OCCASIONAL PAPER

Neurological practice in the Centuriae of Amatus Lusitanus

Paulo Fontoura

Department of Immunology, Faculty of Medical Sciences, New University of Lisbon, Lisbon, Portugal

Correspondence to: Paulo Fontoura, MD, PhD,
Department of Immunology,
Faculty of Medical Sciences,
Campo dos Mártires da Patria, 130,
1169-056 Lisbon, Portugal
E-mail: paulo.fontoura@fcm.unl.pt

Abstract

Amatus Lusitanus, a Portuguese Jew who gained notoriety as one of the most famous physician-scientists in XVI century Europe published collections of case histories—Centuriae—describing his most interesting patients. The Renaissance was a transitional period for medicine and the neurological sciences, which if still dominated by the humoral and ventricular-pneumatic doctrines, were taking the first steps away from them. We analysed the Centuriae for neurological and psychiatric cases in order to appreciate neurological practice in this period and selected one hundred which fit those diagnostic categories. The Centuriae contain cases of CNS infection and trauma, epilepsy, apoplexy and depressed states of consciousness (including coma, carus, lethargy and cataphora), headache and vertigo, tumours, cranial nerve paralysis, melancholy, anatomical and physiological observations, as well as a short treatise on cranial traumatology. The most relevant observations point to the importance of the brain parenchyma in cognition, provide original observations of epidemic lethargic encephalitis, describe the neurological consequences of syphilis, including the first description of tertiary syphilis, attempt to distinguish mania from melancholy, extensively describe medical and surgical treatment of cranial trauma, document the first use of anatomical dissection to study a case of brain abscess, negate Galen’s view of the optic nerves as hollow, and describe the use of new drugs such as guaiac wood for the treatment of headache. The Centuriae not only provide insight into neurological clinical practice in the XVI century, but also emphasize the role of Amatus Lusitanus as an important precursor of this discipline, given his numerous original observations.

Keywords: Amatus Lusitanus; history of neurology; Centuriae; Renaissance; Jewish physicians

Qui toties fugientem animam sistebat in aegro
Corpore, Letheis aut revocabat aquis
Gratus ob id populis, & magnis regibus aequè
Hic iacet, hanc moriens pressit Amatus humum…

He who so often would detain the fleeing soul in the ailing

Body, or summon it back from Lethe’s waters,
Dear, on that account, to peoples, and to great kings, equally,
Lies here, in death Amatus lies upon this soil…

Epitaph by Diogo Pires, Cato minor (Didacus Pyrrhus Lusitanus, 1592–1596) (Tucker, 1998)
Introduction: Amatus Lusitanus and the Iberian medical Diaspora

Neurological science and clinical practice during the XV and XVI centuries benefited, as much as the rest of medical knowledge, from the Renaissance movement in the arts and sciences, and the first globalization phenomenon. Medicine underwent a momentous revolution driven by the advancement of anatomical studies and by rediscovery of the clinical works and ideas of Galen (like the primacy of the brain) (Temkin, 1973). In the neurological sciences, this led to the first steps being taken away from pneumatics and the ventricular theory, and towards the affirmation of pathological anatomy and lesion localization as the basis for neurological diseases. Also during this period, European navigators expanded the world’s known boundaries, and Portugal and Spain assumed the roles of primary first global naval powers (Mahan, 2003), establishing a network of bases and trade routes throughout the world. As a result of this globalization, European pharmacopoeia and the clinical practice of medicine were enriched with several new or more readily available drugs and spices.

At this time both Iberian kingdoms experienced an unparalleled flourishing of their medical schools. Several relevant medical scientists appeared, such as the Spanish anatomists Miguel Servetus (1511–1553), who first proposed the idea of blood circulation (Reristitutio Christianismi, 1553), and Juan Valverde de Amusco (c. 1525–1564) (Historia de la composion del cuerpo humano, 1566), or the Portuguese botanists and pharmacologists Cristovão da Costa (Cristobal Acosta, c. 1512–1580) (Tractado de las Drogas y Medicinas da las Indias Orientales, 1578) and Garcia de Orta (c. 1499–1568) (Fig. 1), whose Coloquios dos simples e drogas e coisas medicinais da India (Aromatum, et simplicium aliquid medicamentorum apud Indos noscentium historia, 1563) was considered the most relevant medical botany work since Dioscorides (Garrison, 1931; D’Cruz, 1991; Martin Araguz et al., 2001; Paweletz, 2002).

In both countries, the development of medical science was associated with their large Jewish communities. Unfortunately, this golden period came to an end in the beginning of the XVI century, with the expulsion of the Jews and the start of the Inquisition (Friedenwald, 1944b). Jewish physicians were one of the most targeted groups, and records from that time list no fewer than 200 indicted for trial and punishment (Friedenwald, 1944b). Entire families were forced to convert to Christianity (so-called ‘New Christians’ or marranos) or flee, mostly to northern Europe, the Middle East, the Papal States (where a protected trade community existed at Ancona), or the new overseas colonies. A great number of Jewish-born physicians migrated to the more liberal cities of Amsterdam and Antwerp, becoming figures of renown in northern Europe (Ferreira de Mira, 1947; Tricot, 1996).

One of the best examples of this exodus is the Portuguese physician João Rodrigues de Castelo Branco (1511–1568) (Fig. 1), better known as Amatus Lusitanus. Considered by medical historians as one of the most representative renaissance physicians (Withington, 1964), during his own time he was listed by Loys Le Roy [Ludovicus Regius (1510–1577), French Roman law scholar and humanist, correspondent with Erasmus of Rotterdam] alongside Jean-François Fernel (1497–1558), Guillaume Rondelet (1507–1566), Jacobus Sylvius (1478–1555), Andreas Vesalius (1514–1564) and Martin Acacia (1497–1551) as the outstanding physicians of that age (Le Roy, 1575). There are a few good biographies that deal in detail with the life of Amatus (Lemos, 1907; Jorge, 1908; Friedenwald, 1944a; Pelner, 1969), which can briefly be summarized. Born in 1511 of a marrano family in the Portuguese–Spanish border city of Castelo Branco, he studied medicine and surgery in Salamanca, and returned to practice in Lisbon around 1529. He moved to Antwerp in 1534 where he wrote his first scientific work on Botany, a set of commentaries on Dioscorides (Index Dioscoridis. En candide Lector, Historiales Dioscoridis campi, etc., 1536) (Tucker, 1998). In 1541, he accepted a job as professor of Medicine at the University of Ferrara, [listed as an eruditi mercatore in legal documents of that time (Gampel, 1997)], traveled throughout Italy to see patients (including Pope Julius III), and collaborated in anatomical and botanical studies with Antonio Musa Brassavola (1500–1555) and Giovanni Batista Cannano (1515–1579). His life in Italy became more complicated after 1555, with the drift to anti-semitism by Pope Paulus IV who implemented the Inquisition in full force. The anti-Jewish riots of 1556 led to his flight across the Adriatic to the independent republic of Ragusa (modern-day Dubrovnik in Croatia) (Dürigl and Fatovic-Ferencic, 2002). Staying only for 2 years in that city, in 1558 he moved to Salonica (modern-day Thessaloniki in Greece) where under the protection of the Turkish Sultan, he lived for the next decade, and was finally able to practice Judaism openly (Melammed, 2004). In 1568, Amatus died fighting an epidemic of plague in this final adopted home.

Curationum Medicinalium Centuriae Septem

Amatus is mostly known for his books of case histories called Curationum Medicinalium Centuriae (Fig. 2). Each Centuria is a collection of 100 cases, organized chronologically, and the collection reflects Amatus’ practice during the whole of his career, from Lisbon to Salonica. All together he published seven volumes of Centuriae (composed from 1546 to 1568, but probably with cases dating as early as 1529), or 700 cases, both medical and surgical, without ‘[…] any other ambitions than to contribute to the health of my patients […] I have done nothing, added nothing or modified anything to profit my reputation’ (Tavares de Sousa, 1972). It is uncertain what case selection criteria were used for publication in the Centuriae. Most observations consist of a detailed clinical description of the case and therapeutic recommendations (curatio), followed by a discussion (scholia). Amatus often cites his contemporaries in these discussions, and does not hesitate to take part in the controversies of the day. Notably, he criticizes Vesalius regarding his 1546 letter De radice Chynae for his ignorance in using guaiac wood, or China root, (Centuria I, Curatio 90, De dolore coxendico & radice chinarum), which he himself describes in detail (Centuria II, Curatio 31, In qua agitur...
The famous discovery of valves in the azygos vein, shared with Cannano (and predating Acquapendente’s claim), is part of the scholia of a case seen in 1547, related to the ongoing dispute regarding the best side for bloodletting in pleurisy and the opinions of Pierre Brissot (1478–1522), (Centuria I, Curatio 52, De pleuritide, ac de vera ratione proper quid in secanda vena sit axillaris eiusdem brachii ubi dolor est) (Baas, 1889; Ferreira de Mira, 1947; Leibowitz, 1957; Tavares de Sousa, 1972).

The Centuriae are a milestone in clinical research, containing original descriptions of disease entities, and oftentimes therapeutic innovations. Several researchers have combed through this work looking for first observations, and Amatus has been credited with describing idiopathic thrombocytopenic purpura (morbo pulicaris absque febre, Centuria III, Curatio 70) (Imbach et al., 2002) and encephalitis lethargica (Centuria II, Curatio 15, 26 and 27) (Jorge, 1921). Naturally, such a haphazard collection of cases has heterogeneous quality, and the medical historian Kurt Sprengel (1766–1833) is quoted as stating that ‘[he] left us a voluminous collection of observations, some excellent and instructive, but others mediocre and mixed with vain ostentation of erudition, and most demonstrating the credulousness and superstitions of the author’ (Friedenwald, 1944a; Ferreira de Mira, 1947). Nonetheless, the Centuriae illustrate the clinical practice of a renowned XVI century physician, during a prolonged period of time, in several countries, who no doubt encountered several neurological diseases. Therefore, an analysis of the neurological cases in the Centuriae might contain valuable clues to understanding the state of neurological clinical knowledge and therapeutics at that time.

Fig. 1 Garcia de Orta (left) and Amatus Lusitanus (right) as portrayed by Veloso Salgado (left picture); detail from ‘The Portuguese’ panel painted in the ‘Sala dos Actos’ of the Faculty of Medical Sciences in Lisbon (inaugurated 1906). A more contemporary portrait of Amatus appears in a medallion labelled ‘Dissentimus’ (we disagree) in the frontispiece of Johannes Bauhinus’ (1541–1613) posthumous Historia Plantarum Universalis (1650–1651) (right, above), together with that the Italian botanist Pietro Andrea Mattioli (1501–1577) one of his more ardent enemies and who accused him of crypto-Judaism (Apologia adversus Amathum Lusitanus, 1558), and the German botanist Melchior Wieland (Guilandinus, c. 1520–1589), (detail below; Amatus is the first on the right).

The Centuriae are a milestone in clinical research, containing original descriptions of disease entities, and oftentimes therapeutic innovations. Several researchers have combed through this work looking for first observations, and Amatus has been credited with describing idiopathic thrombocytopenic purpura (morbo pulicaris absque febre, Centuria III, Curatio 70) (Imbach et al., 2002) and encephalitis lethargica (Centuria II, Curatio 15, 26 and 27) (Jorge, 1921). Naturally, such a haphazard collection of cases has heterogeneous quality, and the medical historian Kurt Sprengel (1766–1833) is quoted as stating that ‘[he] left us a voluminous collection of observations, some excellent and instructive, but others mediocre and mixed with vain ostentation of erudition, and most demonstrating the credulousness and superstitions of the author’ (Friedenwald, 1944a; Ferreira de Mira, 1947). Nonetheless, the Centuriae illustrate the clinical practice of a renowned XVI century physician, during a prolonged period of time, in several countries, who no doubt encountered several neurological diseases. Therefore, an analysis of the neurological cases in the Centuriae might contain valuable clues to understanding the state of neurological clinical knowledge and therapeutics at that time.
Methods and Results

Selected neurological case histories from the Centuriae

A careful search and selection was performed on the seven-volume complete edition of the Centuriae (using the translated Portuguese version, composed between 1940 and 1970 by Firmino Crespo [Crespo, 1980], of the Bordeaux 1620 complete edition of Amatus’ work) for cases that might be classified as neurological or neuropsychiatric, which were then divided into general categories of disease corresponding to modern clinical criteria (Table 1). This is naturally difficult given the differences in clinical concepts in the XVI century and the language used to express them. Some disease entities were clearly recognized in this period, making classification easier (epilepsy, trauma, headache), while other cases were fitted into probable categories (e.g. infections, psychiatric) that might explain the clinical presentation (e.g. fever with neurological dysfunction, mood and behaviour abnormalities). Selected cases where read through and analysed for clinical and scientific content, in order to confirm or propose a diagnosis, and evaluate therapeutic options. Surprisingly, of 700 cases published by Amatus, a full 100 met the criteria for selection, belonging to the following categories (in decreasing number): infections (29 cases), psychiatric (22 cases), trauma (14 cases), headache (13 cases), vertebral column and spinal cord diseases (seven cases), stroke (five cases), cranial nerve paralysis (four cases), seizures (four cases), tumours (three cases), vertigo (three cases), poisoning/exposure (three cases), anatomy and physiology (three cases), malformations (two cases), movement disorders (one case) and pharmacology (one case). Again, this cataloging might be debatable, and some cases belong to more than one category. The most interesting cases in some of these categories will be presented and commented, but given the large number overall no attempt will be made to exhaustively describe their clinical characteristics or therapy, which is beyond the scope of this work.

Infection

Infectious diseases comprise the largest category of cases, and include descriptions of canine and feline rabies (VII-41, VII-65), tetanus (VII-10, VII-66) and Pott’s disease (I-84, V-47). Morbus gallicus or syphilis [so baptized in 1530 by Girolamo Fracastorio (1483–1553)] was a well-known entity in Europe by this time, and just a few years before the Centuriae appeared Ruy Diaz de Ysla had published his Tractado contra el mal serpentino (1539), one of the earliest detailed studies of this disease (de Ricon-Ferraz, 1999). The protean neurological complications of syphilis were still being discovered, and Amatus describes cases of syphilitic paralysis of the recurrent nerve (II-70), syphilis with facial paralysis cured after an attack of malaria (I-85) and syphilitic neurolabyrinthitis (VI-25). This last case refers to the Croatian poet Sabo Bobaljevic Glušac (1529–1585) observed by Amatus in Ragusa, whose writings are testimony to his chronic vertigo (Dürrigl and Fatovic-Ferencic, 2002).

Case VI-42 (In qua citatur casumarius de quodam nobili Gallo, imaginatrice corruptam habende, et eiusdem curatione faceta) is probably the earliest description of tertiary syphilis with dementia and mania: ‘The Frenchman Jacob, dignitary of King Henry of France in the oriental regions […] was suffering from his country’s disease, that is morbus gallicus […] He was delirious and had continuous mental disarray […] In effect, his mental faculties were corrupted, except, however, for his imagination’. He developed a severe paranoid delusion of having an abscess in his head, claiming ‘[…] that noxious and deadly vapors were taken from the abscess to his nose, and, more ridiculous still, showed in his fingers a very white and thick sputum […] Things had gone to the point where the patient hid his will and
### Table 1 List of neurological and psychiatric cases in the *Centuriae*, by order of appearance

<table>
<thead>
<tr>
<th>Centuria-Curatio</th>
<th>Identification</th>
<th>Clinical description</th>
<th>Outcome</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-4</td>
<td>M, adult</td>
<td>‘Melancholy’, headache (‘sinciput’)</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>I-9</td>
<td>M, 27 years</td>
<td>Headache, fever, stupor, seizures</td>
<td>Death in 48h</td>
<td>Infection</td>
</tr>
<tr>
<td>I-19</td>
<td>F, child</td>
<td>Right temporal fracture with bone depression</td>
<td>Full recovery</td>
<td>Trauma</td>
</tr>
<tr>
<td>I-34</td>
<td>F, adult</td>
<td>Fever, headache, delirium and agitation (‘possession’) post-partum</td>
<td>Recovery after 1 month</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>I-35</td>
<td>F, 30 years</td>
<td>‘Mania’ from excessive hair washing and sun exposure</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>I-36</td>
<td>F, 11 years</td>
<td>Obesity, ‘sanguine’. Acute right hemiparesis</td>
<td>Death within 1 month</td>
<td>Stroke</td>
</tr>
<tr>
<td>I-41</td>
<td>F, 20 years</td>
<td>Menstrual retention, speech difficulties, headache</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>I-44</td>
<td>M, 12 years</td>
<td>Groaning and bruxism during sleep</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>I-51</td>
<td>M, child</td>
<td>Cranial horn with encephalic substance inside</td>
<td>Death after removal</td>
<td>Malformation</td>
</tr>
<tr>
<td>I-62</td>
<td>M, adult</td>
<td>Fever and headache after killing a snake</td>
<td>Death in 10 days</td>
<td>Poisoning?</td>
</tr>
<tr>
<td>I-68</td>
<td>M, 30 years</td>
<td>Vertigo, loss of appetite, gastric pain</td>
<td>Full recovery</td>
<td>Vertigo</td>
</tr>
<tr>
<td>I-69</td>
<td>Newborn, 15 days</td>
<td>Soft head tumour</td>
<td>Full recovery in 3 days</td>
<td>Tumour</td>
</tr>
<tr>
<td>I-76</td>
<td>M, 48 years</td>
<td>Extracranial abscess with bone invasion</td>
<td>Full recovery</td>
<td>Infection</td>
</tr>
<tr>
<td>I-81</td>
<td>M, 50 years</td>
<td>Ischiatic pain, loss of movement in the legs</td>
<td>Full recovery in 3 days</td>
<td>Spinal</td>
</tr>
<tr>
<td>I-84</td>
<td>F, 8 years</td>
<td>Low fever, T10 gibbus spinal deformity, lower left quadrant pain</td>
<td>Partial recovery, spinal deformity</td>
<td>Infection</td>
</tr>
<tr>
<td>I-85</td>
<td>M, 25 years</td>
<td>Syphilis, right facial paralysis</td>
<td>Full recovery after malaria</td>
<td>Cranial palsy</td>
</tr>
<tr>
<td>I-90</td>
<td>M, adult</td>
<td>Lumbar and sciatic pain</td>
<td>Full recovery</td>
<td>Spinal</td>
</tr>
<tr>
<td>II-2</td>
<td>M, 6 years</td>
<td>Occipital trauma with fracture, vomiting and loss of consciousness</td>
<td>Full recovery</td>
<td>Trauma</td>
</tr>
<tr>
<td>II-6</td>
<td>Child, 9 years</td>
<td>Uncharacterized seizures after leg wound</td>
<td>Full recovery in 2 months</td>
<td>Seizures</td>
</tr>
<tr>
<td>II-7</td>
<td>F, adult</td>
<td>Facial paralysis during pregnancy; Post-partum right hemiparesis and generalized seizures</td>
<td>Death within days</td>
<td>Cranial palsy; Stroke?</td>
</tr>
<tr>
<td>II-9</td>
<td>M, fifth decade</td>
<td>Emprostothonus</td>
<td>Not mentioned</td>
<td>Movement disorders? Infection?</td>
</tr>
<tr>
<td>II-11</td>
<td>M, young</td>
<td>Urinary incontinence after spinal trauma</td>
<td>Full recovery</td>
<td>Trauma</td>
</tr>
<tr>
<td>II-14</td>
<td>M, young</td>
<td>Catalepsis</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>II-15</td>
<td>F, 18 years</td>
<td>Fever, lethargy, confusion (‘catechos’)</td>
<td>Full recovery after 20 days</td>
<td>Infection</td>
</tr>
<tr>
<td>II-19</td>
<td>M, 5 years</td>
<td>Occipital trauma followed by lethargy and left hemiparesis</td>
<td>Full recovery in 1 month</td>
<td>Trauma</td>
</tr>
<tr>
<td>II-26</td>
<td>F, 34 years</td>
<td>Fever, lethargy – (‘caros’ or ‘subet’)</td>
<td>Death in few days</td>
<td>Infection</td>
</tr>
<tr>
<td>II-27</td>
<td>F, adult</td>
<td>Fever, lethargy, somnolence</td>
<td>Full recovery after 8 days</td>
<td>Infection</td>
</tr>
<tr>
<td>II-36</td>
<td>M, adult</td>
<td>Fainting after seeing/smelling roses</td>
<td>Recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>II-52</td>
<td>F, adult</td>
<td>Post-partum depression</td>
<td>Full recovery in 1 month</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>II-57</td>
<td>M, 16 years</td>
<td>Sunstroke followed by agitation, ‘mania’ and fever</td>
<td>Recovery after 25 days</td>
<td>Exposure</td>
</tr>
<tr>
<td>II-64</td>
<td>M, adult</td>
<td>Post-purging fever and agitation</td>
<td>Full recovery after 1 month</td>
<td>Infection?</td>
</tr>
<tr>
<td>II-66</td>
<td>M, adult</td>
<td>‘Melancholy’</td>
<td>Recovery after 2 months</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>II-67</td>
<td>M, adult</td>
<td>‘Mania’ after wound closure</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>II-70</td>
<td>F, adult</td>
<td>Syphilitic neck tumour with recurrent nerve paralysis</td>
<td>Loss of speech</td>
<td>Infection</td>
</tr>
<tr>
<td>II-76</td>
<td>F, 14 years</td>
<td>‘Double tertian’ fever followed by lethargy or ‘caros’</td>
<td>Full recovery in 15 days</td>
<td>Infection</td>
</tr>
<tr>
<td>II-83</td>
<td>M, adult</td>
<td>Severe head wound from sword fight</td>
<td>Full recovery after 50 days</td>
<td>Trauma</td>
</tr>
<tr>
<td>II-90</td>
<td>F, under 20 years</td>
<td>Fainting after bad news</td>
<td>Not described</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>III-1</td>
<td>M, adult</td>
<td>Fever, headache and disturbed sleep</td>
<td>Full recovery</td>
<td>Infection</td>
</tr>
<tr>
<td>III-3</td>
<td>M, adult</td>
<td>Headache, insomnia</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>III-7</td>
<td>M, 35 years</td>
<td>Intense bilateral orbital pain after traumatic perforation of left eye</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>III-8</td>
<td>M, adult</td>
<td>Back pain after fall from horse</td>
<td>Full recovery</td>
<td>Trauma</td>
</tr>
<tr>
<td>III-9</td>
<td>M, 8 years</td>
<td>Fall from high window, coma for 2 days</td>
<td>Full recovery</td>
<td>Trauma</td>
</tr>
<tr>
<td>III-22</td>
<td>M, child</td>
<td>Left hemiparesis and seizures</td>
<td>Death within hours</td>
<td>Stroke</td>
</tr>
<tr>
<td>III-36</td>
<td>M, adult</td>
<td>‘Melancholy’, pre-prandial headache</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Centuria-Curatio</th>
<th>Identification</th>
<th>Clinical description</th>
<th>Outcome</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>III-40</td>
<td>M, adult</td>
<td>Headache</td>
<td>Not described</td>
<td>Anatomy</td>
</tr>
<tr>
<td>III-41</td>
<td>M, 9 years</td>
<td>Fall from window, multiple head contusions and fractures</td>
<td>Death in 3 days</td>
<td>Trauma</td>
</tr>
<tr>
<td>III-42</td>
<td>M, 12 years</td>
<td>Right temporal head injury, severe headache</td>
<td>Recovery after 30 days</td>
<td>Trauma</td>
</tr>
<tr>
<td>III-55</td>
<td>M, 20 years</td>
<td>Hallucinations</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>III-56</td>
<td>M, adult</td>
<td>Obsessive love</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>III-63</td>
<td>M, 14 years</td>
<td>Chronic headache</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>III-81</td>
<td>M, adult</td>
<td>Fever, headache, thirst, delirium</td>
<td>Slow recovery</td>
<td>Infection</td>
</tr>
<tr>
<td>III-99</td>
<td>M, adult</td>
<td>Sunstroke</td>
<td>Full recovery</td>
<td>Exposure</td>
</tr>
<tr>
<td>IV-6</td>
<td>M, adult</td>
<td>Cranial sword wound</td>
<td>Partial recovery, with ‘loss of reason’</td>
<td>Trauma</td>
</tr>
<tr>
<td>IV-13</td>
<td>F, adult</td>
<td>Anxiety, sighing, agitation, loss of appetite</td>
<td>Not reported</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>IV-22</td>
<td>M, 3 years</td>
<td>Prolonged generalized seizures</td>
<td>Prolonged post-ictal hemiparesis</td>
<td>Seizures</td>
</tr>
<tr>
<td>IV-23</td>
<td>M, 70 years</td>
<td>‘Apoplexy’ and sudden coma</td>
<td>Immediate death</td>
<td>Stroke?</td>
</tr>
<tr>
<td>IV-24</td>
<td>M, 2 years</td>
<td>Seizures, ‘horrendous look and turbid eyes’, motor retardation</td>
<td>Resolution of seizures?</td>
<td>Seizures, Malformation?</td>
</tr>
<tr>
<td>IV-26</td>
<td>M, 43 years</td>
<td>Fever, severe headache</td>
<td>Full recovery after 22 days</td>
<td>Infection</td>
</tr>
<tr>
<td>IV-42</td>
<td>M, adult</td>
<td>‘Melancholy’</td>
<td>Recovery after 4 months</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>IV-47</td>
<td>F, 13 years</td>
<td>Fever, mental disturbances, ‘alienation’, thirst</td>
<td>Full recovery after 40 days</td>
<td>Infection</td>
</tr>
<tr>
<td>IV-54</td>
<td>M, 35 years</td>
<td>‘Melancholy’</td>
<td>Partial recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>IV-87</td>
<td>M, adult</td>
<td>Left ear intense pain followed by facial paralysis</td>
<td>Full recovery after 40 days</td>
<td>Cranial palsy, Headache</td>
</tr>
<tr>
<td>IV-99</td>
<td>M, 35 years</td>
<td>Chronic pulsating headache, insomnia</td>
<td>Full recovery</td>
<td>Anatomy, Physiology</td>
</tr>
<tr>
<td>IV-100</td>
<td>M, 4 years</td>
<td>Left-handedness</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>V-8</td>
<td>M, 8 years</td>
<td>Purulent ear infection followed by painful ‘head tumour’, fever, local bone invasion</td>
<td>Seizures after surgery, death the next day</td>
<td>Infection</td>
</tr>
<tr>
<td>V-40</td>
<td>M, 40 years</td>
<td>Facial paralysis, loss of sensation in the face</td>
<td>Full recovery in 1 month</td>
<td>Cranial palsy</td>
</tr>
<tr>
<td>V-47</td>
<td>F, young</td>
<td>Scrofula, followed by spinal gibbus deformity</td>
<td>Full recovery</td>
<td>Infection, Malformation?</td>
</tr>
<tr>
<td>V-63</td>
<td>M, 2 years</td>
<td>Occipital tumour, followed by left arm paralysis, strabismus and fever</td>
<td>Death in 8 days</td>
<td>Tumour</td>
</tr>
<tr>
<td>V-75</td>
<td>F, 18 years</td>
<td>‘Melancholy’, prolonged seizures with loss of feeling and left arm paralysis</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>V-78</td>
<td>M, 40 years</td>
<td>Right cranial (‘sinciput’) tumour. Headache and fever</td>
<td>Full recovery</td>
<td>Tumour</td>
</tr>
<tr>
<td>V-87</td>
<td>F, adult</td>
<td>Depression during pregnancy</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>V-97</td>
<td>M, 75 years</td>
<td>Episodic speech disturbance, syncope with fall</td>
<td>Full recovery</td>
<td>Stroke?</td>
</tr>
<tr>
<td>VI-5</td>
<td>M, 2 years</td>
<td>Fever, paralysis, loss of speech and hearing</td>
<td>No change after 50 days</td>
<td>Infection</td>
</tr>
<tr>
<td>VI-25</td>
<td>M, 34 years</td>
<td>Syphilis, headache, vertigo and deafness</td>
<td>Worsening</td>
<td>Infection</td>
</tr>
<tr>
<td>VI-28</td>
<td>F, adult</td>
<td>Anguish, depression, amenorrhoea</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>VI-42</td>
<td>M, adult</td>
<td>Syphilis, followed by dementia and delusions</td>
<td>‘Recovery’ after sham surgery</td>
<td>Infection</td>
</tr>
<tr>
<td>VI-44</td>
<td>M, 20 years</td>
<td>‘Melancholy’</td>
<td>Full recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>VI-55</td>
<td>M, adult</td>
<td>Lumbar and sciatic pain</td>
<td>Full recovery</td>
<td>Spinal</td>
</tr>
<tr>
<td>VI-80</td>
<td>M, 38 years</td>
<td>Vertigo, blurred vision, headache, tinnitus, loss of smell, nausea</td>
<td>Recovery after 40 days</td>
<td>Vertigo, Headache</td>
</tr>
<tr>
<td>VI-100</td>
<td>M, adult</td>
<td>Multiple head-wounds and fractures</td>
<td>Not mentioned</td>
<td>Trauma, Surgical techniques</td>
</tr>
<tr>
<td>VII-1</td>
<td>F, adult</td>
<td>Fainting after bad news, ‘melancholy’</td>
<td>Recovery</td>
<td>Psychiatric</td>
</tr>
<tr>
<td>VII-7</td>
<td>F, adult</td>
<td>Post-partum headache and fever</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>VII-8</td>
<td>M, adult</td>
<td>Post-vomiting headache and dizziness</td>
<td>Full recovery</td>
<td>Headache</td>
</tr>
<tr>
<td>VII-10</td>
<td>F, 54 years</td>
<td>Opistothonus, trismus, intense pain</td>
<td>Recovery in a month</td>
<td>Infection</td>
</tr>
<tr>
<td>VII-11</td>
<td>M, 30 years</td>
<td>Chronic lower limb atrophy and muscle spasms</td>
<td>No recovery</td>
<td>Spinal</td>
</tr>
</tbody>
</table>

Table 1 Continued
everything in his house – clothes, gold, horses and precious furnishings, or gave them to strangers. He left nothing for himself except a clay pot which he embraced constantly as it was an elegant woman’ (VI-42). It is usually accepted that the late-stage consequences of neurophilis, such as dementia paraletic or general paralysis of the insane appear to have escaped medical description up until the late XVIII century, when William Perfect and Vincenzo Chiarugi published detailed cases (Hare, 1959; Shorter, 1997). This viewpoint is contradicted by this case of syphilitic dementia, so clearly described in the sixth Centuria (composed in 1558 during his period in Ragusa) which may be the first medical description of the late-stage cognitive and psychiatric complications of syphilis, and pushes back over 200 years the date of discovery.

In curatio I-9 (De sphacelismo depascente), Amatus describes a case of cerebral gangrene (sphacelon) or abscess, coursing with fever, headache, seizures and stupor, leading to death: The Hebrew Alzalain, twenty seven years of age, was attacked by a severe and deadly disease, on the 4th of September 1546, date from which we decided to write these Curationes [...] Fatigued by long vigils [...] he fell into the corruption of the brain which the greeks call sphacelon. This diagnosis was confirmed by these signs: pain felt in the sinciput (anterior fontanelle) and forehead, the permanence of such torpor that, if pricked hard, he did not react; a great lassitude of the body; besides, intense fever, as is usual for this disease. Appearing at the end, together with the previous signs, tremors which shook his whole body and fatal warnings, so that in the space of 2 days he was dead’. Notably, after dissecting the brain of this and other similar patients (quorum capite dissecuimos), Amatus found a pyogenic abscess. This confirmation of clinical diagnosis by pathological examination is a clear example of the impact that the new scientific doctrines and techniques such as dissection were having on medical science, and also of Amatus’ background in anatomical research. It must also be emphasized that up until the XVIII century, anatomical dissection was usually not applied to the study of human disease, and in this case Amatus is clearly a pioneer in neuropathology. Unfortunately, there is no mention of the systematic use of dissection to study other neurological cases in the Centuriae. Although no attempt is made at symptomatic localization of the lesion, a hallmark of modern neurology, this is a step towards the clinical–pathological correlation which would play such an important role in the development of Neurology as a clinical discipline. It would be only in 1710, however, that the French army surgeon Pourfour du Petit (1664–1741) would describe autopsy cases of brain abscess in his Lettres d’un Médecin, and Matthew Baillie (1761–1823) would present his systematic description of brain pathology, including abscess, in his Morbid Anatomy (1793) (Garrison, 1969).

Other interesting observations in this category include several fevers with headache, excessive sleep and depression of consciousness. Since Hippocrates, alterations in sleep patterns had been recognized as pathological and associated with plague (Aphorism 1.2. Somnus, quo voles morbo, si laborem insert, pestiferus; si vero auxilium tulerit, nequaquam pestiferus erit, quoted from Oliverum Popardum, Hippocratis Aphorismi 1580). A recent review on the subject (Koehler and Wijdicks, 2008) describes the evolution of the diverse and often confusing terminology associated with excessive sleep and altered states of consciousness from the XVII to the XX century, beginning with Thomas Willis (1621–1675) who used the terms lethargy, coma and carus in his De anima brutorum (1672) to describe increasing states of loss of responsiveness. In the next century, Herman Boerhaave (1668–1738), classified such states into the four categories of lethargy, cataphora, carus and coma, in which the first two presented with fever, and the last two without. Some of these terms would still be used up to mid-XX century and only gradually disappear from standard medical terminology.
This proposed timeline stops at the XVII century, however. It is, therefore, relevant that diagnostic categories as lethargus, carus, cataphora and coma were also used and described by Amatus in his work, sometimes in relation to his cases (II-26, II-27, II-76). Carus (for which Amatus also gives the Arabic term subet, as well as passio subetica or veternus) was a deep sleep with closed eyes and absence of speech or pain responses, accompanied by slow fever. Lethargy was the opposite of phrenitis (acute confusional state), and a lighter form of carus from which one could be awakened briefly (‘they open their eyes when interrogated, but fall again to an invincible sleep’, II-27). Similar to lethargy, Cataphora was excessive sleepiness, and coma was a form of abnormal deep sleep, which in some cases might show signs of vigil (then called agyropyon coma).

Besides these terms, Amatus also uses the denomination catuchos to describe a form of depressed consciousness associated with fever epidemics. In fact three of his observations in this category, II-15 (In qua agitur de catocho, id est, sopore vigilante, sive dormitione vigilante, dicto morbo), II-26 (In qua agitur de caro.i. veterno morbo: quem Arabes subet appellat) and II-27 (In qua agitur de comate febrem, sanguineam comitante), have been considered original descriptions of encephalitis lethargica: ‘[…] a woman came to see me one day […] attacked […] of a malignant and pestilent fever, which developed into the disease catuchos. In effect, she slept and was awake, because she had her eyes closed yet, if interrogated, she opened them and spoke irreverently, giving no straight answers. [The] posterior areas of the brain are the most attacked by catuchos from which one could be awakened briefly (‘they open their eyes when interrogated, but fall again to an invincible sleep’, II-27). Similar to lethargy, Cataphora was excessive sleepiness, and coma was a form of abnormal deep sleep, which in some cases might show signs of vigil (then called agyropyon coma).

Amatus was familiar with an epidemic of a similar disease in Portugal, called mal de modorra which may have caused the death of King Manuel I (Pinto, 2004). The episode is told in Damião de Góis’ (1502–1574) Crónica do Felicíssimo Rei D. Manuel (1566) and in Luis de Sousa’s (c. 1555–1632) Annais de D. João III (1628–1632): ‘[…] Three years there were after King D. Manuel was married (1521) when at the fifth day of December […] he was attacked by an ardent fever with an inclination to sleep. This disease went around the city, was like modorra, and killed many […]’. Góis, then a page belonging to the King’s Chamber, was a direct observer of the disease and gives more details of the clinical course including periodic ‘accidents’ in which D. Manuel ‘[…] lay in bed, without turning, without moving, still and inert as a dead body […]’. Based on the absence of a rash, Amatus differentiates this case of modorra from tabardillo (exanthematic typhus), a common epidemic belonging to the ‘emerging diseases’ (Nuevas enfermedades) of that period, probably the same as morbus hungaricus. Gomez Pereira of Medina del Campo (Spanish physician and philosopher, c. 1500–1588) also commented on the death of King Manuel, and described the clinical characteristics of the epidemics of modorra in 1521 and 1556–1567, including fever, episodic lethargy, hypersonomolence, and ocular muscle paralysis (Novae Veraeque Medicina Experimentis et Evidentibus Rationibus Comprobatae, 1558) (Pinto, 2004). This disease is also mentioned in other contemporary writings such as in Antonio de Guevara’s (Spanish chronicler, 1481–1545) Libro Aureo de Marco Aurelio (1528): ‘He who is mortally wounded is like one suffering from mal de modorra; he has a clear judgment, but recognizes no-one […]’, as well as by the Spanish historian Andrés Bermúdez (Memorias del reinado de los Reyes Católicos, 1509) ‘From the year 1502 there began to be in Castilla […] much hunger and many illnesses of pestilential modorra and pestilence […] until the present year of 1507.’ (Cook, 1998).

Modorra was apparently exported to the Canary islands and Spanish New World in the early XVI century. Specifically, the 1514 expedition of Pedro Arias de Ávila (1443–1531) to Santa Maria Antigua de Darién (modern-day Colombia) was much affected by this disease, which is said to have caused the death of almost half of his crew of 1500 people (Ashburn, 1947; Cook, 1998). Later, the chroniclers Bernal Díaz del Castillo (1492–1584) (Historia verdadera de la conquista de la Nueva España, 1568) and Francisco Lopez de Gómara (c. 1511–1566) both describe the death of Luis Ponce de León in Mexico city, circa 1526, due to modorra: ‘He fell sick with modorra and it was in this manner. […] He was taken with a high fever, and was for four days heavily with sleep and without his usual senses […] on the ninth day he yielded his soul […]’ (Castillo, quoted by Ashburn(1947)). The reported clinical characteristics of New World modorra have lead authors to diverge as to its diagnosis, candidates including typhus (Grunberg and Chaunu, 1993), epidemic cerebrospinal meningitis (Sticker, 1931), or the effects of severe starvation that afflicted the Spanish colonists (Ashburn, 1947).

Nowadays it is unclear what Amatus’ designation catuchos might have referred to in comparison with Hippocratic and Galenic medicine where it broadly signified a type of neurological lesion or disease, and the confusion is increased by the use of local denominations such as mal de modorra, modorrilla or mazuco. Also, modorra more likely
also quoted in Burton’s treatise (Burton). A few melancholy cases are
from the bowels (IV-54, VI-44). In one case Amatus alleviated such
driacal melancholy (IV-54, VI-44). If this humor accumulated in the abdomen, and affected
the mesenteric veins, it could induce so-called ‘flatuous’ or hypocon-
abilis (IV-42). If this humor accumulated in the abdomen, and affected
strict, and because their diet included foodstuffs prone to create atr-
ca. sive praecordialis, Arabib myrachiiali dicta
A few melancholy cases are
refers to a symptom (lethargy) more than to a specific diagnosis, in the
same way that in the Renaissance ‘fevers’ included several different
nosological categories. In that case, there are several febrile illnesses
that present with modorra, and lacking specific clinical characteristics,
it may be impossible to correlate with modern-day diseases.
Ricardo Jorge (1858–1939), the great public health specialist, writing
in 1921 at the height of the encephalitis lethargica epidemic, commented
on Amatus’ cases and first proposed a connection with it (Jorge, 1921).
Encephalitis lethargica was described by Von Economo in 1916,
and assumed epidemic proportions until 1927. Typically, patients pre-
sented with pharyngitis followed by sleep disturbances, extrapyramidal
movement disorders (such as Parkinsonism and oculogyric crisis) and
neuropsychiatric complications. The cause remains a mystery, although
evidence in favour of an autoimmune reaction against the basal gang-
lia has been mounting (Bentivoglio and Kristensson, 2007). Based on
the paucity of clinical data presented in Amatus’ three cases, there is a
lack of specific findings pointing to the diagnosis of encephalitis lethar-
gica. Therefore, such a comparison appears to be excessive, and mal
de modorra most probably was just a form of epidemic encephalitis
with lethargy.
As stated above, Amatus differentiates catalepsy from catochos or
mal de modorra, and also provides one of the first descriptions of
catalepsy (II-14 In qua agitur de Catalepsi, id est congelatione
morbo) in modern medical literature: ‘One day we went to see [...] a boy that was laying down as if in a deep sleep. His eyes were open,
but the eyelids did not move. [...] He did not reply to questions from
the surrounding people, and did not move [...] He was rigid and cold,
so that it was licit to say that he was suffering from an attack of
catalepsy, or congelatio’ (II-14). In this situation, the ‘animal spirits’
became frozen and incapable of transmitting movement or sensation
to the body parts. By comparison, the first description of this disease in the
English literature only appears in the treatise On Congelation or Taking (1583) by Phillip Barrough, the Elizabethan surgeon and phy-
sician who published the first book on medicine in the English lan-
guage (The method of physic, containing the causes, signs, and cures
of inward diseases in mans body, from the head to the foot, 1583)
(Fink and Taylor, 2003; Shklar, 2004).

Melancholy, seizures and apoplexy
Psychiatric patients in the Centuriae are mostly melancholic young
males and females, with an assortment of complaints, including anxiety,
depression, headache, sleep disturbances and eating disorders. Classical humoral theory stated that excessive black bile (atrabilis)
caused melancholy. Generally, black bile was associated with physical
frailty, a predisposition to malaria (from its accumulation in the spleen)
and melancholic thoughts and dreams, which could be alleviated by
sighing and eructation (IV-42, In qua agitur de varis affectionibus
melancholicis...). Amatus considered Jews to be naturally more pre-
disposed to melancholy from being captive, overzealous, religiously
strict, and because their diet included foodstuffs prone to create atr-
abilis (IV-42). If this humor accumulated in the abdomen, and affected
the mesenteric veins, it could induce so-called ‘flatuous’ or hypocon-
driacal melancholy (IV-54, VI-44). In one case Amatus alleviated such
a condition by the innovative use of a bellows to draw excessive wind
from the bowels (IV-54, In qua agitur de melancholia flatuosa, hypo-
condriaca, sive praecordialis, Arabib myrachiiali dicta), which was commented
in Robert Burton’s The Anatomy of Melancholy (1620)
(Burton). Excessive atrabilis was also associated with headaches (I-4,
III-36, IV-99), and madness, giving rise, for example, to obsessive love
(III-56 In qua agitur de iuvene Hebreo puella Hebrea amore capto),
also quoted in Burton’s treatise (Burton). A few melancholy cases are
also reported to occur during pregnancy or post-partum (I-34, II-52,
V-87).
Mania and melancholy are distinguished by Amatus in I-35 (De
maniae & melancholiae differentia); excessive sun exposure could
induce mania because it caused to yellow bile ‘combustion’, whereas
melancholy was caused by excessive black bile. However, mania could
also be induced by premature wound closure, which prevented the
excretion of atrabilis, as in II-67; alternatively, these patients could
also become epileptic, if the excessive black bile ‘attacked the brain’
(II-6).
As Amatus comments in several scholia, melancholy and epilepsy
were considered two manifestations of excessive atrabilis, affecting
the soul or the brain, respectively (V-75). Their connection and occasional
coexistence are illustrated by the author in several cases presenting as
melancholy and loss of consciousness, seizures and even post-seizure
paralysis. In one of these a Dominican monk had repeated loss of
consciousness after seeing or smelling roses (II-36, In qua agitur de
quodam, qui ob rose odorem, continuo in syncopem & animi deli-
quium incurrat), nowadays probably classified as hysteric pseudo-
seizures (Staudenmayer, 1999). After hearing bad news, other patients
fainted and had convulsions which are also probably non-epileptic pseudoseizures (II-90, VII-1).
Menstrual retention was generally considered unsalutary, causing
‘blood corruption’, and neurological dysfunction such as convulsions
or melancholy (I-41, VI-28, VII-89). For example, in I-41 (De sympto-
matibus quibusdam a menstruum retentione) a 20-year old woman
with menstrual retention complained of tongue enlargement, head-
ache, fatigue and had a ‘ridiculous and stupid laughter’. In another
situation (V-75 In qua agitur de morbo gravissimo, & savissimo: ex
quo agrotans, bis, ter, & pluries, in die corripiebatur: & ita save, ut a
mulierculis assistentibus ab spiritu demoniaco cam vexari crederetur),
a young woman with menstrual retention, thought to be possessed by
her relatives, had daily, 2 h long attacks of loss of consciousness,
agitation and convulsions, and after some time her left arm became
paralysed. Amatus bled her to extract the corrupted blood, and she
was cured after 4 days of treatment ‘to great admiration and enor-
mous glory of medical science’ (V-75). Cases such as these were then
commonly mistaken as demonic possession, but seemed to respond to
medical therapies, denying their supernatural origin. Findings such as
these later led the physician Edward Jorden (1595–1633) to argue
that possession was nothing more than a manifestation of hysteria,
or ‘the mother’ (A briefe discourse of a disease called the suffocation
Epilepsy might also be associated with paralysis, as is described in a
case of prolonged post-seizure hemiparesis, or Todd’s paralysis, in a
young boy (IV-22 In qua agitur de pueru detento symptomate epi-
leptico, & posteaem paralisis im brachi & cruis dextra devemt). Acute
loss of motor function was thought to result from blockage in the
outflow of psychic pneuma from the brain ventricles to the nerves
due to obstruction of ventricular pores, depriving the whole body
(apoplexy), or half of it (paralysis) of movement and sensation
(Riese, 1999; Rocca, 1997). In the case of epilepsy, Amatus’ patho-
physiological interpretation of this phenomenon was that brain and
nerve ‘concussions’ caused nerves to close their pores and there-
fore stopped the flow of ‘animal spirits’ (pneuma physicon) inducing
paralysis (IV-22).
Amatus describes only a few cases of apoplexy, and in one of them
alerts to the necessity of confirming death (describing several practical
tests, such as palpating the metacarpal and carotid pulses, putting a
glass of water on the patient’s chest to observe movement or a
polished metal surface to the nostrils) and waiting for a period of
72 h before sepulture (IV-23 In qua agitur de apoplexia illico
interficiencia, & de apoplectico paroxysmo, tres dias perdurante.

Quoting Petrus Aponensis (Pietro d’Abano, 1257–1315), Amatus agrees that this period of time could allow the cycles of humoral renewal to unobstruct ventricular pores and restore pneumatic flow, and that patients might be revived after that period (IV-23). Recovery of neurological function after a stroke is, of course, possible, both in transient ischemic attacks (TIA) and minor strokes, and such phenomena could give rise to the idea that brain function could remain intact and might resume after clearance of supposed ventricular obstructions. A brainstem TIA could cause a reversible coma, but it is doubtful if after 3 days without irrigation, brainstem function could return to normal, so these commentaries are probably not based on direct clinical observation.

Vertebral column, spinal cord disease and CNS trauma

Spinal diseases are occasionally mentioned in the Centuriae, and range from the more innocuous, such as lower back and sciatic pain (I-90, III-8, VI-55), spinal tuberculosis (mentioned above), to post-traumatic urinary incontinence (II-11) and a case of paraparesis in a young male patient with chronic lower limb atrophy and intense muscle spasms in his legs (VII-11 *In qua agitur de convulsione inanitionem sequente, habita in cruribus*), which Amatus attributed to excessive copulation.

Neurological consequences of cranial trauma are often described in the Centuriae, and cases include a few minor accidental injuries (I-19, II-2), severe trauma causing coma or neurological deficits, including ‘loss of reason’ (III-19, III-41, IV-6), aggressions and assault (III-42, VI-100), resulting in one case in blindness, deafness and amnesiorrhaphy (VII-44), and wounds caused by sword-fighting (II-83, IV-6, VII-32). Unlike most medical contemporaries, Amatus’ extensive background in anatomy and surgery (he studied surgery in Salamanca with Pontano and Olivares) is evidenced by the ease with which he discusses surgical methods for dealing with cranial fractures, including detailed descriptions of the surgical instruments used (VI-100).

Berengario da Carpi’s (1465–1527) *Tractatus de fractura crani* (1535) is usually considered the major contribution to cranial traumatology in the XVI century. In it the author divides cranial trauma in categories (lacerations, contusions and perforations), sets forward the anatomy in the XVI century. In it the author divides cranial trauma in categories (lacerations, contusions and perforations), sets forward the anatomy thoroughly delineated by Berengario da Carpi (1547–1530), Vesalius (1514–1564) and Giulio Cesare Aranzi (1530–1589), who also supported the ventricular-pneumatic doctrine (Garrison, 1969; Olry, 1997). Curiously, Galen was himself not in favour of such a scheme, and considered that brain parenchyma had more functional relevance (Garrison, 1969; Rocca, 1997). In the Renaissance, the ventricular scheme was further elaborated on by Magnus Hundt (1449–1519) and Gregor Reisch (1467–1525), and ventricular anatomy thoroughly delineated by Berengario da Carpi (1547–1530), Vesalius (1514–1564) and Giulio Cesare Aranzi (1530–1589), who also supported the ventricular-pneumatic doctrine (Garrison, 1969; Olry, 1997). Usually, Amatus adheres to this doctrine when explaining, for example, case II-83, where a sword wound to the forehead was said to have caused no neurological damage, because it had passed between the ventricles even though it lacerated the brain parenchyma.

On a few occasions, however, he describes cases that appear to violate these postulates. In case VII-32 (*In qua agitur de miris quibusdam capitis vulneribus, ex quibus & memoria & visus facultas amissa sunt*), a patient with an occipital scalp wound is reported as having lost all memory: ‘[An] individual had a deep wound in the occiput, and lost a small portion of both membranes [meninges], hard and soft, as well as medullary substance, and was well afterwards. However, he lost all his memory […]’ (VII-32). In the ventricular theory, the IV ventricle was considered the seat of memory, and therefore loss of parenchyma in the occipital lobe should not have caused such a pattern of neurological deficit. Historically, this is one of the first descriptions of cognitive loss caused by parenchymal destruction, and was quoted soon after in Johannes Schenk’s (1530–1598) *Observations Medicæ de Capite Humano* (1584) together with other similar cases (Luzzatti and Whitaker, 1995–1996; Whitaker and Luzzatti, 1997). In a few other instances, Amatus again associates death or neurological deficits with the loss of brain parenchyma occurring either through trauma or surgical removal. In his opinion, brain surgery usually caused death, or if the patient
survived ‘[he becomes] mute, deaf or with a facial deformity’ (III-41). In another case accidental surgical removal of brain tissue inside a cranial malformation operated on by another surgeon (I-52 De pueru cum comu in capite nascente) also resulted in immediate death. Again all these observations violate the ventricular theory, since only lesions that infringed upon these structures were thought to be life-threatening. It must be said regarding all of these cases, that in no place Amatus negates the ventricular doctrine, or provides a diverging explanation from it. Most likely he was incapable of providing an explanation for his clinical observations in accordance with what he believed to be the prevailing theory of neurological function. His contribution was to illustrate the possibility of neurological deficit after parenchymal destruction. His and other observations would eventually grow into a body of evidence that led to the discredit of the ventricular theory in the XVII century (Garrison, 1969).

Anatomy and physiology

Finally, a few curationem are almost entirely devoted to anatomical and physiological descriptions (III-40, IV-100 and VII-24). Amatus’ dedication to anatomical studies in Ferrara gave him advantage of first hand observations, and tempered his classical views with more modern conceptions. In result, even though supporting Galen’s standard version of neuroanatomy against Vesalius, including the seven pair scheme of cranial nerves (III-40 In qua docetur, quamodo musculi moveantur suo motu voluntario, simulque quamodo deperditur motus membrri manente sensu, & contrario), he unequivocally states that his research has proven that the optic nerves are not hollow: ‘nowadays, for people dedicated as well as those with a great interest in these matters, [these nerves] have never appeared hollow or perforated, even when seen against the sunlight’. He denies the existence of a true crossover of fibers in the optic chiasma, claiming that the nerves come in contact to facilitate the ‘conjunction of their pores’, avoiding diplopia in normal situations, but making it possible to maintain normal visual capacity with one eye closed (III-40). He describes the existence of four veins that feed the brain (the sphagitidas), as well as two arteries, but fails to mention the existence of the rete mirabile, supported by Herophilus and Galen, and which was eventually denied by Vesalius (VI-100). Also deviating from standard medical doctrine, Amatus provides extensive arguments for the importance of the diaphragm as the seat of laughter, but concludes by saying that in his opinion it should be in the brain (in accordance with the opinion of Hippocrates).

Discussion and historical considerations

The Centuriae are a work of detailed erudition in the best tradition of Renaissance medicine, providing several novel clinical and anatomical observations, and therapeutic innovations both medical and surgical. Amatus appears very much rooted in the scientific mainstream of his time, quoting, for the most, classical authors of the Greco-Roman (Hippocrates, Galen, Celsus, Pliny, Soranus), Byzantine (Paulus of Aegina, Aetius of Amida, Alexander of
Tralles, Ruphus of Ephesus, Oribasius) and Arabic (Rhazes, Avicenna, Averroes) eras. He is also clearly aware of and comments on contemporary works such as the books of Vesalius, Cannano, Bravasola, Curtius, Joseph Struthius, Fuchsis, Andres Laguna, and Vidius. The XVI century was the first time a book was devoted entirely to general neurology (De Cerebri Morbis…, Jason Pratensis 1549) (Pestronk, 1988), but Amatus was apparently unaware of this work, since it is not mentioned in the Centuriae.

Being the work of such a notorious converso physician, the Centuriae appeared regularly in the indices of prohibited books from 1581 onwards, in Portugal, Spain and Italy, and in fact had to be modified in at least in three different places: IV-36, IV-51 and the suppression of the Oath at the end of the book (Front, 2001). The reason behind most expurgations appears to be the portraying of clerics in unfavourable light. Curiously, in one case Amatus comments on a dispute between the Jewish physician of Isabella of Spain and some monks accused of maliciously pronouncing an apoplectic dead (IV-23), where he attempted to conciliate both positions, and justifies the monks’ interference as ignorance instead of malice. It is entirely plausible that this episode was either altered after being written, or originally designed not to give offence. One can wonder, however, why he should decide to mention it at all, if not to somehow protest at the fate of many Jewish physicians at that time, a fate that would also befall him later on. Further evidence that Amatus felt the need to be unusually fervorous in his Christianity is also found in IV-46, where, in passage, he considers the anti-semitic works of Pietro Colonna Galatino (c. 1460–1540) ‘an excellent work and full of erudition’. After residing in Salonica, such deceptions were no longer necessary, and Amatus was free to publicly espouse Judaism.

However, the Centuriae are more than just a collection of cases and erudite discussions. They also provide a clear record of medical practice in the XVI century, and an insight into the problems and difficulties posed by neurological diagnosis and therapy in that era. The impact of the Centuriae on medical knowledge can be measured by the large number of contemporary authors that quote them as a source of interesting medical cases. In scope, number and variety of cases described, the Centuriae provide an important collection of observations. Moreover, Amatus does not limit himself to relating his cases and their therapy, nor is he self-aggrandizing. In several occasions, he describes his therapeutic failures as well as cases which he could not understand. He nearly always attempts to explain to the reader the underlying pathophysiology of his cases, as well as his therapeutic options, based on extensive classic and modern erudition, standard medical theories and his own well-fundamented opinions. On several occasions, he provides insights coming from his own experience, and observations that can only come from a mind trained in the discipline of the autopsy room, as well as rooted in an extensive medical practice.

In therapeutics Amatus is frequently innovative, resorting to surgery without hesitation and often taking risks when using more conventional therapies, in cases where classical and contemporary wisdom was unclear. He also pioneered the use of recently available new medications in neurology, such as guaiac wood (China root) for headache (III-36, IV-99) (Friedenwald, 1944a). Guaiac wood extract (the heartwood and sapwood of Guaiacum officinale L. and/or G. sanctum L.) is still used today as supportive therapy for rheumatic complaints by homeopaths, but has no known application in neurology.

Overall, as a practicing physician Amatus appears to have been very successful, and he made important contributions to contemporary medical science. Unfortunately, the XVI century which mostly was a period of rapid scientific advancement, also saw the destruction of a medical school that had flourished in Southern Europe since the time of the Islamic occupation. The Jewish medical tradition, which had thrived in the tolerant intellectual and religious climate of the Cordoba Caliphate, was eradicated first from Spain and then Portugal, to the detriment of both countries and the benefit of others. The Sephardic Diaspora would prove to be of critical importance in the development of several sciences, including medicine, in northern Europe as well as in the near East. During that period several physicians of great value were condemned to an errant life, and also unfairly driven from the mainstream of medical science. In the case of Amatus, we should recognize his role in the development of neurological science, and in justice, he should be considered one of the precursors of this discipline given his contribution of several relevant clinical observations such as were presented in this work.

Acknowledgements

I wish to express my gratitude to Prof. Christopher Goetz at Rush University, for reviewing an earlier version of this manuscript, to Dr Peggy Ho at Stanford University for her help with obtaining references, and to Mr Alberto Severino at the Faculty of Medical Sciences in Lisbon, for providing the panel photograph in Fig. 1.

References


Jorge R. Amato Lusitano: comentos à sua vida, obra e época. Lisboa: Instituto de Alta Cultura; 1908.


Lemos M. Amato Lusitano, a sua vida e sua obra. Porto: Eduardo Tavares Martins; 1907.


