VISION ACADEMY

people | research | education

Anti-VEGF intravitreal injections in the era of COVID-19: responding to different levels of epidemic pressure

Publication in

Graefe's Archive for Clinical and Experimental Ophthalmology

VEGF, vascular endothelial growth factor.

Objective

To provide guidance, according to different levels of epidemic pressure, for managing patients with retinal disease who require intravitreal injections of anti-VEGF agents during the COVID-19 pandemic

The Vision Academy provides ophthalmic specialists with a forum to share existing skills and knowledge, build best practice, and lead the wider community in the drive towards optimized, compassionate patient care.

Through their collective expertise, the Vision Academy seeks to provide guidance for best clinical practice in the management of retinal disease, particularly in areas with insufficient conclusive evidence.

VEGF, vascular endothelial growth factor.

Alert levels for COVID-19 recommendations

The Vision Academy Steering Committee published a set of considerations for managing patients with retinal disease requiring intravitreal injections during the acute phase of the COVID-19 pandemic[1]

The acute-phase recommendations have been reassessed to determine which should apply depending on the local epidemic pressure, which may vary with time[2]

ALERT LEVEL

- Extreme epidemic pressure; **R_t*** significantly >1; hospital resources strained; lockdown measures likely to be implemented (“**Red alert level**”)
- High epidemic pressure with many clusters of COVID-19-positive people; **R_t*** around 1; hospital resources not strained (“**Yellow alert level**”)
- Low epidemic pressure but no herd immunity through mass vaccination; **R_t*** significantly <1; some physical distancing measures implemented (“**Green alert level**”)

*The expected number of new infections generated at time t by each infectious case, in a population where some individuals may no longer be susceptible.[3-6]
R_t, effective reproduction number.

1. Korobelnik JF *et al. Graefes Arch Clin Exp Ophthalmol* 2020; 258 (6): 1149–1156; 2. Korobelnik JF *et al. Graefes Arch Clin Exp Ophthalmol* 2021 [Epub ahead of print]. https://doi.org/10.1007/s00417-021-05097-0; 3. Flaxman S *et al. Nature* 2020; 584 (7820): 257–261; 4. Gostic KM *et al. medRxiv* 2020; 5. Kucharski AJ *et al. Lancet Infect Dis* 2020; 20 (5): 553–558; 6. Adam D. A guide to *R* — the pandemic’s misunderstood metric. Available at: https://www.nature.com/articles/d41586-020-02009-w. Accessed October 2020.

VISION ACADEMY

GUIDING PRINCIPLES

- **The safety of patients and healthcare staff is of paramount importance in all decision-making**
- Vigilance in identifying suspect cases of COVID-19 is essential
  - Symptoms include dry cough, fever, and fatigue, or less commonly, loss of taste or smell, headache, muscle pain, sore throat, conjunctivitis, dyspnea, nasal congestion, skin rash, or diarrhea[1]
- Diabetic and elderly patients are the most vulnerable to COVID-19 complications[2,3] and should not be exposed to avoidable risk
  - However, continuation of care where possible is important to avoid irreversible vision loss

1. World Health Organization. Coronavirus disease (COVID-19) advice for the public. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public. Accessed October 2020; 2. Garg S *et al. MMWR Morb Mortal Wkly Rep* 2020; 69 (15): 458–464;
3. Docherty AB *et al. BMJ* 2020; 369: m1985.

VISION ACADEMY

GUIDING PRINCIPLES

- DME and BRVO patients may be less likely to suffer irreversible vision loss in the short term[1,2]
  - Carefully consider the medico-legal issues associated with advising such patients that, in most cases, vision will not be significantly adversely affected by interrupted / postponed treatment
  - Consider that many patients with DME and BRVO will have already had their treatment postponed during the initial wave of the COVID-19 pandemic, and further deferral of treatment may lead to permanent visual changes
  - Risk–benefits must be carefully weighed, discussed with the patient, and documented
  - Always consider the local legal / regulatory environment
- It is important that there is clear communication and advice for patients receiving intravitreal injections to ensure they feel supported and reassured that their vision is being appropriately managed

BRVO, branch retinal vein occlusion; DME, diabetic macular edema.

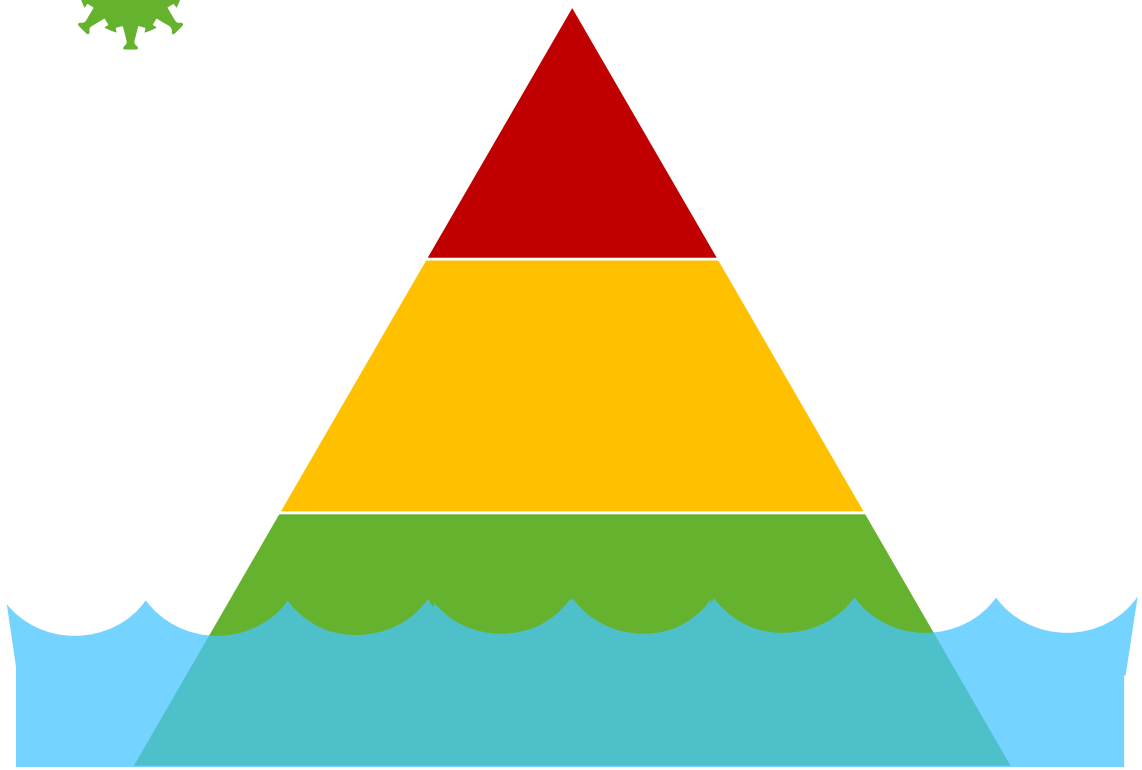
1. Bressler NM *et al. JAMA Ophthalmol* 2018; 136 (3): 257–269; 2. Schmidt-Erfurth U *et al. Ophthalmology* 2014; 121 (5): 1045–1053.

VISION ACADEMY

people | research | education

Low epidemic pressure situations

COVID-19 recommendations – “Green alert level”



Pandemic pressure

Key

Extreme epidemic pressure; **R_t*** significantly >1; hospital resources strained; lockdown measures likely to be implemented (“**Red alert level**”)

High epidemic pressure with many clusters of COVID-19-positive people; **R_t*** around 1; hospital resources not strained (“**Yellow alert level**”)

Low epidemic pressure but no herd immunity through mass vaccination; **R_t*** significantly <1; some physical distancing measures implemented (“**Green alert level**”)
These recommendations are also valid in situations with a higher alert level

*The expected number of new infections generated at time t by each infectious case, in a population where some individuals may no longer be susceptible.
R_t, effective reproduction number.

VISION ACADEMY

GENERAL CONSIDERATIONS

- Medical / healthcare staff should be monitored for signs and symptoms of infection (and quarantined according to national / institutional guidelines)
- Staff should receive regular training on COVID-19 safety practices and they should meticulously follow personal, facility, and instrument hygiene / disinfection rules as per local guidelines
- Consistency in the management and use of PPE throughout the patient journey is essential

PPE, personal protective equipment.

PRIORITIZING PATIENTS ACCORDING TO MEDICAL NEED

- **These considerations should be thoroughly discussed (remotely) with the patient, taking into account the local legal / regulatory environment and the status of the epidemic**
- If necessary, prioritize treatment visits over monitoring visits
  - Inform patients on how to self-monitor their vision (e.g., with Amsler grids or by reading texts with various font sizes)
  - Where feasible, implement the use of home monitoring technologies such as smartphone apps[1]
- Appointments of COVID-19-positive / suspect patients
  - Should be deferred until total resolution of symptoms or risk
  - Emergency surgery / intervention to prevent imminent danger of severe vision loss should proceed in an adequate facility with PPE

PPE, personal protective equipment.

1. Wong TY *et al. Retina* 2020; 40 (4): 599–611.

PRIORITIZING PATIENTS ACCORDING TO MEDICAL NEED

- Prior to the appointment, inform patients about safety and hygiene measures, including:[1-3]
  - The importance of physical distancing by 1 or 2 meters
  - The potential benefits of wearing a mask
- Provide a “Dear Patient” letter that reiterates the importance of attending appointments and offers advice on what to do should they be unable to attend[4]
- Provide support via an emergency contact number manned by a senior ophthalmologist for consistent patient-triaging advice

1. Chu DK *et al. Lancet* 2020; 395 (10242): 1973–1987; 2. Feng S *et al. Lancet Respir Med* 8: 434–436; 3. Leung NHL *et al. Nat Med* 2020; 26 (5): 676–680;
4. Korobelnik JF *et al. Graefes Arch Clin Exp Ophthalmol* 2021 [Epub ahead of print]. https://doi.org/10.1007/s00417-020-05042-7.

REDUCING EXPOSURE DURING THE PATIENT VISIT

- Patients and staff should wear a mask to reduce the potential transmission of COVID-19 to healthcare staff or other patients
  - An N95 or FFP2 mask is preferred; where these are not available, a surgical mask should be worn[1]
- Good ventilation is recommended in all rooms to reduce any potential viral vector load[2]
- Limit exposure in waiting rooms by:
  - Encouraging use of masks
  - Enforcing 1- or 2-meter distance, per local guidelines
  - Spacing out appointments
  - Allowing only one accompanying adult, if absolutely necessary
  - Queuing outside

1. Chu DK *et al. Lancet* 2020; 395 (10242): 1973–1987; 2. World Health Organization. Coronavirus disease (COVID-19): Ventilation and air conditioning in public spaces and buildings. Available at: https://www.who.int/news-room/q-a-detail/q-a-ventilation-and-air-conditioning-in-public-spaces-and-buildings-and-covid-19. Accessed November 2020.

REDUCING EXPOSURE DURING THE PATIENT EXAMINATION

- Staff must wear PPE (masks, gloves, goggles, and suits) for patients who are COVID-19-positive / suspected positive (or for all patients), as directed by local authorities and institution
  - The selection of appropriate PPE should be determined by local risk assessment and national authority guidance
- Keep examination as brief as possible; consider distancing measures between patients, HCPs, and staff
- Thoroughly disinfect hands and equipment, including keyboards, between patients
- In addition to the use of masks, affix large plastic / plexiglass shields to slit lamp and OCT
- Tape the upper edges of the face mask during intravitreal injection procedures to prevent air jets from radiating towards the eyes, thereby avoiding any associated risk of contamination[1]
- Emergency surgery / intervention in symptomatic or suspected COVID-19-positive patients should take place in an appropriate setting with PPE

HCPs, healthcare professionals; OCT, optical coherence tomography; PPE, personal protective equipment.

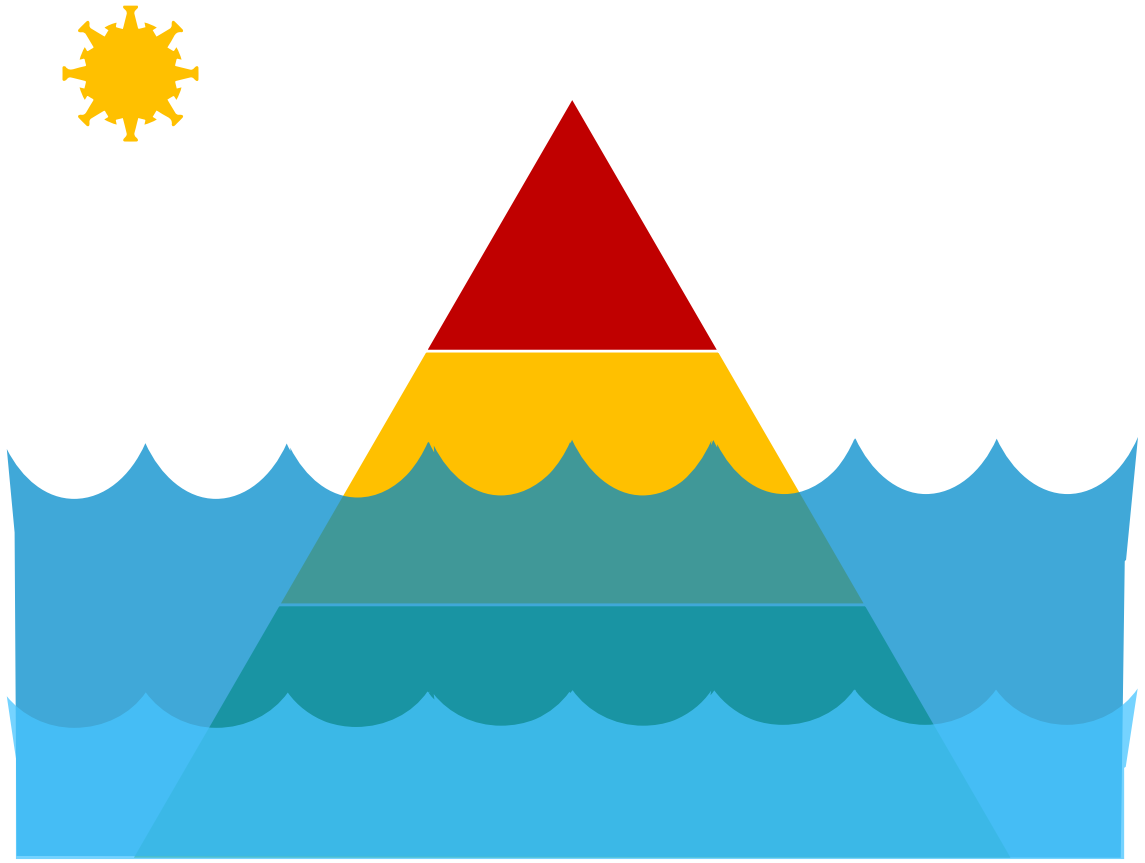
1. Hadayer A *et al. Retina* 2020; 40 (9): 1651–1656.

VISION ACADEMY

people | research | education

High epidemic pressure situations

COVID-19 recommendations – “Yellow alert level”



Pandemic pressure

Key

Extreme epidemic pressure; R_t^* significantly >1; hospital resources strained; lockdown measures likely to be implemented (“**Red alert level**”)

High epidemic pressure with many clusters of COVID-19-positive people; R_t^* around 1; hospital resources not strained (“**Yellow alert level**”)
These recommendations are also valid in situations with a higher alert level

Low epidemic pressure but no herd immunity through mass vaccination; R_t^* significantly <1; some physical distancing measures implemented (“**Green alert level**”)

*The expected number of new infections generated at time t by each infectious case, in a population where some individuals may no longer be susceptible.
R_t, effective reproduction number.

VISION ACADEMY

PRIORITIZING PATIENTS ACCORDING TO MEDICAL NEED

- Pre-screen patients by phone to identify symptomatic or suspected COVID-19-positive patients and direct them to an appropriate setting with enhanced protection measures and PPE (e.g., a designated section of the clinic or hospital)
- In general, patients with nAMD (especially those in the first 2 years of treatment), new patients with significant vision loss, neovascular glaucoma, and monocular or quasi-monocular patients (only one eye >20/40) should be prioritized and their treatment schedules maintained
- Consider postponement of appointments for non-monocular patients
  - Appointments for patients with significant vision loss from recent DME, proliferative diabetic retinopathy, acute-phase RVO, and ischemic RVO should not be postponed
- Avoid prolonged treatment postponement (>4–6 months) and reassess the situation within 2–3 months
- Patients with DME and BRVO who already had their treatment postponed >6 months during the initial wave of the COVID-19 pandemic should have their treatment maintained

BRVO, branch retinal vein occlusion; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; PPE, personal protective equipment; RVO, retinal vein occlusion.

REDUCING EXPOSURE DURING THE PATIENT EXAMINATION

- Limit OCT examinations and the use of special instruments, for example:
  - Tonometer
  - Fundus camera
  - Angiograph
- Special instruments should only be used if they are deemed critical to decision-making for the management of a particular patient

OCT, optical coherence tomography.

TREATMENT REGIMEN CONSIDERATIONS

- Treatment regimens and regimen changes that require frequent monitoring to adjust dosing intervals should generally be avoided
  - Avoid switching treatment regimen unless clear lack of response
  - Avoid changing treatment intervals in patients with nAMD who are responding to a fixed-dose regimen, if possible
  - For patients with AMD on variable-interval regimens (T&E, PRN), consider reverting to the last effective treatment interval and use this for fixed dosing, to minimize the need for monitoring
  - In new patients, maintain the loading phase schedule and select longer-acting drugs if possible
  - In patients with DME / RVO, only consider reimplantation of a dexamethasone implant if the patient is responding well and has a history of normal IOP under such treatment
  - PRP may be a preferable treatment choice for patients with severe proliferative diabetic retinopathy to reduce the potential risk of developing tractional retinal detachment
- Reassure patients who are used to an individualized treatment approach that fixed-dosed anti-VEGF regimens are an effective way of delivering treatment[1-3]

AMD, age-related macular degeneration; DME, diabetic macular edema; IOP, intraocular pressure; nAMD, neovascular age-related macular degeneration; PRN, *pro re nata* (as needed); PRP, panretinal photocoagulation; RVO, retinal vein occlusion; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

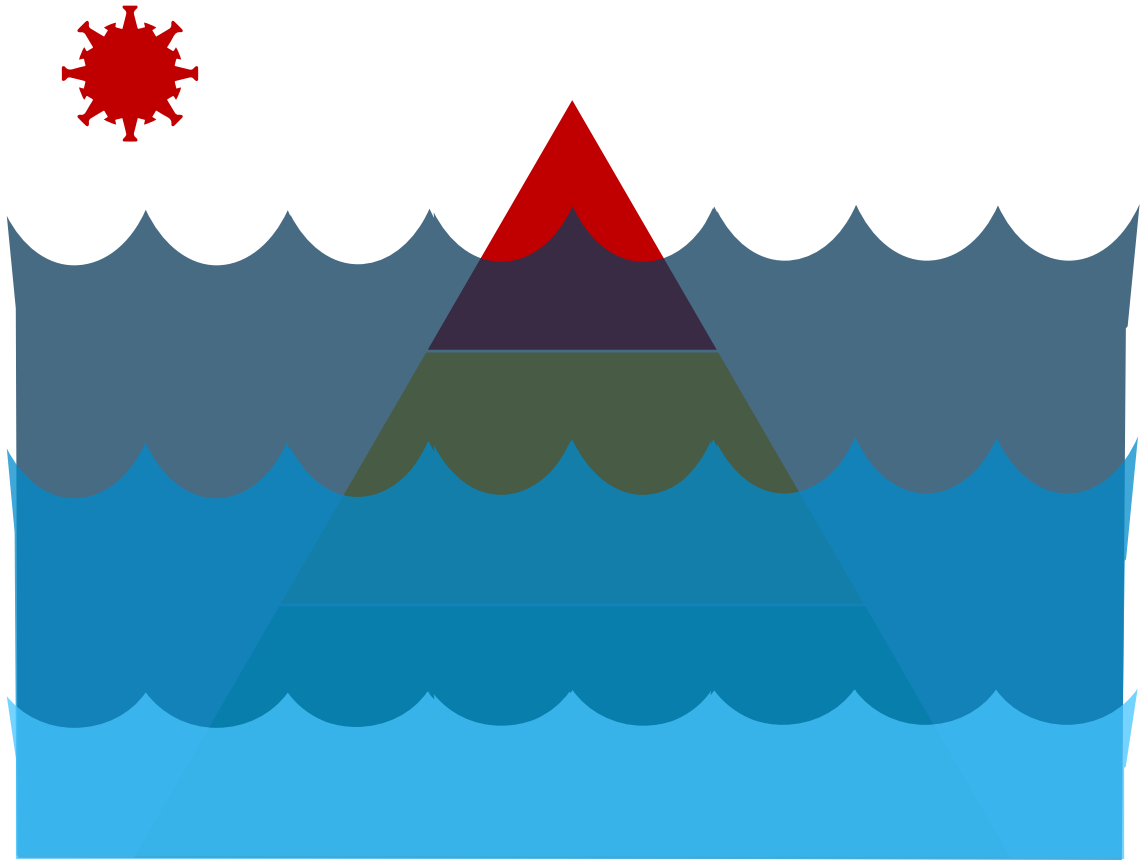
1. Schmidt-Erfurth U *et al. Ophthalmology* 2014; 121 (5): 1045–1053; 2. Rosenfeld PJ *et al. N Engl J Med* 2006; 355 (14): 1419–1431;
3. Brown DM *et al. N Engl J Med* 2006; 355 (14): 1432–1444.

VISION ACADEMY

people | research | education

Extreme epidemic pressure situations

COVID-19 recommendations – “Red alert level”



Pandemic pressure

Key

Extreme epidemic pressure; **R_t*** significantly >1; hospital resources strained; lockdown measures likely to be implemented (“**Red alert level**”)
These recommendations are only valid at this alert level

High epidemic pressure, with many clusters of COVID-19-positive people; **R_t*** around 1; hospital resources not strained (“**Yellow alert level**”)

Low epidemic pressure but no herd immunity through mass vaccination; **R_t*** significantly <1; some physical distancing measures implemented (“**Green alert level**”)

*The expected number of new infections generated at time t by each infectious case, in a population where some individuals may no longer be susceptible.
R_t, effective reproduction number.

VISION ACADEMY

PRIORITIZING PATIENTS ACCORDING TO MEDICAL NEED

- Non-urgent appointments should be postponed where there is capacity to reschedule within a reasonable time period (≤4–6 months)
- For asymptomatic / non-COVID-19-suspect patients who need treatment:
  - Referral to a non-hospital-based clinic may be preferable, especially in areas with high infection rates / medical facility shortages
- Telemedicine consultations can be useful to help physicians assess which patients should attend the clinic in person
  - They could also be particularly useful for monitoring patients whose in-person appointments have been postponed; it may be acceptable in the short term (≤4–6 months) to monitor the disease on function only
- Consider implementing home care where feasible, particularly for patients under lockdown
  - Home injections may be acceptable in some countries
  - Home care should only be provided with adequate PPE and hygiene measures

nAMD, neovascular age-related macular degeneration; PPE, personal protective equipment.

REDUCING EXPOSURE DURING THE PATIENT EXAMINATION

- Avoid thorough visual acuity testing
  - A simple test, ideally self-performed, may be sufficient (e.g., near-reading chart)
  - Perform brief visual acuity testing if an important vision change is reported, jumping to the smallest-achievable line

CONCLUSIONS

- Strategies for managing patients should be reassessed at regular intervals and adjusted in response to local infection rates and the availability of healthcare resources
- Measures should be intensified in situations of high or extreme epidemic pressure to minimize the risk of exposure to COVID-19 for both patients and healthcare staff
- Anti-VEGF treatment regimens should be simplified to reduce the need for frequent monitoring
- Treatment should be prioritized for those at greatest risk of irreversible vision loss

The Viewpoint ‘Anti-VEGF intravitreal injections in the era of COVID-19: responding to different levels of epidemic pressure’ can be downloaded from: https://www.visionacademy.org/vision-academy-community/COVID-19-materials

VEGF, vascular endothelial growth factor.