

# Texts and Documents

## THROMBO-EMBOLIC DISEASE AND HEART-BLOCK IN VESALIUS

by

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WHILE working on the history of coronary disease and myocardial infarction I searched the older medical literature for references preceding the definitive diagnosis. The information gathered from the *Fabrica* under the chapter 'Heart' is useful—more detailed, but hardly more revealing than the anatomical description of the coronary vessels by Galen (*On Anatomical Procedures*).<sup>1</sup>

However, a much more interesting passage was added to the second edition of the *Fabrica* (1555), interpolated in a section which deals not with the heart and its vessels, but with the anatomy of the cranium (Lib. I, cap. 5, p. 24). The information gathered from this important though brief passage is rounded off in Vesalius's *Anatomicarum Gabrielis Falloppii Observationem Examen*, 1564, p. 154. Both of these Vesalian passages must be put together to reconstruct an unusual case history with a remarkable pathological finding. Vesalius's digressions from anatomy to morbid anatomy are not infrequent and I alluded to one of them in a previous paper.<sup>2</sup> This inclusion of morbid manifestations in his anatomical works sheds light on Vesalius's life history and helps to explain the mystery of his renouncing the anatomical chair of Padua. In a relatively brief endeavour he spent his earlier years<sup>3</sup> in producing the *Fabrica*, an example of scientific method almost freed from Galenic teleology. However, it is evident from his Preface that he saw anatomy as the necessary foundation of rational medicine and surgery, and not as a theoretical and purely scientific discipline. He became court physician, with all the limitations of this rank. Nevertheless, in the first years of his court service Vesalius did have the opportunity to work as a physician and to verify his diagnoses by autopsies. The sad feeling expressed in the last sentences of his *Anatomicarum . . . Falloppii . . . Examen*, where he complained of not having occasion to undertake a dissection at the imperial palace, where he could not conveniently obtain even a skull, refers to the last period of his court career (27 December 1561). The enigma why Vesalius resigned from his anatomical chair remains unsolved. A recent publication<sup>4</sup> brought a new attempt at explanation: his position as anatomist did not give him full satisfaction, either socially or academically, or even financially. It is still admitted that his resignation is to be attributed primarily to emotional causes with a psychosomatic background, but it is also possible that Vesalius was drawn towards the actual practice of medicine and surgery. At least in the years when Vesalius accompanied his sovereign, Charles V, chiefly in Brussels and Regensburg, until 1555, when Charles V abdicated in favour of Philip II, he often had occasion to treat members of the Court, to be called into consultation, especially in surgical cases, and sometimes also to perform autopsies. Such was the case of 'the most noble and also learned Dominus de Imersel' to whom Vesalius refers in both passages mentioned above. Their brevity is deplorable, for clinical and pathological detail is lacking, but so also are 'discussions, theoretical and vague', as in the six Vesalian 'Consilia' which have been preserved (Harvey Cushing, *A Bio-Bibliography of Andreas Vesalius*, New York, 1943, p. 171–81).

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The translation of the first passage from the *Fabrica* did not present much difficulty (except for the exact evaluation of the word *ictus*) since here the peculiar features of the Vesalian Latin style were not so apparent. The second passage, however, from the *Anatomicarum . . . Falloppii . . . Examen*, shows the arbitrary and difficult style which I encountered while working on the translation of another item from this book, bearing on the valves of the veins.<sup>5</sup> I wish to thank Dr. F. N. L. Poynter and Mr. R. J. Durling for their friendly assistance in the translation. The rendering of the passages into English follows, together with the original Latin.

Almost at the same time, our astonishment was roused by the [anatomized] heart of a most noble and also learned man; in the left ventricle of his heart we found almost two pounds of glandulous\* (though somewhat dark) flesh, whereby the heart was distended like a belly† around this flesh and similar to the brain of the above-mentioned girl. This man was, before his death, in a persistent melancholic and somewhat wakeful state, his pulse being really astonishingly unequal and changeable, manifestly demonstrating the contraction of the artery. For, during many months before death (though he walked about generally as a fit person), it was observed that the pulse—or more accurately the artery—was contracted, and remained constricted during the interval of three or four pulsations, or beats, as if labouring upon the expulsion of the blood. Indeed, during the last weeks of his life it was sometimes possible to palpate out of a [time-] interval of nine beats only three or two dilations of the artery. Then, to the very time of his death, he possessed enough of animal faculties as to the principal functions of the soul, death being not so nearly related to a fault of the heart as to the gangrene of the left leg; the gangrene, naturally, was provoked by the impediment of the arterial pulsations, as if these beats, intermittent through the fault of the heart, were insufficient in providing the natural heat for the legs; even more so as some years ago the artery leading to the fibula had been contused by a bullet.

Quemadmodum eodem fere tempore non vulgariter nos mirare coegit, nobilissimi et una doctissimi viri cor, in cuius sinistro ventriculo glandulosae (sed subnigricantis interim) carnis libras propemodum duas reperimus, corde instar uteri, ac puellae illius cerebri, ad eius carnis molem extenso, et homine ante mortem habitu utcunque melancholico, et admodum vigili, et pulsu praedito miris sane modis inaequali et vario, quique arteriae contractionem manifeste ostendebat. Ita enim multis mensibus ante mortem (quum tamen alioquin veluti sanus obambulare) pulsus aut arteria potius contrahi visa fuit, ut trium aut quatuor pulsationum ictuum've intervallo contracta maneret, velutque expulsionem moliretur. Imo postremis vitae septimanis, ex novem ictuum intervallo tres tantum aut duo dilatationes arteriae, tactui subinde occurrerunt. Dein animalis facultas cum principis animae functionibus ad mortem usque satis constabat, quae non tam ex cordis vitio proxime obvenit, atque ex sinistri cruris gangraena, quae ab impedito arteriae pulsu occasionem perinde duxit, ac si intermissi illi ex cordis vitio pulsus, cruris illius nativum calorem parum apte eventillasset; potissimum quum ex sclopeti ictu ante annos aliquot ipsi vitiata esset arteria quae fibulam petit.

Vesalius, *Anatomicarum Gabrielis Falloppii Observationum Examen*, Hanoviae, Typis Wecheliani apud Claudium Marnium et heredes Ioan. Aubrii, 1609, pp. 236–7.‡

Since I have already discussed with you the nerves of the heart, there is no need for me to refer to them again here, unless I may recall to your memory those [cases] who have long borne an astonishing glandulous fleshy mass in the left ventricle of the heart, or other affections, and have died from gangrene of the legs or of some other part, evidently because their innate

\* I have retained the word glandulous (glandulosae carnis) eliminating the more common expression 'glandular'. By doing so I took advantage of the *New English Dictionary* which lists in older English literature the adjective 'glandulous' for glandlike, but not glandular in essence.

† Corde instar uteri.

‡ I have used the rare Hanau edition, Wellcome Historical Medical Library, printed Catalogue (1962) No. 6564; reproduction of the title-page in Cushing's *Bio-Bibliography of Andreas Vesalius* (1943), fig. 89. Cushing's census lists but four copies known, and not that in W.H.M.L.

vital heat could not be recreated on account of the scarcity of the pulsations, before they complained of some sad feeling or of pain in the heart, and had not the pulse persuaded [one] that some fault lay hidden about the heart, nobody would have considered heart disease before death. Several imperial physicians saw an example of this same kind, who as they had been called in to the most noble and learned Master de Imersel to treat, in the first instance, a gangrene of his leg, so they were present also while I examined [i.e. at the post-mortem] his heart. For when they saw in the same year the heart of a servant of the Master de Mol, whose gangrene had a similar origin, we amputated first his leg below the knee, and then his forearm at about its mid-length a few days before his death (though meanwhile with little hope of success). But indeed, these [things] have another treatment and that [treatment], at least as I think, a very opportune one, not to say supremely necessary, to the use and precepts of the art of medicine.

Quia iam antea, de cordis neruis tecum egi, non est quod de illis papyrum hic occupem; nisi illi ad memoriam tibi vocandi sint, qui in sinistro cordis ventriculo miram glandulosae carnis molem, aliosve quosdam affectus diu gesserunt, & ex crurum alteriusve alicuius partis gangrena (quum scilicet illius nativus calor ob pulsuum penuriam recreari non posset) mortui sunt, priusquam de aliquo tristi in corde sensu doloreve, conquererentur, & nisi pulsus, circa cor vitium aliquod latitare persuasisset, de cordis morbo, ante mortem, ne cogitatum quidem fuisset. Huiusmodi exemplum viderunt plerique Augustani medici, qui ut ad nobilissimum & iuxta doctissimum Dominum de Imersel adhuc viventem, cruris gangrena affecti in primis occasione, vocati erant, ita quoque mihi cor illius perlustranti, astitere. Vti etiam eodem anno cor famuli Domini de Mol spectarunt, cui gangrenae item causa, primum crus sub genu, & dein manum circa medium longitudinis cubiti aliquot ante mortem diebus serra (etsi interim exigua spe) absecuimus. Verum haec aliam tractationem, & eam sane quantum reor, ad artis medicae vsum praeceptaque, imprimis opportunam, ne dicam summe necessariam, habent.

In examining both of these accounts and taking into consideration the accumulated historical evidence as well as the more recent knowledge of cardiology, we may justly make the following deductions.

1. Vesalius assumed that '*a sad feeling and pain in the heart*' is associated with some form of heart disease. He reported that the patient, de Imersel, died before some sad feeling at the heart became manifest, and, had not the irregularity of the pulse indicated heart disease, nobody would have thought of it. Apparently Vesalius inferred that precordial pain does denote some disease, this narration having preceded Heberden's masterly description by more than two hundred years. The narration in the *Fabrica* stressed the fact that the patient was able to walk about ('obamulare') like a healthy person. This detail, in the very short report, seems to imply Vesalius's notion that a person afflicted with a diseased heart of the type of '*tristi in corde sensu doloreve*' would have not been capable of free ambulation. The precordial pain without dyspnoea was one of the constituents of the diagnosis stressed in the early description of ischaemic heart disease.

2. The striking post-mortem finding of a *big fleshy mass in the left ventricle* of the heart is obviously an intra-cardiac parietal or lateral thrombus, possibly embedded in a partial aneurysm of the heart. The details make this very probable and they preclude taking the finding for a 'heart-polyp'. The '*polypi cordis*' were described many times in the older medical literature, but they proved to be agonal artefacts of no pathological significance. Vesalius's fleshy mass or mole has features of a real thrombus. Since the description is so brief, there is no possibility of more precise pathology. The state of the valves has not been reported and no evidence is brought out as to the existence of mitral stenosis which could have explained some form of arrhythmia and the occluded vessels of the leg (systemic arterial embolism).

In the absence of fuller clinical and anatomical indications it is perhaps safer to

admit an arteriosclerotic thrombo-embolic disease. The description was given by Vesalius long ago before the concept of thrombosis and embolism was presented by Virchow in several publications beginning 1846. As to arteriosclerosis, it existed in ancient Egyptian mummies<sup>6</sup> which have been studied histologically quite extensively since 1868, and it was beautifully depicted by Leonardo da Vinci. However, the first adequate description and illustration of the 'dis-organization of the arteries and especially the internal coats' was given by Scarpa<sup>7</sup> in 1804, while the name arteriosclerosis was coined in 1833 by Lobstein<sup>8</sup>, who tried also to develop the pathogenesis and to differentiate arteriosclerosis from inflammatory processes.

In the passage from the *Anatomicarum . . . Falloppii . . . Examen* Vesalius does not restrict himself to the mention of his impressive clinico-pathological case, that of Imerisel, but adduces another, that of the 'famulus' of the Master de Mol. Again there is a finding of thrombo-embolic disease, in which the reference to the heart is shorter, and limited to the statement that 'his gangrene had a similar origin' (cui gangraenae item causa), i.e. depending on the heart disease.

The inclusion of a second case shows that Vesalius attributed a more general significance to his finding. While the word 'famulus' means a servant at large and not a younger one (as the modern German usage likes to name a final-year medical student working at a hospital under the guidance of a physician), it can be supposed that Vesalius adopted the same usage (cf. NED: attendant; esp. on a scholar or a magician. These attendants were mostly younger). Under this assumption the servant of de Mol may have been younger, more prone to active rheumatic heart disease, vegetations of the valves, and to a spread of detached thrombi causing systemic arterial embolism. Indeed, it is reported that this 'famulus' had a gangrene of his leg, then of his forearm, which substantiates the proposed retrospective diagnosis.

An interesting historical parallel to Vesalius's cases is found, much later, in the printed lectures of G. Dupuytren<sup>9</sup> (1839), who described gangrene coexisting with disorders of the heart (enlargement, yellow and black fibrinous clots, ossified coronary arteries) and the great arterial trunks. Dupuytren's contribution has been exhaustively dealt with in a recent paper by A. Buzzi.<sup>10</sup> Neither Dupuytren nor Vesalius had the benefit of the support given to later scholars by the concept of thrombosis. So Dupuytren describing coronary 'ossification' did not consider the same etiology for the morbid state of the arteries in the limbs and he took it for an arteritis which is an inflammatory condition. While Vesalius was fortunate in finding an important and spectacular pathology, apparently a huge thrombus in a heart-aneurysm, he failed to describe the underlying pathology of the coronaries leading to impaired nutrition of the myocardium; or a thrombo-embolic phenomenon in mitral stenosis in the sketchy record of the 'famulus'.

As to the treatment given to the unfortunate 'famulus' of de Mol, Vesalius censured the exclusive application of an emergency amputation. He, however, was discreetly silent on what other treatment was to be given in a period when no anti-coagulants were available to prevent further spread of thrombo-embolism, nor anti-rheumatic agents and steroids in case of rheumatic disease, nor penicillin for subacute bacterial endocarditis, nor digitalis or anti-shock treatment in the advanced stage of the disease. At any rate Vesalius had reason enough to think that another treatment was necessary, more 'opportune to the use and precepts of the art of medicine'.

3. The third cardiological point to be discussed on the basis of the Vesalian passages quoted is that bearing on *irregularity of the pulse*. Here, in both passages, Vesalius did not commit himself and did not use for the description of the pulse anomaly any type

of the Galenic terminology,\* which was very well known to him and often mentioned in medical books of the sixteenth century. Not even the intermittent pulse was mentioned, although from Galen on (Kühn IX, 294) it was regarded as most dangerous and was often referred to by Renaissance authors (Amatus Lusitanus,<sup>11</sup> Petrus Salius Diversus<sup>12</sup> and many more).

The diagnosis of the irregularity named since Galen 'pulsus intermittus' found the most warm acceptance among Renaissance and later physicians, almost as the contemporary diagnosis of auricular fibrillation promulgated in Britain chiefly by Sir Thomas Lewis. This form of arrhythmia has been illustrated by Galen in his case history of the physician Antipater,<sup>13</sup> which has recently been published by R. E. Siegel,<sup>14</sup> and further discussed<sup>15</sup> by me in an additional note. During the last three months, in pursuing a study of a cardiological item without special relevance to the Antipater case, I came across eight references to it in the literature between the sixteenth and twentieth centuries.<sup>16</sup> Instead of the term 'arrhythmia' Vesalius used more general and less scholarly expressions: in the *Fabrica* 'unequal and changeable' with the addition of 'really astonishing' (miris sane modis inequali et vario), and in *Anatomicarum . . . Falloppii . . . Examen*, 'scarcity of pulsations' (pulsuum penuriam). In this way Vesalius escaped the Procrustean bed of the school terminology in which the phenomenon described would not fit.

Moreover, the description of the pulse sequence in the *Fabrica* is an early example of quantitative relations and records in the history of medicine, thus heralding later quantitative methods in biology. Vesalius stated that 'it was sometimes possible to palpate out of an interval of nine beats only three or two dilations [radial pulses] of the artery'.

The interpretation of this last phrase depends upon the proper meaning of the technical word 'ictus' in Vesalius's time and in ancient medicine. That Vesalius used 'ictus' for heart- or apex-beat is highly improbable, since we have never come across this meaning in Renaissance and earlier medicine. Besides, Vesalius did not say that only 2–3 radial pulses could be palpated during nine heart beats (which would induce one to think of ectopic extrasystolic beats, or frustrate contractions), but that 2–3 pulses could be palpated in the period (intervallus) of nine beats: *ex novem ictuum intervallo*. This formulation strongly recalls that of Galen (Kühn VIII, 456: 'in ictuum intervallo'). Moreover, Galen himself gives the definition of ictus as 'movement of the artery occurring on palpation' (*ibidem*). In a similar way Pliny uses the word 'ictus' for pulse (XI 37, 88, p. 209): 'ictus creber aut languidus'. The dictionaries render 'ictus', in medical usage, always with pulse.<sup>17</sup> For the later periods the most widely used dictionary is that of B. Castelli. This lexicographer gives the following explanation of 'ictus'; it is used for the movement of the artery in [the process of] pulsation, which is called the diastole of the arteries.<sup>18</sup> On philological evidence, and being as yet unable to find in older literature any information that the word 'ictus' was used as apex-beat, or that the heart-beat was referred to in the records of clinical examination, we think it safe to assume that Vesalius meant by 'ictus' really the pulse.

On this assumption the case could be compatible with intermittent atrio-ventricular block, while the word 'sometimes' in the report rules out a persistent block. In a paper on the history of heart-block Flaxman<sup>19</sup> quotes Gerbezius, on page 117: 'pulse so slow, that before a subsequent pulse followed the preceding one, three pulsations would have certainly passed in another healthy person'. Vesalius is more correct in comparing the scarcity of the pulsations not with the pulse rate of 'another healthy person', but with the normal rate of the patient, when in a time-interval of expected

\* p. intermittens, intercalens, caprizans, dicrotus, etc.

nine pulsations only three or two could be palpated. Gerbezius's and Morgagni's cases are connected with fits of unconsciousness, while Vesalius described a case without these Adams-Stokes episodes, which could properly have been diagnosed only in modern times with the advent of electro-cardiography. The previous historians of heart-block could easily overlook the Vesalian report since it is inserted in the chapter on the cranium, where a cardiologistical item was not expected to find its place.

We have followed Vesalius for a while in his capacity as 'cardiologist'. As usual he reveals himself in some clinical costume when he takes a digressing step from his vocation as anatomist. Neither of the passages quoted is generally known. However, they did not escape totally the attention of Vesalius's most informative biographer so far, M. Roth,<sup>20</sup> who devoted to them eleven lines. Likewise, Testa,<sup>21</sup> in his early textbook of heart diseases, quotes in the historical preface the passage from Vesalius's *Anatomicarum . . . Falloppii . . . Examen* in the Latin original in extenso without much comment.

The discussion has tried to prove that Vesalius is to be credited with a knowledge of precordial pain as a cardiac symptom, with a description of thrombo-embolic phenomena, and with a clinical appraisal of one form of arrhythmia which is compatible with the diagnosis of intermittent atrio-ventricular block, seemingly the first in world literature.

I wish to thank Dr. A. Schott for his kindness in discussing with me the intricacies of the reported arrhythmia. Dr. Schott is joint author of the book *Extrasystoles and Allied Arrhythmias*, London, 1952, of which the outstanding historical preface, prepared with Dr. F. N. L. Poynter's inspiring help, I used also for another historical study. And last, but not least, I am greatly indebted to Dr. Walter Pagel, who with unfailing sympathy and vast knowledge introduced me to a better understanding of the essence and terminology of the text on which this paper is based.

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