

Historical note**The adrenal glands: a brief historical perspective**Basil Leoutsakos¹, Agnes Leoutsakos²¹Department of Surgery, Athens University Medical School, ²World Health Organization, Geneva, Switzerland

There have been numerous references to the existence of the adrenal glands ever since ancient times, with an increasing amount of knowledge being accumulated and recorded from the 16th century on.¹ Although it would evidently not be possible to cover the plethora of historical references to these glands, a historical outline is herein undertaken.

According to Professor R. B. Greenblatt, probably the first account in the western world of the adrenal glands is to be found in the Bible.² In his work *Search the Scriptures* (1977), he cites the clear case of monozygotic twins, the Biblical twins, Esau and Jacob, the first being described as exceptionally hairy and strong, possibly presenting the symptoms of congenital adrenal hyperplasia, whereas the other was completely normal. This author proposed that the ancient Hebrews knew about the adrenal glands and their disturbances.

During Roman times, better documented descriptions are to be found on the adrenal glands as compiled by Claudius Galen (130-201 AD), although there is a debate as to their accuracy. Galen refers to a particular tissue as “loose flesh” – the assumption being that reference is being made to an accessory to renal tissue – and clearly describes the left adrenal vein connected to the left renal vein. Several historians³ believe that Galen’s description of the left adrenal vein is proof that he was the first to discover and describe the adrenal glands in mammals, while

others⁴ have not accepted this contention.

The first to unambiguously describe the adrenals, while including several accurate illustrations, was the anatomist Batholemeus Eustachius⁵ (1520-1574) who in 1563 published his works describing the kidneys in detail and referring to the adrenals as *Glandulae renibus incubentis*, a term that implies an auxiliary renal role. A few years later, in 1568, a researcher by the name of Archangelo Piccolamineus⁶ (1562-1605) refuted the accuracy of Batholemeus Eustachius’ findings and wrote, “... sometimes, one may see two or more glands lying on the kidneys, but we do not think that they deserve special attention... They may thus be considered as renal excrescences.”

Several years later, Gaspar Bauchin⁷ (1550-1629), Giulio Casserio⁸ (1561-1616) and Adrianus Spigelius⁹ (1578-1625) commented on the existence of the adrenal glands. Giulio Casserio termed them *Renes succentuari* and Adrianus Spigelius *Capsular renales*.

The anatomist Gaspar Bartholin¹⁰ (1586-1629) believed the adrenals to be hollow organs filled with “black bile” and named them *Capsulae atrabiliariae*, and Johan Vestling (1598-1649) in his treatise published in 1653 supported Bartholin’s view on the adrenals. However, several investigators including Dominicus de Merchetis (1526-1688), A. Molinetti¹¹, Nathaniel Higmore¹² and others, were detractors of Bartholin’s theory. In addition, Jean Riolan the younger¹³ (1538-1605) stated in 1655 that “... I have never seen a cavity in them. Should they have a cavity, no pea would find a place in it.” He named them *Capsulae suprarenales*. In 1640 Andre du Laurens¹⁴,

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also doubting the existence of these organs, wrote, “Eustachius claims to have found a gland above the kidneys. Sometimes we have also noted this; often however we did not”.

Further insight was provided by Marcus Aurelius Severinus (1580-1658) who first described an excretory duct issuing from the adrenal gland and connected to the left epididymis. Later on Antonio Maria Valsava¹⁵ (1666-1723) also described a duct between the left adrenal gland and the left ovary in a woman. Valsava also indicated that the adrenals regulate the libido.

Cuvier (1769-1832) was the first to recognize that the outer portion of the gland is morphologically distinct from that of the centre¹⁶. Thirty years later, in 1836, N. Nagel¹⁷ made substantial reference to the human adrenal glands and for the first time used the terms *cortical* for the outer part and *medulla* for the inner part.

However, it was only during the first decades of the 19th century that scientists had at their disposal an improved compound microscope enabling them to make accurate observations of the morphology of the adrenals. Alexander Ecker¹⁸ (1816-1887), one of the first to make use of this new instrument, pointed out in 1846 that the adrenal medulla is remarkable for its brightness. Credit, however, for the first complete microscopic description of the anatomy of the adrenals goes to R.A. Von Kölliker¹⁹ (1817-1905) who in 1852 stated that “The cortical and medullary substances are physiologically distinct and have different functions ...”

It was not until the latter half of the 19th century that, by virtue of a large number of in-depth studies, it was unequivocally recognized that the adrenal medulla is functionally, histologically, embryologically and in many other respects separate from the cortex.

Starting from the early times of Eustachius, a range of functions of the adrenals were proposed by several investigators. In 1657 Thomas Wharton¹⁵ (1610-1678) associated the function of the adrenals with that of the nearby solar plexus. Wharton is believed to have been the first to correlate the adrenals with the nervous system.

In 1806 Johan Friedrich Meckel²⁰ (1714-1774)

associated the adrenal glands with sexual functions. Meckel stated that the basis for this relationship was “... their simultaneous considerable development in several orders of mamalia...” and furthermore maintained that abnormalities of the adrenals were also connected with abnormalities of the sexual organs such as those, for example, in gestation or arising from syphilis.

Several authors including Coxe and Shumacker have pointed out that early investigators clearly described miscellaneous functions of the adrenals. For example, Jean Baptiste Senac (1693-1770) suggested that the adrenals secreted foetal mecomium, Jean Von Helmont (1577-1644) assumed that they secreted a juice which prevented the formation of renal calculi, while Giovanni Morgani (1622-1771) believed that these organs drained the lymph from the intestines during the life of the foetus, since the cisterna chili were observed not to be filled with lymph during this period.

Most significantly, John Goodsir (1814-1867) published a paper in 1846 declaring that the adrenals, the thymus and the thyroid have embryologically the same origin and therefore may function similarly. Goodsir writes “[these glands]... elaborate the matter which has already been absorbed by other parts and is now circulating in the vessels of the more perfect individuals...”. In this idea we find the seed of modern endocrinology. Since very ancient times, and through the period of intense observation from the 16th to the 20th century, endocrinology has emerged worldwide, as a highly specialized discipline of medical sciences.

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