

# History

## The History of Urticaria and Angioedema

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### Names for urticaria before 1769

Probably the earliest description of the disease we now call urticaria is to be found in *The Yellow Emperor's Inner Classic* (Huang Di Nei Jing), which was written sometime between 1000-200 BC (1, 2). In chapter 64 of "Sin Wen" (Basic Questions), urticaria is called "Feng Yin Zheng," which means wind-type concealed rash. "Feng Yin Zheng" is still the Chinese word for urticaria, which was thought to be caused by an excess in lesser Yin, producing an obstruction of fluid in the skin.

Hippocrates, who lived from 460-377 BC, described elevated itching lesions caused by nettles and mosquitoes, which he called *knidosis* after the Greek word for nettle (*knido*). He also mentions that the weals sometimes occur in patients with gastrointestinal disorders, but then often with less itching. Hippocrates' term was taken up by Jean-Louis Alibert in Paris, in his book on skin diseases published in 1833 (3). Hebra used the term *knidosis* for the chronic type of nettle rash, whereas Andrew's and Domonko's textbook from 1963 used it synonymously with urticaria.

Plinius (32-79 AD) introduced the name *uredo* which means "burning." The term was later adopted by such Latin-speaking doctors as Carolus Linnaeus to denote "red, evanescent itching eruptions." In the 10<sup>th</sup> century, Ali Ibu Al-Abba called it *essera*, which means "elevation" in Persian. After the decline of the Roman empire, this term was used for centuries in both the Arabic and the European world.

In his book *King Richard III*, Thomas More gives an excellent description of the condition, but without giving it a name (4). However, this book is of interest since it is the first case of urticaria reported as able to cause death. In 1480, before the coronation of King Richard, some lords wanted to please him by serving him a cup of strawberries. A few hours later, he suddenly assembled the lords, opened his shirt and showed them his chest, which was covered with red elevated and itching spots. He accused one of the lords of trying to poison him and had him executed on the spot.

### Introduction of the name *urticaria*

In the early 18<sup>th</sup> century, laymen used the term "nettle-rash." The most stinging nettles belong to the genus *urticaria*. In his "Grosses vollständige Universallexikon" from 1734-1740, Zedler changed *uredo* to *urticatio* (5). The word "urticaria" was first introduced in 1769 by William Cullen in his book *Synopsia Nosologiae Methodica* (6). It also appeared in the first

edition of Encyclopaedia Britannica (1771), written under the pseudonym of "a society of gentlemen in Scotland." The term *urticaria* was later accepted by Peter Frank in Vienna and in other centers of medical science. Cullen, who was professor of medicine in Edinburgh, started to classify the skin disorders in the same way that Linnaeus had done with plants. Cullen was a Quaker, as were several of the doctors from the University of Pennsylvania who came to visit him (7). Philadelphia, still called the Quaker City, is home to the first medical school in North America, founded in 1765. The school's first professors were all trained in Edinburgh, and thus the name "urticaria" was introduced into North America.



William Cullen (1710-1790) at age 58, after William Cochrane, Royal College of Physicians in Edinburgh.

Also a Quaker, Robert Willan from England was for that reason not allowed to study in Oxford or Cambridge. He began his medical education in Edinburgh in 1777 and came under the influence of Cullen's ideas on the classification of skin disorders. In 1783, Willan returned to London, where he was soon appointed physician at a newly established public dispensary in Carey Street. Here he saw a great many poor people and also visited their homes. Willan was known for his kindness to his patients, and for being a sincere and reserved man and a good teacher, with an intense dislike for alcohol, which was a common cause of premature death among his patients. He was especially interested in skin disorders and perfected the classification of cutaneous diseases based on the morphology of the lesions. He had read a book on the subject by Josef Plenck, published in 1776, but since it described a mixture of lesion type, location and etiology, he did not cite it (8). Willan's findings, which brought order to the existing classification, were published in separate parts from 1798 to 1808 (9).

In 1801, Willan met Thomas Bateman, who had just finished his medical studies in Edinburgh. Bateman joined him at the dispensary. Bateman, who was very religious and fond of music, was said never to waste a minute and always have his pen in his hand. Bateman embraced Willan's approach to skin problems and soon became his trusted assistant, friend and eventually his successor. Willan was stricken with heart problems at the height of his fame. In 1811, he retired and sailed for Madeira in the hopes of

being cured, but died there at the age of 55. His work, completed by Bateman, became the influential masterpiece, *A Practical Synopsis of Cutaneous Diseases*, published in 1813 and translated into many languages (10). In the book, several different types of urticaria were described: 1. *Urticaria febrilis*, where the patient has fever and abdominal pain for some days before the skin lesions appear. This urticaria usually lasts for a week; 2. *Urticaria evanida*, where new lesions can continue to appear for many months or years and most of the itching occurs at night. This makes it correspondent to chronic urticaria; 3. *Urticaria perstans*, where the single central weal remains for some days and feels hard. The initial reddening around the weal soon disappears. This description corresponds to *urticarial vasculitis*. Bateman also described *lichen urticatus*, or *papular urticaria*, in children, which he differentiated from the real urticarias.

However, there were those who did not accept Willan and Bateman's system. One was Jean Louis Alibert, who was the leading dermatologist in Paris at the time. As mentioned above, he preferred the Greek word *knidosis* to *urticaria* and wanted a new classification, since Willan's study was based on outpatients without a follow-up of possible etiology. Alibert was an excellent teacher and observer who attracted doctors from all over Europe to Hôpital Saint-Louis. When the lecture room became too small, he lectured in the hospital garden under the trees. Alibert stood on a wooden platform and called up patients by the

name of their disease (11, 12). A book on skin diseases by Alibert was admired by King Louis XVIII, who appointed him as his personal physician, granting him an important social position. After the death of Louis, King Charles X kept him as physician and he was awarded the title of baron. Since he was thus away from his department for many years, his best pupil, Laurent Bielt, took over. Bielt visited Bateman in England in 1816 and reintroduced the Willan-Bateman method to Paris. When Baron Alibert returned to Saint Louis Hospital in 1829, he tried to introduce his own construction of a tree with dermatosis on the branches, but it was so complicated and worthless that it never caught on (33).

### **The physical urticarias and *urticaria pigmentosa***

Several physical urticarias were mentioned early in history. *Solar urticaria*, for instance, was described by Borsch in 1799, but it was not until 1887 that Veiel showed that it was solely solar rays and not heat from a stove or candle that were responsible (13, 14). *Factitial urticaria* was first documented in the Middle Ages, when people with this condition were beheaded or burnt alive because they were believed to be related to the Devil (15). It was first described in the medical literature by Heberden in 1767, with Gull coining the name *factitious urticaria* in 1859 (16, 17). Cold urticaria was described by Frank in 1792 (18). A form of urticaria caused by heat and mental or physical exertion, producing distinctive, small, short-lasting weals, was documented by Duke in

1924 in JAMA (19). When the underlying mechanism became known, it was also called *cholinergic urticaria*. Duke also reported the rare heat contact urticaria (19). Pressure urticaria was described by Urbach & Fasal in 1929 (20). Aquagenic urticaria was reported by Shelley & Rawnsley in 1964 and adrenergic urticaria by Shelley & Shelley in 1985 (21, 22).

*Urticaria pigmentosa* was described by Edward Nettleship early in his career (1869), before he specialized in ophthalmology (23). He called it "chronic urticaria leaving brown stains." Sangster called it *urticaria pigmentosa* and Unna discovered the mast cells in the lesions (24, 25).

### Angio-oedemas

Angio-oedema was described in 1586 by Marcello Donati, who saw it in a young count who was sensitive to egg (26). A patient with hereditary angio-oedema was reported by Osler in 1885 (27). It was a fatal case due to suffocation, which was a common cause of death in the family. In Sweden, the causes of people's deaths have long been registered by the State church. Therefore, Arnoldsson et al., in 1966, could trace one family back to the 17<sup>th</sup> century (28). In 1963, Donaldson & Evans found that patients often had low levels of inhibitor to C1 esterase, which caused the swelling (29).

And what about Heinrich Iraneus Quinke? He was made professor in Kiel in 1878, where he remained for 30 years. He made significant contributions on various internal disorders

and introduced the practice of lumbar puncture as a diagnostic and therapeutic aid. Quinke also introduced new equipment into medicine. One of his doctoral students, Eugen Dinkellacker, published a thesis in 1882 on acute oedema, with 12 references to previous reports. Quinke wrote a summary of it the same year (30), which appeared as an original report with no reference to the previous reports, although he was well aware of their existence. To honour Quinke, Dr F. Mendel published a paper in *Berliner Wochenschrift* in 1902 on circumscribed oedema and proposed the name Quinke oedema. Within that same year, this name had spread and was being used around the world, which just shows how you can get your name connected with a disease if you are clever enough.

### Pathophysiology of urticaria

I would also like to briefly mention some important findings on the pathophysiology of urticaria. Dr Chemniz in Copenhagen described a circulatory obstruction in the skin from nettle-rash, which caused the lesions, due to the formation of special fluids. He could also explain why the lesions disappeared fairly quickly, only to reappear later in other areas of the skin (31). Jean Astruc (1684-1766), the founder of modern dermatology and histology, also assumed that the weal was due to a local obstruction (32). The French researcher M. J. Marey sent a paper to Lord Lister in 1858 describing the triple response. He did not say where it had been published, but Lister mentioned the findings in the transactions of the Royal

Society (33).

Imidizolethylamine was first synthesized by Windaus & Vogt (34). Dale & Laidlow showed that the tissue (histos) contained an amine which affected smooth muscles and vessels. This led them to call it histamine and later establish that it was imidizolethylamine (35). The first antihistaminic compound was discovered by Bovet & Staub (36). Recent advances in diagnosis and treatment have included the use of the RAST, the corticosteroids and the non- or less sedating antihistamines.

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