University of Pisa
Division of Paleopathology,
History of Medicine and Bioethics

Gino Fornaciari

The challenging case
of Cardinal Carlo de’ Medici

The First Clinical Challenge:
Eminence versus Evidence in Spondyloarthritis
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Paleopathology, defined by Sir Armand Ruffer, one of the founders of discipline, – “the study of disease in ancient human remains” – diagnoses diseases directly in ancient human bodies, skeletons or mummies.

Skeletons
 XI century burial, Monte di Croce castle, Tuscany

Mummies
 (Renaissance mummies, Basilica of S. Domenico Maggiore, Naples)

Sir Armand Ruffer (1859-1917)
PALEOPATHOLOGY

INTEREST

Anthropology

Life style of ancient populations

(trauma, arthritis..)

Medicine

Origin and evolution of diseases

(infectious diseases, cancer..)
The Paleopathology Group of Pisa University obtained some important results:

XV century colon cancer, with gene K-ras mutation (1996)

XVI century HPV virus (2003)

XII century American trypanosomiasis (1992)

XVI century venereal syphilis (1989)

Smallpox virus (1986)

Treponema pallidum (1989)

Malaria and Leishmaniasis of the Medici (2011)
The Medici were one of the most powerful families of the Italian Renaissance. Starting from the 14th century, their careful management of banking ventures and skilful political actions brought them to the forefront of social and political power in Tuscany and in Florence, the intellectual center of the Western world.

Lovers of art and science, the Medici were patrons of Michelangelo, Leonardo da Vinci, Botticelli, Galileo, and Benvenuto Cellini.
In 2002, dr. Antonio Paolucci, Superintendent of Florentine Museums, granted permission to examine 49 of the Medici burials in the Basilica. The "Medici Project" focuses on the Grand Dukes, who are less known than Lorenzo and his descendants.

The project involved collaboration among the University of Pisa, the University of Florence, and the Superintendence of Florentine Museums.

The most recent biomedical techniques were employed in order to obtain as much information as possible about the life style, the health and the environment of these famous rulers of Renaissance Florence.

I present here an important case of symmetrical polyarthritis found in the course of the “Medici Project”.
In order to conduct this study, we set up a temporary laboratory in the Lorena Chapel, the funerary crypt of the Grand Dukes of the Lorena dynasty, which ruled Florence and Tuscany after the Medici until 1859.
THE CRYPT OF SAN LORENZO

The crypt of the Basilica of San Lorenzo in Florence, Mausoleum of the Grand Dukes of the Medici family.

Map of the crypt, with the Medici tombs already explored in yellow.
THE “RICH” PATHOLOGY OF THE MEDICI FAMILY
(from archive documents)

INFECTIONOUS AND PARASITIC DISEASES
- smallpox
- tuberculosis
- malaria
- syphilis

METABOLIC DISEASES
- obesity
- anemia
- urinary stones

JOINT DISEASES
- ARTHRITIS

CARDIOVASCULAR DISEASES
- arteriosclerosis

TUMORS
- breast cancer

MALFORMATION
- dwarfism

Francesco I (1541-1587)
Maria Cristiana (1609-1632)
Anna Maria Luisa (1667-1743)
Cosimo I (1519-1574)
Cosimo III (1642-1723)
Maria Salviati (1499-1543)
Ferdinando II (1610-1670)
Cardinal Carlo (1596-1666)
Ferdinando (1663-1713)
Francesco Maria (1660-1710)

Maria Cristina (1609-1632)
Cardinal Carlo (1596-1666)
Anna Maria Luisa (1667-1743)

Cardinal Carlo (1596-1666)
Position of the tomb of Cardinal Carlo de’ Medici
Cardinal Carlo (1596-1666)

Sustermans (c.1640), Florence
**Anthropology**

Carlo (1595-1666), younger son of Ferdinand I, became cardinal in 1615 and dean of the Sacred College of Cardinals in 1652. His skeleton is that of a senile man aged more than 60 years, 1.70 m tall, with severe osteoporosis, especially of the lower limbs.

**Autopsy**

There are two transversal cuts on the upper part of the sternum (blue arrows); the sternal extremities of the 4th, 5th, 6th and 8th right ribs, and the 5th of the left, appear completely sectioned (red arrows), probably with scissors.
We know that, at 8 years of age, he was affected by tuberculosis of the column (Pott’s disease), upper thoracic or cervical. From 24 years of age he suffered from an acute articular disorder of the feet, hands and knees, diagnosed as 'gout' by the physicians; the documents report on 18 severe attacks from the ages of 35 to 59, with worsening between 60 and 65. From the ages of 50 to 70 he was affected by recurrent bronchitis and finally died of bronchopneumonia.

“Clinical history”

Sustermans (c.1650), Florence, Palatina Gallery
Paleopathology

The facial skeleton shows a marked hypoplasia of the right mandibular corpus, with right deviation of the face and probable chronic torticollis, as appears in a rare engraving (white arrow).

Haelvegh, engraving

X-ray Prof. N. Villari (University of Florence)
A block, involving the vertebral bodies with wedge-shaped collapse, fusion, and formation of an angular kyphosis (green arrows), is at the level of C6-C7. X-ray confirms body fusion (green arrows).

There is also diffused periostitis of the internal surface of the ribs (blue arrows), typical of tuberculosis.

These are the results of the cervical spine tuberculosis (Pott’s disease), characterized by neck *fistula* and *gibbus*, well described in the archival records, at 8 years of age.
“The portraits”

The portraits, at about 60 years of age, show symmetrical, severe arthropaty of the hands, with evident deformity and atrophy of 1st, 4th and 5th finger of the left hand.

Sustermans (c.1650), Florence, Palatina Gallery
The post-cranial skeleton shows an ankylosing disease, symmetrical and extremely severe, of the great and small articulations, characterized by:

- Fusion of the elbow (in flexion at 55°) (a, a');
• Bilateral fusion of wrists, carpal bones, and some fingers (b, b’), with bilateral swan-neck deformity (c).
• Fusion of the right sacroiliac joint (d) (red arrow)

X-ray Prof. N. Villari (University of Florence)

• Fusion of knees and *rotulae* (in flexion at 90°) (e)
This data, together with the very severe osteoporosis, in particular of the lower limbs, demonstrates the cardinal’s total disability, in the last years of life, as reported by the archival documents. Indeed, from 1658 (at the age of 63), the cardinal was no longer able to sign any letters or documents. In a letter to a nephew he writes: “Y(our) H(ighness) please excuse me for not being able to sign in my own hand (writing), because my hand does not function”

(4 December 1658)
Results of the PCR-SSP genotyping test for **HLA-DRB** locus of Cardinal Carlo:

The band positions of PCR products at *lines* 8 and 23 correspond to

**DRB1*04**

**DRB4**

alleles

(*Line 1* represents the negative control).

The remaining positive bands define the second alleles of Cardinal Carlo, exactly DRB1*11 (serotype DR11, *lines* 13 and 16) always co-expressed in conjunction with DRB3 (serotype DR52, *line* 22).

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Dr. G. Fontecchio,
Regional Centre for Immunohematology and Tissue Typing,
San Salvatore Hospital, L'Aquila
Results of the PCR-SSP genotyping test for **HLA-C** locus of Cardinal Carlo:

The band positions of PCR products at *lines 6 and 12*, correspond to

**Cw*04**

**Cw*12**

alleles.

(Line 1 represents the negative control).

Dr. G. Fontecchio,  
Regional Centre for Immunohematology and Tissue Typing,  
San Salvatore Hospital, L’Aquila
The genotype of Cardinal Carlo de’ Medici for the DRB1 and C loci was **DRB1*04/*11** and **(Cw*04/*12)**.

He was bearing the specificity **HLA-DR4** predisposing to **Rheumatoid Arthritis** (RA), but **not HLA-Cw6**, the strongest risk factor for **Psoriatic Arthritis** (PsA) and Psoriasis.

The DRB1*11, Cw*04 (Cw4 in serology) and Cw*12 alleles are not involved in the onset of RA, PsA or other rheumatic diseases.
The “clinical”, pathological and molecular picture clearly shows severe **rheumatoid arthritis (RA)**, excluding psoriatic arthritis characterized by similar, but not identical, macroscopic lesions.
Institutions involved

University of Pisa
Superintendence of Florentine Museums
University of Florence
Opificio delle Pietre Dure
Opera Mediceo-Laurenziana
University of Long Island
University of Minnesota
MGM Biotechnology, Pisa