# COMPANIE TO DON'T MISS OUT DOWNload the free Community Eye Health Journal app today! bit.ly/CEHJ-app bit.ly/CEHJ-app VOLUME 36 · NUMBER 118 · 2023



## Medicines for eye health

Teamwork is vital if we want to support patients to access and use their eye medication.



#### Fatima Kyari

Associate Professor: International Centre for Eye Health, London School of Hygiene & Tropical Medicine, UK. Consultant Ophthalmologist: College of Health Sciences, University of Abuja, Nigeria.



#### **Elmien Wolvaardt**

Editor-in-Chief: *Community Eye Health Journal*, ICEH, LSHTM, London, UK.

edicines have a vital role in eye care, not only when patients are in the hospital or eye clinic, but also when they have to continue caring for their eyes at home.

For patients to adhere with the prescribed use of eye medicines, two conditions must be met:

- 1 The medication prescribed must be locally available, at a cost the patient can afford (also in the long term if they have a chronic eye condition). To address this, we have included articles on advocacy, local production of eye drops, and the management of eye medicines in a hospital or clinic setting.
- 2 Patients must also understand how and why to use their eye medication. We therefore have an article on empowering patients and a one-page instruction sheet which you can copy and share directly with patients.

Each member of the eye care team has a role in meeting these two conditions, and good communication is essential.

- Pharmacists can check prescriptions for safety and accuracy, give feedback to clinicians, and support patient education and adherence.
- Clinicians and prescribers can ask pharmacists which medicines are locally available and affordable.
- Nurses and allied health personnel can support
  patients by checking they have the correct prescription
  and/or medication before leaving the hospital,
  and by teaching them how to use their medication
  correctly.
- **Managers and policy makers** can support advocacy efforts or consider producing eye drops locally.

However, as we hope to show in this issue, these eye care team members will be most effective in their role if they can recognise that the patient is the most important member of the eye care team. If the patient's needs, abilities, circumstances and preferences are not taken into account at every step, adherence will remain a challenge and even the best medication will not be effective.



#### About this issue

Medicines play a vital role in eye care; not only in the hospital, but also when patients must care for their eyes at home. Ensuring the availability, safety and effective use of eye medicines requires a team effort, with patients and their needs firmly at the centre.

#### Contents

- Medicines for eve health Fatima Kyari and Elmien Wolvaardt
- **Management of medicines** in an eye hospital Ushalini Rasiah and Dhivya

Ramasamy

How we help our patients get their medicines and use them safely

> Bitrus Dauda, Hamida Musa and Farouk Garba

**Empowering patients to** manage their eye medication at home

Nyawira Mwangi, Leah Kenan and Funmi Bankole

How to use your eye medication

Nyawira Mwangi and Leah Kenan

Improving adherence with eye medication: a patientcentred approach to prescribing

Boateng Wiafe, Nisha Iha, Elmien Wolvaardt and Mohammed Abdull

- 10 Supporting patients with adherence to glaucoma medication in Ghana Boateng Wiafe
- 11 Inclusion of eye medication in national health care systems

Junu Shrestha, May Ho and Jude Stern

- 12 Valuing pharmacists as members of the eye team Parvesh Patel
- 13 Providing eye care education for pharmacists **Boateng Wiafe**
- 14 The impact of oral and systemic medications on the eye

Shalinder Sabherwal and Abeer H A Mohamed-Ahmed

17 Local production of eye drops in the hospital or pharmacy setting: considerations and safety tips

> Abeer H A Mohamed-Ahmed and Dan Kuguminkiriza

- 19 Ruharo Mission Hospital eye drop production facility Dan Kuguminkiriza and Abeer H A Mohamed-Ahmed
- 21 How to prepare chlorhexidine eye drops Abeer H A Mohamed-Ahmed, Christina A R Picken and Dan Kuguminkiriza
- 23 Picture quiz Louis Oteng-Gyimah and Victor H Hu
- 24 Improving the distribution and uptake of medicines: lessons from the global trachoma programme

Angelia Sanders, PJ Hooper, Scott McPherson and Tim Jesudason



Ushalini Rasiah Manager: Quality, Aravind Eye Care System, Madurai, India.



Dhivya Ramasamy Senior Faculty: LAICO, Aravind Eye Care System, Madurai, India.

## Management of medicines in an eye hospital

Medication management is essential for safe and effective eye care.

edication forms a large part of ophthalmic treatment - a significant proportion of patients who undergo outpatient consultation at tertiary eye care facilities and primary eye care facilities are prescribed medication.

So it is important that the management of eye medication is integrated into eye care services at all levels. Great advancements in ocular medication therapy have resulted in a wide range of medicines being available, each with a specific use. This complexity makes it crucial for hospitals to implement a systematic and safe approach to drug dispensing. Without proper protocols, errors in medication dispensing can have serious consequences for patients.1

#### The hospital or clinic pharmacy

A hospital or clinic pharmacy is required to manage stock of medication for two distinct purposes:

1 Medicines used within the clinic for diagnosis and procedures. These include dilating drops, anaesthetic drops, and medication used for emergency treatment or during surgery.

#### **Community Eye Health** *Journal* VOLUME 36 • NUMBER 118 • 2023







#### **Editor-in-Chief**

Elmien Wolvaardt editor@cehjournal.org

**Editor: South Asia Edition** Kriti Shukla

**Medical Editor** Victor Hu

Consulting Editor: issue 118 Abeer H A Mohamed-Ahmed

**Editorial Administrator** Anita Shah admin@cehjournal.org

Online and social media

Astrid Leck **Hugh Bassett** Romulo Fabunan

**Editorial Committee** Simon Arunga (Uganda) João M Furtado (Brazil)

Esmael Habtamu (Ethiopia) Fatima Kyari (Nigeria) Ciku Mathenge (Rwanda) Nyawira Mwange (Kenya) GVS Murthy (India) Heiko Philippin (Germany) Thulsiraj Ravilla (India) Serge Resnikoff (Geneva) Jude Stern (Australia) Sumrana Yasmin (Pakistan) David Yorston (UK)

**Editorial Advisors** 

Nick Astbury (Partnerships) John Buchan (Ophthalmology) Jenny Evans (Systematic reviews) Michelle Hennelly (Ophthalmic nursing) Islay Mactaggart (Disability) Priya Marjoria (Optometry) Daksha Patel (Education)

#### **Regional Consultants**

Hannah Faal (AFR) Kovin Naidoo (AFR) Van Lansingh (AMR) Andrea Zin (AMR) Ian Murdoch (EUR) Janos Nemeth (EUR) GVS Murthy (SEAR) R Thulsiraj (SEAR) Babar Qureshi (EMR) Mansur Rabiu (EMR) Leshan Tan (WPR) Hugh Taylor (WPR)

Design

Lance Bellers

Printing Newman Thomson

**Proofreading** Astrid Leck Anita Shah

#### **Download our app**

Download the free Community Eye Health Journal app today: bit.ly/CEHJ-app

Visit us online www.cehjournal.org

**Subscribe** Visit: www.cehjournal.org/

subscribe Email: web@cehjournal.org

Readers in low- and middle-income countries receive print copies free of charge. To subscribe, send your name, occupation, and postal address to:

**Anita Shah, International Centre** for Eye Health, London School of Hygiene and Tropical Medicine, **Keppel Street, London WC1E** 7HT, UK.

Email: admin@cehjournal.org

Clare Gilbert (UK)

2 Medicines prescribed and dispensed to the patient for use at home. Some hospitals will give the patient a prescription to take to a pharmacy in the community.

The medications stocked in a hospital-based pharmacy depends on the services provided. For example, primary and secondary care facilities will stock common ocular medication used for allergies and infections, and tertiary care facilities may stock a more complex variety of medications for conditions such as glaucoma, diseases of the uveal tract, etc.

It is important to have a holistic view of the medications that patients may need. For instance, although glaucoma is not treated at a primary eye care facility, it would be helpful to stock common glaucoma medicines so that patients are able to get refills locally.

#### **Standardisation**

It is important to standardise the list of medications and the brands that a hospital will use or dispense. This allows better price negotiation and stock management, and can help to ensure the quality and efficacy of the drugs.

#### **Prescription writing**

A legible and complete prescription is essential for safe drug dispensing.

Prescriptions should be written **legibly** – possibly in capital letters. Where possible, printed prescriptions are preferred.

Prescriptions must be **complete**. It must have the patient's name and medical record number, the name of the drug, the strength, dosage, and duration. Any special instructions should be clearly and unambiguously written. Prescriptions must also carry the doctor's name and signature, and the date.

Ensure that only authorised personnel are permitted to prescribe medication. If an assistant writes down a doctor's orders, a policy of reading back what was written will help to prevent errors.

Where possible, give patients a consolidated set of instructions that factors in drugs from previous prescriptions as well as those prescribed at the latest visit.



#### **Inventory management**

Having an adequate supply of medicines in stock helps to ensure that patients receive treatment without delay. Medicines must be in date, and of good quality. It is therefore important to monitor stock levels (inventory) on a regular basis, and to check the quality of purchased medicines as they come in: check for any leakage, discoloured liquids, contamination, etc.

It is also important to develop good working relationships with a few reliable suppliers, as this can help hospitals to avoid fake drugs, negotiate better prices, and ensure sufficient stock levels. When there is a long-standing relationship, and mutual trust, suppliers may agree to replace medicines nearing their expiry date and respond to special drug requirements. Some suppliers may also provide stock on consignment, meaning that the hospital pays for medicines only when they have been sold.

Set up systems to ensure that stock is always dispensed according to a first-in, first-out method, so that medicines purchased first are dispensed first. Usually, this is done by stacking newly purchased packs at the back and dispensing packs from the front. A computerised inventory system can greatly enhance inventory management of drugs and alert staff about medicines nearing the expiry date.

A pharmacy assistant counsels a patient about his eye medicines and how to use them. INDIA

#### Support our work

We rely on subscriptions and donations from charities and generous individuals to carry out our work.

To support us, visit: www.cehjournal.org/donate or contact Anita Shah: admin@cehjournal.org

Published by the International Centre for Eye Health, London School of Hygiene & Tropical Medicine.

Unless otherwise stated, authors share copyright for articles with the *Community Eye Health Journal*. Illustrators and photographers retain copyright for images published in the journal. Please note that some articles are published online first and may have been shortened to fit the available space in this printed edition.

Unless otherwise stated, journal content is licensed under a Creative Commons Attribution-NonCommercial (CC BY-NC) license which permits unrestricted use, distribution,

and reproduction in any medium for non-commercial purposes, provided that the copyright holders are acknowledged. ISSN 0953-6833.

#### Disclaimer

Signed articles are the responsibility of the named authors alone and do not necessarily reflect the views of the London School of Hygiene & Tropical Medicine (the School). Although every effort is made to ensure accuracy, the School does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the School in preference to others of a similar nature that are not mentioned. The School does not endorse or recommend products or services for which you may view advertisements in this Journal.





Look-alike medications are clearly labelled in this store room. INDIA

#### Storage and disposal

Always store medicines as recommended by the manufacturer. Make sure the storage area is well-lit, well-ventilated, and checked often to make sure no one is taking them without permission. Ensure that all medicines are kept at the correct temperatures.

Medicines that look alike and/or sound alike (also known as LASA) can result in dispensing and administering errors. Display a list of LASA drugs where pharmacists and other staff members can see it, and encourage the use of non-proprietary (generic) names for medicines. At Aravind, we train staff members to colour code LASA drugs and physically separate them within the storage area. Further guidance from the World Health Organisation is available at bit.ly/WHOlasa

Carry out regular audits to identify and remove expired drugs, and dispose of all medicines safely.

#### Safe dispensing

Processes at the pharmacy must be standardised to ensure that staff always verify the prescription, ensure correct drug, strength and quantity, correct billing, and handing over with clear instructions. Medicine dispensing must be accompanied with detailed do's and don'ts – including how to open the eye drops bottle (not using a pin to perforate), hygiene, dosage and frequency to be followed, how long to wait between two medications, how and when to dispose of a medicine, and any special storage instructions (refrigeration, etc.).

#### **Enhancing adherence to medication**

Counselling during dispensing is important and should include information about why and how to take the medication. Where necessary, explain about drug-drug

..... Figure 1 After getting their medicines, patients at Aravind Eye Hospital take the prescription home. The prescription shows the name of the eye drops, which eye(s) to use them for, how many days to use them, how often, and how many drops to use. The QR code (top right) links to a video that explains how to instil the drops.



#### Considerations when developing a standard drug list or formulary

An essential first step is to set up standard treatment protocols and a standard operating protocol for patient examination.

Include medicines based on evidence of efficacy. The World Health Organization's Model List of Essential Medicines is a good place to start (sections 14.1 Diagnostic agents: Ophthalmic medicines and 21. Ophthalmological preparations). The latest version is available from https://bit.ly/WHO-em.

Ensure that the list not only has the "best" medication, but also includes affordable alternatives that are locally available. Review the list by continuously monitoring outcomes and looking out for new alternatives.

The standardised drug list should be communicated to the following people working in the hospital: doctors, counsellors (nurses or allied health personnel who counsel patients), pharmacists, and the people responsible for inventory management and purchasing. Some government-run eye facilities receive medications from the government without the option to choose brands or vendors. In such cases, hospital managers should advise purchasing officers about which drugs to order.

Figure 2 Medicines

numbers, which are

(or prescription) sent

home with patients.

are clearly labelled with

repeated in the instructions

or food-drug interactions. The information should be provided in simple and clear language that the patient can understand. These oral instructions should be accompanied by printed or digital information for future reference. A QR code printed on the prescription can help patients and their family to access this information at a later date (see Figure 1).

To make it easier for patients who have to use multiple medications, we add coloured or numbered labels (Figure 2). The prescription also refers to this number.

This makes it easy for everyone to follow instructions, not just for those who are unable to read.

For patients taking medications for chronic conditions, counselling should include the importance of long-term adherence and instructions on how and where to get refills.

## @ aurolab DEXA AUROFLOX

#### **Adverse drug reactions**

Adverse drug reactions are undesirable events that follow the use of a drug. This can range from a simple rash to serious conditions, such as pulmonary oedema. Every drug reaction must be documented and analysed to understand whether the reaction is due to the medication itself, an interaction with another medicine, or whether there is an issue with a particular batch of medication.

Having a structured reporting system for this helps pharmacovigilance committees or local health care associations to track adverse drug reactions across the country, so they can make a collective decision on medicine about medicines and how to manage adverse reactions.

#### Reference

1 Kalita IR, Singh HV, Veena K, Mouttappa F. Primary eye care in pediatric population-I study (PREPP-I study): Demographic and clinical profile of pediatric patients treated in six major vision centers of a tertiary eye care facility in South India. Indian Journal of Ophthalmology.

#### **Further reading**

Two previous issues of the Community Eye Health Journal contain useful and relevant content related to managing medicines.

Comm Eye Health Vol. 34 No. 111, 2021. Running a safe eye service for patients and personnel bit.ly/ SafeEye

Comm Eye Health Vol. 24 No. 76, 2011. Instruments and consumables. bit.ly/ CEHJ76



**Bitrus Dauda**Manager:
Eye Clinic, Hajiya
Gambo Sawaba
General Hospital,
Zaria, Nigeria.



Hamida Musa Deputy Sister: Eye Clinic, Hajiya Gambo Sawaba General Hospital, Zaria, Nigeria.



Farouk Garba
Senior Lecturer/
Consultant
Ophthalmologist:
Department of
Ophthalmology,
College of Medical
Sciences, Ahmadu
Bello University,
Zaria, Nigeria.

## How we help our patients get their medicines and use them safely

Setting up a pharmacy inside the eye clinic helped patients get their medicines safely, quickly, and without incurring additional expense.

ajiya Gambo Sawaba General Hospital is a secondary centre in Zaria, in the northern part of Nigeria. The majority of patients who come to the hospital have no medical insurance and have to make out-of-pocket payments for treatment and medication.

Since the hospital pharmacy did not stock eye medicines, eye clinic personnel directed

patients to pharmacies in the local area which were known to sell good quality medicines at reasonable prices. Patients were asked to return to the eye clinic afterwards so that the nurses could check they had purchased the correct medication.

However, we noticed that patients coming from small villages had difficulty finding their way around, even inside the hospital, and struggled to find the pharmacies the eye department recommended. We also noticed that patients were spending additional funds to transport themselves in search

funds to transport themselves in search of medications elsewhere, making the experience overwhelming and expensive.

#### A new approach

To address this issue, the eye clinic and resort to out manager and his team advocated of pocket payment for a pharmacy to be set up right inside the eve clinic itself. The hospital of health services administrators agreed, and the eye and purchase of clinic pharmacy was set up in November 2021. It is overseen by the main hospital medications." pharmacy and stocks commonly prescribed medicines such as antibiotics, anti-inflammatories, analgesics, and glaucoma medication. Consumables, such as viscoelastic, dilation drops, and blocking agents, are also kept in stock.

Now that the pharmacy is inside the eye clinic, eye patients can easily and quickly get the medication they need. They would only be sent to a local pharmacy if an item was out of stock in the hospital. When this happens, a health worker will first call the pharmacy to ensure that the medicine is available, or find a suitable alternative, before sending the patient to that pharmacy.



After surgery and a postoperative examination, cataract patients and their care givers gather in a hall where health workers give explanations and answer questions about postoperative care, including how to use their medicines. NIGERIA

This approach assists patients and caregivers greatly by preventing them walking around in an unfamiliar area, looking for a particular medication and perhaps being vulnerable to being exploited or taken advantage of.

#### **Quality and safety**

"The majority of

patients have no

medical insurance

Hospitals in Nigeria receive medication from the central store in their state. The central store carries out quality control and other checks before accepting medicines from pharmaceutical companies and distributing them

to hospitals in the area. The eye clinic pharmacy sends the list of medicines it needs to the hospital pharmacy, which in turn requests these from the state's central store.

Any expired medicines are sent to the hospital pharmacy, which returns it to the central store for safe disposal.

For drug surveillance and adverse drug reactions, the eye clinic pharmacy follows the same protocol as the main pharmacy. Pharmaceutical companies also visit the eye clinic at intervals

actively enquire if there have been any problems with their medicines.

#### The "Show and Teach" system

The ophthalmic nurses in the eye clinic have a system they call "show and teach". After purchasing medicines, and before leaving, patients are asked to "show" their medicines and prescription to the nurses for verification. This is used as an opportunity to carefully "teach" how the medicines are to be used, and to explain what possible side effects to expect. The date for the patient's next appointment is also confirmed.



Mwangi Deputy Director: Academics, Kenya Medical Training College, Nairobi, Kenya.



Leah Kenan Ophthalmic Nurse: City Eye Hospital, Nairobi, Kenya.



**Funmi Bankole** Director: Eye Unit, Lagos Ministry of Health, Lagos, Nigeria.

## **Empowering patients to manage their** eye medication at home

Eye patients must manage their own treatment once they leave the clinic; our role is to ensure they can do so safely and effectively.

efore patients leave the clinic, we need to be confident that they - and their care givers - know

- 1 Get the right medication
- 2 Manage their medication safely
- 3 Administer their medication correctly.

#### 1. Get the right medication

Before the patient leaves the clinic, talk to them about the medication they have been prescribed.

- Trained eye care personnel, or the hospital pharmacist, can check that the prescribed medication is safe for the patient. Ask the patient about any other conditions or allergies, or about any other medications that they may be taking, including herbal medication and over-the-counter items, such as vitamin supplements and aspirin. Report any concerns to the pharmacist or prescribing clinician.
- Next, explain where the patient must go to get their medication, and what they have been prescribed (the number of medicines and the type, e.g. drops or ointment).
- Encourage the patient to check their medication before they leave the pharmacy: do they have the correct number of medicines, the correct type, and is it in date? In some hospitals, patients are told to come back to the eye clinic so that the nurse can check their medication before they take it home (see page 5).
- Explain to patients how they can get the prescription refilled or renewed, if they are on long-term medication.

#### 2. Manage medication safely

#### Storing medication

Tell the patient or care giver to store the medication out of the reach of children and to check the package insert (containing printed information about the medication) to see whether it needs to be stored in a refrigerator.

#### **Expiry dates**

Expired medication may become contaminated, which can lead to infection and damage to the eye, or it may become ineffective.

- If the expiry date on the packaging is after today's date, the medication is in-date and is safe to use.
- If the expiry date on the packaging is **before** today's date, the medication has **expired** and must be disposed of.

Expired medication must be disposed of safely, ideally by returning it to the pharmacy. Warn patients who are prescribed medication for long-term or chronic conditions to refill their prescription only when needed. If they purchase several months' worth of medication at once, some of the medication may expire before it can be used.



Talk to patients about their medicines and how to use them. NIGERIA

Medicines that don't need to be refrigerated have to be kept in a cool, dry place, such as a storage cabinet, pouch, box, shelf, or drawer. The kitchen is usually too warm, and any place with exposure to direct sunlight is not appropriate.

Remind patients to replace the cap or lid immediately after use (to avoid contamination) and to keep the package insert in a safe place for the entire duration of treatment, in case they need to refer to it later.

#### Checking medication before use

Encourage patients to check their medication before using it.

- Check the expiry date. Do not use any medicine that has expired. If you cannot see the expiry date, for example, because it has rubbed off, return the medicine to the pharmacy for safe disposal, then renew or refill your prescription.
- Do not use medicine that was initially clear but has now become cloudy, or which has visible particles.
- Check the duration of treatment in the instructions given by the clinician. Stop when you have taken the medicine for long enough, and discard any leftover medicines. Once opened, eye drops can get contaminated over time. So it is important to use the medication as instructed, for the period advised by the physician. Do not save any remnants to use later. Usually, eye drops should be discarded within one month of opening the bottle.
- While administering the drops, you may accidentally touch the tip of the bottle or the dropper, which can cause contamination. It is therefore important not to share your medication with others, as this may spread infection.

#### 3. Administer medication correctly

#### Managing patients' expectations

 Tell patients if the drug they have been prescribed is likely to cause irritation or stinging in the eye. Reassure them that this will only last a few seconds and is not something to worry about.

• Tell patients that, with some eye drops, they may experience a drug taste in the mouth. Reassure them that this is normal and nothing to worry about.

#### **Timing and dosage**

Tell patients to use their drops exactly as prescribed. The timing of eye drops can make a big difference to the success of treatment. Suggest specific times for them to instil their eye medicine, e.g. 7 am and 7 pm for twice-a-day drops. Explain why it is important to take the eye drops at those times; usually because the timing is related to the duration of action of the medication.

Remind patients to apply the number of drops prescribed. If they are prescribed eye drops and eye ointment, they must instil the eye drops first and wait 5–10 minutes before instilling the eye ointment. This will ensure that the correct amount of medicine is absorbed.

#### Instilling the drops or ointment

Demonstrate the steps on page 8 to the patient and the person helping them, and to allow them to practice while still at the clinic.

For **postoperative patients**, it is advisable that someone else, such as a family member or friend, instils the eye medication. This can reduce the risk of infection resulting from accidental contact between the eyelashes and the tip of the bottle dropper or tube, which can easily happen when someone instils eye medication on their own. It is also easier for the person helping to check that only one drop enters the eye at a time.

It is useful to empower **patients with long-term eye conditions**, such as glaucoma, with the skills and confidence needed to instil their own medication.

#### **Tips and support**

Some patients find it extremely difficult to keep their eyes open during the process. The **closed-eye technique** could be useful for them:

- 1 Lie down on a couch or a bed or sit on a chair and recline your head back as far as is comfortable
- 2 Keep your eyelids lightly shut
- 3 Hold the eye drop bottle with your thumb and first two fingers
- 4 Put the other two fingers of your hand on your nose to stabilise your hand
- 5 Without touching the tip of the bottle to your eyelid or face, instil an eye drop in the corner of your eye, near your nose.
- 6 While your head is still tilted back, open your eyes and blink several times until the drop rolls into the eye.

If the bottle feels too small or slippery, suggest to patients that they wrap a paper towel or tissue around it. If this doesn't help, recommend any drug-delivery devices that are available and affordable in your area.

#### **Further challenges**

Some people may continue to struggle, especially if they have anxiety, severe visual impairment, painful or shaky hands, a disability affecting their hands or fingers, or if they don't have the coordination or strength needed to instil their own medication. For these patients, suggest that they ask someone to help them, such as a family member, friend or neighbour, and ask the person to come along to their next appointment, so that the doctor or nurse can train them to instil the medication.

#### **Common mistakes**

This is not limited to patients only; health care workers who are not trained in this skill make these errors too.



#### From the field

## How I advise and support my patients

**Funmi Bankole** is an ophthalmologist working for the ministry of health in Lagos State, Nigeria.

"I routinely advise that my patients get someone to instil the eye medication for them. Even as an ophthalmologist, I sometimes miss when I instil my own eye drops – it is difficult. Having someone instil the patient's eye drops for them ensures that the medication gets into the eye and avoids mistakes that could lead to injury to the eye. This is especially important for postoperative patients."

- 1 Retracting the upper lid, instead of the lower lid. This usually results in the eye drop spilling over the eyeball and onto the patient's cheeks. The quantity of the eye drop that gets into the eye will be very small, so the patient will not get the required dosage.
- 2 **Retracting the lower lid, but instilling more than one drop at a time.** Patients may do this if they are not sure whether the first drop has gone in. This is often the reason that patients say their eye drops run out very quickly.
- 3 **Not waiting 5 minutes between two different eye medications**. The second eye drop formulation may 'wash' the first one out of the eye before it has been absorbed. This is often the reason a physician will not see improvement, even if a patient is instilling their medication.

#### **Troubleshooting**

If patients say they are using their eye drops, but the physician does not see any effect, ask them direct questions about when and how they are using the medication.

- Are they waiting at least 5 minutes before instilling a different eye medication, and instilling just one drop at a time?
- How many times a day are they using their medication?
- Check that they have the correct strength of the medication
- Ask the patient to describe each medicine they are on and when they apply or instil them. If they don't wait long enough between different medicines, they may still have the washout effect and lose the benefit.
- Check how they are storing their medication medicines that require refrigeration will lose their efficacy if not stored in the fridge. So, even if they use the medication as advised, it will not have the desired effect.
- Ask if they have stopped using their medication at any time since their last visit. Unless you ask specifically, they may not volunteer this information.

#### Avoiding eye infections: advice for patients

- If a finger touched a dropper bottle by accident, it is best to discard the medication and buy more. If this is difficult for any reason, *immediately* clean the bottle.
- If the dropper bottle lid or ointment cap falls on the ground, pick it up immediately and clean it using a sterile alcohol swab before putting it back.

#### Reference

1 World report on vision. Geneva: World Health Organization; 2019. CC BY-NC-SA 3.0 IGO.



**Nyawira Mwangi** Deputy Director: Academics, Kenya Medical Training College, Nairobi, Kenya.



**Leah Kenan**Patient Care
Manager: City Eye
Hospital, Nairobi,
Kenya.

## How to use your eye medication

Once you have your medication, what is the procedure you should follow?

#### Before you start

- 1 Assemble the items you need: the medication, clean tissue paper or paper towel, mirror, soap and water, or hand sanitiser (note: hand washing is preferred).
- 2 Read the written instructions on how to use each of the medications. This could be on the bottle, on the package insert, or on a separate sheet given to you at the hospital or pharmacy.
- 3 If using a drop, gel, and/or ointment, use them in this sequence; drop first, then gel, and then the ointment.
- 4 If the medicine is for treating a problem on your eyelid, it should be administered on the eyelid and not in the eye.
- 5 Do not instil medication into an eye that has been injured. Visit the eye clinic for review of the injury as soon as possible.
- 6 If the eye has discharge, clean the eye using sterile cotton wipes dipped in cooled, boiled water or bottled water before instilling the medication.

#### **Preparation**

- 1 Take off your spectacles if you are wearing any.
- 2 Wash your hands with soap and water and dry them using a paper towel. Hand washing is preferred, but if you are in a situation where this is not possible, you can use hand sanitiser instead.
- 3 If you are wearing contact lenses, take them out unless your doctor has told you to leave them in.
- 4 Place a clean tissue or paper towel on the nearest surface
- 5 If using eye drops, shake the bottle gently.
- 6 Remove the cap and place on the tissue or paper towel. Do not touch the tip. Make sure the dropper (or tube) and the cap stay clean.

#### If you are instilling the drops yourself:

- 1 Tilt your head back, open both eyes and look up towards the ceiling. Focus on a specific point on the ceiling. Do not blink or wipe the eye.
- With the thumb and forefinger, pull your lower lid down and outwards to expose the lower conjunctival sac: the pocket where you instil the medication. You can stand in front of a mirror, or ask someone to hold a smaller mirror for you.
- 3 Hold the dropper bottle or tube between the thumb and index finger of your other hand. (If someone is helping you, they can hold the dropper bottle or tube and instil the drops or ointment.)
- 4 Position it so the tip is directly over the eyelid pocket.

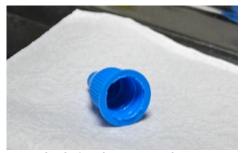


Opening the eye drops. KENYA

- 5 Ensure the tip is not touching the eye, eyelids, or eyelashes; this avoids contaminating the drug.
- 6 Squeeze the bottle or tube gently to instil the eye drop (just one drop) or gel into the pocket (conjunctival sac), as instructed. Avoid letting the medication make contact with the sensitive cornea.

#### **Getting the dosage correct**

- 1 You may feel the cold drop or gel/ointment once it enters the eye, especially if the medication was stored in the refrigerator.
- 2 As long as you feel the medication in your eye or on the edge of the eyelid, you've been successful. You don't need to add more than one eye drop. The drop may spill over onto your cheek; this is okay as long as you felt it hit the surface of your eye.
- 3 If the medicine falls on your face or clothes or floor, but not actually into the eye, try again.
- 4 After instilling the drop, shut the eyelids lightly for a few seconds (up to one minute) while pressing your finger lightly on the inner corner of our eye, nearest your nose. This is known as the canthus and is the location of your tear ducts (visible as small holes). Doing this prevents the medicine draining into your nose, which improves absorption of the medicine where it is needed most in your eye. Try not to blink.
- 5 If any liquid drops leaked out from your closed eyelids, blot around your eyes using a clean tissue or paper towel to remove the excess.
- 6 Repeat the steps with the other eye, if instructed to
- 7 If using more than one type of eye drop, wait for 5–10 minutes between each of the different medications.
- 8 Wash hands with soap and water when done.



Correctly placing the cap on a clean paper towel.



Positioning the patient.



Instilling eye drop in the conjunctival sac.



**Boateng Wiafe**Technical Advisor:
Operation Eyesight
Universal, Accra,
Ghana.



Nisha Jha Professor: Department of Clinical Pharmacology and Therapeutics, KIST Medical College and Teaching Hospital, Lalitpur, Kathmandu, Nepal.



Elmien
Wolvaardt
Editor-in-Chief:
Community Eye Health
Journal, ICEH, LSHTM,
London, UK.



Mohammed Abdull

Chief Consultant/ Associate Professor: Ophthalmology Department, Abubakar Tafawa Balewa University, Bauchi, Nigeria.

"The term 'adherence'

prescription is the result

process between the

of a joint decision-making

patient and the clinician."

recognises that a

## Improving adherence with eye medication: a patient-centred approach to prescribing

Managing infectious eye conditions such as ulcers, or chronic conditions such as glaucoma, requires that patients regularly instil eye medication, often for long periods of time. How can prescribers support patients to do so?

or eye medications to work, they must be used as prescribed and for as long as needed. In chronic diseases, such as glaucoma, this is for life.

There are many challenges when it comes to medication adherence. These include the availability and affordability of the medication, instilling the medication correctly, remembering when to do it, and doing it always, as is the case with long-term or chronic eye conditions.

Clinicians must therefore carefully consider patients' ability to adhere to a medication regimen when deciding how to manage their condition. For example:

- Should we admit the patient with a serious corneal infection, or send them home with eye drops?
- If a patient has glaucoma, should we prescribe eye drops to lower intraocular pressure (IOP), or offer surgery/laser?

#### What is adherence?

We prefer to use of the term 'adherence' instead of 'compliance' when talking about how well a patient is able to follow the medication regimen that was agreed between them and the prescriber/clinician.

The term 'compliance' is associated with the idea that a patient must follow a set of instructions imposed on

them. When health care workers adopt this perspective, patients may be viewed as a passive recipient of health care, and health workers may blame or shame them if they don't use their medication as prescribed.

The term 'adherence', however, recognises that a prescription is the result of a joint decision-making process between the patient and

the clinician. This recognises the patient as an active participant in their own health care (or a co-producer of health) and acknowledges their right to choose as well as their individual circumstances and challenges. When



Giving patients the right medicines starts during the prescribing process. INDIA

something goes wrong, and a patient does not adhere to the prescribed medication regimen, health workers who adopt this perspective can work with patients to explore causes and solutions.

#### **Prescribing to support adherence**

Consider the following aspects when deciding on the best medication regimen for your patients.

- The local availability of the medication, and patients' ability to pay. If it is not available locally or is too expensive, consider an alternative medication or other treatment options such as surgery, if appropriate. If it is not covered by health or medical insurance, or not on the list of medicines approved (or provided) by your country's health service, consider advocating for change (see article on page 11). Generic medications are an important alternative where available as they are often cheaper and as effective as the expensive branded products.
- The complexity of the patient's overall medication regimen. Ask what other medication a patient is taking, particularly long-term medication, and consider any adverse drug interactions that could lead to the patient discontinuing their eye medication. You can also help patients to remember to use their eye medication, e.g., by suggesting that they instil eye drops at the same time of day as they would normally take their long term medication or time the instillation of medication with routine activities they carry out daily, such as prayer times for muslims.
- Support networks. Does the patient have family members or others who can remind them to take their medication, or motivate them to continue when they want to stop? It is always important to counsel a trusted family member, partner or friend on the medications the patient is being given so they

- can help them maintain adherence by reminding them and helping them to instil the medication.
- Patients' physical health. This can include their ability to administer eye medication, for example, if they suffer from arthritis. Can someone else help them? Find out if there are installation aids available locally, which make it easier for patients with conditions such as arthritis to instil their own drops.
- Patients' cognitive health. Patients with cognitive impairments, dementia, or attention deficit disorder may struggle to remember when to use their eye drops and may require support from others or electronic reminders (e.g., by programming mobile phones to remind them of medication times).

#### A note on patient comfort

Stinging sensation or blurring of vision is a common side effect of many eye drops. As this is transient, it is usually better to educate the patient about this possibility and teach them to cope if it is not severe, as changing medication may not be possible, or will be prohibitively expensive. One exception is chlorhexidine, which can be locally manufactured using a buffer solution which reduces stinging sensation (see page 21).

#### **Q&A: Prescribing glaucoma medication**



Abdull

My preferred choice for most of my glaucoma patients is to prescribe a combination drug treatment, used just once or twice a day.

#### Q. Why a combination drug?

**A.** It is better to prescribe as few different types of drops as possible, because the chance of poor adherence increases with the number of medications used. Therefore, if multiple medications are needed, it makes sense to use drug combinations: one eye drop bottle that has two or more active ingredients that work together safely and effectively.

#### Q. Why less often?

**A.** It is always preferable to give patients medications that require as few instillations per day as possible. This is because the chance of poor adherence increases with increasing instillation frequency of the drug. So, an eye drop that is used just once a day is usually better adhered to than one that must be used four times a day. In this respect, it makes sense to use slow-release preparations, if available.

#### **CASE STUDY**



**Boateng Wiafe** Technical Advisor: Operation Eyesight Universal, Calgary, Canada.

## Supporting patients with adherence to glaucoma medication in Ghana

Patients need help in many areas - including advocacy for affordable eye medicines.

n Ghana, as in many other low- or middleincome countries, patients who are prescribed medication for glaucoma often stop using their medicines and only come back when their sight has worsened considerably. It is important, from the beginning, to educate patients about the chronic nature of glaucoma and for them to understand that any treatment is lifelong.

Here are some of the reasons patients have given:

- "I used the eye drops only when I felt the symptoms."
- "I felt better with eye drop treatment. I did not feel the need to use the eye drops all the time, so I use them sometimes."
- "The frequency of use instructed by the ophthalmologist or pharmacist is too much."
- "The price of eye drops is too high, so I do not buy it all the time because my pension is very small."

It is important, from the beginning, to educate patients about the chronic nature of the disease (glaucoma) and for them to understand that any treatment is lifelong. Some patients view the disease to be like malaria, where a stated dose of drug is taken and is sufficient for a cure. They need to understand that this is not the case for glaucoma.



Meeting of a chapter of the Glaucoma Patients Association of Ghana with a guest facilitator. GHANA

The first and most important step in supporting adherence is therefore patient education and counselling about the importance of – and reasons for – adherence. High patient loads in many eye clinics don't allow specialist eye health care providers to spend much time with the patient, so talking to patients about medication and adherence is often done by nurses, allied health personnel, or trained community eye health volunteers.

In Ghana, patients are counselled by community eye health volunteers, who are trained according to the WHO Afro Primary Eye Care training manual (www.afro.who. int/publications/primary-eye-care-training-manual), which has a strong emphasis on health education and counselling, including counselling patients on using their eye medication.

Other strategies we use to support adherence include:

**Involving family members or care givers.** Making sure that family members or care givers understand what the patient must do, and why, really helps to improve adherence to eye medications, particularly those for long-term conditions such as glaucoma. We always advise elderly patients to come with a care giver if possible. The caregiver is also taught how to apply or instil the medication.

**Phone calls.** We keep a register of all our glaucoma patients, and we call them within 2–3 months to ask how things are going with the medication. We also try to help solve any problems they have.

**Counselling and continuous health education in the community.** Peer counselling, via patient groups, is another means to support patients. Clinicians can encourage patients to form associations and share personal experiences with each other. In Ghana, for example, there is an association of patients with glaucoma called the Ghana Glaucoma Patients Association. The GGPA provides education for new patients, invites counsellors

to meetings to address patient concerns, carry out advocacy, and participate in World Glaucoma Week activities to create awareness of glaucoma.

Advocacy for reduction in medication costs. Patients can't be expected to be adherent with medication if the medication is not affordable. In countries with health insurance schemes, it is important to talk to insurance providers and make sure that effective eye medication is included on the list of medicines they cover, or on the national approved list. Another option is to ask for donations from pharmaceutical companies and non-governmental organisations on behalf of those who really need medication but cannot afford to pay for it. Operation Eyesight Universal has set aside funds to support some patients in Ghana who are unable to afford their medication, but this is only a short-term solution. Advocacy is key, and one of the things we are working on right now is advocacy to persuade Ghana's national health insurance agency to add more glaucoma medications to their list.

#### **ADVOCACY**



Junu Shrestha
Policy & Advocacy
Manager:
International Agency
for the Prevention
of Blindness,
London, UK.



May Ho Optometry & Primary Care Adviser: The Fred Hollows Foundation, Melbourne, Australia.



**Jude Stern** Head of Knowledge Management: IAPB, Sydney, Australia.

## Inclusion of eye medication in national health care systems

Advocacy for eye medicines is easier with these helpful resources and guidance.

he World Health Organization (WHO) maintains a model list of essential medicines. The essential medicines include those that satisfy the priority health care needs of a population. The medicines are the most effective, safe, evidence-based available and are comparatively cost-effective. They are intended to be available in health systems at all times. WHO recommends that countries make these medicines available in the appropriate form and dosage, and ensure that they are available, accessible, and affordable to everyone in need. Universal access can only become possible only when medicines are included in a country's essential medicines list and funded by the national health financing system.

The WHO model list of essential medicines includes ophthalmic medicines in section: 14.1 diagnostic agents: ophthalmic medicines; and section 2: ophthalmological preparations. This information needs to be communicated to the policy makers and referred when advocating for universal eye health. The latest list is available here: bit.ly/WHO-em

The WHO's Package of Eye Care Interventions (PECI), launched at the World Health Assembly in 2022, is a set of evidence-based eye care interventions and the resources needed for their implementation. PECI – which includes the list of ophthalmic medicines in the WHO essential medicines list – is designed to support policy makers and technical decision makers to integrate eye care into the health care services system of a country. This tool is an important resource when advocating for the inclusion of essential eye medicines



With so many eye medicines available, the WHO model list provides helpful guidance.

in a national essential medicines list and in health financing benefit packages.

When advocating for eye medicines, also refer to the United Nations' Sustainable Development Goals, target 3.8. This target focuses on achieving universal health coverage, including financial risk protection, access to high quality essential health care services and access to safe, effective, high quality affordable essential medicines and vaccines for all. Without provision for equitable access to essential medicines for eye conditions, achieving universal eye health coverage is not possible.

Access to essential ophthalmic medicines also aligns with the principle of integrated people-centred eye care (IPEC). The IPEC was adopted by the 73rd World Health Assembly resolution in 2020. To know more about advocating for IPEC, check out IAPB's IPEC Advocacy to Action Toolkit. The toolkit includes PowerPoint slides, letter and IPEC policy brief templates that can be adapted and used to approach stakeholders for policy dialogues.

The WHO has also produced guidelines on using the WHO Model List of Essential Medicines to update the national essential medicines list. See https://bit.ly/useWHOem



## Valuing pharmacists as members of the eye team

Pharmacists have extensive knowledge about the ever-increasing number of eye medicines available; their input is vital to protect patients and ensure effective treatment.

harmacists are valuable members of the eye team. They can support the eye care team to make effective, patientcentred decisions by sharing their extensive knowledge about:

- the range of medicines available locally for eye conditions
- the interactions between different medicines
- how to improve adherence, e.g., by suggesting a change in the type of bottle being used, or a change in formulation (e.g., with a preservative-free product to reduce stinging sensation).

The role of the hospital pharmacist as part of a multidisciplinary team is usually understood and accepted. However, the role of the community pharmacist may not be well understood.

In the community setting, the pharmacy is often seen as a simply the location at which patients collect their medication. The community pharmacy is, however, an essential point of contact for primary health care, including primary eye care. Patients come to seek advice about a wide range of conditions and about over-thecounter or prescribed medication.

Community pharmacists play an essential clinical role in assessing the nature of patients' primary concerns (e.g., is it allergic, infective, or acute?) and deciding whether they need to be referred. Pharmacists can also offer support, information, and reassurance to their patients.

#### **Good working relationships**

Effective teamwork between community pharmacists and other members of the eye team is essential to ensure patient safety and improve patient outcomes, so it is therefore important to create opportunities for collaboration and to set up effective communication channels between community pharmacists and the eye team. Here are a few ideas.

#### **Prescription checking**

- Recognise that prescription errors are often picked up by pharmacists, who are specifically trained to do so. Acknowledge that this is in the best interests of both patients and doctors. Acknowledge that this is in the best interests of patients and doctors. Respect pharmacists' role and training.
- Share the eye team's contact details with community pharmacists, so that it is easy and convenient for pharmacists to resolve queries and potential errors.
- When giving patients a prescription to take to the



Every contact between pharmacist and patient is an opportunity to improve patients' eye health. GHANA

pharmacy, it may be helpful to attach a copy of their hospital or discharge notes (containing their diagnosis, the medication they have been prescribed, and the dates of any follow-up appointments). This will make it easier for the pharmacist to detect inconsistencies or prescription errors. (In the UK, patients who leave the hospital receive a 'discharge summary' which is shared with pharmacists via an electronic medical records system; this allows pharmacists to follow up on the prescribing and dispensing of medication for each patient.)

#### Referral and feedback

Set up a referral and feedback mechanism between the eye clinic and community pharmacists.

- Ensure pharmacists have up-to-date information about clinic days and times, so patients don't have the expense of a wasted journey.
- Give feedback to pharmacists who refer patients to you. For example, you can thank them for referring the patient, confirm whether or not they were right to refer them, and offer support or guidance to improve future referrals.
- You could be proactive and give all the community pharmacists in the area a set of referral forms with your hospital or clinic details and space for them to add their contact details, the reason for referral, and to indicate whether or not this is an emergency.
- The clinic administrators can also send the patient's discharge information directly to the pharmacist.

#### **Training**

The multidisciplinary eye team does not stop at the hospital door - it extends out to the community. Some ideas for bringing community pharmacists into closer contact with the hospital-based eye team include the following.

- Offer training sessions for community pharmacists and outreach nurses/eye care workers. Offer sessions on basic eye care, specialist sessions, e.g., eye infections or glaucoma care, or practical sessions such as referral guidelines and procedures
- Invite pharmacists to share their knowledge about the latest eye medications or formulations. This is a great opportunity for learning for all members of the

multidisciplinary eye team to learn about the role of community pharmacists/nurses.

#### Care for long term eye conditions

 For chronic eye conditions such as glaucoma, the community pharmacist may see the patient more often than the ophthalmologist. Sharing the patient's care plan with the pharmacist can help, as every contact they have with the patient is an opportunity for them to support adherence and safety, and to reinforce key messages.

•••••

Pharmacy in eye care is an ever-growing industry, with new drugs and formulations coming onto the market every few months. Pharmacists undergo many years of training, and their input is vital to ensure patient safety and effective treatment. They can advise clinicians about potential interactions, suitability, availability, and alternatives. Therefore, collaborating closely with community pharmacists will help eye care providers to offer effective and safe treatment options in both hospital and community settings.

#### **Further reading**

Waszyk-Nowaczyk M, Guzenda W, Kamasa K, Pawlak K, Bałtruszewicz N, Artyszuk K, Białoszewski A, Merks P. Cooperation between pharmacists and physicians — Whether it was before and is it still ongoing during the pandemic? J Multidiscip Healthc. 2021 Aug 7;14:2101-10.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8357703/

#### **CASE STUDY: GHANA**



Boateng Wiafe Technical Advisor: Operation Eyesight Universal, Accra, Ghana.

## Providing eye care education for pharmacists

Community pharmacies are often the first place people will go to for help with an eye condition, so it makes sense to enhance their knowledge of eye care.

I discussed the following:

**Health promotion** 

• The normal and abnormal eye

the rationale for their management

The practice limitations of pharmacists.

harmacists play an important role in eye care.
Many patients will go to their community pharmacy
to seek over-the-counter or self-care medication
for eye conditions. Some prescribed systemic medications
may also contribute to eye problems (see article on
page 14), so there really is a need to have a very close
relationship between eye care practitioners and
pharmacists.

Community pharmacies are often the first place many patients with eye problems will go to for help, especially in low- and/or middle-income countries, such as Ghana. So it is useful to empower the people who work there with basic knowledge of common eye disorders.

In 2018, I was invited to present at a series of workshops for pharmacists, hosted by Novartis Ghana. We spent time discussing what might bring the patients to pharmacists. These were the most common reasons shared by the pharmacists:

- 1 Red painful eye
- 2 Eye injuries
- 3 Itchy eyes
- 4 Not seeing well, both near and distance
- 5 Glaucoma
- 6 Growths and swellings
- 7 Various childhood conditions.

- For example:
- Counsel people with diabetes about the importance of having regular eye checks, so that any early signs of diabetic retinopathy can be detected.

The signs and symptoms of common eye conditions,

Pharmacists' role is to provide first aid and then refer,

patient presenting with pain in the eye should be

especially for eye injuries. As a rule of thumb, any

referred for further investigation immediately.

Pharmacists also play an important role in health

promotion by providing patient education and counselling. Although pharmacists are not experts in treating eye

conditions, they can give useful advice based on patients'

presenting symptoms and whether they came to purchase

prescription or over-the-counter medicines. Pharmacists

can also explain how the medicines should be used.

- When refilling eye drop prescriptions for patients with glaucoma, ask them to encourage other family members to get their eyes checked
- Encourage parents to take their children for a sight test once a year

General eye messages to help people avoid vision loss and maintain good eyesight can also be delivered by pharmacists – whether in person or via posters and or leaflets. For example<sup>1</sup>:

- Your eyes are an important part of your health
- Have a comprehensive eye examination at least every two years
- Keep your blood sugar levels within a healthy range
- Know your family eye health history
- Eat right to protect your eyes
- Maintain a healthy weight
- Wear protective eye wear and do not leave children to play unsupervised by an adult
- Quit smoking or never start smoking.

#### Reference

1 Centers for Disease Control and Prevention (CDC). Tips to Prevent Vision Loss.

www.cdc.gov/ visionhealth/ risk/tips.htm

## Top tips when treating common eye conditions with over-the-counter medications

- Avoid prescribing steroid drops if someone has a red, painful eye.
   Steroids are prescribed only by the ophthalmologist. For example, if the person has a corneal ulcer, steroids can weaken the immune response, which will worsen the infection. (What other reasons might there be?) Topical steroid drops can cause an increase of intraocular pressure and can lead to secondary, steroid-induced glaucoma. Advise the patient to visit the nearest clinic for further management.
- In case of an injury, never instil or prescribe any eye medication in the affected eye. Refer immediately. This is an emergency.



**Shalinder** Sabherwal Director: Public Health and Projects, Dr Shroff's Charity Eye Hospital Network, New Delhi, India and Research Fellow: London.



Mohamed-Ahmed Research Fellow in Pharmacology and Clinical Trials Management: London School of Hygiene & Tropical Medicine, UK.

## The impact of oral and systemic medications on the eye

Knowing which systemic and oral medications can affect eye health, and how their adverse effects present, can help you to identify and manage patients correctly.



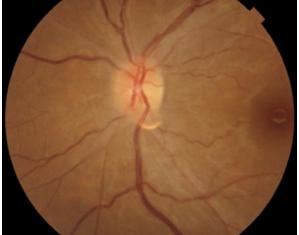


Figure 1 Bilateral toxic optic neuropathy with disc oedema in a 32-year-old female patient with a history of ethambutol intake and on tacrolimus after a renal transplant

variety of oral and systemic medicines can have a harmful effect on the eyes.1 Some of the adverse effects may be dose-related, while others may not be.

Patients may not be aware of the relationship between the medication and their eye condition, and may not think to mention this to you, unless you specifically ask what medicines they are currently taking. They may not remember the name of their condition or the names of the medicine.

It is therefore helpful to be familiar with the different adverse effects of oral or systemic medications, so you can better identify and manage the eye condition the patient presents with. In addition to reporting the adverse reaction via the usual channels, it is advisable to contact the clinician who prescribed the medication so they can consider alternatives.

#### Reporting of adverse drug reactions

There are national adverse drug reporting centres in 153 countries worldwide. Reporting of adverse reactions is mostly voluntary, and is done by health care professionals. At the global level, the World Health Organization Programme for International Drug Monitoring collates the reports from the national centres to ensure timely identification of suspected safety problems. To find out more, including how to set up an adverse drug reporting centre in your country, visit https://bit.ly/DrugWHO.

In addition to eye care professionals, physicians prescribing these drugs must also be made aware of any potential adverse reactions. That would enable them to warn the patients to report early symptoms and to undergo regular eye check-ups wherever indicated. A list of medications which can cause ocular toxicity is given in Table 1.

#### Remember:

- Patients are unlikely to tell you what other medication they are taking, unless you ask.
- Some patients may not remember the name or dosage details, so you may need to check their records, if available.

Some adverse reactions can affect vision and are potentially sight-threatening, while others may not cause loss of vision but can lead to hazy vision or discomfort.

#### **Sight-threatening adverse reactions**

#### Raised intraocular pressure

Patients may present with raised pressures in the eye caused by the intake of the following drugs.

- **Corticosteroids** (such as prednisolone or dexamethasone)<sup>2</sup> are used as long-term medications for some joint disorders, skin diseases, auto-immune disorders and in transplant patients. They are administered by various routes: topically, orally, intravenous, nasally or as injections in joints and can raise intraocular pressure, resulting in secondary glaucoma.
- Antihistamines, beta blockers, antidepressants, antipsychotics and some diuretics can cause angle-closure glaucoma in pre-disposed patients who have shallow anterior chambers. These are drugs with anti-cholinergic effects and are used to treat conditions like urinary incontinence, chronic obstructive pulmonary disorder, allergies, or mental health conditions. This group of medications generally causes pupillary dilation leading to angle closure. Some sulfa-based drugs are also known to cause a similar reaction.<sup>3</sup>

 Topiramate, which is used to treat epilepsy, can cause uveal effusion with very high intraocular pressure. The symptoms include blurred vision, difficulty seeing, and eye pain, and usually happen in the first month of taking the medication.

Patients on these drugs must be monitored for intraocular pressure (IOP) and AC depth. Some patients are 'high responders' and can have significantly increased IOP. In case, corticosteroids cannot be tapered or replaced, IOP must be controlled medically.

#### Cataract

- Corticosteroids. Long-term use of corticosteroids can also lead to posterior sub-capsular cataract. This form of cataract leads to vision-related issues early in its course and may warrant early surgery.
- Some other less-used drugs known to cause cataracts include phenothiazines, used for behavioural disorders and busulfan, an antineoplastic drug.<sup>3</sup>

#### Toxic optic neuropathy

Patients with toxic optic neuropathy may present with bilateral, painless loss of vision (Figure 1). This has been reported with various drugs<sup>4</sup>:

- Ethambutol and isoniazid, which are commonly
  prescribed for tuberculosis in countries where
  tuberculosis is endemic; the risk of toxic optic neuropathy
  is greater in patients who also have renal disease
- Ciprofloxacin and chloramphenicol, both antimicrobial medications
- Antimetabolite medicines used in the treatment of malignancies
- Amiodarone used for arrhythmias
- Amoebicidal medications.

Patients on these drugs must be screened for visual acuity, colour vision, and central vision testing. The majority of these defects can be reversed with timely discontinuation and thus, timely monitoring is essential.

**Retinal haemorrhages and internal ocular bleeding**Bleeding in retinal tissues can lead to sight loss. This may be caused by the following medication:

- **Anticoagulants**<sup>5</sup> used for the prevention of heart disease and stroke
- Antineoplastic drugs used for malignancies.

This can be monitored using blood tests and medication may need to be discontinued in some cases, especially where a minor bleed has already occurred. These drugs can also lead to bleeding during eye surgery and may have to be discontinued prior to some eye surgeries. It is therefore vital that eye surgeons know about patients' usage of such drugs.

#### **Retinal toxicity**

Some drugs can cause damage to one of the layers of the retina (retinal pigment epithelial loss). Unfortunately, some of these patients may already have central visual loss when they present. Retinal toxicity is irreversible, thus early recognition by regular screening, and early discontinuation, is imperative.

- Chloroquine and hydroxychloroquine<sup>6</sup> are antimalarial drugs. They are more likely to cause retinal toxicity when used for longer periods of time, either to treat other inflammatory conditions of the joints or – more recently – as prophylaxes for COVID-19.
- **Thioridazine** and **chlorpromazine** are phenothiazines used for the treatment of anxiety, depression, and other behavioural disorders.

Check patients' vision using manual or automated visual field testing or spectral-domain optical coherence tomography (if available). Multifocal electroretinogram (mfERG), if available, can be used for objective corroboration with visual fields.

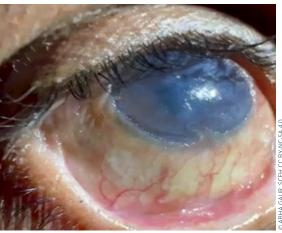
#### Other potentially sight-threatening adverse reactions to medication

- Central serous retinopathy. Corticosteroids can cause central serous retinopathy (CSR) in some patients.
- Intracranial hypertension. Tetracycline, which is used long-term for conditions like rosacea can lead to intracranial hypertension or pseudotumor cerebri, which may lead to optic atrophy if left untreated.
- **Stevens-Johnson syndrome.** This is a relatively rare drug reaction, characterised by skin and mucosal involvement. It has an acute phase with severe pseudomembranous conjunctivitis (Figure 2) and a chronic phase with extreme dry eye and cicatricial features (Figure 3) and can be caused by common drugs such as painkillers or cold and flu medication. Over one hundred drugs have been associated with this syndrome. In the acute phase, treatment includes management of pain, topical and systemic anti-inflammatory medications, and antibiotics to control infection.

Figure 2 A 12-year-old child with acute Stevens-Johnson Syndrome. INDIA



**Figure 3** A 27-year-old man with sequelae of Stevens-Johnson Syndrome. **INDIA** 



#### Non-sight-threatening adverse reactions

These side effects may cause discomfort but may not be directly sight threatening.

#### **Corneal vortex keratopathy**

This is a whorl-like pattern on the cornea and is generally not visually significant. These are mostly caused by amiodarone, a drug used to treat cardiac arrhythmia. Some of the other drugs which can cause this are chloroquine, hydroxychloroquine, indomethacin, and tamoxifen.<sup>6</sup> The dosages need to be reduced only if the corneal condition causes extreme discomfort or blurring of vision.

#### Floppy iris syndrome

Another specific drug-induced condition is one in which there is an effect on the constrictor muscles of the iris, leading to poor dilation and floppy iris during cataract surgery. This is generally caused by alpha-1 blockers like tamsulosin (used for prostatic hypertrophy).8 These technical issues during cataract surgery can be prevented if adequate precautions are taken, so patient's usage of these drugs must be known to the surgeon. It is sometimes recommended that tamsulosin be stopped two weeks before surgery, but it may be more important that the surgeon is made aware that the patient is taking one of these drugs.

#### Dry eye

A diverse group of orally administered medications have been linked with dry eye. These include antihypertensive drugs such as atenolol and acebutolol, antihistamines such as cetirizine, antivirals such as aciclovir, analgesics (e.g., ibuprofen) and some antidepressants, antipsychotic, and anti-arrhythmic medications (see Table 1).3 Other conditions, like epiphora, blepharitis, and conjunctivitis can also be side effects of some anti-malignancy drugs that are administered systematically.9

Table 1 Drugs that can cause ocular toxicity.1

Oral drugs	Use	Possible ocular side effects	
Topiramate	Treatment of epilepsy	Secondary angle-closure glaucoma, visual field defects, oculogyric crisis, uveitis	
Gabapentin	Treatment of epilepsy	Nystagmus, diplopia and visual field defects	
Vigabatrin	Treatment of epilepsy	Visual field constriction, optic nerve atrophy	
Bisphosphonates (e.g., alendronate sodium,, risedronate, zoledronic acid	Treatment and prevetion of osteoporosis	Inflammation in the eye leads to conjunctivitis, episcleritis, scleritis, keratitis or uveitis, or corneal and scleral melting	
Chloroquine-based drugs (chloroquine, hydroxychloroquine	Treatment of malaria	Maculopathy, peripheral retinopathy	
Corticosteroids (e.g., prednisolone, dexamethasone)	Anti-inflammatory	Corticosteroid-induced raised intraocular pressure can lead to glaucoma, acceleration of cataract progression, and subcapsular cataracts.	
Ethambutol	Treatment of tuberculosis	Optic neuropathy characterised by bilateral central visual loss, decreased colour vision, central visual field defects, and (eventually) optic atrophy	
Fingolimod	Treatment of multiple sclerosis	Macular oedema, blurred vision, distortion, and impaired reading vision	
Isotretinoin and vitamin A	Acne and vitamin A deficiency treatment, respectively	Blepharoconjunctivitis, chalazia, corneal opacities, dry eyes, retinopathy	
Mitogen-activated protein kinase kinase enzyme (MEK) inhibitors, e.g., crizotinib	Treatment of advanced non-small cell lung cancer	Decreased visual acuity, visual field defects, dry eye symptoms, eyelid abnormalities, retinal vein occlusion, and retinopathy	
Pentosan polysulfate	Relief of bladder pain and discomfort related to interstitial cystitis	Maculopathy, retinal pigment epithelial lesions	
Phenothiazines	Treatment of schizophrenia and other psychotic disorders	Abnormal pigmentation of the eyelids, conjunctiva and cornea. Corneal epithelial changes (high dose). Corneal oedema (rare).	
Phosphodiesterase type 5 inhibitors, e.g., sildenafil, tadalafil	Treatment of erectile dysfunction	Persistent blurred vision, non-arteritic ischaemic optic neuropathy, cilioretinal artery occlusion, or central serous chorioretinopathy.	
Tamoxifen	Treatment of breast cancer	Intraretinal crystalline deposits, macular oedema, and punctate retinal pigmentary changes.	
Tetracyclines, e.g., doxycycline, tetracycline	Antibiotics	Nausea, vomiting, and morning headaches may be symptoms of idiopathic intracranial hypertension which can lead to permanent loss of vision	
Thiazolidinediones, e.g., glitazones, pioglitazone, rosiglitazone	Management of type 2 diabetes mellitus	Macular oedema	

#### References

- 1 Ahmad R Mehta H The ocular adverse effects of oral drugs. Australian Prescriber. 2021:44(4):129-36.
- 2 Tripathi RC, Parapuram SK, Tripathi BJ, Zhong Y, Chalam KV. Corticosteroids and glaucoma risk. Drugs Aging. 1999;15(6):439-50.
- 3 Li J, Tripathi RC, Tripathi BJ. Drug-induced ocular disorders. Drug Saf. 2008;31(2):127-41.
- 4 Grzybowski A. Zülsdorff M. Wilhelm H, Tonagel F. Toxic optic neuropathies: an updated review. Acta Ophthalmol. 2015;93(5):402-410.
- 5 Shieh W-S, Sridhar J, Hong BK, Maguire JI, Rahimy E, Shahlaee A, et al. Ophthalmic complications associated with direct oral anticoagulant medications. Semin Ophthalmol. 2017;32(5):614-9.
- 6 Tehrani R, Ostrowski RA, Hariman R, Jay WM. Ocular toxicity of hydroxychloroquine. Semin Ophthalmol [Internet]. 2008;23(3):201-9.
- 7 Gomes JÁP, Milhomens Filho IAP. latrogenic corneal diseases or conditions. Exp Eye Res. 2021;203:108376.
- 8 Chang DF, Osher RH, Wang L, Koch DD. Prospective multicenter evaluation of cataract surgery in patients taking tamsulosin (Flomax). Ophthalmology. 2007;114:957-64.
- 9 Omoti AE, Omoti CE. Ocular toxicity of systemic anticancer chemotherapy. Pharm Pract (Granada). 2006;4(2):55-9.



Abeer H A
Mohamed-Ahmed
Research Fellow in
Pharmacology and
Clinical Trials
Management:
London School of
Hygiene & Tropical
Medicine, UK.



Dan Kuguminkiriza Pharmacist: Eye Drop Production Unit, Ruharo Eye Centre, Ruharu Mission Hospital, Mbarara, Uganda.

## Local production of eye drops in the hospital or pharmacy setting: considerations and safety tips

Some eye drops can be locally prepared to improve patients' access to medication. Here is what you will need to consider.

ost eye medicines for topical use are prepared by pharmaceutical companies using special automated mixing and filling machines. However, some eye drops can be prepared in a pharmacy setting in a hospital. There are several reasons<sup>1,2</sup>:

- Patients may be unable to afford commercially available eye drops, and locally prepared eye drops are often more affordable.
- Eye drops may be unavailable due to manufacturing shortages or because a product is discontinued; this can be overcome by preparing eye drops in hospital or pharmacy settings.
- Combinations of drugs that are not commercially available might be prepared locally; for example, eye drops combining anaesthetic and dilating agents.
- In some cases, the drug might be available in a formulation or strength that is not intended for ophthalmic use and needs to be adapted. One example is the preparation of amphotericin B eye drops from intravenous solution.
- Some eye drops need to be patient specific and therefore prepared individually; for example, autologous serum eye drops that are compounded using the patient's own serum.

The main ingredients for preparation of topical ophthalmic eye drops usually include:

- The active pharmaceutical ingredient (API), either as powder or as a concentrated solution.
- A solvent: either sterile water or buffer solution
- A preservative: an antimicrobial agent added to the eye drops to prevent microbial contamination of the liquid during use.

In general, eye drops are prepared in one of two ways:

- 1 Dissolving the active pharmaceutical ingredient/ preservative (in powder form) in a suitable vehicle (either sterile water or a buffer solution).
- 2 Diluting a concentrated solution of the active pharmaceutical ingredient using sterile water or buffer solution.

There are several important elements that should be considered when preparing eye drops.



Eye drops preparation in Ruharo Mission Hospital. UGANDA

#### 1. Sterilisation

Eye drops must be sterilised to ensure they are free of microbial contamination. The method of sterilisation depends on the stability of the drug at high temperature. The options are:

- Autoclaving. Autoclaving is used to sterilise pharmaceutical products (solutions, suspensions, powder) which are stable at high temperature<sup>1</sup>. Eye drops in the final packaging (filled and sealed eye drop bottles) are usually sterilised at the end of the production process (terminal sterilisation) using autoclaving (saturated steam at 121–132°C) for 15 minutes to kill microorganisms.<sup>1</sup>
- **Filter sterilisation.** If the drug is not stable at high temperatures, eye drops in solution form can be sterilised by filtration through a 0.22 µm filter into a sterile final container. This method is called filter sterilisation and it should be conducted under aseptic conditions using a laminar flow cabinet. Filter sterilisation is not suitable for use with eye drops in suspension form, as the 0.22 µm filter will remove the finely dispersed drug particles and make the eye drops ineffective.

#### 2. Inherent toxicity of the drug

The pharmacist should check the drug-specific data safety document (the drug safety data sheet) to get information about the toxicity of the drug. The pharmacist should adhere to the established guidelines for handling each drug.<sup>3</sup>

#### 3. Removal of particulates

All compounded eye drop solutions should be filtered using a 5 µm filter to remove any visible particulate matter.<sup>2</sup> This can be done using glass sintered filters or polypropylene fibre filters under minimal pressure. This pressure can be generated using either a hand-held or foot suction pump.

#### 4. pH

The pH of eye drops is important for drug solubility and for the stability of some drugs.<sup>3</sup> For optimal ocular comfort, it should be similar to the pH of natural tears (pH 7.4). However, sometimes it is not feasible to prepare eye drops with pH 7.4 due to drug stability or solubility issues. The acceptable pH range for eye drops is in the range of 6.5–7.8 to ensure patient comfort. A more acidic or alkaline pH can induce tearing, discomfort and pain.<sup>4,5</sup> A suitable buffer can be used to control and maintain the pH of the eye drops during storage, such as citrate or acetate buffer.

#### 5. Tonicity

Tonicity is defined as the ability of water to enter or exit through a membrane (e.g. cell membrane), via osmosis. The tonicity of the eye drops depends on the concentration of dissolved solutes (e.g. buffer salts and the active pharmaceurical ingredient). Ideally, the tonicity of eye drops should be similar to natural tears, which have a tonicity equal to 0.9% saline. In general, a range of 0.5–2% saline tonicity is well tolerated by most patients. Hypertonic solution (higher than the tonicity of 0.9% saline) can cause tearing. This increase in tear flow reduces the concentration of the drug in the eye, leading to reduction of drug efficacy.<sup>3,6</sup> Hypotonic solutions (lower than tonicity of 0.9% saline) do not cause tearing, but might cause ocular discomfort.<sup>3,6</sup>

#### 6. Preservatives

The addition of preservatives to multi-dose eye drops is crucial to prevent secondary contamination during storage and application.<sup>7</sup> Several studies have reported severe ocular infections related to preservative-free ophthalmic preparations prepared in local pharmacy settings.<sup>7,8</sup>

Selection of suitable and safe preservatives is important.<sup>7</sup> Eye drops that are intended for long-term use, e.g. for chronic eye conditions, should ideally be preservative free. These medications are not suitable for local production as they require highly specialised production facilities and special packaging, e.g., single-use packaging that avoids contamination during use. **Note:** some drugs, such as chlorhexidine, do not require the addition of preservative when prepared in the form of eye drops, because the drug itself acts as a preservative.

#### 7. Stability

The drug should be stable in the selected solvent (e.g., buffer solution or sterile water). The stability of eye drops prepared within hospitals or pharmacies should be assessed according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines to determine the optimum storage conditions and drug shelf life. The shelf life (expiration date) should be determined based on the documented stability data and the potential for microbial contamination. The chemical stability of the active pharmaceutical ingredient(s), preservatives, other excipients (non-active pharmaceutical ingredients), and packaging should be considered when assessing the overall stability of the final ophthalmic product.

## 8. Packaging and storage of the final product

The final container/packaging should be suitable for ophthalmic use and should not compromise the stability and efficacy of the topical preparation.<sup>2</sup>

Many compounded ophthalmic eye drops can be packaged in either sterile plastic bottles with integrated dropper tips (a standard eye drop container) or in glass bottles with separate droppers. The stability of some eye drops might be affected by the type of eye drops container used; for example, cyclosporine is absorbed by polyvinyl chloride, a polymer used in some plastic dropper bottles.

#### Safety tips

According to the American Society of Health-System Pharmacists (ASHP) Pharmacy-Prepared Ophthalmic Products guidelines, the following should be considered when preparing eye drops in the pharmacy/hospital setting<sup>2</sup>:

- Adhere to aseptic techniques and sterilisation procedures to ensure that eye drops are sterile (free from microbial contamination).
- Ask a colleague to double check your calculations of the amount of each ingredient that will be used in preparing the eye drops; this will minimise error.
- All ingredients should be mixed in sterile, empty containers. When using more than one container for compounding a sterile

- preparation, each container should be labelled.
- Compounding should be performed in a certified laminar airflow hood or, for a cytotoxic or hazardous product, inside a biological safety cabinet.
- The compounded eye drops should be clearly labelled according to the hospital or pharmacy policy for prescription labelling. The label should contain information about the concentrations of active ingredients and preservatives and information about storage conditions, handling requirements, and expiration dates.
- The storage instructions on the label should be clear. For example, room temperature means 15–25 °C, refrigerator means 2–8 °C, and freezer means below 0°C.

#### References

- Sandle T. Sterile
   Ophthalmic Preparations and Contamination
   Control. Journal of GXP Compliance. 2014;13(3).
- 2. Alghamdi AE, Al Qahtani AY, Sanjab M, Alyahya MK. Guidelines of The American Society of Health-System Pharmacists (ASHP) on Pharmacy-Prepared Ophthalmic Products. Extemporaneous Ophthalmic Preparations. Switzerland: Springer Nature Switzerland AG; 2020. p. 21-3.
- 3. Awwad S, Mohamed Ahmed AHA, Sharma G, Heng JS, Khaw PT, Brocchini S, et al. Principles of pharmacology in the eye. Br J Pharmacol. 2017;174(23):4205-23.
- 4. Freiberg JC, Hedengran A, Heegaard S, Petrovski G, Jacobsen J, Cvenkel B, et al. An Evaluation of the Physicochemical Properties of Preservative-Free 0.005% (w/v) Latanoprost Ophthalmic Solutions, and the Impact on In Vitro Human Conjunctival Goblet Cell Survival. J Clin Med. 2022;11(11).
- 5. Garcia-Valldecabres M, López-Alemany A, Refojo MF. pH stability of ophthalmic solutions. Optometry. 2004;75(3):161-8.
- 6. Fletcher E, Brennan N. The Effect Of Solution Tonicity On The Eye. Clinical and Experimental Optometry. 1993;76(1):17-21.
- 7. Tu EY. Balancing antimicrobial efficacy and toxicity of currently available topical ophthalmic preservatives. Saudi J Ophthalmol. 2014;28(3):182-7.
- 8. Goldberg RA, Flynn HW, Jr., Miller D, Gonzalez S, Isom RF. Streptococcus endophthalmitis outbreak after intravitreal injection of bevacizumab: one-year outcomes and investigative results. Ophthalmology. 2013;120(7):1448-53.
- ICH. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. https://database.ich. org/sites/default/ files/Q1F\_Stability\_ Guideline\_WHO\_2018. pdf Annex 10.



Dan Kuguminkiriza Pharmacist: Eye Drop Production Unit, Ruharo Eye Centre, Ruharu Mission Hospital, Mbarara, Uganda.



Abeer H A
Mohamed-Ahmed
Research Fellow in
Pharmacology and
Clinical Trials
Management:
London School of
Hygiene & Tropical
Medicine, UK.

## Ruharo Mission Hospital eye drop production facility

After just four years, this hospital-based facility in Uganda has become licenced to produce ten different eye medicines, making them more affordable for patients and easier to obtain.

uharo Eye Care Centre is part of Ruharo Mission Hospital in Uganda and offers care for patients suffering from a wide range of eye diseases, such as cataract, glaucoma, and corneal infections.

In order to provide high quality eye drops for common eye

conditions, at a price people can afford, an eye drop production unit was set up in 2019.

The unit began as a small laboratory that prepared eye drops in small batches, starting with 50 units at a time. A bucket system was used for sterilisation. As demand increased, the unit began producing 100 units per batch and eventually this grew to 400 units per batch.

However, meeting the demand and sourcing ingredients soon became a challenge. The unit decided to apply for a manufacturing permit, which would enable them to import their own raw materials and packaging. During the application process, Uganda's National Drug Authority, which regulates manufacturing permits, inspected the facility and stated that a more sterile working environment would be needed before they could approve a permit.

This required a significant financial investment, of around US \$30,000. The eye unit could cover the cost using the funds it had accumulated over the preceding two years. Since the unit was already providing 90% of the eye medicines used in Ruharo Eye Centre at that time, the long-term benefits made this a worthwhile investment.

The eye drop production facility is now fully licenced by the Ugandan National Drug Authority to produce terminally sterilised eye drops. It produces more than ten different eye medicines and diagnostics, including fluorescein, cycloplegics, mydriatics, antibiotics, anti-inflammatories, and specific treatments for glaucoma, microbial keratitis, allergic conjunctivitis, and dry eyes.









**Figure 1** Ruharo Mission Hospital's eye drop production facility. Clockwise from top left: the external building, the clean production room, the quality control room, and the raw material preparation room. Adapted from¹.

Most raw materials are imported from China; cleaning agents are sourced in Uganda, and packaging materials are imported from the UK and China.

The eye drop production facility acts an independent unit under the general management of the hospital. The facility is run by four technical and two non-technical staff members:

- a chemist, who is also the production officer
- a pharmaceutical scientist and a laboratory scientist, who act as quality control officers
- a pharmacist, who is also the supervisor and quality assurance officer.

The cost of production per bottle is approximately US \$0.50, and units are released for an average cost of US \$1.70 per unit. The revenue generated is either reinvested into the facility or used to support the running costs of the hospital.

The biggest consumer of the locally manufactured eye drops is Ruharo Eye Centre clinic, which uses 60% of the eye drops produced. Other eye hospitals in the region also order from the unit, and steps are being taken to acquire a national distributor.

#### The facility

The eye drop production unit consists of a clean room (class C), a sterilisation room, and a quality control room (see Figure 1). The clean room is equipped with an airflow-controlled environment HVAC (heating, ventilation, and air conditioning) system, which includes a 0.4 µm filter capable of removing dust and particulates from the air. The HVAC system provides clean air and temperature control within the facility.

**Figure 2** Ruharo Mission Hospital eye drop production facility **a.** Static pass-box for UV sterilisation of items. **b.** Laminar air flow booth to weigh ingredients and materials under aseptic conditions.





## Equipment and critical processes used in Ruharo eye drops production unit

The equipment used and the process are described below:

#### 1. Storage of raw materials

Raw materials are stored in a room in which both temperature and relative humidity are controlled and monitored using a hygrometer/thermometer digital reader.

#### 2. Weighing raw materials

- Raw materials are transferred from the storage room to the weighing room passing through a static pass-box with UV lamp (Figure 2). The UV lamp sterilises the raw materials, packaging and powder containers by irradiation.
- The weighing room has an extraction fan which creates negative air pressure in the room, causing the entry of fresh air through the 10-micron filters.
- Weighing is carried out in sterile conditions provided by a laminar air flow booth with HEPA filters (Figure 2), using a digital balance with a range from 0.01 g to 5,000 g.

#### 3. Transfer of raw materials from the weighing room to the clean room

Weighed powders and other raw materials are passed through a second pass box (with UV irradiation) to the Class C clean room (Figure 2).

#### 4. The clean room

The cleanliness of this room maintained by:

- Cleaning all surfaces, including floor, walls, and ceiling, with antiseptic solution, prepared according to the manufacturer's instructions.
- Spraying all surfaces using 70% ethanol prior to start of production.
- An HVAC system, which maintains the purity of air circulated in the room.

#### 5. Mixing and filtration of eye drop solutions

Mixing and filtration of eye drop solutions is done using a batch processing unit (Figure 3), comprising:

- A 20 litre capacity mixing tank with motored rotating pedals and water jacket which can be heated or cooled depending on required temperatures for mixing.
- Filtration chamber with 5 micron filter and suction pump to provide pressure for flow of filtrate.

**Figure 3** Ruharo Mission Hospital eye drop production facility **a.** Batch processing unit. **b.** Manual capping machine.





 A 20 litre capacity holding tank in which the filtrate is stored before dispensing into primary packaging glass bottles.

#### 6. Filling eye drop solutions into bottles

- The eye drop solutions are dispensed in a specific volume into bottles using a metered 'pressmatic' dispenser.
- The caps and droppers (pipettes) are then pressgripped onto the bottles using a manual capping machine (Figure 3).

#### 7. Sterilisation

Capped eye drop bottles are placed onto autoclave trays and transferred to the autoclave machines for terminal steam sterilisation (Figure 4).

#### 8. Visual examination of the filled eye drop bottles

Visual inspection for leakage, particles, and clarity of eye drop solutions is done with the help of white light against both white and black backgrounds.

#### 9. Quality control

A random selection of eye drop bottles from each batch is subjected to quality control analysis to assess pH, sterility, and drug content. Some of these analytical processes are in-house, whilst others are subcontracted to Mbarara University.

Products which pass the quality control tests are dispatched to the hospital stores and issued to the dispensary.

#### Reference

1 Picken CAR, Brocchini S, Burton MJ, Blundell-Hunter G, Kuguminkiriza D, Kaur H, et al. Local Ugandan Production of Stable 0.2% Chlorhexidine Eye Drops. Transl Vis Sci Technol. 2023;12(1):27.

**Figure 4** Automated autoclaves used in Ruharo Mission Hospital eye drop production facility.



RUHARU MISS



## Abeer H A Mohamed-Ahmed Research Fellow in Pharmacology and Clinical Trials Management: London School of Hygiene & Tropical Medicine, UK.



Christina A R Picken Research Fellow: School of Pharmacy, University College London, UK.



Dan Kuguminkiriza Pharmacist: Eye Drop Production Unit, Ruharo Eye Centre, Ruharu Mission Hospital, Mbarara, Uganda.

## How to prepare chlorhexidine eye drops

Preparing chlorhexidine eye drops in a buffered acetate solution can help to improve patient comfort; here is how.



Figure 1 a. pH meter to measure the pH of buffer solutions and eye drops. b. Conductivity meter for water analysis.

hlorhexidine eye drops can be used for the treatment of fungal keratitis as a second line therapy where natamycin eye drops are not available.<sup>1,2</sup> Chlorhexidine eye drops typically used in the clinic are prepared by diluting a concentrated solution of chlorhexidine using sterile water without controlling for pH or tonicity<sup>3</sup> and are reported to cause patient discomfort (stinging sensation). The pH and tonicity of chlorhexidine eye drops can be controlled by using acetate buffer (141.4 mM, pH 6.75) to improve patient tolerance/comfort.3 Controlling the pH of the chlorhexidine eye drops can also improve the stability of the drops: chlorhexidine eye drops prepared using acetate buffer (141.4 mM, pH 6.75) were shown to have stable pH (~6.75) and drug concentration at 40 degrees Celsius for 21 months.3

In this article, we share the protocol we used for the local preparation of acetate-buffered chlorhexidine eye drops at Ruharo Mission Hospital's eye drop production facility in Uganda.<sup>3</sup> This protocol will produce 2,000 ml of buffered chlorhexidine eye drops, which is enough to fill 200 bottles containing 10 ml eye drop solution per bottle.

#### Facilities/space

Ideally, eye drops should be prepared in a certified clean room equipped with an air control system complete with a filter that removes dust and other potential sources of contamination. A laminar flow cabinet can be used for local preparation of eye drops in the certified clean room or in a normal room with air conditioning. In the absence of a clean room/air control system and laminar flow cabinet, we recommend you take the following measures:

- Use a room that is dedicated for eye drop production only, with air conditioning and a double door entry system to avoid air disturbance, minimising contamination (airlock system).
- Less than 2 hours before each eye drop production session, clean the floors and surfaces of the production room (or the room and airlock) by wiping with distilled water and an antiseptic (such as Dettol or cetrimide 0.5% w/v), followed by spraying with 75% ethanol.
   Follow the same cleaning procedure after using the production room.

 Once surfaces are dry, spray production surfaces with 70% ethanol to further reduce the presence of microbes.

#### What you will need

#### Ingredients

- Chlorhexidine digluconate solution (20% w/v)
- Sodium acetate
- Acetic acid (20% v/v)
- Sodium hydroxide (10 M)
- Freshly distilled water

#### Equipment

- Volumetric flasks (20 ml, 2000 ml) + stopper
- Measuring cylinders (10 ml and 1000 ml).
- Pipette (1 ml) and pipette tips
- Metal jug
- Filtration system (filter funnel, 5 µm filter membrane, filter clamp/support, vacuum pump, conical flask/bottle)
- Syringes (with 10 ml graduations)
- Amber glass eye drop 10 ml bottles
- Bottle lids with or without dropper (Use HDPE or PP)
- Class II or electronic balance
- pH meter (Figure 1a)
- Conductivity meter (Figure 1b)
- · Autoclave or steam bath
- Labels

#### Method

- Wash hands before entering airlock room.
- Wear protective clothes (production gown, gloves, boots, hair net or head cap, mask and eye protection) in the airlock room.
- Ensure the production room and equipment are clean.
- Rinse all containers three times using distilled water, by filling them to the top and then discarding the water. Then sterilise using an autoclave or water bath.
- Wash and sterilise the empty eye drop bottles at 121°C for 15 minutes.
- Wash the filtration system by filling it with hot distilled water, flushing it using a vacuum pump, and discarding the water. Repeat this three times. Then backwash the filtering system three times by reversing the filtering head and filling the filtration system with hot distilled water using a vacuum pump.
- Collect 2,500 ml freshly distilled water.

#### Prepare acetate buffer

 Dissolve sodium acetate (23.198 g) in 2,000 ml of freshly distilled water in a large mixing beaker. Then add 4.46 ml of acetic acid (20% v/v) to the sodium acetate solution and mix the solution.

Figure 2 Volumetric flask

(2,000 ml) for dilution of

chlorhexidine 20% w/v to

0.2% w/v by addition of

acetate buffer.

Using a portable pH meter, adjust the pH by dropwise addition of sodium hydroxide (10 M), adding approximately 1.938 ml to reach pH 6.75.

#### Prepare chlorhexidine 0.2% (2,000 ml batches)

- Measure 20 ml of 20% chlorhexidine using 20 ml volumetric flask.
- Transfer 20 ml of chlorhexidine (20%) into 2,000 ml volumetric flask (Figure 2). Rinse the 20 ml flask three times with buffer and transfer the rinsed solution into the 2,000 ml volumetric flask (Figure 2).
- Fill the 2,000 ml volumetric flask containing the chlorhexidine solution to 2,000 ml mark with the acetate buffer.
- Place lid on flask, invert flask and shake to stir.
- Assemble filter membrane onto filter bed and secure with clamp/support. Pass solution through filter

into rinsed conical flask/bottle using pump vacuum.

• Transfer filtrate into a jug or a bottle.

#### **Dispensing**

- Lay out the empty eye drop bottles on a clean surface.
- Dispense the eye drop solution using syringes or measuring cylinder or pressmatic pump dispenser

in 10 ml portions into the amber glass eye drop bottles.

Seal the bottles with tightly fitted lids (either polypropylene plastic dropper or HDPE cap) (Figure 3a) using a manual capping machine (Figure 3b) or by hand if a capping machine is not available.

#### Sterilisation

Sterilise the bottles using a water steam bath at 100°C (at atmospheric pressure) for 30 minutes. If an autoclave is available, sterilise by autoclaving at 121°C for 15 minutes.

#### Visual inspection and quality control testing

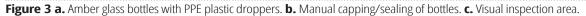
- Do a visual inspection in bright light. Shake the eye drop bottle and observe the contents against white and black backgrounds to check for visible particles or debris (Figure 3C).
- Check lids cannot be tightened further.
- Check correct fill volume.
- Check for the presence of leaks by turning the filled eye drop bottles upside down.
- Send the first, middle, and last bottles of each batch for sterility testing and recall the batch immediately if any samples are positive for microorganisms.
- Check drug concentration, ideally using high performance liquid chromatography (HPLC). In case HPLC is not available, use a UV spectrophotometer to check the concentration of chlorhexidine in the eye drop solution.

#### Labelling

Allow the sterilised bottles to stand for at least 12 hours to cool and dry before labelling.

The label should contain:

- Name and strength of the drug: chlorhexidine digluconate 0.2% w/v.
- Composition of the eye drops: pH buffered in acetate buffer, no added preservative.
- Storage conditions: store below or at 25°C and protect from light. Once opened, store at 4°C and use within 7 days.
- Shelf life of unopened sterile bottles: 24 months at 25°C.









#### References

- 1 Arunga S, Mbarak T, Ebong A, et al. Chlorhexidine gluconate 0.2% as a treatment for recalcitrant fungal keratitis in Uganda: a pilot study. BMJ Open Ophthalmol 2021; 6(1): e000698.
- 2 Hoffman JJ, Yadav R, Sanyam SD, et al. Topical Chlorhexidine 0.2% versus Topical Natamycin 5% for the Treatment of Fungal Keratitis in Nepal: A Randomized Controlled Noninferiority Trial. Ophthalmology 2022; 129(5): 530-41.
- 3 Picken CAR, Brocchini S, Burton MJ, et al. Local Ugandan Production of Stable 0.2% Chlorhexidine Eye Drops. Transl Vis Sci Technol 2023; 12(1):27.
- 4 World Health Organisation. The local small-scale production of eye drops. Geneva, 2002.



Oteng-Gyimah Ophthalmologist: Sunyani SDA Hospital, Sunyani, Ghana.



Assistant Clinical Professor: International Centre for Eye Health, London School of Hygiene & Tropical Medicine and Consultant Ophthalmologist: Mid Cheshire NHS Hospitals, UK.

### Picture quiz

This quiz is based on a real patient. Read the information, then use your knowledge and clinical skills to answer the questions. We suggest you use a separate sheet of paper, then compare your answers with those provided at the bottom of the page.

A 14-year-old girl presented with painful swelling of her right lower eyelid. The swelling started seven days earlier, after the eyelid was scratched by a tree branch. There was no other past ocular or medical history. The vision in the left eye was 6/6 unaided, but vision in the right eye could not be assessed because of the swelling.

Figure 1 Swelling of the right eyelid in a 14-year-old. GHANA

#### Learning outcome

By the end of this quiz, you will be able to reflect on your clinical approach and strategy for managing cases, as well as other unusual ocular presentations.

#### **Question 1**

What are your initial thoughts on seeing this presentation?

#### **Ouestion 2**

What could you consider in your differential diagnosis?

#### **Question 3**

Are there any other examination findings or tests you would like to do?

#### **Ouestion 4**

Based on your diagnosis, what immediate treatment would you start for this patient?

- a. Monitor over the next few days to see how she progresses
- **b.** Antibiotic eye ointment
- **c.** Urgent incision and drainage
  - **d.** Start with oral antibiotics and ask her to come back in three days.

When considering the differential diagnosis of any presentation it can be helpful to use a mnemonic (a memory aid). One example of this is the phrase 'Vitamin C & D.' Each letter in this phrase corresponds to the name of a type of disease process that should be considered when assessing an unusual presentation, such as the one in this quiz. (Note: there can be more than one condition for some of the letters.)

- Vascular disease (i.e., to do with blood vessels and blood supply)
- Ī Infectious or inflammatory

Т

Α

Metabolic M

Ī N

C Congenital (present from birth)

&

Degenerative

#### **ANSWERS**

l's altogether. Remember that there are two T's and five D: degenerative

C: congenital (present from birth) и: neopiastic (i.e., tumours or cancer) (genetic in origin) idiopathic (cause unknown), or inherited I: iatrogenic (caused by treatment),

M: metabolic A: autoimmune or allergy T: traumatic or toxic I: infectious or inflammatory vessels and blood supply) V: vascular disease (i.e., to do with blood

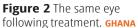
to the following: 5. The letters in Vitamin C & D correspond treat the infection.

suripiotics should also be used to help will need to be drained. A course of systemic will be very tender). A large amount of pus incision site (given very slowly, as the area be done using local anaesthetic over the requires incision and drainage. This would right lower lid. An abscess of this size 4. c. This child has a large abscess of the

future infections. that treatment can be initiated to prevent intections; a test may be indicated in order ре шоле іікеіў то делеіор зелеге растегізі деізу. ілоге тлаг реоріе іічіпв мітп ніч тау and treatment should be initiated without this stage as this is most likely an infection rests; they are probably not necessary at would depend on the availability of these back behind the eyeball. However, this the swelling, such as whether it extends useful to gain further information about imaging scan (e.g., CT or MRI) might be

a raised white cell count. Some form of infection include a raised temperature and Other symptoms which would suggest an would be consistent with an infection. front of the ear and under the jaw, as this lymph glands (lymphadenopathy), e.g., in 3. It would be helpful to look for swollen

develop this rapidly or look like this. however, they would not be expected to haemangiomas, can cause lid swelling; rapidly). Vascular disease, such as Merkel cell tumours can develop more slowly, over weeks to months (although but these would usually develop more 2. Lid swelling can be caused by tumours, most likely to be some sort of infection. some trauma, which makes the diagnosis been there for 7 days. It also occurred after painful. The history is important: it has only lid, which looks likely to be tense and very 1. There is a very large swelling of the lower







**Angelia Sanders** Chair: International Coalition for Trachoma Control, Atlanta, USA.



PI Hooper Vice Chair: International Coalition for Trachoma Control, Atlanta, USA.



Scott McPherson Immediate Past Chair: International Coalition for Trachoma Control, USA.



Tim Jesudason Special Projects and Campaign Partnerships: International Coalition for Trachoma Control, London, UK.

## Improving the distribution and uptake of medicines: lessons from the global trachoma programme

Access to, and uptake of, safe and effective medicine is a pillar of the World **Health Organization** (WHO)-endorsed SAFE strategy to eliminate trachoma as a public health problem.

cale-up of the SAFE strategy (surgery, antibiotics, facial cleanliness, environmental improvement), including the distribution of more than one billion doses of donated Zithromax® since 1999,¹ has

contributed to a 92% reduction in the number of people at risk of trachoma<sup>2</sup> and the validation of 17 countries as having eliminated trachoma as a public health problem since 2002.3

As the global trachoma programme has matured, several lessons have been learned that have enabled countries to increase antibiotic coverage to effectively reduce transmission in the community and reduce the re-emergence of infection.

#### **Lesson 1: Supportive supervision**

Supervision of community health workers and community drug distributors (CDD) is essential to ensure that optimal coverage is achieved, medicines are distributed appropriately and safely, and strategies for further performance improvement are identified.

Across the global trachoma programme, supervisors receive training according to the International Coalition for Trachoma Control preferred practice manual, titled Supportive Supervision for Mass Drug Administration with Zithromax®.

After receiving training, supervisors play an important role in trachoma teams, providing support, troubleshooting challenges experienced by CDDs, and gathering information on any cases of severe adverse events after taking the medicine.

Supervisors are also responsible for the evaluation of individual CDD performance through a supportive supervision framework, which means evaluation is conducted in order to improve the performance of the individual and that of the team. Supportive supervisors should have strong communications skills, be a team builder, and serve as a mentor.



A mother administers azithromycin (Zithromax®) as a powder for oral suspension (POS) to her child. ZAMBIA

#### **Lesson 2: Review programme data**

The global trachoma programme regularly emphasises the power of data for improving programming. This includes carrying out systematic assessments of mass drug administration (MDA) campaigns to ensure high quality performance. All MDA campaigns are advised to collect and analyse:

- 1 Inventory results and accuracy
- 2 Coverage rates, based on districts' distribution numbers
- Coverage rates, based on districts' reported leftover inventory
- 4 Coverage rates, based on leftover physical inventory counting.

Some programmes may also consider coverage surveys after MDA or use intra-process monitoring tools such as the Supervisory Coverage Tool to confirm reported data.

#### **Lesson 3: Patient safety**

Global health programmes have an obligation not only to provide benefits to populations, but also to minimise harm to individuals. Zithromax® is pharmacologically safe; however, protocols must be in place to ensure prompt investigation, management, and reporting of serious adverse events, such as incidents of choking.

Ensuring that MDA programmes are implemented safely is essential to build trust with communities and sustain high MDA coverage. However, MDA safety ultimately depends on the quality of the interaction between CDDs and the person taking the medicine (or in the case of young children, the child's parent or guardian). CDDs must follow treatment guidelines and be adequately trained, prepared, and able to effectively communicate with parents and children.



The International Trachoma Initiative's Zithromax® Management Guide⁴ provides recommendations that national trachoma programmes can implement to improve patient safety. Furthermore, lessons to improve patient safety from trachoma and eye health programmes could inform other disease programmes that benefit from Zithromax®, including typhoid and yaws programmes.

#### Conclusion

More than two decades of coordination and partnership across the global trachoma programme has facilitated the sharing of lessons and experiences, thereby enabling strategies to be refined to improve coverage rates and ensuring that trachoma interventions are implemented effectively, efficiently, and safely.

Notably, in 2021, more than 64 million people<sup>2</sup> were reported to have received antibiotics for trachoma globally, despite ongoing challenges associated

with COVID-19. Moreover, the proportion of treated districts achieving coverage of over 80% (a benchmark for acceptable coverage rates), was more than 80% globally.

Going forward, the trachoma community is continuing to share lessons to ensure that high coverage is achieved equitably. In particular, tailored strategies are being adopted so that special populations, including refugees, internally displaced persons, indigenous and nomadic populations, and people with disabilities, are not left behind within trachoma programmes. The lessons learned and documented by the trachoma community, including supportive supervision, monitoring and evaluation, and patient safety, will be essential for achieving high coverage both for trachoma and other NTDs amenable to preventive chemotherapy, to accelerate progress towards the global NTD road map targets, and to ensure that no one is left behind.

#### References

- Pfizer and International Trachoma Initiative Deliver One Billionth Zithromax® Dose Toward Trachoma Elimination by 2030. 30 January 2023. Available from: https://bit.ly/3lgTBN0
- 2 Weekly epidemiological record. 5 August 2022. World Health Organization. Available from: https://bit.ly/308UJpD
- 3 Global Health Observatory data repository. World Health Organization. 28 April 2023. Available from: https://bit.ly/3MuTAYh
- 4 International Trachoma Initiative. Zithromax® Management Guide. 2019. Available from: www.trachoma.org/zithromax-management-guide