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SCIENTIFIC EVALUATION OF MEDICINAL PLANTS USED FOR THE TREATMENT OF ABNORMAL BLEEDING AND HEMORRHAGES

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Abstract:
Abnormal uterine bleeding (AUB) is one of the prevalent gynecological disorders that cause considerable morbidity and management of that plays an important role in protecting women's health. This review focuses on medicinal plants mentioned by Avicenna, a great Iranian philosopher and physician Medicinal plants mentioned in Canon for treatment of AUB were elicited and searched in electronic databases including PubMed, Scopus, Google Scholar and Cochrane library to find studies that confirmed their efficacy. Data were collected for the years 1980-2014.The findings included 23 plants belonging to 18 families. Scientific findings have revealed that these plants control AUB through four mechanisms of action including inhibition of inflammatory process, inhibition of prostaglandins production, antiproliferative activity on human cervical cancer cells (HeLa), and estrogenic activity. All of the plants exhibited anti- inflammatory activity in vitro and/or in vivo. Cuscuta chinensis and Portulaca oleracea exhibited estrogenic activity. Boswellia carteri, Lens culinaris, Myrtus communis, Polygonum aviculare, Pistacia lentiscus, and Punica granatum have revealed inhibitory activity on biosynthesis of prostaglandins. Some of the mentioned plants including: Ceratonia siliqua, Cuscuta chinensis, Cuscuta epithymum, Cydonia oblonga, Paeonia sp., Portulaca oleracea, Solanum nigrum, Rumex acetosa and Onopordum acanthium have shown antiproliferative activity on HeLa cells.
Key words : Bleeding, Mechanisms, Treatment, Plants for treatment

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INTRODUCTION:

BLEEDING

Bleeding, also known as a hemorrhage or hemorrhage, is blood escaping from the circulatory system from damaged blood vessels. Bleeding can occur internally, or externally either through a natural opening such as the mouth, nose, ear, urethra, vagina or anus, or through a wound in the skin. Hypovolemia is a massive decrease in blood volume, and death by excessive loss of blood is referred to as exsanguination. Typically, a healthy person can endure a loss of 10–15% of the total blood volume without serious medical difficulties (by comparison, blood donation typically takes 8–10% of the donor's blood volume). The stopping or controlling of bleeding is called hemostasis and is an important part of both first aid and surgery. The use of cyanoacrylate glue to prevent bleeding and seal battle wounds was designed and first used in the Vietnam War.[1]Today many medical treatments use a medical version of "super glue" instead of using traditional stitches used for small wounds that need to be closed at the skin level.

BLOOD LOSS

Hemorrhaging is broken down into four classes by the American College of Surgeons' advanced trauma life support (ATLS).

Class I Hemorrhage involves up to 15% of blood volume. There is typically no change in vital signs and fluid resuscitation is not usually necessary.

Class II Hemorrhage involves 15-30% of total blood volume. A patient is often tachycardic (rapid heart beat) with a reduction in the difference between the systolic and diastolic blood pressures. The body attempts to compensate with peripheral vasoconstriction. Skin may start to look pale and be cool to the touch. The patient may exhibit slight changes in behavior. Volume resuscitation with crystalloids (Saline solution or Lactated Ringer's solution) is all that is typically required. Blood transfusion is not usually required.

Class III Hemorrhage involves loss of 30-40% of circulating blood volume. The patient's blood pressure drops, the heart rate increases, peripheral hypoperfusion (shock) with diminished capillary refill occurs, and the mental status worsens. Fluid resuscitation with crystalloid and blood transfusion are usually necessary.

Class IV Hemorrhage involves loss of >40% of circulating blood volume. The limit of the body's compensation is reached and aggressive resuscitation is required to prevent death.

This system is basically the same as used in the staging of hypovolemic shock.

Individuals in excellent physical and cardiovascular shape may have more effective compensatory mechanisms before experiencing cardiovascular collapse. These patients may look deceptively stable, with minimal derangements in vital signs, while having poor peripheral perfusion. Elderly patients or those with chronic medical conditions may have less tolerance to blood loss, less ability to compensate, and may take medications such as betablockers that can potentially blunt the cardiovascular response. Care must be taken in the assessment.[2]

MASSIVE HEMORRHAGE

Although there is no universally accepted definition of massive hemorrhage, the following can be used to identify the condition: "(i) blood loss exceeding circulating blood volume within a 24-hour period, (ii) blood loss of 50% of circulating blood volume within a 3- hour period, (iii) blood loss exceeding 150 ml/min, or (iv) blood loss that necessitates plasma and platelet transfusion." [5]

TYPES

Upper head

Intracranial hemorrhage – bleeding in the skull.

Cerebral hemorrhage – a type of intracranial hemorrhage, bleeding within the brain tissue itself.

Intracerebral hemorrhage – bleeding in the brain caused by the rupture of a blood vessel within the head. See also hemorrhagic stroke.

Subarachnoid hemorrhage (SAH) implies the presence of blood within the subarachnoid space from some pathologic process. The common medical use of the term SAH refers to the nontraumatic types of hemorrhages, usually from rupture of a berry aneurysm or arteriovenous malformation(AVM). The scope of this article is limited to these nontraumatic hemorrhages.

Eyes

Subconjunctival hemorrhage - bloody eye arising from a broken blood vessel in the sclera (whites of the eyes). Often the result of strain, including

sneezing, coughing, vomiting or other kind of strain

Nose
Epistaxis - nosebleed
Mouth
Tooth eruption – losing a tooth
Hematemesis – vomiting fresh blood
Hemoptysis – coughing up blood from the lungs
Lungs
Pulmonary hemorrhage
Gastrointestinal
Upper gastrointestinal bleed
Lower gastrointestinal bleed
Occult gastrointestinal bleed
Urinary tract
Hematuria – blood in the urine from urinary bleeding
Gynecologic
Vaginal bleeding
Postpartum hemorrhage
Breakthrough bleeding
Ovarian bleeding - this is a potentially catastrophic and not so rare complication among lean patients with polycystic ovary syndrome undergoing transvaginal oocyte retrieval.[7]
Anus
Melena - upper gastrointestinal bleeding
Hematochezia – lower gastrointestinal bleeding, or brisk upper gastrointestinal bleeding
Vascular
Ruptured Aneurysm
Aortic transection
Iatrogenic injury

CAUSES OF HEMORRHAGE

Bleeding arises due to either traumatic injury, underlying medical condition, or a combination.
Traumatic injury
Traumatic bleeding is caused by some type of injury. There are different types of wounds which may cause traumatic bleeding. These include:

Abrasion - Also called a graze, this is caused by transverse action of a foreign object against the skin, and usually does not penetrate below the epidermis.
Excoriation - In common with Abrasion, this is caused by mechanical destruction of the skin, although it usually has an underlying medical cause.
Hematoma - Caused by damage to a blood vessel that in turn causes blood to collect under the skin.
Laceration - Irregular wound caused by blunt impact to soft tissue overlying hard tissue or tearing such as in childbirth. In some instances, this can also be used to describe an incision.
Incision - A cut into a body tissue or organ, such as by a scalpel, made during surgery.
Puncture Wound - Caused by an object that penetrated the skin and underlying layers, such as a nail, needle or knife.
Contusion - Also known as a bruise, this is a blunt trauma damaging tissue under the surface of the skin.
Crushing Injuries - Caused by a great or extreme amount of force applied over a period of time. The extent of a crushing injury may not immediately present itself.
Ballistic Trauma - Caused by a projectile weapon such as a firearm. This may include two external wounds (entry and exit) and a contiguous wound between the two.
The pattern of injury, evaluation and treatment will vary with the mechanism of the injury. Blunt trauma causes injury via a shock effect; delivering energy over an area. Wounds are often not straight and unbroken skin may hide significant injury. Penetrating trauma follows the course of the injurious device. As the energy is applied in a more focused fashion, it requires less energy to cause significant injury. Any body organ, including bone and brain, can be injured and bleed. Bleeding may not be readily apparent; internal organs such as the liver, kidney and spleen may bleed into the abdominal cavity. The only apparent signs may come with blood loss. Bleeding from a bodily orifice, such as the rectum, nose, or ears may signal internal bleeding, but cannot be relied upon. Bleeding from a medical procedure also falls into this category.[3]

Medical condition
"Medical bleeding" denotes hemorrhage as a result of an underlying medical condition (i.e. causes of

bleeding that are not directly due to trauma). Blood can escape from blood vessels as a result of 3 basic patterns of injury:

Intravascular changes - changes of the blood within vessels (e.g. ↑ blood pressure, ↓ clotting factors)
Intramural changes - changes arising within the walls of blood vessels
(e.g. aneurysms, dissections, AVMs, vasculitides)

Extravascular changes - changes arising outside blood vessels (e.g. *H pylori* infection, brain abscess, brain tumor)

The underlying scientific basis for blood clotting and hemostasis is discussed in detail in the articles, coagulation, hemostasis and related articles. The discussion here is limited to the common practical aspects of blood clot formation which manifest as bleeding.Some medical conditions can also make patients susceptible to bleeding. These are conditions that affect the normal hemostatic (bleeding-control) functions of the body. Such conditions either are, or cause, bleeding diatheses. Hemostasis involves several components. The main components of the hemostatic system include platelets and the coagulation system.Platelets are small blood components that form a plug in the blood vessel wall that stops bleeding. Platelets also produce a variety of substances that stimulate the production of a blood clot. One of the most common causes of increased bleeding risk is exposure to nonsteroidal anti-inflammatory drugs (NSAIDs). The prototype for these drugs is aspirin, which inhibits the production of thromboxane. NSAIDs inhibit the activation of platelets, and thereby increase the risk of bleeding. The effect of aspirin is irreversible; therefore, the inhibitory effect of aspirin is present until the platelets have been replaced (about ten days). Other NSAIDs, such as "ibuprofen" (Motrin) and related drugs, are reversible and therefore, the effect on platelets is not as long-lived.There are several named coagulation factors that interact in a complex way to form blood clots, as discussed in the article on coagulation. Deficiencies of coagulation factors are associated with clinical bleeding. For instance, deficiency of Factor VIII causes classic hemophilia A while deficiencies of Factor IX cause "Christmas disease"(hemophilia B). Antibodies to Factor VIII can also inactivate the Factor VII and precipitate bleeding that is very difficult to control. This is a rare condition that is most likely to occur in older patients and in those with autoimmune diseases. Another common bleeding disorder is Von Willebrand disease. It is caused by a deficiency or abnormal function of the "Von Willebrand" factor, which is involved in platelet activation. Deficiencies in other factors, such as factor XIII or factor VII are occasionally seen, but may not be associated with severe bleeding and are not as commonly diagnosed.In addition to NSAID-related bleeding, another common cause of bleeding is that related to the medication, warfarin ("Coumadin" and others). This medication needs to be closely monitored as the bleeding risk can be markedly increased by interactions with other medications. Warfarin acts by inhibiting the production of Vitamin K in the gut. Vitamin K is required for the production of the clotting factors, II, VII, IX, and X in the liver. One of the most common causes of warfarin-related bleeding is taking antibiotics. The gut bacteria make vitamin K and are killed by antibiotics. This decreases vitamin K levels and therefore the production of these clotting factors.[4]Deficiencies of platelet function may require platelet transfusion while deficiencies of clotting factors may require transfusion of either fresh frozen plasma or specific clotting factors, such as Factor VIII for patients with hemophilia.

INTRACEREBRAL HEMORRHAGE

It include headache, one-sided weakness, vomiting, seizures, decreased level of consciousness, and neck stiffness. Often symptoms get worse over time.[5] Fever is also common. In many cases bleeding is present in both the brain tissue and the ventricles.Causes include brain trauma, aneurysms, arteriovenous malformations, and brain tumors. The largest risk factors for spontaneous bleeding are high blood pressure and amyloidosis. Other risk factors include alcoholism, low cholesterol, blood thinners, and cocaine use. Diagnosis is typically by CT scan. Other conditions that may present similarly include ischemic stroke.

Treatment should typically be carried out in an intensive care unit. Guidelines recommended decreasing the blood pressure to a systolic of 140 mmHg. Blood thinners should be reversed if possible and blood sugar kept in the normal range. Surgery to place a ventricular drain may be used to treat hydrocephalus but corticosteroids should not be used. Surgery to remove the blood is useful in certain cases. Cerebral bleeding affects about 2.5 per 10,000 people each year. It occurs more often in males and older people. About 44% of those affected die within a month. A good outcome occurs in about 20% of those affected. Strokes were first divided into their two major types, bleeding and insufficient blood flow, in 1823.[6]

PULMONARY HEMORRHAGE

Pulmonary hemorrhage (or pulmonary haemorrhage) is an acute bleeding from the lung, from the upper respiratory tract and the trachea, and the alveoli. When evident clinically, the condition is usually massive. The onset of pulmonary hemorrhage is characterized by cough productive of blood (hemoptysis) and worsening of oxygenation leading to cyanosis. Treatment should be immediate and should include tracheal suction, oxygen, positive pressure ventilation, and correction of underlying abnormalities (e.g. disorders of coagulation). A

blood transfusion may be necessary.
Medications

Nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs, such as ibuprofen (Advil, Motrin IB, others) or naproxen sodium (Aleve), help reduce menstrual blood loss. ...
Tranexamic acid. ...
Oral contraceptives. ...
Oral progesterone. ...
Hormonal IUD (Liletta, Mirena).

Mechanisms to prevent bleeding (i.e., hemostatic mechanisms) are essential to maintain the closed blood-circulatory system. ... Blood-clotting proteins generate thrombin, an enzyme that converts fibrinogen to fibrin, and a reaction that leads to the formation of a fibrin clot.

Arterial and venous thromboses and microcirculatory disturbances such as erythromelalgia and neurologic and visual symptoms are the thrombotic manifestations occurring in Polycythaemia Vera and Essential Thrombocythaemia. The increased in vivo thromboxane A2 generation existing in these patients and the selective sensitivity of erythromelalgia to aspirin suggest that platelet PGG/H synthase products may be involved in transducing the increased thrombotic risk. The relationship between Thromboxane A2 production and thrombotic accidents will be investigated by the European Collaboration on Low-Dose Aspirin in Polycythaemia Vera (ECLAP) which will test the efficacy of low-dose aspirin by a randomised clinical trial. The haemorrhagic diathesis of polycythaemic and thrombocythaemic subjects is generally mild and spontaneous bleeding usually manifests in patients with very high platelet count. Its mechanism may be related to quantitative as well as to qualitative platelet changes. Possible mechanisms linking the high grade thrombocytosis to bleeding are consumption of von Willebrand factor and clot fragility due to a mechanical effect of the high platelet count or to inhibition of fibrin polymerization by platelet Glycoprotein Ib.[7]Hemostasis or haemostasis is a process to prevent and stop bleeding, meaning to keep blood within a damaged blood vessel (the opposite of hemostasis is hemorrhage). It is the first stage of wound healing. This involves coagulation, blood changing from a liquid to a gel. Intact blood vessels are central to moderating blood's tendency to form clots. The endothelial cells of intact vessels prevent blood clotting with a heparin-like molecule and thrombomodulin and prevent platelet aggregation with nitric oxide and prostacyclin. When endothelial injury occurs, the endothelial cells stop secretion of coagulation and aggregation inhibitors and instead secrete von Willebrand factor which initiate the maintenance of hemostasis after injury.

MECHANISM OF CLOTTING

Hemostasis has three major steps: 1) vasoconstriction, 2) temporary blockage of a break by a platelet plug, and 3) blood coagulation, or formation of a fibrin clot. These processes seal the hole until tissues are repaired.Aggregation of thrombocytes (platelets). Platelet-rich human blood plasma (left vial) is a turbid liquid. Upon addition of ADP, platelets are activated and start to aggregate, forming white flakes (right vial)Hemostasis occurs when blood is present outside of the body or blood vessels. It is the innate response for the body to stop bleeding and loss of blood. During hemostasis three steps occur in a rapid sequence. Vascular spasm is the first response as the blood vessels constrict to allow less blood to be lost. In the second step, platelet plug formation, platelets stick together to form a temporary seal to cover the break in the vessel wall. The third and last step is called coagulation or blood clotting. Coagulation reinforces the platelet plug with fibrin threads that act as a "molecular glue". Platelets are a large factor in the hemostatic process. They allow for the creation of the "platelet plug" that forms almost directly after a blood vessel has been ruptured. Within seconds of a blood vessel's epithelial wall being disrupted platelets begin to adhere to the sub-endothelium surface. It takes approximately sixty seconds until the first fibrin strands begin to intersperse among the wound. After several minutes the platelet plug is completely formed by fibrin.[8] Hemostasis is maintained in the body via three mechanisms:

1) Vascular spasm (Vasoconstriction) - Vasoconstriction is produced by vascular smooth muscle cells, and is the blood vessel's first response to injury. The smooth muscle cells are controlled by vascular endothelium, which releases intravascular signals to control the contracting properties. When a blood vessel is damaged, there is an immediate reflex, initiated by local sympathetic pain receptors, which helps promote vasoconstriction. The damaged vessels will constrict (vasoconstriction) which reduces the amount of blood flow through the area and limits the amount of blood loss. Collagen is exposed at the site of injury, the collagen promotes platelets to adhere to the injury site. Platelets release cytoplasmic granules which contain serotonin, ADP and thromboxane A2, all of which increase the effect of vasoconstriction. The spasm response becomes more effective as the amount of damage is increased.

Vascular spasm is much more effective in smaller blood vessels.

2) Platelet plug formation- Platelets adhere to damaged endothelium to form a platelet plug (*primary hemostasis*) and then degranulate. This process is regulated through thromboregulation. Plug formation is activated by a glycoprotein called Von Willebrand factor (vWF), which is found in plasma. Platelets play one of major roles in the hemostatic process. When platelets come across the injured endothelium cells, they change shape, release granules and ultimately become 'sticky'. Platelets express certain receptors, some of which are used for the adhesion of platelets to collagen. When platelets are activated, they express glycoprotein receptors that interact with other platelets, producing aggregation and adhesion. Platelets release cytoplasmic granules such as adenosine diphosphate (ADP), serotonin and thromboxane A2. Adenosine diphosphate (ADP) attracts more platelets to the affected area, serotonin is a vasoconstrictor and thromboxane A2 assists in platelet aggregation, vasoconstriction and degranulation. As more chemicals are released more platelets stick and release their chemicals; creating a platelet plug and continuing the process in a positive feedback loop. Platelets alone are responsible for stopping the bleeding of unnoticed wear and tear of our skin on a daily basis. This is referred to as primary hemostasis.

3) Clot formation - Once the platelet plug has been formed by the platelets, the clotting factors (a dozen proteins that travel along the blood plasma in an inactive state) are activated in a sequence of events known as 'coagulation cascade' which leads to the formation of Fibrin from inactive fibrinogen plasma protein. Thus, a Fibrin mesh is produced all around the platelet plug to hold it in place; this step is called "Secondary Hemostasis". During this process some red and white blood cells are trapped in the mesh which causes the primary hemostasis plug to become harder: the resultant plug is called as 'thrombus' or 'Clot'. Therefore, 'blood clot' contains secondary hemostasis plug with blood cells trapped in it. Though this is often a good step for wound healing, it has the ability to cause severe health problems if the thrombus becomes detached from the vessel wall and travels through the circulatory system; If it reaches the brain, heart or lungs it could lead to stroke, heart attack, or pulmonary embolism respectively. However, without this process the healing of a wound would not be possible.

TRADITIONAL PLANTS USED FOR THE TREATMENT OF HEMORRHAGE

NEW YORK (Reuters Health) - The leaves of Aspilia africana, a plant used in African traditional medicine, can stop bleeding, block infection and speed wound healing, a new study from Nigeria confirms.The leaves and flowers of A. Africana, a bristle-covered herb known as the "hemorrhage plant," have been used to stanch bleeding, remove foreign bodies from the eyes, treat scorpion stings, and for several other purposes across the African continent, note Dr. Charles O. Okoli and colleagues at the University of Nigeria. Dr. Okoli is currently located in Sydney, Australia at the University of New South Wales.To test the plant's medicinal properties, Okoli and his team performed a series of lab and animal experiments comparing the effects of an extract of the powdered leaves in methanol, and two different portions or fractions containing hexane or methanol.They report their findings in BMC Complementary and Alternative Medicine.The extract and the fractions of the plant significantly reduced bleeding and clotting time in rats, the researchers found, with the methanol fraction having the strongest effect.All components also slowed the growth of Pseudomonas fluorescens and Staphylococcus aureus, two common wound-infecting bacteria, and reduced wound healing time. For both halting bacterial growth and speeding healing, the methanol fraction again had the most powerful effect.Analysis of the plant extracts and fractions identified a variety of plant components that could be responsible for its medicinal properties, Okoli and his colleagues note, including saponins and tannins."The results of this study indicate that extracts of leaves of A. Africana have good potentials for use in wound care and further provide a rationale for the use of the leaves of this plant in wound management in traditional medicine practice". Investigation of traditional Iranian medicine literatures can lead to the identification of effective natural medicines for the management of AUB; however, conclusive confirmation of the efficacy and safety of these treatments needs more evaluations.[9]survival times for the Surgicel and ABS groups were 42.7 and 53.4 minutes, respectively. Rats in the ABS and Surgicel groups survived significantly longer than rats in the control group ($P<.05$). There were no significant differences between the ABS and the Surgicel groups in survival ($P=.128$).ABS is as effective as Surgicel in achieving hemostasis and lengthening survival time following partial nephrectomy in an experimental rat model.

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CONCLUSIONS:

Bleeding, also known as a hemorrhage or haemorrhage, is blood escaping from the circulatory system from damaged blood vessels. Bleeding can occur internally, or externally either through a natural opening such as the mouth, nose, ear, urethra, vagina or anus, or through a wound in the skin. Hypovolemia is a massive decrease in blood volume, and death by excessive loss of blood is referred to as exsanguination. Typically, a healthy person can endure a loss of 10–15% of the total blood volume without serious medical difficulties (by comparison, blood donation typically takes 8–10% of the donor's blood volume). The extract and the fractions of the plant significantly reduced bleeding and clotting time in rats, the researchers found, with the methanol fraction having the strongest effect.All components also slowed the growth of Pseudomonas fluorescens and Staphylococcus aureus, two common wound-infecting bacteria, and reduced wound healing time. For both halting bacterial growth and speeding healing, the methanol fraction again had the most powerful effect.

REFERENCES:

1. Bleeding articles althline. Archived from the original on 2011-02-10. Retrieved 2007-06- 18.
2. "Dictionary Definitions of Exsanguination". Reference.com. Archived from the original on 2007-07-11. Retrieved 2007-06-18.
3. "Blood Donation Information". UK National Blood Service. Archived from the originalon 2007-09-28. Retrieved 2007-06-18.
4. Manning JE (2003-11-04). "Fluid and Blood Resuscitation". In Tintinalli JE, Kelen GD, Stapczynski JS (eds.). Emergency Medicine: A Comprehensive Study Guide, Sixth edition. McGraw Hill Professional. p. 227. ISBN 978-0-07-150091-3.
5. ^Irita K (March 2011). "Risk and crisis management in intraoperative hemorrhage: Human factors in hemorrhagic critical events". Korean J Anesthesiol. 60 (3): 151– 60. doi:10.4097/kjae.2011.60.3.151. PMC 3071477. PMID 21490815.
6. Webert K, Cook RJ, Sigouin CS, Rebulla P, Heddle NM (November 2006). "The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia". Haematologica. 91(11): 1530–37. PMID 17043016.
7. Liberty G, Hyman JH, Eldar-Geva T, Latinsky B, Gal M, Margalioth EJ (December 2008). "Ovarian hemorrhage after transvaginal ultrasonographically guided oocyte aspiration: a potentially catastrophic and not so rare complication among lean patients with polycystic ovary syndrome". Fertil. Steril. 93 (3): 874–879. doi:10.1016/j.fertnstert.2008.10.028. PMID 19064264.
8. ^ Wang, Ye; An, Fei-Fei; Chan, Mark; Friedman, Beth; Rodriguez, Erik A; Tsien, Roger Y; Aras, Omer; Ting, Richard (2017-01-05). "18F-positron-emitting/fluorescent labeled erythrocytes allow imaging of internal hemorrhage in a murine intracranial hemorrhage model". Journal of Cerebral Blood Flow & Metabolism. 37 (3): 776–786. doi:10.1177/0271678x16682510. PMC 5363488. PMID 28054494.
9. "Hemorrhage Origin". dictionary.com. Archived from the original on 20 July 2015. Retrieved 16 July 2015.