

“Like a virgin”: Absence of rheumatoid arthritis and treponematosi, good sanitation and only rare gout in Italy prior to the 15th century

“Come una vergine”: in Italia, niente artrite reumatoide o sifilide, solo poca gotta, e buona sanità prima del XV secolo

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RIASSUNTO

Obiettivi: Lo studio è stato condotto con lo scopo di compiere alcune valutazioni e di verificare, anche indirettamente, una serie di ipotesi: 1. che l'artrite reumatoide e la sifilide siano malattie originate nelle Americhe e che siano state trasmesse nel Vecchio Continente successivamente ai viaggi di Cristoforo Colombo; 2. che l'intossicazione da piombo, causa di iperuricemia e quindi di gotta, fosse frequente ai tempi dell'antica Roma; 3. valutare lo stato di salute pubblica in Italia prima del XV secolo, attraverso la stima della prevalenza delle spondiloartriti; 4. valutare la frequenza dei traumi ossei nell'Italia antica, grazie all'analisi dei fenomeni di reazione periosteale focale.

Metodi: Gli scheletri provenienti da diversi siti archeologici di epoca diversa (età del bronzo/peste del 1485-86) sono stati esaminati macroscopicamente per documentare segni di reazione periosteale focale e caratteristiche peculiari di artrite reumatoide, gotta, spondiloartriti e treponematosi ossea.

Risultati: L'esame di 688 campioni ha rivelato una bassa frequenza di reazione periosteale con distribuzione focale (perlomeno nel periodo compreso fra 3400-700 anni fa), con una brusca impennata nel XV secolo. Una reazione periosteale di tipo diffuso è stata messa in evidenza solo in singoli soggetti con un quadro isolato di osteoartropatia ipertrofica. Le erosioni ossee sono risultate poco frequenti e sempre con distribuzione oligo-articolare. Non si sono osservate erosioni marginali, a parte un unico caso, a livello metatarsale, con le caratteristiche tipiche della gotta. Erosioni subcondrali, fusione di articolazioni periferiche e coinvolgimento dello scheletro assiale suggestive di spondiloartrite sono state rilevate nell'1-3% dei campioni esaminati, indipendentemente dalla datazione del sito archeologico.

Conclusioni: L'Italia, prima di Cristoforo Colombo, si presentava “come una vergine”. Malattie come artrite reumatoide ed infezioni da treponema (in particolare sifilide) non sarebbero state presenti, fornendo così un'ulteriore prova che si tratta di forme morbose originarie delle Americhe. Segni di reazione periosteale dovuta a traumi minori erano rare prima del XV secolo, ovvero ai tempi dell'epidemia di peste del 1485-86. Ciò suggerisce il ruolo potenziale di attività domestiche, piuttosto che di quelle esterne, nello sviluppo di questo particolare tipo di lesione. L'ipotesi di un ruolo dell'intossicazione da piombo come cofattore causale nel declino dell'impero romano appare poco probabile, data la rarità dei casi di gotta osservati. La frequenza di spondiloartriti è risultata ridotta rispetto a quella che si osserva su popolazioni in precarie condizioni igienico-sanitarie, lasciandoci così intuire buoni standard di salute pubblica nell'Italia di quei tempi.

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INTRODUCTION

Origin of disease has special interest for rheumatologists, for whom absence of etiologic information generally mandates empirical approaches.

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Hypotheses have been offered that rheumatoid arthritis and syphilis were New World diseases, only transmitted to the Old World subsequent to the passages of Christopher Columbus (1-7). The pertinent search is for polyarticular erosive disease, sparing axial joints (8-10) and for oligostotic or polyostotic periosteal reaction (3, 4). The phenomenon of interest is not the focal periosteal reaction that occurs secondary to trauma (9, 10), but rather the more diffuse reaction indicative of pres-

ence of a systemic disease (e.g., treponemal or hypertrophic osteoarthropathy) (9-11). Four thousand years of Italian cemeteries provide fertile ground to assess those hypotheses.

Skeletal examination also provides a unique opportunity to indirectly test the hypothesis that the demise of the Roman Empire was related to lead poisoning (12). That hypothesis is controversial because of difficulty distinguishing simple environmental lead contamination of the skeletons (13). This, however, may be a resolvable issue, as one manifestation, saturnine gout, is recognizable on the basis of characteristic bone changes (9, 10, 14).

Examination of skeletons also provides a window on sanitary conditions of ancient Italy. Spondyloarthropathy, especially of the reactive type, is a complication of infectious agent diarrhea (9, 10, 15). Frequencies of that disease increase from normal background rates of 1-2% to 7-8% in the presence of oral fecal contamination (16-18).

Sites ranging from the Bronze Age to the Black Plague epidemic of 1485-1486 were evaluated for focal periosteal reaction and for the cardinal signs of rheumatoid arthritis, treponemal disease, gout and spondyloarthropathy.

MATERIALS AND METHODS

The Italian sites (19-20) delineated in table I were chosen to assess the population frequency and nature, extent and character of focal (e.g., bump) and non-focal periosteal reaction or sabre shin tibial modification, as well as peripheral and axial joint erosion or fusion. Skeletal remains were subjected to visual examination of all articular and cortical surfaces - to identify all occurrences of alterations throughout each skeleton, specify the types of bony alterations at each occurrence, and map the distribution of occurrences in each skeleton.

Diagnosis of rheumatoid arthritis was predicated upon presence of polyarticular erosive arthritis, compatibility of all the findings with our current understanding of that disease and identity of skeletal pathologic changes with those noted in unequivocally diagnosed individuals (8-10). The latter findings included marginally distributed erosions, axial skeleton (atlas-atlantal junction excepted) sparing and absent joint fusion (9, 10, 16, 21, 22).

Diagnosis of spondyloarthropathy was predicated upon the presence of axial joint disease or periph-

eral arthritis and identity of skeletal pathologic changes with those noted in clinically unequivocally diagnosed individuals (10, 23). Specific identifying characteristics included joint fusion, erosions with subchondral distribution and reactive new bone formation (10, 23).

Diagnosis of gout was predicated upon recognition of the characteristic spheroid lesion with overhanging edge (9, 10, 14).

Such lesions have only rarely been reported in other diseases (9, 10). The only disorders known to produce a similar x-ray appearance are multicentric reticulohistiocytosis (an extremely rare, polyarticular disorder), amyloidosis (another metabolic deposition disorder) and type IIA hyperlipoproteinemia (related to abnormal lipid metabolism) (9, 10). The latter two only very rarely affect bone.

Fisher exact tests were used to compare frequency of diffuse non-monostotic periosteal reaction in pre-Columbian Italy with that found in populations with syphilis and polyarticular erosive disease with that found in populations with known rheumatoid arthritis. Chi-squared analysis was used to compare frequency of spondyloarthropathy in pre-Columbian Italy with known sanitarly-challenged populations and of relative frequency of periosteal signs of minor trauma among the sites.

RESULTS

Periosteal reaction

Examination of 688 individuals (Table I) from 3600 to 500 years before present in Italy revealed focally distributed periosteal reaction (bumps) in 14 individuals from Cancelleria (10%), 11 (7%) from Civitanova Marche, 3 from Urbino (5%), 3 from Herculaneum (4%) and one each from Olmo di Nogara (1%), Porto Recanati (1%) and San Ercolano (2%). Lesions were unilateral in all but two individuals (1%) from Civitanova Marche, one each with bilateral tibial and bilateral fibular involvement.

Osteomyelitis was present in one individual from Cancelleria (1%).

Diffuse periosteal reaction was present, but limited to only a single bone in one individual from Porto Recanati (3%), one from Herculaneum (1%) and two from Civitanova Marche (2%). Three additional individuals were identified with polyostotic periosteal reaction, one each from Porto Recanati, Herculaneum and Cancelleria. Involvement

Table 1 - Character of pre-15th century Italian Periosteal Reaction and Arthritis.

Site	Olmo di Nogara	Sala Consilina	Porto Recanati	Herculaneum	Urbino	Civitanova Marche	San Ercolano	Cancelleria
Date (Century)	16 th BCE	7 th -6 th BCE	1 st BCE -3 rd CE	1 st CE ^(*)	1 st -3 rd CE	1 th -4 th CE	7 th -8 th CE	15 th CE ^(**)
Sample size	111	24	79	75	66	154	41	138
Periostitis								
- Focal	0	0	1	3	3	10	1	14
Tibia	7	13	2	2	0	1		
Fibula	1	0	1	1	0	0		
Femur	2	1	1	0	1	0		
Diffuse								
- Monostotic	1	0	2	1	1	3	0	0
Tibia	0		2	1	0	2		
Fibula	1		0	0	1	0		
Femur	0		0	0	0	1		
- Polyostotic	0	0	1 ^(***)	1 ^(***)	0	0	0	1 ^(***)
Osteomyelitis	0	0	0	1	0	0	0	1
Rheumatoid arthritis	0	0	0	0	0	0	0	0
Spondyloarthropathy	1	0	2	0	0	2	0	1
Gout	0	0	1	1	0	0	0	0
(*) 79 CE eruption; (**) 1476-1479 plague epidemic; (***) hypertrophic osteoarthropathy - distribution.								

in those individuals spared proximal diaphyses and was associated with dramatic distal diaphyseal thickening (Fig. 1). Sabre shin was not present among the 688 individuals studied.

Postmortem environmental damage (referred to as taphonomic) altered the appearance of diaphyseal bone to a variable degree among the sites. Taphonomic alterations were especially prominent in Por-



Figure 1 - Distal diaphyseal thickening with sparing proximal diaphysis in a case of polyostotic periosteal reaction.

to Recanati, Urbino, San Ercolano and Sala Consilina. These changes were distinguishable from periosteal reaction, as tangential viewing revealed that they were below the surface of unaffected cortex. This contrasts with surface elevation that occurs with periosteal reaction (10, 24).

Erosive arthritis and joint fusion

Erosive disease was uncommon in the studied skeletons. Two examples of peripheral joint erosion were noted. One in the Porto Recanati site was a metatarsal phalangeal joint with a slight bony overhang. The erosion itself appeared as if the hole had been occupied by a space occupying mass (e.g., urate tophus).

No individual with marginal erosions was identified. Subchondral erosion was noted in a proximal interphalangeal joint from Olmo di Nogara and fusion of a proximal interphalangeal joint was found in one individual from Cancelleria.

Sacroiliac joint fusion was present in one individual each from Porto Recanati, Civitanova Marche; syndesmophytes in one individual each from Porto Recanati, Civitanova Marche and Olmo di Nogara.

DISCUSSION

Treponemal disease

“Virgin state”:

Absence of polyostotic periosteal reaction (as other than isolated population phenomenon) from pre-16th century Italy documents a ‘virginity’ with respect to entities that commonly cause periosteal reaction. Periosteal reaction diffusely affecting multiple bones of more than 2% of the population is basically a manifestation of treponemal disease (i.e., yaws, bejel and syphilis) (3, 4, 9, 10). Limited occurrence in Italian populations (i.e., Porto Recanati, Herculaneum and Cancelleria) is below the 2-14% frequencies which have been found in syphilis and the 20-40% frequencies found in populations afflicted with bejel or yaws (3, 4). The other polyostotic periosteal disorder, hypertrophic osteoarthropathy, is actually quite rare in unselected populations (9, 10, 11), and was found at only the 1% level in Porto Recanati and Cancelleria.

Presence of any polyostotic periosteal reaction (even if one includes those with hypertrophic osteoarthropathy) among only 2 of 688 individuals precludes diagnosis of syphilis (Fisher exact test $P < 0.012$), let alone those treponemal diseases (i.e., bejel and yaws) with much higher population penetrance (3, 4, 25).

Thus there is no evidence for treponemal disease in Italy prior to Columbus. This study also explains the disparate suggestion by the Hennebergs (26) that there was a high frequency of periosteal reaction at Metaponto. One of the current authors (AC) had the opportunity to scan the Metaponto skeletons and perceived the visual changes as taphonomic in origin. Given the challenges that many anthropologists have in distinguishing taphonomic changes from periosteal reaction (27-30) and the documented efficacy/reliability of the current authors’ technique (24), 4 millennia absence of significant periosteal reaction in Italy documents the virgin state prior to post-Columbian introduction of syphilis. This observation is parsimonious with Ruffer’s (31) report of absence of treponemal disease in 25,000 Egyptian skeletons that he examined and our experience in North Africa (32).

Differential diagnosis:

Non-treponemal disorders associated with periosteal reaction do not occur with sufficient population frequency (9, 10) to merit serious consideration in differential diagnosis. Further, they have very different patterns of skeletal affliction.

Hypertrophic osteoarthropathy is predominantly a disease of distal diaphyses (9-11), as was noted in Porto Recanati, Herculaneum and Cancelleria. Thyroid acropachy spares the proximal appendicular skeleton, predominantly producing hand and foot bone periosteal reaction (9, 33). Infantile cortical hyperostosis is a disorder afflicting clavicles, scapulae, and ribs (9). Hypervitaminosis A is predominantly an enthesial disease, and fluorosis produces highly characteristic trabecular alterations (9, 19, 34).

Rheumatoid arthritis

As no individuals with polyarticular erosive arthritis were present among 613 individuals, there is no evidence for pre-Columbian rheumatoid arthritis in Italy (Fisher exact test, $p < 0.0001$). The perspective that rheumatoid arthritis is a New World disease (1, 22) is still unblemished.

Gout and lead poisoning

Identification of only two instances of gout among 688 individuals suggests it was uncommon. Limiting evaluation to the Roman period, this represents two occurrences among 439 individuals. There is certainly no evidence for the high frequency of saturnine gout associated with lead poisoning (35, 36). The hypothesis for a role of lead poisoning in the demise of the Roman Empire is not supported by this analysis.

Spondyloarthropathy and sanitation

Spondyloarthropathy was present in 1-3% of individuals studied. This frequency is significantly below that found in sanitarily challenged (16) populations (Chi-square = 12.51, $p < 0.001$). Absence of significant variation over 4 millennia, suggests no major sanitary challenges in pre-Columbian Italy.

Minor trauma

Periosteal signs of minor trauma were significantly (Chi-square = 6.55, $p < 0.015$) more common in fifteenth century Cancelleria than the other early sites. Frequencies were indistinguishable among the other sites (Chi-square = 3.69).

The fifteenth century witnesses great ‘*sturm und drang*’ with the passage of repetitive plagues. It seems that this was a time not only of psychological stress but also uniquely of physical injury, as manifest by periosteal signs of minor trauma. During times of plague, there is a tendency to retreat into one’s domicile. Said retreat might hypotheti-

cally reduce exposure to plague, but certainly increases exposure to minor injuries at home. Presence in the Cancelleria site indicates that measures taken did not save them from plague death. Perhaps such evidence of minor trauma might be an indicator for domicile, rather than outside environmental activity. This is an intriguing question for future investigation.

Implications

Claude Bernard stated that it's not what we don't know that gets us into trouble, so much as what we know that isn't so (37).

Contrary to preconceived notions, there is no evidence of treponemal disease or rheumatoid arthritis

in pre-Columbian Italy and no evidence for increased frequency of spondyloarthropathy or gout. The former observations support New World origins for rheumatoid arthritis and at least the syphilis form of treponemal disease. The latter falsify hypotheses that lead poisoning and sanitation were major problems in pre-Columbian Italy. Perhaps we should not be surprised that the civilization that brought us aqueducts would have also solved sanitation issues.

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SUMMARY

Objectives: This study was conducted to test several hypotheses: 1. That rheumatoid arthritis and syphilis were New World diseases, only transmitted to the Old World subsequent to the passages of Christopher Columbus; 2. To indirectly test the hypothesis that lead poisoning was prevalent in Roman Italy by looking for its byproduct, gout; 3. To test the hypothesis of compromised sanitation in ancient Italy, on the basis of spondyloarthropathy frequency; and 4. To assess variation of trauma frequencies in ancient Italy, by examining frequency of focal periosteal reaction.

Methods: Skeletons from sites ranging from the Bronze Age to the Black Plague epidemic of 1485-1486 were macroscopically evaluated for focal periosteal reaction and for the cardinal signs of rheumatoid arthritis, treponemal disease, gout and spondyloarthropathy.

Results: Examination of 688 individuals revealed low frequency of focally distributed periosteal reaction (bumps) in sites dated from the 3400-700 years before present, sharply increasing in the 15th century. Diffuse periosteal reaction was present only as isolated occurrences secondary to hypertrophic osteoarthropathy and sabre shin reaction was notably absent. Erosive disease was uncommon and always oligoarticular in distribution. No marginal erosions were present, with the exception of an isolated metatarsal with classic overhanging edge sign of gout. Subchondral erosions, peripheral joint fusion and axial skeletal involvement identified spondyloarthropathy frequencies of 1-3%, independent of the antiquity of the site.

Conclusions: Italy, prior to Columbus was like a virgin. Rheumatoid arthritis and treponemal disease (specifically syphilis) were not present, further supporting the contention that they are New World-derived diseases.

Periosteal signs of minor trauma were rare prior to fifteenth century plague times. This suggests a potential role of domestic (as opposed to outside environment activities) in its development. The hypothesis for a role of lead poisoning in the demise of the Roman Empire is falsified by the rarity of gout. The frequency of spondyloarthropathy was significantly below that found in sanitarily challenged populations, suggesting high standards of hygiene in ancient Italy.

Key words - *Treponematoses, spondyloarthropathy, rheumatoid arthritis, gout, syphilis, sanitation, lead poisoning, trauma, paleopathology.*

Parole chiave - *Infezioni da treponema, spondiloartrite, artrite reumatoide, gotta, sifilide, intossicazione da piombo, trauma, sanità pubblica, paleopatologia.*

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