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The eye of Vesalius

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ABSTRACT.
In the time of Vesalius, knowledge of ocular anatomy was limited. The first description of the anatomy of the eye comes from Democrites, for whom the eye was surrounded by two 'coats', filled with a homogenous fluid. The optic nerve was hollow and the lens was considered to be a postmortem artefact. Until the 15th century AD, medicine was influenced by the writings of Galenus and the model of the eye he proposed was still considered valid, even after Vesalius. According to the Alexandrian tradition, the lens was considered as the seat of visual perception. Although Vesalius rightly deserves the title of father of modern anatomy, his description of ocular anatomy was rudimentary and often incorrect. He described a musculus retractorius bulbi, which is found only in lower mammals, not in primates. The lens, the role of which as an optical device he recognized correctly, was placed too centrally in the eye. The optic nerve was not correctly placed and, following Galenus, Vesalius described only seven cranial nerves. The Galenian concept of ocular anatomy was to endure until the development of the microscope by Anthony van Leeuwenhoek. Modern ocular anatomy, in fact, can be dated from the works of Zinn.

Key words: Galen – history – ocular anatomy – Vesalius

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Introduction

Ophthalmology is one of the oldest medical specialties. Iry was the first ophthalmologist whose name was to be recorded. He lived during the 6th dynasty (about 2400 BC) and his tomb can be found near the pyramid of Cheops. Iry's title was 'Royal Oculist and Shepherd of the Rectum'. A number of ocular diseases are described in the Edwin–Smith papyrus (1800 BC), now in the library of the New York Historical Society. The Ebers papyrus, found in 1862 between the legs of a mummy and now owned by the University of Leipzig, contains no anatomical references except for a claim that blood to the eyes is supplied by temporal vessels. It does, however, discuss a number of ocular diseases, such as blepharitis, chalazion, ectropion, entropion, trichiasis, pinguecula, leucoma, staphyloma, iritis, cataract, dacryocystitis and ophthalmoplegia (Hirschberg 1982).

In the *Codex Hammurabi* (*c.* 1800 BC) the fee for ocular surgery is indicated. To operate on a free man, the ophthalmologist was entitled to ask for the considerable sum of 10 silver shekels (about the annual salary of a workman); a poor man was charged five and a slave two shekels. However, if the patient lost his eye after an unsuccessful operation, the surgeon was penalized by having his hand cut off. Possibly this punishment was inflicted not on the surgeon himself, but on one of his slaves. If the eye of a slave was lost, the surgeon was required to replace the slave.

Ocular anatomy before Vesalius

Duke-Elder and Wybar (1961) published an excellent survey of the history of ocular anatomy. Democrites (*c.* 460–370 BC) gave what is probably the first anatomical description of the eye. He described two 'coats' and stated that the eye was filled with a homogenous fluid, there was no lens and the optic nerve was hollow. Alcmaeon of Croton (*c.* 500 BC) is considered to have given the first description of the optic nerve, indicating that it is connected to the brain. For him, the brain, rather than the heart, was the seat of the soul and also the organ of movement and sensation.

Hippocrates of Cos (*c.* 460–375 BC) is considered to represent the father of medicine. He insisted on careful observation of the patient. He was probably the first to describe what would later be called Behçet's disease and he noted the cardinal symptoms of the disease as fever, aphths in the mouth and genitalia, joint and ocular inflammation.

No dissections were performed in the early Greek period because reverence for the dead body required that it be given a proper and intact burial.

Aristotle (384–322 BC) probably dissected animal eyes. He described the eye as a spherical organ consisting of three layers filled with a homogenous fluid. He believed that the eye maintained contact with the brain by means of three tubes, one of which connected with a similar tube originating from the other eye. This may represent the first observation of the optical chiasm. The

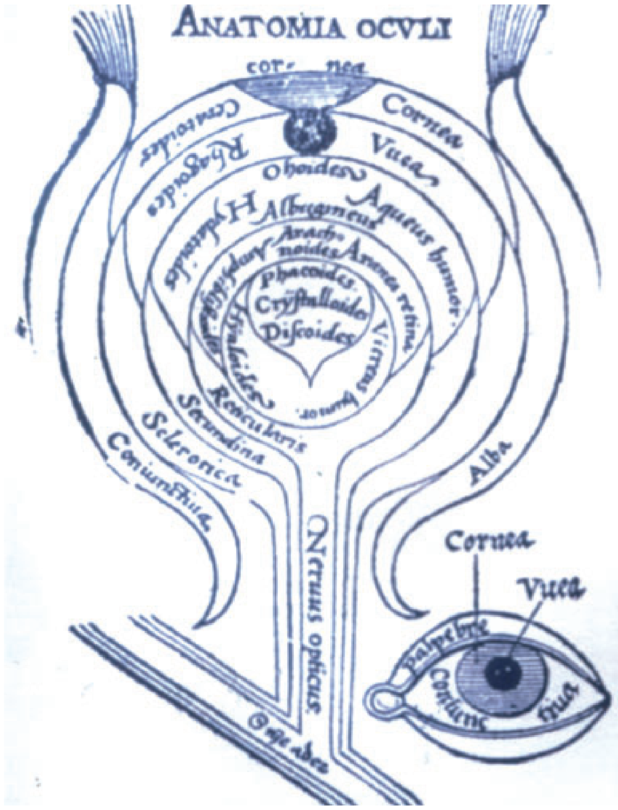

Fig. 1. Ocular anatomy according to Galen. Permission obtained from Jean-Paul Wayenborgh.

two other tubes possibly represent blood vessels and the trigeminal nerve. The lens was considered as a postmortem artefact caused by the accumulation of phlegma.

In Alexandria, dissections were performed on convicts and Roman anatomical knowledge was based on the Alexandrian school. The Romans were quite superstitious and thus, for them, dissection of the human body was unthinkable.

Aurelius Cornelius Celsus (*c*. 25 BC–50 AD) lived under the Emperor Tiberius. His description of ocular anatomy is probably based on papyruses from the Alexandrian Library. Celsus described three ocular layers and the lens (crystalloides), which was still considered as the seat of visual perception. It was Celsus who made first mention of the anterior chamber (locus vacuus) and the vitreous body.

Rufos of Ephesus (98–117 AD), a contemporary of the Emperor Trajan, mentioned a fourth ocular layer, the conjunctiva, which he called the 'epidermis'. He distinguished the anterior chamber filled with an aqueous fluid from the posterior segment of the eye, which, he wrote, contained a substance resembling the white of an egg.

Claudius Galenus (130–200 AD) is the best-known physician of the Roman period and his writings were considered to represent all that was essential in medicine until the period of Vesalius. Galenus originated from Pergamon, studied in Alexandria and became physician to the emperors Marcus Aurelius and Commodus. His writings on ophthalmology have been lost, although his description of ocular anatomy survived. Galen considered seven layers: the conjunctiva, which for him was an extension of the periost of the orbit; the ocular muscles and their tendons; the sclera; the choroid; the retina; the vitreous body, and the crystalline lens. The corneoscleral limbus represented the junction of the choroid and retina. The optic nerve was hollow, allowing the passage of pathological humours which were believed to provoke ocular diseases. There were seven ocular muscles, including the musculus retractor bulbi, which is found only in lower mammals. It is worth noting that Vesalius, much later, did not rectify Galen's mistake. He described the retina as an extension of the optic nerve that nourished the vitreous and, through the vitreous, the crystalline lens. The lens (divinum oculi) was considered to represent the centre of visual perception. Visual corpusculi or emanations were believed to be sent from the lens to the object being looked at and to return via the lens to be transported through the hollow optic nerve to the third ventricle of the brain, where the soul was thought to be located.

After Galen, there began a period of scientific inertia, especially in Western Europe. The burning of the Alexandrian Library in 641 AD resulted in the loss of a mass of knowledge, fortunately partially transmitted by the Arabs to the West through the schools of Toledo and Salerno. Rhazes (Al Razi, 865–925) described the reaction of the pupil to light. The mathematician Alhazen (Ibn Al Haitham, 965–1038), who worked in Cairo, dismissed the corpuscular emission theory of vision.

Averroes (Ibn Rushd, 1126–1198) wrote extensively on optics and suggested that the retina and not the crystalline lens was responsible for vision.

A few schematic descriptions of the eye are known of, especially from Alhazen and Hunain Ibn Ishak. These continued to be based on the Galenic concepts: the optic nerve was hollow and the crystalline lens, which was considered the most essential part of the eye, was centrally located and connected to the optic nerve. Cataract was considered to represent a corrupt humour in front of the lens and thus could not be located immediately behind the iris.

The ophthalmological treaties written during this period in the West are far from original. Peter the Spaniard, who will probably prove to be the only ophthalmologist ever to become a pope (John XXI, 1210–1276) wrote the *Breviarium magistri Petri Hypanide egritudinibus oculorum et curis* which at his time was already considered as valueless (Hirschberg, 1985a). The most popular work on ophthalmology dating from this period is the *Practica Oculorum* of Benvenutus Grassus (or Grapheus).

Even Roger Bacon (1214–1294), a Franciscan and a philosopher, considered the crystalline lens as the site of visual perception and believed the optic nerve to be hollow to allow the visual spirit or pneuma to pass through it.

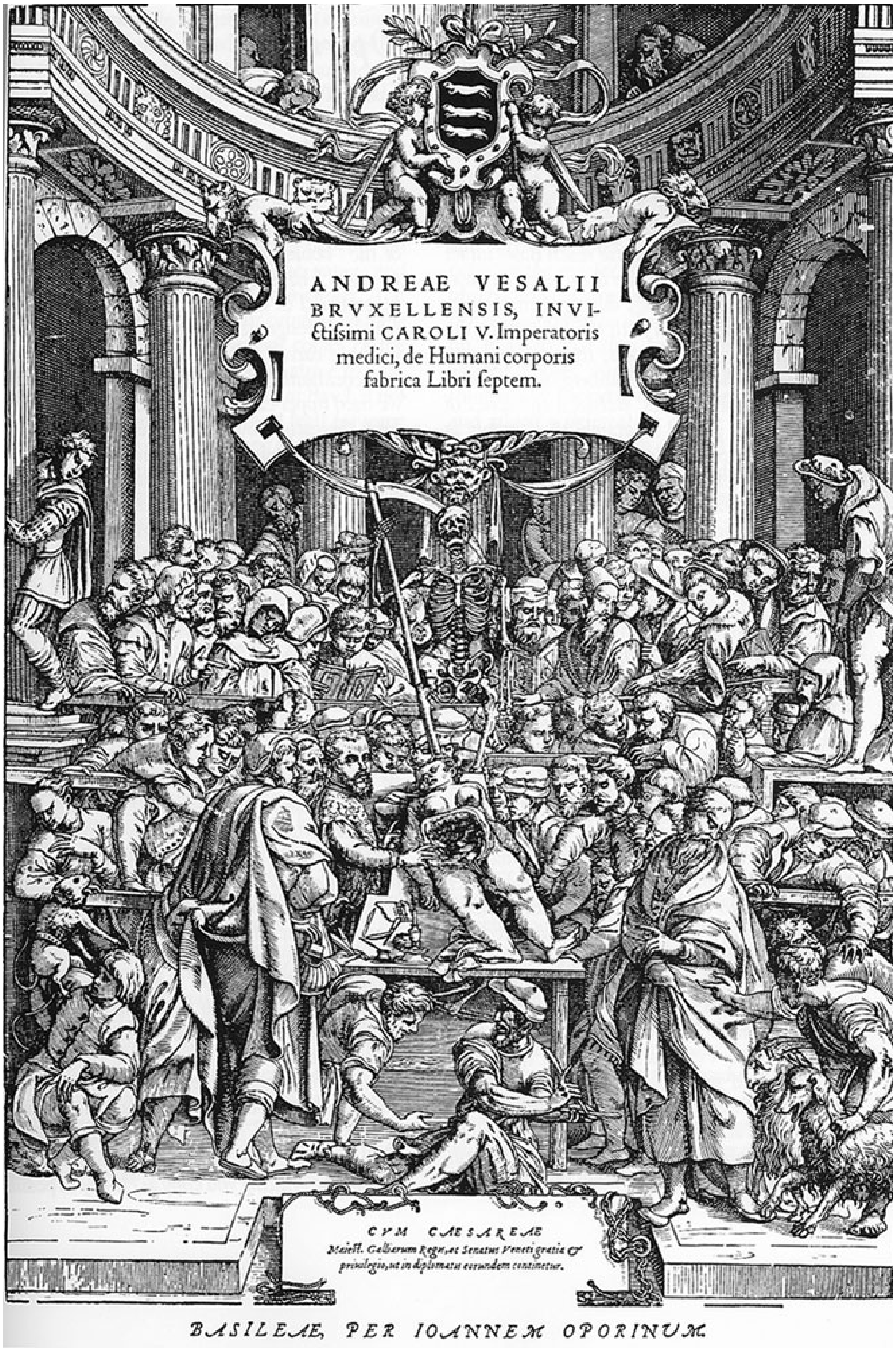

Fig. 2. Frontpage of *De Humani Corporis Fabrica* depicting Andreas Vesalius performing a dissection. Note Vesalius' coat of arms (three weasels). (Private collection).

The most renowned surgeon of his time, Guy de Chauliac of Montpellier, wrote in his *Chirurgia Magna*: 'I am not interested in knowing whether the cataract is present between the cornea and the iris, as Jesus proves, or between the aqueous and the lens as Galen pretends.' This sentence illustrates the total lack of scientific interest displayed by even the most respected physicians in the Middle Ages.

Leonardo da Vinci (1452–1519) adhered to the old anatomical description of the eye, but for one point: the

Fig. 3. Andreas Vesalius painted by Jan van Calcar, the Hermitage, St Petersburgh. (Jdanov 1964)

lens was no longer responsible for visual perception. He described the double refraction of light by the cornea and the crystalline lens before it reached the optic nerve. The lens in da Vinci's drawing is relatively too large and centrally located, and the optic nerve is hollow and connected to the third ventricle. Leonardo may have been the first to consider a technique for fixing ocular tissue. He proposed placing the eye in the white of an egg and boiling it to make it easier to dissect.

Vesalius and the eye

Vesalius rightly deserves the title of father of modern anatomy. He was born Andreas van Wesel on 31 December 1514, in Brussels, into the family Wytinck, which had originated from Wesel in the Duchy of Cleves and had close links with the court. Vesalius' great-grandfather Johannes had obtained his medical degree in 1427 at the University of Padua and had been appointed professor at the recently created University of Louvain in 1429. In 1449 he became the city physician for Brussels. The Emperor Frederic III delivered him a coat of arms showing three weasels. This coat of arms is to be seen on the front page of the *Fabrica*. Johannes' eldest son Everaert studied medicine in Louvain and became physician to the Emperor Maximilian of Austria. He did not marry, but had a number of illegitimate children, one of whom was Andries, who became an apothecary and worked for Margaretha of Austria and later for Charles V (Van Hee 2000).

Andreas Vesalius started his medical studies first in Louvain and later in Paris, where he became a pupil of Jacques du Bois (Jacobus Sylvius) and of Johann Günther d'Andernach. In Paris, Vesalius performed his first public dissection, in which, contrary to the custom of the day, which decreed that the teacher supervise a dissection performed by an assistant, Vesalius himself, not an assistant, performed the task (Elkhadem et al. 1993).

Vesalius returned to Louvain, where he studied for a further semester before leaving for Padua in 1537. On 5 December in that year he obtained his doctoral degree 'cum ultima diminutione'. The term 'diminutione' means that because of the excellence of his defence he was required to pay a markedly reduced fee of only 17 and a half ducats for the diploma. One day after graduating he was appointed Professor of Anatomy and Surgery at the University of Padua. He began work immediately and, the same semester, obtained a corpse for dissection. Vesalius had already realized, while living in Paris, that Galen's anatomy was based on the dissection of animals and did not necessarily correspond to human anatomy. In Paris he had had the opportunity to collaborate with Günther van Anderach on a new edition of Galen's *Institutiones Anatomicae*. In Padua Vesalius was to further adapt this work for his students and to include not only his own drawings, but also illustrations by his friend Jan Stevens van Calcar, a former pupil of Titian. This work is entitled *Tabulae Anatomicae Sex*. Van Calcar most probably also produced the front page of the *De Humani Corporis Fabrica Libri Septem* and drew the skeletons. A portrait of Vesalius painted by van Calcar can be seen in the collections of the Hermitage in St Petersburg. The *Fabrica*, dedicated to the Emperor Charles V, was published in Basel by Vesalius' friend Johannes Oporinus in 1543. A shorter (and less expensive) version for students and artists, the *Epitome*, was dedicated to Philip II of Spain, Charles' son. The *Fabrica* became a bestselling book. However, Vesalius' corrections of some of the errors he had detected in Galen's work were not unanimously accepted and some contemporaries, among them his former teacher Sylvius, were to heavily criticize Vesalius for daring to contradict the unfailing Galen. Vesalius went on to write the *Epistola Rationem Modumque Propinandi Radicis Chynae*, a letter to Joachim Roelants, physician to Margaretha of Austria, who had asked him

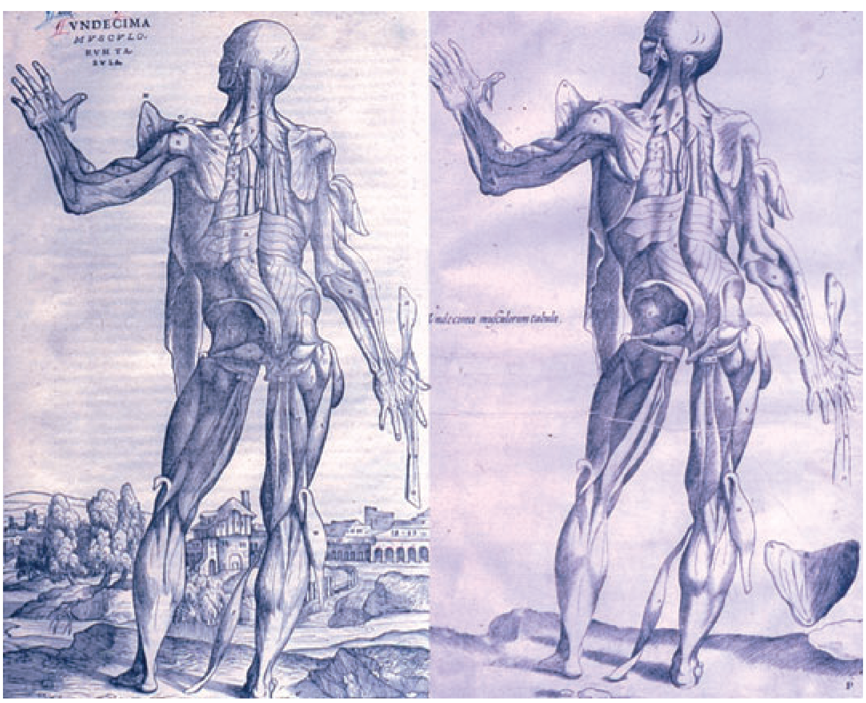

Fig. 4. Description of the human musculature. Left as reproduced in the *Fabrica*, right in the *Epitome*. (Private collection).

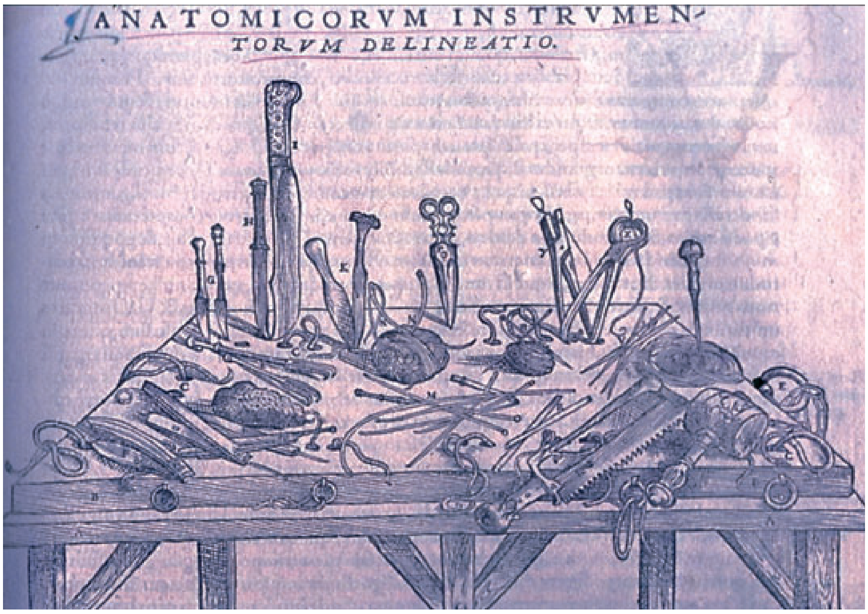

Fig. 5. *De Humani Corporis Fabrica*. Instruments used by Vesalius for dissection. (Private collection)

about the use of the china root, and a communication which gave him the opportunity to respond to Sylvius' accusations (Hahn et al. 1962). He had, meanwhile, been appointed physician to the Emperor and subsequently to his son Philip II and was thus required to live in Brussels.

Vesalius was to have the opportunity to visit Padua again, where his pupil Colombo had succeeded him. In 1550 he was sent by Philip II to Paris, where King Henri II had been fatally injured by the Earl of Montgomery during a tournament. There, Vesalius met Ambroise Paré. After the death and the subsequent autopsy of Henri II, Vesalius returned to Brussels, from whence he accompanied Philip to Madrid. He was not, however, particularly well received in Spain, where his autopsies provoked marked criticisms. Possibly to escape from this animosity, but also possibly by order of the Inquisition or, perhaps, motivated by his own religious beliefs, Vesalius undertook a pilgrimage to Jerusalem. His journey was certainly approved by Philip II, who entrusted him with the sum of 500 ducats to be given to the guardians of the Holy Places. Vesalius was to receive a letter of thanks addressed to Philip, which represented a clear indication of his intention to return to Madrid and not to accept the chair in Padua, as had been proposed when the seat became vacant in 1563 on the death of Gabriele Fallopio, professor of anatomy at Padua after Colombo. However, during the return journey the boat on which he was sailing was struck by a heavy storm near the Greek island of Zanten. In all probability, Vesalius did not drown. His death is recorded as occurring on 15 October 1564 on the island of Zanten, possibly from typhus (Elkhadem et al. 1993).

Vesalius was a true innovator and the quality of his anatomical descriptions, particularly of the skeleton and muscles, heralded a new era in medical understanding of the body. By sharp contrast with this is his limited contribution to ocular anatomy. In the 16th century there were no adequate fixation techniques and the instruments available did not allow for minute dissections. Vesalius concurred with Galen in his description of the extraocular muscles and persisted in mentioning the musculus retractorius, which is only to be found in lower mammals. He also adhered to Galen's classification of seven pairs of cranial nerves, comprising: the nervus opticus (I); the nervus oculomotorius (II); the sensible branch of the trigeminal nerve and the nervus trochlearis (III); the motor branch of the trigeminal nerve (IV); the facial acoustic complex including the nervus abducens (V); the nervus glossoparyngeus (VI), and the nervus vagus (VII).

Fig. 6. *De Humani Corporis Fabrica*. The brain. (Private collection)

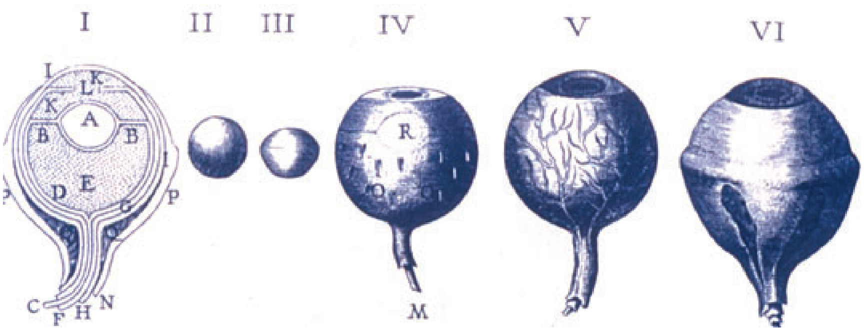

Fig. 7. *De Humani Corporis Fabrica*. Ocular anatomy. (Private collection)

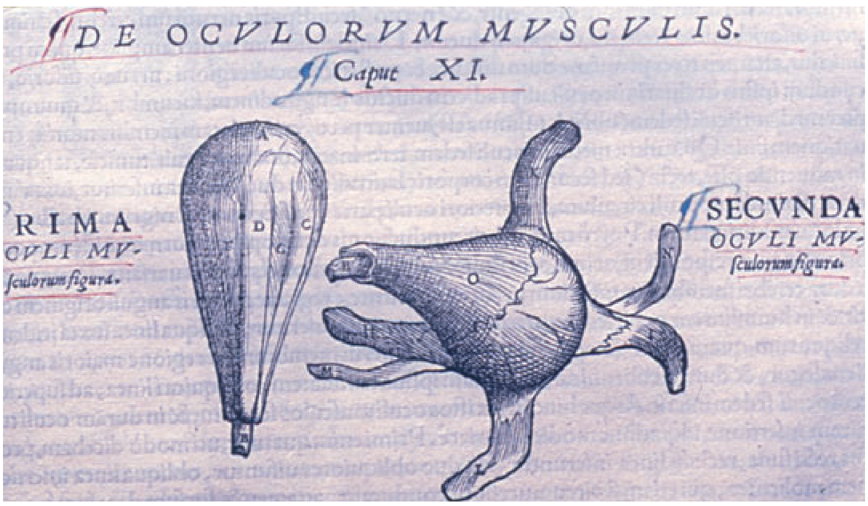

Fig. 8. *De Humani Corporis Fabrica*. The extra-ocular muscles, including the musculus retractorius. (Private collection)

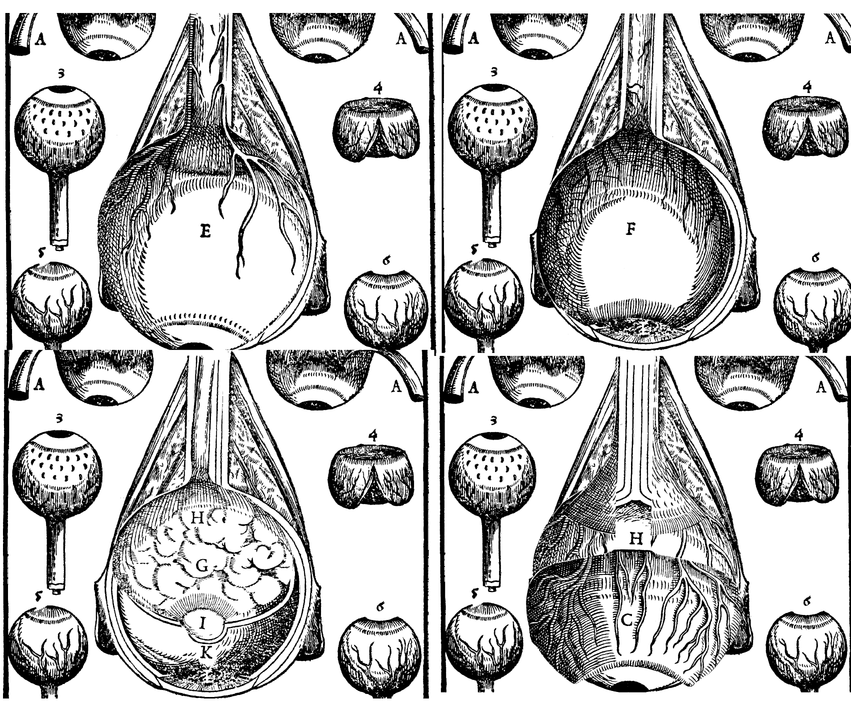

Fig. 9. Georg Bartisch. Ocular anatomy in Ophthalmodouleia. Permission obtained from Jean-Paul Wayenborgh.

Vesalius described the crystalline lens as located in the centre of the eye. He did, however, recognize the optical role of the lens 'quodammodo ad lentis similtudinem'. He also showed that the anterior lens curvature differs from the posterior curvature, but considered each as separate parts. He pointed out that the colour of the iris is caused by iris pigmentation and not by the aqueous humour. He described the ciliary body as follows: 'Tunica ab uvea unitatem ducans, cilii seu palpebrarum pilis imagine correspondens ac interstitium pariter vitrei humoris ab aqueo [A tunic starting from the uvea and with an aspect corresponding to eyelashes or eyelid hair as well as interspaces that equally divide the vitreous and the aqueous].' This description may indicate that Vesalius noticed the ciliary processes and the zonular fibres, but, unfortunately, his drawing is unclear in that respect. He described the retina as: 'Tunica quam reti assimilamus quamqui resoluta visorii nervi efficit substantia [A tunic which we compare to a net which is detached from the substance of the optic nerve].' Vesalius' optic nerve was no longer hollow, as it had been in the opinion of previous anatomists, including Jan Yperman and da Vinci, but he continued to locate it exactly opposite the centre of the cornea.

Vesalius' anatomic studies of the eye did not match his other achievements. His descriptions held fast to the Galenic tradition and a more accurate description of ocular anatomy was not to be made until the 18th century.

Ocular anatomy after Vesalius

Vesalius was to be plagiarized without scruple: his description of the ocular anatomy (with an identical drawing of the eye) was used by Felix Platter in his *De Corporis Humani Structura*, published in 1583 by Oporinus. Platter reiterated the opinion introduced four centuries earlier by Ibn Rushd that the retina, not the crystalline lens, was the place where visual stimuli were processed.

Whereas Galen had considered the conjunctiva as an extension of the orbital septum, Giacomo Berengario (1470–1530) showed it to be a separate

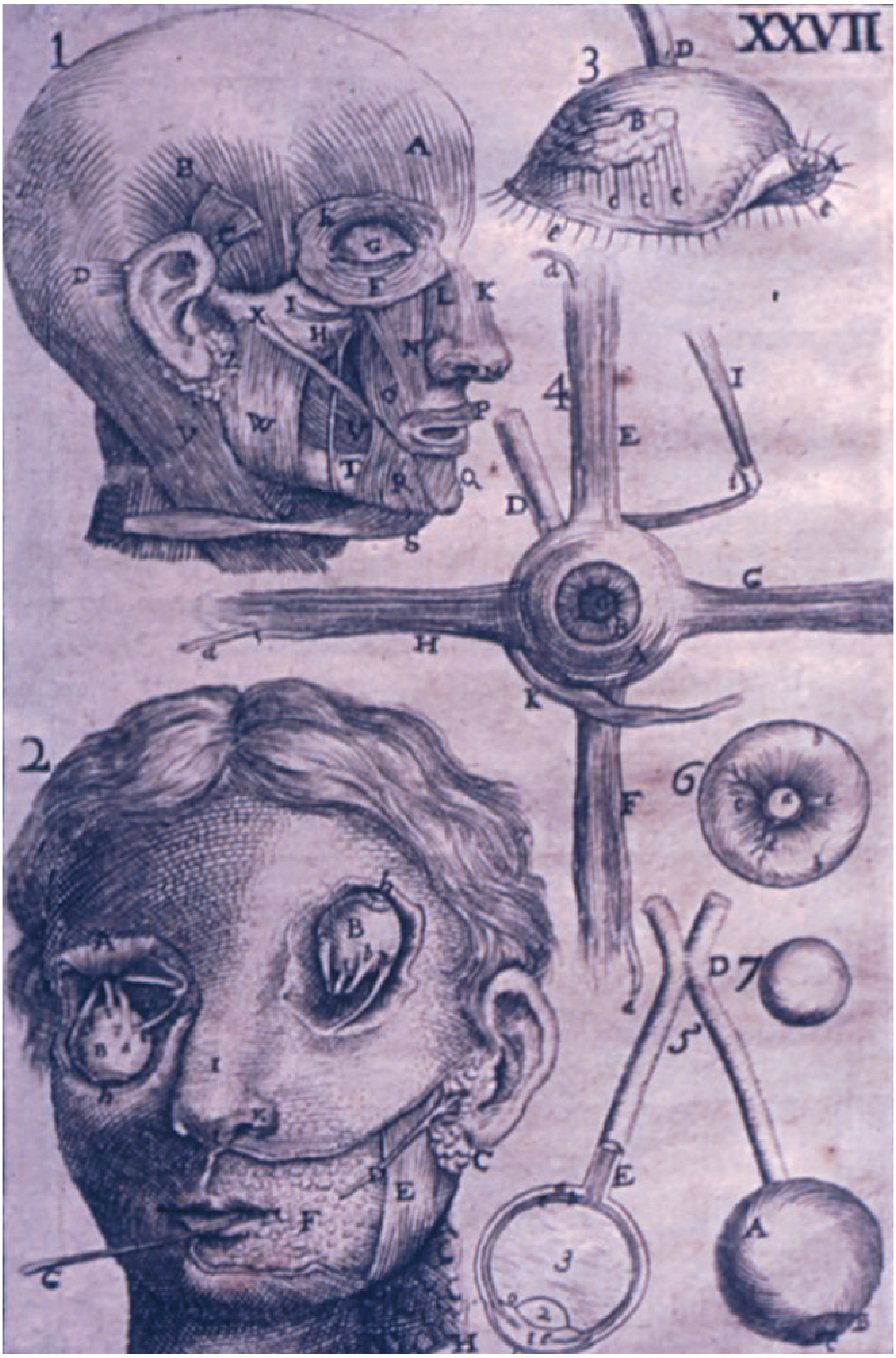

Fig. 10. Philip Verheyen (1710). Corporis humani anatomica. (Private collection).

structure. Gabriele Fallopio (1523–1563), who became professor of anatomy at Padua after Vesalius and Colombo, denied the existence of a musculus retractorius bulbi in humans. He also described the musculus levator palpebrae, gave a more correct description of the musculus obliqui and added the trochlear nerve to Galen's seven cranial nerves (Duke-Elder & Wybar 1961). Georg Bartisch (1535–1606), an oculist and lithotomist from Dresden, authored the first book on ophthalmology to be written in German, *Ophthalmodouleia, das ist Augendienst*, published in Dresden in 1583 (Hirschberg 1984b; Bartisch 1996). It contained a number of colourful illustrations and

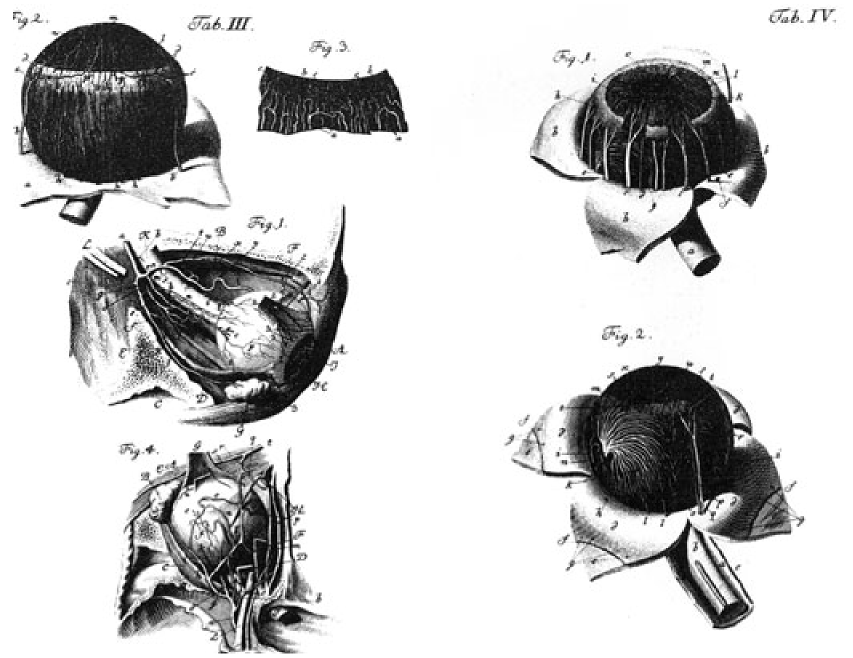

Fig. 11. Johannes Zinn (1755). Descriptio anatomica oculi humani. Permission obtained from Jean-Paul Wayenborgh.

descriptions of a series of eye diseases and ocular surgical procedures. However, Bartisch was highly superstitious. He believed that ocular surgery was best performed under the constellations of Libra, Sagittarius or Aquarius. In emergencies, one might also intervene under Virgo, Scorpio or Pisces (Bartisch 1996). His book contained remarkable drawings of the eye and the brain, with consecutive sheets which could be flipped over to show the various structures layer by layer (Bartisch 1996). Bartisch sited the crystalline lens more anteriorly than Vesalius had and believed that it contained fluid surrounded by arinea. He continued to describe the musculus retractorius bulbi around the optic nerve and seemed to be unaware of the chiasm, despite its mention by Aristotle.

Hieronimus Fabricius ab Aquaponte (1537–1619), disciple and successor of Fallopio, was to establish the correct location of the crystalline lens, but it was not until 1619 that the first more or less acceptable diagram of the eye appeared. Christophorus Scheiner (1575–1650), a Jesuit priest, demonstrated that the radius of the cornea was smaller than the radius of the sclera, placed the lens where it belongs and moved the optic nerve to the nasal side.

Frederik Ruysch (1638–1731) was the first physician to study the ocular vessels using injection techniques, with which he described the central retinal artery and the vortex veins.

Antony van Leeuwenhoek (1638–1731), the inventor of the microscope, discovered the corneal epithelium and was the first to observe rods and cones in the retina (Duke-Elder & Wybar 1961).

Two French scientists, Antoine Maître-Jean (1650–1730) and François Pourfour du Petit (1664–1741), demonstrated the lamellar structure of the lens, and the latter introduced the technique of freezing sections, which allowed for more accurate representation of the ocular tissues. At this point the posterior chamber was observed for the first time (Hirschberg 1984a).

The true father of ocular anatomy is, however, Johann Gottfried Zinn (1727–1759) (Hirschberg 1985b). Zinn studied anatomy and botanical science in Göttingen and Berlin and was appointed professor at the Medical Faculty of Göttingen in 1753, where he also became the director of the botanic garden. His reputation as a botanist is suggested by the fact that Linnaeus named the genus *Zinnea* after him. In his *Descriptio Anatomica Oculi Humani*, published in 1755, Zinn described the various ocular structures layer by layer, correctly reproducing the ocular muscles. Zinn introduced the notion of ciliary processes, and described the zonular fibres and the blood vessels around the optic nerve head. Three ocular structures are named after him: the zonula of Zinn, the annulus tendineus of Zinn, and the circulus of Zinn. This clearly indicates the importance of this brilliant anatomist, who died in 1759 at the young age of 31 years. Other scientists who continued the work of Zinn and his predecessors included Fontana, Cloquet, Schlemm and Bowman. The improvement in fixation and coloration techniques developed by Purkinje, and the subsequent inventions of the microtome, phase contrast microscopy, polarization microscopy and, finally, electron microscopy, were to lead to our current knowledge of the anatomy and histology of the visual system.

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