

D12/S(HSS)/b

**2013/14 NHS STANDARD CONTRACT
FOR OPHTHALMIC PATHOLOGY SERVICE (ALL AGES)**

PARTICULARS, SCHEDULE 2 – THE SERVICES, A – SERVICE SPECIFICATION

Service Specification No.	D12/S(HSS)/b
Service	Ophthalmic pathology service (All Ages)
Commissioner Lead	
Provider Lead	
Period	12 months
Date of Review	

1. Population Needs

1.1 National/local context and evidence base

Ophthalmic pathology represents a ‘microcosm’ of general histopathology and is informed by specialist knowledge of the anatomy of the eye, the diseases that affect it and the wide range of surgical interventions used. The diseases seen therefore cover a remarkably wide range of conditions.

For many conditions, for instance where management of the condition depends on an accurate diagnosis, the role of ophthalmic pathology is so evident that specific studies designed to demonstrate the importance would be unethical. The following summarises some specific areas where the role of diagnostic ophthalmic pathology has been defined.

2. Scope

2.1 Aims and objectives of service

The overall aim of the service is to ensure excellence in the provision of a national service that delivers full access to high quality expert specialist ophthalmic pathology reporting from anywhere in the country. The service can be accessed by ophthalmologists or by histopathologists and deals with specimens from patients of all ages.

In designating the service it is identified that the four centers ensure expert diagnostic ophthalmic pathology, facilitate succession planning in this small specialty, and provide improved opportunities for teaching, research and development.

The service was developed following discussions with the Royal Colleges of Ophthalmologists and Pathologists in recognition of the difficulties in local trust or university resourcing of such a highly specialised service and the benefits of creating a cohesive national service.

Ophthalmic pathology is an integrated national service, provided by clinical and academic ophthalmic pathologists. It provides diagnostic and management advice for the clinical management of a number of conditions of the eye following examination by an Ophthalmologist. The service runs alongside the ocular oncology services in Royal Liverpool & Broad Green University Hospitals NHS Trust, Liverpool, Institute of Ophthalmology, University College London, London, and Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield. National ophthalmic pathology services set up in Liverpool, London, Central Manchester University Hospitals NHS Foundation Trust, Manchester and Sheffield by NHS England from the National Specialist Ophthalmic Pathology Service (NSOPS).

The service includes:

- expert and rapid diagnostic reporting for the ocular oncology services
- expert and rapid diagnostic reporting for the clinical management of a number of conditions involving the eye and the ocular adnexa (including eyelids)
- provision of diagnostic reporting of intraocular biopsies, such as vitreous and chorioretinal biopsies
- provision of diagnostic reporting of ocular cytology specimens (including impression cytology and in some centres fine needle aspirates)
- provision of (or access to) complementary diagnostic studies (e.g. immunofluorescence, electron microscopy, microbiology, PCR, cytogenetic studies).

Description of the disease/condition

A. Intraocular tumours

Uveal melanoma

For ophthalmic pathology services uveal melanomas, with an incidence of six per million per year, are a particularly important condition. They affect both sexes in equal numbers. The age at presentation peaks at 60 years. Without timely treatment, these tumours cause loss of vision and eventually an inflamed, painful and unsightly eye. Despite successful ocular treatment, about 50% of patients develop metastatic disease, which almost always involves the liver and which is almost invariably fatal within a year of the onset of symptoms. Metastatic disease occurs almost exclusively in patients whose tumour shows mutations known as monosomy 3 and polysomy 8.

Ocular treatment is aimed at conserving a useful eye, if possible, while preventing metastatic spread to other parts of the body. In most centres, the first choice of treatment is brachytherapy administered with a radioactive plaque containing ruthenium-106 or iodine-125. When such therapy is unlikely to succeed, patients may be treatable with proton beam radiotherapy. Another possible form of radiotherapy is stereotactic radiotherapy, using a Leksell Gamma Knife or linear accelerator (LINAC).

Some tumours are considered unsuitable for radiotherapy, because of their large size or proximity to the optic nerve, and these may be treatable by trans-retinal local resection (endoresection) or trans-scleral resection. Trans-scleral resection requires specialist surgical expertise and facilities for profound hypotensive anaesthesia. Endoresection is controversial because of concerns about iatrogenic tumour dissemination around the eye. Therefore such excision may be reserved for patients who have had prior radiotherapy.

Transpupillary thermotherapy involves heating the tumour by a few degrees for about one minute, by means of an infra-red, diode laser beam. It is used for very small choroidal melanomas.

Enucleation (i.e. removal of the eye) is performed when the chances of conserving vision and a comfortable eye are unacceptable, for example, if the tumour is very large or involves the optic nerve). The ophthalmic pathologist confirms the diagnosis, looks for histological risk factors, facilitates or in some instances carries out molecular diagnosis and assesses extent of disease, particularly along the draining (vortex) veins at the back of the eye.

Metastatic disease

Intraocular metastases arise mostly from breast and lung cancers. Accurate diagnosis is challenging and many are mis-diagnosed as melanoma prior to the patient being assessed at the specialist ocular oncology centre. In many patients, the diagnosis is confirmed by biopsy, which is usually performed in an operating theatre under local anaesthesia.

Metastases usually respond to a small dose of external beam radiotherapy, which can usually be administered at the patient's local hospital. Asymptomatic metastases may be observed without treatment. If the patient is about to receive chemotherapy then ocular treatment is withheld in case the choroidal metastases regress with such chemotherapy.

Intraocular lymphoma and other malignant tumours

Intraocular lymphomas are rare; they comprise vitreo-retinal lymphomas and uveal lymphomas. Vitreo-retinal lymphomas are highly-malignant B-cell lymphomas, and usually involve the brain with a fatal outcome within a few years of diagnosis. Most uveal lymphomas are indolent, with a good prognosis for survival. Treatment is with low-dose radiotherapy, with intraocular methotrexate injections for recurrent

vitreoretinal lymphoma. With vitreoretinal lymphoma, there is a trend towards administration of systemic chemotherapy instead of radiotherapy, in the hope of delaying or preventing brain disease, and in the hope of reducing dementia, one of the main side effects of radiotherapy.

Vitreous and/or chorioretinal biopsy provide an important and especially challenging role in the diagnosis of and management of intraocular lymphoma with both cytological and molecular techniques being of value.

Intraocular adenocarcinomas are very rare and tend to be locally invasive and destructive with little metastatic potential. Another rare intraocular malignant tumours is malignant medulloepithelioma.

Retinoblastoma

Retinoblastoma is the most common primary intraocular tumour of childhood, and arises from the sensory retina. The incidence of retinoblastoma is 1/18,000 live births or approx. 11 cases/million children under 7 years. There are two forms of retinoblastoma: an inherited autosomal dominant type, which constitutes 30-40% of the cases, and a non-inheritable sporadic form, which constitute the remaining 60-70%. One third of heritable cases result from the inheritance of a mutation of the retinoblastoma gene, located on 13q14.1-q14.2. The remaining two thirds are caused by new germline mutations that were not present in the parents but that can be transmitted to future offspring. Heritable retinoblastomas may be bilateral or multiple in one eye. These patients are also at risk of developing trilateral retinoblastoma – i.e. bilateral retinoblastoma as well as involvement of the pineal gland.

As well as in assisting in diagnosis (rarely intraocular biopsies or cytology specimens, more frequently enucleation specimens) ophthalmic pathology is critical in assessing extent of disease as treatment differs when there is significant involvement of the choroid or extension of tumour into or beyond the optic nerve head.

Benign Intraocular Tumours

Choroidal naevi are common intraocular tumours, affecting about 10% of the population. Most are easily diagnosed as such and ignored. Patients are referred to an oncology centre only if the naevus is atypical and bulky so that differentiation from melanoma cannot be made with certainty. These patients require life-long surveillance, with examination every 4-6 months initially, then once every year or so.

Melanocytoma is a rare type of naevus, which can undergo malignant transformation to melanoma. Congenital ocular melanocytosis is a birth-mark consisting of an over-population of melanocytes (i.e., pigment cells) in and around the eye. This condition predisposes to intraocular melanoma so that patients require life-long surveillance.

Choroidal haemangiomas are rare. They tend to develop near the macula and optic

nerve, causing retinal detachment, with loss of vision and, in some cases, the development of a painful eye. Most are mistaken for melanoma or metastasis. Treatment is with photodynamic therapy whereby a 'cold' infra-red laser beam is used to activate a drug that is injected into the arm a few minutes before.

Other benign intraocular tumours include: choroidal osteomas, choroidal neurilemmomas and cysts, all of which are rare and sight-threatening. Most patients require some form of ocular treatment. Retinal haemangioblastoma can occur alone or as part of von Hippel Lindau syndrome, which causes brain tumours as well as cancers of the kidneys and other parts of the body. Apart from ocular treatment, it is necessary to exclude systemic disease by performing scans and other investigations and by genetic tests. Surveillance needs to be life-long.

The key role of the ophthalmic pathologist in these conditions is one of diagnosis.

B. Non-neoplastic intra-ocular disease

The range of conditions that can affect the eye and that may give rise to an ophthalmic pathology specimen is colossal. The following gives an overview, without seeking to be comprehensive but by category of clinical context.

Differential diagnosis of intraocular tumour mass

Retinal and subretinal haemorrhages, including those arising in the context of disciform scarring in age-related macular degeneration and those arising in patients with diabetic retinopathy can resemble an intraocular melanoma.

Vaso-proliferative tumour or massive retinal gliosis can present as an intraocular mass that mimics a malignant tumour but in fact represents an abnormal, self-limiting reactive process. Ophthalmic pathology can be critical in making the diagnosis. Most respond to photodynamic therapy, but some large tumours require plaque radiotherapy.

Tuberculosis and other infections or infestations can also present as an intraocular neoplasm.

Rarely, developmental abnormalities of the eye can mimic retinoblastoma and/or make it impossible to visualise the back of the eye. In these circumstances it is sometimes appropriate to remove the eye. Diseases diagnosed in this context include primary hyperplastic primary vitreous, Coats' disease, familial exudative vitreoretinopathy and Norrie's disease.

Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a birthmark consisting of a black spot under the retina. This can very rarely give rise to adenocarcinoma.

Differential diagnosis of malignant lymphoma

Chronic intraocular inflammation (uveitis) can be impossible to distinguish from intraocular lymphoma and cytological or histological examination of intraocular specimens can be of great value to the clinician. Non-neoplastic conditions that can be diagnosed this way include a wide range of autoimmune disorders, infections such as toxoplasmosis and viral retinitis.

Removal of a painful blind eye and evisceration specimens

Many conditions lead to an eye that is completely blind and painful (and sometimes disfiguring) and where the patient will benefit from removal and the eye and its replacement with an artificial eye. Longstanding glaucoma is just one, albeit relatively common disorder where end-stage disease is manifest in this way. In many instances it is not possible to see precisely what is going on in the eye and it is important to exclude covert malignancy. Occasionally, the diagnosis made in the removed eye may have an impact on management of optimal visual outcome in the fellow eye. In some circumstances (particular after trauma or multiple intraocular operations) the damaged eye can set up an immune reaction that is capable of threatening vision in the remaining eye. Ophthalmic pathology has a role in ascertaining whether or not there is evidence of this process, known as sympathetic ophthalmia, in the eye that has been removed.

Increasingly, rather than removing the eye, the front of the eye and the intraocular contents (lens, ciliary body, retina etc) are removed instead. The outer white coat of the eye (sclera) is left in situ and a prosthesis fitted to the remaining 'shell'.

Inevitably, the normal anatomical structures within the eye are disordered in these specimens and a deep understanding of the anatomy and pathology of the eye is of great value in achieving optimal interpretation.

Removal of a phthisical eye

Some eyes lose their internal pressure and shrink, often with internal bone formation and distortion of the cornea. It may be very difficult to provide insights into the nature of the underlying disorder but it is critical that these eyes are examined to ensure, again, that there is no hidden malignancy.

C. Corneal disease

The unique properties of the cornea, which lead to its transparency in health and a wide range of genetic so-called dystrophies, make for a remarkable range of pathologies distinct from those found at other sites or, if similar, with potentially very different clinical consequences. The ophthalmic pathologist's expertise in this area is most important.

Corneal inflammation

Infection is an important cause of corneal inflammation and the ophthalmic pathologist plays an important role in diagnosis. The critical role of the cornea in

allowing visual information to reach the retina means that corneal biopsies are of necessity very small and great care is required in handling these tiny specimens. Infections range from a variety of bacterial causes, through fungi to important and cornea-specific conditions such as *Acanthamoeba keratitis* as well as emerging/exotic infectious agents such as microsporidia. As well as helping in diagnosis the ophthalmic pathologist can assist in management by clarifying whether or not organisms appear to have been completely cleared when a disease cornea is transplanted.

Corneal 'melting', where the connective tissue stroma of the cornea essentially dissolves away can occur in both infective and non-infective inflammatory states including in the context of rheumatoid arthritis. The ophthalmic pathologist works with clinical colleagues to reach an accurate diagnosis.

Corneal transplantation is the commonest transplantation procedure carried out in the NHS and ophthalmic pathologists examine the host tissue when a new donor cornea is transplanted to replace a failed graft.

Corneal dystrophies and degenerations

There is a wide range of epithelial, subepithelial, stromal and endothelial dystrophies and even with current advances in genetics the ophthalmic pathologist can define characteristics of the disease that are important in making a diagnosis. There are

other degenerative disorders such as keratoconus where ophthalmic pathologists routinely confirm the clinical diagnosis.

D. Conjunctival disease

Tumours

Conjunctival melanomas are rare, with an incidence of about 1 per ten million per year. They occur in two forms: melanoma in situ (otherwise known as primary acquired melanosis [PAM] with atypia) and invasive melanoma, which can be nodular, diffuse or mixed. These tumours tend to invade the orbit and the eye and to metastasize to regional lymph nodes and systemically. Melanoma in situ requires biopsy to be distinguished from benign melanosis (i.e., PAM without atypia). Some centres also advocate sentinel node biopsy in high risk patients. The overall survival is about 70% at ten years, being much worse if the caruncle is involved (i.e., the fleshy lump in the inner corner of the conjunctiva).

Melanomas tend to be treated by local excision of any nodules, with adjunctive radiotherapy in some cases and topical chemotherapy if there is extensive, superficial disease. Many patients with conjunctival melanoma are referred to an oncology centre only after undergoing biopsy or local excision at their local hospital and in these patients the prognosis may be worse, because of incomplete excision or iatrogenic seeding.

Other malignant conjunctival carcinomas include squamous cell carcinoma (and related pre-invasive conditions) and sebaceous gland carcinoma, both of which are relatively rare in the UK. These are treated in a similar way to conjunctival melanoma. Sebaceous gland carcinoma, apart from potentially showing aggressive invasive behaviour, is well known to spread along the conjunctiva continuously or as skip lesions (with portions of normal conjunctiva in between) which requires multiple mapping conjunctival biopsies. Depending on results of biopsies and staging the treatment ranges between local resection and ocular/orbital exenteration.

Conjunctival rhabdomyosarcoma occurs especially in children, presents with a recent onset (few weeks), and is rapidly growing and potentially life threatening if not diagnosed and treated promptly.

Benign conjunctival tumours include papilloma (often human papillomavirus (HPV) associated), haemangioma, oncocytoma (usually caruncular), naevi.

Lymphoproliferative tumours of the conjunctiva and other ocular adnexal structures include the malignant lymphomas and the benign reactive lymphoid hyperplasias. The most common lymphomas occurring in this site are the B-Non Hodgkin lymphomas (B-NHL), with the most frequent subtype being the extranodal marginal zone B-cell lymphoma (also known as MALT lymphomas). These are low-grade B-cell lymphomas, which can usually be treated with a combination of excision and low-dose radiotherapy. Other lymphoma subtypes occurring in the conjunctiva (and ocular adnexa) include the follicular lymphomas, diffuse large B-cell lymphomas, and the mantle cell lymphoma.

Non-neoplastic conjunctival disorders

Non-neoplastic conjunctival conditions include cysts, conjunctivitis (infectious or non-infectious), granulomatous inflammation, and autoimmune conditions (e.g. ocular cicatricial pemphigoid). The latter is sight threatening due to exaggerated conjunctival lid scarring with consequent conjunctival/corneal exposure. Biopsy with immunofluorescence analysis is necessary to establish the diagnosis.

A particular challenge is the rapid pace of change of surgical approaches to corneal grafting. Pathologists have a role in understanding what pathology is due to surgical intervention as opposed to initiating pathology and also in assisting in the process of refinement of surgical technique by examination of corneal tissue from patients where the outcome was suboptimal.

E. Eyelid

The particular anatomy of the eyelid and a rather different distribution of disorders than is seen on skin elsewhere make this another tissue where the ophthalmic pathologist has important expertise to offer patients.

Eyelid tumours

These include basal cell carcinomas, squamous cell carcinoma, Merkel cell carcinoma, sebaceous gland carcinoma, melanoma, as well as malignant tumours of the eccrine and apocrine glands of the eyelid. They must be differentiated from inflammatory conditions, benign epithelial/skin adnexal tumours, cysts, vascular tumours, xanthomatous lesions as well as metastatic tumours to the eyelids. Sebaceous gland carcinoma is a notorious mimic of chronic blepharitis and even histopathologically can sometimes be difficult to distinguish from other epithelial malignancies. Ophthalmic pathologists are especially familiar with the challenges of this condition including detailed analysis of invasive and intraepithelial disease of resection specimens and the need to study mapping biopsies to access conjunctival involvement.

The challenging and critical anatomy of the eyelid, with regard to preservation of cosmesis and visual function, make it sometimes impossible for oculoplastic surgeons to leave the same margin of apparently disease free tissue around a resection specimen as they would if the resection was from most other areas of the body. As a result of this and the complex anatomy of the eyelids, especially medially and laterally, the ophthalmic pathologist brings special skills in determining whether or not a malignant tumour has been completely excised.

F. Orbital disease

Tumours

These can be divided into those arising in the lacrimal gland and those arising in other orbital structures. The former include pleomorphic adenoma, carcinoma ex-pleomorphic adenoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, adenocarcinoma not otherwise specified, as well as malignant lymphomas.

Tumours arising within the orbit but not involving the lacrimal gland include myogenic tumours (i.e. arising from smooth muscle and striated muscle, such as rhabdomyosarcoma); peripheral nerve sheath tumours (e.g. neurofibroma); those tumours arising from blood vessels (haemangioma and haemangioblastoma); adipose tissue (e.g. lipoma, liposarcoma); bone or cartilage (e.g. osteosarcoma or mesenchymal chondrosarcoma); optic nerve sheath tumours (e.g. meningioma); lymphomas and plasmacytomas; and miscellaneous tumours (e.g. solitary fibrous tumour, alveolar soft part sarcoma).

Inflammatory disease

Inflammatory and benign conditions of the lacrimal gland and orbit include non-specific chronic inflammation, granulomatous dacryoadenitis (e.g. sarcoidosis, tuberculosis, and Wegener's granulomatosis) as well as the recently-described IgG4-related sclerosing disease. Idiopathic (sclerosing) orbital inflammation is a progressive condition which must be differentiated from orbital tumours and other causes of granulomatous inflammation.

Rarely, muscle is received for investigation of myopathy.

As in other conditions, the ophthalmic pathologist is a key member of the multidisciplinary team with responsibility for both diagnosis and assessment of completeness of excision of malignant disease. Excision specimens may come from

relatively small biopsies through to exenterations where the entire orbital contents are removed, generally with parts of the eyelids.

G. Lacrimal sac lesions

Lacrimal sac tumours are rare and both malignant and benign tumours tend to be of epithelial origin (e.g. squamous cell carcinoma/papilloma, transitional cell carcinoma/papilloma, mucoepidermoid carcinoma). Non-neoplastic lacrimal sac conditions include dacryolith, granulomatous and non-granulomatous inflammation).

- to ensure high quality clinical and diagnostic ophthalmic pathology
- to facilitate succession planning in this small specialty
- to provide improved opportunities for teaching, research and development.

The objectives of the service – strategic

The objectives of the Ophthalmic Pathology Services in England are to diagnose ocular and ocular adnexal tumours in a rapid and accurate manner to aid the Ocular Oncology Services in patient management. Identify and differentiate accurately non-neoplastic and inflammatory conditions.

2.2 Service description/care pathway

The following specimens are analysed by the services

- **small lid biopsy** – all tissues should be sent for histopathology except clinically-typical chalazia and blepharoplasty specimens as per Royal College Pathologist /Royal College of Ophthalmologist guidelines
- **full thickness lid resection except** ectropion/entropion repairs – these excisions should only be submitted if there is any evident clinical abnormality (but the threshold for sending should be low)
- **corneal specimens and conjunctival biopsies** (including caruncle, pterygium and pinguecula) these should all be sent for histopathological examination
- **trabecular meshwork** These can be discarded unless the case is of particular research interest
- **iris, ciliary body, choroid** These should all be sent for histopathological examination with the exception of peripheral iridectomy tissue from glaucoma or cataract surgery
- **lens** An intact lens removed in intracapsular cataract extraction may be sent for histopathological examination. Material from phacoemulsification can be discarded

- **vitreous** This fluid should be sent in any case in which there is a suspicion of inflammatory disease (after bacteriological samples have been taken) or malignancy (e.g. lymphoma). Histological examination is not appropriate for removed intravitreal blood or vitreous opacities such as asteroid hyalosis (although the latter may be useful for research or teaching)
- **epiretinal membrane** These should all be sent for histopathological examination in centres where there is a research interest
- **subretinal membranes** Excisions of disciform scars are of research and teaching interest only
- **eviscerations and enucleations** These should all be sent for histopathological examination. There is a very small but appreciable risk of a blind eye with opaque media harbouring occult malignancy
- **orbital Biopsies** These should all be sent for histopathological examination EXCEPT normal soft tissues - removed during orbital decompression and squint surgery
- **lacrimal gland excision/biopsy and lacrimal sac excision** These samples should all be sent for histopathological examination.

Risk management

Care delivered by the Ophthalmic Pathology service providers must be of a nature and quality to meet the care standards, specification and agreement for the service. It is the trust's responsibility to notify the commissioner on an exceptional basis should there be any breaches of the care standards. Where there are breaches any consequences will be deemed as being the trust's responsibility.

Diagnostic histopathology and cytology tests are essential part of the clinical management of ocular oncology patients and a proportion of those with benign disease. A timely delivery of a high-quality service is essential part of the patient pathway.

Days/hours of operation

Monday – Friday: 0900 – 1700 hours.

2.3 Population covered

This service covers patients resident in England.

Patients from Scotland, Wales and Northern Ireland are not part of this commissioned service and the trusts must have separate arrangements in place.

2.4 Any acceptance and exclusion criteria

The service is accessible to all patients within the scope of this specification regardless of age, sex, race, or gender.

Providers are required to provide staff with mandatory training on equality and diversity.

The provider has a duty to co-operate with the commissioner in undertaking Equality Impact Assessments as a requirement of race, gender, sexual orientation, and religion and disability equality legislation.

Referral criteria, sources and routes

- internally: within a large department e.g. difficult cases discussed
- informally between colleagues in adjacent hospitals e.g. generalist pathologist seeking advice from a pathologist in sub-specialist practice
- formally where a second 'primary' diagnostic opinion is required. This is most often in relation to complex lymphoma, dermatology or soft tissue tumour cases
- tertiary referrals linked to patient pathways.

Referred material is received in the form of whole specimens, ocular fluids, blocks and/or slides. Rarely, images may be received for opinion. The material may be submitted for expert opinion or simply for ancillary testing (e.g. clonality analysis, chromosomal analysis, using prognostication and genetic tests MLPA, FISH or MSA, electron microscopy, PCR, microbiology etc) when the analyses are not available to the referring pathologist.

Exclusion criteria not applicable.

2.5 Interdependencies with other services

Currently, in the UK, in addition to the above centrally-funded services, specialist ophthalmic pathology diagnostic expertise is provided by histopathologists and neuropathologists, who are members of the British Association for Ophthalmic Pathology (BAOP). Whilst the four centrally-funded laboratories provide centres of excellence and expertise free of charge, the geographically more disparate BAOP pathologists provide a more locally-based service but have access to NHS England commissioned laboratories. All National Specialist Ophthalmic Pathology service and most BAOP pathologists participate in the UK National External Quality Assurance

Scheme (UKNEQAS) in Ophthalmic Pathology and regularly attend the BAOP annual meeting at which quality assurance is discussed.

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

NHS England and the provider will conduct a formal Joint Service Review at each

centre at least annually and would expect to meet with the national clinical teams annually.

Guidelines for reporting of Ophthalmic Pathology specimens have been agreed by a joint working party of the Royal College of Ophthalmologists and the Royal College of Pathologists (see Appendix 1). Two NSOPS pathologists participated in the working party. This document, together with some additional information, is published on the Royal College of Ophthalmologists website. Its aim is to set out best practice for the reporting of Ophthalmic Pathology in the UK. NSOPS centres should provide services in line with this document.

4. Key Service Outcomes

The desired high level outcomes of the service, including clinical outcomes where appropriate

To provide a rapid turnover of ocular specimens with provision of accurate and reproducible diagnoses, incorporating morphological, immunohistochemical/immunofluorescence and molecular data where appropriate.

There are no clinical outcome measures but the service providers must participate in the UK National External Quality Assessment Scheme (UKNEQAS), in the NSOPS internal quality investigations and attend (and preferably present clinical or research material at) ophthalmic pathology meetings (e.g. BAOP) or major ophthalmology meetings on a regular basis.

5. Location of Provider Premises

National Specialist Pathology Service, NSOPS, comprises specialised ophthalmic pathology laboratories in:

- Liverpool (Royal Liverpool & Broad Green University Hospitals NHS Trust)
- London (Institute of Ophthalmology, UCL)
- Manchester (Central Manchester University Hospitals NHS Foundation Trust),
- Sheffield (Sheffield Teaching Hospitals NHS Foundation Trust).

Appendix 1

ROYAL COLLEGE OF OPHTHALMOLOGISTS AND ROYAL COLLEGE OF PATHOLOGISTS

GUIDANCE ON REFERRAL OF OPHTHALMIC PATHOLOGY SPECIMENS

OPHTHALMIC PATHOLOGY

What should the Ophthalmologist send?

This document contains recommendations for ophthalmologists on when to send tissue generated during diagnostic or therapeutic procedures for histopathological assessment.

Tissue taken for diagnostic purposes will be submitted for histological or cytopathological assessment. For therapeutic procedures it may be acceptable to discard some tissue and these specific circumstances are described in this document.

These recommendations are provided for routine diagnostic NHS laboratories. Specialised research laboratories may accept specimens, which would not normally be submitted.

Who should report Ophthalmic Pathology specimens?

Information on the reporting of ophthalmic pathology specimens is provided by the Royal College of Pathologists.

This document was written in collaboration with the Royal College of Ophthalmologists. In brief, it states that pathologists reporting ophthalmic pathology specimens should participate in an appropriate external quality assessment (EQA) scheme (such as the National Ophthalmic Pathology EQA Scheme). In addition, pathologists reporting ophthalmic pathology specimens should be encouraged to participate in the annual meeting of the British Association of Ocular Pathology, where the results of the National EQA scheme are discussed. A list of pathologists who participate in the National Ophthalmic Pathology EQA Scheme, as well as, details of the National Specialist Ophthalmic Pathology Service (NSOPS) laboratories is available on the EyePath UK website: www.eyepathuk.co.uk/pathology_specialist.html

What should the Ophthalmologist send?

1. Small Lid Biopsy

All tissue should be sent for histopathological examination EXCEPT

Clinically typical chalazia – In a patient under age of 40 years with an otherwise typical chalazion it is acceptable to discard the first two samples unless there are any clinical suspicions. The second recurrence (*i.e.* third sample) should be sent.

In a patient over the age of 40 years with otherwise typical chalazion it is acceptable to discard the first sample unless there are any clinical suspicions. The first recurrence (*i.e.* second sample) should be sent.

Blepharoplasty – excess skin removed for blepharoplasty can be discarded unless there is any clinical abnormality.

Other cosmetic procedures e.g. lid lowering, tightening *etc.* – if tissue is removed it can be discarded unless there is any clinical abnormality.

2. Full thickness lid resection

All tissue should be sent for histopathological examination EXCEPT

Ectropion/Entropion repairs – these excisions should only be submitted if there is any evident clinical abnormality (but the threshold for sending should be low).

3. Corneal specimens and Conjunctival Biopsies (including caruncle, pterygium and pinguecula)

These should all be sent for histopathological examination

4. Trabecular Meshwork

These can be discarded unless the case is of particular research interest.

5. Lens

An intact lens removed in intracapsular cataract extraction may be sent for histopathological examination.

Material from *phacoemulsification* should be discarded.

6. Iris, Ciliary Body, Choroid

These should all be sent for histopathological examination with the exception of peripheral iridectomy tissue from glaucoma or cataract surgery.

7. Vitreous

This fluid should be sent in any case in which there is a suspicion of inflammatory disease (after bacteriological samples have been taken). Similarly if malignancy (*e.g.* lymphoid infiltration) is suspected fluid must also be submitted for histopathology. Histological examination is not appropriate for removal of *intravitreal blood* or *vitreous opacities* such as asteroid hyalosis (although the latter may be useful for research or teaching).

8. Epiretinal Membrane

These should all be sent for histopathological examination in centres **where there is a research interest.**

9. Subretinal Membranes

Excisions of disciform scars are of **research and teaching interest only**

10. Eviscerations and enucleations

These should all be sent for histopathological examination. There is a very small but appreciable risk of a blind eye with opaque media harbouring occult malignancy.

11. Orbital Biopsies

These should all be sent for histopathological examination EXCEPT.

Normal soft tissues - removed during orbital decompression and squint surgery.

12. Lacrimal Gland Excision/Biopsy and Lacrimal Sac Excision

These samples should all be sent for histopathological examination.

13. Orbital Exenteration Specimens

These should all be sent for histopathological examination.

14. Cytology

Impression cytology of the conjunctiva and cornea.

Fine needle aspiration cytology of periocular or intraocular masses.

These samples should all be sent for histopathological/cytological examination

15. Other Biopsies

This is not a prescriptive list and obviously, any material taken for the purpose of diagnosis (e.g. aqueous tap, temporal artery biopsy) should be submitted for histopathological/cytological examination. Temporal arteries need not necessarily be submitted to an ophthalmic pathologist. Ophthalmologists are encouraged to discuss any tissues they are uncertain of whether or not to submit with their local pathologist or an NSOPS ophthalmic pathologist.

Adopted

Appendix 2

JOINT WORKING PARTY OF THE ROYAL COLLEGE OF OPHTHALMOLOGISTS AND ROYAL COLLEGE OF PATHOLOGISTS ON RECOMMENDATIONS FOR REFERRAL OF OPHTHALMIC SPECIMENS

February 2010

The Royal College of Ophthalmologists



OPHTHALMIC PATHOLOGY

Background

Diagnostic ophthalmic pathology is integral to the work of all ophthalmic departments/units in which tissue or fluid is removed during diagnostic or therapeutic procedures, in order to provide a timely, high quality diagnostic opinion and to avoid delayed or missed diagnosis of disease. Ophthalmic pathology (ophthalmic histopathology, ocular pathology) is a subspecialty of histopathology, as it makes use of materials, methods and expertise that allow morphological, chemical, immunological, and, in some cases, molecular genetic analysis of glass-mounted sections of tissue or fluid preparations, obtained from biopsy, excision, aspiration or scraping. Electron microscopy may also be used. Pathologists and biomedical scientists within ophthalmic pathology provide a specialty diagnostic service from a laboratory that is similar in almost all aspects to a general histopathology laboratory and which may be embedded within such a larger laboratory unit which serves a variety of histopathology subspecialties.

In England, ophthalmic pathology is a nationally commissioned specialised service (National Specialist Ophthalmic Pathology Service – NSOPS) funded centrally by NHS England of the NHS.^{1, 2} In Scotland the Scottish Executive (SE) centrally part-funds the Scottish Regional Ophthalmic Pathology Service. Thus the four NSOPS laboratories and the single Scottish Regional Ophthalmic Pathology Service laboratory provide a diagnostic service which is free of charge for specimens generated within NHS units within England & Scotland respectively. Details of the pathologists and laboratories which provide the National Specialist Ophthalmic Pathology Service (NSOPS) and Scottish Regional Ophthalmic Pathology Service are available on the [EyePathUK website](#).³

Currently, in the UK, in addition to the above centrally funded services, specialist ophthalmic pathology diagnostic expertise is provided by histopathologists and neuropathologists who are members of the British Association for Ophthalmic Pathology (BAOP). Whilst the five centrally funded laboratories provide centres of excellence and expertise free of charge, the geographically more disparate BAOP pathologists provide a more locally based service but have access to NHS ENGLAND and SE funded laboratories. All NSOPS and BAOP pathologists participate in the UK National External Quality Assurance Scheme (UKNEQAS) in Ophthalmic Pathology and the BAOP annual meeting at which EQA case discussion is held.

Guidance

This Ophthalmic Pathology Chapter is based on the joint guidance document of the Royal College of Ophthalmologists (RCOphth) and the Royal College of Pathologists (RCPath) on referral of ophthalmic pathology specimens⁴. This information is also contained within an article published in the RCOphth Focus series. It provides recommendations for ophthalmologists concerning when to send tissue removed during procedures for histopathological assessment and in order to avoid delayed or missed diagnosis of disease; and recommends which pathologists should receive specimens in order to ensure consistent, high quality and accurate diagnosis. The document addresses submission of histopathology and cytology specimens, but not specimens sent for other purposes (e.g. microbiology, molecular diagnostics, or research). Guidance for histopathologists on the reporting of ophthalmic pathology specimens is provided by the Royal College of Pathologists.⁶

Who should report ophthalmic pathology specimens?

The guidance provided by the Royal College of Pathologists ⁶ states that pathologists reporting ophthalmic pathology specimens should participate in an appropriate external quality assessment (EQA) scheme (in most cases this will be the UK National Ophthalmic Pathology EQA Scheme). Pathologists reporting ophthalmic pathology specimens should be encouraged to participate in the annual meeting of the British Association for Ophthalmic Pathology (BAOP), where the results of the Ophthalmic Pathology UKNEQAS are discussed. Submitting specimens for examination by specialist pathologists both ensures that the specimen is handled by an expert in the field, allows the specialist to maintain and increase his/her level of expertise,⁷ and facilitates training opportunities for histopathology trainees who wish to develop an interest in ophthalmic pathology. It is also appropriate for specimens of some tissues adjacent to the eye to be sent to a pathologist with expertise in another relevant subspecialty of pathology, e.g. dermatopathology, ENT pathology, neuropathology, or paediatric pathology.

What specimens should the ophthalmologist send?

Recommendations for different procedures and tissue types are listed below. For therapeutic procedures it may be acceptable to discard some tissue and these specific circumstances are described within the list.

1. Small lid biopsy All tissue should be sent for histopathological examination

EXCEPT

Chalazia – In a patient under age of 40 years with an otherwise typical chalazion it is acceptable to discard the first two samples unless there are any clinical suspicions. The second recurrence (i.e. third sample) should be sent. In a patient over the age of 40 years with otherwise typical chalazion it is acceptable to discard the first sample unless there are any clinical suspicions. The first recurrence (i.e. second sample) should be sent. Blepharoplasty – excess skin removed for blepharoplasty can be discarded unless there is any clinical abnormality. Other cosmetic procedures e.g. lid lowering, tightening etc – if tissue is removed it can be discarded unless there is any clinical abnormality.

2. Full thickness lid resection All tissue should be sent for histopathological examination

EXCEPT

Ectropion/Entropion repairs – these excisions should only be submitted if there is any evident clinical abnormality (but the threshold for sending should be low).

3. Corneal specimens and Conjunctival biopsies (including caruncle, pterygium and

pinguecula) these should all be sent for histopathological examination.

4. Trabecular meshwork These can be discarded unless the case is of particular research interest (the majority of tissues contain scleral tissue only).

5. Iris, Ciliary Body, Choroid These should all be sent for histopathological examination

with the exception of peripheral iridectomy tissue from glaucoma or cataract surgery.

6. Lens An intact lens removed in intracapsular cataract extraction may be sent for histopathological examination. Material from phacoemulsification should be discarded.

7. Vitreous This fluid should be sent in any case in which there is a suspicion of inflammatory disease (after bacteriological samples have been taken) or malignancy (e.g. lymphoma). Histological examination is not appropriate for removed intravitreal blood or vitreous opacities such as asteroid hyalosis (although the latter may be useful for research or teaching).

8. Epiretinal membrane These should all be sent for histopathological examination in centres where there is a research interest.

9. Subretinal membranes Excisions of disciform scars are of research and teaching interest only.

10. Eviscerations and enucleations These should all be sent for histopathological examination. There is a very small but appreciable risk of a blind eye with opaque media

harbouring occult malignancy.

11. Orbital Biopsies These should all be sent for histopathological examination

EXCEPT

Normal soft tissues - removed during orbital decompression and squint surgery.

12. Lacrimal Gland Excision/Biopsy and Lacrimal Sac Excision These samples should

all be sent for histopathological examination.

13. Orbital Exenteration Specimens These should all be sent for histopathological examination.

14. Cytology Impression cytology of the conjunctiva and cornea, and fine needle aspiration cytology of periocular or intraocular masses; these samples should all be sent for histopathological/cytological examination. For aspirates of intraocular fluids see vitreous (above).

15. Other Biopsies This is not a prescriptive list and, obviously, any material taken for the purpose of diagnosis (e.g. aqueous tap, temporal artery biopsy) should be submitted for histopathological/cytological examination. Temporal artery biopsies need not necessarily be submitted to an ophthalmic pathologist. In some cases electron microscopy is appropriate (e.g. confirmation of diagnosis of microsporidial infection). Ophthalmologists are encouraged to discuss with their local BAOP pathologist or an NSOPS ophthalmic pathologist any matters involving uncertainty regarding whether or not to submit tissue for diagnosis.

Additional issues

Communication:

Communication with the laboratory is paramount. If the clinician is unsure of how to handle a particular specimen, if an urgent pathology opinion is required, if fresh material (e.g. for frozen section, IF, or cytopathology) is to be sent, or if electron microscopy may be required, the laboratory must be contacted in advance.

Specimen transport and packaging:

Specimens are normally received by post or by courier arranged by the sending hospital. Fax/phone back arrangements to ensure confirmation of receipt may be made by prior arrangement with the laboratory. Packaging of diagnostic specimens must conform to United Nations Regulations (2005) and Transport of Dangerous Goods Regulations (2005) – see HSE guidance.⁸ In brief, virtually all ophthalmic pathology diagnostic specimens will be Category B biological substances (assigned to UN 3373) and packing instruction PI 650 will apply. The postal service, couriers and the laboratory will be able to provide on request information/protocols regarding appropriate packaging and transport.

Request forms:

Request forms may be provided if required. Request forms must be completed fully. In order to conform with specimen acceptance policy the following information should be supplied:-

- Patient Surname
- Patient Forename
- Date of birth
- NHS number
- Patient Address
- Clinician
- Hospital location
- Date specimen taken
- High Risk status
- Specimen type
- Brief relevant clinical information

Rapid processing of specimens:

Many histopathology laboratories provide a service for intraoperative diagnosis (i.e. frozen section) and/or rapid paraffin processing (e.g. for delayed reconstruction). There is local variation in availability, but, generally, this may be arranged by prior discussion between clinician and laboratory. Frozen section service is very labour-intensive and should only be requested when appropriate.

Fixation and containers:

Patient identification and specimen details must be completed on each specimen pot submitted. Multiple specimens from the same patient should be placed in different, individually identified containers in order to avoid confusion among specimens. Most specimens will require fixation in 10% neutral buffered formalin. Suspected sebaceous carcinoma specimens **do not** need to be submitted fresh and should be formalin-fixed. The volume of fixative (and therefore size of specimen pot) should be appropriate to the size of specimen. For minute biopsies (e.g. retina) it may be more appropriate to place the specimen and formalin within a small container (e.g. Eppendorf tube or similar). (Packaging and transport – see above).

Fresh specimens (frozen section specimens, cytology specimens, and conjunctival specimens for immunofluorescence (IF)):

These specimens must be submitted only after prior arrangement with the laboratory, and must be delivered without delay in time to be received and handled by the laboratory. Conjunctival specimens for immunofluorescence (IF) may be stabilised for transport in Michel's medium or gel transport tubes. Michel's medium in suitably sized containers is readily commercially available, and gel transport tubes may be obtained by prior arrangement from some laboratories. Advance notice of fresh specimens to be delivered and sender contact information is required so that late/non-arrival of specimens can be investigated and tracked.

N.B.:- Frozen sections and IF cannot be performed on High Risk specimens.

Turnaround times: Current information may be obtained by enquiry from the individual NSOPS/BAOP laboratory.

Research:

Samples of ocular tissue may be required for research purposes. In such circumstances where the specimen is required both for diagnostic and research purposes, it is advisable for the ophthalmologist to seek advice from the pathologist involved. This will help ensure adequate tissue sample is taken and it may be best for the pathologist to divide and section the specimen before processing.

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1 <http://www.specialisedservices.nhs.uk/serv/ophthalmic-pathology/>

2 <http://www.specialisedservices.nhs.uk/>

3 http://www.eyepathuk.co.uk/pathology_specialist.html/

4 <http://www.specialisedservices.nhs.uk/doc/10034/>

5 Focus Winter 2010 'Histopathology and cytology specimens – what should you send, and to whom?'

<http://www.rcophth.ac.uk/page.asp?section=355§ionTitle=Focus+Articles/>

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http://www.rcpath.org/resources/pdf/g053v2_guidelinesreportingophthalmicspecs_mar08.pdf/

7 <http://www.rcpath.org/resources/pdf/G004-SpecialistCellularPathologists-Jun06.pdf>

8 <http://www.hse.gov.uk/aboutus/meetings/committees/acdp/050208/acdp88p6.pdf>

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