

Nipple Discharge



BBSG – Brazilian Breast Study Group

Definition and Epidemiology

Nipple discharge is a drainage of intraductal fluid through the nipple outside puerperal pregnant cycle. It's responsible for almost 5–10% of breast complaints in out patient clinic. Milk secretion is called galactorrhea and non-milk secretion is called telorrhea.

Between 60% and 80% of women will have papillary flow throughout their life, more common during menacme, but when it is present in elderly patients, the probability of neoplastic origin increases. About 90–95% of cases have benign origin.

Pathophysiology

It can be caused by factors that are specific to the mammary gland, both intraductal and extraductal, or by extramammary factors related to the control of milk production (Tables 1 and 2).

1. Intraductal: inherent to the inner wall of the duct
 - Epithelial proliferations (papillomas, adenomas, hyperplasia, etc.)
 - Intraductal infections (galactophoritis)
 - Intraductal neoplasm with necrosis
2. Extraductal: pathologies that can partially disrupt the intra ductal epithelium and cause nipple discharge
 - Malignant neoplasms
 - Infections
 - Other pathologies

BBSG – Brazilian Breast Study Group (✉)
BBSG, Sao Paulo, SP, Brazil

Table 1 Main medicines associated to galactorrhea

Pharmacological class	Medicines
Hormones	Estrogens, oral contraceptives, thyroid hormones
Psychotropic	Risperidone, clomipramine, nortriptyline, serotonin reuptake inhibitors, phenothiazine, tricyclic antidepressants, opioids, codeine, heroin, cocaine, sulpiride
Antiemetic	Metoclopramide, domperidone
Anti-hypertensive	Verapamil, methyldopa, reserpine
H2 blockers	Cimetidine, ranitidine, omeprazole

Table 2 Pathologies that may cause an increase in prolactin

Origin	Pathology
Lesions in NCS	Prolactinomas, acromegaly, craniopharyngioma, encephalitis, pituitary tumor, surgical transection, pituitary trauma
Lesions in thoracic wall	Herpes zoster neuritis, thoracotomy, mastectomy, burns, dermatitis, and traumatism
Systemic diseases	Chronic renal failure, Addison's disease, Cushing's disease, adrenal hyperplasia, primary hypothyroidism, diabetes, liver disease
Ectopic production	Bronchogenic carcinoma, hypernephroma
Varied causes	Anovulation, coitus, dilatation and curettage, breast stimulation, hysterectomy, IUD, pseudocystitis, neck surgeries

- Galactorrhea: caused by non-mammary factors, usually by changes that cause hyperprolactinemia. Some patients, however, may present galactorrhea without increasing prolactin levels. The most common cause of increased prolactin levels is the use of dopamine suppressive drugs.

Diagnosis

Anamnesis

In routine gynecological anamnesis, the physician should seek information on family history, use of hormone therapy, use of medications, excessive manipulation of the papilla or trauma, and age, in addition to other signs or symptoms of breast and secretion characteristics. It is also advisable to define the characteristics of the papillary flow, which can indeed determine what should be investigated:

- Laterality (unilateral or bilateral)
- Number of orifices (single or multiple)
- Uprising (spontaneous or provoked to expression)
- Macroscopic aspect (milky; purulent; multicolored, greenish, brown, or yellowish; viscous; crystalline; serous; hemorrhagic)

Physical Examination

At inspection, is important confirm the date of anamnesis and aspects of fluid discharge. Palpation should be oriented in order to promote secretion and establish the location or mammary segment that is causing the effusion (“trigger point”).

The characteristics of the flow that present suspicions to the physical examination are:

- Unilateral
- Spontaneous
- Single ductal
- Hemorrhagic, serohemorrhagic, crystalline, serous
- Presence of associated tumor
- Elderly patients
- Male

Differences in the Effusion Aspect

- Serous (fibrocystic mastopathy, cancer, papilloma, papillomatosis)
- Crystalline (papilloma, papillomatosis, cancer)
- Multicolor (ductal ectasia)
- Viscous (comedomastitis)
- Purulent (galactophoritis)
- Serohemorrhagic, hemorrhagic (papilloma, cancer)

Cytology

There is no benefit in the cytology of this test, since the sensitivity assessed in several studies was very low, ranging from 6% to 17%.

Mammography and Ultrasonography

They have low sensitivity in the diagnosis of the alterations, but their accomplishment is mandatory to evaluate possible concomitant lesions. The sensitivity and specificity of mammography in cancer or high-risk lesions are 10% and 94–100%, respectively.

Ultrasonography can detect some intraductal lesions, such as ductal ectasia, papilloma, and abscesses, in addition to guiding possible percutaneous biopsies.

Magnetic Resonance Imaging

In recent years there has been a progressive increase in the use of magnetic resonance imaging in the papillary flow propaedeutics: despite having a relevant role in the differentiation of benign and malignant lesions, the false-positive rates and the limitation of biopsies make it difficult to perform this exam.

Ductography or Galactography

It consists of catheterization of the duct and water-soluble contrast injection, with sequential mammograms to evaluate the ductal tree and to observe filling or blocking faults. It may be useful in peripheral lesions, but have little applicability due to the discomfort the technique produces, to be unspecific and, mainly due to the advent and evolution of the ultrasound technique, especially when performed by experienced professionals.

Ductoscopy

Is micro endoscope fiber optic, inserted into the duct that allows visualization, biopsy and citologica analysis. with high predictive positive value, but with low sensitivity and painful. This technique is widely used in Japan and China, and there is also a classification system based on the appearance of the lesions, developed by the Japanese Association of Breast Ductoscopy, with reports of experience in other countries. Still, a learning curve and special care handling it are required, and there are no scientific reports of experience in Brazil.

Ductal Lavage

This technique was very promising in the beginning; however, it presents the same drawbacks of the cytological evaluation of the flow; in addition, a benign result does not detract from the continuation of the investigation and positivity does not determine the location of the disease.

Differential Diagnosis

Situations that cause an exudate on the papillary surface, that is, a false effusion are as follows (Figs. 1 and 2):

- Papillary inversion
- Eczematous lesions

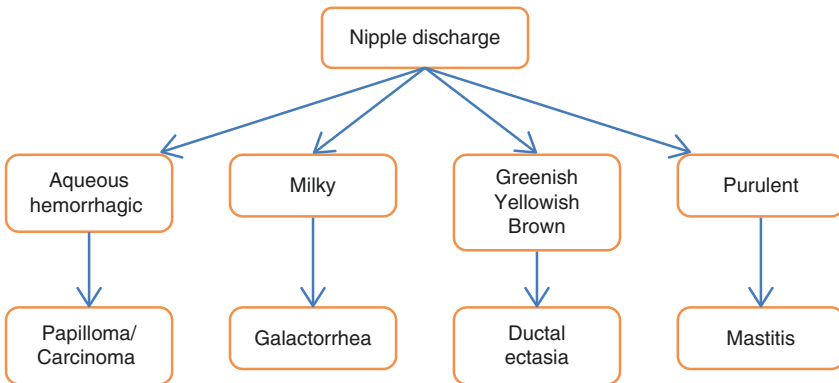


Fig. 1 Flowchart of the characteristics of effusion and possible diagnoses

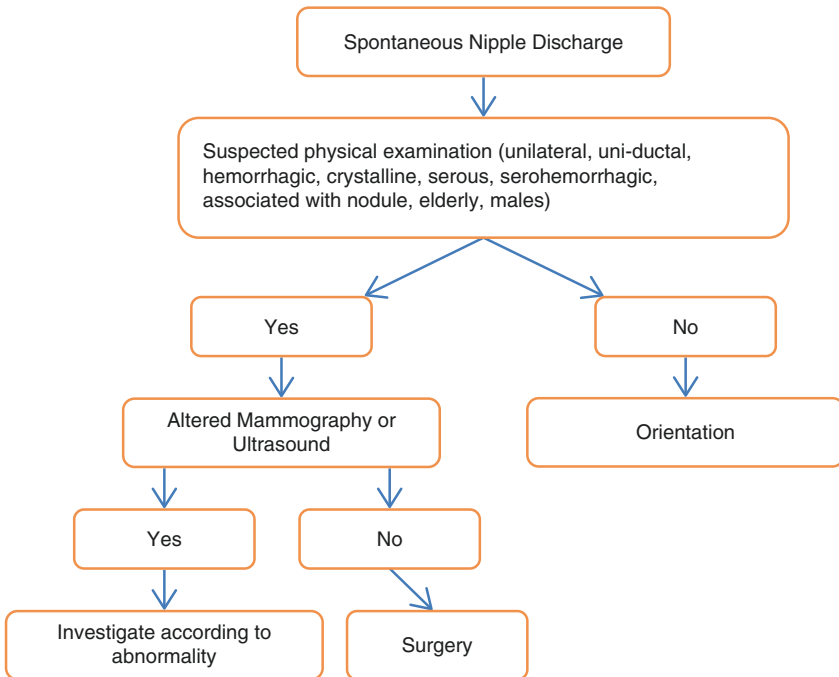


Fig. 2 Flowchart of management of spontaneous papillary effusion

- Traumatic injuries
- Herpes simplex
- Infections
- Ductal fistulas
- Recurrent chronic subareolar abscess

Only excision can provide a definitive histological diagnosis, and it remains the gold standard in suspicious lesions.

Treatment

It will depend on the characteristics of the flow. Most will only need guidance and reassurance, the purulent are treated with antibiotic therapy, and the suspect ones are operated.

Some patients with unsuspected flow (multidrug, bilateral) may require surgery because of the excessive discomfort caused by the continuous effusion.

In the patient who still wants to breastfeed, a selective resection of the affected duct is performed, guided by the “trigger point,” while in women without breastfeeding or postmenopausal desire, selective resection can be replaced by resection of the main ducts. The intraoperative examination has little value in the diagnosis of papillary lesions.

The main anatomopathological findings of patients submitted to surgery due to papillary flow are:

- Papilloma: this is the most common cause of hyaline, serohematic, or bloody secretion. It usually affects the subareolar main ducts, with a diameter varying from a few millimeters to 4.0 cm, a soft and friable consistency, being present in about 35–50% of the operated cases. In the absence of evident lesion on clinical examination or imaging methods, papilloma is the most frequent cause of pathological papillary effusion in more than 95% of patients;
- Ductal ectasia: loss of elastin from the ductal walls and chronic inflammatory infiltration, being evidenced in 15–30% of the operated cases;
- Carcinoma: confirmed in around 5–20% of the operated cases. When there is suspected palpable lesion, or visible by imaging methods, the presence of bleeding effusion is almost pathognomonic of malignant neoplasm.

Recommended Reading

1. Alcock C, Layer GT. Predicting occult malignancy in nipple discharge. *ANZ J Surg.* 2010;80(9):646–9. *It corroborates with most of the published studies that the gold standard diagnosis-treatment for suspected papillary flow is microductectomy.*

2. Liu M, Guo G, Xie F, et al. Mammary ductoscopy and follow-up avoid unnecessary duct excision in patients with pathologic nipple discharge. *J Surg Oncol.* 2015;112(2):139–43. *It shows that ductoscopy, in specialized services, is an excellent diagnostic method for suspicious papillary flow.*
3. Sanders LM, Daigle M. The rightful role of MRI after negative conventional imaging in the management of bloody nipple discharge. *Breast J.* 2016;22(2):209–12. *In patients with suspected papillary flow and conventional negative tests (mammography and ultrasonography), magnetic resonance imaging is indicated by high negative predictive value.*
4. Simmons R, Adamovich T, Brennan M, et al. Nonsurgical evaluation of pathologic nipple discharge. *Ann Surg Oncol.* 2003;10(2):113–6. *Cytological evaluation of 108 patients with suspicious papillary flow, showing low specificity. It concludes that it should not be part of the diagnostic arsenal.*
5. Wong Chung JE, Jeurieus-van de Ven SA, van Helmond N, et al. Does nipple discharge color predict (pre-) malignant breast pathology? *Breast J.* 2016;22(2):202–8. *Evaluation of 184 patients with unilateral and uniductal papillary flow with bloody appearance. Twenty cases of carcinoma and twenty-one cases of atypical lesions were found. It was concluded that the presence of blood secretion should guide the surgical investigation.*