Anders Retzius and the Dental Histologists of the Mid-Nineteenth Century: Their Contribution to Comparative Anatomy, Histology and Anthropology

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Abstract

Anatomy, comparative anatomy and embryology are fundamental to taxonomy and evolutionary biology. In the mid-nineteenth century many anatomists and zoologists made major contributions to more than one of these disciplines and a surprising number of them were also histologists. Historical accounts of discoveries and developments in anatomy, and in particular dental histology, rarely consider the broader contributions and have tended to be concerned with establishing historical
priority about who discovered or described what first. The period 1830 to 1840 saw new developments in light microscopy that enabled studies of histology, cellular pathology and embryology. It also saw a shift away from older ideas such as Naturphilosophie and vitalism towards a more rigorous experimental approach to scientific investigation. Many scientists with diverse research interests were working in parallel on comparative dental histology and were in many cases largely unaware of each other's work. One researcher, Anders Retzius, travelled widely across Europe, corresponded regularly with his scientific colleagues and, probably unbeknownst to himself in his own lifetime, made a lasting contribution to dental histology. Anders Retzius was a clinician, an anatomist, a comparative anatomist, a histologist and latterly an anthropologist. His life and career spanned the whole of this fast-moving period in the history of anatomy and histology.

Introduction

Revisiting aspects of the past and bringing them together in a new or different context can be enlightening. Many nineteenth century anatomists were not just doctors, dentists and/or anatomists but often also physiologists, comparative anatomists, zoologists or anthropologists. Much of the dental histology they first described we now routinely refer to in anthropology and archaeology, more so today perhaps than in clinical medicine or dentistry. Each of the scientists who first studied the histology of the tooth did so, often fleetingly, alongside their other scientific interests. Revisiting the history of how and when this all happened is one way to
ensure their contributions survive beyond just eponyms, which in the case of dental histology, do not always reflect true scientific priority.

**Anders Retzius**

Anders Adolf Retzius was born in Lund, Sweden, on October 13\textsuperscript{th} 1796, the youngest of three brothers. He belonged to a family of considerable academic standing (Nelson, 1920).\textsuperscript{1} His father, Anders Jahan Retzius (1742-1821) was professor of natural history at the University of Lund and a member of the Royal Swedish Academy of Sciences.\textsuperscript{2} His mother was Ulrika Beata Prytz (1764-1808) and his elder brothers were Nils Mathias (1793-1870) and Magnus Kristian Retzius (1795-1871). As a boy he learned a great deal about mineralogy and zoology from his father who had contributed much about the local Swedish fauna, describing many new species of insects and carrying out fundamental work on their classification (Wilson, 1861).\textsuperscript{2} Anders Jahan Retzius had originally trained as an apothecary, but was also a former student of Carl Linnaeus (1707-1778). He was appointed extraordinary professor of natural history at the University of Lund from 1777.\textsuperscript{3} Thereafter, Anders Jahan Retzius held various chairs of natural history, economy and chemistry until his retirement in 1812.\textsuperscript{2}
Even after Anders Retzius had enrolled at the University of Lund his father continued to teach him there. Here also he was taught by Arvid Henrik Florman, (1761-1871), professor of anatomy, surgery and veterinary science. In 1816, aged nineteen, Anders Retzius spent a year at the University of Copenhagen where he studied zoology and comparative anatomy with Ludwig Jacobson (1777-1843) and Johan Hagemann Reinhardt (1776-1845) as well as chemistry and physics with Hans Christian Ørsted (1777-1851). In 1818 Retzius was appointed to the veterinary staff of the Royal Military Academy at Carlsberg, but in 1819 at age 23 he returned to Lund to take his Doctor of Medicine degree. His final MD thesis was on the structure of cartilaginous (chondrichthyan) fish, especially sharks and rays; (Observationes in anatomiam chondropterygium praecipe squali et rajae generum: Lund, 1819). At this time also, he acquired the diploma of master of surgery from the Karolinska Medico Chirurgical Institute. Four years prior to this his elder brother, Magnus Kristian Retzius (1795-1871), had previously graduated in medicine at the University of Lund. In 1823 Anders Retzius was appointed to the staff at the Veterinary School to teach anatomy and returned to live in Stockholm. It was here, and as a result of his continuing and meticulous dissections of comparative material, that he discovered the inter-renal organ in elasmobranch fishes, later shown to be homologous with the adrenal cortex of other animals.
After qualifying in medicine in 1819, Anders Retzius quickly built up a thriving clinical practice in Stockholm and entered military service where he was appointed to the medical staff of a regiment of hussars of the Swedish army, first in Schonen, later in Jämtland. By this time his father was elderly and had suffered a debilitating stroke and so he was brought to Stockholm where both his sons cared for him until his death in 1821 (his mother had died in 1808 when Anders Retzius was just 12). By 1824, aged 28, Retzius was becoming well known among the scientists at the Karolinska Medico Chirurgical Institute. He was friends with Jöns Jakob Berzelius (1779-1848) at the Institute, the physical chemist, mineralogist and well-known proponent of ‘vitalism’. Retzius by now had a growing reputation as an anatomist, in particular with Nils Åkerman, the prosector and anatomist at the Anatomical Institute. The Karolinska Institute was changing and moving towards a more empirical, evidence-based, hands-on approach to medical teaching and Berzelius and Retzius saw eye to eye about this and about its future direction. It followed that in 1824 Anders Retzius was appointed part time professor extraordinary of anatomy at the Karolinska Medico Chirurgical Institute. This part time appointment enabled him to continue with his other activities. During this time, he carried out a series of experimental studies in surgery with the chief surgeon of the Seraphim Hospital, G.J. Ekstrom, on the effects on the digestive tract of vagotomy and of arterial ligation.

In taking up this new part time position at the Karolinska Institute, Anders Retzius set about relocating the anatomical collections put together by the former professor of anatomy and surgery, Anders Jahan Hagströmer. The collections were moved from the old site of the Institute, on the island of Riddarholmen, by barges to the new site in Stockholm. Unfortunately, the greater part of the anatomy collection was lost during the crossing as one of the barges capsized. It was left to Anders
Retzius, with the support and interest of crown prince, to re-establish the anatomy museum almost from scratch. By the mid-1830s the museum had become extensive and consisted of three galleries including a large and varied comparative osteological section upon which Retzius was later able to draw for the purposes of his own comparative research projects.3,4

Besides his surgical experiments with Ekstrom, Anders Retzius explored all things morphological and anatomical that came his way. In 1822 and 1824 he described and published two papers, in Swedish, on the morphology of the cranium, brain, nervous system, gut and vascular system of the hagfish, *Myxine glutinosa*.4 The eyeless and jawless hagfish had been variously regarded as a mollusc, as a worm (by Linneaus) or as a fish or an amphibian by others and these two papers were important contributions. Important as they were, however, it was Retzius’s close friend Johannes Müller who later between 1835 and 1845 published the more widely read and carefully constructed German descriptions of *Myxine glutinosa* and to whom credit usually goes for establishing the hagfish as a primitive vertebrate at this time.4

In 1824 Retzius also became interested in the respiratory system of birds, their air sacs and the communications that extend into long bone cavities. Continuing this work, he went on to draw morphological comparisons with the respiratory system of a python.3 The snake in question had died at sea en route from Java and was a gift to him from the naturalist Sven Nilsson (1787-1883).3 It illustrates well how Retzius seized every opportunity to explore the anatomy and physiology of whatever came before him. Meanwhile, Retzius and his colleague J.S. Billing from the Stockholm Veterinary Institute demonstrated and described the ciliary ganglion and sphenopalatine ganglion in the horse.4 In 1832 he demonstrated by careful
dissection that the rami communicantes of the sympathetic trunk ran between both
the dorsal and ventral roots of spinal nerves.\textsuperscript{2} Turning to the eye, and using injection
methods, Retzius discovered what later became known as the canal of Schlemm as
well as many arterial and venous anastomoses in the body that had not previously
been identified at that time.\textsuperscript{4}

In the summer of 1828 Anders Retzius travelled to Berlin to attend a meeting
of the Society of German Scientists and Physicians where among others, he met
Alexander von Humboldt (1769-1859), who was by then a great patron of the
sciences, as well as the embryologists Karl Ernst von Baer (1792-1876) and Martin
Rathke (1793-1860) and the physiologist and comparative anatomist Johannes
Müller (1801-1858) with whom he enjoyed a close life-long friendship.\textsuperscript{4,5} He was
noted at that meeting for being the only participant to step forward and draw public
attention to von Baer’s important recent discovery of the mammalian ovum, which
appeared not to be attracting the attention it deserved, and for encouraging von Baer
to demonstrate his finding at the meeting, which he duly did in public using a dog.\textsuperscript{4}

In 1830 Anders Retzius was appointed Inspector (Vice Chancellor) of the
Karolinska Institute while still retaining his professorship in anatomy. But he only
finally completely relinquished his connections with the Veterinary School in 1840. In
1832, Anders Retzius’ first wife, Wendela Sophia (née Westerberg) died aged just 26
years old (1806-1832). It might be that during the year that followed he decided to
spend time travelling more extensively than before. From this time onwards travels
abroad played a large role and greatly influenced the direction of his research. He
visited many museums and laboratories across Europe and formed many friendships
with leading scientists of the day with whom he corresponded regularly. Retzius gave
a detailed account of his European travels abroad (Berättelse: öfver en resa l
The list of counties, cities and institutions he visited during that tour is extraordinary and included: Germany, Berlin, Stuttgart, Heidelberg, Munich, Tübingen, Austria, Vienna, Paris, Strasbourg, Breslau (now Wroclaw), London and Glasgow. For each department, museum or institution mentioned in his account he highlights their research specialities and achievements and on occasions mentions some of the academics he spent time with.

**Jan Purkinje and a new era in science and microscopy**

The ten years between 1830 and 1840 saw many new discoveries in dental histology primarily because microscope design improved hugely following the publication in 1830 by Joseph Jackson Lister (father of Joseph Lister of antisepsis fame) of a method to construct achromatic lenses. Lister had worked out a way to combine crown glass with flint glass lenses and so to cancel out chromatic aberration, since each has different dispersion characteristics. Moreover, Lister showed that spherical aberration could also be minimised by the correct separation of different lens combinations. Within a very short time it was possible to purchase high quality optical instruments all across Europe. A review of the instruments available, their merits and costs, appears Kölliker’s *Manual of human histology* of 1853. In Paris, Georg Oberhauser, in Vienna, Simon Plössl, and in Berlin, Philipp Pistor and F. W. Schiek were making relatively affordable achromatic microscopes and among the first to own a Plössl microscope was Jan Purkinje.

In September 1833 Anders Retzius attended the Scientific Congress of Naturalists at Breslau (now Wroclaw). During the conference Jan Purkinje and the Scottish botanist Robert Brown (1773-1858) – of Brownian motion – showed how thin transparent sections of skin and of petrified wood could be imaged under the
microscope. This was also the same year Robert Brown published the first paper describing the cell nucleus.

Jan Evangelista Purkinje (1787-1869) and his students made a major contribution to dental histology and to microscopy in general. Purkinje was born in what was then northern Bohemia in the Austro-Hungarian Empire, now the Czech Republic. From humble beginnings, Purkinje rose from boy chorister educated in a Piarist Monastery to novice monk until in 1807 he managed to change course and enrol at the Universitas Carolo-Ferdinandea, Prague, as it then was, where finally, with interruptions to secure funding, he graduated as Doctor of Medicine in 1818 aged 32 years old. Besides being both a philosopher and a scientist, Purkinje spoke 13 languages, was active in the Czech nationalist movement and not only translated the poetry of Goethe and Schiller but wrote his own.\textsuperscript{10,11} In 1823, after working as an instructor in anatomy, Purkinje was appointed to the chair of physiology and pathology at the Royal Prussian University of Breslau where he remained for 27 years before finally returning to Prague as professor of physiology in the Faculty of Medicine of Charles University.\textsuperscript{11}

Primarily an experimental physiologist Purkinje made many important contributions to science. Early on in his career, as part of his dissertation for the degree of Doctor of Medicine in 1818, he studied the physiology and physics of vision.\textsuperscript{11} This work caught the attention of Johann Wolfgang von Goethe (1749-1832). Purkinje shared with Goethe a passion for literature, poetry and philosophy as well as for science. Indeed, Goethe had previously constructed his own theory of color formation rejecting the findings of Isaac Newton for a theory more befitting his own beliefs in Naturphilosophie. While Newton had shown experimentally that colors
are simply the individual components of white light, Goethe held that color was
shaped by perception, by degrees of darkness and brightness and by the overlap of
one color with another. To Goethe different colors were also associated with different
emotions. Purkinje had observed that color perception changed with decreasing light
intensity. For instance, the brightness of red fades faster than green or blue (and
this, the ‘Purkinje phenomenon’, still bears his name). However, Purkinje explained
his observations differently by proposing there were two different types of
photoreceptor in the retina (i.e. cone vision switching over to rod vision at dusk).¹¹

Naturphilosophie held that it was fundamental for science to search for and
prove the unity of the material world and the mind. The overarching order or
underlying pattern of nature was manifest in all things natural, for example, in the
underlying pattern of animal form. Patterns in natural structures could, therefore, be
recognized and understood by drawing theoretical parallels with our broader human
sensory experiences. Many scientists at this time felt that without this philosophical
blueprint, objective descriptions or experiments alone could reveal no more than a
collection of unrelated facts. There were many, including Goethe’s near
contemporaries in England, for example, the poet and philosopher Samuel Taylor
Coleridge (1772-1834) and the artist and poet William Blake (1757-1827), who felt
the influence of Newtonian reductionism on both art and philosophy was at risk of
dulling human imagination. Nonetheless, Coleridge wrote that if science is performed
with the passion of hope, it is poetical.

New methods in microscopy and dental histology were by their very nature
never going to figure greatly in any bigger debate about the philosophy of science
method. Nevertheless, Purkinje’s more analytical and objective approach to science
had a considerable influence on anatomists and physiologists and helped promote a new more focused way of thinking. The list of Purkinje’s scientific achievements is extraordinary. He classified fingerprints for the first time, introduced the terms protoplasm and plasma, investigated the basis of vertigo, often used himself as an experimental subject to determine the pharmacological action of drugs (and on that basis, incidentally, believed homeopathy to be "nothing but mysticism")11 and besides all this made a major contribution to general histology and to dental histology.11

In the summer of 1832 Jan Purkinje acquired a compound achromatic microscope made by G.S. Plössl of Vienna.12 Purkinje developed methods for processing, sectioning, and embedding biological tissue preparations. With his assistant, Adolf Friedreich Oschatz (1812-1857), he invented the first version of the microtome. Purkinje used ethanol, glacial acetic acid, and potassium dichromate to fix and clear tissue slices and introduced the glass slide for mounting sections with Canada balsam or amber, or copal varnishes. Arguably, his most important discoveries in histology include the description of Purkinje cells in the cerebellum of sheep (1837) and of Purkinje fibers in the endocardium of the sheep heart (1839) that were later shown to be an important component of the conducting system of the heart.10

John Hunter and Thomas Bell

John Hunter (1728-1793) was a Scottish surgeon who became one of the most distinguished scientists of his day. Hunter set up his own anatomy school in London in 1764 and his book, The natural history of the human teeth, first published in 177113 with a second edition in 1778, was the first major treatise to combine descriptions of structure, function, growth and pathology alongside experimental
observations in surgery, transplantation and longitudinal growth of the jaws and teeth. A supplement to the second edition was devoted to the diseases of teeth. Hunter wrote;

“A tooth is composed of two substances, viz. enamel and bone … which when it is broken appears fibrous or striated; and all the fibres or striae are directed from the circumference to the centre of the tooth”. “This in some measure, both prevents it from breaking in mastication, as the fibres are disposed in arches, and keeps the tooth from wearing down, as the ends of the fibres are always acting on the food”.13

To this description, Christian Heinrich Theodor Schreger (1768-1833) then added,

“the bands in enamel course so that their concave surfaces are directed towards the crown and the convex towards the root of the tooth.”14,15

Today it is usual to refer to Hunter-Schreger bands in enamel. Hunter also clearly revealed the incremental nature of tooth growth in labelling experiments in which he fed pigs madder intermittently to leave pink markings at known time intervals. From this he concluded,

“I find that the bony part of the tooth is formed of lamellae, placed one within the another”. The outer lamella is the first formed, and is the shortest: the more internal lamellae lengthen gradually towards the fang, by which means, in proportion as the tooth grows longer, its cavity grows smaller, and its sides thicker”.13

Hunter’s book on teeth was widely read and widely cited and his careful, empirical scientific method laid the foundations on which subsequent dental histologists later built.
Figure 2. Detail of Figure 2, Plate XIII, reproduced from John Hunter, *The natural history of the human teeth*, London, 1771. A deciduous molar and canine (top row) and a permanent molar and canine (bottom row) both grow in stages from right to left. The outline of the crown and root are laid down first. Each tooth then fills in towards the pulp with successively longer 'lamellae'.

In 1829, Thomas Bell, (1792-1880), then professor of zoology at King College London, described in his book, *The anatomy, physiology and diseases of the teeth*, the stages of developing tooth germs and the earliest formation of enamel and dentine. Bell's illustrations, however, were only of isolated mineralizing tooth cusps and did not depict the histological appearance of tooth germs in any detail. Bell nevertheless, wrote that he had observed a “proper membrane of the pulp” from which “the ossific matter [dentine] is secreted”. Bell continued,

“bone [dentine] is first deposited on the points of the teeth covering the pulp and its proper membrane, which retire as it were, as the bone [dentine] continues to be deposited.”
The enamel, Bell described as also produced from the inner layer of the tooth sac which,

"pours out a thickish fluid, which speedily consolidates into a dark chalky substance, and afterwards becomes white and hardened by more perfect crystalisation". The internal lamina alone Bell wrote “performs the office of secretion of bone [dentine] and enamel.”16

Isaac Raschkow and Meyer Fraenkel

Considering that Isaac Raschkow and Meyer Fraenkel made such influential and widely cited contributions to the study of dental microstructure, it is remarkable so little has been written about them. All the more remarkable is the fact that they were both medical students, in the same cohort, whose dissertations on teeth formed part of their exams for the higher post-graduate degree of Doctor of Medicine and Surgery. Both were closely supervised and mentored by Jan Purkinje. Isaac Raschkow was born on 15th May 1809.17 His father was a respected elder of the Jewish community. His mother, Paulina (née Kochanowitz), had died when he was young.17 Gymnasia were elite high schools where pupils who showed great promise were sent, usually for nine years, to prepare for university.5 After attending the Evangelical Gymnasium at Glogow (now in Poland) Raschkow was admitted to study medicine at the Royal Prussian University of Breslau (now the University of Wroclaw) in 1830.17 His dissertation, defended on 16th October 1835, qualified him for the higher degree of Doctor of Medicine and Surgery and was entitled Meletemata circa mammalium dentium evolutionem (Studies on the development of the teeth of mammals).17 Raschkow was taught microscopy by Purkinje with whom he worked closely and clearly revered for his “outstanding kindness and keen intellect”, and who
he wrote, prepared the early drafts for the figures that were lithographed for his dissertation.\textsuperscript{17}

\textbf{Figure 3.} The title page of Isaac Raschkow’s Dissertation\textsuperscript{17}. Image from a facsimile reproduced here courtesy of The Royal Society of Medicine, London.

Raschkow reviewed and built on earlier accounts of tooth structure including Hunter, Schreger and Cuvier,\textsuperscript{13,14,18} by studying developing anterior (incisor) tooth germs in a range of animals including fetal dog, calf, sheep, horse and human
Raschkow illustrated his findings with 12 lithographs of tooth germs made in different planes of section. He described the progression between what we now refer to as the bud, cap and bell stages of tooth formation. Raschkow then described the earliest stages of enamel and dentine formation from the cell layers of late-stage tooth germs. Raschkow’s observations are remarkable for their precision and detail. He made the first clear histological description of the enamel organ (‘organon adamantinae’), he demonstrated that teeth were formed in layers (incrementally) and that dentine was not formed by ossification of the pulp but from ‘granules’ (cells) derived from the dental papilla. He also described the cell layer that forms enamel, the ‘membrana adamantinae’ and the overlying stellate reticulum (or ‘enamel-pulp’). Raschkow (1835) described a ‘membrana praeformativa’, a layer surrounding the dental papilla. This seems equivalent to Bell’s ‘proper membrane of the pulp’. Huxley (1853) later referred to this as equivalent to the ‘basement membrane of Bowman’ and it appears to correspond to what we now refer to as the basement membrane between the inner enamel epithelium and the dental papilla. Raschkow considered that dentine was laid down in successive layers and that the substance of the dentine was formed of fibers made by the pulp that ran at right angles to the canals in dentine and so parallel to the surface of the pulp.

Raschkow’s descriptions of the vessels and nerves associated with the various stages of the developing tooth germ (‘Raschkow’s plexus’) are still cited in textbooks today, of which Mummery’s summary and micrographs remain particularly clear. Raschkow wrote,

“Perhaps there is no part of the body where the extreme ends of the nerves can be seen so beautifully clearly as in the dental pulp”. The groups or bundles of nerves entering the pulp separate into single filaments until “finally
beneath the tip, they again form a plexus from which the rejoined filaments are given off, terminating at the extreme end of the [pulp] tip like bristles of a brush surrounded by vessels”. 17 “[From these nerves,] can be traced the great sensitivity of the tooth, especially in man”. [translated from the original Latin] 17, 25
The enamel organ he described as consisting of a layer of perpendicularly arranged fibers [cells], the ‘enamel membrane’ that can be distinguished, he writes, from an overlying “stellate parenchymatous substance which I shall here call the pulp of the enamel”. The internal surface of the enamel membrane Raschkow described as “composed of almost uniform hexagonal corpuscles [cells] towards the middle of each of which was a round protuberance”. It seems possible this might be the first reference to what we now call the Tomes’ process of the ameloblast.

A completely transparent membrane covers the dental pulp “and since this is where formation of the dental substance [dentine] begins and as the membrane always precedes the latter, I have called it the preformative membrane”. Beneath the membrane,

“lie regularly arranged granules [cells] that have a more elongated form than the rest, partly at right angles to it and partly at slightly acute ones”. “From the tip, the dental substance [dentine] spreads in all directions and seems to be already hard in a very short time unlike the enamel substance which appears soft and easily abraded for a long time after the fibres have been laid down”. “Each one of the perpendicular fibres must be considered as an excretory organ or gland, designed to produce a single enamel fibre corresponding to itself”. [translated from the original Latin]
Raschkow observed, “each one of these enamel fibres shows a pattern of transverse layers”.\textsuperscript{17} This may be the first description of enamel cross striations (although it can be argued that Leeuwenhoek, in 1687, had previously illustrated these).\textsuperscript{22} Raschkow cites Hunter’s description of tooth development\textsuperscript{13} as most closely agreeing with his own observations.

In effect, as Retzius,\textsuperscript{23,24} Nasmyth\textsuperscript{25} and Owen\textsuperscript{26} each later recognized, Thomas Bell\textsuperscript{16} and Isaac Raschkow\textsuperscript{17} between them had documented that enamel and dentine each form incrementally from distinct cell sheets that differentiate from the outer layer of the dental papilla, or pulp, (odontoblasts), or from the cells that derive from the inner enamel epithelium (ameloblasts). What they did not resolve was the origin of the cementum forming cells, which Raschkow, admitting he was not clear about their origins, reasoned formed over the enamel in the calf incisor from the “transformed cells of the enamel pulp”, which we would now refer to as the stellate reticulum.\textsuperscript{17} It took a long time to clarify that ameloblasts are derived from an epithelial down-growth of the dental lamina and that the dental papilla is of mesodermal and ectomesenchymal origin (see Glasstone, 1966, for a historical review of this).\textsuperscript{27}

**Meyer Fraenkel**

Meyer Fraenkel was born in Schneidemühl (then in Prussia, now Piła in Poland) on 1\textsuperscript{st} February 1809 (just 2 days before Felix Mendelssohn and 11 days before Charles Darwin).\textsuperscript{28} He wrote that his mother (Bertha, née Meyer) died prematurely but that in 1827, aged 18, he moved to Breslau (Wroclaw) and completed his primary education at the Elizabeth Gymnasium.\textsuperscript{28} Then aged 22 he entered medical school at the Royal Prussian University of Breslau. He defended his
final MD dissertation on 1st October 1835, just two weeks before Isaac Raschkow defended his.\textsuperscript{17,28} Interestingly, ‘M. Fraenkel’ is listed as an examiner for Isaac Raschkow and ‘J. Raschkow’ as an examiner for Meyer Fraenkel\textsuperscript{17,28} so we may assume there was a lot of good-natured teamwork among these young doctors and their teachers and the other examiners. Fraenkel’s dissertation title was \textit{De penitiori dentium humanorum structura observations} (Observations concerning the internal structure of human teeth).\textsuperscript{28} In the preface, like Raschkow, he states he attended lectures by Purkinje on experimental physiology, general pathology and microscopy. Fraenkel praises Purkinje for his wealth of knowledge, his mental power, goodwill and subtlety of mind as well as for the \textit{“freedom and humanity with which he engages in all things”}.\textsuperscript{28}

Fraenkel’s study was probably the first to use thin ground sections of teeth, cleared in a mounting medium and observed under a new high-quality compound microscope. It was not just a study of fractured surfaces as Leeuwenhoek (1678) and Hunter (1771) and Schreger (1800) had heavily relied on previously.\textsuperscript{13,14,29} Fraenkel also studied teeth that had been demineralized in acid and he was the first to note that the ‘substantia propia’, or dentine, was composed of fibers that could be teased apart. Nasmyth (1839) translates from his dissertation, \textit{“the greater part of the mass of a tooth is composed of a uniform structureless substance and of fibres passing through it”}.\textsuperscript{25} Fraenkel was also first to describe the disposition, cross sectional appearance and orientation of dentine tubules (‘canaliculos’) within a tooth as being vertical over the pulp horns but becoming more horizontal through the crown and root. Although unbeknownst to Fraenkel, Leeuwenhoek (1678, 1687)\textsuperscript{22,29} had previously observed the tubular nature of dentine, but Fraenkel similarly inferred that dentine was a tubular structure. Alexander Nasmyth\textsuperscript{25} translates from Fraenkel\textsuperscript{28}
with his own reference to Müller added on that, “in the teeth of the horse at any rate they are capable of absorbing ink by capillary action – a fact that is also confirmed by Müller”.

Figure 5. The title page of Richard Owen’s personal copy of Meyer Fraenkel’s Dissertation. Reproduced here courtesy of the Natural History Museum Library, London.
Figure 6. Figures from Meyer Fraenkel’s Dissertation\textsuperscript{28} illustrating the arrangement of dentine tubules and enamel prisms in an incisor and molar tooth sectioned in different planes (Figs. 1 to 3). In Figs. 4 to 8, Schreger bands, vertical striae, fissures, prisms and dentine tubules are each depicted at higher power in various planes of section. Reproduced here courtesy of the Natural History Museum Library, London.

Fraenkel’s figures are, like Raschkow’s, a model of how to reconstruct the three-dimensional structure of tooth tissues from sections made in different planes (he, like Raschkow, in the preface of his dissertation, alludes to Purkinje’s help in preparing the figures). Longitudinal ground sections of an incisor, premolar and molar showing the ‘substantia adamantina’ (enamel), ‘substantia propia’ (dentine) and ‘substantia ostoidea’ (cementum), appear side by side with transverse sections through their roots. Fraenkel was the first to clearly document the distribution of cementum over the root surface increasing in thickness towards the root apex and
was the first to describe its cellular inclusions, ‘osseous corpuscula’ (cementocyte lacunae), or as they became know, ‘corpuscles of Purkinje’. Alexander Nasmyth later wrote that Fraenkel’s ‘acute observations’ about cementum ‘ought to be recorded as anticipating his own findings’ and so Nasmyth made a point of translating and citing Fraenkel’s account of cementum distribution in a human tooth;

"In the incisor of an old man of seventy-five we found the whole root surrounded with this substance [cementum], which at the extremity was very thick, and as it ascended thence, became thin by degrees, and extended onwards to that place, where the adamantine substance [enamel] began; moreover, on one side, ascending higher up, it coated a small portion of the adamantine substance itself, and like a single layer could easily be removed". [translated from the original Latin]

This is certainly the first description of cementum extending onto the enamel surface at the cervix in a human tooth (as it often does). At the time, this had implications for comparisons of coronal cementum in other animals as Raschkow and others had already observed, and indeed for early ideas about the developmental origins of cementum that in the end proved to be incorrect.

With regard to enamel, Fraenkel observed, “[E]namel consists of simple perpendicularly-placed fibres increasing somewhat in size towards their upper extremity forming quadrilateral prisms, and often making several curves on one and the same level”. Boyde (1964) notes that when watching the acid dissolution of enamel prisms (‘fibers’) under the microscope, Fraenkel observed that an organic prism sheath remained. Fraenkel’s description of enamel and his illustrations, clearly show alternating ‘fibras Schregerinnas’ or Schreger bands, ‘the enamel cut across by
linear fibres in many places’. They also show the scalloped morphology of the enamel-dentine junction. Fraenkel described the weaving course of enamel prisms at the enamel-dentine junction traversed by what we now refer to as cross striations and described what appear to be tufts or lamellae between them, (‘dein magnas flexuosas fissuras’ or ‘large sinuous fissures’). Moreover, Fraenkel described and illustrated oblique markings within the enamel passing from the enamel dentine junction to the enamel surface that he describes as ‘strias illas subfuscas ad longitudinem dentis percurrentes’, or ‘rather dark longitudinal striae running in line with the tooth’. These we might now, judging from their appearance in Fraenkel’s figures, refer to as striae of Retzius or perhaps accentuated incremental markings.

Throughout his thesis, Fraenkel refers to fibers in enamel and their different orientations. But the term ‘fiber’ (‘fibre’) or ‘fibers’ has been used historically in descriptions of enamel, dentine and cementum microstructure in many different ways. Boyde (1966)\textsuperscript{32} has previously considered how the use of this term has changed over time with respect to descriptions of enamel. John Tomes in 1839, for example, made it clear he regarded the terms fibers and tubules in dentine as interchangeable.\textsuperscript{33} There is, however, hardly a subsequent description of enamel, dentine and cementum histology that does not refer back to this original dissertation of Meyer Fraenkel in 1835.\textsuperscript{28}

Purkinje himself later wrote an account of human tooth histology\textsuperscript{34} in which he drew on Fraenkel’s thesis and referred also to Kolliker’s great volume on human histology.\textsuperscript{9} In this account Purkinje emphasized and illustrated the three-dimensional course of the dentine tubules and enamel prisms using two-dimensional sections and serial cuts through blocks of tissue to explain their complex structure.\textsuperscript{34} His
illustrations include a reconstruction of a single enamel prism 'snaking from its
designing [at the scalloped enamel-dentine junction] to its end at the worn surface.'

Figure 7. The complex 3-dimensional geometry of dentine tubules and enamel prisms depicted with
blocks of tissue and serial sections. Reproduced from Plate 1 in Purkinje, J.E. 1855, Omnia Opera,
Tomus VII, Chapter 2. O ústrojnosti zubů člověčích, Prague, 1954, vol 7, pp.36-49.34 (Image courtesy
of the Wellcome Collection, London).

Anders Retzius as a histologist

Purkinje's and Brown's demonstration at the 1833 Breslau meeting was a
revelation to Anders Retzius and he extended his stay after the conference to learn
from Purkinje how to prepare and mount thin sections and use the microscope. The
practical experience gained at and after this meeting marked a turning point in
Retzius's research career as indeed it did for others who were stimulated to study
the microstructure of tooth tissues. On his return to the Karolinska Institute, Anders
Retzius raised funds to buy his own Plössl microscope, which arrived in the summer
of 1835. At this time, he set out to study the histology of animal tissues and
especially of teeth. There is no specific mention of Purkinje instructing Retzius on how to make thin sections of teeth at the 1833 meeting in Breslau, indeed Retzius later claimed to be completely unaware that two of Purkinje’s medical MD students, Isaac Raschkow and Meyer Fraenkel, were working on tooth histology in parallel with him – indeed it is likely they had not even begun their dissertation work in 1833. Retzius explained in 1837\textsuperscript{23,24} that in fact he sought the help of a Berlin dentist working in Stockholm, Hrn. Bichlier, to help him solve the problem of how to section whole teeth and other teeth that had been demineralized in dilute hydrochloric acid. Åhrén (2017)\textsuperscript{3} notes that there were probably only four licensed dentists working in Stockholm in the 1830s of which Hrn. Bichlier was one.\textsuperscript{3} Always to Retzius there was a keen aesthetic imperative to his research and he felt strongly that illustrations were integral to the science and should represent a direct substitute for the specimens being described.\textsuperscript{3} Retzius collaborated on the drawings and illustrations for his paper with Wilhelm von Wright (1810-1887), the painter and naturalist who at this time was artist in residence at the Swedish Royal Academy of Sciences and who worked with many scientists there illustrating, for example, Scandinavian birds, mammals and fish.\textsuperscript{3}

In 1835, Anders Retzius remarried. His second wife, Emilia Sofia (née Wahlberg) (1813-1903) the mother of Anders Wilhelm, Anna Elizabeth and Magnus Gustaf Retzius (1842-1919), was the sister of Peter Fredrik Wahlberg (1800-1877) the botanist and entomologist.

The results of Retzius’s comparative study on the microscopic anatomy of teeth were first presented as a lecture to the Royal Swedish Academy of Sciences in January 1836 – less than six months after his new microscope had arrived. The published version of the paper appeared in the Transactions of the Royal Academy
of Science in Stockholm (*Mikroskopiska undersökningar öfver Tändernes, särdeles Tandbenets, struktur*) but was only finally published in Stockholm in 1838 in the *Kongliga Vetenskapsakademiens Handlingar* for 1836.\(^{23}\)

Retzius wrote that he had intended to send forthwith a German translation of his paper to Johannes Müller in Berlin, for publication in Müller’s Archive, and another to Jan Pukinje but communications between Sweden and Germany during the winter were difficult and his letters were delayed. By this time in the mid-1830s in Breslau, working with Jan Purkinje as his doctoral students were Meyer Fraenkel and Isaac Raschkow. In Berlin with Johannes Müller were Joseph Linderer and his father and Theodor Schwann and in London were Alexander Nasmyth, Thomas Bell, Richard Owen and John Tomes. It seems many of them were unaware they were working in parallel, each preparing ground sections and describing the histological appearance and development of the various tooth tissues.

**Johannes Müller and his students**

Johannes Peter Müller (1801-1858) played a central role in many advances in dental histology largely through his role as a mentor and friend to others but also as a morphologist, physiologist, microscopist and importantly as the founding editor of an influential journal.\(^{35}\) Müller was born in Koblenz, when the Rhineland was still under French rule, and Johannes was the eldest of five brothers and sisters.\(^{5}\) His father was a shoe-maker, but in reality, more likely a master craftsman and owner of a leather-making business, able to send his young son to the elite Koblenz Gymnasium.\(^{5}\) Because his son was clearly exceptionally bright and because educational opportunities had improved after 1815, when Koblenz became part of Prussia, his father was encouraged not to apprentice him into the leather trade as a
saddle maker. After a short period serving in the Prussian army, Müller attended Bonn University in 1819 where he obtained his first degree in medicine in 1822. He then won a scholarship to study with the anatomist Carl Asmund Rudolphi (1771-1832) in Berlin. Rudolphi was strongly opposed to Naturphilosophie and was clearly a considerable influence on Müller. Rudolphi was also close to Jan Purkinje, who eventually married his daughter Julia Agnes in 1827.

Rudolphi taught Müller microscopy and even gave him his own Fraunhofer microscope when he returned to Bonn on passing his final Prussian state medical exams in 1824 aged 23.

Academics in Bonn and Berlin were direct employees of the Prussian state, and the state both appointed and promoted them, but positions were few and far between and extremely hard to come by. Nonetheless, Müller rose quickly through the ranks to professor and when Rudolphi died applied for and was appointed to his chair in Berlin in 1832 where he remained until 1858. Through each academic year he alternately taught human anatomy, physiology, comparative anatomy and pathology and always insisted on examining all Prussian candidates in medicine himself.

As an academic, but also as a civil servant, Müller was burdened with very heavy administrative responsibilities during the times he was dean of the medical school. This all intensified when he became rector of the university, having to deal with student uprisings and mediate with the state authorities during the March 1848 revolution against King Frederick Wilhelm IV and his autocratic government. Müller also stood up for his colleagues against the Cultural Ministry and the King. Despite the fact Prussia’s Edict of Emancipation had granted Jews full citizenship in
1812 this was never honored and Robert Remak was blocked from a teaching appointment until Müller and Alexander von Humboldt (then in his late eighties) together personally petitioned the King who subsequently instructed the Cultural Minister to comply.\textsuperscript{5} In 1847 Remak was the first unbaptised Jew to ever teach on Berlin’s medical faculty despite the fact that Berlin’s Collegium Medico-Chirurgicum had willingly accepted Jewish students since 1730.\textsuperscript{5}

As an experimentalist and a microscopist Müller made a major contribution to comparative anatomy and physiology. He published an extensive comparative study of genitalia and secretory glands and identified the arteries characteristic of erectile tissue. In particular, he confirmed the Bell-Magendie law experimentally by working on frogs in 1831.\textsuperscript{5,35,36} In 1834 Müller founded the Archiv für Anatomie, Physiologie und wissenschaftliche Medicin (Archive for Anatomy and Physiology and for Scientific Medicine). Every year he wrote an influential annual report (Jahresbericht) summarising key advances in physiology and anatomy. ‘Müller’s Archive’, with his own yearbook summaries, became one of the most widely read and respected scientific journals. Among his many famous students and colleagues were Jakob Henle (1809-1885), Theodor Schwann (1810-1882), Robert Remak (1815-1865), Rudolf Virchow (1821-1902) and Ernst Haeckel (1834-1919).

While not a supporter of Naturphilosophie, Müller, like Anders Retzius’s colleague Jöns Jakob Berzelius, and for that matter John Hunter long before this, was a strong believer in vitalism. It was thought by ‘vitalists’ that the organic matter of living forms and inorganic matter were quite separate such that the former could not be synthesized from the latter and that living matter contained some unknown vital force of life. John Hunter had spent years trying to understand precisely what constituted life and how to recreate it, and more than that, unsuccessfully
experimented on how to bring people who had died back to life again.\textsuperscript{37} Having initially proposed that blood contained some 'vital principle' Hunter later suggested that every particle in the body contained some kind of life force.\textsuperscript{37}

In his textbook, \textit{Elements of Physiology} published in 1838,\textsuperscript{38} Müller described the structure and function of the individual systems of the body in great detail but then argued there must be a vital life force that made every organism indivisible as a whole. Ernst Mayr (1976)\textsuperscript{39} argued that, in Müller's case at least, this was just a way rejecting other crude mechanistic theories of the time and of accepting that some things were simply unknown or unknowable, and in a sense saying, as Mayr put it, that he was "\textit{willing to study the phenomena of life in a detached, objective manner}".\textsuperscript{39} Müller's students, however, particularly Theodor Schwann, were of a younger generation and began to react strongly against vitalism, the evidence for which, at least for Schwann and others, began to fade fast as experimental logic became the basis for scientific enquiry. Müller himself, however, was always respectful of his students' and colleagues' ideas and of their independent scientific thinking and never tried to stifle or influence them. As Schwann himself acknowledged, he continually encouraged all his students to follow up their ideas with experiments and investigations.\textsuperscript{5}
As time passed, Müller himself became less interested in experimental physiology and more in morphology and histology. He was obsessed with understanding how life was organized and to that end avidly collected specimens of all known animal forms that he housed and categorized in his anatomical museum. Otis (2007) wrote that Müller had a compulsion to organize and to communicate and in part he acquired his fame because “he arranged words as well as he arranged animals”. Above all, Müller was consumed by his attempts to classify marine organisms but throughout his life he suffered from serious bouts of anxiety and depressive episodes. One in particular appears to have been triggered by his discovery of slugs developing in the gut cavities of sea-cucumbers (one organism apparently developing inside another), something that was incompatible with the classificatory scheme he was working on. Anders Retzius’s son, Gustaf, reportedly called Müller “the great investigator with the serious often melancholy face and flashing eyes, which no one who once saw them could ever forget”. Johannes Müller died in 1858, a year before the publication of Darwin’s Origin of Species in 1859. The great scheme of life he had been searching for had eluded him.

Johannes Müller and Anders Retzius were close friends and colleagues who shared a common interest in the classification of marine life, especially in sea creatures they regarded as ‘transitional forms’. During the late 1830s specimens of amphioxus, fish-like marine chordates, were discovered on the south west coast.
of Sweden. Retzius enthusiastically collected specimens and carried out dissections as he had done with *Myxine glutinosa* previously. He reported his findings to Müller in 1839 and invited him to accompany him to Bohuslan on the coast of Sweden in order to carry out a more detailed joint study, which Muller did in September 1841. In 12 days apparently, the two friends together described the morphology of *Branchiostoma lanceolatum* and worked through the anatomical and physiological issues that had until then been problematical. It was Müller who presented their results to the Berlin Academy of Sciences on December 6th 1841.

Sadly, much later in life in September 1855 Müller was involved in a tragic accident at sea while returning from one of his research trips to Sweden during which a young zoology student, Hrn. Schmidt, died. This threw Müller into a final depressive bout from which his colleagues and students reported he never really recovered. Ernst Haeckel speculated that Müller might even have taken his own life in April 1858. Anders Retzius gave an account of what happened in a letter written to his good friend the Finnish anatomist Evert Julius Bonsdorff (1810-1898) dated February 10th 1856 (published in Retzius, G. 1902).

“Have you heard about Johannes Müller’s misfortune? He spent the summer in Bergen – on the way home the steam ship collided with another steamer. Müller’s ship sank to the bottom of the sea within 10 minutes. Several passengers barely reached the deck. Müller and a companion threw them self in the sea and were pulled down into the vortex, but came out and were fished up. All their things were lost, no freight was saved – a companion (young Doctor, anatomist) died. – Imagine what a situation! – Microscopes, collections, drawings, books – all lost…” [translated from the original Swedish].

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When in 1837 Müller finally received the translation of Retzius’s paper on comparative tooth microstructure Retzius was surprised to learn from him that Meyer Fraenkel, a student of Jan Purkinje, had already published his final MD dissertation on human tooth microstructure in October 1835. Müller sent Retzius a copy of his summary in Müller’s Archive, Jahresbericht 1836 for Jahre 1835, which he had clearly not seen. He responded that he acknowledged that many of Purkinje and Fraenkel’s findings on enamel were first but that his study emphasized the comparative microstructure of dentine and cementum, as well as enamel.

Finally, with some revision, a German translation of Anders Retzius’s paper was published in 1837 in Müller’s Archive; Bemerkungen über den innern Bau der Zähne, mit besonderer Rücksicht auf den im Zahnknochen vorkommenden Röhrenbau, von A. Retzius: mitgetheilt in Briefen an den Dr. Creplin in Greifswald; aus dem Schwedischen übersetzt von dem Letzten. [Remarks on the inner structure of teeth, with particular regard to the tubular structure which occurs in Tooth Bone, by A. Retzius. Given in letters to Dr. Creplin in Greifswald, translated from Swedish by the latter].

Jacob and Joseph Linderer in Berlin

It is surprising that hardly any mention is made in the literature of the time of Calmann Jacob, later Callman Jacob Linderer (1771-1840) and his son Joseph Linderer (1809-1879). Both father and son were dentists and both made clinical and scientific advances that they published in their textbooks. Callman Jacob Linderer first practiced in Halberstadt and Hildesheim and then as dentist to the University of Göttingen and latterly from 1826, after something of a struggle to retain his title to practice as a dentist, in Berlin. Jacob Callman Linderer had published a
Johannes Müller encouraged Joseph Linderer to make his own observations and carry out experiments to include in the Handbook. To this end Linderer studied microscopy in Müller’s lab in parallel with his clinical training, alongside Theodor Schwann, and completed a comprehensive comparative study of dental histology. Although Joseph Linderer’s histological research was never acknowledged or cited by his German or European contemporaries he was eventually awarded an honorary degree from The Baltimore College of Dental Surgery in 1851 for his contributions to dental science (Alexander Nasmyth, see later, had earlier received the same honor in 1849). The Linderer’s book, Handbuch de Zahnhelkunde, was dedicated to Müller with ‘respect and gratitude’, which implies he had had oversight of the first few sections on general anatomy and physiology. However, Müller only ever made just one brief mention of Joseph Linderer’s observations and that was about altered tooth structure in dental caries in his yearbook summary account of Fraenkel and Purkinje’s studies. Müller would have regarded Joseph Linderer as a student at this time and perhaps simply more as a clinician than a scientist but certainly not as part of the academic hierarchy legitimately involved in scientific research. In Müller’s
Jahresbericht summary for 1835 it is notable that Purkinje is repeatedly credited for the research published by Meyer Fraenkel and Isaac Raschkow in their MD dissertations with only brief mention of their names in a footnote to the dissertation title.\textsuperscript{41} Again, this was likely normal hierarchical deference and was to be expected. Many authors, and indeed colleagues, routinely deferred to Müller in what they wrote, often adding, apparently with pride, that something had been repeated by Professor Müller and shown to be true – or not.
Figure 9. Figures reproduced and rearranged from Tabl. XII and Tabl. XI in Linderer, C.J. and Linderer, J. (1837) *Handbuch der Zahnheilkunde*, Berlin.\(^{44}\) Fig. 1 depicts the outer aspect of an incisor tooth. Fig. 2 illustrates the groups of vertical ‘e’ and transverse ‘d’ fibres in enamel comprising the layer lines and the narrower brownish formation lines ‘o’, ‘g’, ‘f’. Figs 3 and 4 are transverse and outer aspects of the enamel ‘wetted with weak acid’ showing open horseshoe shaped prisms, formation lines, enamel prisms running in different planes and fissures or lamellae. Fig. 6 from Tabl. XI shows two examples of carious lesions in longitudinal section.

Linderer studied developing tooth germs in the calf. He believed the ‘enamel membrane’ consisted of ‘glands’ that produce the enamel, having observed a circular opening though which he thought liquid exuded and congealed on the dentine surface. Linderer later wrote that he disagreed with Theodor Schwann who regarded the ‘enamel membrane’ as a secondary product of the enamel organ, which then layer by layer repeatedly formed and mineralized.\(^{44}\)

Linderer described several kinds of enamel fibers (‘Schmelzfasern’) that we would now refer to as enamel prisms. These included groups made up of vertical, ‘senkrechte’ and transverse fibers, ‘Querstreifen’, that together made up layer lines, ‘Schichtstreifen’, in the enamel that we would now call Hunter-Schreger bands.\(^{20}\) Linderer noted they appeared alternately light and dark to the naked eye because light either hit fibers [prisms] lengthwise or crosswise.\(^{44}\) Linderer took issue with Fraenkel\(^{28}\) and argued that the layer lines, rather than resulting from prisms with a natural bend in their course being cut lengthways or crossways in longitudinal sections, resulted, he believed, from distinct groups of prisms running perpendicular to each other in alternate layers. Fraenkel had observed that what we now call perikymata on the surface of the enamel were the result of differences in ‘fiber
density’, whereas Linderer disagreed and believed they were ‘Querstreifen’ cropping out at the surface.44

Superimposed upon these fibers of different orientation, Linderer described ‘formation layers’ (‘bildungsstreifen’) that in the “tips of the crowns have a brownish appearance and form large arches near parallel with the dentine [surface]” but which intersect the dentine at an angle.44 Formation layers, or bands, he noted, represented increments of enamel growth and became shorter towards the enamel cervix.44 In the second edition of their book Linderer described other ‘temporary formation lines’ that were only visible in immature enamel and in enamel altered by erosion or caries.44 These he observed were often found closer to the cervix and were more closely spaced than permanent formation lines.

Besides these features of enamel microstructure, Linderer described and illustrated bush-like enamel tufts (‘büschelfasern’) or lamellae (‘fissuren’) and correctly observed the open horseshoe shaped cross section of enamel prisms as well as the scalloped nature of the enamel-dentine junction.20,44 Again taking issue with Fraenkel (1835) Linderer failed to confirm the presence of “small cross-fibers” that Fraenkel had suggested connect prisms together, which Boyde (1964)20 has interpreted as Linderer not acknowledging the existence of enamel cross striations (as indeed later neither did John Tomes).

Joseph Linderer is reported to have protested that he had made several observations about enamel and dentine before Fraenkel or Retzius “in the presence of Professor Müller”.15 However, all these histological observations were published with his father as co-author in 1837 and two years after the publication of Fraenkel’s
and Raschkow’s MD dissertations of 1835. Moreover, Retzius’s 1837 paper had by this time also appeared in Müller’s archive.

Nonetheless, Joseph Linderer and his father were probably the first to describe the histological appearance of the carious lesion in enamel and dentine, correctly attributing caries to “acid oral fluids” at a time when ‘animalcula’, ‘animalculis’ or ‘Zahnwürmer’ (originally reported by Leeuwenhoek, 1678, were still at this time thought by some to cause tooth decay.

**Anders Retzius’s paper on the Microscopical Structure of the Teeth**

A number of things about Retzius’s 1837 paper single it out as different and as an original and scholarly contribution. First, it was not just a study of human tooth histology, like, for example, Fraenkel’s or Linderer’s studies of 1835 and 1837, but rather a comprehensive comparative study on many tooth types and on each of the tooth tissues and representing 28 species of mammals, reptiles and fish (and including a fossil horse tooth). It was a near-monographic 88-page text with 18 figures on two fold-out plates. Second, it was intended as a comparative survey to identify histological features that might, as Nasmyth put it, ‘serve as an index of the type of any animal’. Retzius clearly felt it was the dentine that best reflected this aspiration and it is this tissue that dominates his descriptions and illustrations. Third, many authors, including Nasmyth and Owen, subsequently acknowledged Retzius for carefully reviewing what previous authors had published alongside his own observations. In particular, he rediscovered the earlier work of Leeuwenhoek (1678, 1687) that had remained unknown because, as Retzius suggests, his scientific papers on teeth were hard to source and were disorganized. Others have since expressed some sympathy with this view. In fact, Antoni Leeuwenhoek (1632-
1723) sent some 200 letters to the Royal Society in London of which 112 were translated into English by the first secretary of the Royal Society, Henry Oldfield (1619-1677), and published in the Philosophical Transactions of the Royal Society. One of these was on tooth structure (Leeuwenhoek, 1678), another on little animals (‘animalcules’) in the scurf [dental plaque] of teeth (Leeuwenhoek, 1684). Elsewhere Leeuwenhoek published other letters and missives, including a more extensive account of tooth structure in humans and several other animals, which, oddly, while written in London during the only year he ever travelled there, was not eventually published in Philosophical Transactions. Retzius had clearly tracked these publications down. Retzius also refers often to Georges-Frédéric Cuvier’s (1773-1838) 1825 treatise Des dents Des mammifères considérées comme caractéres zoologiques [On the teeth of mammals considered as zoological characters], both agreeing and disagreeing with him in some detail throughout his paper.

Anders Retzius (1837) quoted his colleague the chemist Jöns Berzelius as determining that enamel contains virtually no organic matter losing only 2% of its weight as water when heated and so being 98% mineral. In no sense then could enamel be considered to be a vital tissue. Retzius first examined teeth with a magnifying glass and with loups. He then prepared thin sections of demineralized teeth. Other teeth he ‘filed as thin as writing paper’ and then examined them using both reflected light and transmitted light under his microscope after soaking them in olive-oil and turpentine for different lengths of time to render them transparent to different degrees. He found human enamel to consist of hexagonal solid prisms, like the wax tubes in a honeycomb, on which he observed “transverse lines or streaks, making them appear as if they were formed of several pieces.” Retzius was the
first to publish a description of enamel spindles as isolated projections orientated at right angles to the enamel-dentine junction and also the first to use the term ‘prisms’ in the context of enamel structure. On the tooth surface, elevated undulating lines running parallel from side to side continued round their crowns, formed from enamel fibres “having united into belts”. These we now refer to as perikymata but Retzius correctly cites Leeuwenhoek as identifying these first. In a letter written in April 1687, Leeuwenhoek (1687) had written;

“If we look carefully at the surface of the tooth there are some 50 circular wrinkles or ribbings… the cause of these circular wrinkles around the tooth, in a day, or perhaps a month (in the course of its growth), have pushed outside the gum.” [translated from the original Dutch].

Besides describing what we now refer to as Hunter-Schreger bands, Retzius described,

“generally brownish parallel lines, which in the teeth with their crowns not yet worn down, curve round the coronal apices of the dental bone: but which towards the sides, particularly in teeth with wedge-formed crowns, run nearly parallel with the axis of the tooth”. “They appear to be traces of different stages in the formation of enamel, and are analogous to the lines running round the cavity of the pulp in dental bone”. [translated from the original Swedish].

These are the ‘formation layers’ (‘bildungsstreifen’) of Linderer, also illustrated by Meyer Fraenkel in 1835 as ‘dark longitudinal striae’, or what we now commonly refer to as striae of Retzius.
**Figure 10.** Tab. XXI reproduced from Retzius 1837 in Müller's Arch. Anat. Physiol. 1837,24 courtesy of the Royal Society of Medicine, London. The disposition and numbering of the component figures differs from Retzius, 183723,24 and from the version of this lithograph later reproduced by Nasmyth, 1839,25 Fig 1, is a human bicuspid in LS. Fig. 2 shows dentine tubules x350 cleared with turpentine and Fig. 8, enamel prisms with transverse stripes x350. Figs. 3a, 3b, 4 and 9 are of teeth in TS
showing the distribution of tissues and the hexagonal outlines of enamel prisms. Fig. 5 is the root of an elderly person in TS showing the unusually thick cementum layer. Fig. 6 is a molar of an elderly cow with cementum ‘b’ partially removed from the enamel surface ‘a’. Fig. 7 is of an incomplete human incisor showing dentine tubules, the minute indentations at the enamel-dentine junction upon which rest enamel prisms ‘a’ and brown parallel stripes in the enamel ‘d’.

Dentine was especially interesting to histologists at this time because it was a highly mineralized tissue that forms the bulk of a tooth and a sensitive (vital) tissue but apparently, unlike bone, a tissue that contained no cells. So, turning to human dentine, Retzius described the slightly undulating ‘fibers’ in demineralized dentine, which he discovered were hollow. Retzius again pointed out that in fact Leeuwenhoek was the first to note that dentine is tubular. He continued,

“their trunks opening into the pulp cavity whilst their terminations form extremely fine branches towards the external surface of the tooth.” “Most of the tubules assume more or less the form of a line with three curvatures frequently resembling a Greek ‘zeta’.” [translated from the original Swedish].24,25

At higher magnification an “immense number of other short curvatures are visible”. But contra Fraenkel (1835),28 Retzius observed no similarity whatever between dentine and bone. There was still some debate about this. Nasmyth (1839)25 translates Fraenkel as previously saying, “The interior of the roots of old teeth consists not of dental substance, but of bone properly so called, as does also the deposit on the external surface of the root”, Nasmyth adds, “and this statement is confirmed by Müller”.25 In fact, Müller himself in 183648 had investigated dentine and noted ‘fibers’ sticking out of fractured surfaces that became transparent and
bendable on dissolution with acid. Müller (1836) had concluded the tubules in
dentine have an,

“animal matrix, membrane, that is rigid and fragile in the solid tooth which is
still penetrated with calcium salts” [translated from the original German].\textsuperscript{15,48}

John Hunter (1729-1793) in his book, \textit{The natural history of human teeth}
(1771; 1778),\textsuperscript{13} was the first to observe that tooth tissues do not remodel, or turn
over, like bone since

“madder only reddens those layers which are formed while the animal is fed
with it and does not change at all the colour of those which previously
existed”.\textsuperscript{13}

Retzius was well aware of this, writing that “in the tooth, no renovation of material
takes place” and was also aware of the incremental nature of tooth tissue formation.

In his description of cementum (‘cortical substance’) Retzius noted there were
no cells in young teeth, just a very thin layer, but in thicker cementum,
“communicating tubules and osseous cells in parallel lines deposited in delicate,
coherent layers” were visible.\textsuperscript{23,24,25} Müller in his textbook \textit{Elements of Physiology}\textsuperscript{38}
had previously perpetuated an earlier view that the ‘crusta petrosa’, or cementum,
overlying the enamel in ungulates and some other animals, “seems merely a deposit
from the salts of the saliva and to be essentially the same as what is called the tartar
of the human teeth”. Nasmyth\textsuperscript{25} referring back to this remark in the light of Retzius’s
study subsequently wrote that the organized structure of cementum, now apparent
by microscopic examination, “is sufficient to convince anyone of the fallacy of this
statement”.\textsuperscript{25} But Müller, always fair in his representation of other people’s work, had
actually later in his textbook cited Cuvier as having previously questioned this idea
upon discovering that cementum was formed on the enamel of elephant teeth prior to eruption and so was more likely formed by the inner aspect of the dental follicle.

Against this description of human tooth microanatomy, Retzius then went on to describe each tooth tissue in the teeth of another 27 species he had prepared from specimens in his museum collection. In several plates Retzius illustrates the various ways in which dentine tubules ramify differently in the dentine of human, hare, shark, dolphin, python and horse teeth. He described and explained, for example, the pattern of dentine seen in elephant ivory when sectioned transversely as “cut into rhomboid figures” and “arising from the refraction of the rays of light by the parallel curvatures of the main tubules”.24 Although it must be said, Linderer and Linderer were the certainly first to illustrate this with a drawing of a section through an elephant tusk in their textbook.44 Retzius also described the nature of the characteristic irregular secondary dentine plug formed within the walrus tusk pulp chamber. Retzius concludes,

“these inquiries into the Microscopical Structure of the Teeth have been made with the greatest of care, and have cost me a great deal of trouble: they refute the observations and views of many of my predecessors; but I nevertheless clearly see, that my results to which I have arrived can make no pretentions to completeness.” [translated from the original Swedish].24,25
Figure 11. Illustrations from Retzius, 1837, showing variation in the dentine tubule branching pattern in four contrasting taxa selected from six originally depicted by him. Fig 1b, human incisor, Fig 3 shark (Squalus cornubicus). Fig 5 python, (Python bivittatus) in which the tubules are orientated towards the root. Fig 6 external portion of the tubules in horse dentine. Reproduced and rearranged from the lithographs published by Nasmyth, 1839. Researches on the development, structure, and diseases of the teeth. Churchill, London. Courtesy of the Zoological Society Library, London.

Alexander Nasmyth and Anders Retzius

Alexander Nasmyth (1789-1848) was a Scottish anatomist and dentist and a colleague of John Goodsr (1814-1867), later to become professor of anatomy at the University of Edinburgh. Both had been apprenticed to Nasmyth’s older brother, Robert (1792-1870), himself a surgeon and dentist. Both Nasmyth (1839) and Goodsr (1839) published important papers on tooth development in the same year. Goodsr (1839) described in some detail the timing, sequence and development of, as he put it, human tooth crypts, germs and follicles but apparently soon after began to find dentistry wearisome. As will become apparent, Goodsr was later to go on and make a major contribution to cell biology.

By 1839, Alexander Nasmyth had relocated to London (where among other things he was appointed dentist to Queen Victoria, Prince Albert and their family). His own research sparked a debate that was not satisfactorily resolved for many years. Nasmyth described a membrane that could be separated from the enamel surface of newly erupting teeth, a “persistent capsular investment of the enamel”. Nasmyth’s membrane was wrongly considered (not just by Nasmyth, but also by Richard Owen, John Tomes and Charles Tomes) to be a cementum forming layer continuous with the cementum at the enamel cervix and equivalent to the coronal
cementum-forming layer covering the crowns of some animals.\textsuperscript{21} Thomas Henry Huxley (1825-1895), however, later took issue with this arguing that it was, as he put it, the ‘membrana preformativa’ between the enamel organ and the forming enamel surface.\textsuperscript{19} Nasmyths’s membrane was indeed eventually shown to be of epithelial origin and derived from the reduced and flattened layer of former maturational ameloblasts with an inner amorphous proteinaceous component we now call the enamel cuticle.\textsuperscript{21}

\textbf{Figure 12.} John Hunter (detail of a portrait by Sir Joshua Reynolds (1786) image RCSSC/P 121, courtesy of The Royal College of Surgeons of England), Alexander Nasmyth (detail of portrait by Francis Grant, image 10405750, Courtesy of the Science and Society Picture Library), Richard Owen (image MAM 002887, Courtesy of the Natural History Museum, London), Thomas Bell (image MAM 002887, Courtesy of the Natural History Museum, London), John Goodsir (reproduced from Comrie,
In 1839 Nasmyth published his book, *Researches on the development, structure and diseases of the teeth*. This contains a long and comprehensive review of the history of dentistry from the time of Herodotus (as indeed did the second edition of Linderer and Linderer, 1842) and an up to date account of the most recent developments in dental histology in which Nasmyth translated many long passages from Raschkow, Fraenkel and Retzius. Nasmyth, like Joseph Linderer and his father, was a dentist and his book contains chapters on osteology, head and neck anatomy and a great deal on the vasculature and nerve supply to the pulp, as well as on the histology of the oral epithelium and mucous membrane. Nasmyth restated Goodsir’s findings that the first rudiment of a tooth in the human fetus is represented by a slight prominence of the mucous membrane within a groove in the alveolar arch. This ‘papilla’ or ‘tooth germ’ progressed to a ‘dental follicle’ then a ‘dental sac’ as communication with the mouth is gradually lost. Raschkow had stated he found no evidence of this groove or the papilla in the fetal calf. Nasmyth, puzzled and disbelieving of this, set about dissecting several fetal calves and lambs to check their findings, eventually having to admit that Raschkow’s observations regarding this material were indeed correct.

Nasmyth reported in his book that he first saw Retzius’s paper in April 1838 when his friend Dr Grant loaned him a copy of it. Robert Grant (1793-1874) was a fellow Edinburgh medical graduate and professor of comparative anatomy at University College London from 1827-1874. Nasmyth read the paper and then translated and reproduced much of it in his own book, arguing that it was better to do
this than repeatedly cite Retzius at length. He then sent a copy of his book to Anders Retzius with a cover letter dated May 30th 1839. In his letter Nasmyth writes;

“I have been induced to give the department of comparative anatomy in such minute detail as you see I have done, because there has existed a desire in some individuals here to rob you of your true and well-deserved merit, in supposing that the application of such a system had not been contemplated by you throughout the whole animal Kingdom both recent and extinct.”

Retzius wrote than in 1833 he learned more during his 8 day trip to London than during his 5 month visit to Paris. Nasmyth was well aware that Retzius had travelled to England and spent time at the Hunterian Museum at the Royal College of Surgeons and while we might speculate about who Nasmyth was suggesting might ‘rob’ him or be inclined not to acknowledge the full extent of Retzius’s dental histology studies, he seems in his book only to be determined to make his work better known in England. Nasmyth goes on to write:

“I understand that you were so generous and disinterested as to deposit in the hands of some individual here some prepared sections for the microscope. You would oblige me much if on receipt of this you would have the goodness to let me know, where or in whose hands you did deposit these, and the date. Your doing so at your earliest convenience will very much oblige.”

In reply, Retzius first explained why he had been forced to abandon his microscopic studies but also answered several of Nasmyth’s questions:

“Dear Sir, Allow me to offer you my best thanks for the work on the Development of the Teeth which you had the kindness to send me and for the
honorable mention my researches on the same subject have there received at your hands. I was compelled to abandon these and many other interesting microscopical researches in 1836 in consequence of an affection of the eyes from which I still suffer and which has been the main cause that I have delayed so long in answering your flattering letter. The fact is that the state of my eyes only allows me to read a few minutes at a time, and in this manner only have I been able to read your interesting work.”

“The preparations of teeth, which you ask after, are in the hands of Mr. Clift of the Hunterian, and Mr. Johnson of the St George’s Hospital Museum. Were not my eyes in such a wretched state, I should with much pleasure now send you some newer and finer preparations, which I shall do at all events in case I am happy enough to recover the full use of them. I have the honour to be Dear Sir, Your obliged and obedient humble servant”

But Retzius was rarely active in only one research area at a time. While working on tooth histology, for example, he also published an essay on the castration of cattle. Retzius intimated that he found it hard to write at the same pace he discovered things and especially beyond his mother tongue in German or English. Some of this must have resulted from his intense inclination for multi-tasking and his enthusiasm for practical tasks and experiments. Nelson remarked that Anders Retzius “was a born genius, always bubbling over with original ideas, few of which however were carried to completion”. Wilson, in an obituary notice to the Medico-Chirurgical Society of Edinburgh, was rather more direct about his lifetime achievements as surmised, it would seem, by the medical profession in Scotland at the time;
"Professor Retzius has not contributed any individual work of magnitude to those departments of science which he cultivated so assiduously; but his separate memoirs and monographs have been very numerous".\(^2\)

It seems unlikely these authors were familiar with Retzius’s contribution to dental histology and how careful, insightful and eloquent he was capable of being as a descriptive scientist when fully focused on a topic. Recall, the whole of his comparative study on teeth was completed between Summer 1835 and January 1836 when he first presented his findings at a lecture to Royal Swedish Academy of Sciences.

Erik Müller (1910)\(^40\) writing retrospectively about the early historical achievements of the Anatomical Institute (1765-1910) and cited in Larsell\(^4\), indicates that some scientists of the day felt that Retzius tended to take short cuts in his scientific writing or be careless, his papers appearing then less thorough than they might have been.\(^4,40\) To others his originality and insight more than compensated for this along with his driving ambition and his belief that it was the advancement of science by the widening of its boundaries that was paramount. Retzius himself wrote:

"It comes to this, that I am a poor scribe, it costs me much trouble to write, for I received less foundation in language than I could have wished."\(^4\) And elsewhere: "I am a poor grammarian and must therefor let my essays lie long on the digestion-shelf before I let them leave me."\(^4\)

And in a letter to Arvid Henrik Florman, his former teacher of anatomy, he declared he found written descriptions “complicated and uncertain” in the absence of “reliable specimens to go with them”.\(^4\)
It must be said, however, that Retzius was always quick to respond to criticism and to correct himself. In the final section of his paper on tooth histology he had remarked, almost off the cuff perhaps, that he had found no evidence that "tabescence nor absorption or erosion has anything to do with" the shedding of deciduous teeth.25 A number of people had immediately taken issue with this statement, among them his old professor, Arvid Henrik Florman. In a letter to Florman in 1838 Retzius admitted Florman was right to find fault with this statement and replied, "corrosion of the roots of deciduous teeth is indeed the rule".25,52,53 Similarly, Retzius corrected himself on the same topic with the Parisian physiologist Marie-Jean-Pierre Flourens (1794-1867) and again with Johannes Müller in Berlin, who subsequently published a revision of his observations.52,54 That nobody apparently took issue with anything else in that paper and only seized upon this single obvious error speaks volumes. Taking this criticism seriously, however, Retzius’s immediately made more careful observations to correct himself on this topic.52 He writes,

"the tooth sack of the succeeding permanent tooth swells at the point of contact to a highly vascular, thick body which apparently secretes a liquor which is able to dissolve chemically those parts of the milk tooth with which it comes into contact".25,52

Retzius and Nasmyth also exchanged views on another topic of interest,52 the content of dentine tubules. It is not entirely clear what exactly Retzius was describing in his original 1837 paper but the idea that peritubular dentine fills the periphery (so-called ‘calcarius lime salts’) and that a ‘nourishing and supporting fluid’ circulates within the tubules is not incompatible with what we understand today, except that Retzius did not apparently recognize the presence of the odontoblast cell process.
within the tubule lumen. This was something that Nasmyth appeared to be observing in fresh material as distinct from the empty tubules of dried teeth that Retzius had observed. Nasmyth appears to interpret Retzius’s description as conflicting, as if tubules were either filled with mineral or fluid, even though Retzius seems clear on this and even illustrates dentine tubules seen in cross section composed of an inner and outer zone. Theodor Schwann and John Tomes were both to expand on these observations later.

The good-natured and exacting correspondence between Retzius and Nasmyth reveals so much about their characters, the seriousness with which they both regarded dental histology – and their passion for scientific enquiry in general. In no sense was either author trying to win precedence but simply to get at and understand the truth and be clearly understood. Retzius in his explanatory letter to Nasmyth adds with regard to tooth histology:

“In the mean time it will give me the greatest pleasure to know that they are in the hands of yourself and other able men, who will treat the subject with all the minuteness and critical severity its importance demands.”

Richard Owen and John Tomes in London

Richard Owen (1804-1892) was born in Lancaster, in the North of England, where he was first apprenticed to a local surgeon and apothecary before studying medicine in Edinburgh and then at Bart’s Hospital, London. In 1827 Owen was appointed assistant conservator at the Royal College of Surgeons of England under William Clift (1775-1849), John Hunter’s old assistant, and then following Clift’s retirement in 1842 to conservator until 1856. In 1837, however, he was made Hunterian professor and under the terms of John Hunter’s will became responsible
for delivering 24 Hunterian lectures each year on comparative anatomy and physiology. Owen would have been at the Royal College of Surgeons in 1833 when Anders Retzius met with William Clift there and left ‘preparations of teeth’ with him but neither Owen nor Retzius ever make any mention of meeting each other.

Owen’s 1837 Hunterian lectures (delivered in March, April and May each year) included an account of teeth and dentitions. Owen writes in the introduction to *Odontography* (1840-45) that he had started to collect extensive material for a treatise on the structure of teeth, when in 1837 the fourth number of Müller’s Archive arrived with the summary of Purkinje and Fraenkel’s work. Then shortly after this the fifth number of the same volume arrived with Retzius’s paper in it and so he abandoned his intentions. Nonetheless, Owen still felt there was the need for a more extensive comparative account of dentitions with a different emphasis. Owen’s treatment of dentitions, dental development and histology in the *Odontography* went far beyond the earlier studies of Retzius, Fraenkel and Purkinje. The two-volume work contains 655 pages of text and over 168 illustrations of more than 80 species of fish, 70 reptiles and close to 200 mammals.

Owen championed microscopy and histology in England and co-founded the Royal Microscopical Society in 1839. He began his treatise on teeth by rationalizing what was then a confused dental anatomical nomenclature. He carefully defined the distinct tooth tissues, enamel, dentine, cementum and pulp, in the introduction to *Odontography*. In his descriptions of each animal class, he sought to identify the basic, or archetypal, structural features among them and the ways each dental tissue differed or was modified and how it developed or formed. On his return from the voyage of the Beagle in 1836, Charles Darwin had given Richard Owen fossil
specimens of *Megatherium, Mylodon, Scelidotherium* and *Toxodon* and so Owen turned to palaeontology as an opportunity to use tooth microstructure in living animals as a "test of the affinities of extinct animals".
Owen was also moving away from his early work on the relation of form and function across comparative body systems towards identifying similarities in body plan (homology) and change through time. Owen acknowledged that Retzius had demonstrated beyond doubt that dentine was a completely distinct tissue from bone. Owen wrote,

“I propose to call the substance which forms the main part of all teeth dentine”

and added, “besides the advantage of a substantive name for an unquestionably distinct tissue … the term dentine may be inflected adjectivally … thus we may speak of dentinal pulp, dentinal tubes or cells as distinct from the other constituents of a tooth”.

He also refers to vascular dentine, or vasodentine and osteodentine. Owen’s new nomenclature did not go down well with everyone. Nasmyth for one objected to the term ‘dentine’ on several grounds suggesting it could equally easily be applied to any of the dental tissues, adding that as a description of ivory, ‘dentine’ was the “most objectionable of all terms”. This was just the beginning of a serious rift between Owen and Nasmyth.

Owen carefully cites Retzius’s description of dentine tubules but then, presumably to clarify things, re-describes their course as having three ‘primary curvatures’ and many minute ‘secondary curvatures’. To this he added a
description of ‘contour lines’ in dentine, where the confluence of small deviations of tubules across a tooth crown or root leaves a record of a prior disturbance at the forming front.

Owen questioned Retzius’s observations of ‘corpuscles’ (cementocyte lacunae) in horse dentine saying he had never seen them.26 This raises an interesting question as to whether any of these early authors had clearly distinguished cell lacunae from interglobular spaces (uncalcified spaces between spherical calcification centres), later first identified, described and illustrated in dentine by Czermak in 1850.56 Owen then went on to question (as John Hunter had done) how a non-vascular tissue can be so sensitive, proposing that the circulation of a clear fluid in the dentine tubules may accompany ‘prolongations of nerves’ as well.

“Whosoever has felt the pang produced by contact of a probe with the recently exposed surface of the dentine, must at least allow the tubes to be most efficient conductors of the impression to the sentient pulp”.

This line of thinking about dentine sensitivity remains one of considerable clinical significance and one wonders if around this time Owen might actually have been discussing this issue with a young dentist, John Tomes. Tomes had been working with Owen, helping him to prepare ground sections of teeth and meanwhile conducting his own research into dental histology.57 Neither Hunter, nor Owen nor Tomes, however, would have been aware that the sensitivity of dentine had been considered before. In 1563 Bartholomaeus Eustachius had described, not just enamel and dentine, but the structure of the periodontal ligament as well.58 Moreover, Eustachius had already suggested that the highly sensitive nature of teeth
resulted from the nerves of the pulp chamber branching off and becoming intermingled with the inner substance of the teeth.
Cementum had previously been referred to by Jacques-René Tenon (1724-1816) in 1798\textsuperscript{59} as the ‘cortex osseux’ and then by Robert Blake (1772-1822) in 1798\textsuperscript{60} and 1801\textsuperscript{61} as the ‘crusta petrosa’, by Fraenkel in 1835\textsuperscript{28} as the ‘substantia ossea’, and by Retzius in 1837\textsuperscript{23,24} as the ‘cortical substansen’. But Owen proposed it should simply be referred to as cement, exactly as Cuvier had done.\textsuperscript{26} Nasmyth explained that cementum had originally been observed between the enamel plates of certain animals, elephants for example, and so assumed to hold them together, hence the name\textsuperscript{25}. Owen also continued to refer to enamel exactly as John Hunter had done.\textsuperscript{13,26} While confirming most of what was already described by Fraenkel and Retzius on enamel, Owen added some important observations. He noted that when several overlapping layers of enamel prisms catch the light they appear like ‘dusky brown waves’, exactly as Retzius had described them and as illustrated prior to this by Fraenkel (1835) and Linderer and Linderer (1837).\textsuperscript{23,24,26,28} “Without doubt”, Owen goes on, “they indicate the stratified nature of enamel and the stages in its formation”.\textsuperscript{26} Owen then described a clear link between what we now call striae of Retzius and perikymata. Where these strata, which are arranged obliquely to the vertical surface of the dentine, crop out at the enamel surface, “they occasion those wavy transverse annular delicate markings which Leeuwenhoek noticed”.\textsuperscript{26} This is the probably the first clear description of striae of Retzius being associated with perikymata, something that is usually attributed to Gustav Preiswerk (1895)\textsuperscript{62} and his observations on ungulate enamel.\textsuperscript{62}
John Tomes

John Tomes (1815-1895) was the son of a farmer and was born in the small town of Weston-on-Avon in Warwickshire, England – just 3 months before the battle of Waterloo. In 1831 he was apprenticed to an apothecary in Evesham, Worcestershire, then in 1836 aged 21 studied at Kings College London and The Middlesex Hospital Medical School. As early as 1837, Tomes became expert at making ground sections of teeth under the tutelage of Thomas Bell (1792-1880) who was both a dental surgeon and professor of zoology at King College London. Richard Owen was impressed with Tomes and aged only 23 involved him in preparing ground sections of some of his own modern and fossil teeth. Bell encouraged Tomes to prepare a paper summarizing his findings on tooth histology which Bell, as was the custom for an advisor, then read on his behalf before the Royal Society on 14th June 1838. Certainly, by June 1838 Owen had read Müller’s account of Fraenkel’s MD dissertation and Retzius’s 1837 paper in Müller’s Archive, even if Thomas Bell may not have done. However, Tomes (1839) wrote that “apart from a few facts mentioned by professor Owen at the Royal College of Surgeons”, he knew nothing of the German or Swedish studies already published. Tomes’ paper was subsequently rejected for publication jointly by Owen and Bell (see Berkovitz, 2018, for an account of this) on the grounds that his findings were not new and had already been published by Fraenkel and Retzius. Cohen (1966) notes that Tomes’ paper, signed by him “King’s College, 31st May 1838”, was subsequently received for publication by The London Medical Gazette, but unfortunately did not appear in print until February 9th 1839. The aim of his paper, Tomes wrote, was to “trace the intimate relations existing between dental structure and that of bone”.33
Tomes studied human teeth alongside those of various fish and sharks, and
giraffe teeth, as well as hedgehog, rabbit, pig, elephant, porpoise, dugong, kangaroo
and sperm whale teeth and the fossil tooth of a Megatherion, “the less common”
specimens of which, he noted, were made available to him by Richard Owen and
Thomas Bell. In short it was a comprehensive comparative study that carefully
described many of the structures previously documented by Fraenkel and
Retzius as well as affording several further original observations. Unfortunately,
The London Medical Gazette did not publish the figures accompanying the text that
Tomes had prepared for his Royal Society paper. Tomes fed madder to a pig for 25
days in the same way John Hunter had done (most likely on his father’s farm) and
then observed the growth lines in its teeth. He observed bubbles of gas emerging
from the ends of what were clearly tubules in dentine when demineralized in dilute
muriatic (hydrochloric) acid. Tomes described examples of what we would now call
tubular enamel, as well as comparing tubules and their complex branching patterns
in both dentine and cementum with those in bone. With regard to enamel, Tomes
(1839) noted that enamel fibers (prisms) have the appearance of “somewhat
irregular six-sides figures” when cut transversely but added “I have not seen the
transverse markings of the fibres described by professor Retzius”, adding further, “A
similar appearance may be produced by making a section of enamel in such a
direction as to divide the fibres obliquely” – an issue some still grapple with today.

Tomes stated that the question of greatest interest to him was the function of
the dentine tubules and ‘corpuscles’ (cells) speculating that they “perform some
office important to the vitality of the mass of which they constitute a part”. Tomes
(1839) reasoned that it was not improbable that the tubules “by capillary absorption
carry on a kind of slow circulation of the more fluid parts of the blood” but it was not
until 1856\textsuperscript{63} that he elegantly demonstrated that ‘Tomes fibers’, as they became known, (odontoblast cell processes) also extended into the dentine tubules.\textsuperscript{63} Tomes (1839)\textsuperscript{33} described a ‘granular layer’ towards the tooth surface where dentine tubules “break up into several smaller ones and are lost as they approach it”.\textsuperscript{33} This we now know as the ‘granular layer of Tomes’. Tomes (1848)\textsuperscript{64} illustrated and expanded on this observing that some terminal branches of the dentine tubules may “pass into the interspaces between large granules that form the outer surface of the dentine”\textsuperscript{64} (the term ‘granules’ we would now interpret as minute calcospherites and dilated tubule endings just deep to the hyaline layer and root cementum). In 1839\textsuperscript{33} John Tomes was still only 24 years of age, two years younger than Purkinje and Fraenkel when their MD dissertations were published in 1835, but he had already made new, original and detailed observations about dentine microstructure. John Tomes went on to become a renowned dental surgeon at the Middlesex Hospital, London, and an active political reformer of dental practice in England.\textsuperscript{57,65} In 1848 his course of lectures was eventually published as a book, \textit{A course of lectures on dental physiology and surgery},\textsuperscript{64} of which Rudolf Virchow, by this time Berlin’s greatest pathologist, described as a “\textit{classical work}”.\textsuperscript{15}

\textbf{Figure 15.} Branching dentine tubules (A) passing into the intergranular spaces of the granular layer (B). A transparent layer separates the dentine and cementum (C). One tubule passes into cementum.
It is interesting that Owen’s *Odontography* (1840-45)\(^{26}\) is dedicated to Thomas Bell in the most effusive terms and that Owen was quick to promote Bell’s scientific writings throughout but on occasions less so the work of others. *Odontography* is clearly a monumental work but Owen was accused by some of not properly citing other people’s previous work, Nasmyth’s book of 1839\(^{25}\) for one. This deliberate omission was made worse by a dismissive 7 page footnote by Owen in his introduction denouncing much of Nasmyth’s research.\(^{66}\)

The plates where Owen illustrates human tooth histology (Plates 122, 122a 123 and 124) were almost all reproduced directly from Fraenkel, Raschkow or Retzius.\(^{26}\) Owen altered some previously published lithographs to illustrate his own new findings. For example, Figure 7 in Plate 122, that illustrates Owen’s ‘contour lines’ in root dentine, is an altered copy of Fraenkel’s Figure 3 that has been rotated 180 degrees (and which makes good sense for a lower molar) but with parallel concentric markings added, of a kind that could never actually exist in a human tooth root.\(^{26}\) In this case Owen makes no reference to Fraenkel at all.\(^{26}\) But it would seem this was an exception, as the source of each of Owen’s other illustrations appears clearly in the legends, all be it minimally by simple reference to the author’s surname. Owen made many original histological observations about tooth tissues including new and beautiful illustrations of chimpanzee enamel and dentine showing enamel cross striations and dentine calciospherites and of a human molar from an ovarian teratoma (Owen, 1840-45, Plates 119a and 124).\(^{26}\)
Figure 16. Detail of Plate 119a, reproduced from Owen’s *Odontography*, 1840-45, courtesy of The Zoological Society of London Library. Microstructure of a chimpanzee incisor, showing weaving enamel prisms with cross striations, the scalloped enamel-dentine junction, layers of branching dentine tubules and arcade-shaped calcospherites typical of dentine mineralization.

John Tomes was hurt that he was not acknowledged anywhere, despite having made some of the ground sections for Owen himself but especially so because some of his unpublished findings appeared unreferenced in the text as if they were Owen’s original observations. Tomes was sufficiently upset to openly accuse Owen of plagiarism, such was his strength of character in one so young to
take on a scientist of international stature.\textsuperscript{57} This was not the first or last time this particular accusation was levelled at Owen but the disputatious public exchanges between Owen and Nasmyth that resulted were prolonged and reached epic proportions, eventually prompting the exasperated secretary of the British Association to write that in his view, it “\textit{could all have been settled by any honest schoolboy in five minutes}”\textsuperscript{66}

Despite objections of this kind from some of his contemporaries, Nasmyth and Tomes in particular, Owen’s \textit{Odontography} was hailed a landmark contribution. In it, Owen standardized a lot of over complicated histological terminology and described both the histology of the dental tissues as well as the complete dentitions of an enormous number of living and fossil vertebrates in a seamless and ordered way. Not until 1855 did anything like Owen’s contribution appear again when Giebel’s \textit{Odontographie} was published in Leipzig.\textsuperscript{67} Like Owen, Giebel described and illustrated the dentitions of a huge number of living vertebrates and yet again reproduced the lithographs of Raschkow, Fraenkel and Retzius (Giebel, 1855, Taf. XLIX)\textsuperscript{67} that by now had become an established reference for enamel, dentine and cementum histology.

Tomes later published a number of carefully observed and detailed papers on human and comparative dental histology. For example, in his book, \textit{A course of lectures on dental physiology and surgery}, he illustrated no less than 14 distinct branching patterns of human dentine tubules.\textsuperscript{64} A collection of some 1,880 ground sections made by him and his equally renowned comparative anatomist and dentist son, Charles Sissmore Tomes (1846-1928), still exists at the Royal College of Surgeons of England.\textsuperscript{57,68}
Berkovitz (2018) discovered amongst this collection a letter that reads, 
“Tibia of Dinornis, New Zealand, from Dr Mantell”. Sadly, Gideon Mantell, who had found and described the first Iguanodon fossils in Sussex, England, was, it seems, systematically put down by Richard Owen and was eventually forced to sell his fossil collection to The British Museum to clear his debts. Gideon Mantell’s son, Walter, had emigrated to New Zealand in 1839 and sent important fossils home to his father. Owen acknowledges in his introduction to Odontography that Dr. Mantell had supplied him with fossil teeth of Iguanodon and Gyrodus and it is possible he may also have acquired the giant moa bone at this time. John Tomes did not, apparently, meet Gideon Algernon Mantell (1790-1852), until 1848. This was the year when Tomes was elected Fellow of The Royal Society at the age of 33. His election to FRS in December 1848 was supported by 20 members but Richard Owen and Thomas Bell, both by this time senior Fellows of the Royal Society, were not among the signatories, although Gideon Mantell was. It was perhaps then later that Tomes acquired the Dinornis specimen from Mantell and equally likely that John Tomes’ son, Charles, had subsequently made the ground section from this giant moa tibia.

Meyer Fraenkel (1835) had demonstrated that dentine has a fibrous structure and is “formed layerwise out of material afforded by the pulp”. He had also noted its tubular structure and had, along with Thomas Bell and Isaac Raschkow, gone some way to suggesting that dentine was produced by cells. Johannes Müller’s student, Theodor Schwann (1810-1882), had distanced himself completely from his teacher’s beliefs in vitalism. While comparing details of plant and animal histology with the botanist Mattias Schleiden (1804-1881), who was also working in Müller’s lab, Schwann realized that all living forms conformed to a common principle of
development and growth and were not the manifestations of some mysterious life force (Otis, 2007). \(^5\)

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**Figure 17.** A few of the many forms of dentinal tubules found in the human tooth. Reproduced from Lecture 2, in Tomes, J. (1848). *A course of lectures on dental physiology and surgery delivered at the Middlesex Hospital School of Medicine.* John W. Parker, West Strand, London. \(^6\) Courtesy of the Royal Society of Medicine, London.
In 1839 Schwann announced that the basic unit of all living things, plants and animals, was the cell. In fact, it was Leeuwenhoek’s near contemporary, and another early pioneer of microscopy, Robert Hooke (1635-1703), who first coined the term ‘cell’ in 1665 as the smallest unit of plant specimens visible under his microscope. Theodor Schwann reasoned through the implications of his cell theory in his highly influential book, Mikroskopische Untersuchungen über die Übereinstimmung in der Struktur und dem Wachstum der Thiere und Pflanzen. (Microscopical researches into the accordance in the structure and growth of animals and plants). It was, however, two of Schwann’s colleagues in Müller’s lab, Rudolf Virchow and Robert Remak, who proposed that ‘all cells came from other cells’.

In 1839 Theodor Schwann made some important observations about dentine formation in the context of his new cell theory. Schwann was of course well aware of Müller’s previous observations about dentine and the content of dentine tubules and would also have been well aware of Joseph Linderer’s work on dental histology in Müller’s lab and Linderer’s difference of opinion with him about the formation of dentine. Schwann observed that,

“each of the cylindrical cells of the surface of the pulp extend toward the tooth substance as a short, fine fibre and that these fibres extend beyond the surface of the pulp approximately as the dentine tubules”.

“I once believed that they projected into the dentinal tubes, and that the intertubular tissue was merely the intercellular substance between these elongations of the cells. But I have given up these ideas since I observed nothing of the kind in human teeth, and since this explanation brings with it a
difficulty in regard to the teeth of the pike”. [translated from the original German].

It was, however, John Tomes (1856) who later decisively settled this issue by working on freshly extracted human teeth. By carefully tearing the pulp away from a partially demineralized dentine surface, as Müller had done in 1836, Tomes, however, was now able to demonstrate “unbroken fibrils stretching across from the separated orifices of the tubes to which it belongs”. The mechanism of dentine sensitivity (that Hunter and Owen – and of course Tomes – had alluded to earlier) took a long time to resolve, as did the processes of cellular secretion involved in mineralized tissue formation (see Huxley, 1853 and Glasstone, 1966 for a historical review of this). But John Tomes and his paper on Tomes’ fibers (1856) was the first to convincingly demonstrate dentine was indeed a vital tissue that contained the odontoblast cell processes and moreover, from his clinical experience as a dentist, to discuss the possible mechanisms of dentine sensitivity.

Meanwhile, in Scotland, John Goodsir, having completely abandoned studies of teeth by this date, had also concluded that all life forms were composed of cells. But Goodsir eventually went further than Schwann and described the microscopic components of cells and cell walls in some detail, as well as the processes of cell growth and cell secretion. So influential were Goodsir’s ideas that Rudolph Virchow eventually dedicated his own book Cellular pathology to John Goodsir and it is not hard to see why. Unlike many of the other medically qualified members of Müller’s lab, Virchow was a dedicated clinician who actively campaigned for social change to fight poverty and diseases. From humble beginnings as the only child of a farmer in Schievelbein (now Świdwin in Poland), Virchow had earned his medical
degree with a military scholarship granted to gifted children of poor families to become army surgeons. Virchow was a political and social activist who regarded medicine as a social science, and politics as no more than medicine on a larger scale. In a report on a typhus epidemic in 1848 he wrote “wealth, education and liberty depend on one another and thus, conversely, do hunger, ignorance and servitude”. Through his scientific writings Virchow had continually pressed for more microscopic research to advance and reform clinical practice and this Goodsir’s research had clearly done. In his book Virchow described John Goodsir as “one of the earliest and most acute observers of cell-life both physiological and pathological”. In acknowledgement of his own scientific achievements to cellular pathology, Virchow was awarded the Copley Medal of the British Royal Society in 1892.

A return to Human Anatomy and Anthropology

When in about 1840 it became evident that Retzius’s eyesight had greatly deteriorated, he had to abandon microscopic studies. For the last two decades of his life, he turned again to gross anatomy, chiefly to the skeletal, circulatory, and nervous systems and to topographical anatomy and physical anthropology. Retzius described a gutter-like groove, the pyloric canal, running along the lesser curvature of the stomach in both humans and rodents from the cardia to the pylorus, along which, Kaufmann (1907) later demonstrated, fluid swallowed with a full stomach passes from cardia to pylorus, without mixing with other stomach contents. In 1856 Retzius described a group of gyri forming part of the under surface of the splenium, in the angle formed by the hippocampus and the dentate gyrus of the brain. While inconsistent in the human brain they are important in other species and Triarhou (2013) has recently noted they are conceivably associated with olfaction. Anders
Retzius described the extraperitoneal space deep to the anterior abdominal wall and pubis (the prevesical cavity or ‘cave of Retzius’) into which the bladder may expand and he identified veins, the so-called ‘veins of Retzius’, that occasionally pass from the secondary retroperitoneal parts of the gut directly into the inferior vena cava and not to the portal vein.4

Retzius also engaged himself in the battle to combat alcoholism in Sweden by seeking ways to cure people of their dependency. In 1848 The Lancet76 published a short summary of a treatment Retzius had devised with his colleague Dr. Landblaed in Gotheberg that included a clinical trial of 139 soldiers, of whom 128 were reported to be completely cured.76 Their ‘cure’ consisted of placing the patient in complete confinement surrounded by “every comfort” but all food was mixed with diluted brandy was the only drink available. This regimen was continued until the patient refused food altogether and was “unable to bear even the smell of the once cherished liquor”.76

It is unfortunate that Anders Retzius was perhaps for a long time best remembered as an anthropologist and not as a comparative anatomist and histologist. A number of prehistoric human remains from the Neolithic, Bronze age and Iron age were being discovered in Scandinavia1 and relatively late in his life Anders Retzius became interested in the considerable variation in cranial morphology that was becoming apparent among them.1 Initially curious about their origins, Retzius attempted to quantify the similarities and differences between crania and to do this he invented the cephalic index (the ratio of head length to breadth expressed as a percentage). Retzius first announced his cephalic index in 1840 at a lecture to the Royal Swedish Academy of Sciences.1,4 Initially, he used it to distinguish between the peoples of ‘Slavic and Swedish origins’.4,77 But then, by
including additional measurements to quantify orthognathous and prognathous facial variation, he went further and attempted also to classify peoples of much greater geographical diversity. Eventually he attracted serious criticism for his cephalic index and for his craniometric studies from many other scientists including Rudolf Virchow and Pierre Paul Broca (1824-1880).\textsuperscript{77,78}

Anders Retzius was not the only anatomist and clinician to become fascinated by anthropology and archaeology. Rudolf Virchow (1821-1902) besides being a clinician, histopathologist and a politician not only founded a journal that came to rival Müller's Archive, (\textit{Archiv für pathologische Anatomie und Physiologie und für klinische Medizin} or Virchow's Archive) but was also at the forefront of developments in archaeology, anthropology and ethnology in Germany.\textsuperscript{5} In 1869 and 1870 Virchow founded the German Anthropological Association and the Berlin Society for Anthropology, Ethnology and Prehistory and founded \textit{Zeitschrift für Ethnologie} (Journal of Ethnology). Virchow was personally involved in archaeological fieldwork in Egypt, Nubia, the Caucasus and Asia as well as closer to home in northern Germany. Being the evidence-based scientist that he was he carried out craniometric studies of his own, as well as other studies on eye, skin and hair colour, denouncing the findings of Retzius and others and concluding that all Europeans represented an admixture of peoples and that each had their own origins and that there was no basis for Nordic, Aryan, German or any other racial superiority among them. But when it came to evolution and Darwinism, Virchow strongly opposed the theory of natural selection. He denied that there could be intermediate forms and in particular declared the implications of social Darwinism to be politically dangerous and antidemocratic. Virchow even won a public battle with Müller's younger student Ernst Haeckel (who was for a brief time his assistant) to have natural history and
evolutionary studies banned from the school curriculum on the basis it was, at this
time, unproven science. This was upheld in 1882 by the Prussian House of
Representatives. Virchow was determined to stick to the rigor of evidence-based
science but remained, however, open to the emergence of new evidence and wrote
at one point, "I must confess that to me it appears to be a scientific necessity to
examine the possibilities of changes from species to species".79

In 1872 Virchow examined the original Neanderthal fossil remains, discovered
in 1856 in the Feldhofer Grotto in the Neander valley near Düsseldorf. Virchow
(1872) confirmed his conclusions (made earlier from plaster casts) and further
dismissed the idea of these remains being evidence for a distinct fossil human
species. He reported the remains to be pathological with evidence of arthritis, rickets
and in the case of the cranium, being deformed through injury, premature synostosis
and senile hyperostosis.79 Virchow also pointed out that he felt a single specimen
was insufficient to make the claim for a primitive fossil precursor of Homo sapiens
and, moreover, to claim that the anatomical characteristics it showed could or would
have been passed on from one generation to the next. Later in 1894, Virchow also
dismissed the fossil remains of Pithecanthropus erectus discovered by Eugène
Dubois in Java in 1891 and 1892 as no more than a pathological femur wrongly
associated with the cranium of a giant gibbon.81 Dubois had borrowed the genus
name Pithecanthropus from Ernst Haeckel who had earlier proposed
Pithecanthropus alalus in anticipation of there being a missing link between great
apes and humans that would, he predicted, be found in the Far East, as Dubois
eventually did do, and not in Africa as Darwin had predicted. All this may have
further irritated Virchow given his previous disagreements with Haeckel about
evolutionary biology.
Virchow’s bias towards pathology has been put down in part to his earlier research into cretinism.\textsuperscript{79} In 1849 Virchow was appointed professor of pathology in Würzburg. At this time cretinism was a serious problem in Bravaria and Virchow had made a detailed study of skull growth in which he noted that a striking characteristic of cretinism is cranial deformation through premature closure of some sutures.\textsuperscript{79} Virchow’s apparently dogged refusal to accept the evidence for early fossil human forms and for human evolution was based, in his own view, not just on stubbornness and intransigence but rather on a lack of sufficient scientific evidence to substantiate this claim. He remained interested, curious and open minded and for the last 30 years of his life Rudolf Virchow collected skeletal material from all parts of the globe which he included in his pathological museum. Virchow’s pathology museum in Berlin eventually came to rival Müller’s comparative anatomy museum both in size and diversity.\textsuperscript{5}

Magnus Gustaf Retzius (1842–1919) was, like his father, a physician and an anatomist but is now best remembered as a neuroscientist and for his studies of the membranous labyrinth and the histology of the basilar membrane of the inner ear. Gustaf Retzius was appointed professor of histology at the Karolinska Institute aged just 35 where, like his father, he later became professor of anatomy. His work on teeth was limited but he did demonstrate, using fish and reptiles, the fine network of nerve fibers that run from Raschkow’s plexus into the odontoblast layer and dentine tubules.\textsuperscript{82} In 1908 his contribution to neuroscience was recognized by the Royal Society in London, who invited him to give the prestigious Croonian Lecture on “The principles of the minute structure of the nervous system as revealed by recent investigations”.
Gustaf Retzius also continued his fathers’ anthropological research, drawing much of it together and publishing it, still trying to unravel the origins and history of the Scandinavian peoples.\textsuperscript{1, 83, 84} In so doing, he continued to perpetuate a judgmental view of race that was unfortunately gathering pace across Europe and beyond, the consequences of which, anthropologists and anatomists everywhere remained completely blind to. In 1909 Gustaf Retzius, also now highly regarded as an anthropologist, was invited to give the Huxley Lecture at The Royal Anthropological Institute in London and to present his work on the “So-called North European Race of Mankind”.\textsuperscript{84} In the USA as well as Europe, respected scientists such as Henry Fairfield Osborn all too easily absorbed these studies as support for their views about eugenics.\textsuperscript{85}

The preoccupation of many early anatomists and anthropologists with racial classification is nowadays considered ill-informed and unacceptable. Originally, in recognition of his contribution to anthropology, the Swedish Society for Anthropology and Geography (\textit{Svenska Sällskapet för Antropologi och Geografi} founded in 1877) had, besides the Vega Gold Medal, established the Anders Retzius Gold Medal, but strong feelings about awarding a medal for outstanding achievements in modern anthropology in the name of Anders Retzius is now considered inappropriate and in 2015 led to the withdrawal of this medal. Today the cephalic index of Retzius has its place in studies of comparative primate anatomy and palaeoanthropology and although its original ill-conceived use remains deeply controversial and is widely challenged and questioned, Anders Retzius can still be regarded as one of the founders of quantitative anthropometry and craniometry,\textsuperscript{4} and of modern cephalometrics that nowadays underpins, for example, aspects of evidence-based clinical orthodontic practice.
Anders Retzius the Teacher

As a teacher of anatomy Anders Retzius believed it was his duty to train his students to think for themselves.

“In the Autumn of 1824 I began a course in microscopic and general anatomy for about twenty auditors, and continued in the Spring months with comparative anatomy, while in the meantime presenting the descriptive anatomy of the human cadaver” [translated from the original Swedish].

His son, Gustaf Retzius, wrote (cited in Larsell, 1924) that while still quite young he had once been allowed to listen to his father late on in his life give a lecture on the trachea and its structure and that he spoke,

“with a vivacity which for a man of sixty years must be phenomenal, with a youthful verve and enthusiasm, of which few teachers even in their prime are in possession”. “His mobile features made clear the shades of meaning with a clever mimicry. His hearers followed with intense attention they by no means arranged, but all through, spirited exposition. One immediately caught the contagion of zeal and laughed heartily at the original fancies which spiced the lesson, which had quite a different feel from that of the ordinary dry lecture.”

An early interest in comparative morphology and natural history originally inspired by his father Anders Jahan Retzius (1742-1821) never diminished and was part of family life. Again, his son Gustaf Retzius (and cited in Larsell) illustrates this well in an account of what family life was like, continually exploring the local flora and fauna together and surrounded by collections of all kinds at home.
“I remember even yet so well how a large human skeleton stood beside my bed, and how in the window were placed aquaria and jars with lizards and tree-frogs, indeed one of the bellowing giant frogs of Brazil, which when it got loose made room-high jumps. There were casks with young salmon-fry, whose further development my father studied. And each Spring when the ice broke up, he took me with him to Kungsholmbrunn, where we clattered down on the stone piers to the water's edge and gathered small water animals, infusoria, bryozoans, and worms, which we took home to the aquaria. I shall never forget my father's enthusiasm when he observed under the microscope the wonderful life which was unfolded in the water of these aquaria, and of which he with his spirited descriptive art tried to give me an inkling. I shall never forget his burning interest, his love of truth and the alert, keen look, concerning which a foreigner one time said that in case there was any proof needed for immortality, Anders Retzius' glance was such a proof.”

Quite late in his life in 1858, The Royal Academy of Science of Stockholm, of which he had long been a member, elected Anders Retzius as their president. His brilliance as a scientist had already been widely acknowledged by election to many academic societies. In October of that year he wrote to Charles Wilson that he “felt age creeping on” and that he “had now lectured in the Institute since 1824 and still found his greatest pleasure in teaching youth, and in directing the dissections”. Anders Retzius died on April 18th 1860 after a brief illness aged 63. Wilson (1861) in a very personal account of his life reported that he died of endocarditis that escalated suddenly over nine days, more than likely triggered by a volvulus of the small intestine. In his spare time, he was active in many things but had a particular love for his orchard. Erik Müller, cited by Olof Larsell, pictures
“a man of small stature and slight of frame, in simple working clothes, but with the distinguished mien of the patrician, who with mattock and spade labored diligently in his orchard where he sought outlet for his love of activity.”

Retzius, like so many dental anatomists, had always had a particular love of horticulture and introduced many new plants into Sweden.

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