The ROYAL COLLEGE of OPHTHALMOLOGISTS

Ophthalmic Services Guidance

Ophthalmic Pathology

March 2024

Review Date: Mar 2027

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Contents

1. What is ophthalmic pathology?

Ophthalmic pathology is a laboratory-based discipline which provides an essential service to ophthalmologists and related professionals by providing a diagnostic opinion on samples taken from patients. It is a subspecialty of cellular pathology (including histopathology and cytopathology), with much of its methodology based around light microscopic examination of glass slides on which are mounted sections of tissue, or fluid preparations derived from the patient samples. Staining methods including histochemistry and immunohistochemistry highlight salient features and aid in diagnosis. In some cases, especially in oncology, ancillary studies (eg molecular and/or genetics studies) are also needed.

For the clinician, the "result" of an ophthalmic pathology specimen is typically a written report. It usually concludes with the reporting pathologist's opinion on what the diagnosis is or, in less clear-cut cases, suggestions as to possible diagnoses and what could be done (by the ophthalmologist or pathologist or another party such as a geneticist) to achieve more clarity. For cancer diagnoses, reports should include items such as tumour size, structures involved and completeness of excision. The Royal College of Pathologist publishes datasets for the more common tumours to help standardise reporting[1].

2. Where is ocular pathology provided?

Reports on ophthalmic pathology specimens are provided either by consultant histopathologists and advanced practitioners who specialise fully in ophthalmic pathology, or by consultant histopathologists and neuropathologists who have a special interest in ophthalmic pathology as part of a broader diagnostic repertoire. Both groups of pathologists belong to the British Association for Ophthalmic Pathology (BAOP), and they all work within the structure of their own laboratories. There are some differences between the two groups in the provision of services described below.

In organisational terms, ophthalmic pathology services are provided through histopathology laboratories, with most dedicated ophthalmic pathology services being part of larger histopathology laboratories within hospitals. In England, ophthalmic pathology is nationally designated as a "highly specialised service" (all such services are listed at https://www.england.nhs.uk/publication/nhs-providers-of-highly-specialised-services/). Central funding is provided to four ophthalmic pathology services based in Liverpool, Manchester, Sheffield and London. These laboratories make up the National Specialist Ophthalmic Pathology Service (NSOPS), where the full-time specialists in ophthalmic pathology are based. NHS specimens from England may be submitted to any of the NSOPS laboratories for examination (either primary reporting or second opinion) without charge to the referring organisation. There is a similar arrangement in Scotland.

Non-NSOPS BAOP members include pathologists who have eye pathology as a special interest, but who also have other areas of practice. NSOPS laboratories do not charge for NHS referrals, but non-NSOPS pathologists provide a more locally based service with tighter clinicopathological integration and responsiveness to local needs, in addition to having access to input from the centrally funded laboratories if desired.

3. Who should report ophthalmic pathology specimens?

Guidance provided by the Royal College of Pathologists states that pathologists reporting ophthalmic pathology specimens should participate in an appropriate external quality assurance (EQA) scheme[2]. EQA participants receive a set of scheme-specific diagnostic cases twice a year for which they submit their responses (diagnoses) to the scheme organiser. Their responses are then scored against those of their peers, the other participants. Pathologists are expected to participate in schemes relevant to their area(s) of practice. For ophthalmic pathology, this is the Ophthalmic Pathology National EQA Scheme. NSOPS and BAOP pathologists and other Ophthalmic Pathology EQA Scheme participants are encouraged to attend the annual BAOP meeting, where the cases from the year's scheme are discussed.

For certain types of tissue, it may be appropriate for the specimen to be reported by a pathologist with a different but related area of specialist pathology (who participates in the relevant EQA scheme), such as dermatopathology or neuropathology. Reporting of specimens by pathologists with the appropriate specialist knowledge, skills and experience is good clinical practice and reduces risk of misdiagnosis as well as allowing the specialist pathologist to maintain and enhance their level of expertise. Additionally, it facilitates training for future specialists.

4. Why should ophthalmologists send tissue to the laboratory?

It is not necessary for the ophthalmologist to send all tissue removed from every patient who has surgery. The major risk of discarding tissue is of missing a significant diagnosis (e.g. malignancy, epithelial downgrowth or sympathetic endophthalmitis), but it may be equally as valuable to know that removed tissue was histologically innocuous if the patient develops a subsequent lesion at the same site.

5. What specimens should ophthalmologists send?

The table below lays out which surgically removed material should be submitted for histological/cytological examination based on current UK clinical practice. These recommendations may be amended/updated in future as other diagnostic and treatment modalities evolve.

Specimens/surgery	What can be discarded	What to send
Small lid biopsy	• First occurrence of a chalazion in a patient age >40 years • First or second occurrence of a chalazion in a patient age <40 years • Excess skin removed at blepharoplasty • Normal tissue removed during cosmetic procedure	**All** other material including recurrent chalazia (except as previously stated)
Full thickness eyelid	Normal tissue removed during lid shortening, ectropion or entropion procedures	**All** other material
Conjunctiva		**All** material should be sent including pterygia and pingueculae
Cornea		**All** material should be sent including Descemet membranes
Trabecular meshwork	It is not necessary to send tissue removed at trabeculectomy	If there is a research interest, material may be sent by local agreement
Iris, ciliary body, choroid	Peripheral iridectomy tissue from glaucoma or cataract surgery	**All** other material
Lens	It is not necessary to send material removed at cataract surgery	If there is a research interest, material may be sent by local agreement
Vitreous	It is not necessary to send intravitreal blood or opacities (e.g. asteroid hyalosis)	Send material when there is suspicion of inflammatory disease (after bacterial samples have been taken) or malignancy (e.g. lymphoma)
Epiretinal or subretinal membrane	It is not necessary to send these unless there is clinical concern e.g. malignancy	If there is a research interest, material may be sent by local agreement

Evisceration and enucleation		**All** of these should be sent for examination. There is a small but appreciable risk of there being an occult malignancy
Orbital biopsy	It is not necessary to send normal soft tissue or bone removed during orbital decompression or squint surgery	**All** other tissue removed at surgery should be sent
Lacrimal gland		**All** removed tissues should be sent for examination
Lacrimal sac	It is not necessary to send bone removed during DCR	Lacrimal sac excisions should be sent for examination
Orbital exenteration		**All** of these should be sent for examination
Cytology		Impression cytology of the conjunctiva and cornea, and fine needle aspiration cytology of periocular or intraocular masses should be sent for examination. For aspirates of intraocular fluids see vitreous (above)

Note: *This is not a prescriptive list. In any case where the surgeon has a clinical concern or question it is appropriate to send tissue for examination with a low threshold. Obviously, tissue taken for the purpose of histological/cytological diagnosis, such as a temporal artery biopsy, should be submitted for examination, even if it does not fall into one of the categories covered in the table.*

Ophthalmologists are encouraged to discuss with their local BAOP pathologist or an NSOPS ophthalmic pathologist cases where there is uncertainty about whether/what to submit for examination.

6. Practical points

Communication

Communication with the laboratory is key. If there is clinical urgency, if the clinician is unsure how to handle a particular type of specimen, or if there may be a need for non-routine handling of the specimen (such as fresh material or electron microscopy), the laboratory should be contacted in advance.

Request forms

Histopathology/cytology request forms vary between hospitals, but include standard information fields. It is therefore acceptable for the ophthalmologist to use a request form available locally, even if the specimen is to be submitted to a laboratory elsewhere.

The request form should be completed fully including the following:

- Patient details: Surname, forename, date of birth, hospital number, NHS number
- Clinician details and hospital location. A telephone number is useful if clarification is needed, or if there is a need for urgency
- Date specimen taken
- High risk status
- Specimen type (e.g. fine-needle aspirate, incisional vs. excisional biopsies, etc.)
- Specimen location and tissue of origin, including specimen orientation if relevant
- Relevant clinical information

It is useful if the surgeon indicates whether the intention is for complete excision of the lesion, or whether the biopsy is diagnostic (e.g. for planning surgical or non-surgical subsequent treatment). In the former case, the pathologist will explicitly assess margin involvement, but in the latter this may not be relevant.

It is also helpful for the surgeon to state the precise anatomical location of the specimen on the request form. This allows correlation with any previous specimens or with future persistent or recurrent lesions.

Fixation and containers

Patient identification and specimen details should be completed on each specimen pot submitted. Multiple specimens from the same patient should be placed in different individually labelled containers to avoid confusion. Unless agreed otherwise in advance (see "Unfixed specimens" below), specimens should be fixed in 10% neutral buffered formalin. **This includes suspected sebaceous carcinoma specimens which do not need to be submitted fresh.** The volume of fixative (and therefore size of specimen pot) should be appropriate to the size of the specimen. As a rule of thumb, 10x the specimen volume of formalin is sufficient for adequate fixation.

Specimen packaging and transport

Specimens which are not dealt with by the ophthalmologist's hospital laboratory service will usually be sent to the examining laboratory by post or courier. Packaging of diagnostic specimens (usually classified as Category B biological substances) must conform with the UN3373 and P650 packaging instruction[3]. Further information is available from the postal service or courier selected. It is recommended that arrangements are implemented (e.g. phone or email) to ensure confirmation of receipt by the laboratory. It may be easier for

specimens to be sent via the ophthalmologist's local laboratory rather than directly from the ophthalmology department.

Unfixed specimens

Rarely, it is appropriate to submit unfixed material for examination, e.g. for frozen section examination or immunofluorescence. These specimens should only be submitted following prior arrangement with the laboratory including contact details of the responsible clinician, so that any late or non-arrival of the specimen may be notified to the clinician. Specimens must be delivered without delay to allow handling in a timely fashion. Conjunctival specimens for immunofluorescence may be stabilised for transport in Michel's medium.

Note: High Risk specimens, i.e. those in ACDP Group 3 or above (e.g. Hepatitis B, tuberculosis[4]) pose a health hazard to laboratory, administrative and transport staff. They should never be submitted unfixed.

Rapid processing specimens

Many histopathology laboratories provide a service for intraoperative diagnosis (frozen section) and/or rapid paraffin processing (for delayed reconstruction). These services are provided by local arrangement, and ophthalmologists should discuss their requirements with their chosen laboratory.

Turnaround times

The Royal College of Pathologists Key Assurance Indicators document recommends that anticipated turnaround times be included in agreements between laboratories and service users, without mandating specific targets[5].

Research

Sometimes the ophthalmologist wishes to sample ocular tissue for research. If the tissue is also potentially of diagnostic significance, it is recommended that the ophthalmologist communicates with the pathologist who will be handling the specimen for diagnostic purposes, even if the pathologist is not involved in the research project.

Awareness of errors

As previously stated, the histopathology report provides the pathologist's opinion on the submitted specimen. There is potential for mistakes to occur at any point of the specimen's pathway, including misidentification of the patient or specimen, technical malfunctions, and errors in diagnosis by the pathologist. If the clinical impression and pathology report do not "fit" with each other, it is better for the ophthalmologist to discuss this with the pathologist sooner rather than later.

7. References

1. 1. Royal College of Pathologists. Cancer Datasets and Tissue Pathways https://www.rcpath.org/profession/guidelines/cancer-datasets-and-tissue-pathways.html (accessed 16/2/24)
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4. 4. Advisory Committee on Dangerous Pathogens. The Approved List of biological agents. https://www.hse.gov.uk/pubns/misc208.pdf accessed 4/3/24
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