Eponyms and the Diagnosis of Aortic Regurgitation: What Says the Evidence?

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Background: **Chronic aortic regurgitation can lead to significant morbidity and mortality. For more than a century, numerous eponymous signs of aortic regurgitation have been described in textbooks and the literature.**

Purpose: **To compare current textbook content with the peer-reviewed literature on the eponymous signs of aortic regurgitation and to assess the role of these signs in clinical practice.**

Data Sources: **11 textbooks, MEDLINE (1966 through October 2002), and bibliographies of textbooks and relevant papers.**

Study Selection: **English-language reports that were related to the properties of a sign on physical examination, incorporated more than 10 adults, and did not involve prosthetic heart valves or acute aortic regurgitation.**

Data Extraction: **Three investigators independently analyzed relevant textbook extracts and 27 reports, using predetermined qualitative review criteria. Data relating to diagnostic accuracy and properties of the index test were also extracted.**

Data Synthesis: **Twelve eponymous signs were described as having varying degrees of importance by textbook authors. Only the Austin Flint murmur, the Corrigan pulse, the Duroziez sign, and the Hill sign had sufficient original literature for detailed review. Most reports were low quality, with varying sensitivities for all signs. Except for the Hill sign, specificity tended to be poor. Evidence for the Hill sign also suggested a correlation between the popliteal–brachial gradient and aortic regurgitation severity.**

Conclusions: **Prominent textbook support of the eponymous signs of aortic regurgitation is not matched by the literature. Clinicians and educators should update and improve the evidence for these signs to ensure their relevance in current medical practice.**

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Clinical Scenario

You are presiding over morning report, but the pickings seem slim. It was a quiet night for the on-call team, and the only admission was an 82-year-old man with dehydration who was transferred from a nursing home. His medical history was significant for hypertension and rheumatic heart disease. On physical examination, the resident thought he heard an early diastolic murmur at the aortic area but was unsure of its significance. He suggests echocardiography for further evaluation. Seizing this teaching opportunity, you lament the sad state of medical education and clinical practice, in which thoughtful clinicians have been replaced by "techno-junkies." You decry the need for this expensive test and closely question the residents about the physical findings related to aortic regurgitation, particularly the signs of Hill, Quincke, and Duroziez. To your dismay, you are met with an assortment of blank stares and shrugs. You reminisce fondly about the good old days, when hallowed names such as these rolled effortlessly off the tongues of students, housestaff, and attendings. The residents interrupt your soliloquy, remarking that they have never been taught these signs, and ask for literature references they can review. You pause, realizing that because your knowledge of these signs has come from your mentors and from personal observation, you have never been compelled to review the literature. Confident that you will find journals abounding with evidence, you promise to return to a future report with supporting articles. Energized, you proceed to the library.

Introduction

Aortic regurgitation is a common valvular abnormality that is often well tolerated (1). However, if aortic regurgitation progresses and patients become symptomatic or develop left ventricular dysfunction, substantial morbidity can result, with mortality rates similar to those for symptomatic aortic stenosis (1). Recent guidelines from the American College of Cardiology/American Heart Association emphasize the complementary roles of history, physical examination, and echocardiography in guiding subsequent management of patients with aortic regurgitation (1). However, the guidelines do not elaborate on the value of specific physical findings in the clinical assessment. Although an early diastolic murmur is generally felt to be the quintessential finding of aortic regurgitation (2), for more than a century a variety of other physical signs known by eponyms have been proposed as ancillary findings useful in the diagnosis of aortic regurgitation (3, 4).

To acquire a perspective on the apparent importance of these eponymous signs to the contemporary diagnosis and management of aortic regurgitation, we reviewed recent editions of widely used textbooks in the disciplines of internal medicine (5–7), cardiology (8–10), and physical diagnosis (11–15). The texts varied substantially in the signs mentioned by eponym or description, the clinical importance attributed to them, and the citation of relevant evidence. This paper critically examines the peer-reviewed literature to further explore this variability as well as the possible role of these signs in the clinical evaluation of chronic aortic regurgitation.

Methods

We used a systematic process to develop a qualitative estimate of the clinical importance ascribed to each epon-

Table 1. **Eponymous Signs of Aortic Regurgitation: Textbook Content and Reports in the Literature**

Sign	Description	Important Mentions/Texts	Literature Reports Meeting Inclusion Criteria
		n/n	*n*
Austin Flint murmur	Low-pitched, rough, rumbling murmur that begins in mid-diastole and terminates at the end of diastole	11/11	12
Hill sign	Increase in manually measured blood pressure of the lower extremity compared with the upper extremity	4/4	7
Corrigan pulse	Rapidly swelling and falling arterial pulse by palpation	10/11	6
Duroziez sign	Intermittent to-and-fro femoral artery murmur (occurring in systole and diastole, respectively) generated by femoral artery compression	7/9	5
Quincke sign	Exaggerated capillary pulsations of the nail beds	6/8	2
Traube sign	Double tone on auscultation with light compression of the femoral artery	4/6	2
de Musset sign	Anteroposterior bobbing of the head	6/8	1
Mayne sign	More than a 15–mm Hg decrease in diastolic blood pressure with arm elevation from the value obtained with the arm in the standard position	0/1	1
Rosenbach sign	Pulsatile liver	0/1	1
Mueller sign	Pulsatile uvula	3/3	0
Becker sign	Accentuated retinal artery pulsations	2/2	0
Gerhard sign	Pulsatile spleen	0/1	0

ymous sign in the 11 textbooks selected for review. First, the physician member of the investigative team reviewed each textbook to identify relevant sections. Next, the physician-investigator and the remaining two investigators, one trained in outcomes research and the other a nonphysician clinician, independently evaluated the selected textbook sections. We developed a standardized protocol to review descriptive words or phrases to simulate the importance a reader may ascribe to a sign in establishing the presence or severity of aortic regurgitation. For instance, signs associated with descriptors such as "often seen" or "characteristic of" were graded "important." Signs characterized with descriptors such as "rarely seen" or "useless" were graded "unimportant."

We performed a structured search of MEDLINE (1966 through October 2002) for evidence regarding the identified signs, using the following MeSH headings: *aortic valve insufficiency*, *echocardiography*, *angiography*, *eponyms*, *auscultation or heart auscultation*, and *physical examination*. The search was limited to English-language reports that studied humans 19 to 80 years of age or older. A total of 1539 citations was identified. In addition, we used text word combinations representing each eponym as search terms, yielding a further 1711 citations. These 3250 citations were reviewed by the physician-investigator. When a citation did not provide sufficient information for determination of eligibility, a detailed abstract was obtained and reviewed. If an abstract was unavailable or inconclusive, the entire paper was procured and analyzed. The physician-investigator hand searched bibliographies of all retrieved papers, as well as prominent review articles on aortic regurgitation, to locate possible additional reports. Studies that contained analyzable data related to the diagnostic accuracy or prognostic value of a sign on physical examination, incorporated more than 10 adults, and did not involve prosthetic heart valves or acute aortic regurgitation were retained. Twenty-seven papers met our inclusion criteria; 13 were identified through MEDLINE, and the remainder were found through the hand search.

Signs with three or more studies meeting inclusion criteria were reviewed in depth, and each investigator independently reviewed identified reports to assess study quality. Criteria for grading (**Appendix Table 1**, available at www.annals.org) included elements of study design that have been empirically shown to be sources of bias (16), as well as problematic design features that have been cited in the expert literature (17, 18). Disagreements were resolved by consensus. Where feasible, sensitivity and specificity estimates were calculated for individual reports.

RESULTS

Table 1 illustrates the identified eponymous signs, the number of textbooks that mentioned a given sign, our qualitative estimate of a sign's importance, and the number of reports in the literature that met our inclusion criteria. Four signs—the Austin Flint murmur, the Corrigan pulse, the Duroziez sign, and the Hill sign—were found to have sufficient original reports to meet criteria for in-depth review. Evidence for signs with fewer than three published reports that met our inclusion criteria is presented in **Appendix Table 2**, available at www.annals.org.

Austin Flint Murmur

Origin

In 1862, while Austin Flint was professor of medicine at the New Orleans School of Medicine in Louisiana and an attending at Charity Hospital, he reported two cases of aortic regurgitation that also demonstrated a "blubbering presystolic murmur," which seemed characteristic of mitral stenosis (19). However, normal mitral valves and apparatus

were revealed at autopsy. Of interest, although his perspicacious observation led to his name being attached to the sign, Austin Flint himself was categorically opposed to eponyms. He wrote, "So long as signs are determined from fancied analogies, and named from these or after the person who describes them, there cannot but be obscurity and confusion" (20).

Description

The murmur typically begins in mid-diastole, often has a presystolic accentuation, and terminates at the end of diastole. It is low-pitched, with a rough and rumbling quality, and best heard at the apex. An Austin Flint murmur can be deemed present only in the setting of aortic regurgitation without coexisting mitral stenosis, since the latter can generate a similar murmur.

Pathophysiology

Austin Flint postulated that regurgitant blood flow in severe aortic regurgitation impinges on the leaflets of the mitral valve, leading to a functional stenosis. Diastolic inflow across this narrowed mitral valve orifice generates turbulence that is clinically appreciable as a mid- to late diastolic murmur (19). Later investigations have advanced a variety of other theories as causes for the murmur, including overlap of aortic regurgitation and mitral inflow jets (21), fluttering of mitral valve leaflets (22), and left ventricular endocardial vibrations due to the aortic regurgitation jet (23). However, a universally accepted explanation remains elusive.

Elicitation

The murmur is best heard on auscultation at the apex by using the bell of the stethoscope, with the patient in the left lateral position.

Evidence

The Austin Flint murmur was mentioned in each of the 11 textbooks (5–15), and all mentions were categorized as important (**Table 1**). Studies of this sign have focused more on investigating its mechanism than documenting its existence or diagnostic accuracy. Twelve studies met our inclusion criteria (22–33). Three reports (31–33), which dealt with patients who had both aortic regurgitation and mitral stenosis, were excluded from further analysis because an Austin Flint murmur cannot occur in the presence of mitral stenosis. The remaining 9 studies are detailed in **Appendix Table 2**, available at www.annals.org. Only 2 involved more than 35 patients (27, 28). In addition, selection bias was a significant methodologic flaw, since all studies included only patients with aortic regurgitation. Failure to blind examiners to the results of reference tests was a potential source of test review bias in 6 of 9 reports. Conversely, readers of the reference test were potentially aware of the index test results in 7 of 9 cases. Different reference standards were used to establish the diagnosis of aortic regurgitation, both across and within studies. Earlier studies frequently used phonocardiography as a reference standard (22, 24–27), while later studies largely incorporated angiography or echocardiography (23, 25–30).

There was extreme variation in the reported sensitivity of the studies (**Table 2**), from 25% (30) to 100% (24). Limiting the analysis to patients with known severe aortic regurgitation yielded sensitivities ranging from 57% (30) to 100% (24). Low sensitivity, ranging from 0% (30) to 50% (28), was reported among patients with known mild to moderate disease. Although some researchers have reported specificity for the Austin Flint murmur (30), we have refrained from doing so. By definition, the murmur can occur only in the setting of aortic regurgitation; therefore, estimates of specificity are meaningless.

Corrigan Pulse

Origins

Sir Dominic Corrigan wrote the seminal paper on aortic regurgitation in 1832 while at the Jervis Street Hospital in Dublin, Ireland (20, 34). Corrigan emphasized the visual nature of the pulse (sometimes referred to thereafter as a Corrigan sign), but the eponym has come to represent its tactile qualities. Common synonyms include "collapsing pulse" and "water-hammer pulse."

Description

This sign is characterized by a rapidly swelling and falling arterial pulse that is typically appreciated by palpating the radial artery and accentuated by wrist elevation.

Table 2. **Specificity and Sensitivity Ranges for Selected Signs***

Sign	Specificity	Sensitivity	Mild to Moderate AR		Moderately Severe to Severe AR		Indeterminate AR Severity†	
			Sensitivity	Studies/Patients	Sensitivity	Studies/Patients	Sensitivity	Studies/Patients
	%		%	*n/n*	%	*n/n*	%	*n/n*
Austin Flint murmur	Not applicable	25–100	0–50	4/32	52–100	6/90	13–63	4/118
Corrigan pulse	16	38–95	85	2/41	100	1/1	38–95	4/294
Duroziez sign	35–100	33–81	0	1/4	0	1/5	33–81	4/227
Hill sign	71–100	0–100	0–93	3/42	75–100	2/14	62–100	4/41

* AR = aortic regurgitation.
† Severity was categorized as indeterminate when the report provided insufficient information about this variable.

Pathophysiology

Numerous hypotheses have been advanced over the past century and a half. A recent investigation found that patients with aortic regurgitation had increased amplitude of the pulse, lower mean arterial pressure, and narrower pulse pressure than normal patients (35). The investigators concluded that these characteristics reflected an increase in the compliance of the arterial wall in patients with aortic regurgitation.

Elicitation

The examiner palpates the patient's radial artery while elevating the wrist. If the pulse clearly increases in amplitude, then the sign is present.

Evidence

The Corrigan pulse was mentioned in 11 textbooks (5–15); 10 of these mentions were categorized as important (**Table 1**). Six studies met our inclusion criteria (27, 36–40). One study was excluded because it used the presence of a collapsing pulse as an inclusion criterion (39). The remaining 5 studies are detailed in **Appendix Table 2**, available at www.annals.org. All reports involved more than 35 patients yet suffered from selection bias. Three studies were prospective (27, 38, 40), and 1 used blinded examiners for both index and reference tests (38). Two studies used angiography as the gold standard (27, 40), another used echocardiography (38), and a fourth used autopsy (37). One study did not report a reference standard (36).

Sensitivity ranged widely, from 38% to 95% (27, 36–38, 40). One study examined the impact of aortic regurgitation severity on sensitivity (38) and found no significant effect. It should be noted that this report had a low prevalence of hemodynamically significant aortic regurgitation. The same study reported specificity, which was extremely low (16%) among 103 patients (38). Ranges for sensitivity, stratified by severity of aortic regurgitation, and specificity are presented in **Table 2**.

Duroziez Sign

Origin

Paul Duroziez was a noted French physician with a special interest in the heart. In 1861, the same year he described the "double intermittent murmur" over the femoral arteries, he also wrote a classic treatise on pure mitral stenosis (20).

Description

The sign denotes an intermittent to-and-fro femoral artery murmur (occurring in systole and diastole, respectively) generated by femoral artery compression.

Pathophysiology

Duroziez believed the systolic portion of the murmur was caused by forward flow into the lower extremity and that the diastolic segment was caused by aortic regurgitation toward the heart (20). Despite earlier controversy (41), subsequent investigations support this theory (42–44).

Elicitation

Duroziez auscultated the femoral artery while applying digital compression proximal and distal to the stethoscope (20). Blumgart and Ernstene (42) replaced digital compression with cephalad and caudad tilting of the stethoscope. Luisada (41) showed that the optimal compressive pressure needed to successfully evoke a Duroziez sign was about three quarters of the pulse pressure above the diastolic pressure.

Evidence

The sign was mentioned in 9 texts (5–10, 12, 13, 15); 7 mentions were classified as important (**Table 1**). Five reports met our inclusion criteria (27, 37, 42, 44, 45) (**Appendix Table 2**, available at www.annals.org). Of these, 3 had sample sizes exceeding 35 patients (27, 37, 42). All studies suffered from selection bias. Two included patients without aortic regurgitation (42, 44), and all but 1 study (37) were prospective. Examiners were blinded to reference test results in a single study (45). Two studies did not specify a consistent reference standard (42, 45). Of the 3 remaining studies, 1 used autopsy (37) and 2 used angiography (27, 44).

Sensitivity was highly variable, ranging from 33% to 81% (27, 37, 42, 44, 45). Similar variations were seen in specificity, from 35% (based on 31 patients) to 100% (based on only 2 patients). We are unable to comment on the impact of aortic regurgitation severity on the Duroziez sign because data were inadequate. **Table 2** shows ranges for sensitivity, stratified by aortic regurgitation severity, and specificity.

Hill Sign

Origin

Sir Leonard Hill was an English physiologist. W. Holtzmann, one of his assistants, chanced to observe that lower-extremity blood pressures in patients with aortic regurgitation were consistently higher than pressures in the upper extremity. Hill and colleagues reported these findings in 1909 (46), followed by a similar study of healthy young men in 1911 (47). This sign is also known as the popliteal–brachial gradient.

Description

Hill and colleagues described a "marked" increase of systolic blood pressure in the lower extremity compared with the upper extremity in patients with aortic regurgitation, without specifying numerical criteria (46). Frank and coworkers subsequently proposed that the degree of regurgitation is correlated with the increase in the popliteal–brachial gradient above 20 mm Hg (48). This criterion has been generally accepted and used in some later studies (45)

and textbook descriptions (5, 6, 10, 14), as well as in this review.

Pathophysiology

Etiologic investigations have yielded conflicting results. From later studies, it is apparent that there is no true increase in intra-arterial lower-extremity blood pressures compared with the upper extremity in patients with aortic regurgitation (48–50). The Hill sign, therefore, remains an unexplained artifact of indirect blood pressure measurement that is consistently more common and pronounced in patients with aortic regurgitation than in those without.

Elicitation

The blood pressure is manually obtained over the brachial and femoral arteries by using appropriately sized cuffs, with the patient in the recumbent position. The difference in systolic pressures denotes the gradient.

Evidence

The Hill sign was mentioned in four textbooks (5, 6, 10, 14), and all mentions were classified as important (**Table 1**). Seven reports met our inclusion criteria (45–48, 51–53) (**Appendix Table 2**, available at www.annals.org). Only 1 study had more than 35 patients (48). Selection bias was uniformly present. With the exception of 1 study that blinded examiners (45), there was no evidence of blinding to index or reference test results. Five studies did not specify a reference standard (45–47, 51, 52). A sixth study used more than one standard (angiography, phonocardiography) within the cohort (53), and the seventh study incorporated angiography (48). Reported sensitivity was extremely variable, ranging from 0% to 100% (45–48, 51–53). There were 4 reports of specificity, ranging from 71% in 14 patients (52) to 100% in 3 studies with 5, 23, and 24 patients, respectively (46–48).

One study attempted to correlate indirectly measured popliteal–brachial blood pressure values with angiographic findings (48). The investigators concluded that the degree of the popliteal–brachial gradient predicted severity of aortic regurgitation. For patients with more than mild aortic regurgitation, an increase in popliteal–brachial gradient above 20 mm Hg had a sensitivity of 89%. However, the sign did not distinguish between patients with mild aortic regurgitation and normal persons. This was confirmed by a later report, which found a sensitivity of 0% for the diagnosis of mild aortic regurgitation in 22 patients (53). The threshold of 20 mm Hg was used to calculate the sensitivity and specificity estimates in **Table 2** and in **Appendix Table 2** (available at www.annals.org).

DISCUSSION

Aortic regurgitation is a chronic valvular disorder that can lead to substantial morbidity and mortality (1). The long-term prognosis of chronic aortic regurgitation is closely linked to the severity of regurgitation and the development of left ventricular dysfunction (1). Asymptomatic patients with normal left ventricular function rarely warrant aortic valve replacement but may benefit from therapy with vasodilators, such as nifedipine (1, 54, 55). Aortic valve replacement is usually considered for patients with severe aortic regurgitation accompanied by significant symptoms or onset of left ventricular dysfunction (1). It is therefore vital to determine both the presence and severity of aortic regurgitation.

The history and physical examination are the first steps in this process. These assessments can guide the choice of ancillary tests, such as echocardiography, that may be necessary to reach a diagnostic conclusion with an acceptable degree of certainty. The key physical finding of aortic regurgitation is an early diastolic murmur. However, this murmur can be difficult to appreciate (27, 56) and has poor sensitivity (57–59). In addition, murmur characteristics do not necessarily predict the severity of aortic regurgitation (27, 60). Therefore, consideration of additional physical findings may be valuable, and textbooks are replete with eponymous signs thought to be associated with chronic aortic regurgitation. On review of 11 prominent textbooks, we found 12 such eponymous signs. Although the textbooks generally supported them (**Table 1**), evidence was rarely cited. We therefore conducted a systematic review of the literature and found that only the Austin Flint murmur, the Corrigan pulse, and the signs of Duroziez and Hill had sufficient evidence to meet our criteria for detailed review.

The papers reviewed varied widely in methods, disease definitions, and reference standards. In particular, the use of different reference standards within the same study has been shown to result in a biased estimate of diagnostic accuracy (16). Thus, the available data, particularly from older studies, may not accurately reflect the operating characteristics of these signs in aortic regurgitation.

Reported sensitivities for the four signs reviewed in detail were highly variable. As discussed previously, specificity was not considered for the Austin Flint murmur. The Corrigan pulse had extremely low specificity. The Duroziez sign also had low specificity in the one report of reasonable size (42). Specificity of the Hill sign seems to be quite good but is based on four reports with small samples (46–48, 52).

Evidence regarding the impact of severity of aortic regurgitation on the manifestation of these signs is similarly sparse. Several studies included data on patients with varying severity of disease. However, only three studies specifically examined this question (30, 38, 48). The first examined the Austin Flint murmur and found that sensitivity modestly increased with worsening severity of aortic regurgitation (30). The second studied the Corrigan pulse and found no association between increasing severity of aortic regurgitation and sensitivity (38). Finally, a detailed investigation of the Hill sign reported significant correlation between an increase in the popliteal–brachial gradient and worsening severity of regurgitation (48). All three studies

used the currently accepted reference standards of echocardiography (30, 38) or angiography (48) to determine the presence and severity of aortic regurgitation.

What do our findings mean? Thoughtful educators and clinicians should be mindful that, although textbooks support many of these eponymous signs, there is little evidence in the published literature. This may seem surprising given the longevity of these signs in textbooks and medical lore. However, variance between textbook recommendations and actual literature is not uncommon with respect to the clinical manifestations of disease, as highlighted in a recent editorial (61). The reasons for this are multifactorial and include refinements in the accepted standards of medical evidence, changes in patient populations and disease characteristics, a shift from meticulous physical examination to a greater reliance on technology, and the difficulty of obtaining funding for research to perform primary studies focusing on the physical examination (62–66). Therefore, the absence of evidence to support these signs does not mean that they are without merit. Instead, it attests to the need to rejuvenate the overall literature on the physical examination and attune it to the 21st century. Such an effort would be of value not only to the profession but also to patients because it could potentially reduce the need for expensive and time-consuming ancillary tests.

Our report has limitations. First, the textbooks reviewed to provide an estimate of the current popularity of the signs of aortic regurgitation were works prominent in the United States. Despite the broad international readerships of the works selected, texts that are influential in other parts of the world may have been excluded. Second, our qualitative estimate of textbook content may not accurately represent the attitudes of the medical profession at large. However, textbooks are widely used as fundamental reference sources for physical diagnosis and generally represent an accepted synthesis of expert opinion. Third, our literature review was confined to reports in English, leading to the potential omission of relevant reports in other languages. To minimize the effect of this possible bias, we also reviewed citations of non–English-language reports in our MEDLINE text word search and did not identify any of potential significance. Finally, although summary estimates of diagnostic accuracy for these signs would have been desirable, the heterogeneity among studies precluded such calculations.

Much like the attending physician in our clinical scenario, those who have long embraced time-honored components of the physical examination may be challenged to reexamine their place in contemporary teaching and practice. Such challenges should prompt neither a reflexive defense nor an apologetic retreat. Rather, they should inspire clinicians and educators who value the physical examination to redouble their efforts to update and improve the evidence so the physical examination can earn a more substantial place in current medical practice. If celebrated elements of the physical examination such as the eponymous signs of aortic regurgitation are to prosper in the clinical lexicon, they will need the support not only of tradition but also of science.

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Appendix Table 1. **Grading Criteria for Evaluation of Study Quality***

Grading Criteria	Description
Study type	Prospective trials of randomly selected patients are considered to provide the most valid evidence about a diagnostic test. Prospective studies of patients selected in a nonrandom manner have potentially uncontrolled factors that may bias results. Retrospective studies are considered inferior to prospective designs (16, 68).
Study size	Larger sample sizes are considered to be superior to smaller ones because they increase statistical power and may increase generalizability of results (69). Ranked by preference: 1. >35 patients in both diseased and nondiseased groups 2. >35 patients in the diseased group, but ≤35 in the nondiseased group 3. ≤35 patients with disease in both groups
Test review bias	Readers of the test in question (index test) should be blinded to the gold standard (reference) test (18). Test review bias is considered absent only if the authors specifically state that readers of the index test were blinded to the patient's disease status. It may also be considered absent if the reference test always occurred after the index test.
Diagnostic review bias	Readers of the reference test should be blinded to the results of the index test (18). Diagnostic review bias is considered to be absent only if the authors specifically state that the readers of the reference test were blinded to results of the index test. It may also be considered absent if the reference test always occurred before the index test. When present, this bias has been found to result in an overestimation of diagnostic accuracy (16).
Verification bias	The decision to undergo the reference test should not be contingent on results of the index test (16). When the reference test is highly invasive, expensive, or relatively risky, those referred by the index test may have a higher likelihood of disease. Thus, the study sample will probably be "sicker" than those normally tested.
Selection bias	The inclusion and exclusion criteria should not result in a study sample that is different in important respects from patients normally referred for testing in a clinical setting. Reports with highly selected samples may overstate the diagnostic accuracy of the test (16).

* Numbers in parentheses are reference numbers.

Appendix Table 2. **Summary of Reports on the Eponymous Signs of Aortic Regurgitation That Met Inclusion Criteria***

Study, Year (Reference)	Patients	AR Reference Standard	AR Severity†	Patients with AR	Patients without AR
	n			← *n* →	
Austin Flint murmur					
Currens et al., 1953 (22)	24	AUS, PCG	Unspecified	24	0
Ueda et al., 1965 (24)	13	Autopsy, PCG, AUS	Severe	13	0
O'Brien and Cohen, 1969 (25)	17	ANG, PCG, AUS	Severe	17	0
Parker et al., 1971 (26)	32	ANG, clinical examination, PCG	Unspecified	32	0
Enghoff, 1972 (27)	38	PCG, ANG	Variable	38	0
Rahko, 1991 (28)	51	ANG, Echo	Moderate	4	0
			Moderately severe	29	0
			Severe	18	0
			Total	51	0
Landzberg et al., 1992 (23)	24	AUS, ECG, NMRI	Variable	24	0
Emi et al., 1993 (29)	13	AUS, PCG, Echo	Moderate	7	0
			Severe	6	0
			Total	13	0
Lee et al., 1995 (30)	28	Echo	Mild	15	0
			Moderate	6	0
			Severe	7	0
			Total	28	0
Corrigan pulse					
Stewart, 1908 (36)	50	Unspecified	Unspecified	50	0
Tice, 1911 (37)	124	Autopsy, clinical examination	Unspecified	124	0
Shine et al., 1968 (40)	39	ANG, operation	Variable	39	0
Enghoff, 1972 (27)	81	PCG, ANG	Variable	81	0
Babu et al., 2001 (38)	145	Echo	Mild	34	0
			Moderate	7	0
			Severe	1	0
			No AR	0	103
			Total	42	103
De Musset sign					
Sapira, 1981 (45)	20	Unspecified	Unspecified	20	0
Duroziez sign					
Tice, 1911 (37)	124	Autopsy, clinical examination	Unspecified	124	0
Blumgart and Ernstene, 1933 (42)	41	Unspecified	Unspecified	10	0
			No AR	0	31
			Total	10	31
Folts et al., 1968 (44)	11	ANG, operation	Moderate	4	0
			Severe	5	0
			No AR	0	2
			Total	9	2
Enghoff, 1972 (27)	81	PCG, ANG	Variable	81	0
Sapira, 1981 (45)	12	Unspecified	Unspecified	12	0
Hill sign					
Hill et al., 1909 (46)	15	Unspecified	Unspecified	8	0
			No AR	0	5
			Total	8	5
Hill and Rowlands, 1911 (47)	23	Unspecified	No AR	0	23
Murray, 1914 (51)	13	Unspecified	Unspecified	13	0
Kotte et al., 1944 (52)	21	Unspecified	Unspecified	7	0
			No AR	0	14
			Total	7	14
Frank et al., 1965 (48)	58	Clinical examination, ANG	Mild	6	0
			Moderate	14	0
			Moderately severe	8	0
			Severe	6	0
			No AR	0	24
			Total	34	24
Hughes, 1969 (53)	22	Clinical examination, ANG, PCG	Mild	22	0
Sapira, 1981 (45)	13	Unspecified	Unspecified	13	0
Mayne sign					
Abbas and Sapira, 1987 (67)	17	Unspecified	No AR	0	17
Quincke sign					
Tice, 1911 (37)	124	Autopsy, clinical examination	Unspecified	124	0
Enghoff, 1972 (27)	81	PCG, ANG	Variable	81	0
Rosenbach sign					
Tice, 1911 (37)	124	Autopsy, clinical examination	Unspecified	124	0
Traube sign					
Tice, 1911 (37)	124	Autopsy, clinical examination	Unspecified	124	0
Enghoff, 1972 (27)	81	PCG, ANG	Variable	81	0

* ANG = angiography; AR = aortic regurgitation; AUS = auscultation; Echo = echocardiogram; NA = not applicable; NMRI = nuclear magnetic resonance imaging; PCG = phonocardiography.
† "Unspecified" indicates that a study did not specify distribution of AR severity; "variable" indicates that a study did not specify degree of AR at all.

Appendix Table 2—**Continued**

Patients in Whom the Sign Was Present	Patients in Whom the Sign Was Absent	Sensitivity	Specificity	Comments
← *n* →		%		
11	13	46	NA	Sample of syphilitic patients.
13	0	100	NA	2 additional patients with aortic dissection excluded from the table.
12	5	71	NA	
20	12	63	NA	A separate group of 13 patients studying the *a* wave in patients with AR + mitral stenosis excluded from the table.
5	33	13	NA	All patients had moderately severe or severe AR.
2	2	50	NA	
15	14	52	NA	
13	5	72	NA	
30	21	59	NA	
10	14	42	NA	All patients had moderate or severe AR.
1	6	14	NA	15 normal patients studied echocardiographically but not examined for Austin Flint murmur excluded from the table.
5	1	83	NA	
6	7	46	NA	
0	15	0	NA	Sample preselected to have pure AR. None of 8 normal controls had mid-diastolic murmur.
3	3	50	NA	
4	3	57	NA	
7	21	25	NA	
29	21	58	NA	
118	6	95	NA	
15	24	38	NA	All patients had combined AR and mitral regurgitation.
51	30	63	NA	All 7 patients with mild to moderate AR were sign negative.
29	5	85	NA	Includes additional data not presented in original report; more information can be obtained from authors.
6	1	85	NA	
1	0	100	NA	
87	16	NA	16	
123	22	86	16	
1	19	5	NA	Data extracted from appendix of report.
100	24	81	NA	
8	2	80	NA	Sample included unspecified number of patients in whom the sign was elicited over brachial artery instead of femoral. Among participants without AR, 20 had thyrotoxicosis, 4 had unspecified disorders, and 7 were normal.
20	11	NA	35	
28	13	80	35	
0	4	0	NA	12 patients in original sample; 1 patient with uninterpretable examination excluded from the table. The 2 patients without AR had other cardiac lesions.
5	0	100	NA	
0	2	NA	100	
5	6	56	100	
27	54	33	NA	
8	4	67	NA	Data extracted from appendix of report.
6	2	75	NA	Lower-extremity blood pressure was measured at the posterior tibial or dorsalis pedis arteries. Later studies have used the popliteal site. The 5 patients without AR were normal.
0	5	NA	100	
6	7	75	100	
0	23	NA	100	Sample of young men without AR.
8	5	62	NA	15 patients in original sample; 2 patients without thigh pressures excluded from the table.
7	0	100	NA	Out of 28 patients in sample, only data in 21 measured with a wide thigh cuff are included in the table. Among patients without AR, 6 had hypertension and 8 had unspecified disorders.
4	10	NA	71	
11	10	100	71	
1	5	17	NA	This report determined the correlation between the popliteal–brachial gradient and degree of AR. The 24 participants without AR were normal.
13	1	93	NA	
6	2	75	NA	
6	0	100	NA	
0	24	NA	100	
26	32	76	100	
0	22	0	NA	Report did not specify criteria for positive sign.
9	4	69	NA	Sign noted as positive only if gradient >20 mm Hg.
11	6	NA	35	Authors declared sign "useless." All participants were normal.
112	12	90	NA	
48	33	59	NA	
15	109	12	NA	
26	98	21	NA	
31	50	38	NA	