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Disease in wildlife or exotic species

Ocular pathology in aquarium fish with a focus on the Syngnathidae and Apogonidae families

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This study catalogued ocular pathology in fish histopathology submissions to a specialist diagnostic service and investigated associations with species and systemic disease, with a focus on species of conservation interest. Cross-tabulations and Fisher's exact tests were used to identify associations among the variables and results are reported as prevalence ratios (PRs) with 95% confidence intervals (CI). Of 12,488 reports reviewed, ocular histology examination was available for 4,572 submissions, in which histopathological ocular lesions were identified in 18% (813/4572). Most diagnoses (701/813; 87%) were in marine fish. Inflammatory conditions were most common (608/813; 75%), with identification of a bacterial aetiology in 42% (255/608) and a parasitic aetiology in 30% (183/608). Most bacterial infections were due to mycobacteriosis (153/255; 60%) and most parasitic infections were due to scuticociliatosis (114/184; 62%). The Syngnathidae, Centriscidae and Cichlidae families were each more likely than all other families combined to be diagnosed with ocular manifestations of mycobacteriosis (PRs = 2.6, 4.4 and 2.9, respectively, P <0.0001 for each). The Syngnathidae were also more likely to be diagnosed with ocular scuticociliatosis (PR = 1.9, P <0.0001). Fifty-four percent (39/72) of ocular mycobacteriosis and 38% (9/24) of gas bubble disease cases affected threatened or near threatened Syngnathidae species. The Apogonidae were more likely than any other family to have ocular iridovirus (PR = 10.3, 95% CI = 5.5−19.4, P <0.0001) and neoplasia (PR = 8.2, 95% CI = 4.2−16.3, P <0.0001). The endangered Banggai cardinalfish (*Pterapogon kauderni*) accounted for 13/15 ocular iridovirus and 16/18 mycobacteriosis cases in this family. All cases of neoplasia in the Apogonidae occurred in pajama cardinalfish (*Sphaeramia nematoptera*). These results should inform clinical diagnosis of ocular disease in aquarium fish and influence training for aquarists, highlighting ocular pathology as a potential early warning of systemic disease. The findings also have direct/indirect consequences for the welfare and conservation of some of these popular flagship fish species.

1. Introduction

Primary ocular conditions and ocular manifestations secondary to systemic disease are common in fish [1–3]. Vision is vital to targeting, feeding and schooling/social habits, and ocular disease affects fish welfare and can lead to mortality. Postoperative survival of fish following exenteration of diseased eyes has been reported to be poor [4]. Systemic disease underlying ocular signs probably explains the poor prognosis for many of these fish, but impaired vision may also reduce ability to feed and express normal behaviours. Ocular disease is also noticed by aquarium visitors, with unsightly signs such as exophthalmos common in many cases [5].

Ocular lesions, including keratitis, uveitis and endophthalmitis, and periocular pathology are briefly mentioned in studies of systemic bacterial, viral, fungal and parasitic diseases of fish [2,6–10]. Moreover, ocular pathologies occurring secondary to trauma and gas bubble disease (GBD) have been described [2,11]. Case reports of fish ocular neoplasia have also been published [12–20]. The extensive literature on the effects of environmental, nutritional,

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parasitic, toxic and developmental factors in cataract development focuses on farmed fish species [5,21–35]. However, few studies have documented ocular pathology across large cohorts of aquarium fish.

In this study we catalogue and describe ocular disease diagnosed on histopathological examination in a large cohort of aquarium fish submitted to a single laboratory and report the frequency of occurrence and associations with systemic disease. The findings are compared with previous reports, focusing on the most affected families or species. In doing so, the eye is highlighted as an important externally visible indicator of fish health.

2. Materials and methods

2.1. Sample population

Fish histopathology reports generated from 2003 to 2021 were extracted for retrospective analysis from the database of International Zoo Vet Group (IZVG) Pathology, a specialist zoological pathology practice. The dataset contained the following information: genus and species name, common name, laboratory reference number, year of submission, age, owner/collection name, brief clinical summary, histopathology description, histopathology diagnoses and pathologist comments.

Searches ('eye', 'ocular' and 'ophthalmic') were performed to include only those submissions that had undergone ocular/periocular histopathology (HP) examinations in the extracted study dataset. Cases were sorted by family, subfamily (where applicable), genus, species (where present) and common name. The International Union for Conservation of Nature (IUCN) Red List of Threatened Species (IUCN, 2022; www.iucnredlist.org) and FishBase (www.fishbase.se) were used to assign a conservation status and water habitat type (marine, fresh or estuarine/brackish water) to each case. The seven standard IUCN classifications were grouped into four categories for analysis: critically endangered/endangered/vulnerable; near threatened; least concern; and data deficient/not evaluated.

2.2. Ocular/periocular histopathology

All cases that had undergone ocular/periocular HP examinations were individually reviewed and assigned a diagnosis (any further mention of diagnosis/diagnoses in this article relates to ocular HP diagnoses only). Diagnoses were grouped into nine generic categories for ease of analysis: buphthalmos, cataract, corneal oedema, GBD, inflammation, intraocular haemorrhage, neoplasia, phthisis bulbi, and 'other'. Cases in which no ocular pathology was diagnosed, or where eyes were too autolysed for assessment, were broadly categorized as 'no abnormality identified' and excluded from further analysis.

Cases were submitted by trained aquarists or veterinarians from a variety of international aquarium, zoological or breeding centre facilities (anonymized for further analysis). HP examinations were undertaken by three board-certified veterinary pathologists on formalin-fixed necropsy (or occasionally biopsy) tissues, routinely processed for histology, sectioned (4 μm) and stained with haematoxylin and eosin (HE). Special stains were applied when appropriate. Occasional cases included supporting microbiology from swabs or fluid/tissue samples.

2.3. Statistical analysis

Statistical analysis was performed using the SPSS 28.0 (IBM, www.ibm.com) program. Descriptive statistics are reported as number (n or N) and percentage with 95% confidence intervals (CI) where appropriate. Cross-tabulations of two by two and n by n tables with Chi-square or Fisher's exact tests were used to identify associations among the variables. Prevalence ratios (PRs) were estimated from the two by two tables using the traditional formula for relative risk (RR) in a cross-sectional study. Results are reported for prevalence of a diagnosis in a specific fish family (or species) compared with all other fish families (or species) combined. The level of significance was set at P <0.001 using a Bonferroni correction for multiple comparisons. PRs are reported with 95% CI.

3. Results

3.1. Sample population

A total of 12,488 fish pathology reports spanning a 17.5-year period were reviewed. Thirty-seven percent (95% CI 35.8–37.5; 4,572/12,488) of these submissions had an ocular/periocular HP examination, of which 18% (95% CI 16.7–18.9; 813/4,572) had an ocular/periocular HP diagnosis. In a few submissions, autolysis of the fish (n = 18) or eyes (n = 16) impaired HP evaluation. As age was unreliable and infrequently reported (9% [407/4,572] of submissions and 8% [63/813] of diagnoses), it was excluded from the analysis.

Ocular HP was performed on samples from 128 different collections/owners in 24 countries, including groups of aquaria within larger corporate entities. One such group accounted for 84% (3,852/4,572) of submissions and 86% (699/813) of diagnoses. Collections in the UK accounted for 63% (2,865/4,572) of the submissions. Few were submitted from outside the UK and Europe, hence no further statistical comparisons of geographical origin were attempted.

There were 125 fish families and 555 fish genus and species combinations represented. Most diagnoses were in marine (701/813; 87%) fish followed by freshwater fish (9%), reflecting overall submissions of 91% and 5.5%, respectively. The 10 most commonly submitted families comprised 71% (3,241/4,572) of all submissions (**Table 1**) and 56% (452/813) of all diagnoses. The Syngnathidae (seahorses, pipefishes and seadragons), Pomacentridae (damselfishes and clownfishes) and Apogonidae (cardinalfishes) families accounted for 57% (2,584/4,572) of submissions. The Syngnathidae alone accounted for 26% (208/813) of all diagnoses. Four vulnerable (lined seahorse [*Hippocampus erectus*], spotted seahorse [*Hippocampus kuda*], Barbour's seahorse [*Hippocampus barbourin*] and tiger tail seahorse [*Hippocampus comes*]) and one endangered (White's seahorse [*Hippocampus whitei*]) Syngnathidae species and one endangered (Banggai cardinalfish) species of Apogonidae comprised 65% (96/125) of all threatened (critically endangered/endangered/vulnerable IUCN categories) fish with an ocular diagnosis (**Supplementary Table 1**).

3.2. Ocular/periocular histopathology and associations among variables

Eighty two percent (670/813) of diagnoses were ocular, 11% (90/813) were periocular and 6% (49/813) affected both ocular and periocular structures. The frequency of ocular diagnoses grouped into the nine broad categories are summarized in **Table 2**. There were no significant associations between water habitat type and ocular/periocular disease distribution.

Inflammatory conditions comprised the most common diagnostic category at 75% (95% CI 71.6–77.7; 608/813; **Tables 2** and **3**). The Pomacentridae and Syngnathidae families were significantly more likely to have an inflammatory diagnosis (P <0.0001, **Supplementary Table 2**). A bacterial aetiology was identified in 42% (255/608, **Table 3**) of all inflammatory conditions of which 60% (153/255) were mycobacteriosis (confirmed by Ziehl–Neelsen [ZN]

Table 1
Number and percentage of total number of submissions (4,572) for the 10 most commonly submitted fish families.

Order	Family	Common family name	N	%	n
1	Syngnathidae	Seahorses, pipefishes and seadragons	2,079	45.47	208
2	Pomacentridae	Damselfishes and clownfishes	284	6.21	50
3	Apogonidae	Cardinalfishes	221	4.83	61
4	Serranidae	Sea basses, groupers and fairy basslets	130	2.84	23
5	Acanthuridae	Surgeonfishes, tangs and unicornfishes	102	2.23	17
6	Gasterosteidae	Sticklebacks and tubesnouts	95	2.08	16
7	Centriscidae	Snipefishes and shrimpfishes	94	2.06	10
8	Labridae	Wrasses	85	1.86	29
9	Chaetodontidae	Butterflyfishes	77	1.68	14
10	Congridae	Conger and garden eels	74	1.62	7
	Total		**3241**	**70.89**	**435**

N, number of submissions; n, number of ocular histopathological diagnoses.

staining but not speciation by polymerase chain reaction). An additional 10% (452/4,572) of submissions had mycobacteriosis with no histological ocular manifestation. Therefore, out of a total of 605 mycobacteriosis cases in the database, 25% (153/605) involved the eyes. Thirty families and 58 species had at least one ocular mycobacteriosis diagnosis. The Centriscidae, Cichlidae and Syngnathidae families were significantly more likely to be diagnosed with ocular mycobacteriosis (P <0.0001, Table 4). Thirty-eight percent (59/153) of ocular mycobacteriosis diagnoses occurred in threatened or near threatened species overall, rising to 54% (39/72) in two vulnerable and one near threatened Syngnathidae species (Table 4). In the Apogonidae family, 16/18 ocular mycobacteriosis cases occurred in the endangered Banggai cardinalfish. Histologically, many of the Syngnathidae species with ocular mycobacteriosis had necrogranulomatous inflammation (70%; 51/72) compared with more purely granulomatous or histiocytic inflammatory changes in other fish families (40%; 12/30); this was not statistically significant after correcting for multiple comparisons ($P = 0.016$). All ocular mycobacteriosis cases involved fish with disseminated mycobacterial disease. Granulomatous, histiocytic or necrogranulomatous inflammation affected multiple ocular structures, including the choroid, sclera, episclera, retrobulbar vascular rete and periocular tissues (Figs. 1 and 2). Non-mycobacterial cases were intraocular (panophthalmitis, endophthalmitis, septicaemia associated) in 28% (72/255) and ocular surface/periocular/orbital (keratitis/keratoconjunctivitis, scleritis, periocular cellulitis/dermatitis) in 12% (30/255) of all bacterial ocular/periocular infections (Table 3).

Thirty percent (184/608) of inflammatory ocular conditions were parasitic. Scuticociliatosis occurred in 62% (114/184). The Syngnathidae family were significantly more likely to be diagnosed with ocular scuticociliatosis (85/208, PR = 1.9, 95% CI 1.5–2.4, P <0.0001) but only 26% (22/85) were in threatened or near threatened Syngnathidae species. Uronema-like species and *Philasterides dicentrarchi* were the commonly reported scuticociliates, seen histologically as elliptical ciliated, unicellular organisms with basophilic vacuolated protoplasm containing eosinophilic granular organelles and a single nucleus. Scuticociliate parasites were associated with oedema and a mild-to-marked mononuclear response, as well as necrosis of adjacent myofibres in affected tissues (Figs. 3 and 4). Cryptocaryonosis, found in 14% (26/184) of parasitic diagnoses, was associated with keratitis and periocular dermatitis. Nine percent (16/184) of the 13% helminth infestations seen were due to trematodiasis. Mesomycetozoea infestations (5%), myxozoanosis (2%), microsporidiosis (2%), amoebiasis (0.5%) and crustacean infestations (0.5%) were also seen, but due to their relatively low numbers, no further analysis was carried out and these parasites will not be discussed further.

Table 2
Frequency of ocular diagnoses by category.

Ocular diagnosis categories	N*	%**	Individual diagnoses
Inflammation	608	74.8	See Table 3
Intraocular haemorrhage	34	4.2	29 traumatic, 4 unspecified, 1 vasculitis
Neoplasia	30	3.7	See Table 5
Phthisis bulbi	29	3.6	11 unspecified, 11 traumatic, 4 bacterial infection, 1 marine oodiniosis, 1 secondary to chronic uveitis
Gas bubble disease	24	3.0	–
Cataract	18	2.2	9 Morgagnian (1 ruptured), 7 unspecified, 1 associated with scleral granuloma, 1 bilateral (with lens rupture)
Buphthalmos	13	1.6	1 secondary to endophthalmitis, 3 suspect ‘dropsy’, 9 unspecified
Corneal oedema	11	1.4	9 unspecified, 1 traumatic, 1 fungal with secondary bacterial infection
Other	46	5.7	See footnote
Subtotal diagnoses	**813**	**17.8**	
No. ocular diagnosis	3,759	82.2	
Total submissions	**4,572**	**100**	

N*, number of diagnoses; %**, percentage of total submissions.
Summary of other diagnoses: 6 melanomacrophage hyperplasia, 3 corneal perforation, 2 corneal fibrosis, 2 traumatic lens rupture, 2 periocular haemorrhage, 2 periocular oedema, 2 retrobulbar haemorrhage, 2 retrobulbar oedema, 2 retrobulbar vasculitis and 1 each of choroidal fibrosis, choroidal granuloma, corneal irregularity, exophthalmos due to coelomic fluid accumulation, bilateral exophthalmos due to generalized oedema, exophthalmos due to acute oedema and inflammation in the retrobulbar space, exophthalmos due to intracoelomic dysgerminoma, exophthalmos due to steatosis, glaucoma, intraocular fluid accumulation, metastatic ocular mineralization, ocular cholesterol accumulation, ocular osteochondritis, ocular telangiectasia, ocular trauma, periocular cellulitis due to trauma, phthisis bulbi in left eye with buphthalmos in right eye with no cause identified, retinal atrophy, retinal atrophy and oedema, retinal dysplasia (ocular dysgenesis), scleral and periocular haemorrhage, scleral metastatic mineralization (secondary to renal disease) and unspecified trauma.

Table 3
Inflammation category by type and aetiology for 608 inflammatory diagnoses.

Inflammation categories	Parasitic	Bacterial	Viral	Fungal	Traumatic	Aetiology not identified	Total
Parasitic infestation	183					1	184
Mycobacterial infection		153					153
Periocular cellulitis/dermatitis		22		8		26	56
Panophthalmitis		21		13	7	12	53
Endophthalmitis		25		2	5	19	51
Iridovirus			33				33
Septicaemia		26				1	27
Keratitis		4		1*		12	17
Uveitis					2	8	10
Choroiditis						7	7
Scleritis		2**		1		4	7
Periocular steatitis						5	5
Encephalitis		1					1
Extraocular myositis						1	1
Keratoconjunctivitis		1					1
Meningitis						1	1
Optic neuritis						1	1
Total	**183**	**255**	**33**	**25**	**14**	**98**	**608**

*, one case had secondary bacterial infection; **, one case had concomitant parasitic infestation.

Only 5% (33/608) of inflammatory conditions were of viral aetiology and were all due to iridovirus (*Megalocytivirus*) infections. The Apogonidae family were more likely to be diagnosed with an ocular iridovirus infection than any other fish family (PR = 10.3, 95% CI 5.5–19.4, *P* <0.0001) and 13/15 were seen in the endangered Banggai cardinalfish. Several species in the Pomacentridae and Grammatidae families were also significantly more likely to be affected (*P* <0.0001, **Supplementary Table 3**). Cytomegalic perivascular cells containing intracytoplasmic, basophilic, granular, viral inclusion bodies affecting the vascular rete, choroidal capillaries and retrobulbar connective tissues were seen histologically (**Fig. 5**).

Fungal infections were uncommon, accounting for 4% (25/608) of inflammatory conditions. Fungal panophthalmitis (13/25), periocular cellulitis (8/25), endophthalmitis (2/25), keratitis (1/25) and scleritis (1/25) cases were seen (**Table 3**, **Fig. 6**).

Ocular neoplasia represented 4% (30/813, **Table 2**) of all diagnoses and occurred in 13 species of 12 fish families (**Table 5**). Nine different ocular neoplasms (seven melanomas, six carcinomas, six lymphomas (lymphosarcomas), four spindle cell sarcomas, two round cell sarcomas and one each of neuroectodermal tumour, haemangioma, retinoblastoma, meningioma) and one unspecified neoplasm occurred. The Apogonidae were eight times more likely to be diagnosed with ocular neoplasia (PR = 8.2, 95% CI 4.2–16.3, *P* <0.0001) compared with all other fish families. Three other families (Gasterosteidae, Leptobarbidae and Monacanthidae) were also significantly more likely to be affected by ocular neoplasia (*P* <0.0001). All 12 cases of ocular neoplasia in the Apogonidae occurred in pajama cardinalfish [*Sphaeramia nematoptera*] (**Table 5**, **Figs. 7** and **8**).

Intraocular haemorrhage (34/813) and phthisis bulbi (29/813) each occurred in 4% of diagnoses. Trauma was suggested as an aetiology/contributing factor in 13% (104/813) of pathologist comments, including in 2% (14/608) of inflammatory conditions, 38% (11/29) of phthisis bulbi cases (**Fig. 10**), 85% (29/34) of intraocular haemorrhages (**Figs. 11** and **12**) and one case of corneal oedema. GBD (**Fig. 9**) was reported in 3% (24/813) of cases; 14 of these were in species in the threatened IUCN categories, nine of which were Syngnathidae.

Buphthalmos was an uncommon diagnosis (2%, 13/813) occurring in nine families. Buphthalmos was used by the pathologists to describe enlarged eyes that had corneal and scleral oedema,

Table 4
Selected families, genera and species and IUCN categories* of fish diagnosed with ocular mycobacteriosis

Family/genus/species	n	N	PR	95% CI	*P* value
Apoginadae	18	61	1.6	1.1–2.5	0.0195
Pterapogon kauderni (16**, EN), *Sphaeramia nematoptera* (NE), *Zoramia leptacantha* (NE)					
Centriscidae	**8**	**10**	**4.4**	**3.1–6.2**	**<0.0001**
Aeoliscus strigatus (DD)					
Cichlidae	**8**	**15**	**2.9**	**1.8–4.8**	**<0.0001**
Astronotus ocellatus (3, NE), *Heros severus* (NE), *Pterophyllum scalare* (3, NE), *Melanochromis* sp (LC)					
Serrasalmidae	3	8	3.0	0.8–5.0	0.0130
Pygocentrus nattereri (LC)					
Syngnathidae	**72**	**208**	**2.6**	**1.96–3.4**	**<0.0001**
Hippocampus genus	52	157	2.2	1.6–2.9	<0.0001
Syngnathus genus	10	21	2.6	1.6–4.2	0.0001
Hippocampus erectus (VU)	23	34	4.1	3.1–5.4	<0.0001
Hippocampus reidi (NT)	13	20	3.7	2.6–5.3	<0.0001
Hippocampus comes (VU)	3	6	2.7	1.2–6.1	0.017
Syngnathus typhle (LC)	8	16	2.8	1.7–4.6	0.0001
Phyllopteryx taeniolatus (LC)	5	11	2.5	1.3–4.8	0.0080

*, IUCN classification: DD, data deficient; EN, endangered; VU, vulnerable; NT, near threatened; LC, least concern; NE, not evaluated.
**, number stated if >1.
n, number of ocular mycobacteriosis cases; N, total number of diagnoses in each family; PR, prevalence ratio; CI, confidence interval.
Families in bold text were more significantly affected at the corrected *P*-value of <0.001.

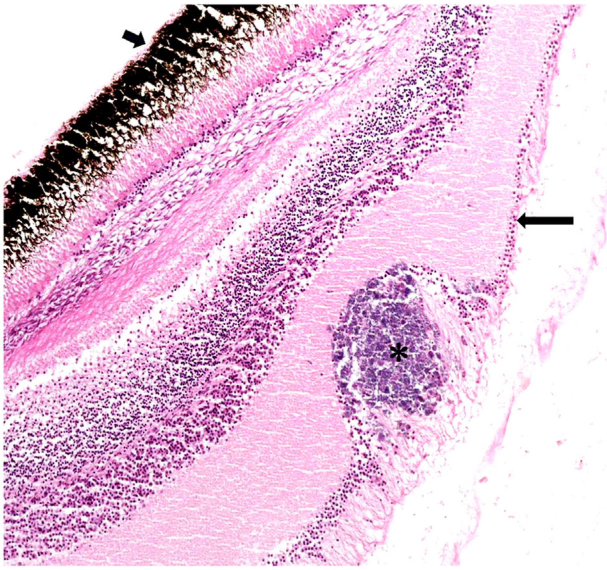

Fig. 1. Mycobacteriosis, retina, long snouted seahorse (*Hippocampus guttulatus*). Focal area of necrosis (*), mixed inflammatory cell population and abundant intralesional mycobacteria. Retinal pigment epithelium (short arrow), ganglion cell layer (long arrow). HE. ×100.

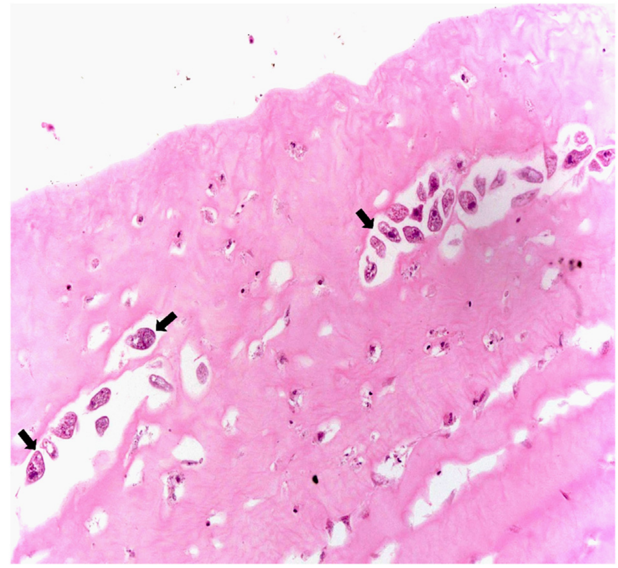

Fig. 3. Scuticociliatosis, cornea, Atlantic horse mackerel (*Trachurus trachurus*). Unicellular scuticociliates with basophilic vacuolated protoplasm containing eosinophilic granular organelles and single nucleus (arrows) embedded in oedematous corneal stroma. HE. ×200.

intraocular fluid accumulation and, in some cases, perivascular lymphohistiocytic infiltrates in the periocular connective tissues and other organs (cranial muscles and connective tissues, branchial arch, kidneys and spleen). In these cases, ocular enlargement was commonly part of a wider syndrome of generalized oedema (referred to by aquarists as 'dropsy'). A single case of buphthalmos had signs of retinal atrophy suspected to be secondary to intraocular pressure elevation due to glaucoma (Fig. 13A). Cataracts were uncommon (2%, 18/813), occurring in 13 families; 50% (9/18) of all cataracts were characterized as Morgagnian on histology. The Gadidae (cods, haddock, whiting, pollock) were more likely than any other fish family to have both buphthalmos and cataracts (PR = 17.6, 95% CI 4.0–76.7, $P = 0.0001$ and PR = 55.2, 95% CI 16.2–188.7, $P < 0.0001$). Exophthalmos ('pop-eye') was mentioned in 1.4% (64/4,572) of clinical summaries of all cases submitted for ocular HP examination and in 2.46% (20/813) of those with a diagnosis.

4. Discussion

This study afforded a unique opportunity to characterize ocular pathology in a large cohort of aquarium fish submitted for histopathological surveillance. Thirty-seven percent of all submissions had ocular HP examination with an ocular pathology diagnosed in 18% of these fish. This is consistent with other publications in which fish ocular disorders have been reported to be relatively common

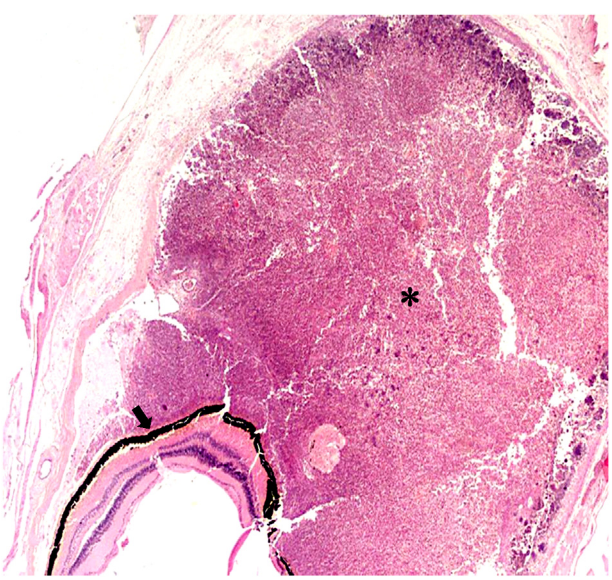

Fig. 2. Mycobacteriosis, periocular tissue, tiger tail seahorse. Massive cavitating necrotizing lesion (*), aggregates of mixed inflammatory cells and myriad intralesional mycobacteria. Retinal pigment epithelium (arrow). HE. ×20.

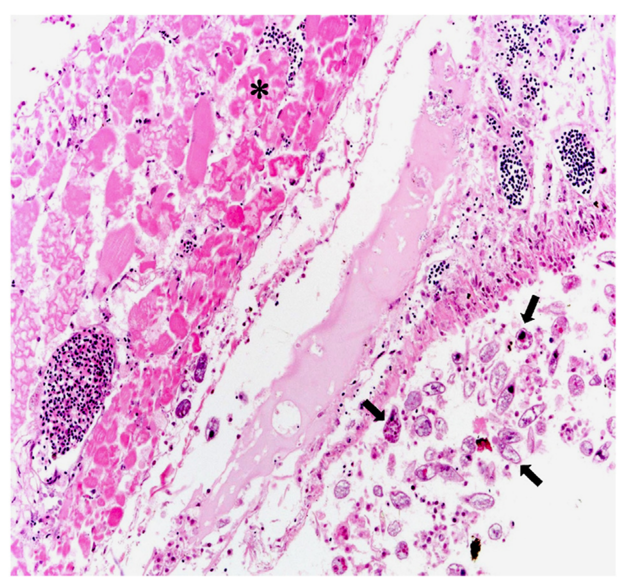

Fig. 4. Scuticociliatosis, episcleral tissue, Atlantic horse mackerel (same specimen as in Fig. 3). Many scuticociliates (arrows) associated with oedema, myofibre separation and necrosis (*). HE. ×200.

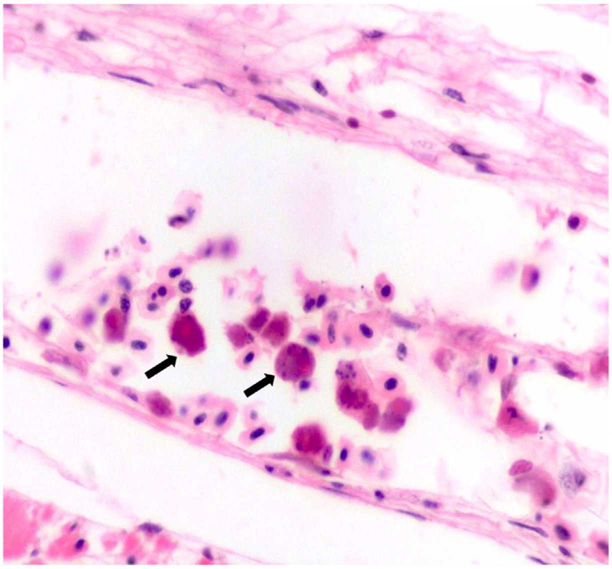

Fig. 5. Iridovirus infection, retrobulbar vascular rete, Banggai cardinalfish. Cytomegalic endothelial cells contain intracytoplasmic, basophilic, granular iridovirus inclusion bodies (arrows). HE. ×600.

[1–3,5,36]. Inflammatory/infectious disease were the most common (75%) lesions. Although there are no multispecies fish ocular pathology studies for direct comparison, retrospective studies of multisystem pathology in smaller numbers of fish species have also identified inflammatory/infectious diseases to be the most common [37–39]. Ocular mycobacteriosis and scuticociliatosis occurred at a high frequency, most significantly in the Syngnathidae. The Apogonidae were particularly affected by ocular neoplasia and iridovirus infections. These disease processes and the two fish families will therefore be discussed in greater detail.

Intraocular bacterial infections (eg, endophthalmitis) of fish are usually sequelae of systemic bacterial foci and are relatively common. Isolated, more localized, ocular surface (eg, keratitis), periocular or orbital bacterial infections are often secondary to

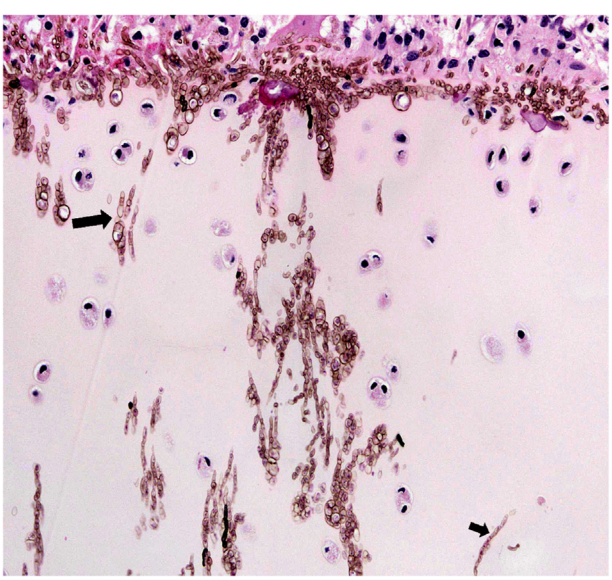

Fig. 6. Fungal infection, periocular cartilage, bull huss (*Scyliorhinus stellaris*). Many pale brown irregularly bulbous fungal pseudohyphae (long arrow) and true hyphae (short arrow), chondritis and cartilage necrosis. *Fusarium* species suspected. HE. × 200.

traumatic ulceration or parasitic infestations [2]. This is reflected in the present study where more intraocular (28%) than ocular surface/periocular/orbital (11%) non-mycobacterial bacterial infections occurred, and all ocular mycobacterial infections were associated with disseminated mycobacteriosis. Mycobacteriosis is one of the most common diseases of cultured, wild and aquarium fish worldwide, and is a significant source of morbidity and mortality [9]. Unilateral or bilateral exophthalmos due to panophthalmitis is the most commonly reported ocular sign and ocular involvement is widely reported [1,8,9,40–43]. Findings in this study are consistent with previous reports; mycobacteriosis accounted for most (60%) bacterial ocular infections and 25% of all mycobacterial infections identified in the archive were diagnosed with ocular manifestations. Atypical, environmentally-derived, non-tuberculous species (eg, *Mycobacterium marinum, Mycobacterium fortuitum* and *Mycobacterium chelonae*) usually cause mycobacteriosis in teleost fish [6,8,38]. Common aquarium fish from the Anabantidae, Characidae, Cyprinidae, Cichlidae and Syngnathidae families have been reported to be more susceptible to mycobacteriosis [8,40,41,44–46]. Two of these families, the Cichlidae and Syngnathidae, had significantly more diagnoses of ocular mycobacteriosis in the present study, with the latter family almost three times more likely to be affected compared with all other families. It has been suggested that a lack of interferon-gamma, a key element of the adaptive intracellular immune response to mycobacteria, could explain this increased susceptibility in syngnathids [46]. Mycobacterial lesions in syngnathid species typically lack granuloma formation and involve large numbers of acid-fast bacilli. In contrast, many other teleosts develop chronic granulomatous inflammation involving fewer bacteria [46]. Although not statistically significant, a similar difference in lesions between the Syngnathidae (70% with necrogranulomatous inflammation) and other fish (40% with granulomatous or histiocytic inflammation) affected by ocular mycobacteriosis was seen in this study. The endangered Banggai cardinalfish accounted for 16/18 ocular mycobacteriosis cases in the Apogonidae family. The vulnerable or near threatened (IUCN, 2022) lined seahorse, slender seahorse (*Hippocampus. reidi*) and tiger tail seahorse comprised 54% of the ocular mycobacteriosis cases in the Syngnathidae. With low host specificity, ongoing transmission in densely stocked aquaria, absence of effective treatment or vaccines and depopulation/destruction of affected fish and extensive disinfection of tanks required to control mycobacteriosis [8,9,47], the loss of high-value, flagship, popular, display aquarium species such as these has a significant economic impact. The zoonotic risk of *M. marinum* to aquarists must also be considered [8,48–51].

Parasites are rarely reported as a primary ocular pathogen in fish, although their importance in pet and aquarium fish is well recognized [1,41]. The most prominent (62% of all parasitized cases) parasites to infect ocular and periocular tissues in the present study were ciliophoran scuticociliates. Consistent with other reports [10,38,45], scuticociliates, primarily *Uronema*-like species (most likely *P. dicentrarchi*, although organisms were not speciated by molecular methods in any case) commonly parasitized the Syngnathidae. Species in this family were nearly twice as likely to be affected by ocular scuticociliatosis than other fish. Ulcerative keratitis or periorbital dermatitis can facilitate entry of the parasite and exophthalmos, periocular hyperaemia, periorbital oedema and haemorrhage have all been reported to occur with scuticociliatosis [52–54]. The histological changes identified in the present study were similar to those reported [54]. Cryptocaryonosis was the second most diagnosed parasitic disease (14%). The ability of the parasitic stage (trophonts) of *Cryptocaryon irritans* to inhabit the epithelial tissues of the cornea and skin [3] explains the keratitis and periocular dermatitis seen in all cryptocaryonosis cases in this study. The severe pruritus and irritation sometimes associated with

Table 5
Twelve fish families with 184 submissions for ocular histopathology had an ocular diagnosis of neoplasia (n = 30)

Family	Neoplasia	Total	PR	95% CI	*P* value	Genus/species	Type of neoplasia (n if > 1)
Apogonidae	**12**	**61**	**8.2**	**4.2–16.3**	**<0.0001**	***Sphaeramia nematoptera***	Carcinoma (5), lymphoma (2), melanoma (2), neuroectodermal, retinoblastoma and round cell sarcoma
Cyprinidae	2	9	6.4	1.8–22.8	0.004	*Carassius auratus* *Cyprinus carpio*	Spindle cell sarcoma (2)
Gasterosteidae	**5**	**16**	**10.0**	**4.4–22.7**	**<0.0001**	***Gasterosteus aculeatus***	Lymphoma (3), meningioma and unspecified
Labridae	1	29	0.9	0.1–6.6	0.9	*Ctenolabrus rupestris*	Melanoma
Leptobarbidae	**1**	**1**	**28.0**	**19.6–40.0**	**<0.0001**	***Leptobarbus hoevenii***	Spindle cell sarcoma
Leuciscidae	2	17	3.3	0.9–12.9	0.08	*Leuciscus idus*	Round cell sarcoma and spindle cell sarcoma
Lutjanidae	1	7	4.0	0.6–25.2	0.1	*Lutjanus kasmira*	Melanoma
Monacanthidae	**2**	**5**	**11.5**	**3.7–35.9**	**<0.0001**	***Acreichthys tomentosus***	Carcinoma and melanoma
Myliobatidae	1	3	9.3	1.8–48.0	0.008	*Myliobatis californica*	Lymphoma
Priacanthidae	1	5	5.6	0.9–33.3	0.06	*Pristigenys serrula*	Haemangioma
Serranidae	1	23	1.2	0.2–8.3	0.9	*Anthias anthias*	Melanoma
Toxotidae	1	8	3.4	0.5–22.5	0.2	*Toxotes jaculatrix*	Melanoma

PR, prevalence ratio; CI, confidence interval. Families in bold text were more significantly affected at the corrected *P* value of <0.001.

cryptocaryonosis and scuticociliatosis have welfare implications in infected fish. Infection rates are reported to be higher in warmer water with higher salinity for scuticociliatosis [10,55] and in higher water temperatures for cryptocaryonosis [56]. This information could influence prevention and control of these parasitic diseases in aquaria. However, water quality and environmental parameters were not uniformly available for all fish in this dataset, preventing investigation of any association between these variables and disease.

Iridovirus (*Megalocytivirus*) infection has been described in Banggai cardinalfish and, as in this study, the associated changes are characterized by cytomegalic perivascular cells containing intracytoplasmic, basophilic, granular, viral inclusion bodies in a variety of tissues, including the choroid [57]. The Banggai cardinalfish was by far the most frequently affected of all species, with the Apogonidae family to which it belongs 10 times more likely than any other fish family to be diagnosed with this disease. Iridoviral involvement of the vascular rete, choroidal capillaries and retrobulbar connective tissues would be consistent with the exophthalmos recognized as a common clinical sign of this disease [57–59]. Banggai cardinalfish can be bred in captivity but continue to be harvested from the wild and subjected to transport and handling stressors during transglobal shipment. Such stressors, coupled with poor aquarium conditions, are likely to enhance the risk of clinical disease [57,58] and may be factors resulting in increased iridovirus susceptibility in this fish species. Infection in wild-caught aquarium fish may also reflect rates of infection in the wild populations from where they are sourced, a concern in highly threatened species such as the endangered Banggai cardinalfish. Iridoviruses affect every sector of the ornamental fish industry and are not tightly host specific, with outbreaks of disease causing high mortality rates and significant economic losses [58–61].

Ocular neoplasia occurred infrequently (4% of all diagnoses) and only in a few families and species in this dataset. Primary ocular neoplasia in fish has been considered rare [2] and there are reports of neoplasms in the eyes of single species or in a small series of fish species [12–20,62]. Nine different ocular neoplasms were identified in this study, affecting several fish families/species. Ocular melanomas were most frequently seen (7/30), showing significant

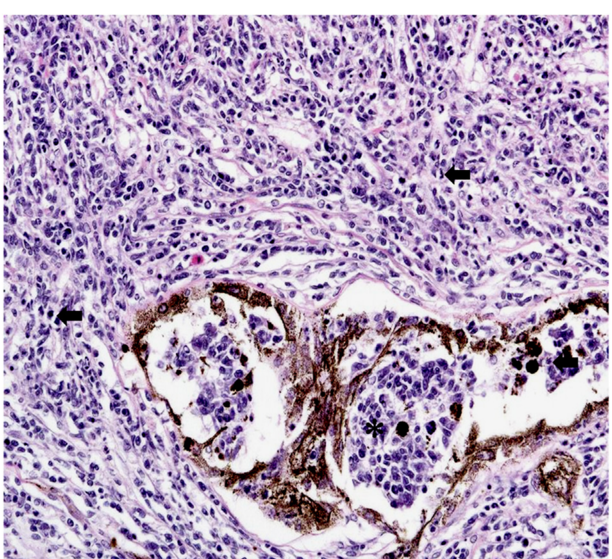

Fig. 7. Ocular melanoma, sclera, pajama cardinalfish. Sheets of polyhedral to spindloid cells with indistinct borders efface and disrupt normal tissue architecture. Frequent mitoses (arrows). Cluster of intravascular neoplastic cells (*) with anisocytosis, anisokaryosis and fine intracytoplasmic melanin granules. HE. ×200.

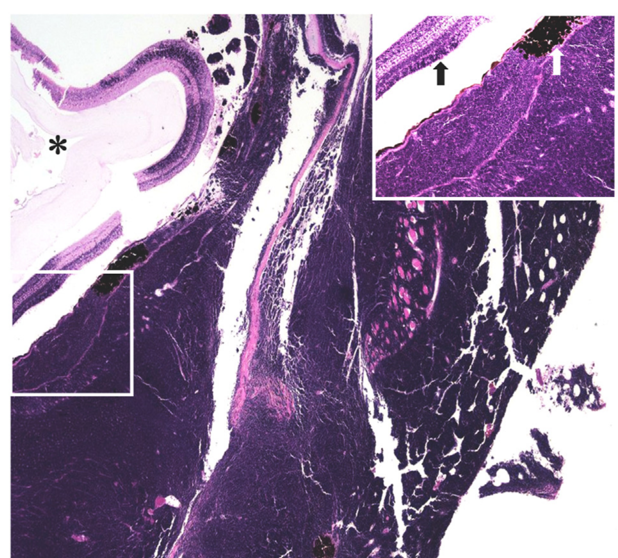

Fig. 8. Ocular/periocular round cell sarcoma, eye and periocular tissues, pajama cardinalfish. Densely packed basophilic round cells diffusely infiltrate and efface eye (*) and surrounding tissues. HE. ×20. Inset: neoplastic cells invade retina (black arrow). Melanomacrophage aggregate (white arrow) within periocular neoplastic cell population. HE. ×100.

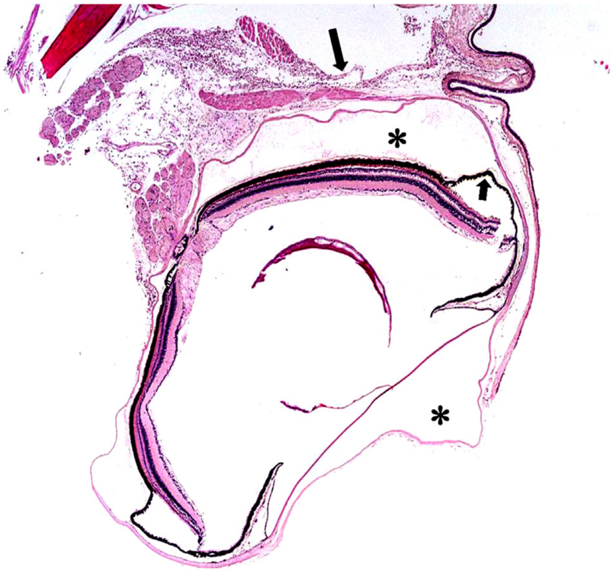

Fig. 9. Gas bubble disease, eye and periocular connective tissue, snake pipefish (*Entelurus aequoreus*). Cavernous bubble-like spaces in cornea and sclera (*). Retinal detachment with 'tomb-stoning' of retinal pigment epithelium (short arrow). Periocular connective tissue separation (long arrow) with oedema and haemorrhage. HE. ×20.

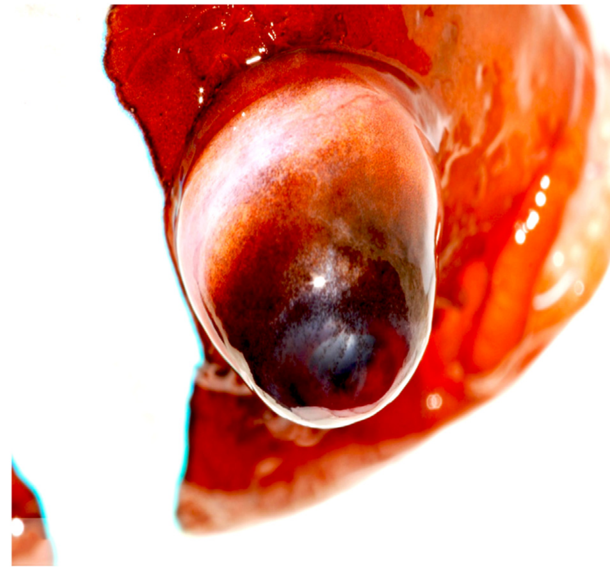

Fig. 11. Exophthalmos and hyphaema, right eye, common clownfish (*Amphiprion ocellaris*).

invasion of multiple intraocular structures. This is in contrast to a single report of iridociliary melanoma in a long-horned cowfish (*Lactoria cornuta*) in which a more localized ciliary body mass extended into the iris base and retractor lentis muscle with secondary lens luxation [19]. The pajama cardinalfish accounted for all 12 ocular neoplasms seen in the Apogonidae in this study, and this family was eight times more likely than any other family to have ocular neoplasia. This was an unexpected and previously unrecognized finding. A conference abstract presentation of retinoblastoma-like tumours in six pajama cardinalfish is the only previous report of ocular or any other type of neoplasia in this species [63]. This study shows that apart from retinoblastomas, ocular carcinomas, lymphomas, melanomas, neuroectodermal tumours and round cell sarcomas can all affect pajama cardinalfish. This fish species has adaptations for nocturnal vision, including a larger eye and retina than diurnal species [64], and has been proposed to be more sensitive to retinal damage due to ultraviolet (UV)/blue light [63]. This might explain the apparent propensity for ocular neoplasia in pajama cardinalfish.

Ocular fungal infections were rare (only 4% of inflammatory pathology cases) in this study and most of these were panophthalmitis (13/25) and periocular cellulitis (8/25) cases. These are likely to have occurred secondary to systemic mycoses or to other ocular surface/periocular diseases. It has been suggested that primary ocular fungal infections of fish are uncommon [1,2,7].

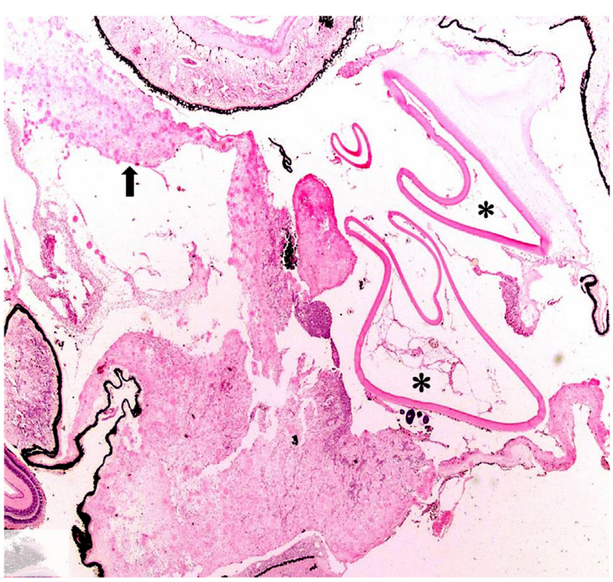

Fig. 10. Phthisis bulbi, eye, banded archerfish (*Toxotes jaculatrix*). Protein-rich fluid, neutrophils, erythrocytes, macrophages and fibroblasts in posterior chamber (arrow). Ruptured lens with lens capsular tissue containing remnants of lenticular debris (*). HE. ×20.

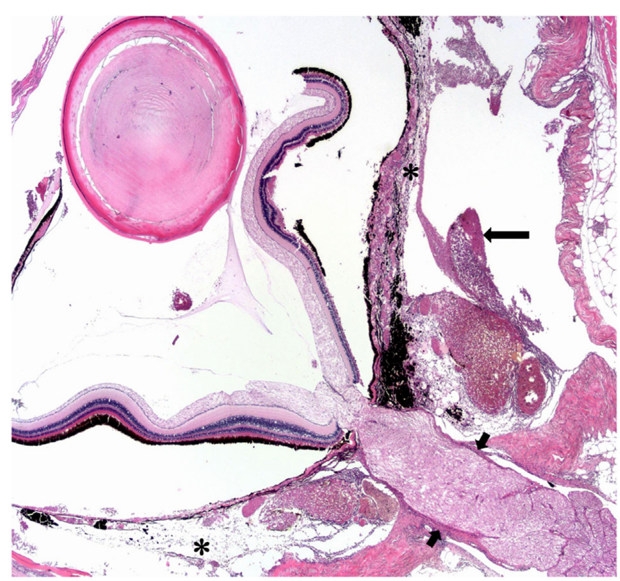

Fig. 12. Hyphaema, enucleated right eye, common clownfish (same specimen as in Fig. 11). Dilated and congested periocular blood vessels with extravasation of erythrocytes (long arrow). Artefactual retinal detachment and markedly distended, oedematous, congested and haemorrhagic choroid (*). Optic nerve (short arrows). HE. ×20.

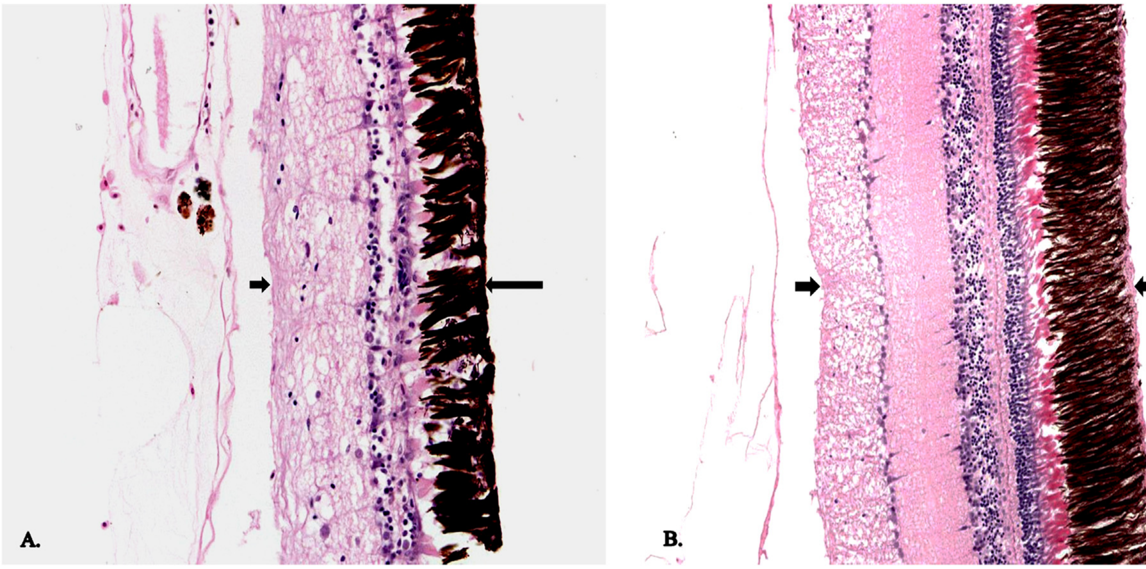

Fig. 13. (A) Retinal atrophy, ballan wrasse (*Labrus bergylta*). Retinal atrophy suspected secondary to glaucoma. Unremarkable retinal pigment epithelium (long arrow), thin photoreceptor layer, thin but distinct outer nuclear, outer plexiform, inner nuclear and inner plexiform layers and absence of distinguishable nerve fibre layer (short arrow). HE. ×200. **(B)** Normal retina, ballan wrasse for comparison. Retinal pigment epithelium (long arrow) and nerve fibre layers/inner limiting membranes (short arrow). HE. ×200.

Trauma was the most likely aetiology (29/34) in cases of intraocular haemorrhage in this study, which is consistent with reports of ocular trauma being common in fish [2]. Aquarists and veterinarians might diagnose trauma at aquarium level [39], especially when obvious lesions such as periorbital abrasions, corneal ulceration and hyphaema are present, consequently reducing the number of submissions for histological confirmation. This might account for the low frequency of pathologist suspicion of trauma (only 13% of cases) in this study. Conspecific or interspecies aggression, particularly in overcrowded exhibits, collisions, handling stress and recent transportation can all contribute to ocular trauma in fish [1,2,37]. Globe rupture may occur in severe cases of trauma and may have been the cause in 11/29 phthitic eyes in this study. However, phthisis bulbi is a chronic, non-specific, end-stage sequela to a range of severe ocular diseases. Determining a definitive cause histologically can be very challenging in such distorted globes.

GBD occurred at a low frequency (3%) in the submitted case material. The Syngnathidae have been shown to be particularly predisposed to GBD [38] and 38% of GBD cases in this study were from this family. The histological changes associated with GBD have been described in detail [2,11]. It is possible that GBD was underdiagnosed histologically when obvious gas accumulations were not seen in tissues or a history of a gas supersaturation event was not provided. Some of the cases diagnosed with intraocular haemorrhage, endophthalmitis/panophthalmitis/uveitis, cataracts or phthisis bulbi without another obvious cause could have been initiated by GBD.

With few eyes (2% of all diagnoses) diagnosed with a cataract, even in the Gadidae, which were shown to be more frequently affected, this study identified an apparently low level of cataracts in the aquarium fish species submitted for histological examination. Under aquarium management, cataracts (particularly mature/hypermature cases) are visible to aquarists and visitors. With limited budgets, aquaria may elect to allow otherwise healthy fish that are coping well to continue in an exhibit rather than submit them for histology. Enucleation may also be considered unnecessary when the diagnosis is obvious, and fish that are not able to cope with cataract associated blindness might be euthanized. Cataracts have been reported to be the most economically important disease of many farmed fish [31] and may be induced by a variety of insults including inappropriate nutrition, environment, chemical exposure and infectious organisms including parasites [65]. For example, actinic damage from UV light may incite lens damage in fish [26] and aquaria may have artificially high levels in comparison with exposure levels in the wild [66]. Although most fish cataracts are irreversible, osmotic cataracts and those caused by water temperature fluctuation may be reversible [5] and adjustment of diet can influence the rate of fish cataract development [32]. Submission of more examples of cataractous eyes with whole fish may enable additional conclusions to be drawn about suspected causes that could be addressed by modifications to aquarium management systems. Buphthalmos usually refers to an enlarged globe, secondary to chronically elevated intraocular pressure/glaucoma in other animals. Only one case of buphthalmos in this study had clear evidence of retinal atrophy, potentially correlating with chronic intraocular pressure elevation. Retinal ganglion cell loss has been seen in experimental zebrafish with a genetic mutation causing raised intraocular pressures [67]. All other buphthalmos cases (2% in total) in this study were associated with whole body oedema (‘dropsy’), which is a non-specific presentation due to failure of osmoregulation, caused by a range of underlying conditions in fish.

Corporate groups of aquaria frequently have standardized collection planning, including sourcing and distribution of fish. Transfer of some fish between related centres also occurs. General husbandry/feeding, quarantine and health management practices may also be standardized. The details of these practices were not available in this dataset, precluding reliable intercomparison of different facilities and of the effects such factors could have on the species and disease frequencies. An absence of detailed histories, environmental (eg, water quality and temperature) parameters, stocking information/species distribution and clinical observation in many cases limited opportunities to investigate associations between such variables and ocular pathology. Factors such as levels of aquarist training and observation and the relative importance ascribed to different species within collections may have introduced bias into the range and prevalence of ocular diseases diagnosed. Future work could involve prospective studies focussing on the more significant ocular diseases in single or small numbers of fish families/species. Detailed histories and environmental data could be collected alongside questionnaires for participating aquarists in order to address some of these limitations, with more detailed routine ophthalmological clinical examination of fish to corroborate histopathological findings.

5. Conclusion

In this study we identified the frequency of ocular diseases in a large cohort of aquarium fish comprising 125 fish families. These results will guide clinicians in formulating differential diagnosis lists and determining the prognosis for ocular diseases in aquarium fish. Training for aquarists and veterinarians in the use of ocular signs to improve early detection, surveillance, treatment and control of these diseases will improve health, longevity and welfare in aquarium populations, and have both direct and indirect benefits for the conservation of endangered fish species in captivity and the wild.

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Statement of Author contributions

KV Kumaratunga: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – original draft preparation, Visualization. **VJ Adams:** Methodology, Software, Validation, Formal analysis, Data curation, Writing – review & editing, Supervision. **D Donaldson:** Writing – review & editing, Supervision. **R Tetas Pont:** Writing – review & editing, Supervision. **MF Stidworthy:** Conceptualization, Resources, Writing – review & editing, Imaging, Supervision.

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Declaration of competing interests

The authors declared no conflicts of interest with respect of the research, authorship or publication of this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcpa.2022.11.002.

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