The Evolution of Eisenmenger's Eponymic Enshrinement

Clyde Partin, MD

Victor Eisenmenger (Figure 1) was born of German parents in Vienna, Austria, on January 29, 1864. In 1897 he published a treatise describing a congenital heart defect, a study that would later serve to enshrine him in medical history. Subject to poor health, the rigors of clinical practice proved too much for him and he became a court physician to the royal Hapsburg family. He died in Vienna at age 68 on December 11, 1932. His famous article served as a beacon that illuminated his name for posterity but shed no light on his otherwise obscure life.

His father, August Eisenmenger, was described by his son as a "distinguished painter and an enthusiastic and beloved teacher." He was a professor at the Akademie der Bildende Kunste in Vienna.[1] Victor grew up in Vienna and received his education there; he obtained his medical degree from the Medical Faculty of the University of Vienna on February 23, 1889. In a memoir chiefly concerned with the medical care he provided to one celebrated patient, Eisenmenger wrote that, in his youth, he was in "constant touch with artists and natural scientists so that there was soon developed within me a love for art and nature which was to govern my entire life. An artistic career and a study of natural science were both denied to me, the former because my talent was not sufficiently pronounced the latter because I was forced to earn my living as soon as possible. Thus, I decided to study medicine. I hoped thereby to satisfy my predilection for natural science and my inherited liking for a teacher's calling."[1]

Likely influenced by his father's example, Eisenmenger gravitated toward the academy. In 1891, he held an unpaid position as an assistant surgeon at the Chirugisches Operationsinstitut Prof. Allerts (personal communication, Kurt Muehlberger, MD, February 2002) He later joined the respected laryngology clinic of Professor Leopold von Schrötter in 1894. Of this appointment, Eisenmenger commented, "My dearest wish was fulfilled and I could see the clinical career to which I wished to devote my life stretching out smoothly before me."[1] Unfortunately, the emotional bliss concerning his circumstances was ephemeral. He was hampered by "precarious health and repeated illness,"[1] and suffered another setback in his health in July 1895.

Professor von Schrötter, a friend and fatherly figure, in an effort to assist Eisenmenger with his recovery, asked him to examine a sputum sample obtained from the Archduke Francis Ferdinand, which Eisenmenger found laden with tubercle bacilli, confirming an observation von Schrötter had already made. von Schrötter had surreptitiously arranged for Eisenmenger to become the personal physician to the Archduke, a job that would not be too physically demanding. He advised Eisenmenger, "If you are clever, this may turn into a good position for you." Thus, Eisenmenger reported to Ferdinand's castle at Chlumetz in Bohemia to discover a gravely ill Archduke. Eisenmenger would go on to maintain a relationship with the Archduke until the latter's assassination at Sarajevo in 1914. It was not always an easy relationship. During the first 2 of those years, Eisenmenger reminisced that a "fight was waged between him and me with great tenacity and stubbornness on both sides. Success varied, but, on the whole, I fortunately prevailed. . .a real friendship never existed between us, although he took me largely into his confidence. Neither do I owe him any debt of gratitude. My career would have been a better one and my declining years more pleasant, had I never met him."[1]

FIGURE 1. Victor Eisenmenger (1864 to 1932).

In the book Eisenmenger penned to chronicle the years spent with the Archduke, (Figure 2) he offers only an occasional glimpse into his personal life and the memoirs are bereft of biographical details. In 1902, he was disappointed when the medical *Doktorenkollegium* rejected his request to become a lecturer in medicine. To what extent Eisenmenger was incorporated into the medical elite of Vienna is not clear, but he does recount a story describing a day of traveling through the countryside, followed by dinner at a country inn where he was invited by Dr. Roentgen to join him at his table. Various vignettes portray Eisenmenger as observant, principled, clinically as-

From the Emory University School of Medicine, Atlanta, Georgia. Manuscript received March 9, 2003; revised manuscript received and accepted July 14, 2003.

Address for reprints: Clyde Partin, MD, Emory Internal Medicine Clinic, 1525 Clifton Road, Third Floor, Atlanta, Georgia 30322. E-mail: clyde_partin@emoryhealthcare.org.

0002-9149/03/$–see front matter
doi:10.1016/j.amjcard.2003.07.028

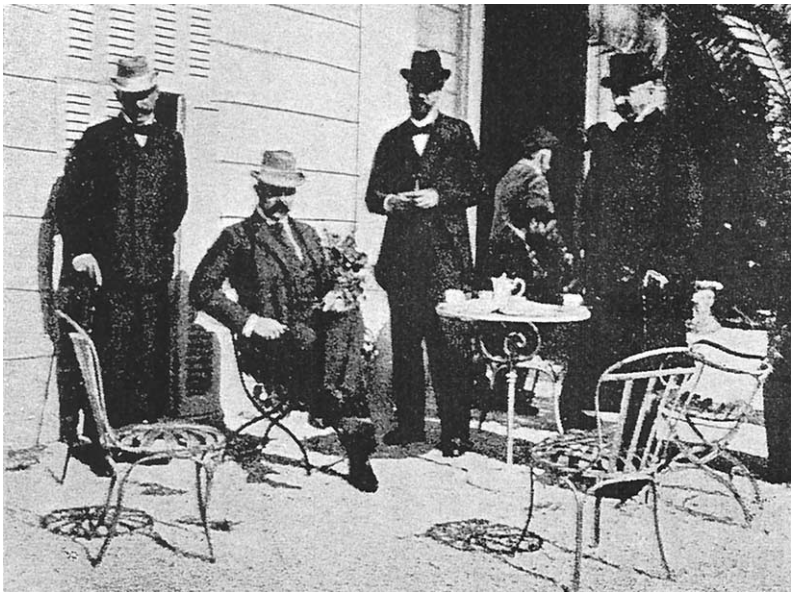

FIGURE 2. ***Left to right*****: Baron Bronn, Archduke Francis Ferdinand, Victor Eisenmenger, Count Cavriani.**

tute, and humane. It is a testimony to Eisenmenger's diplomacy that, in a time of tense relations between Austria and Germany, he became a physician in ordinary and chief of the board of health of the Habsburg court (personal communication, Muehlberger, February 2002).

As the Archduke's physician, he received many unsolicited therapies to consider. One of these was Professor Maregliano's serum cure for tuberculosis. The clinically savvy Eisenmenger invoked his usual "principle to use a new medical treatment with one of my patients only after it has withstood criticism and tests for a considerable time" and declined to employ the untested preparation. In another incident, the Archduke expressed his displeasure with Eisenmenger's restrictions on his activities after he had noted the similarly afflicted Grand Duke "was permitted to do as he likes." After the dressing down, Eisenmenger simply replied that he was not the Grand Duke's physician and "withdrew to let the firestorm pass." The next day the Grand Duke suffered a severe hemorrhage. Eisenmenger reassured, with difficulty, the now contrite and downcast Archduke that his own recovery would require patience. Later, Eisenmenger inadvertently made a remark that was indirectly disrespectful of the Archduke. Recognizing his indiscretion, he tendered his resignation, but the Archduke accepted his apology, declined the resignation, and retorted, "This settles the incident. As a physician you have my confidence now as before. I still need you."[1] Eisenmenger lamented, "I stayed on. The year was drawing to an end; the way back to the Clinic was barred." Eisenmenger also relates an episode that occurred while traveling in Egypt with the Archduke. He spent an hour bargaining a lad down to 1 schilling for an antiquity, "during which my knowledge of Arabic was enriched mainly by oaths and imprecations." Noting the boy's dire circumstances, he gave the merchandise back to the child after the purchase.

Although Eisenmenger provides a number of anecdotes in his recollections about his experiences and sojourns with the Archduke, he never refers to his own research. The edifying study that was to bring him posthumous fame was published in Berlin in 1897, about 2 years after he started in the employ of the Archduke. One can only speculate that he had already done most of the research for the study because the Archduke and his entourage spent virtually no time in Vienna, devoted as Franz Ferdinand was to traveling in warm climates and enjoying mountain hideaways. Presumably, Eisenmenger wrote his report in what must have been ample free time.

The evolution of Eisenmenger's eponymic escalation is worthy of examination. One commentator acerbically noted, "it would be difficult to think of a term which caused more long term disputation among pediatric cardiologists and others interested in the physiology of the circulation. The problem was, this was a useful shorthand phrase, but the longhand concept it represented was still unknown. The pulmonary vascular resistance bed was still foreign territory. Eventually, by the mid 1970s,* the term became useful once pulmonary vascular resistance and pulmonary vascular obstructive disease had reached at least our present interim phase of understanding."[2] Today his name is interchangeably used in reference to Eisenmenger syndrome or to Eisenmenger physiology and is particularly entrenched in the pediatric cardiology literature. Eisenmenger's physiology is one of the earliest pathophysiologic concepts medical students learn, its multisyllabic rhythm rolling off the tongue like an etude, yet the term is rooted in anatomic soil. The original description of the Eisenmenger complex, as it was first known, referred to a "ventricular septal defect with dextroposition of the aorta without any pulmonary stenosis or hypoplasia."[3] The absence of pulmonary stenosis makes this congenital syndrome distinct from the tetralogy of Fallot. Some anatomic descriptions include right ventricular hypertrophy as part of Eisenmenger's complex, thus an occasional reference to "tetralogy of Eisenmenger" can be found.[4,5] The world renowned pathologist Maude Abbott, an understudy of Sir William Osler, whose use of the term 'Eisenmenger complex' in her writings on congenital heart disease provides the most persuasive

*The early 1960s may be more accurate. Heath and Edwards of the Mayo Clinic reported in *Circulation* in 1958 a grade 1 to 6 classification of the pathology of pulmonary vascular disease with special reference to congenital cardiac defects (personal communication, Robert Franch, MD, August 2002).

genesis for widespread dissemination of the Eisenmenger eponym. As she wrote, "This term has been used by the writer, in default of a better, to designate an unusual combination reported by Eisenmenger."[3] She goes on to address the issue of aortas that arise from the right ventricle as opposed to those emanating astride the ventricular septal defect, noting "both these types form a single clinical group, we are still in need of a generic name, if that adopted by the writer is discarded." In 1924, she and Wilfrid Dawson, of Philadelphia, had referred to "Eisenmenger's case" in an article about classifying congenital cardiac lesions, relegating it to "Cases of Venous-arterial Shunt (Morbus coeruleus)" with a subheading of "Cyanosis, Moderate."[6]

As the nuances of Eisenmenger's complex began to be appreciated, his name began to be less associated with the originally described anatomic blemishes but rather the physiologic aberrations occasioned by the defect. The irony of this was that Eisenmenger had had little to say about the physiology of the defect and what he did mention was flawed. Peter R. Fleming surmised that Eisenmenger "was puzzled by the cyanosis in his patient, a man of 32 in whom it had been present since early childhood. He could not conceive that there had been a right-to-left shunt in the absence of pulmonary stenosis and was forced to invoke systemic venous congestion as the cause of the cyanosis. He clearly did not appreciate that it was an increase in pressure in the pulmonary artery, and, therefore, the right ventricle, now well-recognized as a serious complication of septal defects in general, which had caused a right-to-left shunt and, consequently, cyanosis."[7] Rashkind had also noted "Eisenmenger discussed neither pulmonary artery pressure, nor pulmonary hypertension, nor pulmonary arteriolar disease. The entirety of his attention to the pulmonary vascular aspect of his single patient's problem was: 'The slightly dilated pulmonary artery showed endarteritic thickening on its inner surface, which continues into the main branches of the vessel.' Thus his attention did not go beyond gross examination of the main pulmonary artery and its primary branches. He should be known instead for his much more valuable analysis of the mechanism of overriding (*reiten*) of the aorta . . . from his 1898 study."[8] The luster of Eisenmenger's description is slightly tarnished by the recognition that Dalrymple[†] may have first reported this condition in 1847/8.[8,9] Under the heading of "Diseased Heart, In Which the Root of the Aorta had an Opening Common to the Two Ventricles," Dalrymple described his postmortem examination of the heart of a delicate 25-year-old woman, noting that "the root of the aorta opened between the two ventricles by an aperture of the size of a sixpence."[10]

Paul Wood, (notably not a pediatric cardiologist) in his 1951 textbook, referred to "Eisenmenger's syndrome or pulmonary hypertension with reversed shunt." This may have been the first use of the term "Eisenmenger syndrome." There had been a misconception that the displacement of the aorta over the ventricular septal defect was a result of the shunt. However, by 1950, there was appreciation that the right-to-left shunt was the consequence of increased pulmonary vascular resistance. Wood redefined Eisenmenger's complex as "pulmonary hypertension with reversed interventricular shunt."[11] Thus, the shift of the eponym from an anatomic to a physiologic construct was effected. Wood initially suggested that "complex" should refer to a reversed shunt at the ventricular level and "syndrome" to a reversed shunt at any level, but abandoned this distinction in 1958, further refining the definition as "pulmonary hypertension due to a high pulmonary vascular resistance with reversed or bidirectional shunt at aorta-pulmonary, ventricular or atrial level."[12] The expanded eponym was associated with at least 12 different congenital cardiac defects,[13] was firmly ensconced in the literature, and synonymous with the unwieldy term "pulmonary vascular obstruction syndrome." As claimed in one textbook describing the syndrome, "the clinician who first encounters these patients sees a relatively homogeneous clinical profile, irrespective of the underlying anatomy."[14] Wood was quite emphatic in defending the use of the term Eisenmenger syndrome, despite opposition from the editor of the *British Heart Journal*, who had opined that *maladie de Roger* and Eisenmenger's complex were opposite ends of a continuous spectrum with regard to ventricular septal defects and that the terms "have outlived their usefulness and should no longer be used in clinical medicine."[15] A similar sentiment was expressed for Wood's term "Eisenmenger's syndrome," "which adds confusion rather than clarity."[15] Wood went on to say:

> An eponymous title may be justified, however, when it has been introduced by someone singularly entitled to do so (Abbott and Dawson, 1924), when it has become familiar by customary use on an international scale over a period of 34 years, when the etiology and precise mechanism of the syndrome are still controversial, and when there is no convenient alternative title likely to stand the test of time. Nothing is gained by changing customary nomenclature prematurely. To dispense with the term altogether, and to regard the Eisenmenger complex simply as a variety of ventricular septal defect, is to deny the very essence of the syndrome, for, as it will become clear later, its distinguishing feature lies not in the anatomy of the defect, but in the behavior of the pulmonary circulation.[12]

Modern echocardiographic technology has allowed the issue to come full circle as more precise anatomic delineations of the Eisenmenger ventricular septal defect are described. Using such data, Gatzoulis et al[16] reported that "the position of the outlet septum in relation to the remainder of the muscular subpulmonary infundibulum represents a hallmark of tetralogy of Fallot, permitting its differentiation from Eisenmenger ventricular septal defects," the former having

[†]John Dalrymple (1804 to 1852) was an English oculist whose 1834 description of exophthalmos associated with hyperthyroidism became known as Dalrymple's sign.

a rightward and anterior deviation of the malaligned infundibular septum and the latter exhibiting no narrowing of the subpulmonary infundibulum. Modern medical textbooks continue to make an anatomic[17] and physiologic[18] distinction when defining Eisenmengers's complex/defect and syndrome.

Eisenmenger's densely written thesis[19] was published in Berlin as a supplement to a journal of clinical medicine, *Zeitschrifft fuer Klinische Medizin*, of which von Schrötter was 1 of 6 editors (3 from Berlin and 3 from Vienna) listed on the cover of the periodical. One scholar advised that Eisenmenger's article "should not be embarked upon by anyone making their first dive into historic papers."[2] Eisenmenger organized his study into 5 numbered but untitled sections. In the first section, he rejected established dogma concerning congenital heart disease, arguing persuasively and with clarity against Hunter-Morgagni's theory that the flow of blood was mechanically responsible for the origin of congenital cardiac defects. Eisenmenger favored the ruminations of Rokitansky, who argued "all existing forms derive from developmental inhibition, and by far the majority have their origins in abnormal separation processes of the truncus arteriosus communis." Eisenmenger displayed considerable lucidity on the intricacies of embryonic cardiogenesis. In section 2, he devotes much discussion to the topic of the overriding aorta. The 1 and only case in question is introduced in section 3. In a flawless manner, he describes a powerfully built 32-year-old man with clubbing and early childhood cyanosis, moderate dyspnea, and a "buzzing systolic murmur over the apex and a loud second sound."[8] The patient likely came to Eisenmenger's attention upon referral from von Schrötter in January of 1894, when the patient presented with increased dyspnea and peripheral edema. The patient was readmitted in August, in congestive heart failure, and survived until November 13, when he collapsed "following a large haemptysis."[12] The clinical impression of ventricular septal defect (notably, a round 2- to 2.5-cm diameter defect in the membranous septum and placed in such a way that the lumen of the aortic orifice fell half over the left ventricular outflow tract and half over the right) and hemorrhagic pulmonary infarction was confirmed at necropsy. A discussion of ventricular septal defects, associated murmurs, and cyanosis occupies section 4. The fifth section provides a limited discourse on the differential diagnosis.

As pointed out earlier by Rashkind and Fleming, Wood also noted that, remarkably, Eisenmenger failed to appreciate the right-to-left shunt, a misinterpretation eloquently defended by Wood, who feels Eisenmenger had no way to realize that "first, since the cyanosis had been present from birth, he could not attribute it to reversed shunt from thrombo-obstructive pulmonary hypertension, for the thromboses were terminal; second, the absence of a giant V wave in the jugular pulse forced him to ascribe the systolic murmur and thrill to a left-to-right shunt through the defect rather than to tricuspid incompetence."[12] Poetic justice would prevail. For the first half of the twentieth century, most researchers believed that the overriding aorta played a causal role in the etiology of the cyanosis, although an overriding aorta is absent in 7 of the 12 defects associated with Eisenmenger physiology.[12] In another article published in 1898,[20] thought by some to be his more significant treatise, Eisenmenger further discussed the overriding aorta, proposing that it was irrelevant to the cyanosis and hypothesized that enhanced pulmonary vascular resistance may account for diminution of the left-to-right shunt and ensuing cyanosis. In 1947, Bing followed up on this suggestion, as did others, all reaching a similar conclusion, which was succinctly summarized by Selzer in 1951 as, "The most characteristic feature of Eisenmenger's complex is the presence of severe pulmonary hypertension,"[5] secondary to the markedly elevated pulmonary vascular resistance. Thus Eisenmenger's work of 1898 vindicated the perceived deficiencies of his better-known 1897 article. Reactive intimal proliferation with resultant luminal diminution of the pulmonary arteries and arterioles, the subject of a 1950 thesis, came to be appreciated as the cause of the pulmonary artery hypertension as a result of the nonrestrictive interventricular communication. This histologic observation led to yet another variation on a theme—Eisenmenger's reaction. Suprasystemic pulmonary vascular resistance promulgates reversal of the shunt.

How did Eisenmenger, a man without obvious cardiology specialty training, a German working in a Viennese otolaryngology clinic, come to write his study? Vienna was then a bastion of medical scholarship, clinical excellence, and superior teaching. Any serious North American student of medicine made a pilgrimage to Vienna after graduating from medical school. Sir William Osler wrote in an awed manner of his time in Vienna. Although he never mentions Eisenmenger by name, he refers to von Schrötter, among others, as a "brilliant specialist (in laryngology). . .responsible for the successful development of these specialties in the United States."[21] Although some made the ambiguous criticism that the teaching was too clinically oriented and the more scientifically minded student went to smaller German universities,[22] it was in this medical milieu, "emphasizing the Viennese and German physiological approach to pathology in contradistinction to the Parisian school,"[23] that Eisenmenger found himself an understudy in the clinic of the brilliant laryngologist von Schrötter. It was von Schrötter[‡] who actually made the first correct antemortem diagnosis of Eisenmenger's complex. Yet it is Eisenmenger we laud for delineating the salient features of the syndrome that has etched his name into eternity.

[‡]This unusual otolaryngology–cardiology connection was revisited years later in a published report concerning a young female with Down's syndrome, ventricular septal defect, and upper airway obstruction from hypertrophied tonsils. Tonsillectomy and adenoidectomy reversed the bidirectional shunt to a strictly left-to-right shunt with marked diminution in the pulmonary artery pressure. Clairmont AA, Hart NJ, Rooker DT, Franch RH. Upper airway obstruction and ventricular septal defect. *JAMA* 1975;233:813–814.

Acknowledgment: Appreciation is extended to Kurt Muehlberger, MD, and Brigitta Galian of the University of Vienna, Austria; Mia White, MILS, of the Emory University Medical School, Health Sciences Center Library; and Dawn McInnis, MILS, Clendening History of Medicine Library, for her research assistance. Editorial advice was kindly provided by William Aronstein, MD, of Procter & Gamble, Cincinnati, Ohio; Robert Franch, MD, of Emory University; Martha Clabby, MD, of the Sibley Heart Center, Atlanta, GA; Myron Schultz, MD, of the Centers for Disease Control, Atlanta, GA; and Ray Smyke, EdD, Webster University, Morge, Switzerland.

1. Eisenmenger V. Archduke Francis Ferdinand. Translated by James A. Galston. London: Selwyn & Blount, 1928:17, 18, 28.
2. Neill CA, Clark EB. The Developing Heart: A 'History' of Pediatric Cardiology. Dordrecht, The Netherlands: Kluwer Academic, 1995:120–121.
3. Abbott ME. Atlas of Congenital Heart Disease. Facsimile edition by American Heart Association. New York, American Heart Association, 1954:44.
4. White PD. Heart Disease. New York, NY: Macmillan, 1931:309.
5. Selzer A, Laqueur GL. The Eisenmenger complex and its relation to the uncomplicated defect of the ventricular septum. *Arch Int Med* 1951;87:218–241.
6. Abbott ME, Dawson WT. The clinical classification of congenital cardiac disease, with remarks upon its pathological anatomy, diagnosis and treatment. *International Clinics* 1924;4:156–188.
7. Fleming PR. A Short History of Cardiology. Atlanta, GA: Rodopi Press, 1997:47.
8. Rashkind WJ, ed. Congenital Heart Disease: Benchmark Papers in Human Physiology. Vol 16. Stroudsburg, PA: Hutchinson Ross, 1982:91, 96, 180.
9. Stewart HL, Crawford BL. Congenital heart disease with pulmonary arteritis: interventricular septal defect, dextroposition of the aorta and dilation of the pulmonary artery. *Am J Pathol* 1933;9:637–653.
10. Dalrymple J. Diseased Heart in which the root of the aorta had an opening common to 2 ventricles. *Trans Path Soc London* 1848;58:31–32.
11. Wood P. Diseases of the Heart and Circulation. Philadelphia, PA: JB Lippincott, 1956:392.
12. Wood P. The Eisenmenger syndrome: or pulmonary hypertension with reversed central shunt. *Br Med J* 1958;2:701–709 , 755–762.
13. Young D, Mark H. Fate of the patient with Eisenmenger syndrome. *Am J Cardiol* 1971;28:658–669.
14. Nadas AS. Pediatric Cardiology. Philadelphia, PA: WB Saunders, 1963:601.
15. Brotmacher L, Campbell M. The natural history of ventricular septal defect. *Br Heart J* 1958;20:97–116.
16. Gatzoulis MA, Soukias N, Ho SY, Josen M, Anderson RH. Echocardiographic and morphological correlations in tetralogy of Fallot. *Eur Heart J* 1999;20:221–231.
17. Alexander RW, ed. Hurst's The Heart Arteries and Veins. 9th ed. New York, NY: McGraw-Hill, 1998:205.
18. Franch RH. Cyanotic congenital heart disease. In: Fowler NO, ed. Cardiac Diagnosis and Treatment. 3rd ed. Hagerstown, MD: Harper & Row, 1980:419–501.
19. Eisenmenger V. Die angeborenen defekte der kammerscheidwand des herzens. *Z Klin Med* 1897;32(suppl):1–28. Translated in Rashkind, *op. cit.,* as Congenital defects of the ventricular septum:176–184.
20. Eisenmenger V. Origin of the aorta from both ventricles in ventricular septal defect. *Klin Ther Wochenschr (Vienna)* 1898;11:26–27.
21. Osler W. Vienna after thirty-four years. *JAMA* 1908;151:1523–1525.
22. Bonner TN. American Doctors and German Universities: A Chapter in International Intellectual Relations 1870–1914. Lincoln, NE: Univ. of Nebraska Press, 1963:69.
23. Acierno LJ. The History of Cardiology. New York, NY: Parthenon, 1994: 171.