

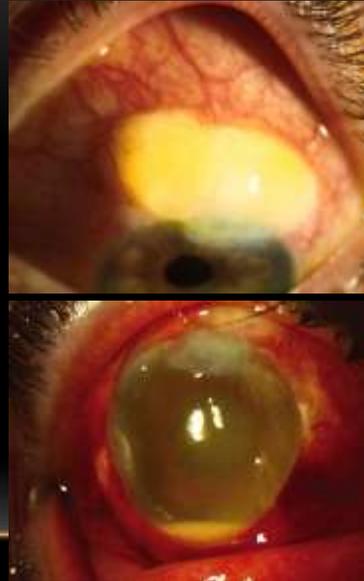
## BLEB ASSOCIATED ENDOPHTHALMITIS

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Trabeculectomy with antimetabolites is the most commonly performed surgery worldwide for glaucoma patients with progressive optic nerve head injury and visual field loss despite maximum pharmacologic intraocular pressure lowering therapy.



Bleb-associated infections remain one of the most feared early and long-term complications of trabeculectomy surgery because of their poor prognosis and variable response to antimicrobial therapy.



## INCIDENCE

The incidence of BAI varies among different studies according to

- The study design
- Follow-up period
- Surgical technique (fornix based Vs limbal based, use of antimetabolites)
- Statistical methods

## INCIDENCE

### INCREASED WITH USE ANTIMETABOLITES

- Before the use of antimetabolites with trabeculectomy the rate of BAI was between 0.2 and 1.5%.
- The incidence of BAI for 5-FU treated eyes with a follow-up of 12 years is between 1.9 and 13.0%.
- Incidence ranges from 1.5% to 13.8% in cases utilizing MMC over 16 months to 8 years of follow up.

Solomon A, Ticho U, Frucht-Pery J. Late-onset, bleb-associated endophthalmitis following glaucoma filtering surgery with or without antifibrotic agents. *J Ocul Pharmacol Ther.* 1999;15(4):283e93

Uchida S, Suzuki Y, Araie M, et al. Long-term follow-up of initial 5-fluorouracil trabeculectomy in primary open-angle glaucoma in Japanese patients. *J Glaucoma.* 2001;10(6):458e65

Shigeeda T, Tomidokoro A, Chen YN, et al. Long-term follow-up of initial trabeculectomy with mitomycin C for primary open-angle glaucoma in Japanese patients. *J Glaucoma.* 2006;15(3):195e9

## INCIDENCE

- However, there is cumulative evidence that the incidence of BAI has reduced over time.
- The Collaborative Initial Glaucoma Treatment Study found a 5-year risk of **blebitis** and **bleb-associated endophthalmitis** (BAE) of 1.5 and 1.1%, respectively

Zahid S, Musch DC, Niziol LM, Lichter PR. Risk of endophthalmitis and other long-term complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol.* 2013;155(4):674e80, 680.e1.

## PRESENTING SYMPTOMS AND SIGNS

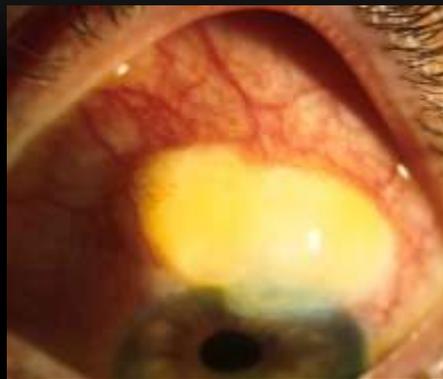
Bleb Associated Infection (BAI) may present with nonspecific symptoms and clinical findings that mimic a viral or bacterial conjunctivitis. So it needs high suspicion from the clinician

- Conjunctival hyperemia, discharge,
- foreign body sensation, irritation, pain
- lid swelling
- VA in the early stages may be normal or minimally effected
- Development of AC inflammation
- Corneal edema
- Vitreous involvement results in a progressive decline in VA.

## CLASSIFICATION OF BAI

- **Stage I (blebitis):**

Milky fluid within the bleb, conjunctival congestion, absence of cells in the anterior chamber, no or minimal visual impairment.



Yamamoto T. Bleb-related infection: clinical features and management. *Taiwan J Ophthalmol.* 2012;2(1):2e5

Yamamoto T, Kuwayama Y. Interim clinical outcomes in the collaborative bleb-related infection incidence and treatment study. *Ophthalmology.* 2011;118(3):453e8

## CLASSIFICATION OF BAI

- **Stage II (aqueousitis):**

Stage I, plus cells and flare in the anterior chamber, absence of cells in the anterior vitreous of the phakic, and rare cells in the aphakic or pseudophakic, eye.



Yamamoto T. Bleb-related infection: clinical features and management. *Taiwan J Ophthalmol.* 2012;2(1):2e5  
 Yamamoto T, Kuwayama Y. Interim clinical outcomes in the collaborative bleb-related infection incidence and treatment study. *Ophthalmology.* 2011;118(3):453e8

## CLASSIFICATION OF BAI

- **Stage III (vitritis):** stage II, plus cells in the anterior vitreous

A- fundus details are visible

B- fundus details are not visible



Yamamoto T. Bleb-related infection: clinical features and management. *Taiwan J Ophthalmol.* 2012;2(1):2e5  
 Yamamoto T, Kuwayama Y. Interim clinical outcomes in the collaborative bleb-related infection incidence and treatment study. *Ophthalmology.* 2011;118(3):453e8

## OCULAR RISK FACTORS

- **Bleb location:** Inferior Vs superior bleb
- **Conjunctival incision:** (Fornix based > limbal based)
- **Antifibrotic agents:** 5FU, MMC
- **Bleb leakage:**
- **Bleb manipulation:** massaging, releasable sutures, needling, autologous blood injection
- **Contact lens and punctal plug**

## OCULAR RISK FACTORS

- **Prophylactic antibiotic use:**
  - long-term topical antibiotic use did not eliminate the risk of BAI
  - The risk ratios for BAI in patients who were receiving episodic and continuous topical antibiotics were **2.13** and **9.07**, respectively.
  - Conjunctival swabs showing Staph-epidermidis resistant to Levofloxacin in **66%** in eyes using continuous prophylactic antibiotics Vs only **25%** in other eyes

## OCULAR RISK FACTORS

- **Blepharoconjunctivitis**
- **Intravitreal injections** (antivascular endothelial growth factor, steroids)
- **Lens status:** aphakia, pseudophakia, and absence of post capsule were statistically more associated with vitritis (stage III)
- **Trabeculectomy versus combined phacoemulsification and trabeculectomy:**
- **Hypotony:** The risk for developing an infection is increased by 50% for every 3 mm Hg decrease in IOP

## SYSTEMIC RISK FACTORS

- DM
- Age

## DIAGNOSTIC WORK UP AQUEOUS AND VITREOUS SAMPLES

- **Stain**

Gram stain is positive in approximately 45% of endophthalmitis cases.

- **Culture**

blood, chocolate, and Sabouraud's dextrose agar, anaerobic media, and thioglycolate broth.

Vitreous culture has a higher positive culture yield than aqueous humor.

The rate of positive culture in vitrectomy samples (90%) is greater than with vitreous tap (75%)

Six of 7 culture-negative cases of BAE in a study were later confirmed to be *Moraxella* species by polymerase chain reaction (PCR) analysis of aqueous humor samples

## DIAGNOSTIC WORK UP AQUEOUS AND VITREOUS SAMPLES

- **PCR**

- PCR requires only a small sample (10-50 mL)
- diagnosis can be made quickly (real-time PCR takes 60 minutes)
- PCR identifies the presence of bacteria with sensitivities ranging from 66% to 95%, compared with 34%-% for cultures
- Six of 7 culture-negative cases of BAE in a study were later confirmed to be *Moraxella* species by polymerase chain reaction (PCR) analysis of aqueous humor samples

## DIAGNOSTIC WORK UP AQUEOUS AND VITREOUS SAMPLES

### PCR

- Each organism or class of organisms under consideration must be ordered individually and requires its own portion of sample of 10-50 mL.
- There is no commercially available kit that looks for the full spectrum of pathogens involved in BAI.
- The clinician's degree of suspicion and clinical expertise guides PCR requests for appropriate primers, tags, and targets for analysis.
- Testing with PCR may also amplify bacteria that are conjunctival contaminants and lead to false-positive results.
- Quantitative PCR allows the amount of pathogen in a sample to be measured, which helps to differentiate a bacterial contaminant from true infection

- CoNS are the most common cause of **early-onset BAE**, similar to cataract surgery

## LATE ONSET BAE

No of Cases	Years studied	Positive culture rate (%)	Streptococcus species (%)	Staphylococcus aureus (%)	Coagulase negative staphylococcus (%)	Haemophilus influenza (%)	Gram-negative organisms (%)	Microsp
36	1969-1984	83	57	7	8	34	6	
32	1985-1995	87	48	9	23	16	7	
49	1996-2001	80	41	30	15	2.5	13.5	
40	1996-2001	40	20	20	—	—	—	
71	1985-2007	44	50	8	14.6	16.7	—	
49	1987-1996	86	79	30.1	28	4.7	11.2	
68	1989-2001	59	26.5	3	13.2	—	14.7	
54	1996-2001	—	33	1.5	14.8	—	25	
31	2003-2010	31.1	3.8	—	25.1	—	7.2	
13	1991-1994	63.2	23.1	—	7.7	23.1	7.7	
33	1981-1985	34.3	27.7	—	27.7	5.5	20.3	
18		67	33	34.8	41.6	—	8.3	
6	1990-1993	83	40	—	20	—	—	
12	1984-1993	67	8	62.5	—	12.5	25	
85	1996-2009	63	25	—	11	—	18	
20	1993-1998	55	27.2	18.1	—	—	9	
71	1996-2008	83	30	12	28	—	28	
157	2005-2010	54.8	60	3.5	10.7	7.1	—	

(note: NEP, no light perception; —, not isolated; —, not commonly isolated organisms in lab-associated infection; not all isolated organisms in the studies and the percentages may do not add to 100% each row.

## TREATMENT

- No randomized controlled clinical trials have been conducted to determine the most effective method of treatment (medical vs surgical) or antibiotic regimen for BAI.
- To date, there have been no established or official guidelines for the treatment of BAI.
- Current opinions on optimal treatment for BAI rest on the data collected primarily from retrospective case series.

## TREATMENT

### STAGE I,II

#### Topical antibiotics

- Fortified amikacin or ceftazidime (G -ve)
- Fortified vancomycin (G +ve)
- Fluoroquinolone ( moxifloxacin)

Fortified topical antibiotics should be started every 5 minutes for 3 doses as a loading dose and then every 30-60 minutes.

The patient should be monitored closely, daily or twice a day to early detect any change in severity scale (increase in AC reaction or start vitreous reaction)

## TREATMENT

### STAGE I,II

#### Other topical treatment

- Cycloplegics
- CAI drugs: for the bleb leak which is found in 84% of BAI

## TREATMENT

### STAGE I,II

#### systemic antibiotics

- It has been suggested that oral antibiotics may prevent stage I and II BAI from becoming stage III
- Oral fluoroquinolones yield vitreous levels higher than in aqueous following topical administration alone.
- The most profound effect on the aqueous and vitreous concentration has been observed with combined topical and oral administration of fluoroquinolones, up to a 7-fold increase.

## TREATMENT

### STAGE I,II

#### Subconjunctival antibiotics

To increase the concentration of the antibiotics inside the eye, subconjunctival antibiotic injection may be considered. The relative efficacy of the subconjunctival antibiotics is unproven. Although, it may allow a higher concentration of antibiotic in the anterior chamber, the concentration in the vitreous cavity remains low

## TREATMENT

### STAGE I,II

- If no clinical improvement is observed over the following 24-48 hours (e.g., a decrease in the anterior chamber reaction and/or improvement in visual acuity) or inflammation is detected in the vitreous cavity at any time, surgical intervention (tap and inject or pars plana vitrectomy [PPV]) should be considered.

## TREATMENT

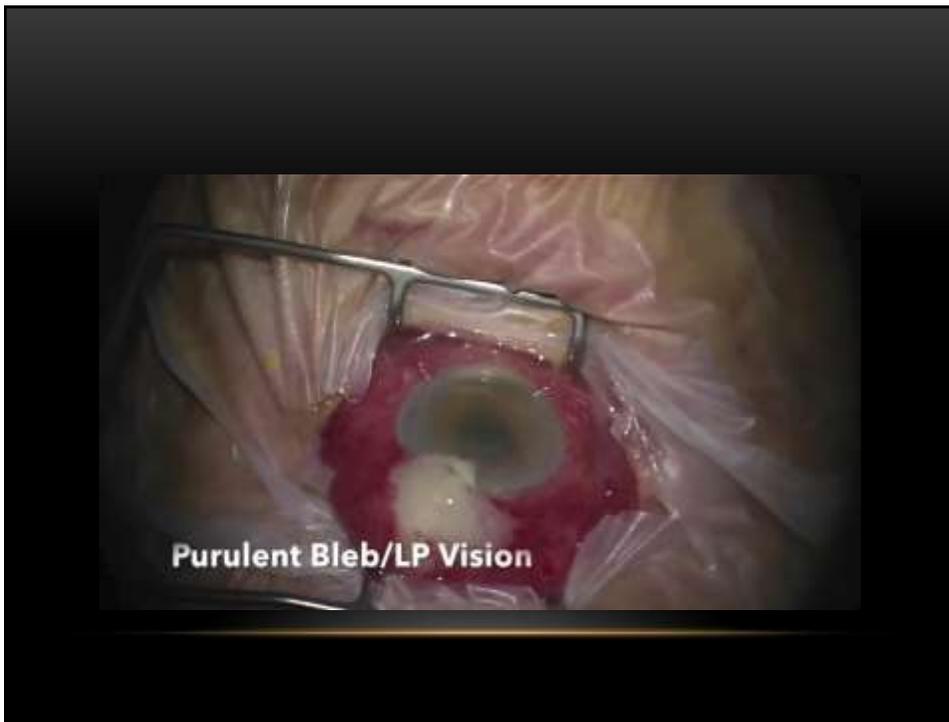
### STAGE III (BAE)

- Stage III treatment often requires surgical intervention: vitreous tap and inject or PPV.
- BAE patients treated with initial vitrectomy had better visual outcome and a lower incidence of no light perception vision than those treated with tap and inject

Al-Turki TA, Al-Shahwan S, Al-Mezaine HS, et al. Microbiology and visual outcome of bleb-associated endophthalmitis. *Ocul Immunol Inflamm.* 2010;18(2):121e6  
Busbee BG, Recchia FM, Kaiser R, et al. Bleb-associated endophthalmitis: clinical characteristics and visual outcomes. *Ophthalmology.* 2004;111(8):1495e503, discussion 1503.

## VITRECTOMY AND ITS MODIFICATIONS TO PRESERVE BLEB FUNCTION

- The preservation of their filtering bleb is critical for preventing further glaucomatous optic neuropathy.
- Reducing conjunctival manipulation when employing suture-less PPV, the lack of conjunctival sutures reduces risk of intraoperative subconjunctival hemorrhage and its extension into the bleb area, and decreased conjunctival inflammation further contributes to a decreased risk of bleb failure.



## INTRAVITREAL ANTIBIOTICS

- Combination intravitreal therapy effective against both gram-positive and gram-negative bacteria can be administered as an empirical treatment of BAE even before the culture results are available
- Vancomycin and ceftazidime cover gram-positive and gram-negative microorganisms, respectively.

## INTRAVITREAL ANTIBIOTICS

- Amikacin can be used instead of ceftazidime in beta lactam sensitive patients with cephalosporin cross reactivity.
- Although the ocular toxicity of intravitreal injection has not been well studied for most antibiotics, it is possible that toxicity may develop with repeated injections.

## FREQUENCY OF INTRAVITREAL ANTIBIOTICS

Antibiotic	Frequency of repeat intravitreal injection (hours)	Microorganism coverage	Advantages
Vancomycin	72	<ul style="list-style-type: none"> <li>- Gram-positive cocci</li> <li>- Methicillin-resistant Staphylococcus</li> <li>- Multidrug-resistant Staphylococcus epidermidis</li> <li>- Methicillin-resistant Staphylococcus aureus</li> </ul>	<ul style="list-style-type: none"> <li>- Low rate of resistance among commonly isolated organisms</li> </ul>
Ceftazidime	48-72	<ul style="list-style-type: none"> <li>- Aerobic gram-negative bacteria</li> <li>- Pseudomonas aeruginosa</li> </ul>	<ul style="list-style-type: none"> <li>- Low risk of retinal toxicity</li> <li>- Broad therapeutic index</li> </ul>
Amikacin	24-48	<ul style="list-style-type: none"> <li>- Aerobic gram-negative bacteria</li> <li>- Pseudomonas aeruginosa</li> </ul>	<ul style="list-style-type: none"> <li>- Synergistic effect with vancomycin</li> <li>- No precipitation</li> </ul>
Gentamicin	72-96	<ul style="list-style-type: none"> <li>- Aerobic gram-negative bacteria</li> </ul>	

## BLEB LEAKAGE DURING BAI

- No immediate surgical treatment is necessary for bleb leakage during BAI
- Bleb leaks associated with BAI usually do not produce hypotony or AC shallowing.
- In addition, some will seal once the inflammation and infection have resolved.
- If the bleb leak continues after controlling the infection, it can be addressed as a delayed onset bleb leakage.

## IOP CONTROL POST BAI

- In the Japan Glaucoma Society Survey of Bleb-related Infection
  - There was no change in the IOP in the eyes with stage I and II BAI
  - Stage III A and III B eye demonstrated a 2.7 mmHg and 6.6 mmHg IOP increase, respectively.
- The causes of IOP elevation include
  - formation of peripheral anterior synechiae at the sclerostomy.
  - dysfunction of the filtering bleb from episcleral scarring

Yamamoto T, Kuwayama Y, Nomura E, et al. Changes in visual acuity and intra-ocular pressure following bleb-related infection: the Japan Glaucoma Society Survey of Bleb-related Infection Report 2. Acta Ophthalmol. 2013;91(6):e420e6

# Thank U