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HISTORICAL PERSPECTIVE

Augusto Bonome and his revolutionary studies on leprosy in the early 20th century

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Abstract

Background: Augusto Bonome (1857–1922), professor at the University of Padua until 1922, was involved in a study about a particular kind of pulmonary leprosy, being the first to testify the lepromatous alterations also in the deepest parts of the respiratory tract, even though the same Gerhard Hansen (1841–1912) had denied the possibility that lungs could host Mycobacterium leprae.

Objectives: It is necessary to reevaluate the research done by Bonome to also demonstrate how it can still be relevant today in further comprehension of leprosy.

Methods: Bonome's advances in leprosy studies are testified by some specimens from the Morgagni Museum of Pathological Anatomy of the University of Padua. Among the specimens, there is a peculiar case of advanced tuberous leprosy in an adolescent, who died in 1908, of which the face, the larynx, the hands and genitals are still preserved today in the Museum.

Results: Through autoptic and histological analysis of this specimen, Bonome succeeded in identifying a peculiar case of bone toxoid-infectious dystrophy besides characteristic leprous laryngitis, which caused the death of the young leprosy patient.

Conclusions: The results confirmed the innovative research carried on by Bonome during his medical career, being among the first to offer an important contribution to improving and revolutionary knowledge on leprosy which could still be useful today.

INTRODUCTION

Leprosy is a chronic granulomatous infection of the skin, respiratory tract, eyes and nerves caused by *Mycobacterium leprae*. The damage to peripheral nerves, due to the predilection for Schwann Cells and the immunologic reaction, causes the characteristic deformities and disabilities.[1] Leprosy was widespread across Europe and Asia but occurs nowadays in low- and middle-income countries, especially India, Brazil, Indonesia and in countries in Africa.[2] Leprosy is also called Hansen's disease following the discoveries of Gerhard Henrik Hansen (1841–1912), a Norwegian physician, scientist and leprologist, who in 1873 identified the intracellular *Mycobacterium leprae* as the etiologic agent of the disease (the mycobacterium is also called Hansen Bacillus).[3] Leprosy may have a wide range of effects on the human body, ranging from mild disease limited to some skin alterations (tuberculoid) or severe and systemic spread (lepromatous). In 1966, William Jopling (1911–1997) and Dennis Ridley (1918–2009) classified the disease into five main forms: tuberculoid (TT), borderline TT (BT), borderline (BB), borderline lepromatous (BL) and lepromatous (LL) according to immunity.[4] Nowadays leprosy is a treatable curable disease with multidrug therapy (MDT).[5]

Augusto Bonome (1857–1922) was a professor of Pathology (1891), Bacteriology (1896), and director of the Institute of Pathological Anatomy (1889) at the University of Padua, succeeding Lodovico Brunetti (1813–1899) in both professorship and directorship of the Institute, a role he held until his death. During his career in Padua, Bonome also contributed to enriching the collection of pathological preparations of the Museum of Pathology, founded by Brunetti in the 1860s,

now Morgagni Museum of Pathological Anatomy, including among many also a particular case of Situs Inversus.[6–8]

The objective of this research aims at rediscovering Bonome's revolutionary studies on leprosy, both through anatomical preparations and historical-literary sources, thus confirming his role as the first discoverer of lung leprosy.

MATERIALS AND METHODS

Some specimens of the present-day collection of the Morgagni Museum still testify today the efforts made by Bonome in the study of leprosy: four leprous laryngitis, hands and genitalia of a male individual, a testicle, a whole arm and three heads of male individuals affected by leprosy. The study of the old autopsy registers of the Institute of Pathological Anatomy of the University of Padua has permitted to confirm Bonome's hand in the preservation of these cases.

Furthermore, a review of past and present literature on the subject has been carried out to compare the results obtained by Bonome in early 20th century and prove the validity of his research.

RESULTS

One of the cases described by Bonome was a 16-year-old young individual who died in 1908 at the Dermatological Clinic in Padua and showed a peculiar pathognomonic case of lepromatous leprosy.[9] The cause of death of this individual was described as related to a thickening of the larynx and the epiglottis due to leprosy (Figure 1), which led to severe stenosis of the opening of the glottis, causing frequent chocking episodes, one of which brought him to death. Numerous skin lesions were present in the whole body, particularly well represented in the face, showing a typical *facies leonina* (Figure 2), in the testicles and the leprosy patient's ulcerated hands (Figure 3). The brain had an 'augmented consistency' and showed congestion of the nervous tissue. The inferior lobe of the right lung presented a greyish colour and a further 'augmented consistency'. The peribronchial

FIGURE 1 Larynx of the leprosy patient preserved at the Morgagni Museum showing a thickening (arrows).

FIGURE 2 *Facies leonina* of the leprosy patient preserved at the Morgagni Museum showing nodules and facial alterations.

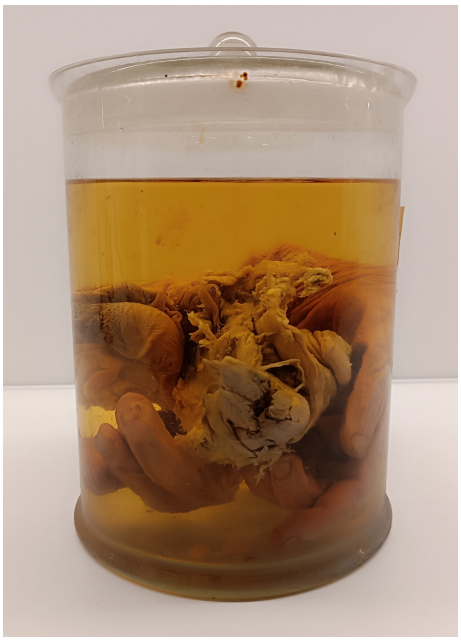

FIGURE 3 Hands and genitalia of the leprosy patient preserved at the Morgagni Museum showing bone alterations of the phalanges.

lymph nodes were also enlarged and thicker than normal, compatible with the other cases of pulmonary and bronchial leprosy described by Bonome. The face, the larynx, the hands and the genitalia of this individual were preserved along with other specimens of other individuals to prove the bone alterations typical of leprosy patients also connected to various levels of infections of this pathology, as he noticed in his studies.

DISCUSSION

Before Bonome's research, lung involvement in Hansen's disease was considered only limited to the upper respiratory tract, per continuity with the typical mucosal involvement of the disease. Hansen performed several investigations of lungs in more than 100 leprosy patients without identifying clear traces of leprosy, thus hypothesizing that some of the bronchial changes were caused by co-infection with Mycobacterium tuberculosis.[9,10] Instead, in 1888 during an autopsy of a leprosy patient, Bonome was able to recognize Hansen's disease spread in the whole body (except for the kidneys, the nervous centres and the thyroid gland). The patient presented laryngeal leprosy that invaded the bronchi, with swollen bronchial mucosa. The consistency of the organs was augmented with many nodules visible at the cutting, which presented hyaline metamorphosis and exudate, typical of leprosy.[9]

Histological and bacteriological analysis performed by Bonome showed a ubiquitous visible infiltration that consisted of 'big granulose cells with a single well-delimited nucleus, piles of leucocytes in the alveoli and bigger elements in the peribronchial lymphatic tissue'. These inflammatory infiltrations also occluded the bronchial space, forming 'granulomatous nodules with giant cells', although recent studies proved that granulomatous nodules with giant cells may be inconsistent with LL leprosy, suggesting a potential sign of either borderline leprosy or a foreign body reaction.[11] Hyaline zones were visible where the process was more advanced, not absorbing any colour and often not containing brown pigmented granules. There was no trace of caseous nodules or ulceration. Anyway, these results were also compatible with a rare form of chronic hyaline tuberculosis.[9]

M. leprae does not affect the tissues directly but it is known to be an immunologically mediated disease, which affection may be related to the different immune responses to the presence of the bacteria.[12] The bacteriological analysis carried out on lung fluids, bronchial mucus, mucosal and skin granulomas, splenic fluid, blood, bone marrow and lymphatic fluid showed only the leprosy bacillus in all samples, also in the form of globi.[9]

In the newer nodules and in the interalveolar septa, where the normal structure was still recognizable, the leprosy cells were visible and consisted of granulated bacilli (coccotrix leprae), easily stainable. The bacillus was mostly visible in the hyaline zones, sometimes so concentrated that the specimen was difficult to decolorate. Therefore, the recognition of leprosy cells analogous to those that were found in the nodules in the skin and mucosal tissue that are in the spleen and lymphatic tissue and bone marrow, made it possible for Bonome to diagnose pulmonary leprosy. A final comparison with lung specimens and sputum rich in T bacilli confirmed the absence of a co-infection and the final declaration of the discovery of lung leprosy.[10]

Bonome also described some typical leprosy alterations of the bones discovered in two autopsies he performed in Padua in 1908.[9] Some samples of these autopsies are still nowadays part of the collection in the Museum of Pathological Anatomy.

He examined two patients affected by 'tuberous leprosy' which we nowadays describe as lepromatous leprosy, these cases presented diffuse bony alterations with hyperostosis of some bones (skullcap, long bones and ribs), ossification of the medullary cavity and a notable thickening of the cortical bone. The analysis made by Bonome revealed that the alteration did not start from a periosteal osteogenic activity as supposed, but it was related to neoformations starting from the deeper part of the bone. Furthermore, some regressive/dystrophic alterations were observable in the main tubular bones, starting from the sub-periosteal circumferential lamellae to Hawers's canals.

Thus, Bonome hypothesized a direct involvement of the catalytical activity of leprosy bacilli on the bone tissue, responsible for both productive and destructive changes, although some of the alterations may be due to the systemic inflammatory response. This may be confirmed also by the presence of Hansen's bacillus in the bone marrow tissue (Figure 4) and the evidence of products (mainly proteins), related to bacilli destruction, in the blood stream.[9]

Bonome noticed that the productive and regressive processes developed at the same time, although the dystrophic results prevailed. A different response in the bone tissue may be related to the intensity of the stimulus on the bone: productive results were connected to lighter affection and vice versa, a stronger stimulus may result in destructive processes. An impairment of the nervous system may play an important part in the development of the disease in the bones: patients are at constant risk of developing ulcers and subsequent osteomyelitis, or neuro-osteo-arthropathy.[13] It is also known that nervous tissue is fundamental in the development and modelling of skeletal tissue, so it is possible that the remodelling also happens because of impaired neural signalling.[14]

Since the first evidence of pulmonary leprosy was made by Bonome, the discovery was later proved by many authors, for example, Joseph Doutrelepont (1834–1918),[15] Giuseppe Scagliosi (nd),[16] Elena Fambri (1886-nd)[17] and Victor Babes (1854–1926)[18] observed the same alterations and confirmed the presence of leprosy in the lungs as described by Bonome.

Thus, Bonome may be recognized as the first to have observed those features and the discoverer of pulmonary leprosy infection. His discoveries might still be useful today

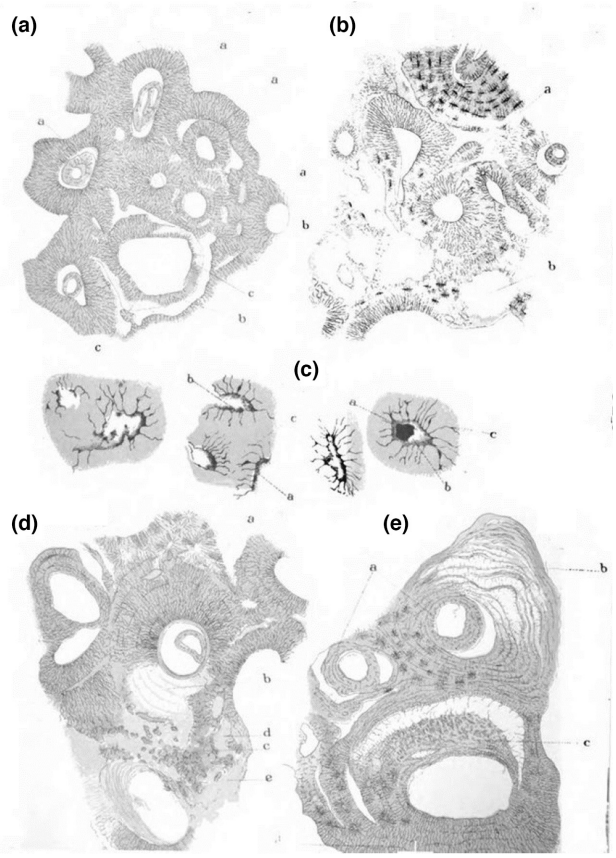

FIGURE 4 Drawing of the bone alteration described by Bonome and edited by the authors.[9] (a) Portions of the femoral diaphysis in transverse section. Reichert, objective 4, compensation 6: (a,a,a) Annular bone neoformations around vascular loops in the Havers canals; (b) Trait of a Haversian system in a state of incipient necrobiosis; (c,c) Metachromatic canal-free zones. (b) Portion of tibial diaphysis seen in transverse section. Reichert, objective 5, compensation 6: (a,a,a) Intermediary lamellar systems in metachromasia with necrobiosis; (b,b) Haversian systems in incipient necrobiosis. (c) Osteoplasts and channels undergoing regressive metamorphosis. Reichert, objective 9, compensation 6: (a, a) Contours of osteoplastic cavities with a grainy and hyper-coloured appearance, alternating with colourless traits; (b,b) Dilated osteoplastic cavities; (c,c) Interrupted channels, partly dilated, partly thinned. (d) Fragment of the humerus in cross-section. Reichert, objective 6, compensation 6: (a) Large Haversian system widely preserved and with several very fine channels, containing a thin newly formed trabecular ring in its cavities; (b) Short section of the aforementioned system free of channels; (c) Homogenous zones without channels with non-metachromatic reaction; (d) Zones with metachromatic reaction and no channels. (e) Transverse section of a femoral disc. The preparation demonstrates that there is a necrobiosis with fibral damages besides the neo formative reaction. Reichert, objective 6, compensation 6: (a, a) Newly formed annular bone trabeculae; (b) necrobiosis zone in a Haversian system with fibral damages; (c) necrobiosis zone with metachromasia in which fibres are not yet damaged; and (d) normal portion of a Haversian system.

since most of the cases of lung involvement are generally linked to superinfection of *M. tuberculosis*, even though quite rare and more common in patients who present immunodeficiency or multimorbidity.[19] Also, according to recent studies, '*lung has never been reported to be affected by leprosy*',[20] although further modern cases reported and confirmed the presence of Hanses' bacillus in the lungs,[21] as discovered by Bonome.

The revision of the ancient discovery made by Bonome during his period in Padua must not be underestimated and it must be re-evaluated to highlight new aspects of pulmonary leprosy, thus maybe allowing a better understanding of this pathology still widespread in the world and providing new effective treatments.

Instead, bone alterations in leprosy are nowadays known and classified as specific and non-specific: specific bony alterations are characterized by cystic brightening, while non-specific bone changes produce absorption of the bone structure and osteoporosis, both compatible with the results obtained by Bonome.[22] Anyway, the frequency of bone changes is still debated: a study puts the percentage to 87,3%,[23] other to 66% for specific alterations, similar to those described by Bonome.[24] Bone marrow involvement, as proved by Bonome, was recently reported in cases of lepromatous leprosy, and used, to some extent, to diagnose the disease.[25]

Concluding, Bonome has offered an important contribution to improving knowledge on this pathology at the beginning of the 20th century, thus giving him the proper credit to be among the first to make these new revolutionary discoveries.

AUTHOR CONTRIBUTIONS

Conceptualization: Filippo Valle, Giovanni Magno; Methodology: Filippo Valle, Giovanni Magno; Formal analysis and investigation: Filippo Valle, Giovanni Magno; Writing—original draft preparation: Filippo Valle; Writing—review and editing: Filippo Valle, Giovanni Magno, Alberto Zanatta; Supervision: Alberto Zanatta.

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CONFLICT OF INTEREST STATEMENT

All authors declared to have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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REFERENCES

1. Ooi WW, Srinivasan J. Leprosy and the peripheral nervous system: basic and clinicalaspects. Muscle Nerve. 2004;30(4):393–409. https://doi.org/10.1002/mus.20113
2. World Health Organization. Global leprosy (Hansen disease) update, 2022: new paradigm – control to elimination. Wkly Epidemiol Rec. 2023;98(37):409–30.

3. Hansen GA. Undersøgelser Angående Spedalskhedens Årsager. Nor Mag Laegevidenskaben. 1874;9(4):1–88.
4. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Mycobact Dis off Organ Int Lepr Assoc. 1966;34(3):255–73.
5. Alemu Belachew W, Naafs B. Position statement: LEPROSY: diagnosis, treatment and follow-up. J Eur Acad Dermatol Venereol. 2019;33(7):1205–13. https://doi.org/10.1111/jdv.15569
6. Zanatta A, Zampieri F, Bonati MR, Frescura C, Scattolin G, Stramare R, et al. Situs inversus with dextrocardia in a mummy case. Cardiovasc Pathol. 2014;23(1):61–4. https://doi.org/10.1016/j.carpath.2013.07.002
7. Zanatta A, Zampieri F. Origin and development of medical museum in Padua. Curator Mus J. 2018;61(3):401–14. https://doi.org/10.1111/cura.12273
8. Magno G, Zampieri F, Thiene G, Basso C, Zorzi F, Della Barbera M, et al. When self-medication goes wrong: the case of argyria at the Padua Morgagni Museum of Pathology. Virchows Arch. 2022;480(6):1283–8. https://doi.org/10.1007/s00428-021-03139-w
9. Bonome A. Distrofie Tosso-Infettive Nel Tessuto Osseo Di Due Esemplari Di Lebbra Tuberosa. Arch Sci Med Torino. 1910;34(15):271–98.
10. Bonome A. Ueber die Lungenlepra. Archiv f Pathol Anat. 1888;111:114–24.
11. Rodríguez G, Arias V. Giant cells lepromatous leprosy. Diffuse dermatitis with exuberant foreign body giant cells in treated lepromatous leprosy. Biomedica. 2019;39(Supl. 2):26–31. English, Spanish. https://doi.org/10.7705/biomedica.v39i4.4493
12. Britton WJ, Lockwood DNJ. Leprosy. Lancet Lond Engl. 2004;363(9416):1209–19. https://doi.org/10.1016/S0140-6736(04)15952-7
13. Slim FJ, Faber WR, Maas M. The role of radiology in nerve function impairment and its musculoskeletal complications in leprosy. Lepr Rev. 2009;80(4):373–87.
14. Rajpar I, Tomlinson RE. Function of peripheral nerves in the development and healing of tendon and bone. Semin Cell Dev Biol. 2022;123:48–56. https://doi.org/10.1016/j.semcdb.2021.05.001
15. Doutrelepont J, Wolters M. Beitrag zur visceralen Lepra. Arch f Dermat. 1896;34:55–86.
16. Scagliosi G. Ricerche anatomiche nei polmoni di un leproso. Riforma Med. 1896;3(39):459–62.
17. Fambri H. Pathologisch-anatomische Beobachtungen über einen Fall von Lepra universalis. Virchows Arch Path Anat. 1914;218:272–99.
18. Babeș V. Untersuchungen Über Den Leprabacillus Und Über Die Histologie Der Lepra. Basel: S. Karger AG; 1898.
19. Keragala BSDP, Herath HMMTB, Janapriya GHDC, Vanitha S, Balendran T, Janani T, et al. Coexistence of mycobacterial infections – mycobacterium tuberculosis and mycobacterium leprae – in Sri Lanka: a case series. J Med Case Reports. 2020;14(1):101. https://doi.org/10.1186/s13256-020-02413-w
20. Mastrangelo G, Marcer G, Cegolon L, Buja A, Fadda E, Scoizzato L, et al. How to prevent immunological reactions in leprosy patients and interrupt transmission of mycobacterium leprae to healthy subjects: two hypotheses. Med Hypotheses. 2008;71(4):551–63. https://doi.org/10.1016/j.mehy.2008.05.016
21. Uguen A, Schoenlaub P, Abalain ML, Grippari JL. Souvenirs d'enfance…. Ann Pathol. 2012;32(3):220–3. https://doi.org/10.1016/j.annpat.2011.12.002
22. Rothschild BM, Rothschild C. Skeletal manifestations of leprosy: analysis of 137 patients from different clinical settings in the pre- and post-modern treatment. Eras J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis. 2001;7(4):228–37. https://doi.org/10.1097/00124743-200108000-00008
23. Choudhuri H, Thappa DM, Kumar RH, Elangovan S. Bone changes in leprosy patients with disabilities/deformities (a Clinico-radiological correlation). Indian J Lepr. 1999;71(2):203–15.
24. Mohammad W, Malhotra SK, Garg PK. Clinico-radiological correlation of bone changes in leprosy patients presenting with disabilities/deformities. Indian J Lepr. 2016;88(2):83–95.
25. Velasco D, Lozano S, Villarrubia J. Leprosy diagnosed by bone marrow aspiration. Br J Haematol. 2013;160(2):121. https://doi.org/10.1111/bjh.12101

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