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Spontaneous Cerebrospinal Fluid Rhinorrhea: A clinical and anatomical study

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Objectives/Hypothesis: Spontaneous nasal cerebrospinal fluid (CSF) fistula represents a rare clinical entity. The possible etiology and the localization of the rhinorrhea remain an ongoing clinical challenge. The purpose of this study was to evaluate the localization of spontaneous CSF fistula and to correlate it with anatomical studies.

Study Design: Retrospective clinical study, prospective anatomical study.

Methods: Twenty-nine patients with spontaneous CSF rhinorrhea were retrospectively studied, 10 males and 19 females. Ages ranged from 10 to 92 years (mean, 50 years). In addition, 48 human skulls from newborns to adults were examined for the postnatal development of the anterior and middle cranial fossa.

Results: In our study isolated cribriform plate defects were found in four patients. The lateral lamina of the ethmoid bone showed defects in three patients. In nine patients the bony defect could be found in the region of the fovea ethmoidalis. The bony defect between the extra- and intracranial space was found in the lateral recess of the sphenoid sinus in eight patients. Five patients had special sites (e.g., supraorbital recess and frontal recess).

Conclusions: This study supports the theory that bony dehiscence in the lateral lamina of the ethmoid bone can be congenital and can also be spontaneously acquired later. The bony dehiscence in the lateral wall of the sphenoid sinus can only develop during pneumatization.

Key Words: Spontaneous cerebrospinal fluid leak, anatomy.

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INTRODUCTION

According to the classification system developed by Ommaya, nontraumatic causes of cerebrospinal fluid rhinorrhea (CSF) can be subdivided into high-pressure leaks, which are associated with tumors or hydrocephalus; normal pressure leaks, which are associated with congenital anomalies; and spontaneous leaks.[1] The possible etiology and the localization of spontaneous CSF rhinorrhea remain an ongoing debate.

The most common site of CSF fistula is found in the roof of the ethmoid sinus or in the floor of the anterior cranial fossa, which communicates with the ethmoid and frontal sinuses. Less often, it is seen in the lateral wall of the sphenoid sinus.[2] Sphenoid bone defects are mostly detected in the area of the cavernous sinus, the internal carotid artery, and optic nerve.[3] Bone dehiscences are also seen in the area of the sella turcica.[4,5] The sphenoid sinus is prone to development of CSF leakage, especially if anatomic variants such as lateral pneumatization are present, which encourage development of a communication with the sella floor or the middle cranial fossa.[6] It has been hypothesized that the floor of the middle cranial fossa harbors small perforations or pits. Normal intracranial pressure dynamics and hydrostatic pulsatile forces may lead to development of small holes or pits at the sites of arachnoid villi with herniation of dura/arachnoid or brain tissue. With fixation of these meninges in the pits, the dura mater progressively thins out, resulting in fenestration, arachnoid diverticula formation, or CSF fistula when the arachnoid membrane ruptures.[6,7]

Several studies deal with the anatomical variations of the sphenoid bone and describe extreme differences in the pneumatization. To understand the pathogenesis of the nontraumatic, acquired, and congenital forms of skull base defects, knowledge of the complex ontogenesis of the sphenoid bone is necessary. The sphenoid bone develops from numerous ossification centers, which are initially separated by synchondrosis.[8] The fusion of these centers is a complex process, which may result in a localized lack of bony tissue. The anterior sphenoid bone, the lesser wings, the posterior sphenoid bone, the greater wings, and the lateral pterygoid processes originate as independent cartilaginous precursors. After their ossification, the union of these separate parts gives rises to the complex sphenoid bone. When

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TABLE I.
Spontaneous Cerebrospinal Fluid (CSF) Rhinorrhea Patients Age, Gender, and the Localization of the Spontaneous CSF Leaks.

Patient	Age, yr/Gender	Site/Localization
1	76/male	Lateral wall left sphenoid sinus
2	41/male	Middle fovea ethmoidalis left
3	59/female	Anterior third cribiform plate left
4	11/male	Anterior fovea ethmoidalis behind anterior etmoid artery left
5	58/male	Fovea ethmoidalis and cribriform plate transition to middle ethmoid right
6	12/female	Posterior ethmoid pterygoid-sphenoid right
7	45/female	Anterior/middle third left cribriform plate
8	61/male	Anterior/middle fovea ethmoidalis right
9	69/female	Middle third behind anterior ethmoid artery
10	56/female	Anterior/middle third right forea ethmoidalis
11	81/female	Lateral recess left sphenoid sinus
12	92/male	Anterior fovea ethmoidalis
13	61/female	Lateral wall of sphenoid sinus left
14	32/male	Supraorbital recess, frontal recess right
15	18/female	Left middle fovea ethmoidalis
16	50/male	Supraorbital recess, right frontal sinus
17	48/female	Left middle cribriform plate
18	74/male	Right anterior cribriform plate
19	10/female	Right middle fovea ethmoidalis
20	32/female	Lateral lamella, left cribriform plate
21	51/female	Posterior wall left sphenoid sinus
22	59/female	Lateral recess left sphenoid sinus
23	52female	Roof right ethmoid sinus, encephalocele
24	65/female	Junction right cribriform plate and middle turbinate
25	46/female	Lateral lamella right cribriform plate
26	44/male	Lateral recess right sphenoid sinus adjacent to large cistern
27	48/female	Lateral lamella left cribriform plate
28	42/female	Lateral wall right sphenoid sinus
29	51/female	Lateral wall right sphenoid sinus

posterior fusion is incomplete, a lateral craniopharyngeal canal is created. This congenital bony defect can communicate with the sphenoid sinus after pneumatization has taken place.[9,10]

Whereas most reports in the literature focus on endonasal, microscopic, or endoscopic techniques for leak repair,[2,7,9,11,12] recently refined monitoring protocols discovered a higher incidence of elevated intracranial pressure in idiopathic cerebrospinal fluid leaks.[13–15] This elevated intracranial pressure may be generalized, local or focal, associated with being overweight or obesity, and lead to multiple fistulas in 14% of the patients.[13] This may be one reason for recurrent fistulas in about 10% of the patients.[16]

The purpose of our study was to identify the clinical localization of spontaneous CSF fistulas treated in our departments and to correlate this with anatomical studies on cadaver specimens.

MATERIALS AND METHODS

A retrospective review to localize the sites of spontaneous CSF nasal fistulas was conducted on 29 patients at the Department of Otorhinolaryngology in Mainz Medical School and the New York Eye and Ear Infirmary/New York Medical College. Nineteen woman and 10 men made up this cohort. Age varied from 10 to 92 years (mean, 50 years). This review covered a period of 20 years in Mainz and 15 years in New York. The age of the patients, gender, and site of the leak are shown in the Table I. Spontaneous CSF fistula is defined as the occurrence of CSF rhinorrhea in the absence of prior surgery to the skull base, nose, face, and without prior craniofacial trauma. One patient in this series did undergo a frontal craniotomy for clipping of an anterior communicating aneurysm, and therefore may not fit our definition of spontaneous CSF rhinorrhea. No other patient had other potential causes of their rhinorrhea. All research was carried out according to the guidelines of the Regional Scientific and Ethical Committee for Reseach (TUKEB 83/1999), and the institutional review board of the New York Eye and Ear Infirmary.

The anatomical part of the study compromised 48 human skulls from newborns to adults in order to evaluate the postnatal development of the anterior and middle cranial fossa (Table II). The bones were macerated in water of 56°C for 1 to 2 months and subsequently whitened in 3% hydrogen peroxide solution. The macerated bones were examined under a stereomicroscope. In order to observe the relationship between the structures of the anterior and middle cranial fossa and the sphenoid sinus, the skulls were cut in different planes with a band saw machine. The blade was specially developed in our technical laboratory with a thickness of 0.2 mm.

RESULTS

Clinical Cases

All patients presented with active CSF rhinorrhea. Rhinorrhea varied from a few drops to overt nasal drainage in the head-down position. Preoperative localization of the fistula in Mainz and in New York consisted of intrathecal contrast-enhanced coronal thin-section computed tomographic (CT) imaging and beta-2-transferrinase analysis of the rhinorrhea. Magnetic resonance imaging (MRI) was employed selectively in both cohorts of patients when brain or CSF dynamics abnormalities or encephaloceles were suspected. With the exception of one individual who had adult-onset hydrocephalus, all other female patients were morbidly obese, often two or more times their normal weight for their age and height. Male patients were only slightly above the norm for their weight. Only one patient had undergone attempted repair of their fistula prior to presentation. At surgery,

TABLE II.
Age and Number of Investigated Human Anatomical Specimens.

Age of Anatomic Specimens	No. of Specimens
Newborn	7
2-year-old child	4
3-year-old child	6
5-year-old child	4
Adult	27
Total	48

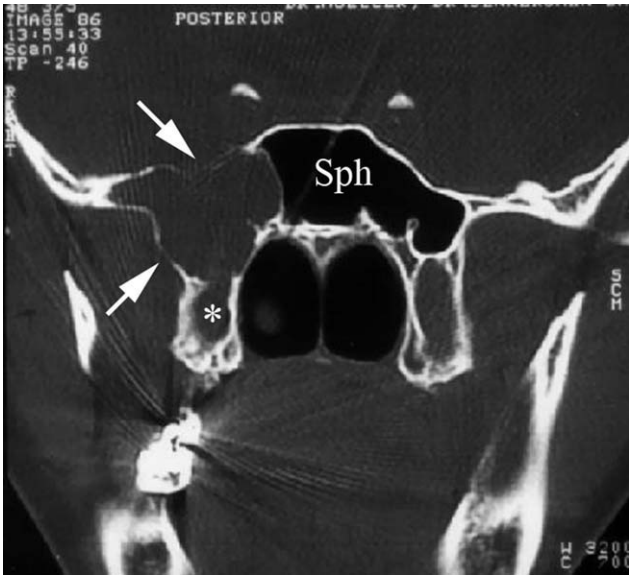

Fig. 1. Coronal computed tomography scan showing a well-pneumatized sphenoid sinus and its surroundings. The bony wall of the sinus reveals defects (arrows) on the right side. Sph = sphenoid sinus, * = pterygoid process.

hypodense intrathecal fluorescein (10 mg/mL) was used in all New York patients to further localize and to confirm closure of the fistula; however, this was not done in the Mainz patients.

The most common sites for spontaneous CSF rhinorrhea were the cribriform plate, with its prolongation laterally, the roof of the ethmoid sinus, and the lateral recess of sphenoid sinus. The roof of the ethmoid sinus is composed of both the fovea ethmoidalis and the frontal bone depending on the extension of the ethmoid cell anlagen into the frontal bone. The bony wall lying between the frontal bone and cribriform plate is usually a thin bony plate, the so-called lateral lamina. In our clinical cohort the isolated cribriform plate defect was found in four patients. The anterior third of the plate had dehiscence in three patients, the middle third in one, and a combination of both areas in one patient. In larger cribriform plate defects, the adjacent skull base may be dehiscent of bone, and this was seen in five patients. The lateral lamina of the ethmoidal bone has shown defects in three patients, whereas the ethmoid roof and the middle turbinate were affected in one case each. A very thin bony plate of the frontal bone covers the ethmoidal cells lying lateral to the cribriform plate. In case of absence of this bony plate, the anterior, middle, and posterior ethmoidal foveae can be found in direct connection with the dura mater, increasing the likelihood of CSF rhinorrhea. In nine of our patients we found bony defects in the region of the ethmoidal foveae. The most frequent site of bony dehiscences was the middle ethmoidal fovea. Isolated defects were observed in five cases, and a combination with the anterior ethmoidal fovea in two cases. The anterior ethmoidal fovea was only affected in two patients, and we did not find any patients with defects of the posterior ethmoidal fovea. In two cases the CSF fistula was found medial to the anterior and middle ethmoidal foveae. The dehiscence of the ethmoidal bone revealed dura prolapse in the supraorbital recess in both cases (Table I).

In extensive pneumatization of the paranasal sinuses, the sphenoid sinus develops an extension laterally, the so-called lateral recess. In our cohort of patients with spontaneous CSF rhinorrhea, the bony defect between the extra- and intracranial space was found in the lateral recess of the sphenoid sinus in eight patients (Fig. 1) and in the posterior wall of the sphenoid sinus in one patient (Table I). All cases had isolated defects without any other communication between the intra- and extradural space. One patient had an extensive bony dehiscence of the lateral wall of the sphenoid sinus within 1 cm of an aneurysm clip. Another patient had developed a bony defect of the lateral recess adjacent to a large cistern, and two patients were diagnosed with an arachnoidal cyst. Large basal cisterns were observed in an additional four of the New York patients. In five of nine patients no other abnormality could be associated with the spontaneous CSF leaks using CT and MRI. Summarizing all the CSF fistulas in our clinical cohort, we identified 21 isolated fistulas, two simultaneous fistulas in seven patients and three fistulas in one patient. Closure of the CSF fistulas varied between the two participating institutions. In Mainz, patients had closure of their CSF leaks localized in the roof of the ethmoid by intradural placement of temporalis fascia plugs covered by an extradural second layer of fascia and secured by fibrin glue and rotation of part of the middle turbinate underneath the defect. For sphenoid sinus fistulas, closure was performed by intradural fascia plugs followed by obliteration of the sphenoid sinus after removal of the sinus mucosa. Lumbar drains were kept in place for 5 days for the latter patients. No patient required a permanent intrathecal shunt. In New York, extracranial free-mucosal grafts, AlloDerm (LifeCell Corp., Branchburg, NJ), or a nasal mucous membrane were applied to the roof of the ethmoid sinus in two patients. Subsequent patients underwent placement of intrathecal abdominal fat, which partially herniated into the nose, and application of free-mucosal or AlloDerm grafts to the roof of the anterior cranial fossa. Intradural and intracranial fat grafts were used to repair all sphenoid sinus fistulas. Lumbar drainage was performed for 3 to 5 days in all but one New York patient. As all patients had active rhinorrhea, opening pressure on insertion of lumbar drains were judged unreliable, and intrathecal pressure was not measured after closure of the fistulas. Three patients had permanent intrathecal shunts placed. One of these patients was shunted after failing the initial repair, and another had severe adult onset noncommunicating hydrocephalus leading to a large meningoencephalocele and mental impairment. One patient presented with bacterial meningitis and was initially successfully treated with antibiotics and then underwent repair of the fistula. No lumbar drains or fluorescein were used. However, this morbidly obese patient subsequently developed Stevens-Johnson syndrome and died. Another morbidly obese female underwent successful closure of her sphenoid fistulas

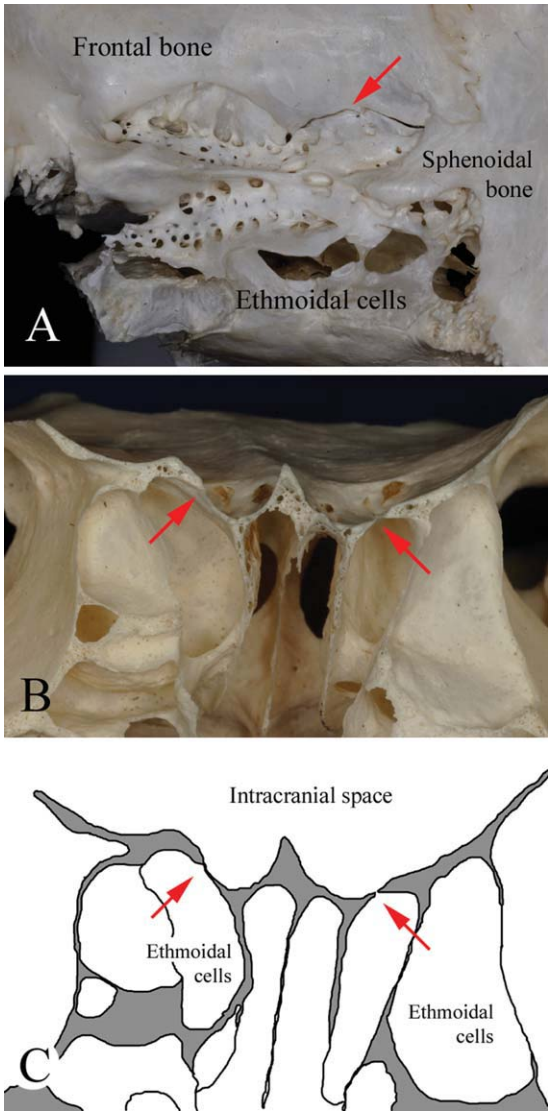

Fig. 2. The developmental border (arrow) between the frontal bone and the ethmoidal cells in adults is still well visible. After removal of the left frontal bone, the ethmoidal cells become uncovered lateral to the cribriform area. (A) Superior view. The optimal view of the border between the frontal bone and the ethmoidal cells is seen in the frontal plane. (B, C) Frontal section, anterior view. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

after several attempted repairs and meningitis at other institutions. Preoperative localization of the fistula in a large lateral recess of the sphenoid by contrast CT cisternogram helped to plan and conduct a successful repair.

Anatomical Specimens

The cribriform plate continues laterally with a thin bony plate, the lateral lamina, which is also part of the ethmoidal bone. More laterally there is a characteristic bony fissure along the free edge of the lateral lamina, which is the developmental border between the ethmoidal and frontal bones (Fig. 2). Although almost all the developmental borders between the neighboring anlagen disappear in the first postnatal years, this border is well visible in adults as well. It seems to be a normal feature of this region. In our specimens the border between the lateral lamina and the frontal bone were always visible irrespective of the age of the anatomic specimens. In many cases the frontal bone has a characteristic triangle-shaped process, which can be found just above the middle ethmoidal fovea. The lateral lamina is larger anterior to this process, and our clinical cases affecting the cribriform plate had bony defects only in this area.

In a three-year-old child there is yet no sign of pneumatization in the body of the sphenoid bone (Fig. 3), but all parts of the sphenoid bone are well developed. The pterygoid canal and the foramen rotundum have the same size and localization as in adults. Pneumatization of the sphenoid bone begins with an air-filled cell, which continuously enlarges to form the sphenoid sinus. The sinus enlarges not only anteroposteriorly but also laterally. According to the degree of pneumatization of the sphenoid sinus in the coronal plane, we were able to distinguish three different types. In normal pneumatization the sinus is shallow (grade I) (i.e., the most lateral part of the sinus extends as far as the foramen rotundum and the pterygoid canal) (Fig. 3B). In more pronounced pneumatization of the sphenoid sinus (grade II), the mucous membrane of the sinus enters the space between the foramen rotundum and the pterygoid canal. If the sphenoid bone shows an extended pneumatization (grade III), a pouch called the lateral recess of the sphenoid sinus develops (Fig. 3). The distance between the foramen rotundum and the pterygoid canal is normally more than 3 mm. In spite of hyperpneumatization, when the foramen rotundum and the pterygoid canal are positioned close to each other, there is no possibility for a lateral extension of the sphenoid sinus (Fig. 3C). We could not find lateral extension of the sphenoid sinus either above the foramen rotundum or below the pterygoid canal.

DISCUSSION

The localization of spontaneous CSF leaks in our clinical cohort was similar to previous reports in the literature; however there is growing evidence that increased intracranial pressure is the major culprit for development of spontaneous CSF leaks.[13–15] Refined monitoring techniques help to identify this group of patients, which previously were classified as idiopathic. Although failure rates of the initial closure are reported in approximately 10% of the patients, only a few authors consider multiple synchronous or subsequent leaks as a cause of failure in closing spontaneous CSF leaks. Identifying patients with increased intracranial, intermittent, or permanent hypertension is the primary goal for adequate treatment; however, knowledge of the embryologic basics of skull base development requires similar attention.[8,17]

The likelihood of developing spontaneous CSF leaks in predestinated areas depends on the completeness of fusion of the various anlagen and last but not least on pneumatization of the sinuses. Especially for the sphenoid sinuses, we were able to describe three types of pneumatization patterns that were related to the

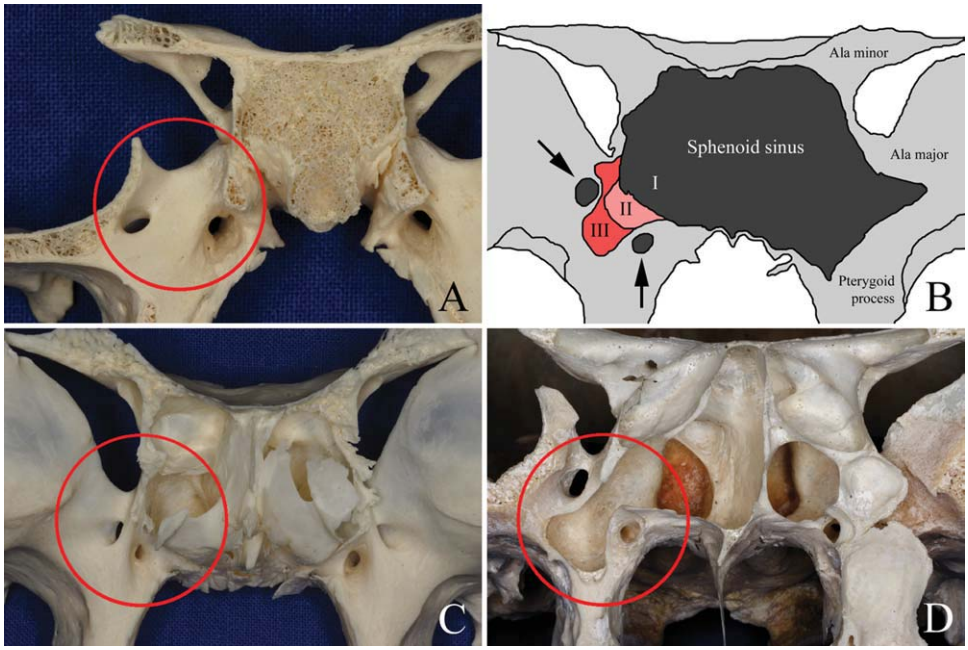

Fig. 3. Sections of the sphenoid bone in the frontal plane in a 2-year-old child (A) and in adults (B–D). (A) In the first postnatal years there is a sign of pneumatization within the body of the sphenoid bone, but the foramen rotundum and the pterygoid canal have already become well developed. (B) Depending on the pneumatization, the sphenoid sinus in adults can be larger or smaller laterally presenting in grade I–III. (C) If the foramen rotundum and the pterygoid canal are positioned near each other, the lateral border of the sinus is bordered with these foramina. (D) In the case of a laterally widely extended sphenoid sinus, there is a relatively large distance between the two foramina. Oblique arrow = foramen rotundum; vertical arrow = pterygoid canal. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

distance from the foramen rotundum to the pterygoid canal. After development of the bony canal around the maxillary nerve (foramen rotundum), and around the greater superficial petrosal nerve and the deep petrosal nerve together (pterygoid canal), the relative distance between the nerves remains essentially unchanged. So the development of the lateral recess of the sphenoid sinus is partially predefined during embryologic life.

In patients with type 3 pneumatization of the sphenoid sinus with a large lateral recess, CSF fistulas seem to be confined to this area, at least in our cohort. As far as leaks in the region of the fovea ethmoidalis, the middle fovea seems to be the most frequent site with the possible occurrence of further leaks in the anterior fovea. The posterior fovea seems to be less likely to develop defects. Although almost all of the developmental borders of neighboring anlagen disappear in the first postnatal years, this border between the lateral lamina and the frontal bone was always visible in our specimens and clinically relevant in our patients. The lateral lamina was larger anterior to this bony process and led to isolated fistulas of the cribriform plate in our patients.

When faced with the problem of localizing spontaneous CSF fistulas, knowledge of the embryologic development of the skull base is helpful when evaluating imaging findings, especially the degree of pneumatization of the sphenoid sinus. This knowledge is helpful to direct attention to predestinated areas and to consider the possibility of multiple leaks. In cases of extensive lateral pneumatization of the sphenoid sinus, focus on this localization should be placed even before contrast media or fluorescein are used prior to surgery so that the occurrence of further leaks in other localizations is unlikely.[18]

CONCLUSION

Based on our study, the most frequent localization of spontaneous CSF fistulas are the lateral recess of the sphenoid sinus and the anterior and middle fovea ethmoidalis. The likelihood of developing spontaneous CSF leaks in predestinated areas depends on completeness of the fusion of the various anlagen, and last but not least on pneumatization of the sinuses.

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