Cancer in Sea Turtles

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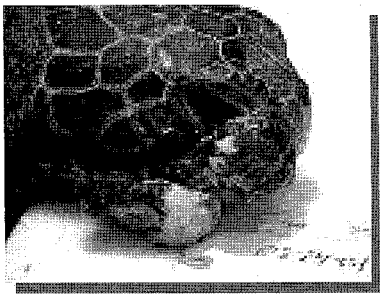
Sea Turtles

Sea turtles are one of the oldest extant groups of animals, and they have changed little in basic anatomy for millions of years. Sea turtles are found throughout the world, and depending on the species, range from warm tropical water to frigid oceans near the arctic. They can be herbivores, omnivores, or carnivores and can be quite large. For example, the largest species of sea turtle, the leatherback, can weigh several hundred kilos. All sea turtles have an oceanic existence. Males spend almost their entire life in the ocean. After mating, females crawl onto nesting beaches where they dig a nest, lay eggs, and return to the ocean. Several weeks later, these eggs hatch, and baby turtles disappear out to sea (no one knows exactly where). Eventually, juvenile turtles return to foraging grounds where they eventually mature to adults. Adults then migrate, sometimes many thousands of kilometers, to their breeding and nesting grounds where the cycle begins again. Sea turtles live for many (40+ years). Of the seven species of sea turtles, all are listed as threatened or endangered by the Endangered Species Act. Major threats to sea turtles worldwide include overharvesting of meat and eggs for human consumption from nesting beaches for consumption, bycatch of sea turtles from fisheries, and disease.

Hawaii has two *coastal* species of sea turtles, the hawksbill (*Eretmochelys imbricata*) and the far more numerous green turtle (*Chelonia mydas*). The major nesting grounds for green turtles in Hawaii are at French Frigate Shoals in the Northwestern Hawaiian islands (~500 miles from Oahu); the main Hawaiian islands harbor the foraging pastures where you can see juvenile and adult green turtles grazing on marine algae.[1] Since green turtles were listed as protected, the numbers of adults on nesting beaches has increased steadily.[2]

Fibropapillomatosis in Sea Turtles

A few cases of cancer have been reported in sea turtles including a leiomyoma in a green turtle from Florida[3] and lymphoma[4] and squamous cell carcinoma[5] in loggerhead turtles from Spain. However, by far the most important disease of sea turtles is fibropapillomatosis (FP). FP was first documented in green turtles from Florida.[6] Since then, it has been found in many species of sea turtles worldwide, including mainly green, loggerhead (Caretta caretta), and olive ridley (Lepidochelys olivacea) turtles. In Hawaii, FP is believed to have been present since the 1950s. FP is unusual among neoplastic diseases of free-ranging wildlife in that it affects a significant



percentage of animals. For example, in Hawaii, depending on method of collection and location, prevalence of FP in Hawaiian green turtles can range from 20-60%.[7]

The most visible manifestation of FP in green turtles is the presence of large tumors on the skin, eyes, and corners of the mouth. In some instance, these tumors can become very large and occlude vision. About 25 % of turtles with FP also have internal tumors, most commonly in the lungs, heart, and kidney. On histology, these tumors are universally composed of a connective tissue matrix and fibroblasts. In the case of skin tumors, these have been characterized as fibropapillomas[8,9] while tumors in internal organs have been classified as fibromas, myxofibromas, or fibrosarcomas of low-grade malignancy.[10,11] Hawaiian green turtles also have tumors in the glottis[12], and as expected, such animals are prone to getting pneumonia and other respiratory inflammatory problems.[11] Interestingly, green turtles with FP from Florida do not get tumors in the glottis. Green turtles afflicted with FP can be found on all major foraging pastures of the Hawaiian Islands, however, the disease is rare on the west coast of the island of Hawaii, and reasons for this are unknown.

In Hawaii, FP is the most significant cause of stranding morbidity and mortality in green turtles.[11] More troubling is that the prevalence of disease in juvenile turtles far exceeds that found in adults[11], and given that juveniles are an important life stage for long-lived species like sea turtles, the disease may have demographic effects in the longer term. A system to score severity of FP in green turtles based on size, number, and location of tumors was developed in Hawaii.[13] Green turtles with moderate to severe FP are over-represented on strandings[13] and are less likely to be recaptured. Green turtles with moderate to severe FP are also lymphopenic[13,14], suffer from chronic inflammation[13], are immunosuppressed[15], and are prone to systemic bacterial infections.[16] All this indicates that FP is more than a mere cosmetic disease and has detrimental impacts on the survival of affected animals. Cases of FP regressing are uncommon.[17] To top it all off, 100% of turtles that strand with FP have concomitant infections with blood flukes[11, 18] that resemble the human disease Schistosomiasis.

Many causes for FP have been proposed including pollutants[19], blood flukes[20], marine toxins[21], ultraviolet light, and viruses. Tantalizing evidence of viruses was found during microscopic examination of skin tumor from Floridian green turtles that revealed intranuclear inclusions compatible with herpes viruses.[22] Follow-up studies in Florida revealed that FP could be reproduced in captive green turtles using cell-free tumor homogenates thus ruling out parasites and further implicating a filterable agent such as a virus as a possible cause.[23] Other potential viral etiologies such as retroviruses[24], and papilloma viruses[25] were thought to play a role. However, more recent evidence from Hawaii[26] and Florida[27] implicates an alpha herpes virus as closely associated with FP. Using polymerase chain reaction, DNA from an alpha herpes virus has been consistently associated with tumored tissue from green, loggerhead, and olive ridleys from Florida[27], Hawaii, Australia, and Costa Rica[28]. Whether this herpes virus is the cause of FP or just happens to be found associated with tumored tissue remains unknown. A big stumbling block in progress with FP has been the inability to culture the virus in the laboratory in spite of the availability of cell culture systems.[29,30] This has hampered both the confirmation of the virus as cause of disease and the development of diagnostic tests. Nevertheless, in spite of these barriers, some progress has been made simply by the ability to detect viral genome in tissues through molecular tools. Viral RNA (suggestive of active replication) is more abundant near the surface of tumors suggesting that direct contact transmission of the virus is likely.[31] Other possible routes of transmission include cleaner fish[32] and parasitic leeches.[31]

Implications for Humans

The study of wildlife diseases for that matter goes beyond mere academic interest. Although FP is not zoonotic, the presence of epizootic disease in an ecosystem suggests an ecological imbalance. Given that most of Hawaii's human population lives near or depends on the ocean, presence of disease in marine ecosystems could indicate threats to the environment that may directly or indirectly also affect humans. Understanding the dynamics and causes of wildlife disease may have ramifications for human health. In addition, few animal models exist for herpes virus-induced neoplastic diseases. Two examples are Marek's disease[33], an alphaherpes virus that causes lymphomas in chickens and FP. Examples of herpes-induced viral cancers in humans include Kaposi's sarcoma (human herpes virus 8).[34] Kaposi's sarcoma in some ways closely resembles FP in that it is a skin tumor that, for many years, was associated with a non-cultivable herpes virus. Understanding the epizootiology and pathophysiology of FP in sea turtles may provide valuable clues to the biology of some human cancers.

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For more information on the Cancer Research Center of Hawaii, please visit our website at www.crch.org.

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