

Heavy metals

The mysterious death of Francesco I de' Medici and Bianca Cappello: an arsenic murder?

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Modern analytical techniques suggest that the grand-ducal couple died of acute arsenic poisoning and not malaria as previously believed

Soon after the sudden and simultaneous deaths of Francesco I de' Medici, Grand Duke of Tuscany, and his wife, Bianca Cappello, in October 1587, rumours spread that the two had been murdered by Francesco's brother, Cardinal Ferdinando.^{1 2} Apparently, Ferdinando had a very good motive to kill his brother and the woman that Francesco had loved and then married after the death of his first wife the Grand Duchess Giovanna of Austria. Ferdinando was at risk of being excluded from the succession if Francesco's illegitimate son Don Antonio was to inherit the title of Grand Duke or, even worse, if Bianca, who was no longer able to have children, was to falsify the birth of an heir.

Deaths of Francesco and Bianca

A couple of weeks after Ferdinando came to the villa at Poggio a Caiano, in the surroundings of Florence, where Francesco and Bianca lived, the couple suddenly fell ill; they died 11 days later, a few hours apart. The behaviour of Ferdinando during Francesco's final days, and after his death as well, raised more than a suspicion about his involvement in his brother's illness. He took charge of the entire matter, drawing up all the medical bulletins and minimising the gravity of his brother's state of health in the dispatches sent to the Holy See. He stressed that his brother's illness had to be attributed solely to his imprudent eating habits and that Bianca's illness was caused by the grief she felt for her husband's condition. He did his best to raise an impenetrable wall of isolation around Francesco and Bianca so that they would not be approached by anyone with the right or authority to be admitted to their presence. He ordered immediate autopsies on the two bodies (which was habitual at that time for princes and rulers but not for a grand duchess) as if he wanted to have flawless documentation on the "non-toxic" cause of death in order to protect himself from future accusations. He arranged a solemn funeral for his brother but reserved a very different treatment for Bianca, whose body was taken to Florence by a small group of courtiers and, as a legend says, immediately buried in a common grave in San Lorenzo.

According to the Florentine diarist Domenico Martinelli,³ however, Bianca Cappello was buried not in San Lorenzo but in Santa Maria a Bonistallo, a church



United in death, too

close to the villa in Poggio a Caiano. Actually, four terracotta jars containing the viscera extracted from the autopsied bodies of Francesco and Bianca were buried in the crypt of this church. This has been recently confirmed by a document discovered in the *Episcopal Diocesan Archive of Pistoia, the Book of Marriages and Deaths, Year 1587*, kept by Monsignor Bernardo Baldovineti: "The day of October 19, 1587: between 4 and 5 am died His Serene Highness Francesco, Grand Duke of Tuscany, and on day 20 of the same month and year died Her Serene Highness Grand Duchess Bianca his wife and their viscera were brought to Santa Maria a Buonistallo in four jars. She died on Tuesday at 3 pm the interval between their deaths being about 12 hours. May God give them rest."

Early investigations

More than two and half centuries later, in 1857, the Grand Duke of Lorena, Leopold II, ordered the Medici

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family tomb to be opened for identification of the bodies and for final burial in the basement of the Medici Chapel, in San Lorenzo. After reading the reports of Francesco's exhumation, referring to a "fairly well preserved" body, and after examining the portraits drawn by two artists present for the recognition of the body, Féynes hypothesised that Francesco's death could be due to arsenic poisoning.⁴ Féynes was well aware that arsenic may slow down the putrefaction processes—as a result of both the direct action of the poison and the considerable loss of liquids from prolonged vomiting and diarrhoea before death—so that bodies exhumed after a long time are often found in a state of mummification.

In 1945, the graves of Francesco I and the other members of the Medici family were opened again on request of the anthropologist Gaetano Pieraccini. His project was to study the bones,⁵ in an attempt to correlate anthropometrical data with behavioural attitudes and lifestyle, under the influence of Lombroso's theories. According to the reports, the remains were exhumed, recomposed, and then replaced in the graves.

Possibility of arsenic poisoning

Two of us (FM and EB) have recently readvanced the hypothesis of arsenic poisoning,¹ on the basis of the following assumptions:

- Most of the symptoms reported by the doctors attending Francesco during his last days are typical of arsenic poisoning: nausea and violent vomiting as initial symptoms; cold sweats; repeated requests for cold drinks because of terrible dryness and constant gastric burning; the persistence of violent and convulsive vomiting; aggressive and delirious restlessness; apparent improvement four to five days after the onset of illness, followed by the sudden return of symptoms. Much less is known about Bianca's illness, though her doctors reported that she had been struck by a disease very similar in nature to that of her beloved husband
- These symptoms are quite different from those typical of a malarial infection, the cause of death hypothesised at the time
- The reports of the Grand Duke's autopsy are also very interesting in view of the hypothesised arsenic poisoning, describing evident gastric inflammation, enlarged and hard to the touch liver, multiple bruises in the lungs, and extensive oedema. Many of these findings were described at autopsy of the Grand Duchess, in addition to the dropsy that had tormented her in life
- White arsenic (arsenic trioxide), also known as arsenious acid or commercial arsenic, was certainly the best known and most commonly used poison in the Medici era.

Samples obtained

In the frame of the Medici Project, an internationally important historical, archaeological, and paleopathological study of the Medici funerary depositions in the 16th to 18th centuries directed by Gino Fornaciari of the University of Pisa, some of us (EB, FM, and DL), with the authorisation and under the supervision of Monica Bietti, director of the Medici Chapels in Florence, had the opportunity to collect biological



Two crucifixes found under the pavement of the crypt in the church of Santa Maria a Bonistallo

material from the grave of Francesco I (a fragment of femur and few beard hairs with one small fragment of skin tissue still attached) in order to determine their arsenic content. Subsequently, on the initiative of DL, some samples were collected from the remains of the broken terracotta jars buried under the pavement of the crypt in the church of Santa Maria a Bonistallo. Two small crucifixes (figure) were found during the inspection of the broken terracotta jars, indicating that these originally contained the organs of two people.

Samples collected in the church of Santa Maria a Bonistallo consisted of three different pieces of dry, thick, and crumbly material (samples A, B, and C) collected within the broken terracotta jars and of two other samples (samples D and E) collected as control samples of the material (mould) surrounding the broken jars. We submitted samples A, B, and C to histological analysis after inclusion in paraffin and haematoxylin-eosin stain and identified them to be biological tissues with rather damaged cells, in which nuclei and cytoplasm were still clearly recognisable. Sample A had a cellular and tissue structure compatible with liver, whereas for samples B and C the type of biological tissue could not be determined.

Arsenic concentrations

The table shows the arsenic content of the samples analysed. To estimate the arsenic concentrations in soft biological tissues at the time of death, the arsenic concentrations measured in samples A, B, and C must be adjusted for the water loss resulting from ageing. Considering that fresh liver contains approximately 70-80% water, and assuming (as an extreme hypothesis) that the water loss in biological tissues after more than four centuries has been complete (which is consistent with the dry and crumbly consistence of the samples), the arsenic content of samples A, B, and C should be reduced to between one third and one fifth of the data reported in the table. According to these calculations, the arsenic content in fresh tissues would have been in the range 5.4-8.2 mg/kg for sample A, 4.2-6.2 mg/kg for sample B, and 6.6-10.0 mg/kg for sample C.

The low arsenic concentrations in samples D and E allow us to exclude the possibility that the arsenic found in the biological tissues is a result of contamination from the material surrounding the broken terracotta jars.

A great part of the difference in arsenic concentrations in sample A measured by inductive coupled plasma atomic emission spectrometry (27.27 mg/kg) and by neutron activation analysis (12.08 mg/kg) is likely to be due to the absence of washing in the second determination. In fact, the material removed from sample A by the washing accounted for more than 40% of the gross weight of the sample.

Arsenic concentration in hair has been used as an indicator of arsenic poisoning. According to Hindmarsh, arsenic concentrations above 10 mg/kg in chronic poisonings and above 45 mg/kg in lethal poisonings are typically detected, whereas arsenic concentrations below 1 mg/kg should be considered normal.⁷ In a group of 50 non-exposed people (trauma victims) the average arsenic concentration in hair was 0.307 mg/kg, with values in the range 0–1.92 mg/kg.

The arsenic concentration measured in the beard hair of Francesco I (sample G) rules out the hypothesis of chronic exposure to high doses of the metal, especially considering that at least part of the arsenic detected could result from external contamination. However, in our opinion, this low concentration does not exclude the possibility that the Grand Duke was poisoned with arsenic, as in this case the survival time (11 days) could have been too short for a significant incorporation of arsenic into beard hair.

The same conclusion can be drawn for the arsenic concentration measured in femur (sample F), as this is lower than those found in bones of modern, non-exposed humans.^{8,9} Francesco I was an expert alchemist and a poisons scholar who might have been chronically exposed to arsenic during his alchemistic activities. This hypothesis is not supported by our findings.

In contrast, the arsenic concentrations measured in all the soft tissue samples (A, B, and C) support the hypothesis of acute arsenic poisoning. In fact, the concentrations in these samples, calculated by adjusting for the water loss due to ageing, are significantly higher than those measured in non-exposed humans (0–0.092 mg/kg in brain, lung, liver, and kidneys) and are in the range of those measured in a series of 49 fatalities attributed to accidental or intentional arsenic poisoning (2.0–120 mg/kg in liver; 0.2–4.0 mg/kg in brain; 0.5–62 mg/kg in spleen; 0.2–70 mg/kg in kidney).¹⁰

DNA profiling allowed us to establish that the DNA of samples A and C has an extremely high degree of similarity with the DNA of the small skin fragment

found attached to the beard hair of Francesco I. Therefore, it is highly probable that these soft tissues were among those extracted from the body of Francesco I at autopsy. DNA profiling of sample B revealed only its female origin. However, its proximity to the remains attributable to Francesco I may indicate that it was among the organs extracted from the body of Bianca Cappello at autopsy.

Conclusion

The results of toxicological investigations carried out on the samples identified as biological tissues and attributable, according to DNA profiling, to Francesco I de' Medici and, tentatively, to Bianca Cappello, and on the femur and beard hair of Francesco I, are consistent with the hypothesis that the Grand Duke and his wife were victims of an acute arsenic poisoning. The 11 day survival time after the onset of the illness could explain the not extremely high—though still in the lethal range, according to the literature—arsenic concentrations measured in soft tissues on the one hand and the very low concentrations detected in bones and hair (insufficient time for significant incorporation) on the other.

These findings, in addition to the historical data collected on the events before and after the almost simultaneous deaths of the grand-ducal couple, allow us to rewrite the historical reconstruction of those events and to affirm that acute poisoning with arsenic was the cause of death of Francesco I de' Medici and Bianca Cappello, in contrast to previous theories that attributed their deaths to malaria.

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Contributors: FM coordinated the study, is the guarantor, and did toxicological investigations on historical documents. AP coordinated the arsenic analysis by neutron activation analysis and wrote the paper. DL did investigations on historical documents and discovered the terracotta jars under the crypt of the church of Santa Maria a Bonistallo. EB collected biological samples in the Medici Chapels and coordinated arsenic analyses by inductive coupled plasma atomic emission spectrometry, histological analyses, and DNA profiling. All authors discussed the results and commented on the manuscript.

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Arsenic content in samples

Sample	Weight (mg)	Washing	Arsenic content (mg/kg)	Method
A (soft tissue, male)	1298	Yes	27.27	ICP-AES
B (soft tissue, female)	1635	Yes	20.81	ICP-AES
C (soft tissue, male)	906	Yes	33.28	ICP-AES
A	186.9	No	12.08	INAA
D (control)	203.0	No	1.26	INAA
E (control)	265.6	No	1.31	INAA
F (femur)	254.1	No	0.22	INAA
G (beard hair)	5.3	No	1.49	INAA

ICP-AES=inductive coupled plasma atomic emission spectrometry; INAA=neutron activation analysis.