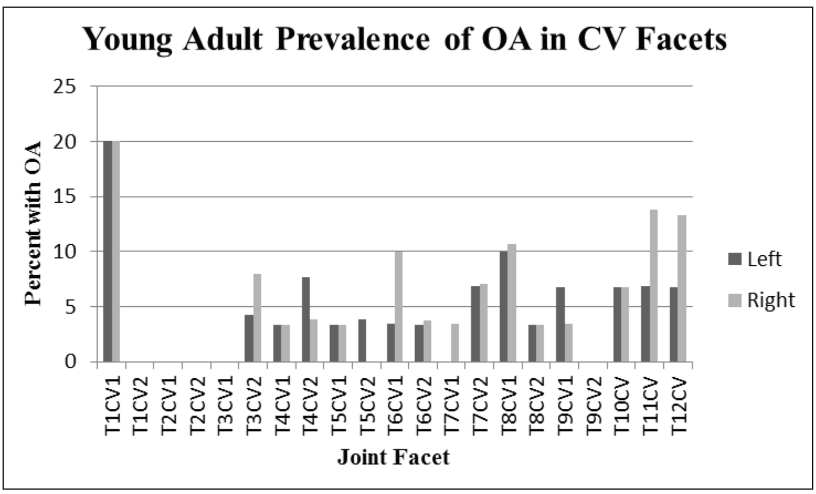

Figure 2: Prevalence of OA in CV joints in young adults.

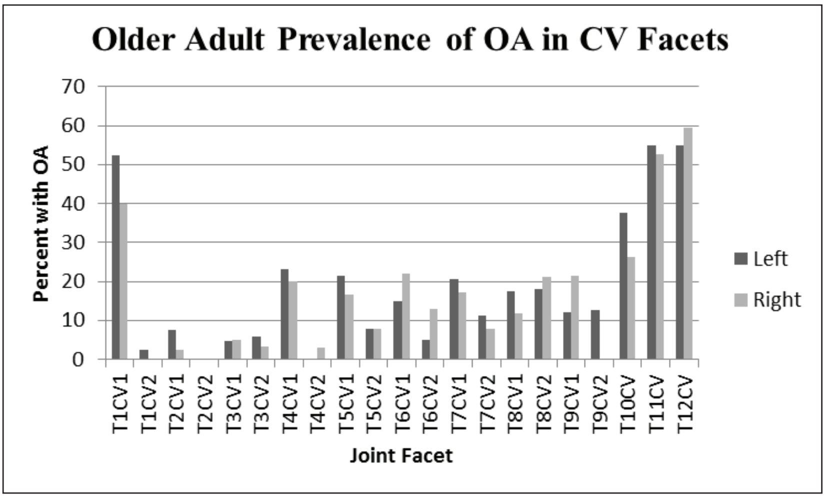

Figure 3: Prevalence of OA in CV joints in older adults.

the CV joints, with pronounced peaks at the levels of the first, eleventh and twelfth ribs (see **Figures 2** and **3**). Generally the superior CV joints had a higher prevalence than the lower, while for the CT joints the highest prevalence was found for the four lowest joints (the seventh to the tenth).

Discussion

Results were compared to those of two other studies, one by Nathan and his colleagues who examined 346 skeletons from the Hamann-Todd collection (Nathan *et al.* 1964) and Bevan's study of 113 skeletons from Medieval and post-Medieval London (Bevan 2007). The Hamann-Todd collection contains approximately 3,000 skeletons that were collected between 1893 and 1938 and is now housed in the Cleveland Museum of Natural History. Nathan and his colleagues found that approximately 48% of the skeletons in their sample had OA in at least one CV joint and that there were peaks in prevalence at the first, eleventh and twelfth ribs, as was found in the Nubian material. Bevan also found that the distribution of OA within the spine in her material from Medieval and post-Medieval London was the same for both time periods, with peaks also at the level of the first, eleventh and twelfth ribs. Nathan and his colleagues did not examine the CT joints but in Bevan's study, the distribution was essentially the same as in the current study, with the highest prevalence in the four lowest levels.

The results from these three studies of material widely separated in time and space, and representing individuals whose ways of life must have differed considerably from each other, strongly suggest that external factors such as environment and occupation or other activities must have contributed much less to the causation of their OA (at these joints, at least) than internal factors such as the structure, and movement of the joints. Osteoarthritis is a chronic disease with a multifactorial aetiology that may affect different joints in different ways (Arden & Nevitt 2006). Recent clinical research suggests there may be a strong genetic component to the development of OA (Garner, Alshameeri & Khanduja 2013), and these genetic risk factors also seem to be specific to different joint sites (Reynard & Loughlin 2013).

Mechanical factors such as repetitive joint loading also increase the risk of OA in a joint (Arden & Nevitt 2006). While the CV and CT joints do not experience joint loading stress in the same way as the weight-bearing joints such as the knee or hip, they do experience biomechanical stress from the constant movement caused by respiration. This, along with chemical mechanisms affecting the articular cartilage metabolism, could influence the presence of OA in non weight-bearing joints such as the CV and CT joints (Garner, Alshameeri & Khanduja 2013).

While genetic and environmental factors likely played a role in the development of OA in the skeletons examined, the remarkable similarity in the pattern of CV and CT joint OA across temporal and geographic regions suggests that biomechanical stress is a particularly strong aetiological factor in the development of OA in these particular joints.

Osteomyelitis

Osteomyelitis is a primary bone infection caused most commonly by the pus-forming bacterium, *Staphylococcus aureus*. Bones usually become infected by the spread of the organism through the blood stream (so-called haematogenous spread) from an infection on the skin; in the past this would most often have been a boil. The infection tends to affect young children when their bones are growing actively, and the knee is one of the most common sites for the infection to settle (Kaplan 2005).

Osteomyelitis was known to the writers of the Hippocratic corpus and to Galen, who practiced in Rome during the first century BCE. It was described by early writers as frequently following a compound fracture, and its treatment was undertaken by surgeons from the Medieval period onwards, most usually by amputation of the affected limb. The first clinical account of haematogenous was made by physicians in the 18th century using terms for the condition such as caries, necrosis, or fever sore (Klenerman 2012: 14–15). The term osteomyelitis was coined by Auguste Nélaton in his thesis of 1836 (Nélaton 1836).

Materials & Methods

Rather than using data from skeletal assemblages, in which the disease is uncommon (not usually occurring in more than *ca* 1% of skeletons) data were obtained from historic hospital records stored on the Historic Hospital Admissions Records Project (HHARP).[1] In this way a much larger number of cases could be obtained. The records are from a number of children's hospitals in London, and the Glasgow Children's Hospital (GCH). For the present purposes, records from the largest of the London hospitals, Great Ormond Street Hospital (GOSH), were used together with those from GCH. The records for GOSH were available from March 1895 to March 1914, and for GCH from September 1890 to January 1904. By this time, the disease was well understood and the term osteomyelitis had been in medical use for well over half a century. The records were searched for all cases admitted with a diagnosis of osteomyelitis over the entire period for which records were available; cases with bony tuberculosis were excluded even though many of these were diagnosed simply as osteomyelitis. From each of the records, personal data were extracted including name, sex, age on admission, bones affected, length of stay, and outcome (cured, relieved, or died). For the fatal cases, the cause of death was ascertained wherever possible.

There were a total of 155 admissions over the whole period: 99 at GOSH and 56 at GCH. The sex ratio was close to unity although with a slight preponderance of females (the ratios were 1:1.3 and 1:1.2 for GOSH and GCH, respectively). A small number of children were admitted on more than one occasion, eleven at GOSH and three at GCH, so that the total number of admissions relates to 129 individual cases. At GOSH the long bones were affected in approximately 83% of cases; in two-thirds of these, the femur and/or the tibia were involved. The situation at GCH was similar; here 87% of cases involved the long bones of the leg. The mean age on admission, case fatality rates and cure rates were similar in both hospitals (**Table 1**). In all instances where it could be determined, death was the result of septicaemia (infection in the blood stream), which was well known to be the most common cause of death in osteomyelitis at the time (Owen 1906).

	GOSH	GCH
Number of cases	99	56
Mean age on admission in years (standard deviation)	5.0 (3.5)	5.8 (3.8)
Number of deaths	19 (13 boys, 6 girls)	14 (10 boys, 4 girls)
Case fatality rate	25% boys, 19% girls	36% boys, 16% girls
Cure rate	29% boys, 33% girls	33% boys, 35% girls

Table 1: Vital data for admissions to Great Ormond Street Hospital (GOSH) and Glasgow Children's Hospital (GCH) for patients admitted with osteomyelitis.

Discussion

The features of osteomyelitis in late Victorian and early Edwardian Britain are similar in many respects to those of the present-day disease, in Westernised countries at least. Thus, in contemporary society it remains a disease predominantly of the young, with the femur and the tibia being most commonly affected (Goergens *et al.* 2005) as was also the case in the late 1920s (Hughes 1927). It was then, and is now a relatively uncommon disease with an incidence reported in a modern study from the Royal Hospital for Sick Children in Glasgow (the successor to GCH) as being 2.9 per hundred thousand (Blyth *et al.* 2001). Unfortunately it is not possible to calculate either the incidence or the prevalence of the disease in the population from the historic admission records as the denominators necessary for these calculations are not known. Nevertheless, it seems reasonable to suppose that the disease was more common in the past than it is now. At GOSH the disease accounted for about 0.15% of all admissions in the five years beginning 1890 but was 0.76% after 1900, an increase that was significant at p = 0.05 Contemporary proportions are generally substantially lower than this although whether the disease is increasing or decreasing in prevalence nowadays is not clear. An Australian study found that the proportion of cases of osteomyelitis admitted between 1968 and 1972 was 0.17%, and 0.12% between 1998 and 2002; this difference was not statistically significant (Blyth *et al.* 2001). An earlier study from Australia, by contrast, showed that the frequency rose after 1951, which has been suggested to be due to the infectious organism (presumably *S. aureus*) becoming resistant to penicillin (Gilmour 1962); it is hard to see how resistance to antibiotics would have affected the numbers presenting with the disease, however, although it may have affected the outcome. More recent data from the USA have shown an increase in frequency, rising from 0.26% to 0.60% of all admissions over a four year period, an increase that was considered to be due the emergence of methicillin resistant strains of *S. aureus* (Arnold *et al.* 2006). Again it is difficult to follow this argument since the knowledge that the infectious organism was resistant to treatment would follow only after treatment had begun.

It is not certain what organisms were responsible for the development of osteomyelitis in the children represented in the historic hospital records, but it was during this period that Bommers (1893) first isolated *S. aureus* from the blood of a patient who had died from the disease. There is little reason to suppose that this was in any way unusual, and so it is likely that *S aureus* was the most common infectious agent then as now.

The most notable differences between the historic and present-day nature of the disease relate to cure rates, case fatality rates, and length of stay in hospital. In the historic period no more than a third of all patient were said to have been cured by surgery to drain the abscess and to remove sequestra, then the only forms of treatment (Klenerman 2012: 42–3). Death rates were high and about a fifth of all children admitted could expect to die; at GCH the death rate for boys (36%) was exactly the same as for children admitted to the same hospital with osteomyelitis between 1936 and 1940 (White & Dennison 1952). With the advent of effective antibiotics (notwithstanding the emergence of some resistant strains), death rates are now so low as to go unreported.

The length of stay in hospital has also declined considerably in recent times. One study (Blyth *et al.* 2001) reports a median length of stay of 15.7 days compared with a median stay of 28.5 days for the historic cohort, with eleven of the children having stays in excess of 100 days. In the later study from GCH, White and Dennison (1952) also found that a number of children had excessively long stays, the record being one patient who remained in hospital for almost 500 days. The authors noted that there were many factors affecting the duration of stay, of which home conditions were often the most influential; this is, arguably, equally likely to have been the case in the earlier period.

In many measures, the epidemiology of osteomyelitis has changed relatively little over the past one hundred and fifty years, which suggests that internal factors have probably also changed little in importance when considering the aetiology of the disease. External factors, on the other hand, may account for the probable decrease in the frequency of the disease. That external factors may be important in the natural history of osteomyelitis, as is shown by a study from Uganda which demonstrated that there patients tended to be much older at diagnosis, and also that the bones most commonly affected were the phalanges of the hand because infection most often followed pricks to the fingers (Ibingira 2003).

In the historic period, the most important external factors were almost certainly the state of nutrition and the lack of cleanliness which gave rise to a high prevalence of skin infections. Nutritional status is important for the maintenance of an effective immune system, and malnutrition is the most common cause of immunodeficiency worldwide (Chandra 1997). During a Victorian childhood, nutritional status was likely to have been considerably worse than today. Victorian working class boys, for example, only approached the first one-tenth of the first percentile of height compared with their modern counterparts. Working class girls fared little better, their height falling short of the first percentile on modern growth charts (Horrell, Meredith & Oxley. 2009). Skin infections, particularly boils and carbuncles were rife during the Victorian period, at times being reported as achieving epidemic proportions (Hunt 1852). Nowadays, few have seen a boil, much less had one. Thus, if there has been a reduction in the incidence and prevalence of osteomyelitis since Victorian times, it seems most probable that it is due in large measure to external factors such as improved standards of nutrition and hygiene.

Conclusion

We have provided two examples of the types of study that might be used to study the relative importance of internal and external factors in the causation of disease in past societies. In the first, it seems likely that internal factors were the most significant since the epidemiology of OA of the CV and CT joints does not seem to have varied to any substantial degree in skeletal assemblages that are widely separated in time and space, and, presumably, in their activities and other ways of life. In the second, using historic rather than archaeological data, it seems that the frequency of osteomyelitis has decreased since the Victorian period and this is most likely due to external factors, most probably improvements in nutrition and hygiene.

There is no reason why this methodology should not be applied to other diseases affecting the skeleton including, for example, osteoarthritis of different joints, Paget's disease of bone, and other infectious diseases such as tuberculosis and syphilis, or the diseases we have considered here but in other assemblages. The requirements for such a study are: that skeletal assemblages should be well preserved so that as much epidemiological information can be obtained from them as possible; that comparisons should be made between assemblages that are widely separated in time and/or space in order to maximise external factors; that any historic medical data should be as complete as possible. Allowances should also be made for differences that may have arisen over time in the nomenclature of diseases and the understanding of their aetiology; care must also be taken to make only valid comparisons if using modern epidemiological data.

The last two points may need a little further clarification. There are fashions in the naming of diseases which have varied over time. For example, it was common in the early part of the 20th century to use the terms osteoarthritis and rheumatoid arthritis interchangeably, whereas nowadays they refer to completely different entities. Earlier, in the 17th and 18th centuries, all joint diseases were subsumed under the rubric of gout, meaning that basing a study on accounts from those times would substantially over-estimate the frequency of gout compared with the present day. In modern studies of disease, the incidence rate is commonly estimated, and it is by no means rare to find this term applied to disease in skeletal assemblages although it is possible only to estimate the prevalence of disease in an assemblage, that is, the number of cases in the group under study. The incidence rate refers to the number of new cases that arise in a study group over a particular time and, of course, new cases can never be recognised in a skeletal assemblage.

When using modern prevalence data it is important to ensure, as far as is practicable, that they are comparable with those derived from the archaeological or historic data. Differences will often be found with denominators; modern studies may use hospital or general practice patients as the study base, or be based on autopsy studies, or be derived from a randomly selection sample of a population. Only the last may be in any way analogous to a study using human remains and even then, care must be taken since an assemblage of skeletons is by means random (Waldron 2007). On the other hand, any form of rank ordering of, or distribution of lesions, is directly comparable with archaeological or historic data, and so are variables such as the relationships between prevalence and age and sex. With these caveats in mind, we believe that the methodology discussed here will prove useful in examining the relative importance of internal and external factors in the production of some diseases and we hope that others will be encouraged to carry out further studies.

Competing Interests

The authors declare that they have no competing interests.

Note

[1] www.HHARP.org. Last accessed 2 February 2015.

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