

# Was Maria de' Medici a diabetic patient?

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**ABSTRACT** Queen Maria de' Medici (1573–1642) died in a miserable, marasmic state. Infections, gangrene, weight loss, fatigue and respiratory problems suggest a progressive decompensation of a previously existing Type 2 diabetes. The lack of biochemical data, however, permits only circumstantial evidence of this hypothesis. The author proposes that the queen developed subclinical diabetes after the age of 45, when she became obese due to excessive eating and lack of exercise. With a clear familial predisposition, she could have become insulin resistant and chronically hyperglycaemic. The presence of an internal deviation of the left eye, visible on several late portraits, suggests a mononeuropathy of cranial nerve VI. Repeated skin infections and gangrene of the lower limbs during the last month of her life complete the clinical diagnosis. Hyperglycaemic ketosis with Kussmaul respiration without adequate treatment may have caused her death.

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Maria de' Medici, Queen of France, died in 1642 in a marasmic and septic state. Abandoned by nearly everybody and heavily in debt, she was living in miserable conditions in an old Cologne brewery, a property formerly owned by her favourite painter, the Flemish master Pieter Paul Rubens. Only an old servant, her physician Riolant and some crooks, mostly spies of Cardinal Richelieu, were her final companions.<sup>1</sup>

How could a French queen, a member of one of the richest families in Europe, come to such an end? Maria was born in 1573 as the sixth daughter of the second Grand-Duke of Tuscany, Francesco I, and his first wife, Giovanna d'Austria. She became the second wife of King Henry IV of France and ruled over France after his death in 1610. However, her regency was not a success. She was hated by everyone: the nobles and the people did not like the 'italianisation' of the court, the Huguenots did not accept her support of the Catholics and nobody agreed with her excessive taste for luxury and her spending of royal funds on jewels and clothing. After her son, Louis XIII, came of age she was exiled to Blois and later to Compiègne, from where she escaped to the Spanish Netherlands to conspire against France. After a long journey through Europe Maria de' Medici arrived in Cologne in 1641.<sup>2</sup>

As recorded in the notes and correspondence of Dr Riolant, Maria's physical condition worsened progressively:<sup>3</sup>

- Over a period of six months she lost half of her weight despite fluid accumulation in the lower limbs and the abdomen.
- She developed fever and erysipelas of the face.
- Despite an enormous thirst, her urine volume decreased, suggesting renal insufficiency.
- Due to extreme fatigue she could not leave her bed.
- Her respiration was slow and very deep.
- On 1 July 1642 gangrene appeared in her right leg; an amputation was proposed but refused by the patient.



**FIGURE 1** Portrait of Queen Maria de' Medici by Pieter Paul Rubens. (With kind permission of the Prado, Madrid.)

- Periods of agitation alternated with subcoma.
- Haematemesis was observed.
- The queen died on 3 July 1642.

It has been suggested that Maria de' Medici was poisoned by one of her servants in the pay of the French court or that she committed suicide.<sup>4</sup> The post-mortem examination, however, found no evidence for either of these theories.<sup>3</sup> It reported:

- extensive gangrene of the limbs
- an enlarged heart with fluid in the abdomen
- a calcified aorta and atheroma of most of the large arteries

- small atrophic kidneys and pancreas
- a small stomach ulcer (a terminal 'stress ulcer' explaining the haematemesis?)

The body was later transported to France, but during the French Revolution the remains were removed from the grave, rendering further research impossible.

During a metabolic meeting last year,<sup>5</sup> the author defended the hypothesis that the queen died in a hyperglycaemic, ketotic coma precipitated by infections and gangrene which was not adequately treated because of the lack of insulin, intravenous fluids and antibiotics. The loss of weight, severe thirst, extreme fatigue and slow, difficult respiration (Kussmaul?) are the clinical arguments to sustain this theory. However, to make the hypothesis acceptable, I had to find arguments showing the presence of a pre-existing Type 2 diabetes. The diagnosis of this type of diabetes, especially in the preclinical period, was practically impossible in the sixteenth and seventeenth centuries. For this reason I have had to refer to circumstantial evidence based on the presence of chronic diabetic complications, described in documents or biographies, or on objective data discovered at the post-mortem or paleopathological examinations.

### 1. Family history

Maria's grandfather, Cosimo I, died at the age of 54 years after repeated cerebrovascular insults.<sup>6</sup> Her grandfather and uncle, Ferdinando I, suffered from gout and diffuse idiopathic skeletal hyperostosis (DISH),<sup>7</sup> both well known to be associated with diabetes.<sup>8</sup> Her mother, Giovanna d'Austria, was found to have a severe hyperostosis of the skull, frontal and occipital.<sup>7</sup> This form of hyperostosis is considered to be part of the osteopathic lesions of Type 2 diabetes.<sup>9</sup>

### 2. Obstetric history

Maria bore three sons and three daughters by Henry IV and no stillbirths. None presented signs or symptoms suggestive of diabetes.<sup>10</sup> There are no data available on their birth weight, but the oldest son, the future Louis XIII, was described by his father as being fat.<sup>11</sup>

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### 3. Personal history

During her stay in France, Maria had never been seriously ill. Her main problem was progressive weight gain, induced by a lack of physical exercise and the continuous eating of *pâtisseries et confitures*.<sup>12</sup> When we compare the slender young bride of 1600 (Jacopo Chimenti, Uffizi, Florence) with paintings made during the Regency (Frans Pourbus II, Rijksmuseum, Amsterdam) this fact is striking. By the age of 57, Maria had become a full-blown, obese *matrona* as shown by the Rubens painting of 1631 (Figure 1). During her exile in the Spanish Netherlands she presented with episodes of fever and migraine from which she recovered well after treatment by Dr Vautier.<sup>3</sup>

### 4. Diabetic complications

The erysipelas during the last month of Maria de' Medici's life is an infection frequently described in uncontrolled diabetes.<sup>13</sup> The gangrene of both legs is a classical complication of macroangiopathy, although not specific for diabetes.<sup>13</sup> It is not impossible that Queen Maria developed a mononeuropathy of cranial nerve VI. Indeed, when we look at Figure 1, the left eye is deviated to the right, an anomaly that can also be seen in the painting of Frans Pourbus II. This eye deviation is not present in any of the paintings made before 1611. Palsies of oculomotor nerves, even transient ones, are well known in Type 2 diabetes, even in the preclinical state, and are the consequence of metabolic abnormalities or diabetic microangiopathy.<sup>14</sup>

## CONCLUSION

In conclusion I would like to propose the following hypothesis: Maria de' Medici developed Type 2 diabetes between the ages of 35 and 45 years. Having a familial predisposition, she became insulin resistant as a consequence of obesity and repeated pregnancies. During the preclinical phase she showed signs of chronic diabetic complications (mononeuropathy). As a consequence of infection, gangrene and physical and emotional stress the diabetes decompensated (severe weight loss, fatigue) and she died in a ketotic, hyperglycaemic coma resulting from a lack of adequate treatment combined with heart and renal insufficiency.

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