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MICROBIOLOGY IN SCHOOLS ADVISORY COMMITTEE
50th Anniversary Articles

Watch out for the fungus – It's behind you and coming up fast!

Another reason to fear Climate Change?

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In recent years, in both animals and plants, an unprecedented number of fungal diseases have caused some of the most severe die-offs and extinctions ever witnessed in species in the wild. They are known as Emerging Infectious Diseases (EIDs). One of the first to be noticed among animal species was a fungal EID that reduced population abundances in amphibians, across many species and over large geographical areas. Fungal EIDs of bats and corals were then identified, and a recently recognised fungal disease of snakes has caused declines in some snake populations in the Eastern United States.

There is also concern over diseases of plants, especially crop plants. An Emerging Plant Pathogen (EPP) causes a new disease, infects a new host, or extends the geographic range of a disease. The rate at which EPPs arise has recently increased, and threatens our food security.

Cutaneous chytridiomycosis of amphibians

This is an infectious disease of the skin that affects amphibians worldwide, caused by the chytrid fungus *Batrachochytrium dendrobatidis*. This colonises the epithelium of adult amphibians causing inflammation that impairs the cutaneous respiration, which is essential to the gas balance and osmoregulation of amphibians. It affects over 700 species on all continents where amphibians occur. The disease was only discovered in 1998, but it has since been linked to dramatic population declines of amphibian species in western North America, Central America, South America, Australia and Africa. Recent disturbances of rain forest habitats may have spread the parasite into susceptible amphibian populations. Subsequent world-wide spread of the disease was probably accelerated by the international trade in exotic 'pets'. In some regions in the wild the population declines of native amphibian species amount to multiple extinction events. It is certainly the largest disease-caused loss of biodiversity ever recorded.

Aspergillosis disease of coral

Because of global warming, ozone depletion, overfishing, eutro-phication, and drainage of poll-utants from the land, the decline of coral reef ecosystems has been a concern since the 1970s. However, disease seems now to be causing significant losses. A disease for which the identity of the pathogen has been proved to a satisfactory level is aspergillosis of the Caribbean Sea fan (*Gorgonia* spp.). The impact of disease ranges from severe (localised mass mortalities) to mild (partial tissue loss and eventual recovery). *Gorgonia ventalina* sea fans suffered mass mortality on reefs in the Caribbean and the Florida Keys in 1995 and 1996.

The pathogen was identified as *Aspergillus sydowii*, a common terrestrial soil fungus. Diseased tissues all contained fungal hyphae at their edges and careful analysis has

demonstrated that sea fan aspergillosis is infectious:

- the same filamentous *Aspergillus* species was isolated from different geographical disease areas,
- the organism could be grown in pure culture *in vitro*,
- mycelium taken from culture and inoculated onto healthy sea fans caused typical disease symptoms,
- the same fungus could be recovered from these experimental disease instances and recultured *in vitro*.

The course of action followed here was established by Robert Koch in the 1870s to identify pathogenic microorganisms (they are called Koch's postulates). Such procedures are necessary to demonstrate unambiguously that a suspected pathogen is the true cause of disease.

Aspergillus sydowii is a common saprotroph that is found in both terrestrial and marine environments as varied as Arctic Alaskan and tropical soils; as well as from subtropical coastal marine waters and oceanic zones as deep as 4,500 m. It had not previously been associated with disease in plants or animals. Non-marine strains of *Aspergillus sydowii* did not cause sea fan disease so it was concluded that isolates taken from diseased corals have acquired pathogenic potential, taking advantage of hosts weakened by factors like elevated temperature and nutrient pollution.

Aspergillosis in various animals, including humans, has increased over the last few decades. Some causing concern recently are: stonebrood mummification in honey bees, pulmonary and air sac infection in birds, mycotic abortion and mammary gland infections in cattle, guttural pouch mycoses in horses, sinonasal infections in dogs and cats, and invasive pulmonary and cerebral infections in marine mammals and non-human primates.

Snake fungal disease

Beginning in 2006, severe skin infections and a rapid population decline were reported in a timber rattlesnake (*Crotalus horridus*) in the northeastern USA. In 2008, similar infections with a possible fungal cause emerged in Illinois, USA in an endangered population of Massasauga rattlesnakes (*Sistrurus catenatus*). This infectious disease became known as Snake Fungal Disease (SFD), and by 2015, SFD had been documented in most of the eastern USA. SFD is caused by *Ophidiomyces ophiodiicola*, which is widely distributed in eastern North America. It has a broad host range and is the main cause of fungal skin infections in wild snakes. SFD has been documented in 23 very different species of snakes, which suggests that other species of snakes in the US might now be infected or susceptible to SFD. *Ophidiomyces ophiodiicola* was found in carcasses and moulted skins from wild snakes collected during 2010-2016 in Great Britain and the Czech Republic, which were screened using DNA detection. The fungus was detected in 8.6% of the specimens and further analysis confirmed that *Ophidiomyces*-SFD occurs in wild European snakes. The European and North American diseases involve genetically different strains of *Ophidiomyces ophiodiicola,* so this is a global emerging pathogen of reptiles in the wild.

White-nose syndrome of bats

White-Nose Syndrome (WNS) of bats is caused by the fungus *Pseudogymnoascus destructans*. This pathogen has decimated North American hibernating bats since its emergence in 2006 and is feared likely to drive several species extinct. WNS was first detected in New York

State in 2006 and was detected in Washington state in March 2016. *Pseudogymnoascus destructans* is endemic in Eurasia, where the disease is less severe with a much lesser impact on bat populations. Bats first become infected when they return to their winter quarters (their hibernacula) in the autumn, and both transmission and fungal growth on bats occurs primarily during winter when bats lower their body temperature and begin to hibernate. Mortality from WNS differs substantially between North American species, even when they hibernate at the same sites. Some species declined more than 90% in the first year following WNS detection, whereas population growth rates in other species only decreased 8%. Despite markedly different mortality rates, most bat populations experience greater than 50% infection incidence, suggesting that variation in mortality is due to variation in response to infection. Differences in the preferred roosting microclimate between bat species determines the impact of the new pathogen. An interesting aspect of this story is that the pathogen, *Pseudogymnoascus destructans*, is extremely sensitive to ultraviolet (UV) light and to chemical mutagens, because the pathogen's genome has lost a key enzyme in its DNA repair pathway. This feature might be exploited for treatment of bats with WNS.

Emerging fungus diseases

The fungal diseases that have affected wildlife populations over the past several decades need to be studied and understood. This is not only important for wildlife conservation, but for us, too. We may be next in line. You might think we don't need more fungal pathogens:

'Fungi cause more than a billion skin infections, more than 100 million mucosal infections, 10 million serious allergies and more than a million deaths each year. Global mortality owing to fungal infections is greater than for malaria and breast cancer and is equivalent to that owing to tuberculosis and HIV...' (quoted from Gow & Netea, 2016; see also Bongomin *et al*., 2017). Emerging plant pathogens threaten the security of our food crops, so it's no surprise that many examples of EPP come from agriculture, including:

- *Ramularia collo-cygni*, a European barley pathogen (*Ramularia* leaf spot) which emerged in South America in 2011 and which has also recently developed virulence against oats and wheat.
- *Magnaporthe oryzae*, known as rice blast disease, was detected on wheat in Brazil in 1985, and Bangladesh in 2015-16.
- Charcoal rot, also known as dry-weather wilt is caused by the fungus *Macrophomina phaseolina*. The fungus has a widespread distribution and large host range but recently emerged as a disease of soybean in both the USA and Africa's Sahel region. The disease is most problematic in hot, arid conditions and is expected to spread to new regions as the climate changes.

These few examples illustrate the main issue, which is that environmental stress can change the balance between being a pathogen and not being a pathogen. Most of the stress can be attributed to human-made changes:

- agricultural monocultures, which provide year-round host availability;
- international trade spreading disease fungi worldwide;
- climate change caused by accumulating CO_2 and reactive nitrogen gases (NO_X).

There is no shortage of plant-pathogenic fungi which might be subject to such stress. But many plants harbour fungi within their tissues that are normally harmless and may be beneficial. Fungi that are simply taking advantage of the habitat of open spaces within plants (particularly the leaf space) are called endophytes and seem to be present in any

healthy plant tissue. And, of course, most terrestrial plants harbour mycorrhizal fungi in root symbiotic associations. Any of these associations could be tipped from mutualistic to pathogenic status by magnifying environmental stresses.

More information

…about fungi as pathogens of animals:
http://www.davidmoore.org.uk/21st_Century_Guidebook_to_Fungi_PLATINUM/Ch16_00.htm

…and fungi as pathogens of plants:
http://www.davidmoore.org.uk/21st_Century_Guidebook_to_Fungi_PLATINUM/Ch14_00.htm

Fones H.N. & Gurr S.J. (2017). NO_xious gases and the unpredictability of emerging plant pathogens under climate change. *BMC Biology*,**15**:article 36. https://doi.org/10.1186/s12915-017-0376-4.

Gow N.A.R. & Netea M.G. (2016). Medical mycology and fungal immunology: new research perspectives addressing a major world health challenge. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **371**: 20150462. DOI: https://doi.org/10.1098/rstb.2015.0462.

Bongomin F., Gago S., Oladele, O.R. & Denning D.W. (2017). Global and multi-national prevalence of fungal diseases - estimate precision. *Journal of Fungi*, **3**: 57. https://doi.org/10.3390/jof3040057.

IMAGE CREDITS: frog icon made by Smashicons, coral icon made by Freepik; both downloaded from www.flaticon.com. Other icons from the Microsoft Icons library in MS Office 365

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Dr David Moore was formerly Reader in Genetics in the Faculty of Life Sciences at Manchester University. His research interests were in fungal physiology and mutant isolation and linkage mapping in *Coprinopsis cinerea*. David has held a number of senior positions in the British Mycological Society including that of President and was creator and webmaster of its web site. He was instrumental in establishing the society's outreach and education work in schools, science fairs and RHS shows for which he has received the society's awards. David is the author of a number of books on mycology.