

# Intraoperative Identification of Lacrimal Sac by Means of Methylene Blue

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*Methylene blue (MB) has many uses in medicine, being applied as a treatment for infections, malaria, methemoglobinemia, as a dye for diagnosis and for staining of cells, tissues and bacteria. In elderly patients with associated high anaesthetic risk, dacryocystectomy is an alternative to dacryocystorhinostomy. This is an observational clinical study for two cases of chronic dacryocystitis where dacryocystectomy combined with MB (1%) staining of lacrimal sac was performed. Case no.1 - an 81-year old female patient with arterial hypertension, atherosclerosis, pulmonary fibrosis, and lower limb varices complained of recurrent epiphora, muco-purulent secretions in both eyes, inflammatory oedema of the left perisacular region for the past 6 months. Case no. 2 - a 74-year old female patient with hypothyroidism suffered from chronic epiphora in the left eye with a purple-red oedema of the inferior eyelid and perisacular region. Symptoms reoccurred in the last 10 months despite topical and systemic therapy with antibiotics and anti-inflammatory drugs. Dacryocystectomy was performed under local anaesthesia in both patients. MB (1%) was used to irrigate the lacrimal sac in order to facilitate its localisation, dissection and excision. Results: Case no.1. Ectopic lacrimal sac. Case no.2. Enlarged lacrimal sac (7.5/14 mm). The histopathological examination revealed a trachomatous dacryocystitis, respectively a chronic non-suppurative non-granulomatous dacryocystitis. Their postoperative evolution was without complications, except for a mild epiphora. In conclusion, dacryocystectomy appears to be a less traumatising alternative to dacryocystorhinostomy. The staining of the lacrimal sac with MB (1%) in dacryocystectomy facilitates its identification and dissection, especially when it is ectopic.*

**Keywords:** dacryocystitis, methylene blue, lacrimal sac, dacryocystectomy

MB was synthesised for the first time in 1876 by Heinrich Caro at Badische Anilin and Sado Fabrik (BASF), being used in textile dyeing [1-3], then 15 years later it was the first antiseptic introduced in clinical cure of malaria [1]. MB is now used in a large variety of dyes for multiple purposes and in medicine for a number of therapeutic and diagnostic procedures [2,4-10].

MB occurs in the form of several different hydrates but not as trihydrate [11]. The structural and molecular formulae of MB is  $C_{16}H_{18}ClN_3S$  [12] (fig.1). MB is synthesized commercially by oxidation of N,N-dimethyl phenylenediamine with sodium dichromate ( $Na_2Cu_2O_7$ ) in the presence of sodium thiosulfate ( $Na_2S_2O_3$ ) followed by further oxidation in the presence of N,N - dimethylaniline [13].

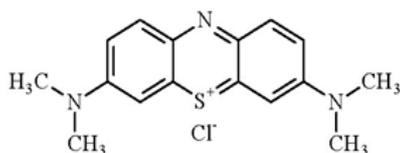


Fig.1.  $C_{16}H_{18}ClN_3S$ . Relative molecular mass (anhydrous form): 319.85. [12]

MB is used clinically in a wide range of indications, including the emergency treatment of methaemoglobinemia, ifosfamid-induced encephalopathy or poisoning by cyanide, nitrate or carbon monoxide, and for intraoperative tissue staining [2,14].

The dacryocystectomy is an oculoplastic surgery representing the complete extirpation of the lacrimal sac [15] and was described for the first time in 1724 by the English ophthalmologist John Thomas Woolhouse [16] and was considered a standard before the introduction of the dacryocystorhinostomy by the Italian Addeo Toti at the beginning of the 20<sup>th</sup> century for the treatment of dacryocystitis and lacrimal fistulae [17]. Nowadays dacryocystectomy is rarely used, having indication in some lacrimal sac malignant tumors [18].

This article presents two cases of dacryocystectomy where we used the technique of lacrimal sac staining by MB (1%) and we highlight the importance of this surgical procedure in elderly patients.

## Experimental part

### Material and methods

Clinical case no.1. An 81-year old female patient was admitted into the 2<sup>nd</sup> Ophthalmology Clinic from Iasi,

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complaining of recurrent epiphora, muco-purulent discharge in both eyes and inflammatory oedema of the skin surrounding the lacrimal sac in the left eye for the past six months. The patient is known with arterial hypertension, atherosclerosis, pulmonary fibrosis and lower limb varices.

Clinical case no.2. A 74 year old female patient with hypothyroidism was hospitalized in the 2<sup>nd</sup> Ophthalmology Clinic, because she presented chronic epiphora, lower eyelid and perisacular (purple-red) oedema of the left eye, which developed in the last ten months.

In both cases, patients were treated prior surgery with local and general large spectrum antibiotics and with steroidal and non-steroidal anti-inflammatory drugs. The symptoms remitted partially after the treatment, but reoccurred later. In the first patient, a high anaesthetic risk was taken into consideration, while the second patient refused the dacryocystorhinostomy, after this procedure was explained to her. In these circumstances, dacryocystectomy under local anaesthesia was performed in both patients. The inferior lacrimal punctum was dilated by a punctum dilator. One mL of MB (1%) was flushed in the lacrimal sac using a cannula through the inferior lacrimal punctum (fig.2 a). Skin and subcutaneous tissue were incised until the reflected tendon of the medial palpebral ligament (1.5 cm) parallel to nose angle. The lacrimal sac stained by MB was easily identified, dissected from the bone wall of its fossa and sectioned at the isthmus level (fig.2 b). The wound was closed in layers with an interrupted absorbable 6.0 suture, antibiotic was applied, and bandage. Resection specimens were sent to the Pathology Laboratory for histopathological examination.

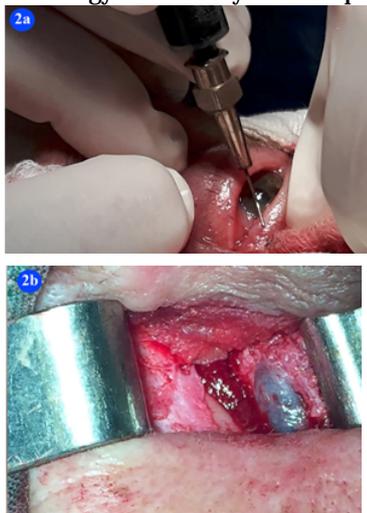


Fig.2. Photographies of our oculoplastic surgery. (a) MB (1%) was flushed in the lacrimal sac through the inferior lacrimal punctum. (b) Easy identification of the blue lacrimal sac during dacryocystectomy

## Results and discussions

During surgery, it was noticed that the lacrimal sac was located below the medial palpebral ligament in the first patient. In the second patient the lacrimal sac had large dimensions (7.5/14 mm). Histopathological examination of the slides from the first case revealed the hyperplasia of the lacrimal sac epithelium, lymphoid follicles in the sac wall, and lymphocytic infiltration along with capillary hyperaemia below the epithelium. All these aspects were suggestive for trachomatous dacryocystitis (fig. 3 a).

The microscopical exam of the slides from the second case showed polypoidal growth of the sac wall due to lympho-plasmocytic inflammation and hyperemia of the newly formed vessels located in the sub-mucosa; lacrimal sac epithelium was denuded in some parts and presented true stratification but with very few goblet cells in some other areas. All these histopathological features concluded the case to be a chronic non-suppurative non-granulomatous dacryocystitis (fig. 3 b).

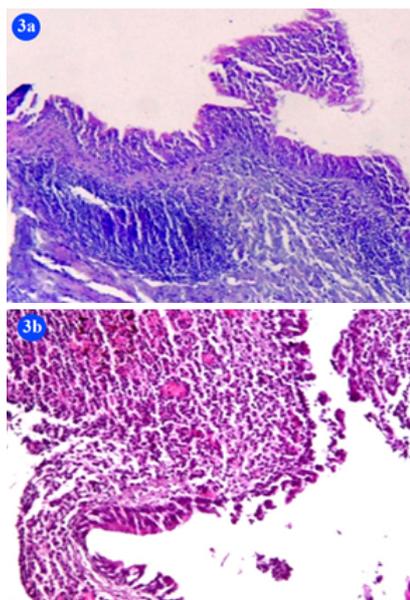


Fig.3. Microphotography of the histological specimens.(a) Case no.1. Chronic follicular dacryocystitis (Hematoxylin - Eosin staining, x 200 original magnification). (b) Case no.2. Chronic non-suppurative non-granulomatous dacryocystitis (Hematoxylin - Eosin staining, x 200 original magnification)

After surgery, the patients did not present complications during routine follow-up, except for a mild epiphora, with no further complaints.

MB is a compound consisting of dark green crystals or crystalline powder, having a bronze-like luster. Solutions in water or alcohol have a deep blue color [19].

The interest for MB in different therapies is due to its relatively low toxicity and its pharmacokinetic properties (the oral absorption is reported to be 53%-97% with plasma peak concentrations after 30-60 min) [20]; but the most important aspect is its low price [21]. About 65-85% of MB is reduced in erythrocytes and peripheral tissues to the leucoMB form [20]. MB and leucoMB are predominantly excreted in urine, but also in bile and faeces [22,23].

Recently, the clinical studies show that MB may have beneficial effects regarding cognitive performances of patients suffering from Alzheimer Disease [24-27].

MB proved its neuroprotective effect, preventing morphologic retinal damage in experimental optic neuropathy induced by mitochondrial dysfunction on a mouse model *in vivo*, which had only one intravitreal dose of rotenone injected [28,29].

Other clinical uses are as a treatment for refractory distributive shock - it inhibits the downstream effect of the nitric oxide [30]; as a treatment for the vasoplegic syndrome in cardiac surgery [31], in dermatology and oncology - in photodynamic therapy as photosensitizer together with iodide laser in order to induce mitochondria release tumoral cell apoptosis [32,33].

It has been used in surgery for precise dissection of anatomical structures [34] and intraoperative marking of the sentinel ganglion in breast cancer [35,36]. MB has tattooing the injected area as a secondary effect and has a risk of 0.6% of anaphylaxis, but the complications have not been reported and are not completely documented [35].

Clinical and experimental studies are not very clear regarding the dose of MB that has secondary effects, but the literature mentions that a dose higher than 7 mg/kg body weight may be associated with paradoxical inducing severe methemoglobinemia and effects on pulmonary function [37,38]. MB rarely causes dyspnea, tremor, vomiting, blue discoloration of body fluids and acute hemolytic anemia with high doses [39]. A higher dose than 7 mg/kg body weight lead to serotonin syndrome [40-42]. The ideal dose is unknown, but in the literature is recommended a dose of 1-2 mg/kg body weight as a single bolus [30,43,44].

In surgery it is used for the precise dissection of anatomical structures [34], endoscopic polypectomy [45],

chromoendoscopy [46,47] and intraoperative staining of sentinel lymph node in early breast cancer [35].

In the two clinical cases of chronic dacryocystitis presented in this article we used the technique of lacrimal sac staining by MB (1%). In both cases the blue-coloured lacrimal sac was easy to identify during dacryocystectomy.

The patients did not present any systemic complications during dacryocystectomy. In both cases, during the irrigation of the lacrimal sac with MB (1%), the regurgitation of dye was flushed with saline solution, without any staining of the bulbar conjunctiva or cornea.

Postoperatively, the patients did not show any complications during follow-ups, but a mild epiphora was objectified, without other complaints. However, secondary epiphora can work a positive effect in elderly patients with dry-eye syndrome.

Giuliano et al. (1994) [46] describe the successful use of MB during the peritumoral injection for lymphatic mapping in patients with breast cancer. In a clinical study, Vuthalurur et al. (2013) [35] on 16 patients diagnosed with advanced malignant eyelid tumours, the authors used without any systemic complications MB to stain the sentinel lymphatic ganglion. In a retrospective study comprising 35 patients, Dorafshar et al. (2010) [48] reported MB use by topic instillation in wounds to facilitate precise surgical debridement and differentiate viable from non-viable tissue. In their retrospective study of 134 patients, Ranjan and Kumar (2016) [49] used MB to irrigate the lacrimal sac during dacryocystorhinostomy.

Therefore, MB is used in medicine in the clinical and experimental therapy, and in surgery because of its low toxicity, pharmacokinetic properties [2, 3, 7] and cost-effectiveness [3, 21].

## Conclusions

Dacryocystectomy appears to be a less traumatizing alternative to dacryocystorhinostomy. The staining of the lacrimal sac with MB (1%) in dacryocystectomy simplifies the identification and dissection of the lacrimal sac, particularly in an ectopic position. Due to a lower surgical risk associated with local anaesthesia, this technique could be suitable for elderly multimorbid patients.

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