

Herpesvirus causing fibropapillomatosis in sea turtles (Infection with)

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AETIOLOGY

Classification of the causative agent

Fibropapillomatosis (FP) of sea turtles, while demonstrably transmissible, has a somewhat unclear aetiology. It is believed these fibropapillomas are caused by a potentially oncogenic alphaherpesvirus, chelonid herpesvirus 5 (ChHV5). Viral DNA is consistently found in fibropapillomas, but occasionally in normal tissues as well. Because Koch's Postulates have not been adequately fulfilled, ChHV5 has not definitively been proven to cause FP. However, due to a strong association between the two, it is putatively considered the aetiologic agent.

The virus itself is widely distributed geographically and may be identified in the skin of outwardly healthy turtles, suggesting latency and/or an asymptomatic carrier state. Additionally, phylogenetic analyses indicate a long history of host-adaptation. It is hypothesized that environmental and/or physiologic stress plays a significant role in the development of clinical disease.

Resistance to physical and chemical action

Temperature: Not well determined; some evidence suggests that in regions with reasonable seasonal variation, tumour growth may be faster when the water is warmer

pH: Not well determined

Chemicals/Disinfectants: Not well determined

Survival: Not well determined

EPIDEMIOLOGY

Hosts

- Marine sea turtles
 - Green (*Chelonia mydas*)
 - Loggerhead (*Caretta caretta*)
 - Kemp's ridley/Atlantic ridley (*Lepidochelys kempii*)
 - Hawksbill (*Eretmochelys imbricata*)
 - Flatback (*Natator depressus*)
 - Olive ridley (*Lepidochelys olivacea*)
 - Leatherback (*Dermochelys coriacea*)

Transmission

- Routes of transmission are still under investigation, but vertical transmission is not believed to occur due to the lack of disease in hatchlings. Suspected routes include:
 - Mechanical vectors, particularly leeches of the genus *Ozobranchus*, Spirorchid trematodes, and reef fishes
 - Direct transmission between cohabiting turtles

Sources

- Tumour keratinocytes and fibroblasts

- Urine
 - It is believed that renal cells, rather than urinary bladder epithelial cells, are responsible for PCR-positive test results in urine.

Occurrence

ChHV5 is identified in marine turtles globally, but the prevalence of FP appears to vary with location and time. Two main hypotheses regarding FP development exist: one considers migration to neritic zones and subsequent recruitment activity to be the impetus for disease; the other assumes most marine turtles are infected with ChHV5, but FP develops secondary to environmental factors. Green turtles appear to be most affected, but all species of marine turtles are susceptible. There is no documented sex predisposition, and hatchlings have not been observed with FP lesions.

A significant proportion of documented FP cases are close to shore near large populations of people in tropical and subtropical regions. It is hypothesized that land use changes, increased water temperature, toxin and pollutant exposure, poor water quality, and other environmental alterations contribute to the development of FP in turtles infected with ChHV5. Oxidative stressors from sources such as UV radiation and heavy metals (namely Pb, Fe, and Cu) are believed to interfere with cholesterol metabolism and therefore increase endogenous reactive oxygen species synthesis.

However, it must be determined whether the incidence of FP is truly associated with coastal habitat and anthropogenic stressors, or if prevalence appears higher due to the ease of sampling when compared to the open ocean. A wide variety of conclusions have been drawn from studies in green turtles. This ultimately indicates uncertainty still exists and much more research regarding the pathogenesis of FP must be performed to truly identify the role, if one exists, of different environmental stressors. Additionally, most of the current literature focuses on green turtles and research efforts should be expanded to other marine turtle species to ensure a full understanding of the disease process.

DIAGNOSIS

Generally, highly reproductive young adults and large juveniles/sub-adults are believed to be most affected. It is believed that the tumours progress from papillomas to fibropapillomas to fibromas with chronicity. FP regression has been documented in rehabilitation as well as trap-and-release research settings, and it may be associated with lesions that are plaque-like in morphology. It is unclear whether adults are less affected due to disease resolution and subsequent protection, or whether most affected individuals succumb to disease and perish before maturation. Morbidity and mortality appear to vary with time and geography as well.

Clinical diagnosis

The appearance of fibroepithelial growths, whether multiple or solitary, is nearly pathognomonic for FP in marine turtle species. These lesions may be visceral or cutaneous, and they may be large enough to hinder normal functions such as vision, movement, and feeding. Papillomas are characterized by epidermal proliferation and sparing of the dermis, whereas fibromas are characterized by dermal proliferation and sparing of the epidermis. Features of both are present in fibropapillomas, which are considered an intermediate stage.

Clinically affected animals show biochemical evidence of chronic inflammation, immunosuppression, and chronic stress. Many are also emaciated. The presence of plaque-like lesions - rather than pedunculated or verrucous - may be a positive prognostic indicator. There is also some evidence to suggest ocular FP is a great negative prognosticator for survival to release in rehabilitation settings.

Lesions

- Cutaneous, mucocutaneous, and/or visceral fibroepithelial tumours
 - 0.1-30 cm in diameter
 - Smooth or warty
 - Plaque-like, sessile, or pedunculated
 - Colour is influenced by the affected tissue type
- Histopathology of the epidermis reveals hyperplasia, orthokeratotic hyperkeratosis, ballooning degeneration, swollen nucleoli, and cytoplasmic vacuoles
- Visualization of capsid aggregates near or within nuclear dense and reticulated bodies using electron microscopy; capsids themselves vary in appearance

Differential diagnoses

- The clinical appearance of fibropapillomatosis is considered pathognomonic

Laboratory diagnosis

Samples

For isolation of agent

- Fibropapilloma lesions/cores, skin biopsies
 - Preferred sample
- Kidney
- Urine
- Central or peripheral nerves
 - Not consistently identifiable by PCR
- Nasal, ocular, and cloacal swabs
 - Considered low sensitivity
 - Not ideal sample for diagnostic testing, but often utilised for field surveys
- Normal skin
 - May test PCR positive if the animal is infected with ChHV5 regardless of FP presence

Serological tests

- Whole blood or serum

Procedures

Identification of the agent

- Immunohistochemistry (IHC)
- Polymerase chain reaction (PCR)

Serological tests

- IgY antibody-capture enzyme-linked immunosorbent assay (ELISA)
 - Currently only utilised in research settings

PREVENTION AND CONTROL

Sanitary prophylaxis

- It is advised that all wildlife rehabilitators and zoological park staff take adequate sanitary precautions in facilities that house sea turtles. ChHV5 is believed to be enzootic in marine turtle populations, but

the unclear pathogenesis of FP indicates continued dedication to environmental and instrumental hygiene and decontamination.

- In these settings, ensure appropriate water quality, temperature, and flow by utilizing best practices for the species housed. Care should be taken to reduce environmental stressors as much as is feasible, e.g., providing an appropriate photoperiod.
- Do not house FP-inflicted turtles with those that appear clinically healthy.

Medical prophylaxis

- There is currently no medical prophylaxis for FP.
- Surgical removal of FP lesions has been attempted in many rehabilitation settings, but the results are variable. It is common for lesions to regrow or for new lesions to appear afterwards.
 - There is speculation that reducing water temperature by 2-5°C post-operatively may reduce the likelihood of recurrence.
 - Anecdotal treatments utilised to prevent regrowth include lysine administration, among other antiviral drugs.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- There is no documented risk of FP to human health.

Risks to agriculture

- There are no documented direct risks of FP to the agricultural industry.
- Some fish species are considered potential mechanical vectors for ChHV5. However, their role in disease transmission is poorly understood at this time, and there is insufficient evidence to suggest any participation of or risk to fish-farming and aquaculture industries in this regard.
- Due to the role marine turtles play in the ecotourism industry, FP may have a negative effect on local economies especially in regions where morbidity and mortality are high.

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<p>The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated 2020. Written by Samantha Gieger and Erin Furmaga with assistance from the USGS National Wildlife Health Center.</p>
