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Padua, the cradle of modern medicine: Bernardino Ramazzini (1633–1714) on headaches

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Abstract A prominent historian of Medicine, Henry Sigerist, quoted the Padua Medical School as “the cradle of modern medicine”. This opinion is currently accepted worldwide. A short outline on the contribution of the Padua Medical School to the development of medical knowledge in its “golden age” is given. In this context, the work of a prominent figure of the 17th century Padua University and the founder of Occupational Medicine, Bernardino Ramazzini, is considered, with focus on his interest in headache.

Key words Ramazzini • Headache • History of medicine • Padua University Medical School

Medical historians agree on the extraordinary role played by the Paduan School in the development of medical knowledge between the 15th and 16th centuries. A second flourishing season took place in the 18th century, with the foundation of Occupational Medicine by Ramazzini [1], and with the shift from humoral galenic medicine to solidistic medicine, through the anatomo-clinical method by Morgagni.

We will try to briefly examine the 16th century golden age first, focusing secondly on the contribution of Ramazzini, specifically to headache.

The fourth decade of the 16th century in Padua represents a turning point in the modern history of medicine.

Here, in the same year, 1543, when Andreas Vesalius' (1514–1564) *De humani corporis fabrica* was published, Giovanni Battista da Monte (1489–1551) originated the method of clinical instruction at the bedside of the patient at the San Francesco Grande Hospital. Therefore, the critical attitude of the Renaissance anatomist had, in a sense, its immediate clinical counterpart with the physician teaching at the bedside of the sick.

Moreover, in 1545, the realisation of the Botanical Gardens permitted the “ostensio simplicium”, that is, the demonstration of real plants, developed from the “lectura simplicium”, or, the single literary description of the sub-

ject. A year later, Girolamo Fracastoro, in his *De contagione et contagiosis morbis*, was the first to hypothesise the presence of “seminaria morbi”, foreseeing the microbial theories established only three centuries later.

Therefore, it can be said that in those years Padua was the centre of the medical Renaissance as Florence was the centre of the artistic Renaissance.

The precedents to these outstanding developments go back almost to the origin of the Padua University (1222). In those years, the rediscovery of numerous classical, philosophical and medical writings took place. In particular, the knowledge of the so-called “physical” writings of Aristotle stimulated renewed attention in the study of nature in opposition to theological themes. As an expression of these interests, at the end of the 1300s, the dissection of the human body began to be performed in the Bologna-Padua area. However, at first the influence of Galen, whose teachings were transmitted in an acritical manner, strictly prevailed, and were emblematically represented by the modality with which the lessons of anatomy were carried out: the professor merely commented *ex cathedra* upon the galenic text, without assuming any direct role in the dissection.

With the Venetian expansion of 1405, Padua became the site of the state university of Saint Mark’s Republic. As we have seen, in our town the studies had assumed a philosophical direction that privileged the empiristic contents of the biological works of Aristotle and favoured, as a result, the observation of nature, an essential aspect of the revival of the anatomical investigations. In this regard, it is useful to remember that from the mid 1400s, examination of the cadaver for academic interest was already codified in the statute of the Paduan School, which established the obligation to proceed yearly with the anatomical dissection of at least two human bodies.

It was upon this background that the activity of the pre-Vesalian anatomists in Padua was situated, and in particular, the teaching of Alessandro Benedetti (1455–ca. 1525), who realised the construction of an anatomical theatre which could be disassembled, aimed at improving instruction based precisely upon objectivity. After Vesalius (1514–1564) followed Realdus Columbus (1516–1559), who first described the lesser circulation, and later Gabrielis Falloppius (1523–1562), who greatly contributed to the knowledge of the cranial nerves and of the female reproductive system.

We have thus arrived at the great moment of the Paduan School of Medicine. It is the golden era of the “Patavina Universitas”, attended by foreign students who converged from all of the European countries.

Indeed, the permanent theatre that Fabrici d’Acquapendente (1533–1619), the successor to Falloppius, had erected in 1594, became the model of the demonstrative teaching of anatomy in the various

European Universities, such that similar structures were to be built by pupils returning from medical studies in Padua to universities such as Leiden, Copenhagen, Basel and Uppsala. Among the other great accomplishments of d’Acquapendente, we limit ourselves to remember his embryological studies, the description of the venous valves, and the realisation of a collection of coloured anatomical paintings, which he bequeathed in his testament to the Venetian State. For this anatomical atlas, d’Acquapendente is credited with being the first to sense the importance of coloured illustrations for anatomical preparations. D’Acquapendente was also the teacher of William Harvey (1578–1657), the discoverer of the circulation of the blood. Attracted to Padua by the reputation of its University, the young Englishman arrived in the city to further his studies, receiving a doctorate’s degree in medicine in 1602. The outstanding discovery of William Harvey is recognised as directly connected with his Paduan education, because here he learned of the existence of the valves of the veins, a unidirectional structure, from d’Acquapendente, and of the connections between mathematics and research within the experimental method from Galilei.

Let us now focus on a prominent character of the second flourishing season of the Paduan Medical School, which took place at the beginning of the 18th century.

Bernardino Ramazzini was born in 1633 in Carpi, near Modena. He graduated from Parma in Philosophy and Medicine in 1659. A year later, he obtained an appointment as district medical officer in the Viterbo countryside. Malarial fever forced him to return to his native city. Later, he moved to Modena, where, in 1682, he was nominated head professor of Medical Institutions and Theoretical Medicine at the “Studio Pubblico di S. Carlo”, the renowned University of Modena, and became court physician of the Duke of Este. In 1700, after almost 30 years in Modena, he was called by the Venetian Senate to the University of Padua. Here, he died of a cerebral haemorrhage, after 14 years of untiring clinical activity and teaching. Our investigations, recently published in *The Lancet* [2], confirmed the traditional belief that the mortal remains of the great physician rest “sine titulo” in the present-day oratory of San Francesco di Sales in Padua. Another recent study allowed us to identify the house where Ramazzini lived.

His scientific production is rich and varied [3]. Most important among his works is *De morbis artificum diatriba*, which lays down the foundation of modern Occupational Medicine. The volume appeared in two editions [4, 5]: in 1700 (Modena), and in 1713 (Padua), enlarged by a supplement. Some personal experiences, among which the observation on a daily basis, during the appointment as district medical officer, of the extremely

poor working conditions of local dwellers, and of some sewer maintenance workers at his own residence in Modena, contributed to drawing the attention of Ramazzini to the diseases of the working class [6].

Among the 69 professions described, accounting for the majority of the occupations of the period, headache is quoted in 15 instances, 12 of which as a disturbance directly related to working conditions. The main categories involved are, according to Ramazzini: pharmacists, carpenters, brewers, tobacco workers and oil producers, confectioners, desk workers and stenographers, Jewish women, lackeys and runners, hunters and sailors, wet-nurses, those working with wine and beer, sewer cleaners, musicians and singers, and soldiers [7]. His remarks on headache are typical of his way of collecting first-hand experience of working conditions, and they underline the importance of occupational hazards in the assessment of headache. In keeping with his clinical approach, he visited the workplaces in person, observing the sanitary conditions, and interrogated the patient in detail on his activities. Ramazzini was really interested in headache and its different aspects, especially as he had often had first-hand experience. From what he writes about his own reaction to bad smells in grimy shops, we may infer that he himself was suffering from migraine.

The importance of a particular contribution given by Ramazzini was recently shown, after nearly two centuries, by the research conducted by our Headache Centre regarding osmophobia. Bernardino Ramazzini refers in more than one passage to the relation between olfactory stimulus and onset of headache (“capitis dolor”), in particular, when he deals with the illnesses of pharmacists, brewers, tobacco workers, oil producers and carpenters. In the chapter, *Of the diseases of pharmacists*, an excellent description of osmophobia as a headache trigger is given: “I noticed that at times not only bad odours are harmful for the pharmacists, as in the preparation of an unguent of

dialthea, which causes nausea and vomiting to some, but also pleasant odours. In spring when they prepare infusions of roses for golden syrups, and when the whole shop smells of the rose beds of Paestum, I have heard some complain of severe headache, others of diarrhoea”.

Our data, derived from a study of 704 patients, of whom 569 were migraineurs (477 suffering from migraine without aura, 92 from migraine with aura) and 135 were diagnosed with tension-type headache, show that more than 40% of migraine patients refer osmophobia during an attack, while none of the patients with tension-type headache complain of this disturbance. Thus, osmophobia can be considered a highly specific symptom of migraine, of great importance in the differential diagnosis with tension-type headache.

Now, at the end of the present outline, the title “Padua, the cradle of modern medicine”, which is precisely the attribute given by the renowned medical historian, Henry Sigerist, to our Medical School, should not seem too ambitious.

In the *Taming of the Shrew*, William Shakespeare has one of his characters express “the grand desire to see fair Padua, nursery of the arts”. I am sure that the unique atmosphere that one feels not only between these ancient walls but also by simply walking in Padua, in its streets and under its arches, which have seen so many great contributors to the key developments of medical thinking, will provide our intellect and soul with an intense emotion that will enrich our experimental and clinical work.

Our medical school is today a very large one, enrolling more than two thousand pupils, and competing at an international level. All of this comes to us from a long, rich tradition, a cultural heritage that we are deeply proud of. We endeavour to pass down to the new generations, to our students, the illustrious, precious legacy of the Paduan Medical School, in order to foster their criticism in clinical judgement and their commitment in everyday practice.

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