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The Final thesis

Epistaxis: Features, Causes, Diversity, Diagnosis. Surgical and Conservative Treatment

Melina Reinhardt, VI year, IV group

Institute of medicine, Clinic of Ear, Nose, Throat and Eye disease

Supervisor — Lect. Arnoldas Morozas
(academic and scientific degree name surname)

Consultant (if applicable) — _____

The Head of Department/Clinic — Prof. dr. Eugenijus Lesinskas
(academic and scientific degree name surname)

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Email of the student: melina.reinhardt@mf.stud.vu.lt

SUMMARY

Epistaxis is one of the most common conditions leading to unplanned hospital admissions and accounts for one third of all otorhinolaryngological related emergencies (1,2).

In 80-90% of cases it is idiopathic, but if taken as a symptom of an underlying condition it is very unspecific and could have a lot of etiologies (3).

There are longstanding treatment methods for epistaxis that are at the same time efficient and safe. Those include nasal packing, cautery, embolization and surgical ligation. All of those have advantages and disadvantages. Some are either invasive or very uncomfortable for the patient. That is why the research was continued and new treatment methods increasing efficacy and patients' comfort are under investigation. Those include several types of haemostatics. The most promising, according to the current research, is an injectable form of tranexamic acid topically applied. Further research with bigger sample sizes is still necessary, but a new treatment regime is forming.

Despite the ongoing development of research, a desperate need for basic care is still essential and studies show the lack of knowledge on First Aid measurements for epistaxis among health care workers and the general public. This needs to be addressed and changed to ensure the safe and most comfortable handling of this unpleasant situation.

KEYWORDS

Epistaxis; Features; Causes; Diversity; Diagnosis; Conservative treatment; Surgical treatment; Nosebleeds.

INTRODUCTION

Epistaxis is a very common condition in the Otorhinolaryngology department. Approximately 60% of the overall population was at least once in their lifetime affected, 6% of those sought medical help. It is one of the most common ENT conditions leading to unplanned hospital admissions and accounts for 1/3 of all ENT related emergencies (1,2).

Despite those numbers showing the relevance of this condition, a high percentage of medical personnel, including family physicians and Emergency Department staff is not able to correctly administer first aid for epistaxis (4).

This impairs patient care and raises the need for more education in the primary care sector to prevent unnecessary complications.

Most hospitals do not have specific guidelines or a treatment regime for epistaxis. A simple step by step guideline with the newest recommendations or first aid measurements could

improve the patients experience in hospitals and could even prevent hospital visits and the need for admission.

To give an overview about the topic of epistaxis, including current treatment strategies and difficulties faced with it, a literature research was performed.

First the clinical presentation including location and symptoms will be discussed. Then the anatomy, specific location of affected vasculature, etiologies and duration will be presented to give a detailed understanding of the mechanism and pathology. The diagnosis will give a more detailed insight on the general approach of medical professionals encountering patients suffering from epistaxis. The research on management and treatment emphasizes on newer treatment methods and how to incorporate them in daily practice and how effective they are in their implementation. The complications again show context to the effectiveness and set an example of a risk-benefit ratio. Finally, the conclusion singles out ways of improving our current handling on epistaxis.

LITERATURE SEARCH STRATEGY

The number of studies performed on epistaxis and everything accompanying this topic is endless. The literature research performed should enlighten the current state of research on the newest treatment methods and deficits in the current management regimes.

The literature utilized for this work was searched primarily using the keywords “Epistaxis”, “Epistaxis surgical treatment”, Epistaxis conservative treatment”, “Epistaxis management”, “Epistaxis medications”. The used platforms were “web of science”, “pubmed”, “science direct” and “google scholar”. Search results were sorted first according to relevance and later according to date of publication. Although the publications with the newest dates were prioritized, to get an overview on such a condition like epistaxis a detailed research of older articles were necessary too. Therefore, this literature search includes articles published in the years from 1965 until 2022.

Later on, more specific topics were searched on the given websites. The keywords changed to “Epistaxis tranexamic acid”, “Epistaxis topical treatment”, “Epistaxis Traumastem” and “Epistaxis coagulation”.

CLINICAL PRESENTATION OF CONDITION

LOCATION

Historically the location of epistaxis can be classified in anterior and posterior (5). The word “anterior” originates from the word “ante”, which means before in Latin and therefore

describes a bleeding that is coming visibly from the nostrils, the front part of the nose. The word “posterior” originates from the word “posterus” which oppositely means “coming after” in Latin. In this case it describes a bleeding coming from the inner part of the nose, also known as the nasopharynx. It is not directly visible from the outside unless the patient spits out the accumulating blood through their mouth. The maxillary hiatus can be used to anatomically draw a line between anterior and posterior nosebleeds (6).
To differentiate the location is crucial for an anticipation of the clinical outcome. Anterior Epistaxis is most often less severe and can be managed more easily, for example by simple first aid measurements. Whereas posterior epistaxis usually requires treatment, like nasal packing.

SYMPTOMS

The word “epistaxis” originates in Greek and is based on the two words “epi”, which means “from above” and “stazo”, which means to drip. The usual amount of blood lost during a common nosebleed is approximately between five and 15 mL. If the blood loss is more severe, Symptoms associated with said blood loss could occur. These include high heart rate, high respiratory rate and low blood pressure. Those symptoms can also occur due to other factors like stress, anxiety, or fever. Commonly used prediction factors to determine if a patient is going into shock are poor capillary refill time, low urine output and extreme temperatures (7). However it is extremely rare, to develop hemorrhagic shock you need to lose 15-40% of your total blood volume, which equals to 750 -2000 mL (8).
In posterior epistaxis the patient is prone to swallow the blood due to anatomical positioning, which leads to Hematemesis as the resulting symptom. The blood could either be fresh and red or clotted due to the stomach acid, looking like coffee ground.

MECHANISMS AND PATHOLOGY

ANATOMY

In Figure 1 an overview about the vasculature of the nasal cavity is given. But when talking about the nose most of the general population just thinks about the visible parts of the external nose. But the external nose only covers about one third of the nasal cavity (9). In conclusion the nose in its entirety is much bigger than generally believed. This misconception has problematic consequences. The volume of both nasal cavities is approximately 15 ml, which is equivalent to a surface area of 150 cm^2. This is only slightly smaller than the average surface area of the oral cavity, which most people are not aware of and therefore

underestimate pathophysiological processes inside the nasal cavities and their influence on our system.

Nevertheless, the lumen of the nasal cavity varies significantly for each individual and can make administration of certain drugs or nasal packing difficult.

In the nasal mucosa we have a lamina propria, specifically rich in blood vessels. It differs from other epithelia of the respiratory tract. First of all it contains venous sinusoids, which are not present anywhere else in the respiratory tract. Normally due to nerve-mediated smooth muscle tone, they are found in a semi-contracted position. Their specific function is humidification, heating and filtration. When extended to the maximum they can block the airway partially or fully (9). One study compared the blood flow per cm^3 in several human tissues. When compared, the blood flow in the upper respiratory tract mucosa is greater than the blood flow in muscle, brain or liver tissue. The only tissues greater in blood flow per cm^3 are the kidneys and the lungs (10). But furthermore the nasal mucosa has arteriovenous anastomoses, like the Kiesselbach's plexus (9). The vessels themselves show specializations in structure by an absence of internal elastic membrane and pronounced porosity of the basement membrane (11,12).

The relevance of the basic anatomy of the nose and its physiological function is important for understanding the main pathophysiological processes and predicting outcomes and potential complications. Therefore it also shows importance for newer treatment strategies and the usage of topically applied drugs and the bodies reaction to said drugs and their distribution possibilities.

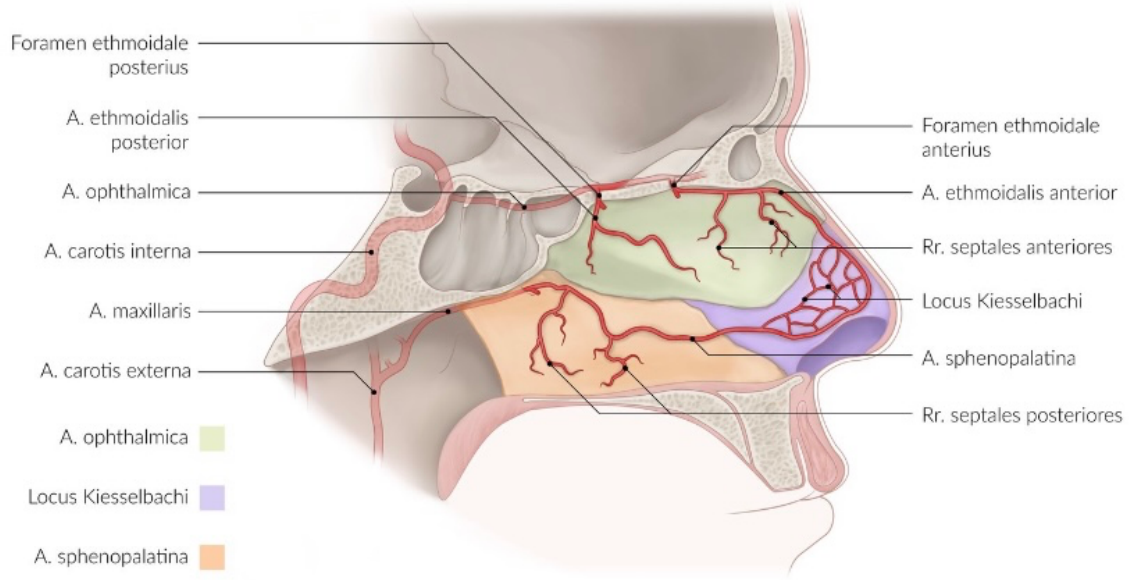

Figure 1: Vasculature of the nose and sinuses (13).

LOCATION OF AFFECTED VASCULATURE

The most common site of bleeding is the nasal septum, followed by the inferior meatus (5). For anterior epistaxis the most common location is the Kiesselbach's plexus, also called Little's area, which is the anastomosis of the terminal branches of both the external and internal carotid arteries, which supplies the nasal septum (Fig. 1). The lateral aspect of the middle or inferior meatus or turbinate is the anatomical location where most posterior bleeds originate from. The damaged vessels include most commonly the maxillary or sphenopalatine artery(6).

ETIOLOGY

Epistaxis is a very unspecific symptom and it can therefore be associated with various etiologies. In the winter months more cases of epistaxis are observed, which indicates a close interaction between environmental factors, quality of air (e.g. extreme temperature, dryness) and the health of our nasal mucosa (14). 80-90%, so the vast majority of cases are labelled as idiopathic, with the etiology remaining unknown (3).

Other causes are, as mentioned before, very variable and Figure 2 and Figure 3 give a detailed list of possible etiologies.

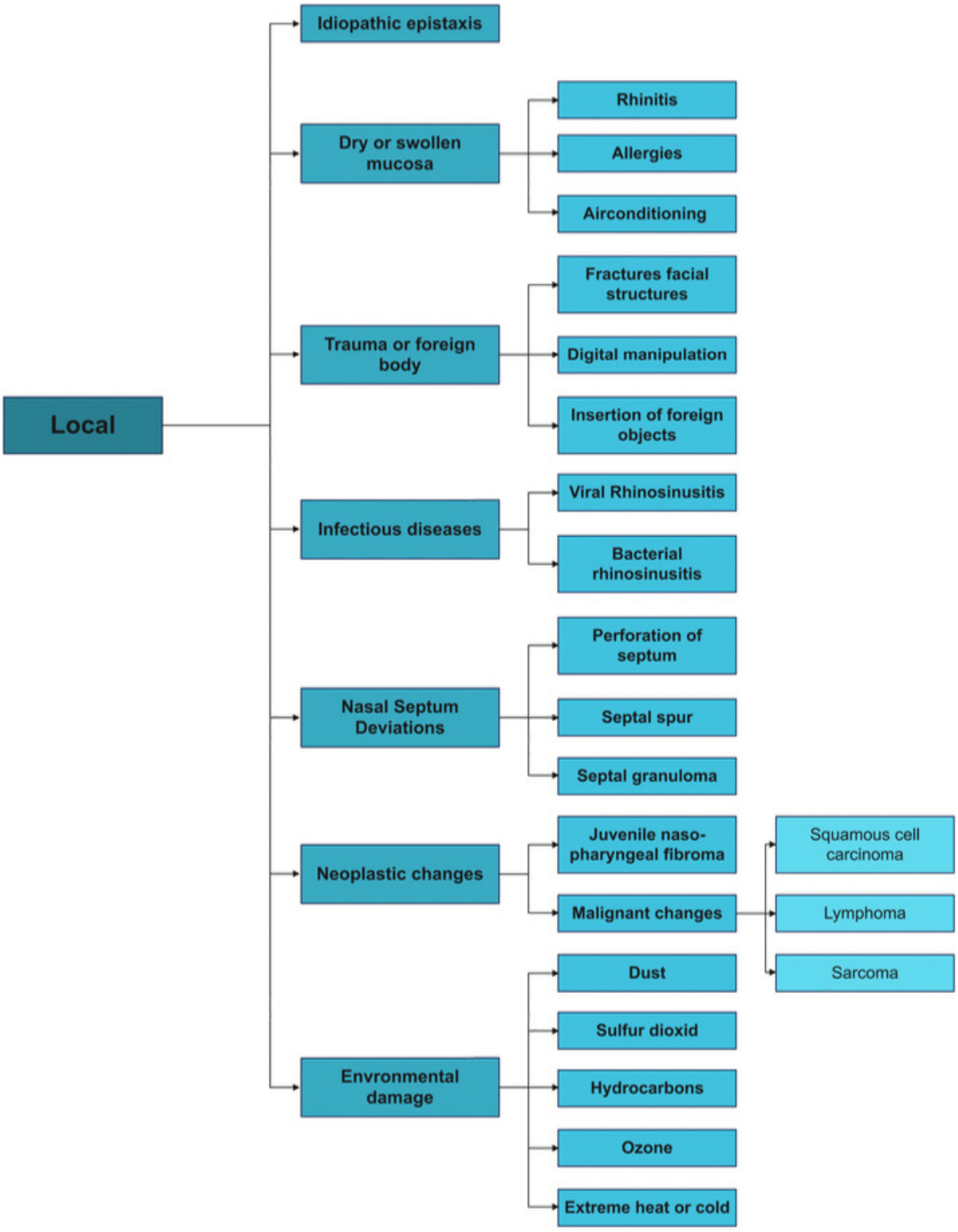

Figure 2: Local etiologies of epistaxis; content according to Thurnher (15).

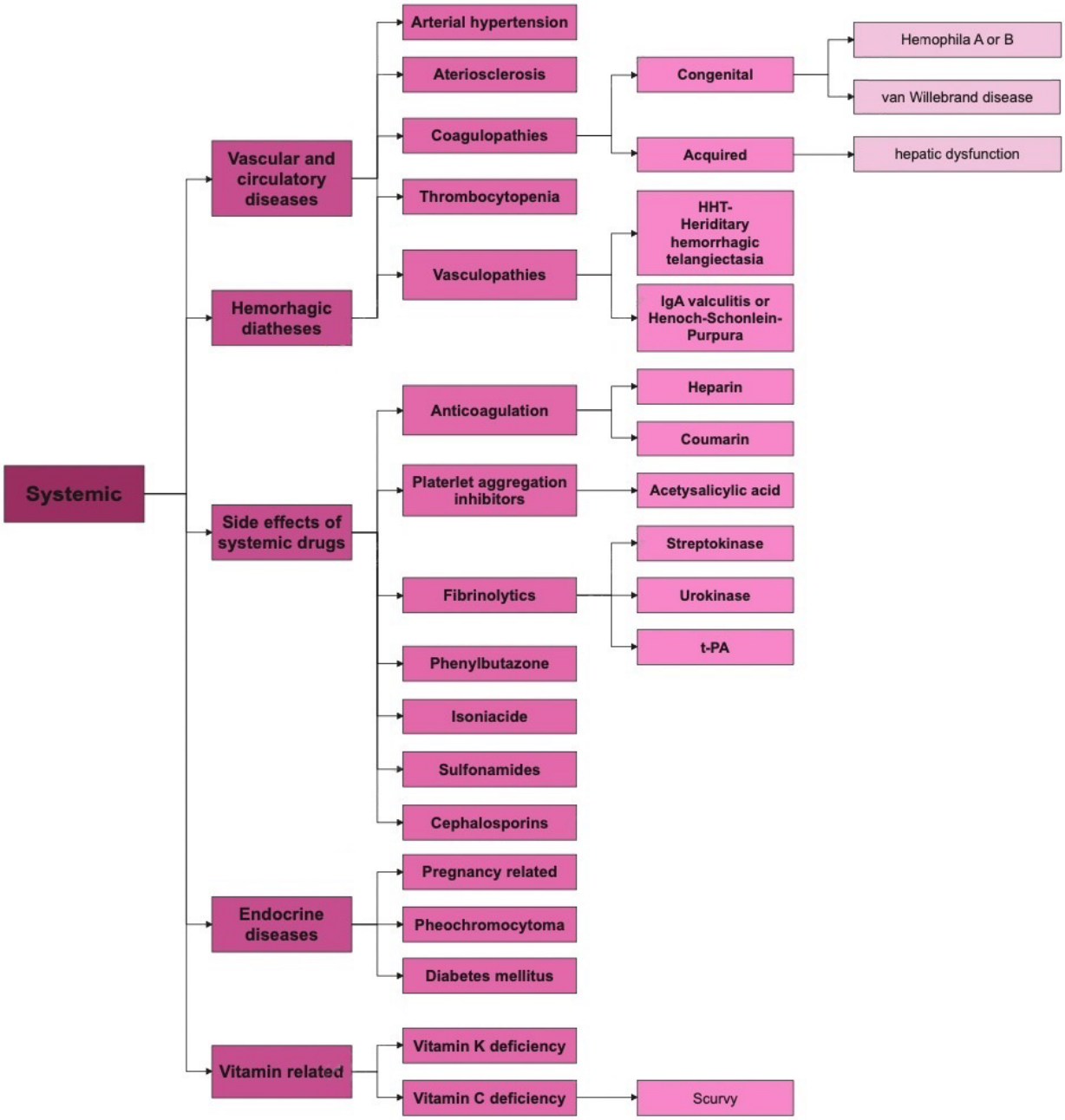

Figure 3: Systemic etiologies of epistaxis; content according to Thurnher (15).

DURATION

Most often idiopathic nosebleeds stop on their own after a few minutes or after directly applied pressure as first aid measurement. If the bleeding has not stopped after fifteen to twenty minutes, patients should seek medical help (14). This time frame only gives a recommendation and does not apply to each case. If the bleeding is very severe or the patient is experiencing accompanying symptoms, like a severe headache, dizziness, syncope or other circulatory related symptoms, they should seek medical help right away. It is also possible

that the bleeding stops after twenty minutes and there is no need for medical intervention at all. If the bleeding is very weak and only a few drops are left coming out of the nose, the patient can decide to wait a few more minutes to check if the bleeding stops on its own. Cohen et al. tried to clarify the rates and risk factors of recurrency of epistaxis. Recurrent hospital Admission, REAs for short, were classified in early, within 30 days, and late, between 31 days and 3 years. In the timeframe of 1999 until 2015 14% of patients included in this particular study had one or more recurrent episodes of epistaxis. Out of those, 7.5% early and 6.5% late presentation (16). In case of recurrent epistaxis episodes, patients should also seek help from a medical professional to exclude underlying conditions.
One of the most important underlying conditions associated with epistaxis is hereditary hemorrhagic telangiectasia (HHT), oftentimes called by its previous name Rendu-Osler-Weber disease. This genetic disorder is transmitted dominant autosomal and is categorized into two major groups, type one and type two. The characteristics of this disease, amongst others. include recurrent, spontaneous episodes of epistaxis (17). It affects 1 in 5000 individuals, so it counts as a rare disorder, but the specificity of the symptoms should be kept in mind by every ENT specialist or family physician (18).

DIAGNOSIS

As mentioned above, the most common cause of Epistaxis is idiopathic (15). It needs no diagnostic procedure and resolves on its own without the affected person visiting the hospital. If the bleeding is strong or persists for a longer period of time and the patient seeks medical attention, diagnosis of the epistaxis itself is clinical. Additionally, general diagnostic measures include taking vital signs to determine if the patient is hemodynamically stable. Also an anamnesis is taken to determine if this is a recurring problem or if they have an underlying disease related to this incidence. The responsible physician can identify a bleeding either via looking at the patient's nostrils or with a diagnostic lamp in the back of the patient's throat. The diagnosis of epistaxis is made and the initial first aid management can be commenced. If the bleeding does persist after the first aid measurements, the physician will try to localize the exact site of bleeding, with the aid of a rhinoscope and light. When the bleeding is anterior, where most of the bleedings are located, he is, with a high possibility, able to identify the origin of the bleeding. If the bleeding is further in the back of the nasal cavity he will use a rhino-laryngoscope, a special endoscope, which can either be flexible or rigid, to identify the bleeding site. This step is important for the determination of treatment, which will be explained in more detail later.

In case of a patient presenting with recurrent epistaxis or hard to manage epistaxis, a detailed diagnostic procedure will be performed. This includes a detailed anamnesis and a family history.
The responsible physician would also check for additional symptoms that might be undiscovered by the patient yet. An example of this would be perioral telangiectasia, which would be a sign of hereditary hemorrhagic telangiectasia. Another example would be signs of easy bruising, other bleeding sites or unusually long bleeding when injured. Those would all be signs of coagulopathies. But since the list of possible etiologies is very long, the list of specific diagnostic tools is equivalently long. If the patient expresses symptoms that could lead to a suspicion of a malignant process, imaging might be performed. The diagnostic procedure can even go as far as tissue biopsy.
In conclusion the diagnosis of epistaxis itself is fairly simple, but if there is an underlying cause there is no limit set for diagnostic procedures.

MANAGEMENT

Anterior epistaxis is usually self-limiting and does not need treatment at all. First aid management at home as described in the First Aid Chapter is completely sufficient. If the bleeding does not stop on its own, medical attention should be sought (14).

GENERAL APPROACH

A stepwise approach for the management of epistaxis is crucial to determine a treatment strategy with the best benefit-to-harm ratio for the patient. The treatment has priority, but the goal is to also include considerations about the patient's comfort and quality of life, especially regarding invasive procedures.
As mentioned above the management should be started by identifying the bleeding site. Depending on the circumstances first aid measurements should already be taken at this point. An evaluation of the amount of blood lost and severity of the current bleeding can be important to identify the underlying cause (6). The statement of the patient should be considered, but it should also be kept in mind that the subjective amount of blood can differ hugely from the objective amount of blood and it often looks like more blood to the patient, than they actually lost. A detailed anamnesis, including the patient's risk factors can be very important and should be taken thoroughly. Risk factors that could lead to serious complications include uncontrolled hypertension, drug use, specific medications and coagulopathies (6).

FIRST AID

The first aid for epistaxis is fairly simple and can be performed at home. By compressing the alae nasi and leaning forward as seen in Figures 4 and 5 we achieve several things. Firstly, direct compression of the Kiesselbach's Plexus or Little's area which encourages clot formation and acts haemostatic. The forward leaning position helps to prevent blood from running down the nasopharynx and entering the oesophagus and finally the stomach, since blood is very nauseating (19,20).

One major problem the society is facing is the lack of knowledge among the general population and health care personnel about the correct use of this procedure. Several studies show that there was a severe lack of knowledge already in the 1990s. Less than 33% of emergency department personnel and less than 50% of trained medical personnel could correctly identify first aid measurements (21). Considering the general public at that time a study by Strachan and England shows that 35% could identify the right location for compression and 36% could identify the correct head positioning, but only 11% could identify both correctly (19). Since the 1990s thirty years have passed, but a study from 2021 shows that the incorrect application of first aid for epistaxis is still very common. Correct answers for both location of compression and position of the head were given by only 21% of emergency medicine attending physicians, 19% of emergency medicine residents, 11% of primary care physicians and 4% of nurses (4). On the other hand, studies suggest that about 70-80% of medical students participating knew the correct position of the head and around 40-60% knew the correct site of compression(22–24). Although those numbers show sufficient knowledge for medical students, it is still problematic, especially considering the technique is easy to learn and the high prevalence of the condition.

Consequently information on how to behave and distribution of first aid should be improved. The information should be broadly available and understandable for different target groups. Those target groups should include the general public, but especially health care personnel, parents, staff at educational institutions and children from an appropriate age on.

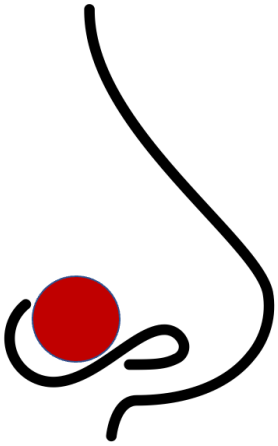

Figure 4: Correct position of pressure point

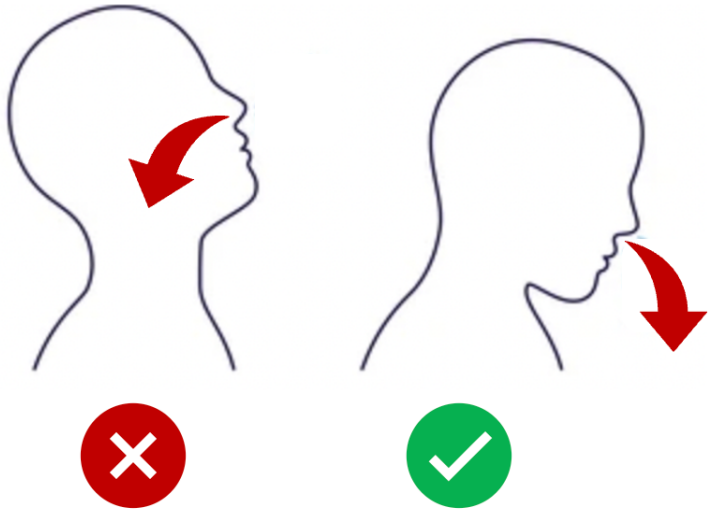

Figure 5: Correct head positioning (arrows indicate way of blood flow).

TREATMENT

Since the most common group of people searching for medical help with epistaxis are either under ten years old or above seventy years old, non-invasive or minimal-invasive procedures are preferred and more commonly used (25). The first try is usually topically applied vasoconstrictors (14). Tunkel and colleagues mentioned in their research that 19.7% of patients presenting to the emergency department with epistaxis had been treated with nasal packing. Out of those over half the patients had additional cautery performed. Another 41% had anterior nasal packing alone and 7% had anterior and posterior packing combined. This treatment regime of the combination or stepwise use of vasoconstrictors, cautery and nasal packing seems to be successful and is more or less used in most of the cases. Embolization or

cautery are only used after the source of bleeding is identified. If the source of bleeding remains unknown, nasal packing is performed without any additional steps (26). But it is also mentioned by Tunkel that there is a desperate need for research and further development to reduce pain and increase patient comfort (2,27).

WARM WATER IRRIGATION

A very old method for treating specifically posterior epistaxis is warm water irrigation. It was first mentioned in 1878 for the management of epistaxis, but was used earlier for the treatment of other bleeding types (28). The water needs to have a temperature of exactly 50°C. There was a study performed by Stangerup and colleagues that showed a clear advantage of warm water irrigation compared to nasal packing, with a 11% higher success rate (29). But considering the study performed was very small, the evidence is not very strong. It is also a relatively old study issued in the year 1999, so the relevance for today's medical practice could be limited. A literature review published in the year 2011 however claimed a success rate of up to 82% (28). Stangerup et al. modified the original method, which was to introduce a catheter into the nasal cavity, fill the balloon with the hot water and afterwards irrigate the posterior nasal cavity with 500 ml hot water in total (29). Novoa and Schlegel-Wagner in comparison used topical anaesthesia (4% tetracaine) and an Epicat balloon catheter, a newer version catheter, which has an irrigation opening proximal to the balloon. They inflate the balloon with normal saline within the epipahrynx. They then gently pull the filled balloon back until the choana is blocked off, to prevent aspiration. The nasal cavity then is irrigated via a caloric stimulator using 500 ml of water, like in the original method too. Further information on the correct placement and waterflow can be taken from Figures 6a and b. Most patients stopped bleeding during the hot water irrigation itself or after 10 minutes of continuous irrigation (28).

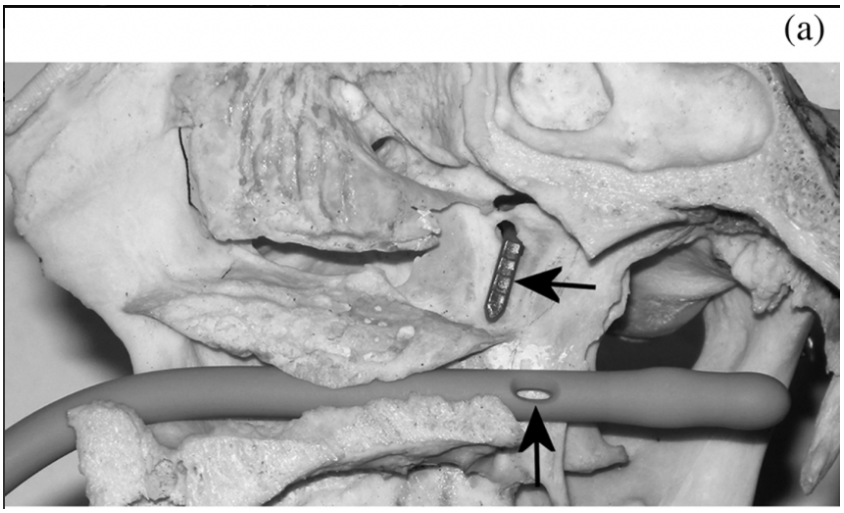

Figure 6 a: Correct placement of the modified balloon catheter along the inferior meatus, with the orifice of the catheter (arrow) placed underneath the sphenopalatine foramen (second arrow) (28).

(b)

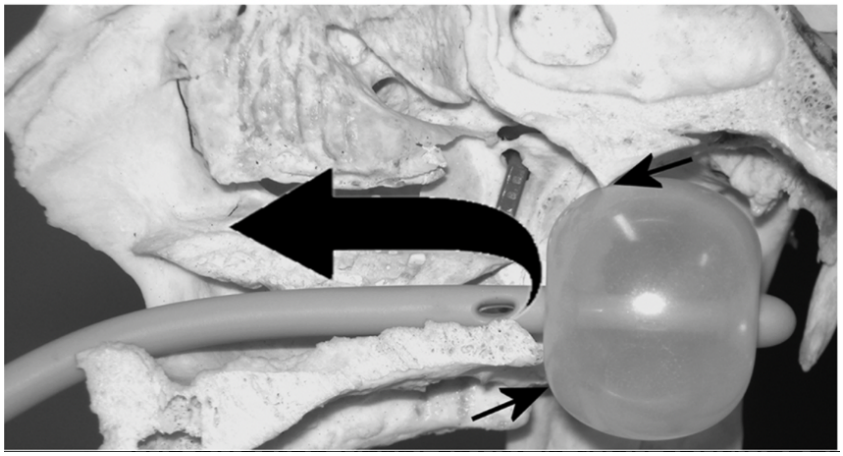

Figure 6 b: The large arrow indicated the direction of water flow through the nose during continuous irrigation, while the small arrows show the correct placement of the inflated balloon, anchored with the choana (28).

VASOCONSTRICTORS

Intranasal vasoconstrictors are routinely used as a first step regardless of the further actions and interventions (14). They are easily accessible and can be applied by non-specialized personnel. Krempl and colleagues showed that 65% of patients can be managed with only vasoconstrictor use, in their case oxymetazoline, to treat epistaxis. They also stated that vasoconstrictors are very useful in combination with silver nitrate cautery. Combining those two methods only 17% of all cases needed to have nasal packing performed (30).

CAUTERY

Silver nitrate cautery, a kind of chemical cautery, is used since the 1980s. Back then after the application of 75% silver nitrate, a cotton pad was applied to the site of bleeding to establish a good burn. Without applying pressure after the cauterization it was previously less sucessful, because the silver nitrate did not stay in place long enough (31). In the 1990s studies were performed trying to establish if chemical cautery or electrical cautery is by any means beneficial over the other. The results showed that they are similar in efficiency and results, but silver nitrate cautery is easier to use, so therefore it should be the method of choice for

simple anterior epistaxis (32). Murthy et al. performed a study in 2001 that concluded that cautery has no benefit compared with the treatment of naseptin, an antiseptic nasal carrier cream, in the treatment of simple epistaxis. The study performed included only 50 patients in total and the presentation of epistaxis was recurrent in all of the patients. Though it did not specifically exclude patients with recurrent epistaxis that is reported to be self-limiting, so the evidence is very weak and further research should be performed on this subject (33).

EMBOLIZATION

This procedure is widely used and safe, but there still are some contraindications which should be considered before applying. Due to the use of contrast media a proper kidney function and the absence of any allergies to contrast media must be ensured. Also accessibility problems can be a contraindication, for example if the vessel is atherosclerotic or the patient is obese to a degree were the access to a vein is severely limited (6).

According to Tseng et al the commonly used technique includes intravenously administered sedation and local anaesthesia. The femoral artery is then punctuated to get access to the blood vessel system of the patient. A selective angiography of the internal and external carotid arteries on the ipsilateral side is performed, to rule out any underlying conditions or malformations of the vessels. The catheter is placed in the external carotid artery and a size three French microcatheter is advanced until the sphenopalatine foramen is almost reached. The embolization itself is performed with polyvinyl alcohol (PVA) particles suspended in iodine contrast media, which is injected through the catheter. Reflux of this material in proximal direction is dangerous and should be avoided (34).

This proceeding shows an initial success rate of 95% in a study from 2009 by Moreau et al. (35). Whereas Christensen et al. state, that 13% of patients had recurrent bleeding episodes within 6 weeks after the procedure and another 14% at a later timing, which accumulates the recurrence rate at approximately 27% (36).

A bigger study performed by Tseng et al. including 114 patients undergoing embolization concluded that the immediate success rate was 93%, in comparison to a long-term success rate of 88%. The rate of complications was 17% with the long-term morbidity rate less than 1% (34). In conclusion the initial success rate shows a high efficiency, with low likelihoods of complications and death, even though data for recurrency rates may vary.

NASAL PACKING

Nasal packing is still one of the most used treatment strategies for epistaxis. Technically the packs are easy to apply and most often are placed in the emergency department, before the patient is admitted or seen by an ENT specialist (37). Nasal packing does not have a lot of contraindications, which makes it safe to use even without direct contact to a specialist. The only known contraindications are facial, nasal bone or basilar skull fractures or emergency conditions, where the patient is either hemodynamically instable or their airway is compromised (14).

The choice of material, device and their combination is highly individual and differs from hospital to hospital and sometimes even from doctor to doctor. There are several studies comparing different nasal devices with one another. Hesham and Ghali compared Merocel nasal packs with rapid rhino nasal packs in 2019 and came to the conclusion that rapid rhino nasal packs were superior in terms of pain and bleeding risk after septal surgery (38). While this study only compared both materials for the preventative use after surgery, Badran and colleagues compared both in regard to epistaxis treatment in 2005. They concluded that the efficacy is similar, but the patients comfort is superior in rapid rhino packing (39).

The material of choice should always be used according to package instructions. Some are soaked in water for approximately 30 seconds before use, while some of them do not need preparation at all. Also, the coating depends on preference and given materials. Some are covering their packing material in antibiotic or antiseptic ointments (e.g. Naseptin cream) or petroleum jelly. (14,27)

The vasoconstrictive agents mentioned above in this case are used in this case to achieve topical anaesthesia.

The medical professional placing the nasal pack should always keep the anatomic structures of the nasal cavity in mind. It is horizontally orientated, and the pack should not be inserted vertically.

The first step is to advance the prepared pack of choice a few centimetres (approximately 1-2 cm) diagonally into the nostrils as seen in Figures 7 a.

Figure 7a: Advancing the Merocel pack horizontally (27).

Then the pack is tilted in a horizontal direction as shown in Figure 7b.

Figure 7b: Advancing the Merocel pack horizontally (27).

The appliyng person should be able to protrude the nasal pack horizontally without any severe resistance until it is completely introduced into the nasal cavity (Figure 7c).

Figure 7c: Advancing the Merocel pack horizontally (27).

After insertion, the nasal pack will expand to some extend on its own due to the contact with blood. But the executing health care professional should inflate the balloon according to the specific instructions for their used material. The combination of nasal packing and usage of hemostatic agents is performed depending on preference and hospital guidelines. Kravchik and her colleagues in their approach on nasal packing mention to either use simple saline (0.9% NaCl), Tranexamic acid or 0.05% oxymetazoline. Close monitoring of the patient for the first ten to thirty minutes directly after the insertion of nasal packs is crucial. The duration of how long the nasal pack should stay in place varies from 24-48 hours for the treatment of epistaxis, but can be up to five days for the prevention of bleeding after surgery or high risk of rebleeding (14,37).

TRANEXAMIC ACID (TXA)

A relatively new treatment strategy is currently investigated in several studies. TXA is an antifibrinolytic agent which is commonly used and has a wide variety of clinical indications. The indication of epistaxis is also mentioned. The application form in the literature varies, some used topical 10% TXA solutions, but most of them topically use the injectable form of TXA with 500 mg/5 ml. One study from 2019 suggest that there is a moderate evidence of statistically significant reduction of bleeding during epistaxis in a randomized trial (40). But another study from 2021indicates that there is no significant benefit compared to a placebo

group regarding bleeding control and reduction of the need for anterior nasal packing (41). R. Zahed and his colleagues performed a study in 2013 that concluded topical tranexamic acid was superior to anterior nasal packing in the initial treatment of idiopathic anterior epistaxis (42). Gholizadeh and their colleagues even stated it is “one of the most effective pharmacological options to control bleeding with cost and tolerability advantages.” (43). Generally speaking, more sources indicated the benefit of TXA as a topical applied medication for epistaxis, which makes it a great alternative to uncomfortable nasal packing or invasive procedures. There is definitely the need for more studies with a larger sample size to confirm the advantages of TXA, but when looking at the already existing data, it looks like it is worth investigating and has great potential.

TRAUMASTEM

Traumastem is an absorbable, sterile powder. It is made of calcium hydrogen salt of oxidized cellulose. In a study performed in 2020 this new treatment method was compared to routine nasal packing, which is highly uncomfortable for the patients (2). There was no difference in bleeding time control between the two groups, but the patient satisfaction was significantly higher in the traumastem group (44). Considering the importance of not only the efficacy of the treatment, but also reducing pain and discomfort for the affected patients, Traumastem seems to be a good alternative treatment option, when regarding given data.

CELOX/CHITOSAN GAUZE

Another haemostatic agent on the market is Celox coagulation powder. The main ingredient is chitosan, a biodegradable and biocompatible monomer (43,45). Shikani and colleagues state that in cases of severe epistaxis that was non-manageable with normal nasal packing, chitosan packing is effective and safe to use. It is also comparable or even superior in regards to discomfort for the patient and a good option for outpatient use (46).

A promising study combines the use of chitosan and tranexamic acid. Gholizadeh and colleagues developed an in-Situ gel that is based on chitosan and loaded with TXA. The gel is prepared and infused with 10 mg/ml TXA. As a control a 1% TXA solution is used. Data about the gelatinous properties, the spray pattern, the nasal deposition in a human nasal cavity, the droplet size and the aerosol deposition. Everything was tested in-Situ on nasal epithelium. Their results show that the gelatinous properties ensure a safe and efficient drug delivery into the nasal cavity, while it prevents nasal run-off and deposition in the lung tissue. The wound healing properties are remarkable and approximately six times faster than that of

the control group with only the TXA solution. There is need for further research, especially in vivo trials (43). It gives rise to the opportunity for a developmental leap with a treatment option that is easy applicable, increases the patients comfort and is a cost and time effective alternative to invasive procedures or nasal packing with subsequent hospital admissions.

CRYOTHERAPY

The basic principle behind cryotherapy is to apply subfreezing temperatures of – 70°C to tissue, which causes the cellular protein to break down. It is supposedly widely used in the ENT field for various other diseases like vasomotor rhinitis, management of tonsillectomies, benign or malignant tumours, and more (47). Anyhow a study concerning the treatment of chronic rhinitis with cryotherapy concluded insufficient evidence for the use of cryotherapy in this specific case(48). Kim and colleagues stated satisfactory results in treating recurrent epistaxis in patients with HHT, but mentioned the need for more studies and reliable data (47).

Cryotherapy in the first aid management of Epistaxis is not performed currently. Studies suggest that there is no benefit in this procedure and emphasize the need for further research (49).

In conclusion the research regarding cryotherapy is not nearly enough and several studies mention the insufficient support of real evidence-based research. As a result, currently there can be assigned no use in the treatment of epistaxis to this technique to assign this technique.

SURGICAL LIGATION

In 1965 Chandler and Serrins presented a preliminary report about controlling recurrent epistaxis with the ligation of the anterior ethmoid and internal maxillary arteries (50). Although Chandler and Serrins reported a success rate of 100 % in their report from 1965, a second report from 1988 from Metson and Lane stated out of 100 performed ligations 15 patients developed postoperative bleeding (50,51).

The surgical ligation of either one or both of the above mentioned arteries can be performed endoscopically or via an external approach. There are several studies suggesting different approaches and it is still performed according to personal preferences of the performing surgeon and external factors, like visibility of the artery (52).

Endoscopic ligation of the sphenopalatine artery or ESPAL for short was described as a treatment method for epistaxis already in the early nineties by Budrovich and Saetti (53).

For this procedure the correct positioning of the ligature is crucial, because there is the possibility of a revascularization by the maxillary artery (52). The anatomy of the sphenopalatine artery is very variable, but gladly extensively researched. For example one big study from Lee et al published in 2009 described the template of branches. The success rate of sphenopalatine artery ligation in the hands of an experienced surgeon is estimated to be 95% or higher (52,54–56). Failure of ESPAL is estimated between zero and 16% and is associated with incorrect usage of the clips and anatomical variations of the arteries, which makes a definite identification of the artery difficult (57).
The ligation of the maxillary and anterior ethmoid artery have a nearly similar failure rate with 5-15% (58).

COMPLICATIONS

GENERAL

Complications of Epistaxis are generally speaking very rare and are either associated with blood loss or the chosen treatment method.
If severe epistaxis is left untreated it could lead to hypovolemic shock. A hypovolemic shock is defined by hypovolemia in addition to decreased peripheral perfusion. This tissue hypoxia can cause necrosis of tissue and ischemic injury of organs, which subsequentially lead to multi-system organ failure if left untreated. If not treated the bleeding would ultimately lead to circulatory failure and death (59).
Awashti et al. reported the death of a patient after the treatment of epistaxis and claimed the cardiac arrest could be attributed to the Trigeminocardiac reflex (TCR), which is stimulated either mechanically or chemically, so the specific treatment method is irrelevant. The trigeminal nerve is the largest cranial nerve and provides sensory innervation to the face, scalp and oral and nasal mucosa. Once the reflex is activated the patient experiences dysrhythmia, hypotension, apnea or gastric hypermobility. This can lead to respiratory or circulatory arrests in patients (60,61).

NASAL PACKING

Since a foreign object is introduced into the body the risk of infection is always present. The duration of nasal packing influences the risk of infection immensely, the longer the tamponade stays inside the nose, the higher the risk of infection. The use of prophylactic antibiotics for nasal packing stays highly controversial. Some studies say that prophylactic antibiotics are still used, especially if non-absorbable packing is utilized. In contrast, several

other studies came to the conclusion that prophylactic antibiotics do not have any benefits, regardless of the packing material (62,63). Correlated with infections is the very rare complication of toxic shock syndrome. It is a complication of a staphylococcal infection and is a life-threatening condition (64,65).

If the nasal packing does not stay at its designated place, it can cause serious complications. There are safety measurements to ensure the correct position of the packing. Those safety measures include stable threads that are secured to the bridge of the nose via tape. If not fixed properly, the tamponade can migrate through the nasopharynx into the trachea or bowels and lead to obstruction. (64,66) The proper use of the fixation and packing should be ensured, because if the thread incises into the skin or the pressure on the mucosa is too high, it can lead to mucosal lesions. Other complications are related to the additional material that is used, like paraffin or ointments and can cause allergies or lipogranulomas (64). Their use is dependent on the procedure and protocol in every individual country or clinic and are therefore very variant.

EMBOLIZATION

As mentioned above the procedure is routinely performed and relatively safe, but obviously a certain risk is unavoidable with every procedure performed. According to Shukla and colleagues minor complications include “facial pain, facial oedema, facial cold hypersensitivity, jaw pain, headache, paraesthesia, anaesthesia, trismus, mild palate ulceration, inguinal pain, inguinal hematoma, altered mental status and fever”. Major complications would be a stroke, loss of vision, necrosis of tissue, facial palsy, scar formation, seizures and a severe allergic reaction to the contrast media used (6). Another possible complication is nasal mucosa necrosis, due to lack of blood supply. Nonetheless the microvascular bed of the nasal mucosa is very prominent, which makes this complication very rare (34).

SURGICAL LIGATION

The procedure is associated with several complications, most of them are nerve related. There are reports about infraorbital neuralgia, persistent upper jaw pain, oroantral fistulas and sinusitis. The most severe complication mentioned, associated with nerve damage, is blindness (50). Moreover Murer et al. presented a case report in 2015 about a patient developing a cerebral abscess after anterior ethmoidal artery ligation (67).

CONCLUSION

The definition of the modern version of Epistaxis is attributed to Cullen, who described it in 1785 (68).

Epistaxis is a well-known disorder that has been around for a long time. The medical research about this topic is very extensive and has been an objective for studies even before Cullen. But the high prevalence of the disease nowadays also emphasizes its still existing relevance. The on-hand research showed that the current practice varies, but nasal packing and cautery are still the leading conservative treatment tactics around the world. Surgical intervention is rarely possible, but surgical ligation is in most countries still preferred over embolization, due to the more extensive training. Great potential is seen in haemostatic agents like tranexamic acid, traumastem or celox gauze. They could revolutionize the current treatment regime, because they are highly effective, easy applicable and increase the patient's experience. Other treatment options like Cryotherapy are not suitable for practical appliance yet.

The lack of basic knowledge of first aid in the general population and among medical professionals is concerning and can and should be addressed with further research on prevention tactics. One way of addressing the general public is designing leaflets for easy and fast understanding and application of the simple first Aid steps. With the help of pictograms, they would be accessible even for small children and people who are not able to read.

Also the need for generalized guidelines has emerged. There is a clinical practice guideline for epistaxis published by the American academy of otolaryngology- Head and neck surgery in 2020 written by Tunkel et al., but a European version is missing (2). Although a European version is strictly necessary, because due to the ginormous differences in health care systems and patient care, the American guidelines are not 100% applicable for European hospitals.

REFERENCES

1. Vasanthan R, Massoumi A, Forde M, Corbridge O, Sood S. 887 A Quality Improvement Project: Implementation of a New Epistaxis Pathway. Br J Surg. 2021 May 4;108(Supplement_2):znab134.501.
2. Tunkel DE, Anne S, Payne SC, Ishman SL, Rosenfeld RM, Abramson PJ, et al. Clinical Practice Guideline: Nosebleed (Epistaxis). Otolaryngol Neck Surg. 2020 Jan;162(1_suppl):S1–38.
3. Parajuli R. Evaluation of Etiology and Treatment Methods for Epistaxis: A Review at a Tertiary Care Hospital in Central Nepal. Int J Otolaryngol. 2015;2015:1–5.
4. Sowerby L, Rajakumar C, Davis M, Rotenberg B. Epistaxis first-aid management: a needs assessment among healthcare providers. J Otolaryngol - Head Neck Surg. 2021 Dec;50(1):7.
5. Khandelwal G, Gupta S. COMMON SITES OF BLEEDING IN EPISTAXIS. J Evol Med Dent Sci. 2019 Jul 1;8(26):2055–8.
6. Shukla PA, Chan N, Duffis EJ, Eloy JA, Prestigiacomo CJ, Gandhi CD. Current treatment strategies for epistaxis: a multidisciplinary approach. J NeuroInterventional Surg. 2013 Mar;5(2):151–6.
7. Sevransky J. Clinical assessment of hemodynamically unstable patients. Curr Opin Crit Care. 2009 Jun;15(3):234–8.
8. Hooper N, Armstrong TJ. Hemorrhagic Shock. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Mar 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK470382/
9. Mygind N, Dahl R. Anatomy, physiology and function of the nasal cavities in health and disease. Adv Drug Deliv Rev. 1998 Jan;29(1–2):3–12.
10. Drettner B, Aust R. Plethysmographic Studies of the Blood Flow in the Mucosa of the Human Maxillary Sinus. Acta Otolaryngol (Stockh). 1974 Jan;78(1–6):259–63.
11. Cauna N. Electron Microscopy of the Nasal Vascular Bed and its Nerve Supply. Ann Otol Rhinol Laryngol. 1970 Jun;79(3):443–50.
12. Cauna N. The fine structure of the arteriovenous anastomosis and its nerve supply in the human nasal respiratory mucosa. Anat Rec. 1970 Sep;168(1):9–21.
13. Nose and sinuses. Amboss; 2022.
14. Kravchik L, Jamal Z, Pester JM. Anterior Epistaxis Nasal Pack. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Mar 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK538304/
15. Thurnher D, editor. HNO-Heilkunde: ein symptomorientiertes Lehrbuch. Wien: SpringerWienNewYork; 2011. 399 p.
16. Cohen O, Shoffel-Havakuk H, Warman M, Tzelnick S, Haimovich Y, Kohlberg GD, et al. Early and Late Recurrent Epistaxis Admissions: Patterns of Incidence and Risk Factors. Otolaryngol Neck Surg. 2017 Sep;157(3):424–31.
17. Pérez del Molino A, Zarrabeitia R, Fernández Á. Telangiectasia hemorrágica hereditaria. Med Clínica. 2005 Apr;124(15):583–7.
18. Parambil JG. Hereditary Hemorrhagic Telangiectasia. Clin Chest Med. 2016 Sep;37(3):513–21.
19. Strachan D, England J. First-aid treatment of epistaxis--confirmation of widespread ignorance. Postgrad Med J. 1998 Feb 1;74(868):113–4.
20. Pearson BW. Epistaxis. Postgrad Med. 1975 May;57(6):116–9.
21. McGarry GW, Moulton C. The first aid management of epistaxis by accident and emergency department staff. Emerg Med J. 1993 Dec 1;10(4):298–300.
22. Alyahya K, Alsaad S, Alsuliman S, Alsuliman N. Awareness about first aid management of epistaxis among medical students in Kingdom of Saudi Arabia. J Fam Med Prim Care. 2019;8(3):914.

23. Mugwe P, Kamau KJ, Nyambaka OK. Knowledge, Attitude and Practice in Frist Aid Management of Epistaxis by Accident and Emergency Clinical Staff at Kenyatta national Hospital. East and Central African Journal of Surgery; 2014.
24. Albouq N, Aljeraisi T, Arabi S, Neyaz H, Alkhurassi H, Alim B. Knowledge and Attitude regarding first aid management of epistaxis among medical specialities students AL-Madinah, Kingdom of Saudi Arabia. 2017.
25. Pallin DJ, Yi-Mei C, McKay MP, Emonds JA, Pelletier A, Camargo CA. Epidemiology of Epistaxis in US Emergency Departments, 1992 to 2001. Ann Emerg Med. 05/05;(Volume 46).
26. Kasle DA, Fujita K, Manes RP. Review of Clinical Practice Guideline: Nosebleed (Epistaxis). JAMA Surg [Internet]. 2021 Jul 7 [cited 2021 Jul 29]; Available from: https://jamanetwork.com/journals/jamasurgery/fullarticle/2781752
27. Leong SCL, Roe RJ, Karkanevatos A. No frills management of epistaxis. Emerg Med J EMJ. 2005 Jul;22(7):470–2.
28. Novoa E, Schlegel-Wagner C. Hot water irrigation as treatment for intractable posterior epistaxis in an out-patient setting. J Laryngol Otol. 2012 Jan;126(1):58–60.
29. Stangerup SE, Dommerby H, Lau T. Hot-water irrigation as a treatment of posterior epistaxis. Rhinology. 1996 Mar;34(1):18–20.
30. Krempl GA, Noorily AD. Use of Oxymetazoline in the Management of Epistaxis. Ann Otol Rhinol Laryngol. 1995 Sep;104(9):704–6.
31. Barr GD. Silver nitrate cautery and epistaxis. Arch Emerg Med. 1989 Sep;6(3):233.
32. Toner JG, Walby AP. Comparison of electro and chemical cautery in the treatment of anterior epistaxis. J Laryngol Otol. 1990 Aug;104(8):617–8.
33. Murthy P, Nilssen ELK, Rao S, Mcclymont LG. A randomised clinical trial of antiseptic nasal carrier cream and silver nitrate cautery in the treatment of recurrent anterior epistaxis. Clin Otolaryngol Allied Sci. 1999 Jun;24(3):228–31.
34. Tseng EY, Narducci CA, Willing SJ, Sillers MJ. Angiographic Embolization for Epistaxis: A Review of 114 Cases. The Laryngoscope. 1998 Apr;108(4):615–9.
35. Moreau S, De Rugy MG, Babin E, Courtheoux P, Valdazo A. Supraselective Embolization in Intractable Epistaxis: Review of 45 Cases. The Laryngoscope. 1998 Jun;108(6):887–8.
36. Christensen NP, Smith DS, Barnwell SL, Wax MK. Arterial Embolization in the Management of Posterior Epistaxis. Otolaryngol Neck Surg. 2005 Nov;133(5):748–53.
37. INTEGRATE (The UK ENT Trainee Research Network), Abbas Y, Abdelkader M, Adams M, Addison A, Advani R, et al. Nasal Packs for Epistaxis: Predictors of Success. Clin Otolaryngol. 2020 Sep;45(5):659–66.
38. Hesham A, Ghali A. Rapid Rhino versus Merocel nasal packs in septal surgery. J Laryngol Otol. 2011 Dec;125(12):1244–6.
39. Badran K, Malik TH, Belloso A, Timms MS. Randomized controlled trial comparing Merocel and RapidRhino packing in the management of anterior epistaxis. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2005 Aug;30(4):333–7.
40. Cai J, Ribkoff J, Olson S, Raghunathan V, Al-Samkari H, DeLoughery TG, et al. The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. Eur J Haematol. 2020 Feb;104(2):79–87.
41. Reuben A, Appelboam A, Stevens KN, Vickery J, Ewings P, Ingram W, et al. The Use of Tranexamic Acid to Reduce the Need for Nasal Packing in Epistaxis (NoPAC): Randomized Controlled Trial. Ann Emerg Med. 2021 Jun;77(6):631–40.
42. Zahed R, Moharamzadeh P, AlizadehArasi S, Ghasemi A, Saeedi M. A new and rapid method for epistaxis treatment using injectable form of tranexamic acid topically: a randomized controlled trial. Am J Emerg Med. 2013 Sep;31(9):1389–92.

43. Gholizadeh H, Messerotti E, Pozzoli M, Cheng S, Traini D, Young P, et al. Application of a Thermosensitive In Situ Gel of Chitosan-Based Nasal Spray Loaded with Tranexamic Acid for Localised Treatment of Nasal Wounds. AAPS PharmSciTech. 2019 Sep 3;20(7):299.
44. Pouraghaei M, Shafiee S, Mesrian F, Ebrahimi Bakhtavar H, Rahmani F. Traumastem Powder in Treatment of Non-Traumatic Anterior Epistaxis in Emergency Department; a Randomized Clinical Trial. Arch Acad Emerg Med. 2020;8(1):e78.
45. Ala A, Rahmani F, Shirzadegan S, Ebrahimi Bakhtavar H, Mehdizadeh Esfanjani R. Non - traumatic Epistaxis Management Using Celox® Dressing: A Randomized Clinical Trial. Iran Red Crescent Med J [Internet]. 2018 May 5 [cited 2022 Mar 13];20(4). Available from: https://sites.kowsarpub.com/ircmj/articles/58374.html
46. Shikani AH, Chahine KA, Alqudah MA. Endoscopically guided chitosan nasal packing for intractable epistaxis. Am J Rhinol Allergy. 2011 Feb;25(1):61–3.
47. Kim JY, Oh JH, Kim GT, Kwon JH. Endoscopic cryotherapy for the treatment of epistaxis due to hereditary hemorrhagic telangiectasia. J Craniofac Surg. 2014;25(2):e120-122.
48. Kompelli AR, Janz TA, Rowan NR, Nguyen SA, Soler ZM. Cryotherapy for the Treatment of Chronic Rhinitis: A Qualitative Systematic Review. Am J Rhinol Allergy. 2018 Nov;32(6):491–501.
49. Berry D, Carlson JN, Singletary E, Zideman DA, Ring J. Use of Cryotherapy for Managing Epistaxis in the First Aid Setting: A Scoping Review. Cureus [Internet]. 2021 May 4 [cited 2021 Jul 29]; Available from: https://www.cureus.com/articles/57398-use-of-cryotherapy-for-managing-epistaxis-in-the-first-aid-setting-a-scoping-review
50. Chandler JR, Serrins AJ. TRANSANTRAL LIGATION OF THE INTERNAL MAXILLARY ARTERY FOR EPISTAXIS.*???: The Laryngoscope. 1965 Jul;75(7):1151???1159.
51. Pearson BW, MacKenzie RG, Goodman WS. THE ANATOMICAL BASIS OF TRANSANTRAL LIGATION OF THE MAXILLARY ARTERY IN SEVERE EPISTAXIS: The Laryngoscope. 1969 May;79(5):969–84.
52. Traboulsi H, Alam E, Hadi U. Changing Trends in the Management of Epistaxis. Int J Otolaryngol. 2015;2015:1–7.
53. Budrovich R, Saetti E. Microscopic and Endoscopic Ligature of the Sphenopalatine Artery: The Laryngoscope. 1992 Dec;102(12):1390–4.
54. Pádua FGM, Voegels RL. Severe Posterior Epistaxis-Endoscopic Surgical Anatomy. The Laryngoscope. 2008 Jan;118(1):156–61.
55. Kumar S, Shetty A, Rockey J, Nilssen E. Contemporary surgical treatment of epistaxis. What is the evidence for sphenopalatine artery ligation? Clin Otolaryngol Allied Sci. 2003 Aug;28(4):360–3.
56. Simmen DB, Raghavan U, Briner HR, Manestar M, Groscurth P, Jones NS. The Anatomy of the Sphenopalatine Artery for the Endoscopic Sinus Surgeon. Am J Rhinol. 2006 Sep;20(5):502–5.
57. Kamani T, Shaw S, Ali A, Manjaly G, Jeffree M. Sphenopalatine-sphenopalatine anastomosis: a unique cause of intractable epistaxis, safely treated with microcatheter embolization: a case report. J Med Case Reports. 2007 Dec;1(1):125.
58. Kamani T, Shaw S, Ali A, Manjaly G, Jeffree M. Sphenopalatine-sphenopalatine anastomosis: a unique cause of intractable epistaxis, safely treated with microcatheter embolization: a case report. J Med Case Reports. 2007 Dec;1(1):125.
59. Taghavi S, Askari R. Hypovolemic Shock. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2022 Apr 9]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK513297/
60. Awasthi D, Roy TM, Byrd RP. Epistaxis and Death by the Trigeminocardiac Reflex:

A Cautionary Report. Fed Pract Health Care Prof VA DoD PHS. 2015 Jun;32(6):45–9.
61. Trigemino-Cardiac Reflex Examination Group (TCREG), Spiriev T, Sandu N, Arasho B, Kondoff S, Tzekov C, et al. A new predisposing factor for trigemino-cardiac reflex during subdural empyema drainage: a case report. J Med Case Reports. 2010 Dec;4(1):391.
62. Hu L, Gordon SA, Swaminathan A, Wu T, Lebowitz R, Lieberman S. Utilization of Prophylactic Antibiotics After Nasal Packing for Epistaxis. J Emerg Med. 2021 Feb;60(2):144–9.
63. Biswas >D., Mal RK. Are systemic prophylactic antibiotics indicated with anterior nasal packing for spontaneous epistaxis? Acta Otolaryngol (Stockh). 2009 Jan;129(2):179–81.
64. Delank K-W. Diagnostik und Therapie der Epistaxis. Laryngo-Rhino-Otol. 2006 Aug;85(8):593–603.
65. Weber R, Hochapfel F, Draf W. Packing and stents in endonasal surgery. Rhinology. 2000 Jun;38(2):49–62.
66. Hashmi SM, Gopaul SR, Prinsley PR, Sansom JR. Swallowed nasal pack: a rare but serious complication of the management of epistaxis. J Laryngol Otol. 2004 May;118(5):372–3.
67. Murer K, Holzmann D, Burkhardt J-K, Soyka MB. An unusual complication of epistaxis: cerebral abscess formation after anterior ethmoidal artery ligation. BMJ Case Rep. 2015 Dec 29;2015:bcr2015213389.
68. Olóriz Marín JA, Prim Espada MP, de Diego Sastre JI. [History of epistaxis since the ancient times to the first half of the XXth century]. An Otorrinolaringol Ibero-Am. 2007;34(5):505–15.

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