

The varying morphology and aetiology of arterial aneurysms. A historical review

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Abstract

Swelling of the arteries of the extremities is an old disease and has been first reported in ancient Egyptian and Indian texts. The term 'aneurysm' has been introduced in the first century by Ruphus from Ephesus. From the beginning, distinction was made between spontaneous and posttraumatic aneurysms. Spontaneous aneurysms were mostly considered to be related to debilitation due to exertion. While the majority of traumatic aneurysms were due to accidental pricking of an artery during bloodletting.

Arterial aneurysms of the aorta and its side branches were first reported in the 16th century. However, it has to be taken into consideration that post-mortem exams were not done before the Renaissance. Most aortic aneurysms were saccular, eroding the neighbouring organs. This is typical for syphilitic aneurysms. However, although suspected, syphilis has not been recognized as the primary cause of aortic aneurysm until the end of the 19th century. In the mean time, fusiform 'degenerative atherosclerotic' aneurysms, especially on the abdominal aorta, became more frequent. It is now generally accepted that the cause of this aneurysm is multifactorial and exciting scientific research is actually done to elucidate this complex pathology.

Key words: history, arterial aneurysm

Arterial aneurysm (AA) has a pathology with a "rich" past, and the recent evolution in the knowledge of its pathogenesis and surgical therapy is fascinating. AA has been recognised since antiquity. Until very recently, the aetiology remained unclear and controversial. Currently, aneurysm formation is invariably associated with severe atherosclerotic damage of the arterial wall, and therefore AA has been traditionally regarded as a consequence of atherosclerosis [1]. However, was atherosclerosis always the underlying pathology? And, moreover, is that indeed a correct description of the etiology?

As with many diseases, the recorded history of aneurysms starts in ancient Egypt. In the Ebers Papyrus of Ancient Egypt, (> 1500 BC), the author describes swellings of the conduits (metu). It is possible that he was speaking of an arterial aneurysm, because the heart is connected to the body by the metu. However, the text is too vague to be certain. In the second half of the 19th century, thousands of mummies were dissected, albeit mostly with little scien-

tific seriousness. They did show that arteriosclerosis occurred amongst the ancient Egyptians, but remnants of calcified aneurysms have not yet been found.

Sushruta (\pm 600 BC?), a surgeon in Ancient India, was the first to distinguish between "post-traumatic" and "spontaneous" arterial swellings. According to Sushruta, pulsatile swellings of the vessels were caused by bodily tumours, related to debilitation due to exertion, especially in tired and weakened persons.

Greco-Roman medicine is the cradle of our Western medicine. In the writings of Hippocrates, there is nothing to be found concerning swellings of blood vessels. The term "aneurysm" was probably written down for the first time by Rufus of Ephesus, (110–180 AD) and is derived from the Greek *ana* (on top of, towards the outside) and *eurunô* (widening). Galen, who mentioned Rufus in his treatise on unnatural swellings, described the spontaneous aneurysm as an arterial dilatation of the open side holes at the mouth of the arteries. The

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Figure 1. First illustration of a traumatic aneurysm after blood letting. Matthaus Purmann (1699) in: *Chirurgia Curiosa*

description is unclear, but it fits into the framework of Galen's concept of the vascular system (it would be wrong to speak of a Galenic concept of circulation). Galen probably encountered only post-traumatic aneurysms. In those days, and until the 18th century (Figure 1), post-traumatic aneurysms were generally the result of accidental piercing of an artery during blood-letting. All superficial veins, especially the veins at the bend of the arm, were considered suitable for blood-letting, and accidental pricking of an adjacent artery was not uncommon. Incisions of small arteries and veins around the ear and in the temporal region were also customary. This procedure might have been the cause of the frequently reported aneurysms in the head, and is still part of traditional medicine in some African tribes.

After the fall of the Roman Empire in 410, there was little interest in medicine in the West. In the East, the Greco-Roman medicine became Byzantine medicine. The encyclopædia of Oribasios of Pergamum (325–403) gives additional information regarding arterial aneurysms. Oribasios described the spontaneous aneurysm as a cylindrical swelling with a lot of foreign bodies deposited on the walls, while the traumatic aneurysm is saccular, round in form and can be ligated at its base. According to Oribasios, when the fingers are pressed

on a traumatic aneurysm, an indistinct sound is heard. Let's assume, for the sake of the story, that the foreign bodies are arterial wall calcifications and that the indistinct sound is a thrill over an arterio-venous fistula. Two centuries later, Aetios of Amida (527–565) was the last eminent Byzantine physician. According to Aetios, a well-vascularised goitre was also an aneurysm, which he called bronchocele. This erroneous diagnosis was still being made in the 17th century.

Fortunately, the Arabs, who flooded like a tsunami over the greater part of the Mediterranean region a few centuries later, preserved the old writings, translated them, further worked on them, and sometimes, unfortunately, altered them. Avicenna (980–1037) called the aneurysm "the mother of blood", whilst the famous surgeon Abucalsis (936–1013) described the spontaneous aneurysm as a swelling at the mouth of the artery, an idea he took from Galen. For more than a thousand years, no new opinions developed regarding the causes of this probably rather rare pathology up until the 16th century, when aneurysm of the internal arteries (the aorta and its side branches) was reported as a new phenomenon by Jean-François Fernel, professor at the Sorbonne (1542). It was postulated by Fernel that aneurysms were due to a dilatation of all coats of the arterial wall. However, for the next four centuries, most reported aneurysms were saccular, filled with a coagulum-like boiled lard (dixit Andreas Vesalius) and covered on the outside with a calcified shell, which, according to Ambroise Paré, was a gift of God to protect the patient against a fatal rupture.

The "new" aortic aneurysm was mostly located on the thoracic aorta and especially on the aortic arch (Figure 2). The aneurysms grew slowly, consuming the surrounding organs and bony structures, whereupon a fatal rupture followed. Ambroise Paré mentioned that the aortic aneurysm occurred primarily after treatment for syphilis because sweat cures and mercury administration caused the blood to boil and thus to seek an escape route. Stress of the arteries by hard work, loud shouting, singing, trumpet playing, and pressing, as in childbirth, were other possible causes. The patients undoubtedly welcomed these ideas, for "work" was then, too, considered the cause of much misery and many diseases. The reality, however, was less prosaic: indeed, the aortic aneurysm was caused by syphilis, a new disease that probably had been successfully imported from the New World by the crew of Christopher Columbus. But the truth appeared only at the end of the 19th century.

Giovanni Lancisi (1654–1720), professor at the Sapienza University in Rome and personal physician of

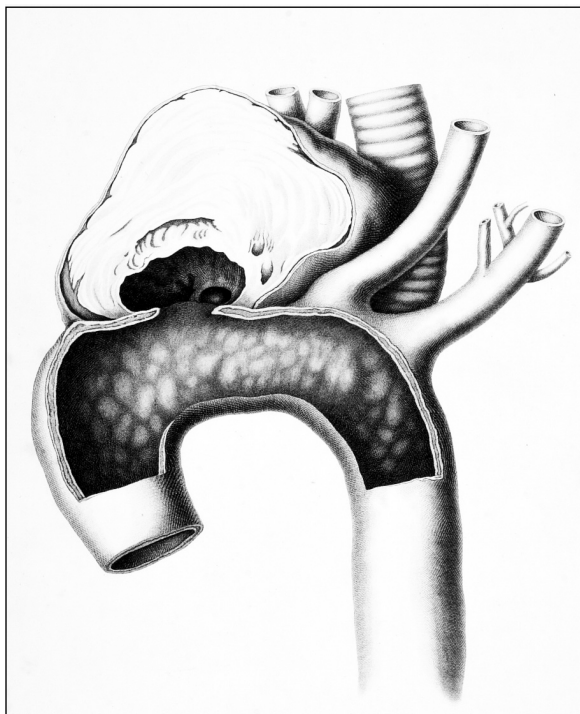


Figure 2. Sketch of a saccular aneurysm on top of the aortic arch. Joseph Hodgson (1815) in: *A Treatise on the Diseases of Arteries and Veins*

three popes in succession, became the first expert in aneurysms. He has been rightly called the first epidemiologist. He described the saccular aneurysm with a narrow entry port as a "legitimate or genuine aneurysm", in contrast to the "spurious or illegitimate fusiform spontaneous aneurysm". In his discourse "de Motu Cordis et Aneurysmatibus", he listed the then current possible causes of aneurysm: stress from the inside by impetus of blood, external stress of the arterial wall due to work, inherent weakening of the arterial wall, and, finally, the impact of bodily fluids (humours) on the vessel wall. Benign watery humours from the hypochondrium or from the womb and malignant lymphatic humours were thought to generate various kinds of diseases, including arterial aneurysms. In gluttons and in patients with syphilis, the lymphatic humour could primarily produce congestion in the bones and the ligaments, secondarily penetrating the outer parts of the artery. This is the first clear reference to syphilis as the cause of "legitimate or genuine" aortic aneurysms.

The search for the pathogenesis of aneurysms continued during the 18th century, the era in which the foundations of scientific medicine were first established, which is called the adolescent period of modern medicine. The names of Morgagni, Monro and Hunter should be recalled here.

Giovanni Morgagni (1682–1771), anatomist and surgeon at the University of Bologna, was also convinced of the luetic origin of the aortic aneurysm. In his book "De Sedibus et Causis Morborum per Anatomem Indigatis", he described in detail the ruptured saccular aortic aneurysm in prostitutes and lecherous wastrels. He also described the syphilitic aortitis with its thickened and expanded vessel wall. For Morgagni, it was clear that the eroding particles that "disturb the spirit of patients with venereal diseases" do not stop at the vessel wall. Morgagni is still (and correctly) considered to be the first anatomopathologist. In his monumental work, he reported on 700 clinical cases supplemented by autopsies, generally performed by his master Antonio Valsalva. The ideas of Lancisi and Morgagni received little response. Hard work, stress of the vessel wall, and generalised weakness were more plausible for the *doctores medicinae* and certainly more attractive for the patients.

In the 18th century, Great Britain was the Mecca of this budding science. In 1733, Donald Monro, an anatomopathologist at the University of Edinburgh, described the adventitia, media, and intima of a vessel wall [2]. Here he demonstrated that an aneurysm was caused by dilatation of the three layers, and not by a local tear, as was until then quite generally accepted. The Hunter brothers of London agreed with him. William Hunter (1718–1783) distinguished the "true" from the "false" aneurysm in the modern sense of these medical concepts. For William, true aneurysms, formed by dilatation of the whole arterial wall, really existed (Figure 3). He also stressed the role that a morbid, probably universal pathology had a part to play in the formation of arterial aneurysms, but he did not comment on the nature of the disease. William Hunter was also the first to describe the post-traumatic aneurysm as the late consequence of an arterio-venous fistula.

Also for John Hunter (1728–1793), the famous anatomist and surgeon, an aneurysm was the result of "a disproportion between the force of the blood and the strength of the artery". For John Hunter, syphilis was not the direct cause of the aortic aneurysm, but at most a risk factor. Exactly 25 years after the appearance of the first edition of Morgagni's *De Sedibus et Causis Morborum*, John Hunter passes off the question of syphilis as a cause of arterial aneurysm with the remark that syphilis does not affect the brain, the heart, the stomach, kidneys nor other viscera; although such cases had been described. Apparently, in those days, arteries were considered to be "internal viscera".

Antonio Scarpa (1752–1832), anatomist and surgeon at the University of Pavia, became, in the first half of the 19th century, the new authority in this field with his

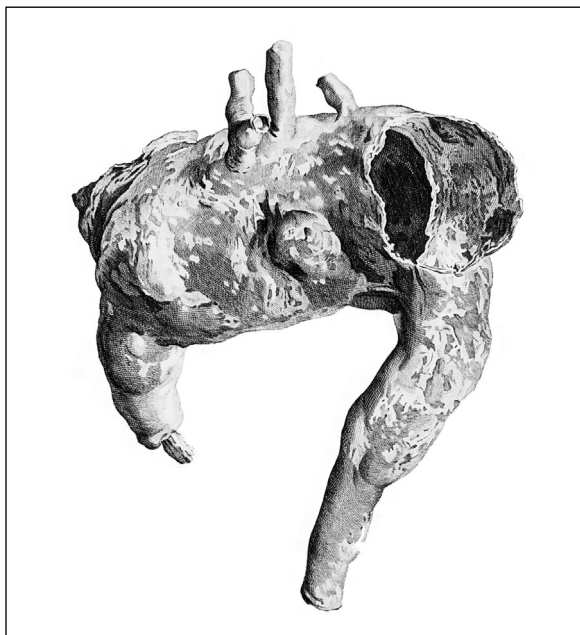


Figure 3. Ruptured fusiform aneurysm of the aortic arch. Willam Hunter (1757) in: *Med Obs Inq Phys*. London 1: 323–357

splendidly illustrated book „Sull Aneurisma” (1804). For Scarpa, it was obvious that all aneurysms were saccular, and caused by a local tear in the intima and media of the vessel wall (Figure 4). He described the diseased vessel wall as „thickened, squamous, fatty and ulcerated”, a pathology that, in his opinion, occurred more often amongst patients with a venereal disease. This description approaches the pathology that one would later describe as atheromatosis. Fusiform dilation of an artery was, according to Scarpa, not an aneurysm, because no clots appeared in it. Actually, it was a semantic discussion in which Scarpa was probably not wrong, if the reference was to the Greek meaning of “aneurysm”.

Meanwhile, the clinical knowledge of aortic aneurysms achieved its highest niveau, and detailed clinical essays came from England, Ireland and France. Corvisart and Laennec achieved diagnostic eminence by carefully examining more patients and corpses than any physician had done previously. They dealt with the same type of pathology: slowly growing saccular thoracic aneurysms, finally reaching huge dimensions with protrusion through the chest wall, compression of neighbouring organs and erosion of the ribs, sternum and vertebrae. Both authors cited syphilis as a risk factor, but not as the primary cause. According to Corvisart, the majority of the aneurysms were dilatations of the whole vessel wall due to the impetus of the blood or to an obstruction „even in the capillaries” distal to the arterial dilation. Laennec agreed with the theory of Scarpa on the pathogenesis of the aneu-

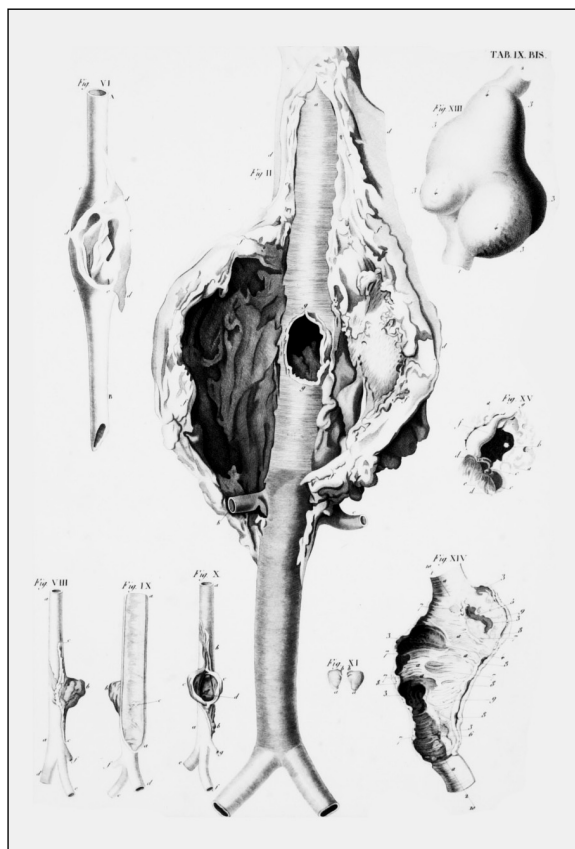


Figure 4. Ruptured saccular thoracoabdominal aneurysm. Antonio Scarpa (1804) in: *Sull'Aneurisma*. Pavia

rysms stating that weakening of the arterial wall by stomatous, ulcerative and squamous degeneration was the main cause of aneurysm formation.

Syphilis was, as it were, intentionally ousted as a possible cause of the aortic aneurysm. Some fanciful conjectures on the causes of aneurysm formation such as excessive sexual intercourse, prolonged holding of breath, and tight neck collars were also proposed. In 1869, there appeared a study in the famous medical journal *The Lancet* on the frequent occurrence of thoracic aneurysms amongst infantrymen. A thoracic aortic aneurysm was, according to the author, caused by stress on the chest during exercise and by constriction of the neck by tight collars! The truth was humiliating: infantrymen were routine visitors of houses of prostitution and many had signs of tertiary syphilis by the time they were in their fifties. Furthermore, in the second half of the 19th century, at the University of Leiden, one could be promoted to *Doctor Medicinae* of thoracic aneurysm without even mentioning syphilis as a possible cause. The eminent promoters should have known better!

Aneurysms of the femoral and popliteal arteries were very common in the 18th and 19th century. In 1847,

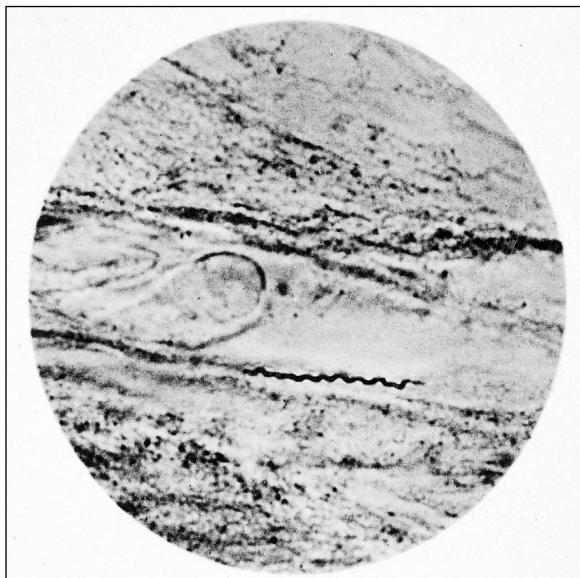


Figure 5. Spirochete in the wall of a diseased aorta. Karl Reuter (1906) in: *Ztschr f Hyg und Infektionskr*, 54: 49–60

the first extensive study on this subject was reported with a review of the English literature over a period of 50 years [3]. The 551 patients included in this review were mostly working-class men aged between 30 and 55. An aneurysm of the popliteal artery was reported in 137 (25%) of the patients. This pathology was, probably correctly, ascribed to the constriction and constant load on the arteries of the lower limbs in horsemen, coachmen, footmen who stand behind carriages, and in young men, like dock labourers, who had physically demanding jobs.

Meanwhile, the truth concerning the formation of aortic aneurysms could no longer remain hidden. After the pioneering work of Pasteur and Koch, many set out zealously in search of all forms of bacterial infection. Was the aortic aneurysm then a manifestation of tertiary syphilis? The first indication came from F. Welch, a pathologist at the Army Medical School in Great Britain. His *post-mortem* studies, published in *The Lancet* in 1875 [4], showed that two out of three corpses with an aneurysm manifested pathognomic signs of syphilis, whilst no aneurysm was evident in 106 corpses without signs of syphilis. Welch's article was met with great scepticism until finally, in 1906, *Spirochaeta pallida* (now called *Treponema pallidum*) was discovered in the wall of a syphilitic aorta [5] (Figure 5). Also, the new Wasserman-Bordet test (1906) showed that 90% of patients with an aortic aneurysm suffered from syphilis. The generally fusiform aneurysms of the femoral and popliteal arteries did indeed turn out to be non-bacterial but degenerative pathologies [6].

Meanwhile, the knowledge of arterial disease progressed rapidly with the advent of the microtome and improved microscopes. In 1893, Joseph Coats of Glasgow [7] postulated that atheromatous patches within the intima were projected by the pressure of blood against the media at every systole of the heart, and that the consequent injury and atrophy of the media was the most important causative factor in aneurysm formation. The increased incidence of the fusiform "degenerative atherosclerotic" aneurysm, which generally affected the infra-renal aorta, was apparently due to the increase in human life span, as elderly people are more susceptible to degenerative vascular disorders. Atherosclerosis was initially considered a consequence of sins and faults of modern civilisation with, of course, syphilis as an important risk factor for atheromatosis and for aneurysms. Rudolph Matas (1860–1957), the American leader of vascular pathology, was the champion of such theories with statements like this one: "The sins, vices, luxuries and worries of civilisation clog the arteries with the rust of premature senility, known as arteriosclerosis or atheroma, which is the chief factor in the production of aneurysm." According to Matas, the Negro slaves, after their emancipation, became, because of their new dissolute life, affected just as much by vascular diseases as their former white masters [8]. William Osler (1849–1919), professor at Oxford University and probably the most prestigious academic around the turn of the century summarised the causes of an aneurysm in three unambiguous words: "Bacchus, Venus, and Hercules" being "Sex, drink, and dissolute living". Fortunately, due to better prevention and appropriate anti-bacterial treatment, syphilis disappeared in the first half of the 20th century, and with it also the syphilitic saccular aortic aneurysm, like snow before the sun.

In the second half of the 20th century, the biomedical sciences made enormous advances. This led to a better understanding of the pathogenesis of the so-called "atherosclerotic aneurysm", which turned out to be a disease of the matrix of the media and the adventitia, whereas atherosclerosis is primarily a disease of the adventitia. In 1962, collagenase, an enzyme that affects collagen, was discovered by Gross and Lapiere [9]. But it didn't stop there. We now know that some specific enzymes called metalloproteinases affect elastin and collagen. These enzymes start to act in inflammatory conditions that are activated by environmental factors, such as nicotine abuse. Some metalloproteinases are found in large amounts in the intra-luminal coagulum and in the media and adventitia of the aneurysm. They are responsible for the further degradation of the arterial wall and growth of the aneurysm [10].

Recently, also, a better understanding has developed of the familial occurrence of the degenerative aneurysm. The first publication on this appeared in 1977 [11]. This concept later attracted the attention of surgeons who hoped to be able to identify the familial aneurysm with echography, and thus to treat it in time. The frequency of abdominal aortic aneurysms in first-degree relatives is 15–19% compared with only 13% in unrelated patients [12]. According to Verloes and colleagues [13] the major determinant factor in the appearance of an AAA could be an inherent defect, possibly of collagen type III or of other components of the connective tissue matrix. The genetics of non-syndromic familial aortic aneurysms remains obscure and much work has still to be done.

In the meantime, learned scientists are enthusiastically searching for an effective pharmacological treatment of aortic wall deterioration. From recent experimental studies it appears that aneurysm stabilization by transforming growth factor-beta 1 may represent a new treatment concept [14]. The end result may, together with a progressive change in our smoking habits, also call a halt to the arterial aneurysm. And this will close another chapter for the surgeons, both literally and figuratively. Surgeons should not be concerned: they will also cross that bridge.

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