

# Diapedesis leading to hematidrosis due to abrupt emotional suffering (Review)

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Received November 21, 2023; Accepted September 13, 2024

DOI: 10.3892/etm.2024.12743

**Abstract.** Hematidrosis constitutes a rare imposing phenomenon encountered millennia ago. It involves the plexus of small, mostly superficial arteries, veins and sweat glands of various parts of the human body. Bloody sweat implies skin pathology. It has been connected to psychogenic impairment and lacks a clear etiology. The present study conducted a historical review using the Thesaurus Linguae Graecae®, Gallica-BNF and Google Books databases. The year 1900 was the mark for full-text works to be included. A second review of the modern literature, over the last 20 years, was carried out using the PubMed/MedLine database. In both eras, the terms h[ematid]rosis, diapedesis, sudor sanguineus, plus various others vocables of Hellenic and Latin origin, were used as key words. Cases of persons suffering hematidrosis during stigmata as partly connected to this study were surveyed and discussed separately. References were obtained from the classical Greece, late Hellenic antiquity and Roman era. A number of 70 cases were registered from the Renaissance to 1900, and 44 cases between 2007 and 2022. The later time interval is considered as the selection of references of all time, while the 1870 to 1884 interval followed. Differences in sex were observed (males, 60.6%; and females, 39.4%; vs. males, 25.6%; and females, 74.4%). The scalp, forehead, face, trunk, arms and legs were the most common areas of appearance in both time intervals.

The eyes and ears were the most common areas of appearance in the modern era. As regards the limitations of the present review, it should be emphasized that not all historical cases were available for survey. Stigmata were studied independently. Records in etiology hypothesis, pathological description and the manifestation of a cluster of post-triggering effects described were similar over time. The modern way of life, major stressful events, a fear of death, hematological disorders, vessel derangements and deep faith may trigger hematidrosis. This spectacular acute event stimulates alertness in patients, family, caregivers and physicians, and may lead to social isolation and unnecessary diagnostic and/or therapeutic interventions. The present narrative review aimed to connect science with history and religion, promote contemplation among health professionals and highlight a medical peculiarity. An open mind is warranted in order to comprehend phenomena in religion. Education for the family and a knowledge update for health professionals is also necessary.

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## 1. Introduction

As reported from the Hellenic Classical Era, hematidrosis is a rare medical cutaneous condition (International Classification of Diseases/ICD-10: L 74.8) which has rarely been noted throughout the ages. It is regarded as an eccrine sweat disorder, which is defined as the spontaneous dermatological excretion

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**Key words:** bloody sweat, sudor sanguineus, psychic disorders, stigmata, dermatology

of a mixture of blood and sweat directly from non-traumatized skin. The pathological mechanism of blood oozing from the skin and mucosa remains unclear. However, it is hypothesized that dermal deficiencies can lead to blood-filled spaces, which may be exuded into follicular canals, or directly to the skin surface, demonstrating this peculiar phenomenon (1,2). As a medical term, it is composed of two Greek words 'hema' (blood) and 'idrosis' (sweating), while certain other associated terms used in the English medical literature include the words stigmata (also of Greek origin, hysterical stigmata), diapedesis (also of Greek origin, meaning jumping through), vicarious menstruation, ephidrosis cruenta (Greco-Latin origin), sudor cruentus and sudor sanguineus (Latin terms) (3). Hematidrosis, is classed as a somatic symptom disorder, almost always related to psychic imbalance, ranging from acute or chronic anxiety to fear (rivalry, scolding, punishment, bullying). Reports exist of extensive unnecessary investigations, which at times, have led towards risky therapeutic interventions (1,2,4). Thomas K. Chambers in 1861, suggested that this strange experience had triggered a 'need to publish' trend of case reports that otherwise may have been neglected. Nevertheless, the majority of available articles on the subject have appeared over the past decades. In Christianity, its notorious appearance was connected to the agony in the biblical historical reference on the 'bloody tears' of Jesus Christ in the Garden of Gethsemane (1,5).

The present study, inspired by the nature of hematidrosis itself, aimed to highlight both the hallmarks in the history of medicine, as well as the currently available scientific evidence. By searching through the archives of the literature in the past and simultaneously conducting a narrative review of the recent research, the present study aimed to provide a clearer picture and a thesaurus for this 'marvel' entity in dermatology.

## 2. Literature search strategy

A research strategy was developed to identify relevant literature. This included selecting key search terms and deciding on the criteria of inclusion and exclusion. Moreover, certain conditions were set that are critical to the quality and breadth of the present scoping review, framed by historical and epistemological sources, starting from their compatibility and retrospective consistency in the clinical context. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were used consultatively to avoid a major quality deficit regarding the studies included (6). The key words which were used to render and describe this clinical entity were verbally similar diagnostic terms concerning their syllabic pronunciation to provide access to appropriate articles, chapters and books and various references, thus explaining the intended dual search. Key words included hemaditrosis, haematidrosis, hemathidrosis, αίμα and ιδρώτας (blood and sweat for the Greek texts), diapedesis, stigmata hysterica, sudor cruentus and sudor sanguineus (bleeding sweat and bloody sweat for the Latin texts). All terms are considered directly related to the research question. The present narrative review was based on original studies, clinical case reports and series, opinion articles, letters to the editor and review articles to investigate recent knowledge. A thorough survey was conducted in the online medical database PubMed/Medline for studies published over the past two

decades until December 1, 2022. To limit the search and to set criteria, full-text articles published in the English language were only included. The eligibility of each citation was based on the title, abstract and full content of the articles considered and retrieved, taking into account the predefined admission criteria, such as methodological excellence, authorship, the relevance of the responsible correspondence author, and the quality and visibility characteristics of the biomedical journal hosting the publication. The factors that were evaluated covered the frequency of recording the clinical entity, management parameters, the time course of clinical manifestations, coexisting pathologic conditions and the socio-demographic and clinical characteristics of the patients. For the historical investigation, a bibliographic review was conducted using a documentary research methodology, applying the same key words as aforementioned. The year 1900 marked the end of the historical research. The survey included the following: i) Texts of antiquity within the online database Thesaurus Linguae Graecae (TLG) in Latin and Greek language; ii) works within Gallica Digital Library (Gallica-BnF) in the French language; and iii) books within online Google Digital Book Index (Google Books) in the English, French, German, Italian and Latin languages. Full-text availability was set as a criterion. Cases associated with religion and religious books were excluded for possible bigotry and deisidaimonía (superstition) to be avoided. On the other hand, this exclusion criterion may provoke a bias concerning cases with true hematidrosis. Thus, cases presenting hematidrosis during stigmata phenomenon were excluded from the main review; however, as they were partly connected to the symptom in study, they are being historically perused, discussed and registered independently.

## 3. Results of the literature search

Historical records unveiled relevant fragments of treatises during Greek antiquity, the case of Jesus Christ in early Christianity and 64 works with case references from the Renaissance until 1900. A summary of nine works had been included from within TLG, seven from Gallica-BnF and 57 from Google Books. Of the cases referred, 29 were in English, 13 in French, 13 in Latin, eight in German and one in Italian. Among the 64 works, 70 hematidrosis incidents were revealed. The mean age of those who suffered was 25.6 years. The time expanse for case reports was 426 years (Table I). The female sex was recorded in 39.7% of the affected individuals (Fig. 1). Articles in other languages (one in Russian, one in Czech and two in Spanish) were excluded, as well as some cases with no full texts (five works). A systematic search of the current medical literature of the past two decades retrieved 56 articles, 37 of which were eligible for all data requirements to have been included in the present review. Non-English articles, nine in total, five publications with no abstract or text available, and five overlapping publications were isolated and excluded. Among the 37 articles identified, a total of 44 cases were recorded. The mean age of the affected individuals was 15.8 years. The female sex exhibited a 74.4% dominance. The total time span was 15 years (2008-2022) (Table II). The number of articles on hematidrosis presents with a peak during the second half of the 19th century and after 2007. Until the end of 19th century, articles had appeared in Latin, Italian, German, French and

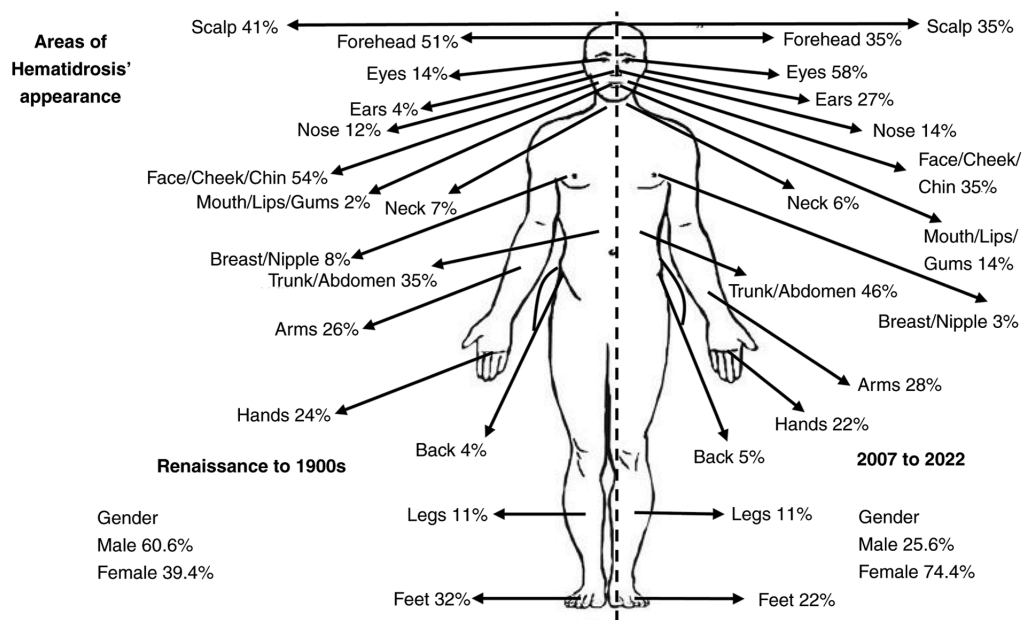


Figure 1. Areas of the body for the appearance of hematidrosis. Comparison of the anatomical body areas of appearance of hematidrosis between the two eras investigated, i) the Renaissance to 1900, and ii) 2007 to 2022.

English languages, with English language encompassing the majority of articles, followed by French and Latin. Over past two decades, all articles are written in English. A comparison of the bodily areas of the appearance of hematidrosis between the two eras in question is demonstrated in Fig. 1. Cases of famous individuals, 26 in total, experiencing hematidrosis under stigmata exposure are registered separately (Table III).

#### 4. Hallmarks in history

The phenomenon of sweat which resembles blood was coined to the observations noted in medicine by the ancient Greeks. Hematidrosis appeared as an affliction from the unbroken surface of the skin and greatly attracted the interest of scholars, medico-philosophers and theologians of antiquity. Aristotle was the first to mention bloody sweat in two fragments of his works, 'if blood gets too wet people get very weak. It becomes like ichor (pus, coagulation disorders) and appears so that many have seen bloody sweat' (7), and 'Instances, indeed, are not unknown of persons who in consequence of a cachectic state have secreted sweat that resembled blood' (8). Theophrastus the philosopher, the successor of Aristotle in the Peripatetic School also mentioned that 'sometimes with sweat blood appears' (9). The Greek historian, Diodorus Siculus, in his masterpiece entitled *Bibliotheca Historica* reported cases of individuals bitten by snakes tormented with pain and seized with a bloody sweat (10). The Pseudo-Galenic collection of works mentioned sweat with blood into two books, 'De Utilitate Respirationi' (Latin text, paraphrasing the reports of Aristotle) and 'De Humoribus Liber' (Greek text, sweats in spring and summer produced by having blood and bile) (11). Marcus Annaeus Lucanus noted that the human body could emit humor, such as blood from various areas such as the limbs and nostrils (12). Hematidrosis was connected with acute anxiety in the case of Jesus Christ prior to his arrest and crucifixion inside the gospel of the physician and evangelist Luke, where Christ is reported

to sweat large drops of blood when he was praying with agony in the garden of Gethsemane (Luke 22:44) (13). This report further enhanced curiosity as opposed to the phenomenon itself, resulting in numerous references by scholars throughout the next centuries and fanatic religious to state that they also similarly suffer. Kings, state officials, military officers and common individuals in agony under fear or hysteria were reported as cases of hematidrosis until the 19th century (14-31). A. Westphal wrote one of the first post-medieval dissertations on the subject, entitled *De Sudore Sanguineo* in 1775 (32). The article of Jules Parrot's entitled 'Study of bloody sweat and neuropathic hemorrhage' in 1859 was considered in its era the most essential work on the subject. This original work attracted attention to the appearance of cutaneous hemorrhages and hematidrosis during paroxysms of a neuralgia, which was extremely severe and variously located (17,33). For some researchers, hematidrosis was classified as an entity related to hemophilia (Greek term meaning friendship for blood) (34), characterized by the suddenness of appearance with various outbreak patterns, connected sometime with the vicarious menstruation (35). It was also closely related to the central nervous paralysis and hysteria, to ecstasy, to agony, to convulsion (spasms), to hallucinations and in general in neurology disorders, reported as a rare symptom (36,37). According to the beliefs of the epoch, blood pure, or mingled with sweat could appear on the surface of the skin in the form of drops or issues from the glandular openings (pilo-sebaceous, Meibomian, ceruminous) in tiny jets. Moreover, dermatorrhagia (bleeding from the sub-epidermic vascular network) could occur simultaneously and the condition have also been considered as a form of hyperhidrosis with fatal symptomatology (weakness, anemia, syncope and death) (38).

The most prolific complete treatise on the subject of hematidrosis was this of Ernst Ziegler in 1895, naming hematidrosis as diapedesis. Diapedesis of the blood through uninjured walls of vessels was considered as something peculiar and a different

Table I. Works with references to hematomatidrosis cases from the Renaissance until 1900.

No.	Original author <sup>a</sup>	Case	Body locations of hematidrosis	Work and year of publication
1	Johannes Müller von Königsberg (32) (Regiomontanus)	Young boy accused for a crime	Whole body	Ephemerides, 1474
2	Leonardo da Vinci (98)	Soldier departing for battle	Forehead, whole body	Ca 1503, La Battaglia di Anghiari era (Malvin Pilato, The Memoirs of Dr. Michael Arthur Creed, 2010)
3	Jacques Auguste de Thou (17)	Italian officer of Monte Maro fortress proposed to surrender or die	Whole body	Historia sui temporis, 1560-1584, (French translation of 1711)
4	Jacques Auguste de Thou (17)	Young Florentine sentenced to death by Pope Sixtus V	Whole body and tears	Historia sui temporis, 1560-1584, (French translation of 1711)
5	Wilhelm Fabricius von Hilden (23)	12-year-old child after drinking red wine	Gums, every part of integuments, nose	Observationem et curationem chirurgicam centuriae sex, 1606
6	Wilhelm Fabricius von Hilden (23)	45-year-old widow losing her only son	Upper part of the body, back of the head, temples, eyes, nose breast, tips of the fingers	Observationem et curationem chirurgicam centuriae sex, 1606
7	Henricus ab Heer (23)	Man	Bloody sweat with worm like coagulation	Observo Medicinalis, ca 1600-1636
8	Georg Spörlin (24)	12-year-old boy with high fever	Whole body	Letter in Wilhelm Fabricius Hildanus. In: Opera quae extant omni, 1627
9	Paolo Zacchia (22)	Young man condemned to die in flames	Whole body	1628 (Quaestiones medico-legales, 1621-1651)
10	François Eudes de Mézeray (17)	Charles IX King of France	Whole body (pores and conduits)	Histoire de France depuis Faramond jusqu'au règne de Louis le juste, 1643-1651
11	François Eudes de Mézeray (17)	Mayor of a town destroyed by a heavy storm and condemned to die	Whole body	Histoire de France depuis Faramond jusqu'au règne de Louis le juste, 1643-1651
12	James Henry Pooley (14)	Sailor during a storm	Whole body	Memoirs of the Society of Arts of Haarlem (Popular Science Monthly, 1884)
13	Thomas Bartholinus (22)	Various cases after vehement terror agonies of torture	Whole body	De nivis usu medico observationes variae Chapter XXII, 1661
14	Du Gard (32)	3-month-old child dying	Nose, ears, hinder part of the head, fingers, toes	Philosophical Transactions, 1674
15	S. Ledelius (25)	Woman nursing	Breasts	Sudor sanguineus. Misc Curiosa, Sive, Ephemeridum MedicoPhysicarum Germanicarum, 1683
16	Herman Boerhaave (19)	Girl suffering from cold finger syndrome	Whole body	Ca 1688-1720 (Index-catalogue of the Library of the Surgeon-General's Office, United States Army, 1889)
17	Johannes Franciscus Vicarius (32)	Newborn boy	Right arm	De sudore cruento frequentiore, Misc. Acad. Nat. Curios., 1694 (Magnet JJ. Bibliotheca medico-practica sive rerum medicarum thesaurus Cumulatissimus, 1698)

Table I. Continued.

No.	Original author <sup>a</sup>	Case	Body locations of hematidrosis	Work and year of publication
18	S. Ledelius (25)	Man with scurvy	Whole body	Manget JJ. Bibliotheca medico-practica sive rerum medicinarum thesaurus, 1697
19	Ido Wolf (32)	43-year-old man, cranial trauma	Cranium	Observationum chirurgico-medicarum libri II, cum scholiis & variis interspersis historiis medicis, 1704
20	J.C. Schilling (32)	Boy in coma and convulsive disorder	Whole body	Case of Bloody Sweat, 1747 (Popular Science Monthly, 1884)
21	Antonii Mesaporiti (32)	Young lady	Whole body	Epistola D. Antonii Mesaporiti, M. C. Genuensis ad Cl. Antonium Vallesnerium, 1753
22	Christiani Ehrenfried Eschenbach (32)	Girl	Whole body	Sudor sanguineus; urina sudore et vomitu rejecta, Observata anatomico-chirurgico-medica rariora, 1769
23	Albrecht Von Haller (32)	Woman, uterus cancer	Whole body	Anfangsgrunde der Physiologie des menschlichen Koerpers, 1772 (Schneider in Fulda. Medicinisch-chirurgische Bemerkungen uber verschiedne Gegenstande ans der Heilkunde, 1848)
24	Gallandat (32)	31-year-old boatman with fatigue	Whole body	Sueur de sang. Soc. Scient. Harleimensis, 1773 (Dictionnaire abrégé des sciences médicales, 1822)
25	Josephi Lanzoni (32)	Young woman suffering from cholera morbus	Whole body	Case of Bloody Sweat, Ephemerid. Acad. Natur. Curios., 1788
26	John Mason Good (32)	Various cases in general regardless of age	Whole body	A History of Medicine, 1795
27	Boivin (33)	45-year-old man with depression and burn out syndrome	Whole body	Observation sur une diaphésèse, Journ. de Méd., Chir., Pharm, 1807
28	F.C. Câizergues (33)	Young lady	Face, neck, chest, armpit	Sueur de sang survenue quatre fois pendant la plus grande vivacité des douleurs d'une colique néphritique. J. de Méd., Chir., Pharm., 1814
29	James Johnson (editor) (33)	21-year-old woman with irregular menstruation	Cheeks and epigastrium	Transactions Médicales, 1830 (The Medico-surgical Review, and Journal of Practical Medicine, 1831)
30	Chauffard M. (33)	21-year-old woman after a parental clash due to religious issues	Cheeks and abdomen	Transactions Médicales, 1830
31	Maur Hoffmann (22)	Man ~50 years of age, fatigue	Arms and feet	Ca 1836, Misc Nat Curios Dec II Ann III Obs 27 (Wochenschrift für die gesammte Heilkunde: 1848)
32	Kaminsky (31)	Young girl	Feet	Tertianfieber mit Ausschwitzung von Blut aus den Füßen. Med. Ztg., Berl., 1837 (Schmidt's Jahrbuecher, 1838)
33	John Gideon Millingen (15)	Catherine Merlin of Chamberg, 46 years of age, received a kick from a bullock in the epigastrium	Scalp and various parts of the body	Curiosities of Medical Experience, 1839

Table I. Continued.

No.	Original author <sup>a</sup>	Case	Body locations of hematomidrosis	Work and year of publication
34	C.A.W. Schneider (31)	50-year-old man, fatigue	Feet	Blutschwitzen. Wochenschrift für die gesammte Heilkunde: 1848
35	Durius (16)	30-year-old male, fear Student placed in prison	Forehead, cheek Hands, chest, arms	(Misscel. cur. Ephemerid.) The Cyclopædia of Biblical Literature, 1851
36	Auguste Nicolas Gendrin (33)	Young lady	Whole body	Des Sueurs de Sang, 1856
37	Huss (31)	23-year-old woman, emotional stress	Whole body	Allg Med Cent Zeitung Nr 97-98, 1856
38	Erasmus Wilson (41)	Women	Forehead, chin, cheeks	On the Diseases of the skin, 1857
39	Julles Parrot (33)	Woman 37-year-old woman with hysteria	Face and various parts of the body	Bulletin De l'Enseignement Médiclae, 1859
40	Thomas K. Chambers (30)	27-year-old woman	Whole body, nose	Case of Bloody Sweat, Lancet, 1861
41	F. Servaes (31)	Man, dementia paralytica Man, dementia paralytica	Face Face, scalp, ear	Ueber Blutschwitzen am Kopfe de Dementia paralytica. Centralblatt für die Medicinischen Wissenschaften, 1863
42	A. von Franque (21)	45-year-old woman, into pregnancy after a previous abortion	Forehead, back	Medicinish-chirurgische Monatshefte: kritisches Sammeljournal für praktische Heilkunde. 1863
43	G. Sous (36)	9-year-old girl	Right eye	1866 (Annales d'oculistique, Sueur sanguinolente, Tircher, 1869)
44	Ferdinand Ritter von Hebra (21)	Female Female Male	Caruncula lachrymalis Nipples Lower limbs	On Diseases of the Skin, Including the Exanthemata, 1866
45	McCall Anderson (18)	15-year-old girl with defective and irregular menstruation	Face, chest, arms and legs	Journal Cutan. M., Lond. (British Medical Journal), 1867
46	Messedaglia & Lombroso (84)	23-year-old man	Whole body	Giornale Italiano delle Malattie Veneree e delle Malattie della Pelle, Volume 2, 1869
47	W.T.P. Douglas (84)	35-year-old woman, fatigue, tetanus	Forehead	Hematidrosis with tetanus, 1870 (Sammuel Wilks, Hematidrosis or Bloody sweat complicating tetanus, Guy's Hospital Reports, 1872)
48	Schneider (16)	Sailors during a storm	Whole body	The biblical museum, 1871
49	Samuel Wilks (84)	Woman with tetanus	Whole body	A case of hæmatidrosis, or bloody sweat, complicating tetanus. Guy's Hosp. Rep., 1872
50	Rudolf Ludwig Carl Virchow (28)	Louise Lateau,	Forehead, dorsal surface of the hands and feet	Professor Virchow on Louise Lateau, The Medical Times and Gazette: A Journal of Medical Science, Literature, Criticism, and News, 1874
51	W.P. Hart (18)	24-year-old young man	Whole body	Richmond and Louisville Medical Journal, 1875

Table I. Continued.

No.	Original author <sup>a</sup>	Case	Body locations of hematidrosis	Work and year of publication
52	M. Tittel (29)	20-year-old man with fatigue	Face	A case of Hematidrosis, Medical record: a monthly journal of medicine and surgery, 1876
53	McCall Anderson (41)	15-year-old young lady with early menstruation	Face, arms, chest, legs	Lectures on Clinical Medicine, 1877
54	R.G. Hill (42)	4-year-old boy, malaria	Face and neck	Case of bloody sweat. Virginia M. Month., Richmond, 1879-80 (The Ohio Medical Recorder, Volume 5, 1881)
55	George William Pollard (42)	4-year-old boy patient of Dr Hill	Whole body	Virginia Medical Monthly, 1880
56	W. T. Mitchell (42)	R.G. suffering from malaria	Whole body	Case of Hematidrosis. Ohio Med Recorder, 1881
57	Juan De Maldonato (13)	Woman, irregular menstruation	Whole body	A commentary on the Holy Gospels, 1888
58	Hehir (93)	Man from Paris sentenced to death	Head, axillae	Indian Medical Record (The Medical News, 1893)
59	Friedrich Albin Hoffman (22)	16-year-old girl	Feet	Lehrbuch der Constitutionskrankheiten, 1893
60	James Craven Wood (27)	Man	Fingers, knees, thighs, chest and grooves of the lower eyelids	A Text-book of Gynecology, 1894
61	Isadore Dyer (26)	6-year-old girl with cicatrized fingers after strumous ulcers on the right hand when 7 months old	Shoulders	A Case of Hematidrosis Combined with Chromidrosis, The Medical News, 1895
62	R. Reynolds (38)	26-year-old American rubber in a local Turkish bath, fatigue	Face	Report of the Department of Health of the City of Chicago, 1895
63	Henri Fournier (32)	Various cases suffering from smallpox	Whole body	Journal des maladies cutanées et syphilitiques, 1896
64	Alma L. Rowe (5)	Magistrate after any excitement	Whole body	Purpura Hemorrhagica Attended with Hematidrosis Complicating Pregnancy, Journal of the American Medical Association, 1900
64	Alma L. Rowe (5)	Pregnant woman	Whole body	

<sup>a</sup>Reference numbers in this column may refer to the study of the named author or to a more recent study that reviews the data presented, as some are historical data without an available reference. For C.A.W. Schneider in reference number 34 and Schneider in 48 there are no data available to support any connection. 'Whole body' in some cases may imply undetermined areas. Works in parentheses indicate the treatises that include the original work mentioned.



Table II. Works with references to hematidrosis cases from 2002 until 2022.

No.	Author(s)	Person	Body locations of hematidrosis	(Refs.)
1	Manonukul <i>et al</i>	14 years old girl	Scalp, palms, and occasionally from trunk, soles, and legs	(2)
2	Carvalho <i>et al</i>	9-year-old girl after strenuous exercise or prolonged exposure to heat	Around the mouth	(49)
3	Mishra	13-year-old girl with platelet factor 3 dysfunction	Eyes	(72)
4	Jerajani <i>et al</i>	72-year-old male, suffered from continuous mental stress	Area confined to the abdomen	(56)
5	Bhagwat <i>et al</i>	12-year-old girl, horrifying incident with psychological stress	Forehead	(51)
6	Patel and Mahajan	13-year-old boy with no underlying disease	Face, arm and trunk	(74)
7	Wang <i>et al</i>	13-year-old girl, emotional excitement	Subungual area, palms, feet, thighs, and trunk	(59)
8	Praveen and Vincent	10-year-old girl, severe headache lasting for few hours on facing stressful situations	Forehead, ear canal, nasal bridge, neck, umbilicus, wrists and legs, hemolacria	(50)
9	Mora and Lucas	18-year-old girl, high stress	Nose, lacrimal ducts, forehead, hands, nails, and navel	(48)
10	Bhattacharya <i>et al</i>	12-year-old girl with no underlying disease	Face, limb, palm and sole	(46)
11	Biswas <i>et al</i>	12-year-old healthy girl with low intelligent quotient and loss of insight	Forehead, face and body	(77)
12	Khalid <i>et al</i>	Female crying as a result of emotional outburst or even sometimes voluntarily	Eyes and ears	(82)
13	Tshifularo	30-year-old woman, stress 26-year-old woman with no underlying disease 34-year-old woman, stress 18-year-old woman, stress	Bloody otorrhea	(63)
14	Deshpande <i>et al</i>	10-year-old boy, behavioral interventions for the child and counseling and psychoeducation to the parents	Navel, eyes, ear lobules and nose	(76)
15	Shen <i>et al</i>	9-year-old girl with no underlying disease	Various parts of the skin on her body, canthi, tongue, nails or Umbilicus	(69)
16	Varalakshmi <i>et al</i>	10-year-old girl, significant psychological stressors, temperamental difficulties and conflicts with mother	Eyes	(52)
17	Jafar and Ahmad <i>al</i>	12-year-old girl with no underlying disease	Face, eye and tear duct	(60)
18	Techasatian <i>et al</i>	9-year-old boy after a novice monk summer retreat	Scalp, cheeks, palms, arms and legs	(57)
19	Yeşilova <i>et al</i>	11-year-old girl when returning from outside cold air into a warm Environment	Forehead	(61)
20	Maglie and Caproni	21-year-old woman, depression and anxiety disorder	Palms and face	(65)
21	Gião Antunes <i>et al</i>	66-year-old male with Henoch-Schönlein Purpura	Hemolacria (bloody tears), hematidrosis and appearance of a palpable purpura on the lower limbs, abdomen, and trunk	(55)
22	Jayaraman <i>et al</i>	10-year-old girl, intense fear secondary to psychosocial stressor ,mixed anxiety and depressive disorder	Scalp	(68)



Table II. Continued.

No.	Author(s)	Person	Body locations of hematidrosis	(Refs.)
23	Shahgholi	11-year-old girl with no underlying disease 11-year-old boy with no underlying disease 9-year-old girl	Forehead, eyes, ears, nails, arm, umbilical area, back, vagina, and gastrointestinal tract Hand and feet Ears lobules, nose and eyes	(58)
24	Alsermani <i>et al</i>	9-year-old girl, bullying at school	Scalp, ear, mouth, and eyes	(4)
25	Meyer <i>et al</i>	10-year-old girl, post-traumatic	Forehead	(62)
26	Hansson <i>et al</i>	9-year-old boy, migraine	Forehead, neck, knee and mouth	(54)
27	Pari	10-year-old girl with no underlying disease	Forehead and chest	(73)
28	Ricci <i>et al</i>	15-year-old girl, major stressful event	Eyelids and body	(79)
29	Murota <i>et al</i>	6-year-old girl with no underlying disease	Palms	(64)
30	Dast <i>et al</i>	15-year-old girl following a head injury 13-year-old girl, anxiety	Ears, nose and eyes Face, eyes, shoulders and forearm	(78)
31	Matsuoka and Tanaka	11-year-old girl presenting dissociative disorders from the age of 7 and self-harming from 9	Scalp, forehead, hands and feet	(80)
32	Shafique <i>et al</i>	10-year-old girl, experiencing significant psychosocial stress due to the recent separation of her parents	Eyelids, ears, scalp, axillae, vagina, rectum, abdomen, chest, neck, and trunk	(47)
33	Hoover <i>et al</i>	9-year-old boy, possible genetic predisposition 6-month-old girl	Ears, eyes, scalp and other sites Ears, eyes, scalp and other sites	(89)
34	Talwar <i>et al</i>	12-year-old boy, separated from relatives, maladaptive response to a psychosocial stressor	Eyes, ear, mouth	(53)
35	Tirthani <i>et al</i>	13-year-old girl, orphan girl living with her paternal uncle and cousins	Mid face and hands	(81)
36	Zheng <i>et al</i>	8-year-old girl, single parent (mother)	Mouth, eyes, forehead, oral, arms and legs and intestine	(44)
37	Alasfoor <i>et al</i>	20-year-old woman, retinoblastoma of the left eye with enucleation and artificial eye placement, prolonged and heavy menstrual cycles and neurological symptoms	Eye	(45)

form the hemorrhage produced by ruptured ones when a rhexis (Greek term for rupture) occurs. This occasional spontaneous oozing of arterial blood from the sweat glands was studied by microscopy and was attributed to the rise of pressure in the capillaries and small veins combined with increased permeability of the vessel walls. As for the hemorrhagic diathesis (Greek term, meaning temper), this had been divided into congenital or hereditary and acquired. A large cluster of diseases could enact the provocation of hematidrosis, named scurvy, morbus maculosus Werlhof, purpura simples, purpura rheumatic, purpura haemorrhagica, melena neonatorum, septicemia, endocarditis, malignant pustule, spotted typhus, cholera, smallpox, plague, acute yellow atrophy of the liver, yellow fever, nephritis, phosphorus poisoning, snake-bites, malnutrition, irritation or paralysis of the vaso-motor nerves, moral shock, terror, thrombosis or embolism or ligation of a vessel complicated with stagnation and many more. The female sex was most vulnerable against diapedesis. Psycho-therapy and palliative interventions were suggested (39). Geranium, a genus of 422 species of plants, was proposed to help

confront hematidrosis (40). The treatise of Ziegler was published the same year with Moriz Kapozi's masterpiece Pathology and Treatment of the Disease of the Skin. However, Kapozi only mentioned the occasional spontaneous oozing of arterial blood from the sweat glands, named hematidrosis, considering it as the rarest case of cutaneous hemorrhage (41).

The terrifying nature of the hematidrosis phenomenon impressed the mind of medical observers and conquered the souls of the uneducated population to assume an almost miraculous character. Diapedesis on the forehead, hands and feet was stated to occur in religious bigots considered by fanatics as a gift of holy marks and bloody sweat of the Christ named stigmata. Those cases, following careful scientific examination, had proven to be, at least most of them, in the sphere of religion and faith or somehow fictitious. Religion enthusiasts bearing hematidrosis made their appearance from time to time mostly in the area of the Catholic church, stating the ability to reveal and confess the real work of God. Even publications were encountered in the form of Letters (famous type of text

Table III. Some cases of famous people bearing stigmata with hematomidrosis.

No.	Person	Canonized
1	Marie d'Oignies (ca 1177-1213) (100)	No
2	Saint Francois d'Assise (1181-1226) (97)	Yes
3	Helen of Hungary (d. ca 1241) (100)	No
4	Cistercian nun Lutgard of Aywières (1182-1246) (100)	No
5	Clare of Montefalco (ca 1268-1308) (100)	No
6	Margaret Ebnerin (d. ca 1351) (100)	No
7	Gertrude D'Oosten (d. ca 1358) (100)	No
8	Sainte Catherine de Sienne (1347-1380) (97)	Yes
9	Saint Liduina of Schiedam (1380-1433) (100)	Yes
10	Sainte Rita de Cascia (1381-1457) (97)	Yes
11	Bienheureuse Lucie de Narni (1476-1544) (97)	No
12	Sainte Catherine de Ricci (1522-1590) (97)	Yes
13	Hieronyme Carvaglio (d. ca 1604) (100)	No
14	Sainte Véronique Giuliani (1660-1727) (97)	Yes
15	Bienheureuse Anne Catherine Emmerick (1774-1824) (97)	No
16	Maria Theresia von Mörl (1812-1868) (97)	No
17	Maria Domenica Lazzeri (1815-1848) (97)	No
18	Maria Beatrix Schuhmann (1823-1887) (97)	No
19	Juliana Weiskircher (1824-1862) (97)	No
20	Sainte Mariam Baouardy (1846-1878) (100)	Yes
21	Louise Lateaua (1850-1883) (97)	No
22	Madeleine Lebouca (1853-1918) (100)	No
23	Sainte Gemma Galgani (1878-1903) (97)	Yes
24	Saint Pio de Pietrelcinaa (1887-1968) (97)	Yes
25	Thérèse Neumanna (1898-1962) (97)	No
26	Marie Rose Ferron (1902-1936) (97)	No

Ca, circa (approximately); d., died.

in religion). Hyperboles, such as for public demonstrations of hysteric or cataleptic poor peasant girls being visited by hundreds of wondering spectators ready to worship them and references of persons that had not slept or eaten for 8 years, compelled scientists to refer to them as simply impostors (14).

Charles T. Scott was the first to publish in PubMed in 1918 under the term haematidrosis, reporting the case of abnormal perspiration of a pink fluid on the forehead of an 11-year-old girl with a nervous temperament (42). Almost a century later, Joe E. Holoubek and Alice B. Holoubek in 1916, two devoted catholic physicians, performed an extensive literature review based upon a selection of 76 cases of Pooley's review ranging from the 17th century to 1980. They had classified all cases under subgroups according to the etiology: Systemic disease (e.g., scurvy and lupus), vicarious menstruation, physical exertion, psychological stress (repeated or unique), religious stigmatics and idiopathy (43). Moreover, 2 cases were reported during 2022 in the PubMed/MedLine database (44,45).

## 5. Findings in the modern literature

Hematidrosis depicts an eccrine sweat disorder, strongly characterized by one or more transient, yet recurring episodes

of a spontaneously mixed fluid of sweat and blood from the intact epidermis. Although it presents a notoriously rare and fascinating condition, the prevalence and incidence of this condition remain unknown, as illustrated by the small number of cases published and the almost complete absence of case series. However, over the past two decades the number of cases and studies has increased, despite the fact that most of the cases which have been reviewed displayed a stereotypical presentation of bleeding pattern, background etiology and therapeutic approach (1,4). Female patients presented the majority of the cases, mainly young between the ages of 9 to 15 years (46-52). Male patients have been less frequently reported, but are usually also at a young age (53,54) with a small number of exceptions of patients >65 years of age (55,56). The geographic distribution testifies a tendency towards the Asian region (India and Pakistan) as one of the two cases of those reported refers to the Indian population. A genetic predisposition was proposed to explain this geographic predilection (1,4).

The most common areas of appearance of the phenomenon, without being limited to these, are namely the forehead, scalp, face, eyes and ears, and secondary trunk and limbs. The majority of the cases were clinically examined and interdisciplinary observed by more than one specialized physician, as

in numerous reports, there were suspicions that the symptom may be factitious (5). Moreover, in some reports, the diagnosis was based only on clinical criteria with insufficient laboratory examinations, accompanied by a misdiagnosed hypothesis of self-traumatism. However, fully clinically examined patients, undergoing histopathological examinations, is the trend observed over the past decade (57). Psychiatric disorders and severe stress have been proposed (1,58-60), while a post-traumatic appearance has been reported by 61. Yeşilova *et al* (61) and Mejer (62). Various areas of appearance may be noted in a multiple concurrent emergence. Otorrhea, hematuria, epistaxis, bleeding from the intestines the oral cavity and the eyelids have also been mentioned (1,41,59,60,63). Pathology usually reveals a free medical history, and records have demonstrated no family incidents; laboratory tests of complete blood count, coagulation, immunology, renal and liver function have yielded inconclusive results (60). Dermatological evaluation have disclosed no cutaneous lesions. Histological findings following skin biopsy have ranged from congested blood vessel capillaries, extravasation of erythrocytes within the follicular lumen, leakage of red blood cells in dermis, or even just normal skin layers (1,2,43). In a case where an increased number of CD34-positive cells were observed around the eccrine sweat glands in a young female with palmar hematidrosis, the authors suggested that high pressure applied in the plantar surface of the hand (horizontal bar exercise) subsequently damaged the balance of her small blood cells, thus increasing the CD34-positive cells (64). As regards diagnosis, the following criteria have been suggested: i) testified bleeding by medical personnel; ii) red blood cell detection in the examination exudates; iii) the absence of trauma, self-injury, telangiectasias, purpura and no evidence of oozing after wiping of the area (65). Differential diagnosis included self-injury, vasculitis, connective tissue disorders (increased vascular fragility and secondary bleeding), Munchausen's by proxy syndrome, scurvy, hematomas, petechial, purpuric lesions, pseudochromhidrosis, and chromhidrosis and psychogenic purpura (5,62,66). To avoid confusion, it must be noted that chromhidrosis is characterized by the excretion of colored sweat from eccrine sweat glands, while pseudochromhidrosis sweat is colorless, later acquiring color due to its contact with chromogenic chemicals of the skin (66,67).

The patho-physiological mechanisms involved in the development of hematidrosis are not completely clarified. It has been calculated that half of the cases of hematidrosis remained with an undetermined causative etiology. The rupture of the small capillaries that supply sweat glands has been suggested to be the key factor of blood seepage (1). Physical fatigue and emotional stress, fear of death, school examinations, inter-family conflict and orphanage are being indicated as the most frequent triggers of this condition (1,68). Tonic seizures resolved with anti-epileptic medication may cause hematidrosis, as recorded in a 9-year-old girl by Shen *et al* (69) in 2015. It has been hypothesized that the hyper-reactivity of the sympathetic nervous system following a major or acute stressful event, may result in vessel vasoconstriction, altering the blood supply to the eccrine glands. In the post-stress phase as vasodilatation occurs, tinny ruptures of the nutritional vessels of the sweat glands occur and the secretion of bloody sweat droplets to the skin is implemented. A distinctive vasculitis with intra-dermal bleeding and obstructed capillaries has also been reported as

the pathological basis of hematidrosis cases (70,71). Platelet factor-3 dysfunction has been also implicated (72).

Currently, there is no available treatment of choice. The benign and transient nature of the disease should be explained to the family and caregivers. Convincing the parents about the nature of the disease is mandatory for the successful management of any case. Moreover, holistic emotional support of all implicated appears to be of paramount importance (72-76). Personalized therapy and individualized interventions based on the needs of patients and caregivers are strongly recommended. The reduction of anxiety followed by the administration of benzodiazepines, such as lorazepam and diazepam has been proven efficacious (1,60). Hemostatic drugs and vitamin C are being used without any notable results. Some cases have responded to atropine transdermal patches (77), while others to adrenaline gauze wipes (73,75). The administration of  $\beta$ -adrenoceptor antagonists has been reported to be an effective treatment for hematidrosis by regulating sympathetic nervous system activation and reducing intense psychological excitement (4,47,78-80). Wang *et al* (59) in 2010 reported a complete resolution and recovery of the bleeding episodes in a 13-year old girl treated with propranolol. Oxybutynin, an anticholinergic drug, was successfully used in a 13-year-old patient (81). There are cases reporting that apart from medical personnel, patients were searching for various spiritual treatments, homeopathy and quackery (personas who fraudulently sell a product or service to supposedly cure a patient) (82).

## 6. Summary and deliberation of hematidrosis

Diapedesis from the plexus of the vessels surrounding the sweat glands has intrigued scholars and scientists; this has led to the appearance of records in medical and historical books. Shallow skepticism of the medical community denied the phenomenon for centuries, until only when it was directly observed. Apart from plausibility, failure to evolve a comprehensive explanation contributed further to its delayed acceptance. Disbelief strengthened by the fact that recorded cases were being described sporadically and in a number of cases, by completely unrelated authors (83).

A plethora of studies refer to Aristotle as the first to describe hematidrosis. That is not entirely accurate. Aristotle in his work 'On the Parts of Animals', truly described bloody sweat, but as a peculiarity observed in the animal kingdom, but not in humans. He only noted that it is known to exist. Some animals exude reddish fluids from the surface of the skin. This blood-colored exudation is due to color globules, and not merely to blood in the case of the hippopotamus. Flamingos secrete red fluids by their stomachs (84). The observation of domestic animals, horses and cattle reveals more representations of livestock manifesting incidents of real bloody sweat (85). There is also some confusion as regards the referral to Galen as the pioneer to understand hematidrosis. There was an old treatise titled 'De utilitate respiration' bearing the same name given by Galen to one of his works. It was paraphrased by the physician, Richard Mead, in his 1749 publication on the bloody sweat of Jesus Christ. Since then, it was globally celebrated as a true work of Galen's Collection. Nevertheless, the remark was noted by some other scholars who wanted to draw additional attention by falsifying the name of the Greek majesty. Nevertheless, references for bloody sweat

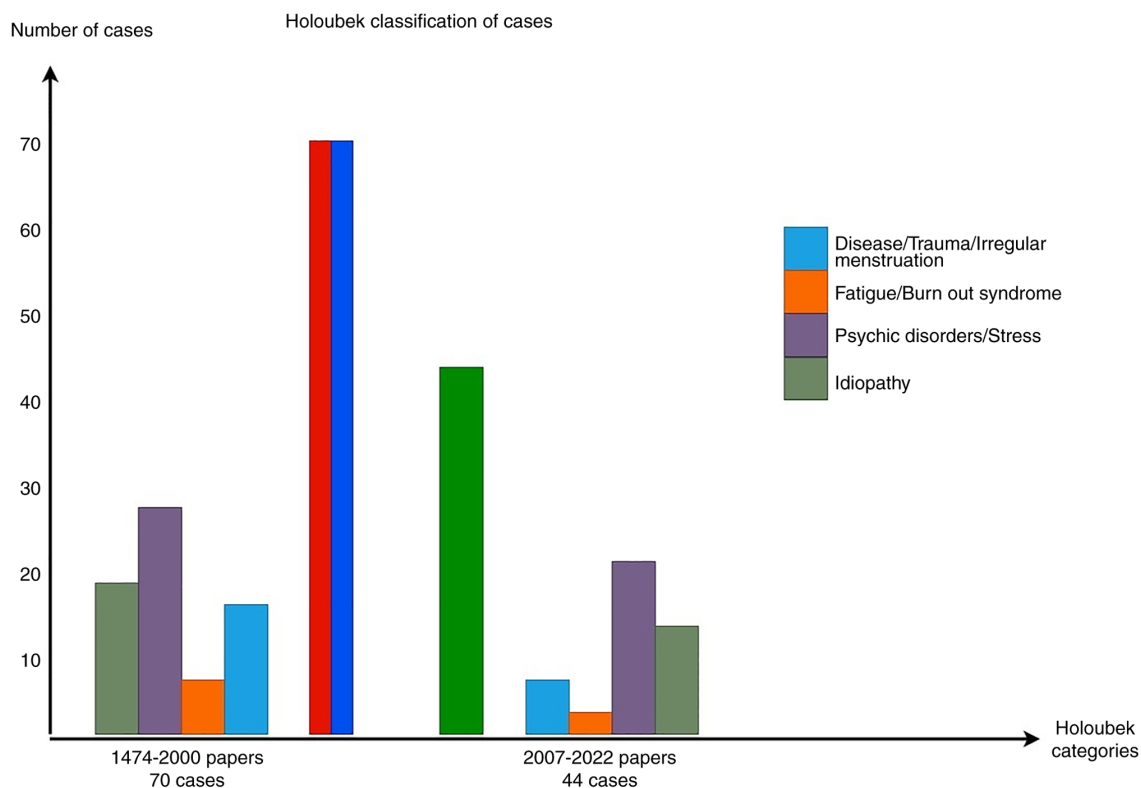


Figure 2. Articles categorized according to the classification by Holoubek and Holoubek (43). The red-blue column indicates the total number of articles until 2000, while the green column indicates the total number of articles included from 2007 to 2022.

exist only in the pseudogalenic texts (43). To verify this fact, the authors analyzed and made a translation of 3,054 of Galens' references to blood (αἷμα) and 78 to sweat (ιδρώτας) by accessing TLG, resulting in no possible much for such a case.

The Latin terms, *sudor cruentus* and *sudor sanguineus*, first appeared in 18th century medical dictionaries and indexes of the era. Hellenic-derived spellings of h[a]e [o]mat[oh/h]idrosis appeared at a later date, during 1854 (43). Apart from the name of the disease, hematidrosis itself, various terms of Hellenic origin are connected to its pathology, such as H[a]emorrhage (blood outflow), hemolacria (blood in tears), otorrhea (outflow from the ears), otorrhagia (blood outflow from the ears) and epistaxis (blood drip from the nose) (86,87). Terminology only implies for an emotive entity in skin pathology. Otorrhagia appears in more articles in PubMed Central than hematidrosis. Authors worldwide have only heard about rare bleeding disorders, and yet, they believe their existence. However, this is not valid concerning cases of hematidrosis, as for many, it depicts a rather controversial theme. This, raises the question of who to choose for reader or reviewer for such an article (88). Cases such as the one reported by Hoover *et al* (89), of two siblings presenting hematidrosis, apart from witnessing genetic predisposition, further complicates emotions and beliefs.

In both eras investigated, during the 15th-19th century and the past 20 years, the female sex has been registered as the dominant inside scientific texts. However, the numbers of reported cases prior to 1900 are markedly lower when comparing with those reported over the past two decades. Masculine restrictions, deficiency in physical strength and limitations to intellectual developmental activities had undermined the education and intelligence of the female sex and particularly that of younger

females of the humbler social casts (90). In many cases, young girls presenting hematidrosis were peregrinated for religion and profit reasons being considered as stigmatics gathering pilgrims and coin. Although a bleeding episode of a young girl may cause embarrassment, social isolation, panic and depression, the majority of those girls never attended a physician or registered as an official case (14). This fact may also explain the following: i) The difference in mean age, which was 25.6 years until 1990 and 15.8 years over the past two decades, when presumably all cases were examined by health professionals; and ii) the female sex percentage recorded until 1900 was 39.4%, while that over the past two decades increased into 74.4%. The analogy report of the anatomical areas of bloody sweat oozing through the skin demonstrates that in both eras, the scalp, forehead, face, arms, trunk and feet are the most commonly recorded regions, while the ears, eyes and mouth demonstrated considerably higher numbers in later years. The time period of the past 15 years presents the highest peak of all time concerning papers on hematidrosis, with the second half of the 19th century to follow (5,43). The second industrial revolution marked the second half of the 19th century, provoking acute social changes, while nowadays, the excessive and harmful use of technology, such as cell phones, video games, personal computers, the internet and in general, the modern way of life, greatly aggravate psychological side-effects such as anxiety, stress and depression, while the youth are often associated with emotional and behavioral issues. Increased psychic disorders increase all diseases associated, perhaps explaining the increase in the incidence of hematidrosis (91,92). Articles categorized according to the classification of hematidrosis by Holoubek and Holoubek (43) are demonstrated in Fig. 2, where

psychotic disorders/stressful events constitute the main trigger factor in both eras. With the exception of the case described by Dr Hehir in India, all other references until 1900 were reported from areas of the European continent, while in the modern literature, the majority of cases are recorded in India, or in Asia. The geographic limitation of reports from Europe may be explained by the medical achievements and progress mainly due to Western European intellectual evolution through the ages, rendering this region as the major point of quotation (93). English works until 1900 comprised 45.3%, while this number increased to 80.4% over the past two 2 decades. To support geography and language results, English was cited as a universal language and globalization of the medical references.

Jesus Christ when reacting to his future and known to him torturous death, he had experienced a passionate agony, an intensified stressful juncture of emphatic emotions, which flared up as epistaxis. A number of medical writers still insist that blood fell to the ground. Richard Mead in his 1749 work was the first to notice and record that actually it was thromboi (clots of blood) which touched the earth. The reddish fluid was thick and viscous and rapidly coagulated (94,95). The Hellenic term stigma was used to reproduce the optical portraiture of the agony bleeding, crucifixion nails, thorny crown, vinegar sponge, lash and spear wounds, which had been inflicted to the palms, soles, head, chest, lips and back of Christ. Stigma in Greek antiquity indicated a bloody wound or a sign marked on a slave, while during the cultural spread of Christianity, it acquired a more mystical meaning. Nuns, priests, saints, common frauds and deep believers all experienced among other painful effects, hematidrosis. Stigmata have never been studied under the prism of a medical scientific approach until the review by Kechichian *et al* (96) in 2018. A cluster of symptoms received by God is reported, including painful purpura, erosions, blisters, scars and bleeding through the epidermis with intact skin layers. Hematidrosis, the symptom of interest, presents an obvious interaction between skin and psyche. In a state of ecstasy, a pure believer may endure the agony felt by his God, triggering the over-activation of the sympathetic nervous system. An acute induce of a sympathetic response of the autonomic nervous system may be held responsible for the vascular mechanisms behind hematidrosis (96). Although the conscious and voluntary fabrication or exaggeration of physical and psychological symptoms for personal gain of frauds do exist, physicians must have in mind the case of an almost 'pure in life' true believer who may experience in the reality of his mind, the passion of the Christ and in some cases, being canonized. Hematidrosis is a condition which remains one of gruesome fascination, but of great psychological suffering for the victim. Neurology, psychiatry, dermatology, angiology and religion must interact to explain some aspects (96-100).

## 7. Conclusions

Throughout the ages, a rarity in daily practice, a sporadic reference in textbooks, an enigma in medicine, a malady that may lead to extensive unnecessary laboratory tests and to hazardous therapeutic interventions, hematidrosis is a spectacular manifestation in skin pathology. It depicts a field where science, the unknown and religion intertwine. The derma, psyche and faith create a triad to explain diapedesis. For some

medical personnel, the condition appears to be an inconceivable phenomenon. For others it is merely an ailment. For the Catholic church, hematidrosis in stigmata constitutes an almost divine phenomenon. As medicine without religion is a science disabled, to paraphrase the words of Einstein, the present review highlights the pathology and illustrates the necessity to believe in both, in order to comprehend the peculiarities of nature. Nevertheless, blurred etiopathogenesis, transdiagnostic variables, interdisciplinary teams of health professionals, symptomatic and inconclusive therapy and blood cells mixed with sweat are the only data that may be presumed as certain.

## Acknowledgements

Not applicable.

## Funding

No funding was received.

## Availability of data and materials

Not applicable.

## Authors' contributions

GT, DA and ES were involved in the intellectual content of the review. GT, DA, AK and NP were involved in the literature search. GT, DA and ES were involved in the acquisition of data from the literature. GT, ES and KK were involved in the analysis from the literature for inclusion in the review. GT and ES were involved in the preparation and editing of the manuscript. ES, KK and DAS were involved in the reviewing of the manuscript. All authors have read and approved the final manuscript. Data authentication is not applicable.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

Not applicable.

## Competing interests

DAS is the Editor-in-Chief for the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

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