# An Introduction to Diagnostic Criteria of Syphilis, Treponarid and Yaws (Treponematoses) in Dry Bones, and Some Implications\*

C. J. Hackett

Department of Morbid Anatomy, Institute of Orthopaedics, London\*\*

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Summary. Diagnostic criteria of syphilis and some other diseases are proposed from a study of 424 crania and calvariae and 250 long bones in 22 medical museums in Europe. Yaws bone lesions in Uganda and changes in Australian aboriginal bones also contributed to the establishment of these criteria. Any deductions about disease in the past or isolated populations must depend upon acceptable diagnostic criteria; post mortem damage must be recognised. In crania and calvariae the sequence of changes of Virchow's caries sicca, and in long bones nodes/expansions with superficial cavitation are sound indicators of syphilis, and of yaws and treponarid in relevant geographical areas.

Attention is called to the cause of sequestra in European calvariae labelled syphilis, the absence of sequestra due to haematogenous pyogenic osteomyelitis in Australian and other aboriginal bones and possibly in Europe before the Middle Ages. The number of bones with diagnostic criteria needed to demonstrate the endemicity of a particular infection in a past community is discussed. There is also need for an extensive application of diagnostic criteria of syphilis to pre-Columbian or pre-European bones everywhere. The uncertain future of old dry diseased bones in medical museums, and the need for reference centres to provide sound advice and guidance in palaeopathology are stressed.

Key words: Diagnostic criteria — Syphilis — Dry bones.

#### 1. Introduction

The origin of syphilis is one of the most controversial subjects of the history of medicine. The story that brings syphilis to Europe from the Americas in the last decade of the fifteenth century is widely known, but in this century it is being increasingly challenged. It is not sufficiently sound to be used as a base from which reliable conclusions may be drawn. Perhaps an already present disease might have been first recognised in Europe then, by more astute observation or because the disease became more severe.

In 1905 the causal organisms of venereal syphilis and, soon after, that of yaws were discovered (Hackett, 1963). Similar organisms were found in treponarid (the preferred synonym of endemic syphilis, Wells, 1973) in the twenties, and in pinta in the thirties. These four diseases make up the treponematoses. In this paper they will be regarded as four separate diseases due to infection by four different though morphologically identical (Ouchinnikov and Delekorskij, 1970)

<sup>\*</sup> This paper is based upon an extensive report to be published in the Records of the South Australian Museum.

<sup>\*\*</sup> The material of the study has been deposited in this department.

organisms. This is supported by the work of Turner and Hollander (1957) on experimental infections in animals. Recently a treponeme, like that from yaws, has been found in wild baboons in parts of West Africa (Fribourg-Blanc, 1972). Pinta affects only the skin.

Some people, however, maintain that there is only one organism, and that differences seen in patients infected with it are due to differences in environment (Hudson, 1965). Although under favourable conditions certain differences can be recognised, at present none has been observed between the bone lesions of the late stages of yaws, treponarid and syphilis. The diagnostic criteria developed in this study for bone syphilis are, thus, equally applicable to all these three diseases.

# 2. Purpose

A brief review (Hackett, 1963) of the origin of syphilis showed that the diagnosis of syphilis in dry bones often left much to be desired. For this reason it was thought that the establishment of diagnostic criteria would be useful.

# 3. The Study

When this study started in 1965 Professor H. A. Sissons kindly made available bench space in the Department of Morbid Anatomy in the Institute of Orthopaedics, London, where much help and encouragement were received from him and members of his staff. The co-operation of many folk in many countries made this study possible. Among these is Professor E. Uehlinger, Zurich, for advice and encouragement during more than ten years.

Between 1965 and 1970 in 22 medical museums in Britain and Europe<sup>1</sup> 424 crania and calvariae and 250 long bones were seen. During a visit to Australia in 1967–68 over nine thousand aboriginal bones were seen in eight national anthropological collections. These Australian specimens can be regarded as pre-European as regards freedom from recently introduced diseases. The findings in these specimens supported the diagnostic criteria that were emerging from the British specimens that had at that time been examined (Hackett, 1968). In New Zealand, Honolulu, Chicago and Washington<sup>2</sup> over five thousand indigenous bones were seen, many of which were probably pre-European.

To simplify the study only skulls and long bones with the changes of syphilis or of other diseases likely to be confused with syphilis were examined. Of some frequent conditions, such as pyogenic osteomyelitis and Paget's disease, only a few typical and a few atypical specimens were selected. The number of bones examined may be a considerable part of all syphilitic bones in all medical museums.

Because pathological terms, such as periostitis and osteomyelitis, are of no value in defining diagnostic criteria, simple terms based upon the four most frequent alterations that make up bone changes in disease, namely, more bone, less bone, dead bone, and deformed bone were used. The most characteristic

<sup>1</sup> London, Cambridge, Edinburgh, Glasgow, Prague, Vienna, Innsbruck, Zurich, Berlin DDR, Copenhagen and Leningrad.

<sup>2</sup> Auckland, Wellington and Dunedin; Bernice Bishop Museum; Field Museum; U.S. National Museum, Smithsonian Institution.

change in a bone became its main change. Seventeen main changes were recognised in crania and calvariae and 14 in long bones. Syphilitic bone changes may be more bone, less bone (destruction) or a combination of both (Beitzke, 1934; Burkhardt, 1970).

Specimens, as packets of photographs, were sorted by their main changes and not by their label diagnoses, which were at first regarded with suspicion in the absence of supporting evidence outside the bone itself. This authentication was found in about 8 per cent of crania and calvariae, but in a few museums only specimens with authentic diagnoses were taken, and in only one long bone.

One should bear in mind that though all bones in medical museums have pathological changes, few of those in anthropological collections will be diseased. In the latter, changes may be early, slight and transient, but these may be rare or absent in medical museums.

# 4. Pseudo-Pathology

Changes in bones occurring after death do not usually resemble characteristic pathological changes (Wells, 1967). They should always be suspected when uncharacteristic loss of bone rather than 'more bone' is present.

#### 5. Diagnostic Criteria

A diagnostic criterion of a disease in a bone should identify changes due only to that disease, and to no other. It is not important if it misses a few specimens with changes due to the particular disease, provided it does not include one bone with changes due to another disease; that is it should be specific rather than sensitive. Only if the diagnosis of a disease in a dry bone is reliable can sound conclusions be reached about disease in the past and perhaps the way of life of the people concerned.

There has been only one bone change up to the present declared, with acceptable authority, as undoubtedly syphilitic. This is the caries sicca stressed by Rudolf Virchow (1896). Williams (1932) of Buffalo, established his own criteria by extensive study of medical museum specimens in many countries, but only briefly recorded them in his report of their application to pre-Columbian bones said to be syphilitic in Europe and America. He illustrated one of Virchow's specimens (No. 18802) with caries sicca (Fig. 1); this important Rosetta-stone-like calvaria is still in Virchow's Institute in Berlin, DDR. It complements his description in 1896.

The popular rough and ready diagnostic indication of syphilis by changes in several bones or in the skull and other bones, without sequestra, Pales (1930) has called a suggestion rather than a diagnosis.

The diagnosis of syphilis in many papers on pre-Columbian bones is often based on the opinion of the author supported by inadequate or no photographs, and without reference to diagnostic criteria.

Changes thought in the past to be syphilitic, but for which adequate support was not found in this study, are regarded as (on Trial) until further application has established their value.

# 6. Findings

# A. Calvariae and Crania

These 424 specimens fall into 17 main groups. Of these specimens 281 (66 per cent) are labelled syphilis, 42 trauma, 40 neoplasms, 16 osteomyelitis and 45 in eight other diagnoses. It must be stressed that these frequencies of changes or label diagnoses can have no value outside these highly selected specimens.

A sequence of changes was found that ends in a healed, thus inactive, multinodulation. This was soon recognised as the caries sicca of Rudolf Virchow (1896).

Caries sicea (Fig. 1), the scar remaining after the healing of superficial gummatous osteitis of the calvaria, Virchow said, was the only pathognomonic bone change of syphilis. He pointed out the difficulty of describing it, although once seen it could never be confused with any other disease. He stressed the smooth nodules coming together to form star-shaped depressions, which may be deep, or wide and flat; the important character was the consistent pattern formed. Caries sicea could never occur in pyogenic caries, lupus or leprosy, he said.

The early stages of this sequence are not often described or illustrated; perhaps they are not recognised. Williams suggested that probably the changes referred to as 'worm-eaten' are really these, namely serpiginous cavitation and the intermediate nodular cavitation. The early stages are of short duration, a



Fig. 1. Caries sicca. Pathologischen Institutes der Humboldt-Universität, Berlin, DDR-No. 18802. Syphilis. Before 1895. Characteristic caries sicca. Diagnostic criterion of syphilis.
The "0/.8" is on the frontal. (I am grateful to Professor L. H. Kettler, Director of the Institute, for this photograph and permission to publish it.)

# **SYPHILIS SEQUENCE CARIES SICCA Contiguous Series** 6 SERPIGINOUS CAVITATION Destruction Bone 7 **NODULAR** CAVITATION Formation Bone 8 **CARIES** SICCA Bone Remodelling

Fig. 2. Caries sicca sequence; contiguous series

few weeks or months perhaps, but caries sicca is for ever. These changes make up the *contiguous* series (Fig. 2) of the caries sicca sequence.

Another important skull with extensive frontal changes, is in the Hunterian Museum, London (No. P716; Fig. 3). In the centre of these changes is some caries sicca, round this is nodular cavitation, and surrounding all is serpiginous



Fig. 3. Caries sicca. Hunterian Museum, Royal College of Surgeons. London. No. P716. Syphilis. Before 1793. Caries sicca in the centre then nodular cavitation with the earliest stage serpiginous cavitation peripherally

cavitation. This clearly demonstrates the reality of the contiguous series of the caries sicca sequence. The central change arises from the middle one, and the middle from the outer and earliest one, which is extending peripherally. In this specimen similar changes are on the posterior parietals.

A sequence is a developmental series of changes due to one disease, hence if in a sequence the cause of one stage (change) is known then this will apply to all the others.

From this contiguous series are readily recognised two others of simpler parallel changes; (i) the *initial* series with clustered pits and confluent clustered pits and (ii) the *discrete* series of three main changes focal superficial cavitation, circumvallate cavitation, and radial scars. Alas new names had to be found for them. The main changes in the discrete series are comparable with serpiginous cavitation, nodular cavitation, and caries sicca.

Of the 117 specimens in these eight caries sicca main groups, 107 are labelled syphilis, two tuberculosis and eight neoplasms. Each of these eight main changes

is a diagnostic criterion of syphilis. Few medical museums have specimens with the full range of these changes, which explains perhaps why they have not been clearly recognised.

Only the earliest changes may be confused with early metastatic osteolytic neoplasms, or tuberculosis.

While the inner surface of the calvaria in syphilis is but little changed beyond a few pits, and sutures are rarely crossed, in neoplasms pits on the inner surface are numerous and rapidly coalesce to produce deep erosions, often before the outer surface has any changes, and sutures are freely crossed. Transillumination of such calvariae will show this and may even reveal translucent foci without inner or outer surface involvement. This is a diagnostic criterion of metastatic osteolytic neoplasms. Transillumination of calvariae with syphilitic changes reveals, localised increased bony density.

In tuberculosis a change like focal superficial cavitation may develop, but through the opening on the outer surface a small sequestrum is seen while on the inner surface already is an extensive superficial erosion, as Erdheim (1932) so well described and illustrated. This is a diagnostic criterion of tuberculosis. Seven specimens with these changes in the study are labelled tuberculosis.

The most numerous cranial changes in medical museums are a grouping of sequestra, depressions and perforations (214 specimens). These changes may be single or multiple, large or small. Superficial sequestra may result in depressions, and whole thickness sequestra in perforations, but there is no constant causal relationship, hence this is a grouping and not a sequence. Some of the sequestra have discoloured patches in small areas of destruction on their outer surfaces. These may indicate where sinuses opened on to the surface of the scalp from some earlier bone change. Such sinuses might have allowed pyogenic infection to be added to an earlier syphilitic infection and lead to the sequestra.

Of these 214 specimens 137 (64 per cent) are labelled syphilis, 14 osteomyelitis, 5 tuberculosis, 16 neoplasms and 42 trauma.

Diagnostic criteria of syphilis can be recognised in some crenated thin-floored depressions and perforations which are surrounded by finely radially striated rims; this relates them to a confluence of circumvallate cavities.

Multiple small discrete, or single larger perforations with circinate finely dentate, or gouged, flared margins, all with no sign of healing, are diagnostic of neoplasms. Perforations from trephination may be found in some populations and may need differentiating from those due to pathological processes, such as other trauma and healed infections that may be associated with sequestra (Lisowski, 1967).

Depressions with protrusions on the inner surface or perforations with pouting inner margins are diagnostic of trauma.

The smooth (healed) surfaced, bored-out, empty nasal tunnel, often with extensive destruction of the palate and anterior maxillary alveolus can be accepted as syphilitic; this was not seen in the medical museums. It occurred in present day communities with yaws and treponarid until penicillin mass treatment campaigns. The continuous nasal destruction of neoplasms, often with extensions into the orbits, cannot be confused with this healed condition.

The diagnostic value of naso-palatine destruction of leprosy, *facies leprosa*, has been established by Møller-Christensen (1961) and Andersen (1969).

Hutchinson's teeth of congenital syphilis are surely a diagnostic criterion of syphilis, though they were not seen in yaws and treponarid, nor in the Australian specimens. None was seen in the European specimens.

But for the early death of Merton Satinoff in 1972 diagnostic criteria for the dry bone changes of the haemoglobinopathies (Satinoff, 1972) would probably have been established by now. These bone changes (Reynolds, 1963), symmetrical osteoporosis, are of immediate archaeological and medical historical interest as indicators of *falciparum* malaria in a past community.

The characteristic appearances of osteomata, Paget's disease, and hyperostosis frontalis interna of the calvaria are well known, and can be accepted as diagnostic criteria.

# B. Long Bones

Williams found the recognition of syphilis in these more difficult than in crania. Nodes and expansions in long bones were, he said, frequently attributed to syphilis, and were largely responsible for the diagnostic difficulties in ancient dried long bones.

These 250 specimens fall into fourteen main groups of which 129 (52 per cent) are labelled syphilis. Other label diagnoses are osteomyelitis 61, tuberculosis and leprosy 11 each, neoplasms 3, Paget's disease 12, chronic leg ulcer 20 and 'others' 3.

There is a grouping, possibly a sequence, of plaques on otherwise normal bone leading to striate nodes. Though these striate nodes are widely regarded as syphilitic, the evidence for this in this study was not conclusive so this change is put (On Trial), although a few specimens of this were seen in Australia.

Another progress may be followed through nodes and expansions with dimpled and trabeculate (rugose) surfaces to expanded bones with gross surface irregularities and either compact, or finely porous, expanded cortices. Of the 103 specimens with nodes/expansions and surface changes, 90 are labelled syphilis, 9 osteomyelitis, 3 Paget's disease and one other. These changes are also put (On Trial). They were not seen in Australian bones nor in yaws bone lesions in Uganda (Hackett, 1951).

Expanded bones with larger than usual striae and pits, are also regarded as diagnostic criteria (On Trial) of syphilis.

Fine striation usually without nodes is frequent in leprosy (Møller-Christensen, 1961; Andersen, 1969) but is of no more value than an indication of inflammation and perhaps vascular congestion.

Nodes/expansions with superficial cavitation in long bones are clearly a diagnostic criterion of syphilis (Fig. 4). In advanced stages the cavities may be in a sclerotic medulla. This change was seen in yaws in Uganda (Hackett, 1951) and in Australian bones, and is reported in treponarid in Syria (Rost, 1942) and Botswana (Murray et al., 1956). Of the thirty specimens in this main group 26 are labelled syphilis, two osteomyelitis, and one each tuberculosis and chronic leg ulcer; these four are revised to syphilis. One of the label diagnoses of syphilis is revised to osteomyelitis.



Fig. 4. Nodes/expansion with superficial cavitation. Hunterian Museum, London. No. P724. Syphilis. Before 1793. A diagnostic criterion of syphilis

There are 94 specimens with nodes/expansions and destruction, of which 29 are labelled syphilis, 48 pyogenic osteomyelitis, 11 tuberculosis, and 6 have other diagnoses.

Other candidates for diagnostic criteria of syphilis would be sternal or vertebral erosion from aortic aneurysm, and Charcot's joints, none of which was seen in this study.

The appearances of Paget's disease, haematogenous pyogenic osteomyelitis, and the bony platforms on the distal third of the tibia resulting from chronic varicose leg ulcer are other diagnostic criteria.

Healed fractures are often numerous in medical museums, but are usually not likely to be confused with infections of bones. A radiograph is a great help in an uncut bone.

Cancellous tissue destruction especially in the vertebral bodies is frequent in tuberculosis but is not included in this study. Of sixteen long bones seen with metaphyseal expansion and with openings, sometimes exposing cancellous tissue sequestra, 10 are labelled tuberculosis. This is regarded as a diagnostic criterion (On Trial) of tuberculosis.

#### 7. Conclusions on Diagnostic Criteria

Every effort has been made to ensure that the proposed criteria will stand the test of use. Diagnostic criteria of syphilis are proposed based on observations in European bones and in the Uganda (Hackett, 1951) yaws bone study (except crania) and on reports in treponarid (Rost, 1942; Murray et al., 1956). In Australian bones were found all the changes of late acquired syphilis in European bones. Calvarial sequestra were, however, absent.

Recent serological surveys (Garner et al., 1972) using treponemal antigens found prevalences of up to 35 per cent in some groups among 899 Australian aborigines over 15 years of age in communities in the north and centre; these were regarded as being due to yaws and treponarid respectively and not to syphilis. There is much evidence that in tribal and near-tribal conditions the Australian aborigine did, and perhaps still does, not contract syphilis because he is protected by a childhood treponematosis. Thus the Australian treponemal bone changes,

with the absence of pyogenic osteomyelitis, can be used to control the label diagnosis of syphilis in European bones.

For simple and immediate diagnostic criteria of syphilis the caries sicca sequence of calvarial changes, and nodes/expansions with superficial cavitation in long bones are recommended with confidence. Because the late bone lesions of acquired syphilis cannot be distinguished from those of yaws and treponarid, diagnostic criteria of syphilis are really evidence of the treponematoses. Which of these three related infections is the cause of the bone changes can only be indicated by the provenance of the specimen (humid or arid), its accurate dating, and the way of life (urban or rural) that the population concerned might have lived.

One diagnostic criterion in a bone is sufficient for the recognition of the disease in a specimen, but does one such bone in a population mean that the disease was endemic therein?

The diagnostic criteria established from European bones are readily applicable to aboriginal bones in Australia. Should they not be equally applicable to pre-Columbian bones in America if a bone damaging treponemal infection were present?

# 8. Implications

# A. Sequestra of Calvariae, and of Long Bones

In European bones most calvarial sequestra are labelled syphilis but in a few diagnoses this is accompanied by (pyogenic) osteomyelitis. Pyogenic osteomyelitis (Burkhardt, 1970) in the calvaria is rare, only about 0.5% of all such bone changes, and is usually not blood-borne but an extension of some adjacent inflammation. The absence of sequestra in Australian calvariae casts doubt on the purely syphilitic origin of these changes labelled syphilis in European calvariae. In Australian long bones sequestra are also absent. Pyogenic infection of any tissue used to be extremely rare in aborigines under tribal ways of living. Pyogenic osteomyelitis is rare in European bones (Wells, 1973; Pales, 1930) before the Middle Ages, except as a complication of open fractures.

Could its possible appearance in European bones about the time that syphilis was first recognised, have any implication for that disease?

Pyogenic osteomyelitis is now appearing in Central Australian aboriginal children perhaps not living in the old tribal ways. This is probably due to the introduction of new organisms by the increased population of white residents and tourists during the last 30 years.

Most of the changes in aboriginal bones in Australian national collections are of the caries sicca sequence. A similar occurrence of yaws bone changes and absence of osteomyelitis were found in the 1950s in Western New Guinea by the first medical service doctors.

# B. Geographical Implications

In the *Pacific area*, skulls from a number of islands have caries sicea changes, e.g. New Hebrides, Solomon Islands, Samoa, and New Guinea, where clinical yaws was present until the recent penicillin mass treatment campaigns.

The diagnostic criteria of syphilis, i.e. of treponematoses, developed from European material have wide application to bones from populations in some developing countries.

Dr. A. T. Sandison (1973) of Glasgow, in 1972 studied disease in aboriginal bones in Australia. His conclusions in general agree with those stated here about treponemal and pyogenic infections.

In American Indian bones only a few were seen in 1968 with changes at all like caries sicca and they were not as characteristic as similar changes in Australian bones. The most likely changes were in skulls from the Aleutian Islands. Dr. T. Dale Stewart of the Smithsonian Institution has pointed out that such infections may well not be indigenous as the populations of those Islands, bought from Russia by the USA in 1867 as part of Alaska, had been exposed to introduced infections. He does not accept them as evidence of pre-Columbian syphilis in America. In 1940 he stressed that there were fewer pre-Columbian bones with syphilis-like changes than would be expected had that disease been present.

Stewart (1973) says that supposedly syphilitic lesions are found in post-Columbian bones, but are fewer in pre-Columbian bones. He thinks that the almost complete absence of these changes in American bones from the unquestionably prehistoric era is remarkable, and points out that the lack of these particular changes in older American bones, like other negative evidence, is seldom mentioned.

Bullen (1972) reported prehistoric syphilis in Florida. Two of the crania from her study might have had rather atypical caries sicca, and the tibiae related to one of these had changes rather like nodes with superficial cavitation. The other Florida specimens did not have diagnostic criteria proposed in this study. Joseph Jones (1876) first described syphilis in pre-Columbian bones in America; these specimens have not recently been re-examined.

The extensive application of diagnostic criteria of syphilis to pre-Columbian American and other bones may better define the problem of so-called 'non-specific' infections (Wells, 1964) and thus help the recognition of their causes.

#### C. Community Implications

The question now arises "How many specimens in a bone population from the past must have diagnostic criteria of syphilis for the recognition of syphilis as endemic in that community?"

In the Australian bone study perhaps 1–2 per cent of the bones examined had changes like those in syphilis, i.e. caries sicca in calvariae, or nodes/expansions with superficial cavitation in long bones. In pre-European days high prevalences (80 per cent) of treponematoses in populations like the Australian aborigines would be expected.

In American bones from acceptable pre-Columbian sites the frequency of caries sicea changes might be fewer than 1 in 500. Some recent American publications have occasional illustrations of calvariae with caries sicea and long bones with nodes/expansion with superficial cavitation (Morse, 1969) from pre-Columbian American populations. These are many fewer than in Australian bones. Diagnostic criteria should be applied to changes in many pre-Columbian American Indian bones to establish the frequency of treponemal changes.

When this problem of "How many?" was raised with Professor F. Fenner, of Canberra in 1973, he replied that upon a solitary bone in a continent with changes like diagnostic criteria no opinion was justified, but with a number that might be anticipated from present day expectations a much better guess could be made.

Williams's study of pre-Columbian bones referred above, found that in none of the bones in Europe said to be pre-Columbian and syphilitic could the diagnosis be confirmed. In pre-Columbian American bones few, four crania and two lots of long bones, he thought had diagnostically acceptable changes but the dating of some of these by the then archaeological techniques has since been challenged. One skull only of these specimens, that from Pecos, New Mexico, has possibly acceptable syphilitic changes, judged by the diagnostic criteria proposed in this study.

#### 9. The Future

# A. Of Old Bones

Few medical museums remain in their pristine glory; another generation of professors of pathology may see their extinction. Space is valuable and new avenues of study are opening up in pathology.

With the disappearance of the infections that caused many of the bone changes discussed above, these old bones will gain prestige as historical documents. They are already irreplaceable and should, therefore, be transferred for safe keeping and ready availability for study to Institutes or Departments of the History of Medicine where they will be cared for. In Prague much of the great collection of the 2nd Institute of Pathology has been wisely transferred to the National Museum.

# B. Of Palaeopathology

The future study of old bones is related to the development of the pathology of past populations and should be in the hands or under the surveillance of bone pathologists.

There is need for national reference centres (Jarcho, 1966) in departments of morbid anatomy; not, perhaps, more than one per country or group of countries. In these centres, 'type' collections of specimens and microscopical preparations, and lists of local relevant publications would be built up, advice would be available and enquiries could be directed to competent authorities in particular fields. Such a centre could be a rallying point at the professional level of palaeopathological activity in its related geographical area. Much preliminary work and coordination could be done at little cost; the development of a centre should depend upon the usefulness of its work.

In time an international reference might be called for by thriving national centres.

#### References

Andersen, J. G.: Studies in the mediaeval diagnosis of leprosy in Denmark, Copenhagen: Costers Bogtrykkeri 1969

Beitzke, J.: Erworbene Syphilis der Knochen. In: Handb. Spez. path. Anat. Hist. (Hrsg. Lubarsch, O., Henke, F., Rössle, R.), Bd. IX/2, S. 469-538. Berlin: Julius Springer 1934

- Bullin, A. K.: Paleoepidemiology and distribution of prehistoric treponemaisis [sic] (syphilis) in Florida. Fla. Anthrop. 25, 133–175 (1972)
- Burkhardt, L.: Pathologische Anatomie des Schädels in seiner Beziehung zum Inhalt spezielle Pathologie des Schädelskelets. In: Handb. Spez. path. Anat. Hist. (Hrsg. Lubarsch, O., Henke, F., Uehlinger, E.), Bd. IX/7, S. 212–234, S. 229–234, Berlin: Julius Springer 1970
- Erdheim, J.: Über Tuberkulose des Knochens im allgemeinen und die des Schädeldaches. Virchows Arch. path. Anat. 238, 368–376 (1932)
- Fribourg-Blanc, A.: Treponema. In: Pathology of Simian Primates (Feinnes, R. N.T.-W. ed.), Part II, p. 255–262. Basel: Karger 1972
- Garner, H. F., Backhouse, J. L., Moodie, P. M., Tibbs, G. J.: Treponemal infections in the Australian Northern Territory aborigines. Bull. Wld Hlth Org. 46, 285-293 (1972)
- Hackett, C. J.: Bone lesions of yaws in Uganda, Oxford: Blackwell Scientific Publications Ltd. 1951
- Hackett, C. J.: On the origin of the human treponematoses. Bull. Wld Hlth Org. 29, 7-41 (1963)
- Hackett, C. J.: Some aspects of treponematoses in past populations. J. Anthrop. Soc. S. Aust., 6, 5–14 (1968)
- Hudson, E. H.: Treponematosis in perspective. Bull. Wld Hlth Org. 32, 735-748 (1965)
- Jarcho, S.: Human Palaeopathology, 175, London: Yale University Press 1966
- Jones, J.: Exploration of the aboriginal remains of Tennessee. Smithson. Contr. to Knowl. 22, 65-73 (1876)
- Lisowski, F. P.: Prehistoric and early historic trepanation. In: Diseases in Antiquity (Brothwell, D., Sandison, A. T., eds.), p. 651–672. Springfield, Ill.: Charles C. Turner 1967
- Møller-Christensen, V.: Bone lesions in leprosy, Copenhagen: Munksgaard 1961
- Morse, D.: Ancient disease in the Mid-West USA, Reports of Investigations, No. 15. Illinois State Museum, Springfield, Ill., Plate 13 A and B (1969)
- Murray, J. F., Merriweather, A. M., Friedman, M. J.: Endemic syphilis in the Bakwena Reserve of the Bechunaland Protectorate. Bull. Wld Hlth Org. 15, 975–1039 (1956)
- Ouchinnikov, N. M., Delekorskij, V. V.: Treponema pertenue under the electron microscope. Brit. J. vener. Dis. 46, 349-379 (1970)
- Pales, L.: Paléopathologie et Pathologie Comparative, 192-225, Paris: Masson et Cie 1930
- Reynolds, J.: The roentgenological features of the sickle-cell disease and related haemo-globinopathies, Springfield, Ill.: Charles, C. Turner 1965
- Rost, W.: Roentgen manifestations of Bejel ("Endemic syphilis") as observed in the Euphrates River valley. Radiology 38, 320-325 (1942)
- Sandison, A. T.: Disease changes in Australian skeletons. Newsletter, 3, 20–22, Canberra: Australian Institute of Aboriginal Study 1973
- Satinoff, M. T.: The origins and geographical spread of the thalassaemias and abnormal haemoglobins. J. Human Evolution 1, 79–82 (1972)
- Stewart, T. D.: Some historical implications of physical anthropology in North America. In: Essays in historical anthropology in North America. Smithson. Misc. Collns. 100, 15–50 (1940)
- Stewart, T. D.: The People of America, London: Weidenfeld & Nicolson 1973
- Turner, T. B., Hollander, E. R.: Biology of the Treponematoses. Geneva, World Health Organization, Monograph Series No. 35, 1957
- Virchow, R. L. K.: Beitrag zur Geschichte der Lues. Derm. Z. 3, 1-9 (1896)
- Wells, C.; Bones, bodies and disease, 100-105, London: Thames & Hudson, 1964
- Wells, C.: Pseudopathology. In: Diseases in Antiquity (Brothwell, D., Sandison, A. T., eds.), p. 5–19, Springfield, Ill.: Charles C. Turner, 1967
- Wells, C.: The palaeopathology of bone disease. Practitioner, 210, 384-391 (1973)
- Williams, H. U.: The origin and antiquity of syphilis; the evidence from diseased bones. A review with some new material from America. Archs. Path. 13, 779-814, 931-983 (1932)

Dr. C. J. Hackett 19 Prince Edward Mansions Moscow Road London W2 4EN, England