

**Supplementary Table 1. List of causative bacteria and fungi**

| Bacteria                           | Fungi                           |
|------------------------------------|---------------------------------|
| <i>Acidovorax</i> sp               | <i>Acremonium</i> sp            |
| <i>Acinetobacter</i> sp            | <i>Alternaria alternata</i>     |
| <i>Bacillus</i> sp                 | <i>Alternaria tenuissima</i>    |
| <i>Chryseobacterium</i> sp         | <i>Alternaria</i> sp            |
| <i>Corynebacterium macrynleyi</i>  | <i>Aspergillus udagawae</i>     |
| <i>Corynebacterium</i> sp          | <i>Aspergillus fumigatus</i>    |
| <i>Cutibacterium acnes</i>         | <i>Aspergillus</i> sp           |
| <i>Cutibacterium</i> sp            | <i>Candida albicans</i>         |
| <i>Haemophilus influenzae</i>      | <i>Candida guilliermondi</i>    |
| <i>Micrococcus luteus</i>          | <i>Candida parapsilosis</i>     |
| <i>Micrococcus</i> sp              | <i>Cladosporium</i> sp          |
| <i>Moraxella catarrhalis</i>       | <i>Colletotrichum fruticola</i> |
| <i>Moraxella lacunata</i>          | <i>Curvularia</i> sp            |
| <i>Moraxella nonliquefaciens</i>   | <i>Fusarium solani</i>          |
| MRSA                               | <i>Fusarium</i> sp              |
| MRSE                               | <i>Lophotrichus</i> sp          |
| <i>Mycobacterium gordonae</i>      | <i>Nigrospora</i> sp            |
| <i>Mycobacterium</i> sp            | <i>Paecilomyces</i> sp          |
| <i>Neisseria</i> sp                | <i>Penicillium</i> sp           |
| <i>Nocardia</i> sp                 | <i>Pleosporales</i> sp          |
| <i>Proteus mirabilis</i>           | <i>Trichosporon</i> sp          |
| <i>Pseudomonas aeruginosa</i>      |                                 |
| <i>Pseudomonas stutzeri</i>        |                                 |
| <i>Serratia</i> sp                 |                                 |
| <i>Staphylococcus aureus</i>       |                                 |
| <i>Staphylococcus auricularis</i>  |                                 |
| <i>Staphylococcus capitis</i>      |                                 |
| <i>Staphylococcus epidermidis</i>  |                                 |
| <i>Staphylococcus haemolyticus</i> |                                 |
| <i>Staphylococcus hominis</i>      |                                 |
| <i>Staphylococcus intermedius</i>  |                                 |
| <i>Staphylococcus lugdunensis</i>  |                                 |
| <i>Staphylococcus</i> sp           |                                 |
| <i>Staphylococcus warneri</i>      |                                 |
| <i>Streptococcus dysgalactiae</i>  |                                 |
| <i>Streptococcus</i> sp            |                                 |
| <i>Streptococcus anginosus</i>     |                                 |
| <i>Streptococcus mitis</i>         |                                 |
| <i>Streptococcus pneumoniae</i>    |                                 |
| <i>Streptococcus viridans</i>      |                                 |

**Supplementary Table 2. Keywords for internet search**

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|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| acanthamoeba                            | herpes keratitis fluorescein           |
| <i>acremonium</i>                       | HSV epithelial keratitis               |
| amoebic keratitis                       | <i>lophotrichous</i>                   |
| anterior chamber empyema                | MRSA                                   |
| aspergillus keratitis                   | <i>moraxella</i>                       |
| bacillus                                | <i>mycobacterium</i>                   |
| bacterial keratitis                     | <i>neisseria</i>                       |
| <i>candida albicans</i>                 | <i>nocardia</i>                        |
| <i>cladosporium</i>                     | <i>penicillium</i>                     |
| <i>corynebacterium</i>                  | <i>pseudomonas aeruginosa</i>          |
| Curvularia keratitis                    | <i>pseudomonas aureus keratitis</i>    |
| filamentous                             | <i>propionibacterium keratitis</i>     |
| fungal keratitis                        | <i>staphylococcus</i>                  |
| fungal keratitis <i>candida</i>         | <i>staphylococcus aureus</i>           |
| fungal keratitis <i>fusarium solani</i> | <i>staphylococcus aureus keratitis</i> |
| <i>fusarium</i>                         | <i>staphylococcus aureus keratitis</i> |
| <i>haemophilus influenzae</i>           | <i>streptococcus</i>                   |
| herpes cornea                           | <i>streptococcus pneumoniae</i>        |
| herpes keratitis dendritic              |                                        |

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**Supplementary Table 3. URL for web images of infectious keratitis**

| <b>Acanthamoeba Keratitis</b> |                                                                                                                                                                                                                                                                                                                                                                                      |
|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1                             | American Academy of Ophthalmology. Acanthamoeba Keratitis.<br><a href="https://eyewiki.aao.org/Acanthamoeba_Keratitis">https://eyewiki.aao.org/Acanthamoeba_Keratitis</a> .                                                                                                                                                                                                          |
| 2                             | American Academy of Ophthalmology. Early signs of Acanthamoeba keratitis.<br><a href="https://www.aao.org/image/early-signs-of-i-acanthamoeba-i-keratitis">https://www.aao.org/image/early-signs-of-i-acanthamoeba-i-keratitis</a> .                                                                                                                                                 |
| 3                             | CDC. Parasites — Acanthamoeba — Granulomatous Amebic Encephalitis (GAE); Keratitis.<br><a href="https://www.cdc.gov/parasites/acanthamoeba/health_professionals/acanthamoeba_keratitis_images.html#">https://www.cdc.gov/parasites/acanthamoeba/health_professionals/acanthamoeba_keratitis_images.html#</a> .                                                                       |
| 4                             | CET points.com. Acanthamoeba Keratitis.<br><a href="https://www.cetpoints.com/cet/acanthamoeba-keratitis/overview">https://www.cetpoints.com/cet/acanthamoeba-keratitis/overview</a> .                                                                                                                                                                                               |
| 5                             | CNN. Alerta por aumento de casos de una rara infección en los ojos por usar lentes de contacto.<br><a href="https://cnnespanol.cnn.com/2018/09/21/alerta-por-aumento-de-casos-de-una-rara-infeccion-en-los-ojos-por-usar-lentes-de-contacto/">https://cnnespanol.cnn.com/2018/09/21/alerta-por-aumento-de-casos-de-una-rara-infeccion-en-los-ojos-por-usar-lentes-de-contacto/</a> . |
| 6                             | eye news. How to diagnose and treat Acanthamoeba keratitis.<br><a href="https://www.eyenews.uk.com/education/top-tips/post/how-to-diagnose-and-treat-acanthamoeba-keratitis">https://www.eyenews.uk.com/education/top-tips/post/how-to-diagnose-and-treat-acanthamoeba-keratitis</a> .                                                                                               |
| 7                             | eye news. Acanthaemoeba keratitis.<br><a href="https://www.eyenews.uk.com/education/medico-legal/post/acanthaemoeba-keratitis">https://www.eyenews.uk.com/education/medico-legal/post/acanthaemoeba-keratitis</a> .                                                                                                                                                                  |
| 8                             | Health Online Unit, Ministry of Health Malaysia. Corneal Ulcer.<br><a href="http://www.myhealth.gov.my/en/corneal-ulcer/">http://www.myhealth.gov.my/en/corneal-ulcer/</a> .                                                                                                                                                                                                         |
| 9                             | Health Jade. Keratitis.<br><a href="https://healthjade.net/keratitis/">https://healthjade.net/keratitis/</a> .                                                                                                                                                                                                                                                                       |
| 10                            | kiyosawa.or.jp. The initial slit lamp findings of Acanthamoeba keratitis resemble resinous keratitis.<br><a href="https://www.kiyosawa.or.jp/%E8%A7%92%E8%86%9C%E7%96%BE%E6%82%A3-2/69508.html/">https://www.kiyosawa.or.jp/%E8%A7%92%E8%86%9C%E7%96%BE%E6%82%A3-2/69508.html/</a> .                                                                                                 |
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### **Bacterial Keratitis**

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## **Fungal Keratitis**

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### **HSV Keratitis**

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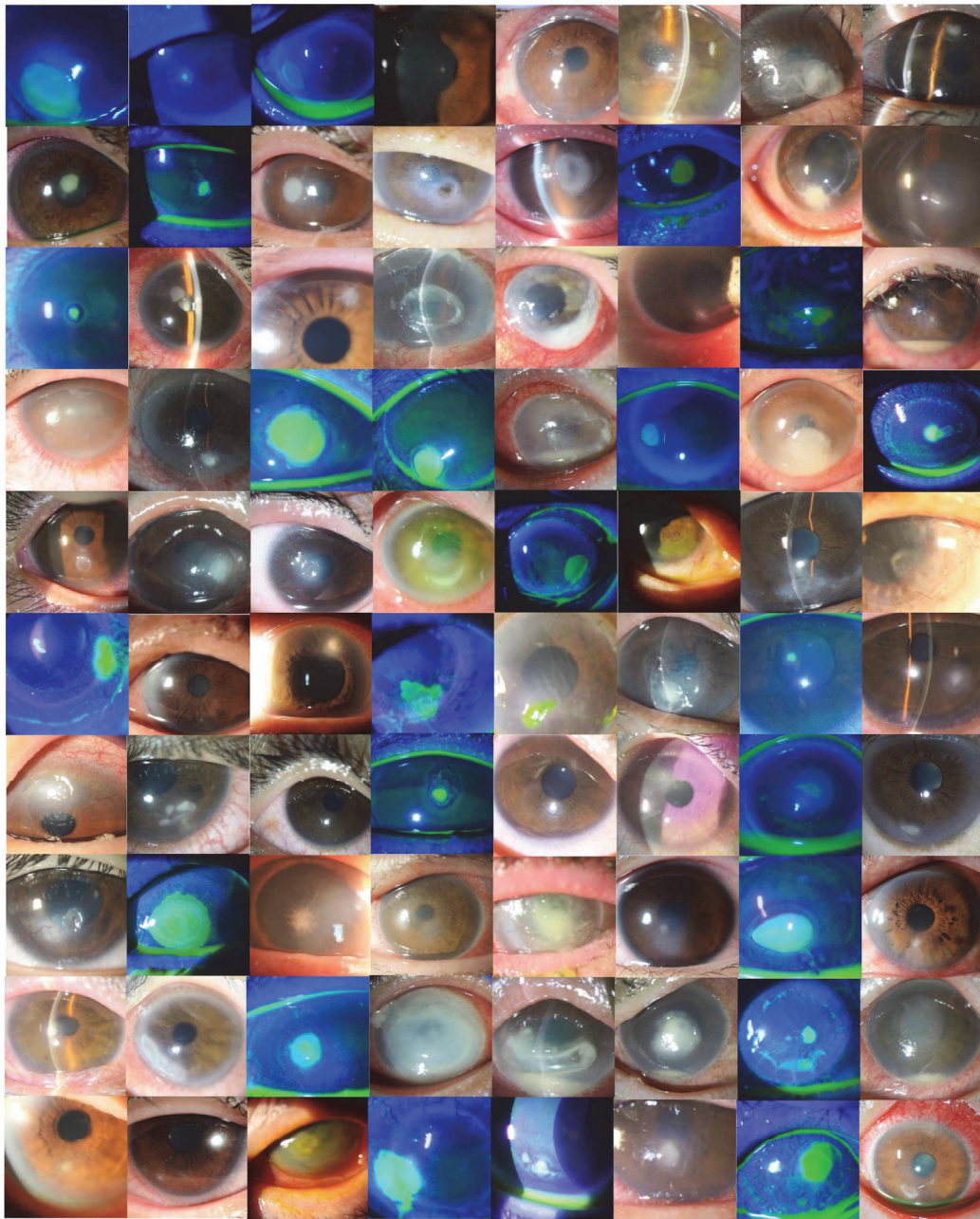
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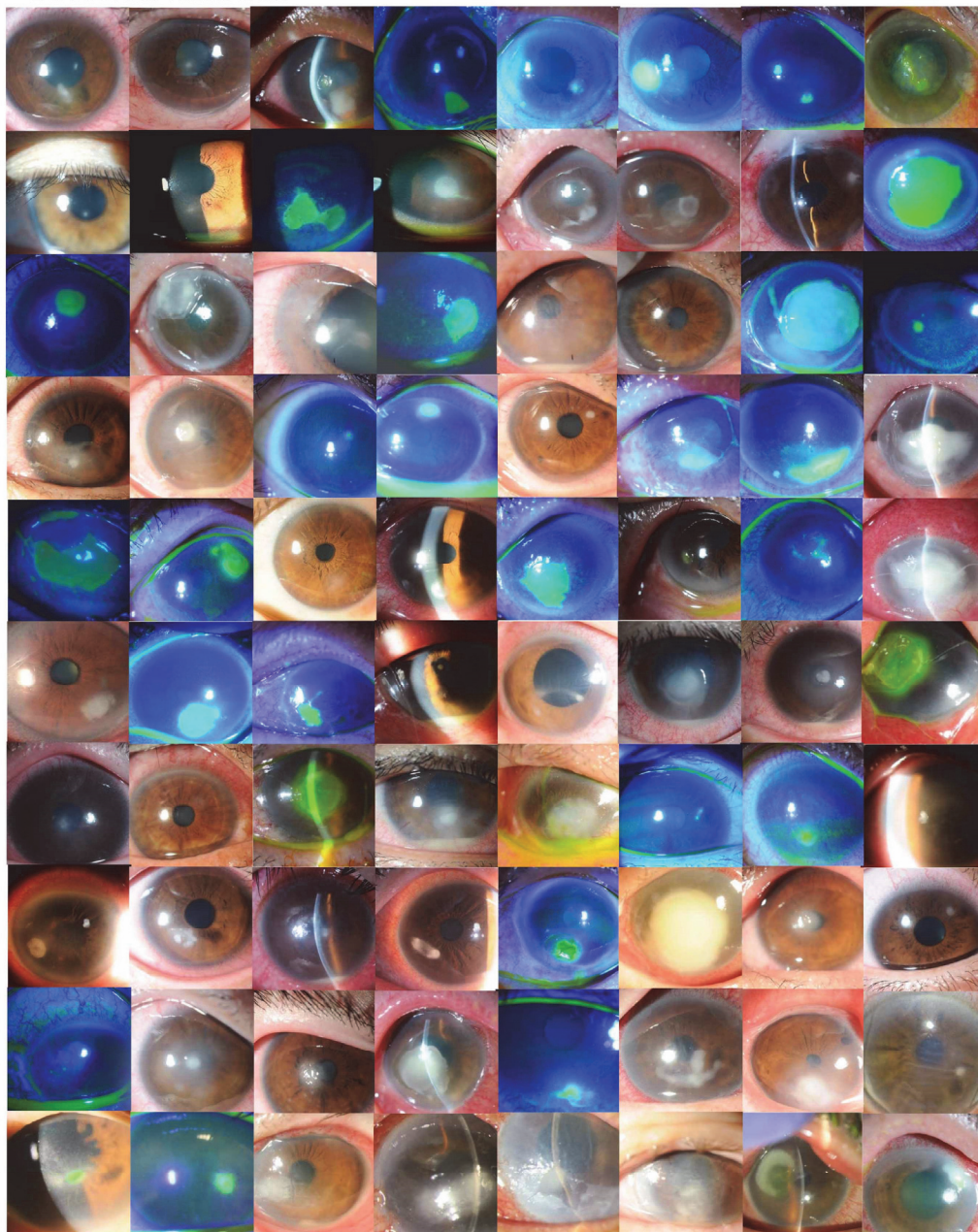
a

## Bacterial Keratitis



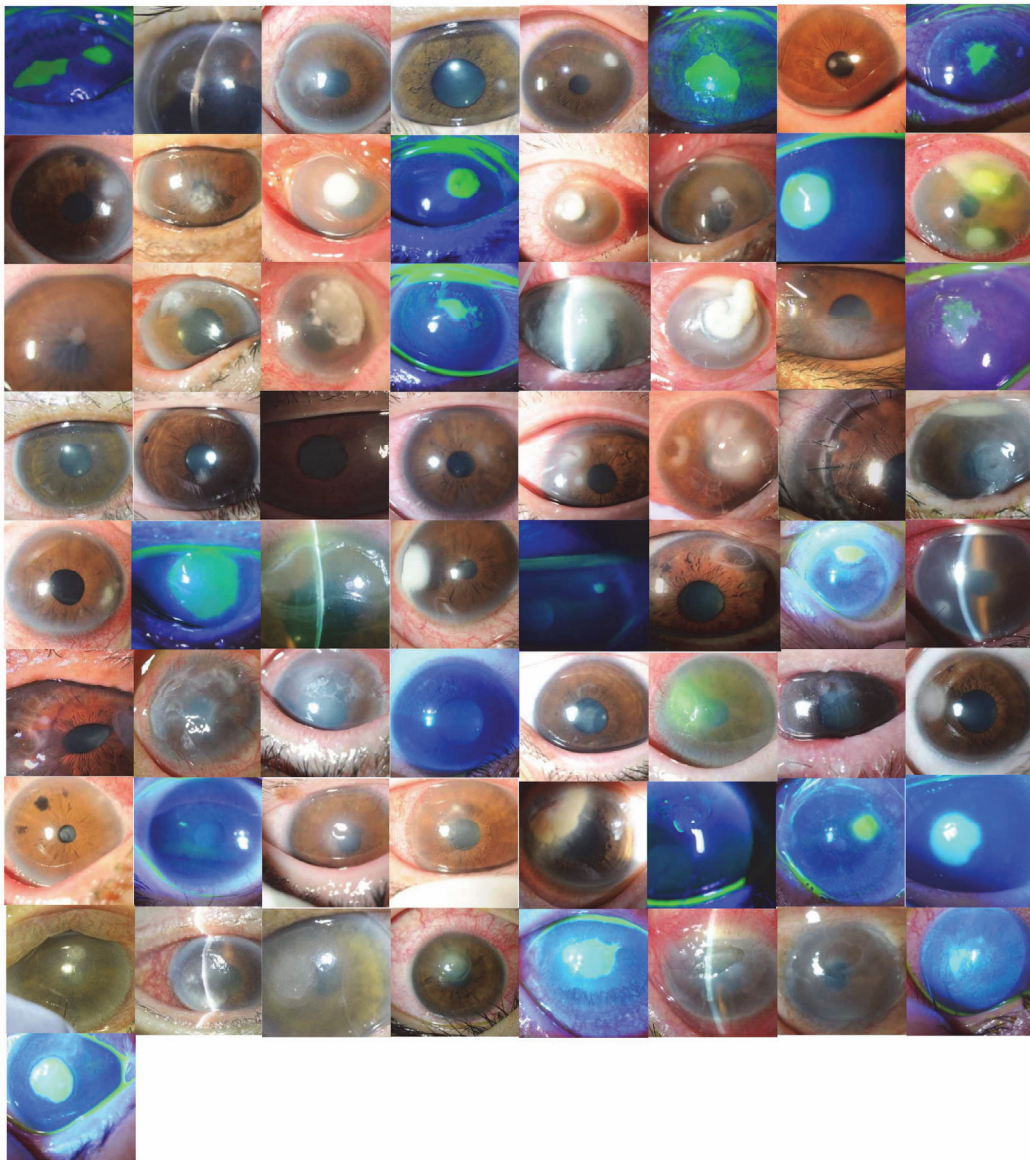
Supplementary Figure 1

## Bacterial Keratitis



Supplementary Figure 1

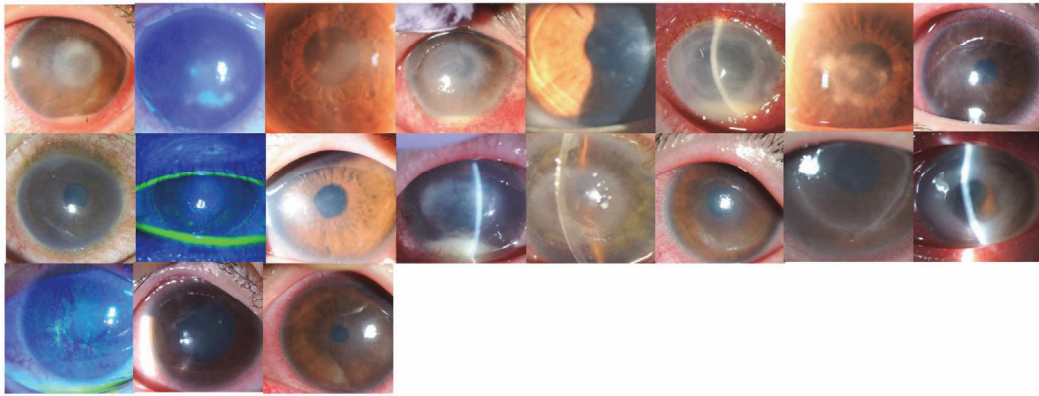
## Bacterial Keratitis



Supplementary Figure 1

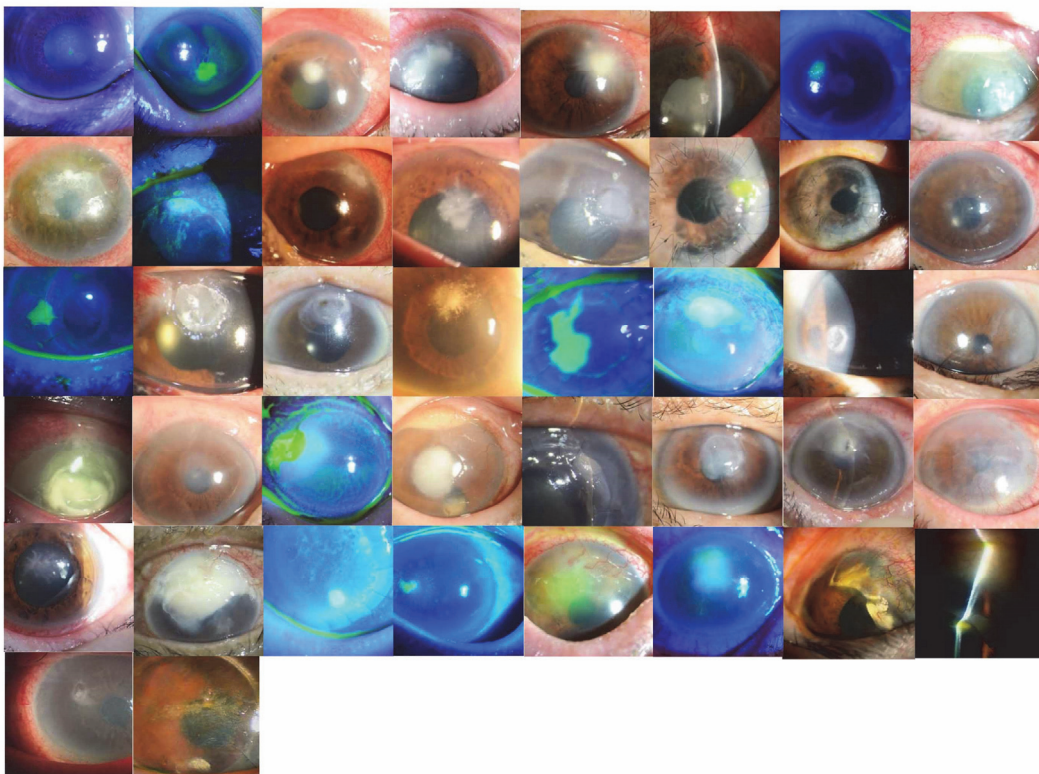
b

### Acanthamoeba Keratitis



c

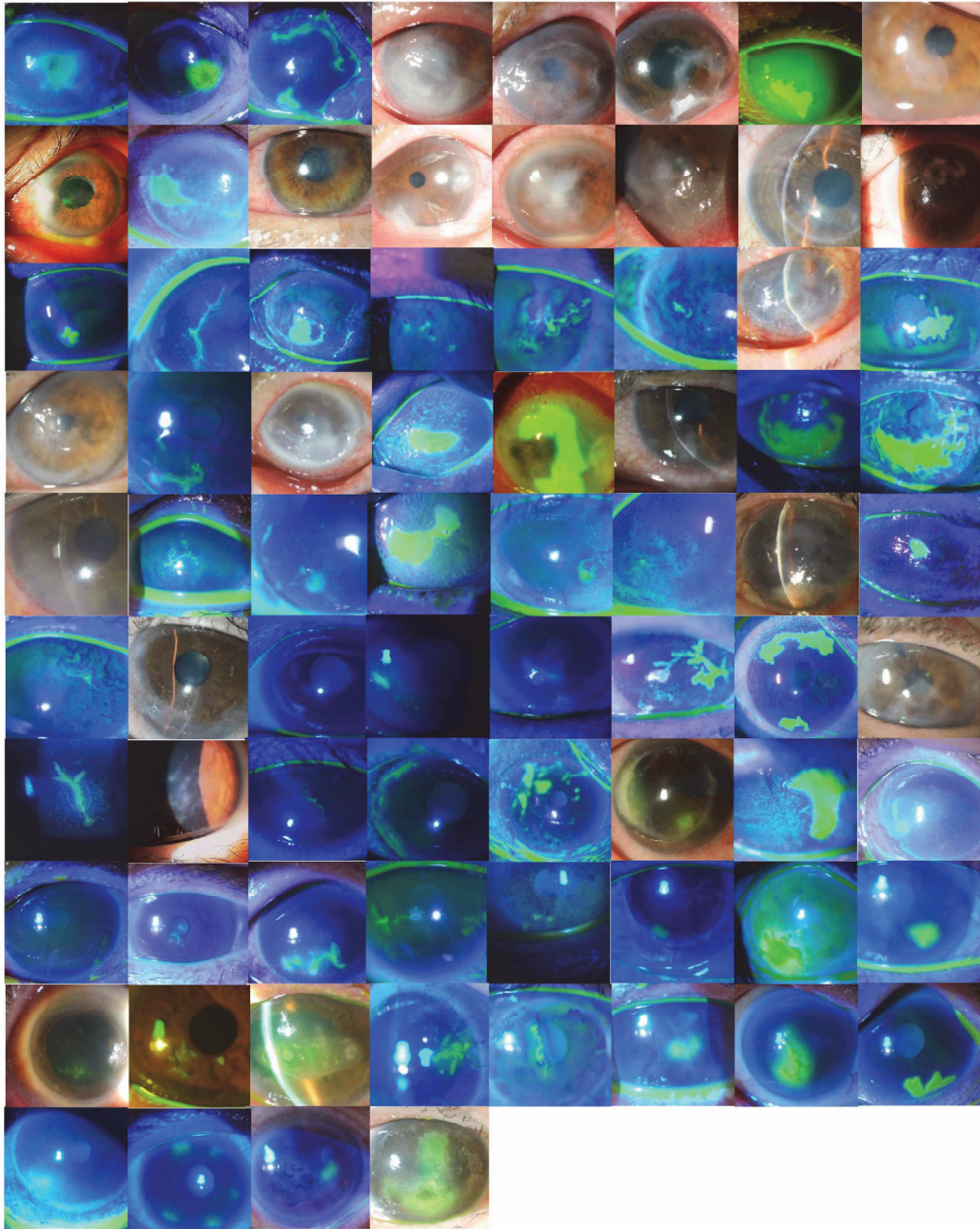
### Fungal Keratitis



Supplementary Figure 1

d

# HSV Keratitis



Supplementary Figure 1

## 1. Deep learning algorithm at developmental stage ResNet50-based two step classifier

1566 images (-2019 march)  
1426 images as training dataset  
140 images as test data set

→Evaluation by algorithm, Keratitest, and expert clinicians

## 2. Deep learning algorithm at final stage Ensemble of InceptionResNetV2-based two step classifier and gradient boosting decision tree

4306 images  
(3994 clinical images (-2020 Aug) and 312 web images)

→Evaluation by algorithm using Group K-fold validation

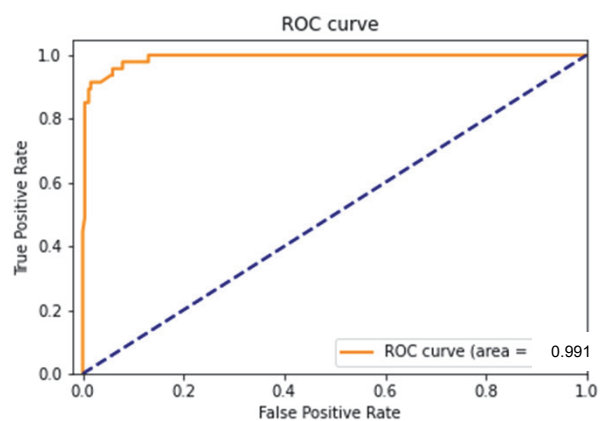
4306 images  
(3994 clinical images (-2020 Aug) and 312 web images)  
3882 images as training dataset  
424 images as test data set

→Evaluation by algorithm

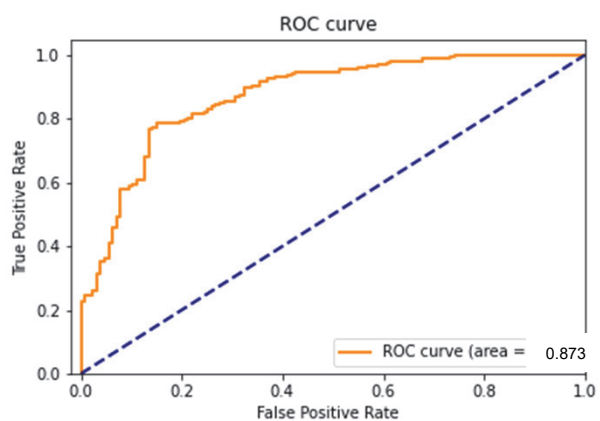
2992 images without fluorescein staining  
(2740 clinical images (-2020 Aug) and 252 web images)  
2692 images as training dataset  
300 images as test data set by algorithm

→Evaluation by algorithm

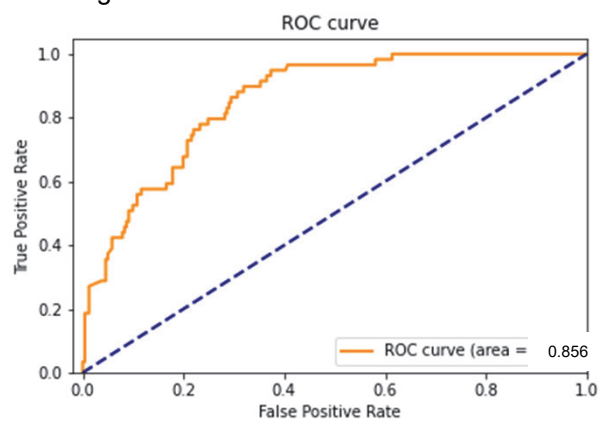
Acanthamoeba



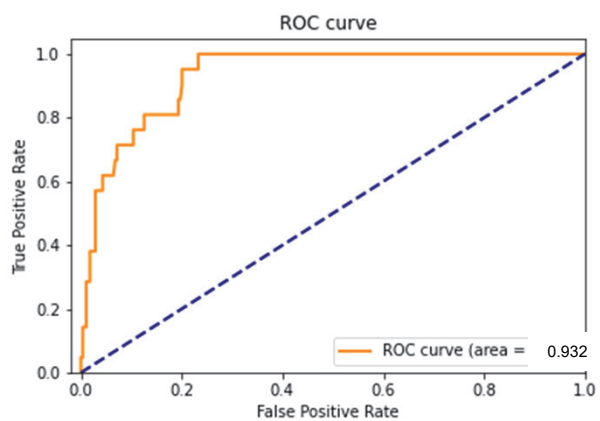
Bacteria



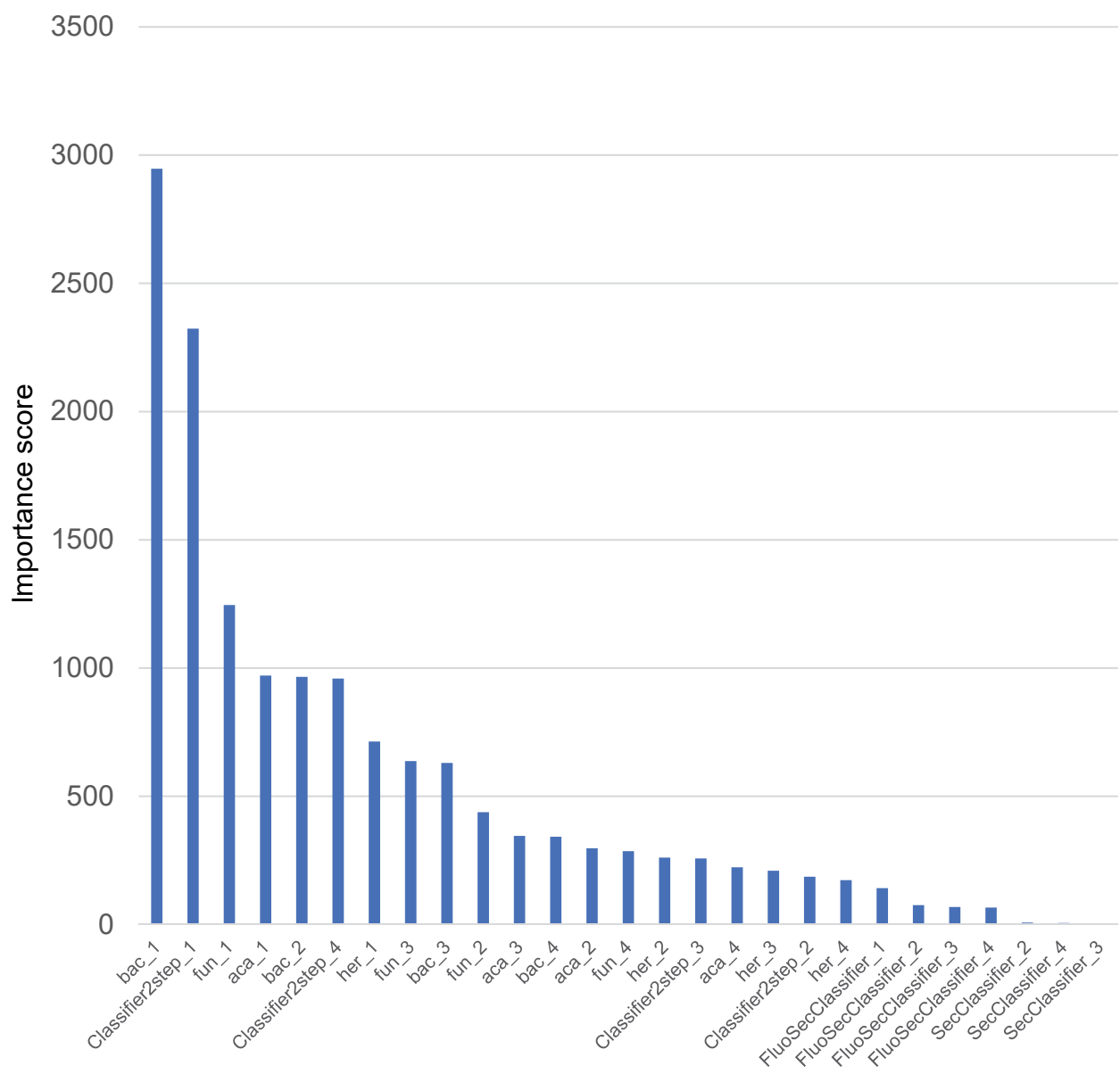
Fungi



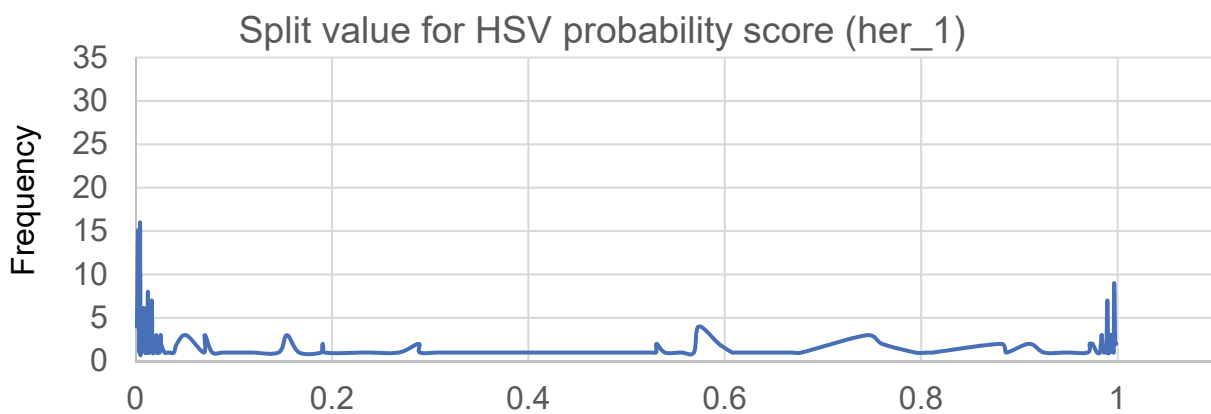
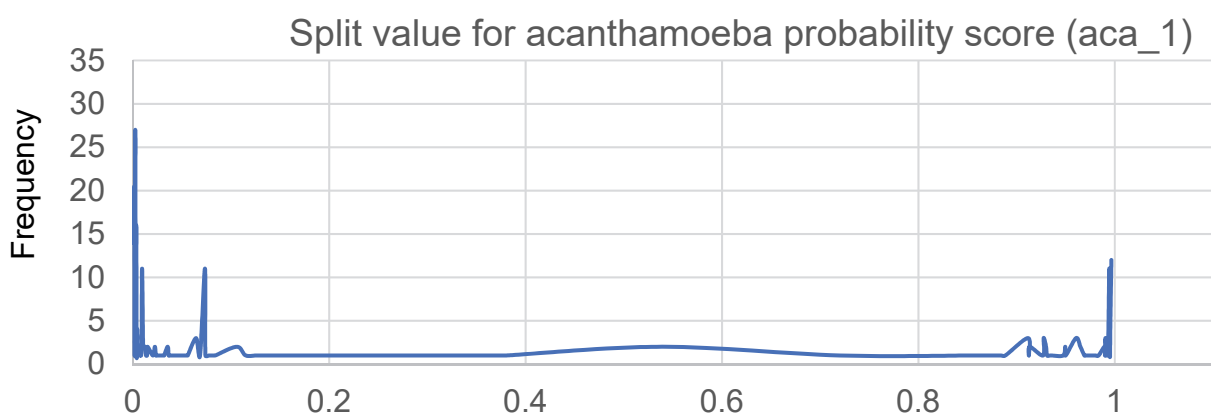
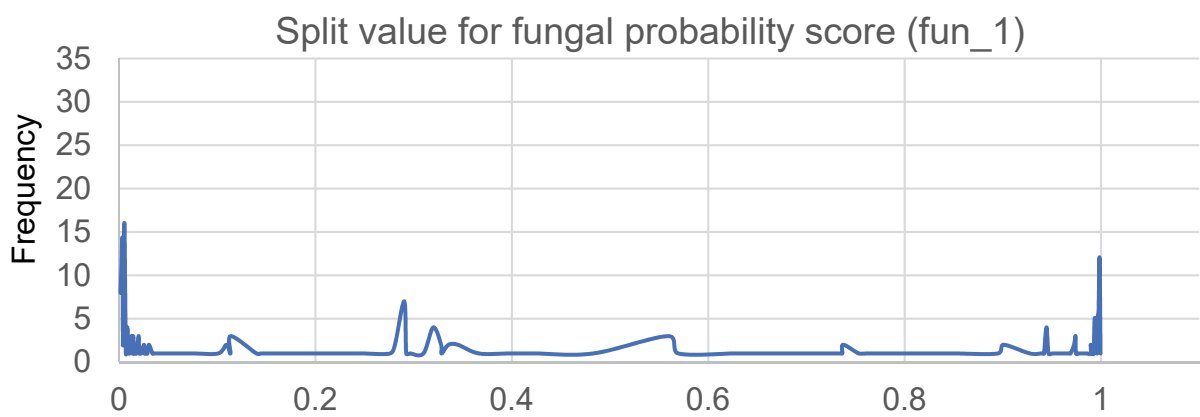
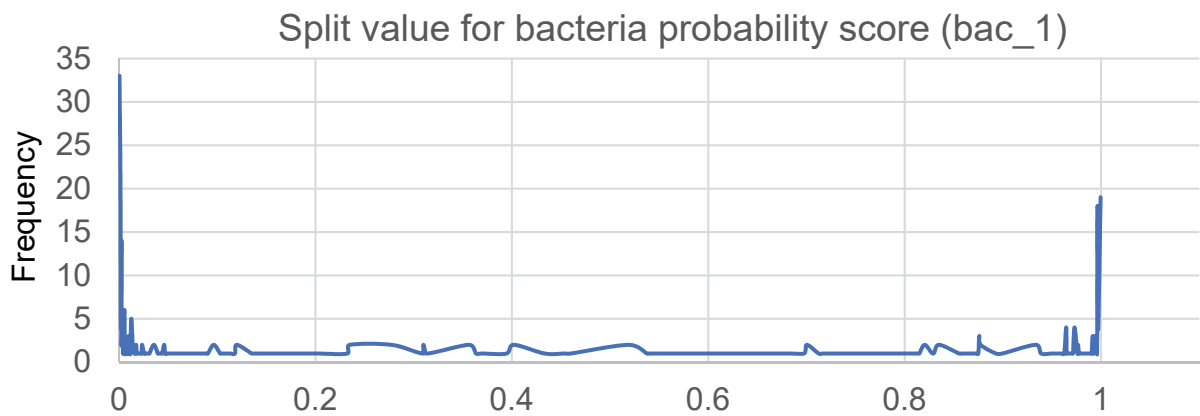
HSV



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5

**Supplementary Figure 1. Clinical images used for development of deep learning algorithm.**

Panels of representative 362 images of 362 patients were shown. Of them, 225 patients were bacterial keratitis, 19 patients were acanthamoeba keratitis, 42 patients were fungal keratitis, and 76 patients were HSV keratitis.

**Supplementary Figure 2. Flow chart of development and testing of deep learning algorithm.**

Deep learning algorithm at developmental stage was constructed based on ResNet50-based twostep classifier (Figure 1). Deep learning algorithm at final stage was constructed as ensemble of InceptionResNetV2-based twostep classifier and gradient boosting decision tree. The algorithm was developed in three different schemes, and evaluated.

**Supplementary Figure 3. Receiver operating characteristic analysis of hybrid deep learning-based algorithm for images without fluorescein staining.**

The 2992 images without fluorescein staining were randomly divided into 2692 training images and 300 testing images. The algorithm was initialized and retrained using the training images and assessed for the AUC using test images in batch of up

to 4 serial images.

**Supplementary Figure 4.** Importance scores for classification by gradient boosted decision tree algorithm.

Deep learning derived probability scores (acanthamoeba: aca\_, bacteria: bac\_, fungus: fun\_, HSV: her\_) and argmax of the pathogen probability scores (Classifier2step\_), argmax of pathogen probability scores in fluorescence second classifier for fluorescein-stained image (FluoSecClassifier\_), and argmax of pathogen probability scores in second classifier (SecClassifier\_) were assessed for total gain change as importance score. Bacteria probability scores showed the highest importance score. Numbers following “\_” (1 - 4) indicate serial number of images for the same batch.

**Supplementary Figure 5.** Distribution of split values in pathogen probability scores for classification by gradient boosted decision tree algorithm. Of the feature values learned for GBDT, probability scores of bacteria, fungal, acanthamoeba, and HSV showed highest importance scores. To confirm their validity for classification, the

frequency of split values for classification are shown as a histogram. For all the feature values, distribution of cut off probability scores for classification was bimodal, and 0 (0%) and 1 (100%) were densely utilized for classification.