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Prof.ssa Maria New

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Ancient History of Congenital Adrenal Hyperplasia

Ancient History of Congenital Adrenal Hyperplasia

Maria I. New

Mount Sinai School of Medicine, New York, N.Y., USA

Abstract

Although there are many erudite reports on the history of endocrinology and endocrine disorders, the history of congenital adrenal hyperplasia has not been published. I have tried to review ancient as well as modern history of CAH.

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Most endocrinologists regard Giuseppe Marzo as the first patient described with congenital adrenal hyperplasia (CAH) (fig. 1). The cadaver of Giuseppe Marzo in figure 1 was described by de Crecchio, who was conducting the autopsy. He published it in the journal *Morgagni* in 1865;7:154. The description indicated marked surprise at finding uterus and fallopian tubes in this patient, who had very large adrenals. The story of the patient, Giuseppe Marzo, was that he was originally assigned as a female called Giuseppina (Josephine), but then was found to have genital ambiguity and was reassigned as a male, called Giuseppe. He was reared as a boy, and as an adult joined the noble household in which his father worked. Giuseppe fell in love with a maid, proposed marriage, and produced his birth certificate, which said Giuseppina. It was reported that she ran away, and that Giuseppe died of a broken heart. Possibly he died of a salt-wasting crisis. Dr. de Crecchio wrote in very flowery language the remarkable size of the adrenals.

However, it is possible that a case of CAH was indirectly reported in 800 AD, when a female pope was said to be elected. This remarkable event is described in a book by D'Onofrio, entitled *La Papessa Giovanna (Pope Joan)* (fig. 2).

The legend of a female pope is first recorded in a manuscript by the friar Jean de Mailly from about 1250 AD. During the late Middle Ages and Reformation, dozens

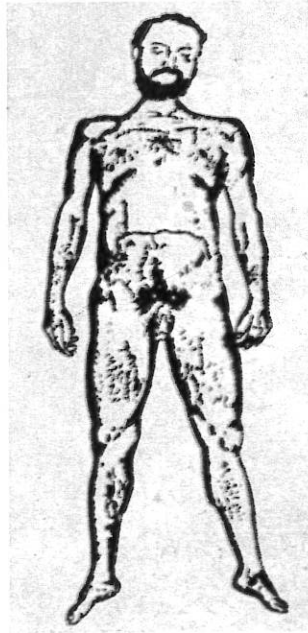


Fig. 1. Giuseppe Marzo from de Crecchio L.
Sopra un caso di apparenze virili in una donna.
Morgagni 1865;7:154.

of people wrote about this scandal, many of them Franciscan and Dominican friars or Protestants, and their stories were widely believed. The most popular version was a bestseller all over Europe for hundreds of years after its publication around 1265. This appeared in Martin Polanus' *Chronicon Pontificum et Imperatum*:

'After. . . Leo, John Anglicus, born at Mainz, was pope for 2 years, 7 months, and 4 days, and died in Rome, after which there was a vacancy in the papacy of 1 month. It is claimed that this John was a woman, who as a girl had been led to Athens dressed in the clothes of a man by a certain lover of hers. There she became proficient in a diversity of branches of knowledge, until she had no equal, and afterwards in Rome, she taught the liberal arts and had great masters among her students and audience. A high opinion of her life and learning arose in the city, and she was the choice of all for pope. While pope, however, she became pregnant by her companion. Through ignorance of the exact time when the birth was expected, she was delivered of a child while in procession from St. Peter's to the Lateran, in a narrow lane between the Coliseum and St. Clement's church. After her death, it is said that she was buried in that same place. The Lord Pope always turns aside from the street and it is believed by many that this is done because of abhorrence of the event. Nor is she placed on the list of the holy pontiffs, both because of her female sex and on account of the foulness of the matter.'

Boccaccio, the Italian humanist, relished the tale and included it in his book, *De Claris Mulieribus*, published circa 1350. This was the first recorded attribution of a woman's name, Gilberta, to John Anglicus (Pope John VIII). There are various accounts of how Pope Joan died; some authors have her torn limb from limb by an angry crowd; others say she was dragged by horses through the streets of Rome. Petrarch (1304–1376), evidently thinking of the plagues of Revelation, added that



Fig. 2. In 800 AD a female Pope was proposed.

after her death it rained blood for 3 days and nights and locusts with six wings and powerful teeth appeared in France.

Is There Any Evidence That Pope Joan Existed?

Is there any factual basis for the fantastic stories about Pope Joan? To answer this question, it helps to have some idea of the historical framework. In 800, on Christmas Day, Charlemagne was crowned Holy Roman Emperor by Pope Leo III in thanks for his help in staving off the Lombards who periodically attacked Rome and for defending him from enemies among the Roman nobility, who had physically attacked him. But after Charlemagne's death in 814, the papacy fell increasingly under the sway of the impious and powerful Roman nobility. The existence of this corruption is central to understanding the birth of the legend. Joan's papacy was placed by Martin Polanus and most of her

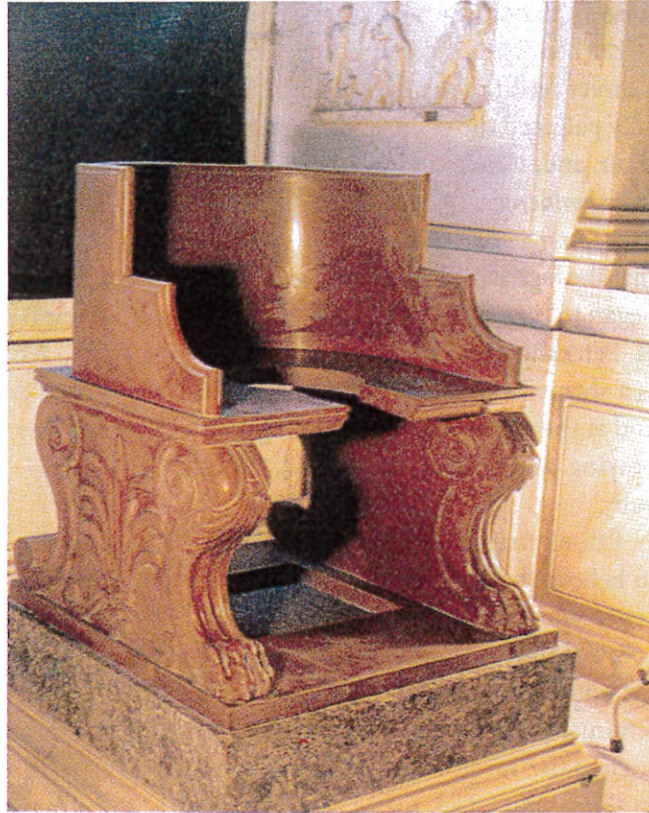


Fig. 3. Porphyry chair with perforated seat dating to classical times. Used in the installation of Popes 1099–1513. Discontinued by saintly Hadrian VI. Used to check the new pope's sex after Joan?

other chroniclers in the years 855–857, between Popes Leo IV (847–855?) and Benedict III (?855–858). Jean de Mailly and some others put her around 1100. But all of these accounts of Pope Joan were written long after she was said to have lived—in most cases 400 years after. The existence of a female pope is not mentioned in any private letters or official communications or histories at the time(s) of the alleged papacy.

Another avenue for this legend might have been the Christian literary tradition of the female saint in male disguise, which derives from the early legend of St. Pelagia the Penitent. Whatever the first source of the Pope Joan legend, turmoil within the Church continued for centuries, culminating in the Protestant Reformation, and so the story lived on, along with growing controversy as to its truth.

Is there any solid evidence that Pope Joan ever lived? There are three facts to weigh. The first is this: In the nave of the Cathedral of Siena is a series of busts representing each of the legitimate popes. The head of Johannes VIII, *Femina de Anglia*, was placed between those of Leo IX and Benedict III until 1600, when Pope Clement VIII ordered it removed, and it was recycled as the head of Pope Zacchary. Was this a cover-up?

Second, there is the famous 'Sedia Gestatoria,' a red marble chair, now in the Vatican museum, which has a perforated seat (fig. 3). It is known that this chair was

used in the ceremonies of installation of the popes between 1099 (Paschall II) and 1513 (Leo X). It is rumored that it was used to ascertain the gender of popes-elect as a direct result of the scandal of a real Pope Joan. The 'junior cleric present' purportedly palpated the genitals of the papal candidate through the hole in the bottom of the chair, and, if he found what he expected, shouted in a loud voice, '*Testiculos habet et bene pendentes. (He has well-formed testicles).*' To which all the clerics replied, '*Habe ova noster papa (Our father is virile).*' Finally, there is the fact that around the time that the legend of Joan was spread by Martin Polanus' book, formal papal processions began to turn off the most direct route between their home in The Lateran Palace and St. Peter's to avoid the place where Joan was said to have given birth. On route, there is a shrine presumably on the spot where Pope Joan gave birth. I walked that route, and at the shrine, there was a pregnant woman praying. I asked her to whom she was praying, and why. She answered, 'I am praying to Pope Joan for me to have a healthy baby.'

I think that the story of Pope Joan must be a legend because it is very hard for me to believe that this fantastic event could have occurred in the 9th century without a contemporary written record. Yet despite the unlikelihood of its truth, this tale has continued to be retold and even believed up to the present day. It has been the vehicle for both ribald mockery and serious accusation of the Church. It has been used for feminist propaganda, as a basis of romantic fiction and drama, and in card games such as the Tarot, which has a card, the High Priestess, first identified with Pope Joan in the famous deck made for the Visconti-Sforza family by Bonifacio Bembo in the 1400s. My brother-in-law is one of the chief librarians of the Library of Congress, and when I was preparing this lecture, I asked him to send me everything he had on Pope Joan. I was amazed to find that there are hundreds of publications about Pope Joan. Many are written by historians sorting through the evidence, but the story has a life of its own.

Real Patients That Could Have Been Pope Joan

If Pope Joan was a legend, why as a civilization have we not lost interest in her after all these centuries? Why do many people persist in believing that her story could have been true? The fact is, on a biological basis, it might have been. I have known a man who if he had lived in the 9th century could have been Pope Joan.

The very masculinized person shown in figure 4a is a patient with CAH whose karyotype is 46,XX and who was never treated. In figure 4b is the recent picture of a female subject who chose to take testosterone to become masculinized. She changed her birth certificate to that of a male, and married a female who had had 2 children by a former husband. The couple wanted a child and so the husband decided to stop taking testosterone and demasculinize. He began menstruating and became pregnant by artificial insemination.

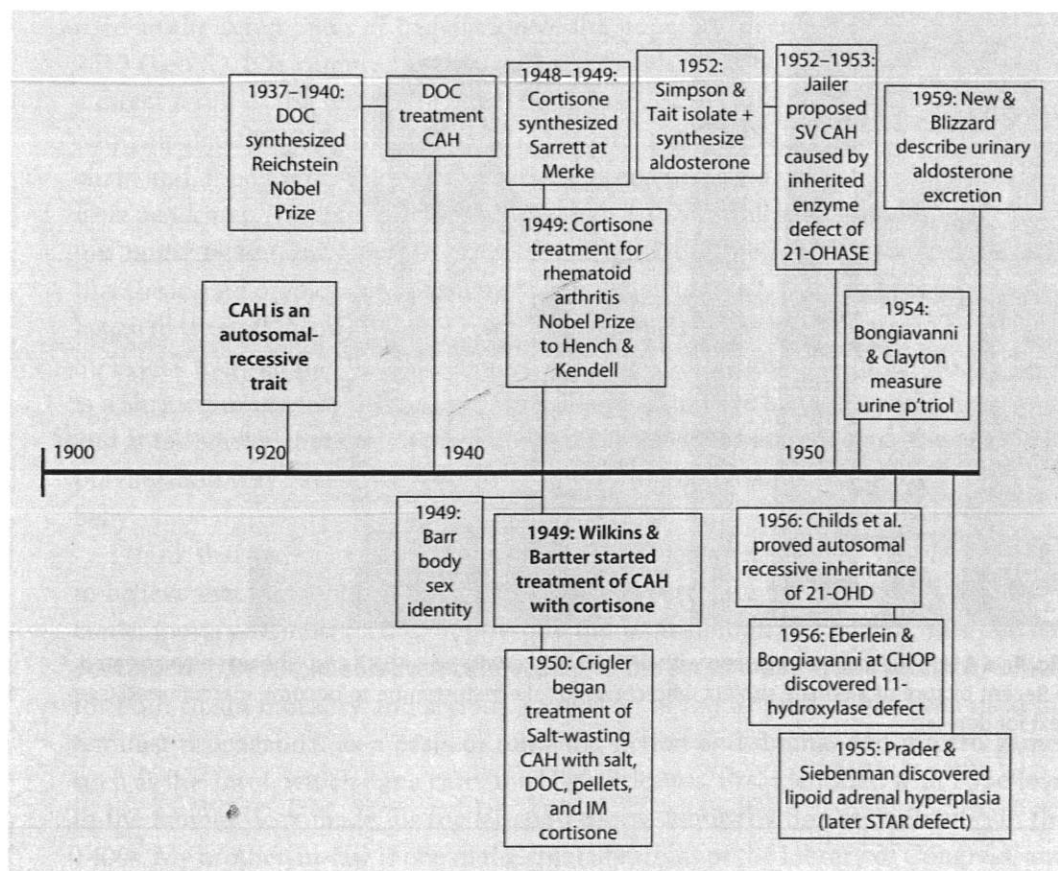


Fig. 6. Modern history of CAH: the timeline indicates that the modern history begins in the 20th century and continues into the 21st century.

In light of such cases, it is possible to imagine the story of Joan would be that Pope John VIII was a female pseudohermaphrodite who had a homosexual liaison, got pregnant, and delivered a child. The endocrinological version of the legend is that Pope Joan had a recognizable syndrome, CAH.

And Even Before 800 AD

The pedigree of the ancient biblical family shows consanguinity and infertility (fig. 5). Abraham married Sarah, who was the daughter of his brother, Haran. Haran died at an early age, and as was the custom, Abraham married the daughter was left orphaned. Further, it was said that Sarah was infertile and told Abraham to take the slave girl Hagar, by whom Abraham has a son called Ishmael. And it is said that at the age of 99, Sarah prayed to God, and gave Abraham a son called

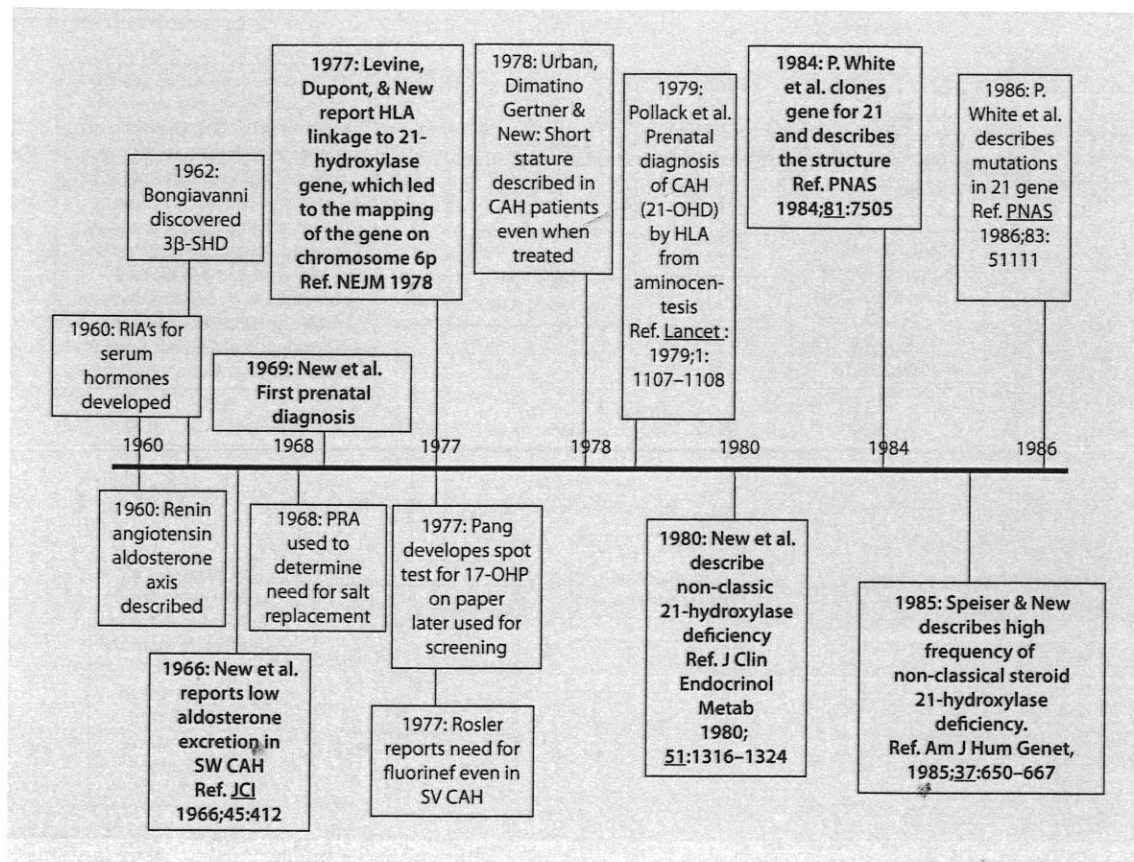


Fig. 6. Continued.

Isaac. Thus, in this ancient pedigree there was consanguinity and infertility, and I may speculate that this ancient family may have suffered from the non-classical form of CAH.

It is no wonder that the story of Pope Joan continues to resurface inspiring art and controversy. Whether or not she really lived and had a recognizable syndrome, Pope Joan is a symbol of the fascination and tragedy of gender ambiguity, and as such is likely to remain in the public eye.

Modern History of CAH

The modern history of CAH is depicted in figure. 6. The timeline indicates that the modern history begins in the 20th century, and continues into the 21st century.

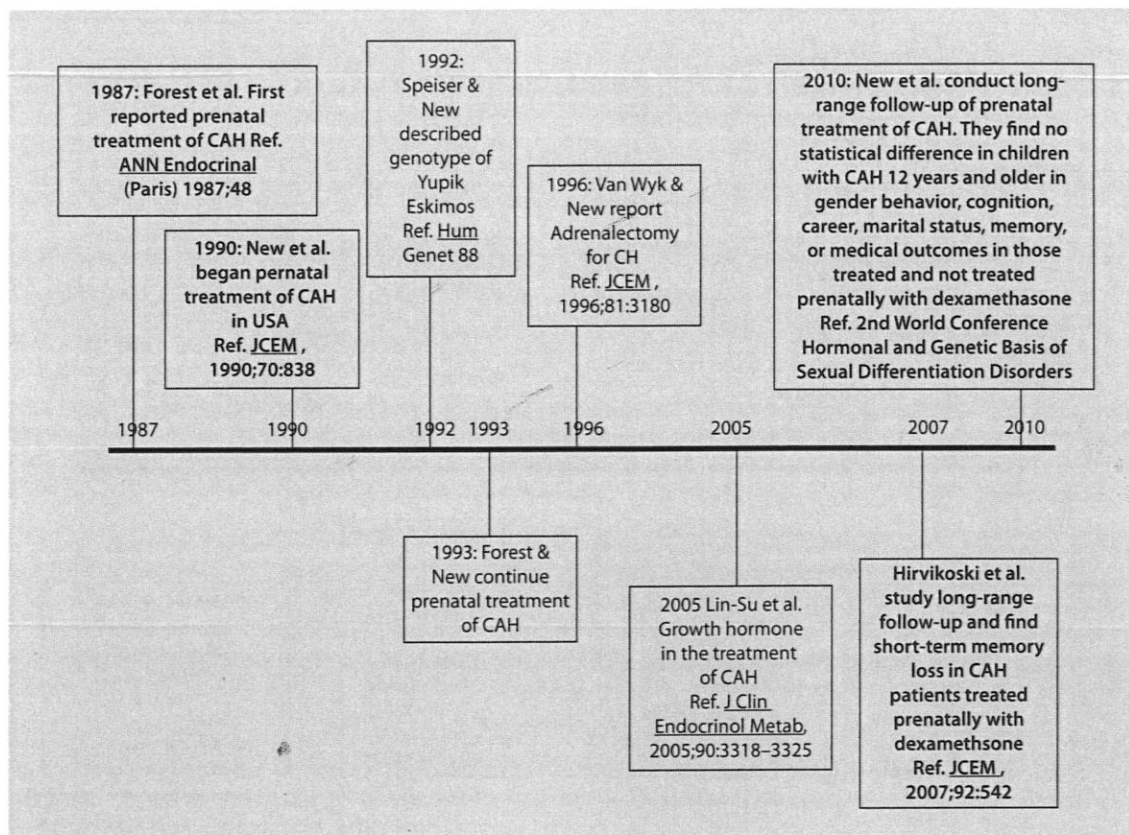


Fig. 6. Continued.

Future of CAH Investigation

The author proposes the following areas for future CAH investigation: (1) gene therapy, (2) non-invasive prenatal diagnosis and treatment, (3) advance understanding of psychoendocrinological factors, (4) improve surgical repair of genital ambiguity, and (5) discover the basis for the high-frequency of non-classical 21-hydroxylase deficiency.

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Suggested Reading

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Prof. Maria I. New
Pediatric Endocrinology, Genetics, and Genomics
1 Gustav L. Levy Place, Mount Sinai School of Medicine
Box 1200, New York, NY10029 (USA)
Tel. +1 212 241 7671, Fax +1 212 241 5405, E-Mail maria.new@mssm.edu