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Review Article

Venothromboembolic signs and medical eponyms: Part II

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ABSTRACT

Eponyms were established to serve the purpose of honoring individuals who have made important observations and discoveries. The use of eponyms remains controversial, and important questions have been raised regarding their appropriateness. Although there have been instances where eponyms were abandoned, the remainder are largely embedded within the established literature making their disappearance unlikely. Physicians used a variety of techniques to describe signs of medical eponyms as a method for diagnosing deep venous thrombosis (DVT), pulmonary embolism (PE) or venothromboembolism (VTE). These methods (observation, palpation, pressure, or maneuvers), were detected during the physical examination and using bedside sphygmomanometer or radiographic imaging. Reviewed are both common and less frequently encountered VTE eponyms identified during the physical examination and radiologic imaging. Most of these signs have not been further studied and, therefore, there is a lack of information regarding their accuracy and reliability in clinical practice.

1. Introduction

Eponyms are structures, signs, syndromes, maneuvers, tests, procedures, or instruments derived from the name of a person who first reported, described, or significantly contributed to the clinical understanding of a certain disease or procedure. They are embedded throughout medicine and used by clinicians to provide a concise description of a phenomenon or imaging finding. Clinicians used eponyms to better recognize VTE and to improve medical communication between different specialists. A variety of signs of the physical examination were described including those involving coughing, tissue infiltration, calf tenderness, and use of a sphygmomanometer as methods for diagnosis. The historical context of medical innovation is also tightly interwoven with advances in imaging, which has further led to the evolution of a number of eponyms in pulmonary embolism (PE).

Described in part II of VTE eponyms are those signs described from 1946 to 1996. Included is brief historical information of the physician who described the sign as originally reported and the sensitivity and specificity of the sign if studied. Our goal is to 1) recognize the pioneers in the field who significantly contributed toward our present understanding of VTE and 2) provide readers with consistent, accurate definitions, and depictions of less frequently encountered VTE eponyms.

2. Methods

PubMed, Medline, online Internet word searches, and bibliographies from source text and textbooks were used. PubMed was searched using the Medical Subject Heading (MeSH) of the name of the eponyms and text words associated with the sign.

3. Discussion

3.1. Moses sign

William Russell Moses (1916–2005) was born in Spartanburg, SC and received his medical degree from George Washington University, D.C. in 1938 [1]. In 1941, at the age of 25, he served as Chief of Surgery at Gallinger Municipal Hospital (later became known as D.C. General which closed in 1953) [1]. He also served as Adjunct Clinical Professor

Abbreviations: DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venothromboembolism

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in the Department of Surgery at George Washington University School of Medicine [1]. In 1941, he had a medical practice in Washington and in 1965 served as a founding member of the Falls Church Medical Center [1].

Moses described a three-part method for testing the skin, subcutaneous tissue, fascia, and calf muscle, independent of the deep vein. During the first part of the test, firm pressure of the fingers is used to identify the area of venous tenderness located on the calf by direct compression in the posterior-anterior direction. During the second part of the test, the calf is firmly compressed from side to side between the fingers and palm of the hand:

> In the presence of bland venous thrombi, the skin, subcutaneous tissue, fascia and muscles show little, if any, tenderness on firm compression, whereas direct pressure on the veins, as executed in the first maneuver causes definite pain. On the other hand, the superficial tissues are extremely tender at the second test if the tenderness resides in their layers. These two stages do not, however, rule out tenderness of the deep calf nerves, such as is present in a peripheral neuritis. The third part of the test is therefore a brief neurologic examination, with a search for alteration of cutaneous sensation and an evaluation of position sense of the toes, the vibratory sense and the deep reflexes [2].

Moses found that this test correctly identified thrombus in all of 12 patients with operative proven thrombosis [2]. In 31 patients with a positive test and suspected phlebothrombosis, thrombus was identified by direct visualization within the vein in 14 patients. In the remaining 17 patients, there was radiographic evidence of pulmonary emboli, with infarction in 12 patients [2]. In 65 patients with suspected phlebothrombosis, the sign was negative in all, with no evidence for thrombosis found on subsequent follow-up [2]. There are no well-designed clinical studies to draw any meaningful conclusions regarding the accuracy of this sign in clinical practice (Tables 1, 2).

3.2. Neuhof sign

Harold Neuhof (1884–1964) received his medical degree in 1905 from the College of Physicians and Surgeons of Columbia University, New York City. He completed his internship and residency at Mount Sinai, New York City and was appointed to the Physicians and Surgeons Division of Surgical Service at Bellevue Hospital, New York City in 1910 [3]. From 1913 to 1923, he was a member of the neurosurgical service at Montefiore Hospital, New York City and subsequently served as Attending Surgeon and Chief of the Surgical Division from 1923 to 1932. From 1932 to 1946, he was appointed Chief in the Department of Surgery at Mount Sinai Hospital, New York City and Consultant Surgeon and Director Emeritus of the Department of Surgery at The Mount Sinai Hospital beginning in 1946 [4]. He was subsequently appointed Director of the Division of Surgery at Beth-El Hospital in Brooklyn, New York City retiring from this position in 1959 [3,4] (Table 3).

He described in 1947:

> A sign which I regard to be valuable (and which apparently is not mentioned in the literature) is infiltration to be felt on palpation of the deep calf musculature. With the patient's heels resting on the bed, the knees flexed and the calf muscles relaxed, palpation reveals thickening and infiltration deep to the gastrocnemius. The area of infiltration, of greater or lesser extent, is vertically disposed. It usually is tender, although tenderness varies with different patients. The area of infiltration, which corresponds to the general region of the deep veins of the calf, may coexist with subjective signs of venous thrombosis or may be present alone [5,6].

Neuhof identified that this finding was present in all patients whom Homans sign was present, as well as in other patients which there was no other objective evidence for venous thrombosis [5] (Tables 1, 2).

3.3. Bailey sign

Henry Hamilton Bailey (1894–1961) received his medical training at the London Hospital Medical School, qualifying in 1916. After the World War I, he served as house surgeon and surgical registrar in London, and was recognized for fellowship in the Royal College of Surgeons in 1920 [7]. He worked as an Assistant Surgeon at the Liverpool Royal Infirmary in 1925, Dudley Road Hospital in Birmingham, Bristol Homeopathic Hospital in 1930, Bath Homeopathic Hospital in 1931, latter posts at the Royal Northern Hospital in Holloway, North London in 1932, and several other hospitals in London [7] (Table 3).

Hamilton Bailey wrote in his textbook *Physical Signs in Clinical Surgery* in patients with suspected thrombophlebitis, “Apply finger-tip pressure over each saphenous opening, and with a stroking motion, run the finger down the course of each femoral vein, seeking a segment of unilateral localized tenderness.” [8]. Oritez-Ramirez and Serna-Ramirez described a new sign of provoked pain and compared this sign with other signs of deep phlebitis including Bailey sign. They did not, however, describe how Bailey sign was performed (Tables 1, 2).

3.4. Rosenthal sign

We were unable to identify any historical information on Randolph Rosenthal. At the time of the publication of his physical finding, he served in the Peripheral Vascular Disease Department at the Bronx Hospital, New York City. He described the foot extension sign as a bedside diagnostic method for detecting DVT of the leg which:

> [c]onsists simply of passively extending the foot 45 degrees or less, depending on the maximum painless mobility of the ankle joint and, if this elicits no pain in the patient, plantar flexing the toes while the foot is held in extension by the examiner's hand. At present the author's practice is to combine these two movements into one, (…) by grasping the toes, flexing them in a plantar direction, and automatically extending the foot up to 45 degrees or less at the same time [9].

The test is considered positive if:

> [t]he maneuver elicits pain anywhere just lateral to the anterior crest of the tibia, but especially at a point 3 in. above the distal end of the tibia, where the position of the anterior tibial vein is most superficial in its course. It is at this point that foot extension produces maximum compression of the anterior tibial vein [9].

Rosenthal found that this maneuver is useful in identifying anterior tibial vein thrombosis (Tables 1, 2).

3.5. Pratt sign

Gerald Hilary Pratt (1906–1979) was born in Montello, Wisconsin and received his medical degree from the University of Iowa in 1928. He was a Clinical Associate Professor of Surgery at the New York University School of Medicine, and Attending Surgeon at St. Vincent's Hospital and Medical Center, St. Clare's Hospital and Health Center, and Doctor's Hospital, New York City [10].

In 1948, Pratt reported on the presence of three dilated veins over the tibia as an early sign of thrombosis of the deep veins of the leg [11]. In his 1949 paper on “An early sign of femoral thrombosis” he stated that, “Since then, this phenomenon has been observed so consistently that the term ‘sentinel’ veins has been coined for this finding” [12]. He found that the sign was present in 84 of 109 patients with thrombosis of the leg and that it is present earlier than Homans' sign [12] (Tables 1, 2).

3.6. Lawrence sign

Elias D. Lawrence (1905–1994) received his medical degree from

Table 1
Thromboembolism eponymous signs.

Name	Year	Description of sign
Moses	1946	Three-part test. Part 1: Using the fingers firm pressure is applied compressing the calf in a posterior-anterior direction to identify the area of venous tenderness. Part 2: Calf is firmly compressed from side to side between the fingers and palm of the hand. Part 3: Brief neurologic examination (alteration in cutaneous sensation, position and vibratory sensation and deep tendon reflexes. Pain elicited by direct compression of an area in the deep posterior calf with the fingers in the anterior-posterior direction toward the tibia (part 1 but not part 2) is considered a positive test for DVT. The presence of pain when the calf is compressed between the fingers and palms in the lateral direction suggests involvement of the superficial tissue or muscle rather than the veins
Neuhof	1947	Patients heels on bed, knees flexed, calf muscle relaxed, palpation reveals thickening and infiltration deep to the gastrocnemius muscle.
Bailey	1947	Fingertip pressure is applied over each saphenous opening. Using a stroking motion, the finger moves inferiorly following the course of the femoral vein. A positive sign if the presence of unilateral segment of localized tenderness.
Rosenthal	1948	Passively extend the foot up to 45°. If no pain occurs than plantar flexed the toes while holding the foot in extension. Alternatively, the entire test can be performed simultaneously. A positive test is the presence of pain located laterally to the tibia crest and at a point 3 in. above the distal tibia.
Pratt	1949	Dilated superficial veins located over the tibia.
Lawrence	1950	Coughing, sneezing or laughing increases pain in an inflamed area in the lower extremity. In early cases of DVT or in proximal thrombosis compression of the greater saphenous vein close to the saphenofemoral junction causes pain to disappear when coughing. In case of DVT below the knee this same maneuver causes the pain to disappear in 50% of cases.
D'Alessandro	1951	Marked diminution or absence of the femoral pulse.
Louvel	1952	Pain in an inflamed area of the lower extremity caused by coughing.
Bellini	1953	Disappearance of the femoral pulse as detected through sphygmanometer and oscillometer and its reappearance using trinitric (nitroglycerin)
Castañeda	1953	Difference in consistency between the diseased (hard) calf compared to the healthy calf due to muscular edema. Also described the sign of the toe in which compression of the edge of the first joint of the first toe cause sudden sharp pain in patients with phlebothrombosis [29].
Lowenberg	1954	The patient's pain threshold is first determined by inflating a pneumatic cuff on the arm rapidly to 250 mmHg. If pain is experienced than a reduced pain threshold is detected. A pneumatic cuff is distended over the calf or thigh and slowly inflated (10–15 s) to 180 mmHg pressure. If pain is elicited before this, the end point has been reached and the cuff is deflated. Pain, grimacing or withdrawal of the limb beneath the inflated cuff at 80, 100, or 120 mmHg (60–150 mmHg) is a positive cuff test. In patients with a reduced pain threshold, pain response below 180 mmHg may indicated a false-positive result.
Rose	?	A small region of the skin is pinched due to the presence of thickening of the dermis and subcutaneous tissue caused by early edema.
Ortiz-Ramírez	1955	Patient recumbent and extremity slightly flexed. A sphygmomanometer cuff is applied above the knee and inflated to 40 mmHg. Pain most commonly occurring in the popliteal region is a positive test and disappears with deflation of the cuff.
Popkin	1960	Patient recumbent with pressure applied using the index finger or thumb over the anteromedial surface of the leg compressing the tissues between the fingers and underling bone. A positive test is the occurrence of pain.
McLachlin	1962	Unilateral swelling of the left ankle.
Lisker	1964	Percussing using the flexed fingers on the broad subcutaneous surface of the tibia, medial to the tibia crest. A positive test is the presence of bone tenderness.
Peabody	1964	The patient is supine and examiner places both thumb against the end of the second metatarsals on the plantar surface of the feet. Pressure is applied against the plantar aspect of the foot such that he is able to raise the feet approximately 20 in. off the bed. The examiner observes for evidence plantar flexion by noting the relative position of the medial side of the 1st metatarsals.
Chang	1965	Widening of the descending pulmonary artery as detected on chest radiograph.
Pataro	1965	The patient is placed in the prone or supine position with the leg flexed on the thigh at a 45° angle. Unidigital pressure is applied at equidistant points from the midline of the diseased calf. A positive test is the presence of fixed-point tenderness detected on the calf.
May	1969	Patient supine, blood pressure cuffs are placed on both calves and inflated to 150 mmHg. Healthy people report that the pressure is uncomfortable. However, on a diseased leg, the patient reports a pressure pain, grimaces and spontaneously withdraws his leg at 80–120 mmHg.
Davies	1972	Patients knee flexed to 90° and the foot resting on a flat surface. Palpation of the calves is conducted using the palmar aspect of the hands gently lifting the muscle up and down in order to detect a difference in weight and hardness of the calf muscles caused by intramuscular inflammatory edema.
Corrigan-Strachan	1973	Inability to fully extend the knee when flexed in the range of 20–25°.
Sigg	1979	Knee extended and downward pressure is applied to the patella using the palmar aspect of one hand while the other hand lifts the heel. A positive test is the presence of a strong pain in the popliteal fossa. This pain can also be provoked by vigorous pressure on the patella with the leg stretched out on a firm support.
Palla	1983	Widening of the descending pulmonary artery in patients with pulmonary embolism detected by chest radiography.
McConnell	1996	Among patients with acute pulmonary embolism and RV dysfunction, there is a distinct, regional pattern of abnormal RV wall motion involving akinesia of the mid-RV free wall.

Table 2
Location of symptoms and signs.

Location	Name of sign
Inguinal ligament	None
Thigh	Bailey, Lawrence, D'Alessandro, Louvel, Bellini, Lowenberg
Popliteal	Ortiz-Ramírez, Sigg
Leg	Rosenthal, Pratt, Lawrence, Louvel, Popkin, Lisker
Calf	Moses, Neuhof, Castañeda-Uribe, Lowenberg, Patero, May, Davies
Foot	McLachlin, Peabody

the University and Bellevue Hospital Medical College in 1929, and completed his internship at Barnett Memorial Hospital in Paterson, New Jersey from 1929 to 1930 [13]. At the time of the publication of his sign, he was Associate Surgeon at Barnett Memorial Hospital. He described the cough-pain sign as a method for diagnosing acute superficial thrombophlebitis of the legs:

> I have noticed that in many cases the pain in the inflamed area was increased by coughing, sneezing, or laughing. In these cases, compression of the greater saphenous vein close to the saphenofemoral junction resulted in the disappearance of the pain on coughing. This was found to be present in practically all patients who were seen early or when they are involved as at the knee or proximal; and in about 50 per cent of the cases with involvement below the knee. I have called this the “cough-pain sign” [14].

He reported that the sign may be absent in cases in which there is resolution of the inflammatory process, or if the superficial thrombophlebitis is below the knee. He believed that if the cough-pain sign remains positive after compressing the greater saphenous vein it may be caused by communicating veins (Tables 1, 2).

Table 3
Noteworthy contributions.

Name	Accomplishments
Neuhof	Made significant contributions to the field of medicine and surgery including his literary contributions to lung cancer, mediastinitis and thrombophlebitis as well as the transplantation of the kidney of a lamb into a human [3]. With colleagues in his department they developed a comprehensive pathophysiologic and surgical approach to lung abscesses [3]. Founding member of the American Board of Surgery and American Board of Thoracic Surgery, Fellow of the New York Academy of Medicine and American College of Surgeons, and Member of the American Association for Thoracic Surgery and American Surgical Association, and Societies of Surgery, Thoracic Surgery and Cardiovascular Surgery in New York [3].
Bailey	Wrote and edited fifteen books including *Emergency Surgery* (1920), *Demonstration of the Physical Signs in Clinical Surgery* (1927), and *A Short Practice of Surgery* with RJ McNeil Love (1932) [7]. His books were unique because of the clarity of presentation and use of illustrations and photography to explain disease or techniques [7].
D'Alessandro	Member of the American Medical Association, The Academy of Medicine of New Jersey and Fellow of the American College of Surgeons (FACS) [15].
Teófilo Ortiz-Ramírez	Founding president of Mexican Society of Cardiology between 1945 and 1946. member of the National Academy of Medicine and the National Institute for Cardiology, and General Director of the Interamerican Society of Cardiology [30].
McLachlin	Awarded the Queen's Jubilee Medal for his dedicated service to the community [37]. Fellow of the Royal College of Surgeons of Canada (FRCSC) and the American College of Surgeons (FACS), and recipient of the Research Gold Medal by the Royal College of Physicians and Surgeons [37].
Pataro	Honorary member of numerous national and foreign scientific societies, founder and President (1954–1957) of the Argentine Society of Angiology and editorial board member of *The Journal of Cardiovascular Surgery* [44].
Sigg	Honorary President of the Swiss Society for Phlebology, and honorary member of the German Society for Phlebology [50].
Palla	Editor of the *Journal of Nuclear Medicine-Allied Sciences* and member of editorial Committee of the *Quarterly Journal of Nuclear Medicine* [53].

3.7. D'Alessandro sign

Arthur Joseph D'Alessandro (1911–1983) graduated from Columbia University College of Physician and Surgeons, New York City in 1935 [15]. At the time of reporting his sign, he served as Assistant Surgeon in the peripheral vascular service at Presbyterian Hospital and Newark City Hospital, and was affiliated with St. James Hospital in Newark, New Jersey [16]. He described a number of important signs and symptoms of thromboembolism and stated:

> To these I should like to add a fairly constant, simple, and early sign that I have found to be of great value in my clinical practice. In the past five years, I have become increasingly aware, particularly on palpating the femoral pulse preparatory to vein ligation, of the significance of marked diminution or even absence of the femoral pulse in the affected extremity. This phenomenon has invariably been present, even in the absence of other appreciable signs or symptoms (…) [17].

He postulated that arterial vasospasm was the physiologic mechanism responsible for the deceased femoral pulse and that this finding occurs early, prior to edema or swelling of the lower extremity. [17] (Tables 1, 2).

3.8. Louvel sign

Jacques Louvel (1898–1983) was born in La Ferté-Macé Normandy, France. He finished his internship at Hôpitaux de Paris and later served as a chief physician of the cardiology clinic at the University [18]. Inspired by their masters, Vaquès and Laubry, Louvel published several articles related to cardiovascular pathology, as well as preventive and curative therapy of phlebitis [18]. Louvel and Laubry described at the March 16th, 1952 French Session of Cardiology entitled "Sur un symptôme peu connu de thrombophlébite" (On a less-known symptom of thrombophlebitis) (Tables 1, 2):

> [a] simple test, which we have used for nearly fifteen years and which we feel it is important to make others aware. This is pain caused by coughing in the presence of thrombophlebitis. When a subject complains of an intense pain in the leg, with or without dilatation of the superficial veins, with more or less marked edema, with or without pain on dorsiflexion of the foot is told to cough, and if cough causes pain in a suspected area of the vein, the diagnosis is phlebitis. The sign thus makes it possible to prove the venous and inflammatory origin of pain. This sign, when one is lucky to have it at the beginning of or during an evolving phlebitis episode, is the factor that guides the clinician on the possible extension of the inflammatory process. Thus, we were able to follow, step by step, even in the depth of the thigh, the ascending progression of a venous thrombus. (…) When coughing sign causes pain in a segment of the saphenous vein it is usually possible to suppress the symptom by exerting a digital pressure on the anastomotic sapheno-femoral junction. This is an indication for venous ligature. If however, despite compression of the saphenous junction, the pain of the underling venous thrombosis is still present by coughing, it is because there is another valvular failure originating below the sapheno-femoral junction communicating with the vein. Thus, the physician must identify the second site of failure and apply venous ligature [19].

Louvel noted that the sign can be used for diagnosing, treating, and determining response to treatment and its absence can be used to confirm resolution of the inflammatory process [19]. They reported that this sign is present in only 40% of cases. Lawrence previously reported in 1950 a positive "cough-pain sign" is as an indication for venous ligature.

3.9. Bellini sign

We were unable to identify any historical information on Dr. Ettore Bellini. At the time of the publication of his physical finding he served at the Ospedali Civili Riuniti di Venezia Prima Divisione Medica diretta dal Primario Prof. Angelo Spanio (United Civilian Hospital of Venice First Medical Division directed by Prof. Angelo Spanio) [20]. He reported in a communication to the Venetian Medical-Surgical Society session on January 29th, 1953 the finding of "a not infrequent observation in phlebitis disease, namely the detection and disappearance of the femoral and popliteal pulses" [21]. Dr. Bellini assessed the thigh and legs of 50 patients daily using a sphygmomanometer and an oscillometer to measure the pressure and pulse respectively. In patients with DVT, he found an increase in minimum pressure values (sometimes caused by increasing the minimum or lowering the maximum pressures), decrease in differential pressure, and decrease in the oscillometric curve and index, compared to the unaffected thigh and leg, or previous values in the same limb if both legs developed thrombosis. He also performed what he referred to as the "trinitric" (nitroglycerine) test as a method for distinguishing vasospastic from previous or coexisting arterial disease. A positive test was reported as a reappearance or increase in the affected limbs pulse rate and oscillometric index, reappearance or lowering of the maximum and minimum pressure, or increase of the differential pressure. Furthermore, to distinguish a coexisting or autonomous functional arteriopathy, he found that the reaction to trinitrine resolved in 30 min compared to those with DVT that

persisted for at least 6 h [21]. He concluded that phlebopathy induced a reflex mechanism and transient arterial vasospasm (Tables 1, 2).

3.10. Castañeda sign

We were unable to identify any historical information about Manuel Castañeda-Uribe. At the time of the description of his physical finding he served as Head of the Vascular Surgery Service at the General Hospital of Mexico and Sanatorium no. 1 of the IMSS [29]. Castañeda-Uribe presented his findings at the Mexican Association of Gynecology and Obstetrics in 1953 [22]:

> In phlebothrombosis edema does not occur early, but begins the third or fourth day and is localized to the supramalleolar region. However, there is another type of edema that is located in the calf muscles, infiltrating them, named "sign of the calf" (Castañeda Uribe), which is of a hard consistency that occurs when there is thrombosis of the veins of the leg due to ascending progression from the foot [22].

Thus, Castañeda Sign refers to the firm consistency of the calf muscle caused by DVT of the leg (Tables 1, 2).

3.11. Lowenberg sign

We were unable to identify any historical information on Dr. Robert I Lowenberg (1917–2000). He practiced as a vascular surgeon in the Department of Surgery, General Service at Grace-New Haven Community Hospital, Connecticut [23]. Lowenberg developed a sphygmomanometer cuff pain test for diagnosing and predicting the onset of phlebothrombosis. His findings were first reported in *Science* in 1954:

> A pneumatic cuff is distended over the calf or thigh slowly to 180 mmHg pressure. If pain is elicited before this, the end point has been reached and the cuff is deflated. A positive cuff test is indicated by pain beneath the inflated cuff at 80, 100, or 120 mmHg. A negative test that becomes positive a few days post-operatively or several days after a patient has been put to bed with a myocardial infarction is presumed evidence of intravascular clot and should be treated as such [23].

He expanded upon this further with more detailed information included in his publication in the *Journal of the American Medical Association* that same year as follows:

> In patients suspected of having phlebothrombosis, the pneumatic cuff is placed about the calf or thigh and slowly distended; distention of the cuff should be accomplished in 10 to 15 seconds. Normally patients do not register discomfort below 180 mmHg over the calf or thigh. In the presence of phlebitis, the patient will complain bitterly of pain at a level of significantly below the normal [24].

The technique involved as described by Lowenberg:

> In performing the test, the patient's threshold for pain must first be determined. In order to accomplish this, the oscillometer cuff is placed on the arm and rapidly distended to two hundred fifty millimeters of mercury. The average patient experiences no pain at this pressure. The test is then performed by similar compression successively of the lower limbs above and below the knee. A blood pressure cuff or an oscillometer cuff serve equally well for this study. A level of one hundred eighty to two hundred millimeters of mercury pressure has been found proper for the lower extremity. If pain is experienced as indicated by the patient's withdrawing the limb, wincing, or crying out, the cuff is immediately deflated. This is considered a positive test. For the purpose of checking the patients' reliability, the test may be safely repeated within a minute or two. The same response should be elicited within twenty millimeters of mercury pressure. (…) In patients with a reduced pain threshold, a pain response at levels below 180 mmHg must be given special interpretation relative to the pain-response level on the upper extremity [25].

A positive sphygmomanometer cuff test occurs if pain is between 60 and 150 mmHg. For confirmation, he recommended repeating the test with the new value being within 10 mmHg of the previous one. [24]. Lowenberg acknowledged that false positive results are found in patients with muscle cramps, trauma, superficial phlebitis, and intermittent claudication, and that no false negative results were identified. He also recommended that the cuff test should not be performed in patients with superficial thrombophlebitis since it may elicit pain and exacerbate the disease [25] (Tables 1, 2).

3.12. Rose sign

We were only able to identify limited historical information about S.S. Rose. He was a member of the Department of Surgery at the University of Manchester and Withington Hospital, Manchester [26]. He served as Vice-Chairman on the Organizing Committee of the First United Kingdom Meeting of the Union International de Phlébologie (International Union of Phlebology) in 1985 [27], and from 1983 to 1987 was Chief Editor of the *Journal of the International Society for Cardiovascular Surgery* [28].

We were unable to identify the original reference to this sign. Bailey described, Rose sign, in his textbook *Physical Signs of in Clinical Surgery* as the method for identifying early edema in patients with suspected DVT. This involves: "pinch up a small portion of skin. In very early edema there is a resistance that is not present on the normal side, owing to thickening of the dermis and subcutaneous tissue" [29] (Tables 1, 2).

3.13. Ortiz-Ramírez sign

Teófilo Ortiz-Ramírez was born in 1901 in Morelia, Michoacán, Mexico and received his medical degree in 1924 at the National University of Mexico. Remaining in the Faculty of Medicine, he earned the title Professor of Introductory to Clinical Medicine from 1929 to 1932, Pathology Physiology in 1930, and Clinical Medicine beginning in 1933 [30]. He also led the Section of Experimental Biochemistry, the Consulting Department, Chemistry, and Pharmacy at various times at the National Department of Health in Mexico between 1927 and 1935 [30]. In 1955, he was Professor at The National University of Mexico (UNAM) [30] (Table 3).

Teófilo Ortiz-Ramírez and R. Serna-Ramírez described a method for detecting phlebitis in the lower extremities (Tables 1, 2):

> With the patient in the recumbent position and the extremity to be explored slightly flexed, a sphygmomanometer mercury cuff was applied above the knee, with a pressure of around 4 cm. Hg. The venous hypertension provoked pain in some place, most often in the popliteal region of the calf in cases of deep phlebitis. The pain increased during the 5 minutes of the test, sometimes it was similar to pain occurring spontaneously, and disappeared almost instantaneously after releasing the pressure [31].

They reported a positive sign requires that pain appears or increases with pressure and decreases with release of the sphygmomanometer. The cuff sign was found in 32 (100%) with phlebitis as compared to 81% identified by Homans sign [31]. Oritz-Ramirez and Serna-Ramirez postulated that compression of the thigh causes distention of the venous system and pain within 1–2 min [31]. They believed that pain in patients with thrombophlebitis is caused by venous distention, the sign was not pathognomonic for DVT since it was assessed in a non-homogenous population, and venous thrombosis was not definitively confirmed [31].

3.14. Popkin sign

There is limited historical information available about Roy J. Popkin. He received his medical degree from the University of Minnesota in 1930 [32], and served as an attending in medicine and later as Chief of the Peripheral Vascular Clinic at the Cedars of Lebanon Hospital, Los Angeles, California [33]. He described the "finger pressure test" in patients with venous stasis of the lower extremities:

> [b]est performed with the patient recumbent and the shoes and stockings removed. Sufficient pressure is applied with the index finger or thumb over the anteromedial surface of the leg compressing the tissues between the fingers and underlying bone. The pain is usually more intense distally and disappears proximally. The intensity of the pain produced frequently surprises the patient. It is often unexpected. The complaint of pain and evidence of pitting are found more often in the afternoon or when the patient has been up and about for several hours [34].

Popkin reported that the sign was present in a variety of conditions associated with venous insufficiency or obstruction causing venous stasis. He hypothesized that the source of pain may be due to afferent fibers along the veins. This sign is believed to be a sensitive but non-specific finding in DVT (Tables 1, 2).

3.15. McLachlin sign

John Adams McLachlin (1915–2004) received his medical degree from the University of Western Ontario in 1940. He served during WWII as a Surgeon (Lieutenant Commander) in the Royal Canadian Navy [35], followed by positions as Chief of Surgery at St. Thomas-Elgin General Hospital, and Instructor at the University of Western Ontario. At the time of his publication he worked at Westminster Hospital, Department of Veterans Affairs, and the Departments of Medical Research and Surgery at the University of Western Ontario [36]. McLachlin was the recipient of a number of honors and awards for his contributions to medicine [37] (Table 3).

McLachlin et al. reported in their paper entitled "An evaluation of clinical signs in the diagnosis of venous thrombosis" that (Tables 1, 2):

> Unilateral swelling of the ankle is, by far, the best single test in the clinical diagnosis of venous thrombosis. If asymmetrical swelling of the ankle is noticed, the diagnosis of venous thrombosis must be suspect. (…) It must be emphasized, however, that swelling of the ankle seems to be of diagnostic validity for the left leg only [36].

MacLachin et al., in their small necropsy series showed that an increased circumference of the left ankle, identified in 83% of patients, was the only finding among local tenderness, changes in skin temperature, Homans' dorsiflexion sign, and venous dilation useful in detecting DVT [36].

3.16. Lisker sign

We were able to identify only limited historical information about Dr. Samuel Lisker. At the time of the publication describing his sign, he served as Assistant Professor of Medicine and Director of the Division of Peripheral Vascular Diseases and Clinic at Graduate Hospital, University of Pennsylvania, Philadelphia [38]. Edward W. Knox, MD, MRCPI, a fellow of Dr. Lisker, described the clinical findings of thrombophlebitis in a series of 20 unselected patients at the University of Pennsylvania [38]. In this series, he used the tibial tap sign, or Lisker sign that involved percussing using the flexed fingers on "the broad subcutaneous surface of the tibia medial to the crest" [38]. A positive sign is the presence of bone tenderness. In cases where the sign was uncertain, percussion tenderness over the patella is compared to the tibia. The tibia test is considered insignificant if tenderness is equivalent over both sites. In Knox's series, tenderness over the upper third of the tibia resolved faster than the lower two-thirds. Furthermore, tenderness presents more acutely and is more common in the lower two-thirds of the tibiae. They hypothesized that bone tenderness was caused by increased inter-osseous pressure due to venous thrombosis and obstruction of venous blood flow [38].

Knox identified a positive Lisker sign in 26 of 30 patients' legs. Tenderness was found distributed throughout the tibia in fourteen patients, more severe in the lower two-thirds in ten patients and the upper area in two patients [38]. This sign is said to be present in 65% of patients with thrombophlebitis [39] (Tables 1, 2).

3.17. Peabody sign

There is limited historical information on Dr. Charles Newton Peabody (1925–2011). Peabody received his medical degree from Harvard University in 1946 [40]. At the time of his publication he was a member in Department of Surgery, Framingham Union Hospital, Framingham, Massachusetts [41]. Peabody later became an Assistant Professor at the Boston University School of Medicine. He was a navy veteran of the Korean War and remained a member of the Naval Reserve until his retirement as a commander in 1976 [41]. Peabody described the plantar flexion spasm technique as a later sign to diagnose thrombophlebitis:

> The examiner stands at the end of the bed with the covers pulled back and the legs exposed. The feet are placed opposite each other. The examiner then places both his thumbs against the ends of the second metatarsals on the plantar surface of the feet. He then applies enough pressure against the bottom of the foot so that he can raise the feet off the bed about 20 inches. He observes the difference in plantar flexion by looking down at the feet. This is done by noting the relative position of the medial side of the end of the first metatarsals. When the internal malleoli are touching or nearly opposite each other, the bunions in the normal person will remain opposite each other. But if there is calf muscle spasm, the bunion in the diseased foot will be more plantar flexed [42].

He postulated that thrombophlebitis causes a low-grade spasm of the gastrocnemius and soleus muscles resulting in foot plantar flexion. The degree of plantar flexion seen was proportionate to the amount of resistance caused by spasm of the gastrocnemius muscle. In 25 patients with thrombophlebitis, Peabody found the plantar flexion sign in 20 (80%), calf tenderness in 24 (96%), Lowenberg's sign in 21 (84%), and Homans' and plantar flexion signs in 20 (80%). Thus, the sign was as reliable as Homans and Lowenberg signs [42] (Tables 1, 2).

3.18. Chang sign

There is limited historical information available about C.H. Joseph Chang and Clayton Davis. Chang was a member in the Department of Radiology at West Virginia University School of Medicine, Morgantown, West, Virginia. Davis, coauthor of this manuscript, was a Fellow of the American College of Surgery (FACS) and Associate Chief of Surgery, Man Memorial Hospital, Man, West Virginia [43]. They reported:

> The most consistent roentgen sign of pulmonary embolism in our patients were dilation of the descending pulmonary artery, parenchymal densities and pleural fluid. The earliest consistent sign was widening of a previously normal descending pulmonary artery. This sign usually appeared within 24 hours of the onset of chest pain and shows its maximal measurement within two or three days. Dilation of the descending pulmonary artery persists for a period of one to two weeks and usually returned to normal in three to four weeks [43].

In their series of 23 consecutive patients with pulmonary infarction, all patients were found to have dilation of the right (19), or left (4)

descending pulmonary arteries. The size of the right descending pulmonary artery ranged from (17–22 mm normal upper limit on inspiration 16 for adult males and 15 mm for adult females) and of the left descending pulmonary artery ranging from 17 to 26 mm (normal range < 17 mm) [43] (Table 1).

3.19. Pataro sign

Vicente Francisco Pataro (1907–1983), professor of surgery at the Faculty of Medicine in Buenos Aires, Argentina was one of the most important figures of Argentine surgery of the twentieth century. He was born in Buenos Aires on March 2, 1907 and received his medical degree from the Faculty of Medicine of the University of Buenos Aires [44]. In 1935, he initially served in Room V of the Pirovano Hospital, and later became Head of the Surgical Clinic at the Dr. Ricardo Finochietto Polyclinic, Avellaneda, Buenos Aires [44]. Pataro also served as a surgical consultant of the Naval Hospital of Buenos Aires from 1962 until his death.

Sfarcich described in his paper entitled "La presión unidigital de pantorrilla como signo thrombosis venosa aguda de los miembros inferiors" (Calf unidigital pressure as a sign of acute venous thrombosis of the lower limbs), a sign that was initially described in 1954 in the *Interpoliclínicos Days of the National Institute of Social Medicine*:

> The sign taught by Dr. Vicente F Pataro, which he calls McBurney's calf, is in our opinion the most useful sign in the investigation of acute venous thrombosis. It is the first one that appears and the last to disappear after treatment. When the calf is painful, and when systematically investigated, a fixed point of pain is always found. It is similar to that which occurs in acute appendicitis - although the entire right iliac fossa is painful, there is a point of exquisite pain named McBurney's point. That's why Dr. Pataro called this one McBurney's sign of the calf. The obvious value of this sign is that a calf can hurt for several reasons, but the well-located and fixed painful point is an unambiguous sign of acute venous thrombosis [45].

The test is performed as follows: "The patient is placed in the prone or supine position with the leg flexed on the thigh at a 45° angle. (…) To assess for the presence of pain, unidigital pressure is applied at equidistant points from the midline of the diseased calf" [45] (Tables 1, 2).

3.20. May sign

Robert May (1914–1984) was born in Klagenfurt, Kärnten and studied medicine in Innsbruck, Austria from 1933 to 1938 [46]. He was taught phlebology by René Lehriche and C.L. Olivier in Paris and completed his surgical preparation in Vienna and London [46]. In 1956, he was head of the Vascular Department at Krankenhaus der Kreuzschwestern (Hospital of Cross Sisters), University of Innsbruck, Austria [46,47] and in 1982 was named Professor of Phlebology [46].

May reported in his paper entitled "Frühdiagnostik peripherer venöser und arterieller Durchblutungsstörungen" (Early diagnosis of peripheral venous and arterial circulatory disorders) a method for detecting venous thrombosis:

> With the patient lying, blood pressure cuffs are placed on both calves. Both cuffs are inflated to 150 mmHg. Healthy people report that the pressure is uncomfortable. However, on a diseased leg, the patient reports a pressure pain, grimaces and spontaneously withdraws his leg at 80-120 mmHg [47].

Thus, May described an early method for detecting DVT using a sphygmomanometer (Tables 1, 2).

3.21. Davies sign

There is limited historical information available about Ieuan John Treharne Davies. At the time of his publication he was a member in the Department of Medicine, University Hospital of Wales [48]. He described a method for detecting DVT in the calf:

> Palpation of the calves should be performed with the flat of the hand by gently lifting the muscle up and down with the knee flexed to 90° and the foot resting on the bed. Palpation is aimed at detecting a difference in weight of the calf muscles and a difference in hardness of the muscles due to intramuscular inflammatory oedema [48].

Thus, Davies sign refers to the palpatory firmness of the calf muscles in patients with DVT (Tables 1, 2).

3.22. Corrigan-Strachan sign

There is limited historical information about Drs. Corrigan or Strachan. At the time of the publication, Thomas Corrigan and Colin J.L. Strachan were members of the Department of Surgery at King's College Hospital Medical School, London and Mater Misericordæ Hospital, Dublin, Republic of Ireland [49]. They described two patients with extensive DVT with or without superficial thrombosis in which the knee was flexed in the range of 20–25°, "short of full extension and the patient was unable to extend it beyond this point." [49]. They reported that DVT "should be kept in mind in the presence of a flexed knee of recent onset whether no joint lesion is found." They attributed this finding to muscle spasms and/or sciatic neuritis (Table 1).

3.23. Sigg sign

Dr. Karl Sigg (1912–1986) was born in Basel, Switzerland and completed his medical training in this same city. In 1939, he established a practice for the management of venous diseases [50]. He was Head of the Polyclinic for Venous Diseases at the University Gynecological Clinic Basel (Table 3).

Wupperman described a sign of pain in the knee-joint during hyperextension for diagnosing DVT that he dedicated in gratitude to his revered teacher Karl Sigg. The maneuver is performed as follows:

> Pressure is applied to the patella with one palm and simultaneously, the heel is lifted with the other hand, and causes a strong pain in the popliteal fossa. This pain can also be provoked by vigorous pressure on the patella with the leg stretched out on a firm support [51].

In patients with phlebographically proven thromboses, a mean positive accuracy of 0.83 and a mean specificity of 0.56 was found for Sigg sign [51]. They found that Sigg sign, compared to Lowenberg, Bisgaard, Payr, Homans, Deneke, and Pratt signs, as well as pressure pain in the calf, showed the highest observed overall mean positive postoperative accuracy (0.57), while the overall specificity did not differ from the other signs of thrombosis (0.62) [51] (Table 1).

3.24. Palla sign

Antonio Palla received his degree in medicine and surgery from the University of Pisa in 1974 [52]. In 1963, he served at the CNR Institute of Clinical Physiology and Second Medical Clinic, from 1977 to 1980 he was an Assistant at the Institute of Clinical Medicine, in 1980 was appointed Chair of the Department of Respiratory Diseases at the University of Pisa, and in 2011 was named Ordinary Professor of Respiratory Disease at the University of Pisa [53,54] (Table 3).

Palla et al. conduced a quantitative radiographic analysis of the right descending pulmonary artery in 73 (118) patients with confirmed pulmonary embolism (61 scintigraphy and 12 pulmonary angiography) and in 85 (147) patients with unconfirmed suspicion of pulmonary embolism (perfusion lung scan). They found that:

> (…) the enlargement of descending pulmonary artery may be useful to raise the suspicion of pulmonary embolisms. As documented here,

the descending pulmonary artery was wider in patients with confirmed pulmonary embolism than in those without confirmation. The typical “sausage” appearance of the descending pulmonary artery, easily recognizable without any measurement, was present in about one-fourth of the patients with confirmed pulmonary embolism, and it was never observed in patients in whom the original clinical suspicion of pulmonary embolism was rejected subsequently [54].

It is of historic interest that transient enlargement of the pulmonary artery had been previously described by Fleishner in 1958 [55]. It was Palla and colleagues who performed the first accurate and quantitative analysis of the descending pulmonary artery in pulmonary embolism (Table 1).

3.25. McConnell sign

Michael V. McConnell received his medical degree from Stanford University, California, in 1990 and completed his internship and residency in Internal Medicine at Bingham and Women's Hospital, Harvard Medical School, Massachusetts, followed by a fellowship in Cardiology and Cardiovascular Imaging at Brigham and Women's' and Beth Israel Hospitals, Boston in 1996 [56]. From 2000 to 2015, he served as Director of the Cardiovascular MRI program and from 2010 to 2013 was Director of Preventive Cardiology Clinic in the Stanford Division of Cardiovascular Medicine [56]. From 2008 to 2015, he served as Director of the NIH Training Program in Cardiovascular Imaging at Stanford (CVIS) and from 2014 to 2015 served as Director of the Cardiovascular Health Innovation [56]. He is Clinical Professor of Medicine in Cardiovascular Medicine where he has appointments in preventive medicine and cardiovascular imaging [57]. His current focus involves using technology as a means to prevent, detect, and manage disease as Head of Cardiovascular Health Innovations at Verily Life Sciences [57]. In a study cohort of 41 patients and a validation cohort of 85 patients, McConnell and colleagues found in the right ventricle (RV):

> Among patients with acute pulmonary embolism and RV dysfunction, there is a distinct, regional pattern of abnormal RV wall motion. Both quantitative and qualitative analyses of 2-dimensional echocardiograms in patients with acute pulmonary embolism revealed normal wall motion of the RV apex but akinesia of the mid-RV free wall [58].

They reported a sensitivity, specificity, positive and negative predictive values of 77%, 94%, 71%, and 96% respectively. Casazza et al. retrospectively compared two-dimensional echocardiographic recordings in 107 patients with pulmonary embolism and 54 patients with right ventricular infarction through independent and blind review. They found that the McConnell sign had a sensitivity of 70%, specificity of 33%, positive and negative predictive values of 67 and 36% respectively [59]. Vaid et al. retrospectively studied 37 patients who had the McConnell sign identified on ECHO-CG. All patients underwent another confirmatory diagnostic study including a computed tomography pulmonary angiography, ventilation-perfusion scan, lower extremity doppler ultrasound or autopsy. They found that the PPV of McConnell's sign was 40% (CI, 24%–56%) [60].

Evidence suggests that the sign lacks sufficient specificity to be used alone in the diagnosis of acute pulmonary embolism, (Table 1). Additionally, assessing right ventricular afterload, right and left ventricular diameters, tricuspid insufficiency using flow velocity pattern, and intraluminal thrombosis and/or embolism provides useful information to further support the diagnosis of acute pulmonary embolism [61–63].

4. Conclusion

Eponymic signs are believed to have a low specificity and predictive accuracy and do not appear to be useful in distinguishing patients with or without DVT. There are a number of limitations that may affect this conclusion including methodology, sample size, imaging techniques used as the gold standard, and use of control population. Nevertheless, despite gaps in knowledge regarding their validity and reliability, they remain historically important since many were conceived prior to the advent of noninvasive laboratory and imaging techniques that have tremendously facilitated the accurate diagnosis of VTE. The use of eponyms confers historical, literary, and cultural information that reaches beyond and therefore conveys the dignity of a broader educational background and understanding.

Accurate knowledge of eponyms of VTE and a familiarity with the clinicians and their stories, provides interesting background information and in some instances, an easier milieu for remembering their sign. Although most eponyms are infrequently used by clinicians, the information conveyed by these signs may lead to further proficiency in clinical skills and performance and may assist in considering venous thrombosis when used in conjunction with the history and other clinical signs and symptoms. Advancements in imaging techniques led to an enhanced understanding of findings that can be used to detect VTE. Further interest to rigorously study these signs was supplanted when routine use and availability of duplex ultrasonography to screen patients for DVT became commonplace in medical practice.

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