The Fungal Kingdom

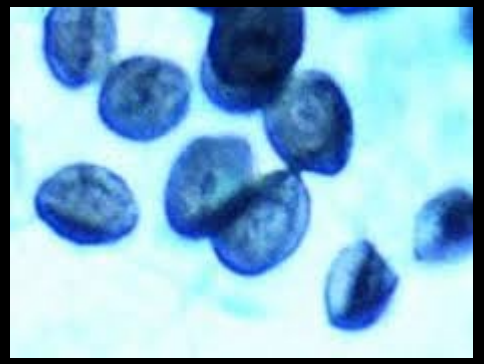
- **> 6 million species**
- **Includes major pathogens of plants, insects, invertebrates and ectothermic vertebrates**
- **Fungi currently devastating major ecosystems**
  - **Bats devastated by ‘white nose syndrome’**
  - **Catastrophic amphibian declines from *Batrachochytrium dendrobatidis***
  - **Salamanders declines in Europe from *Batrachochytrium salamandrivorans***
  - **Snakes in North America**
- **Mammals are remarkably resistant!**

Relatively few fungal species are pathogenic for humans

Host Associated

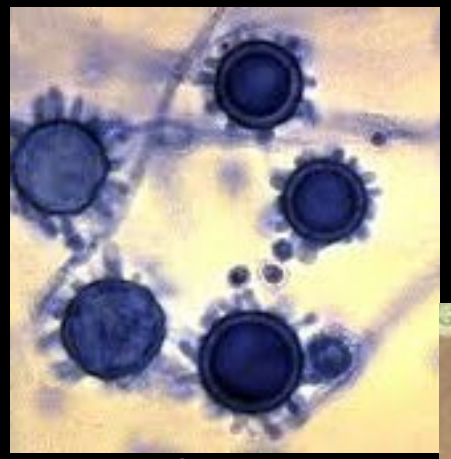
***Candida* spp.**

Dermatophytes

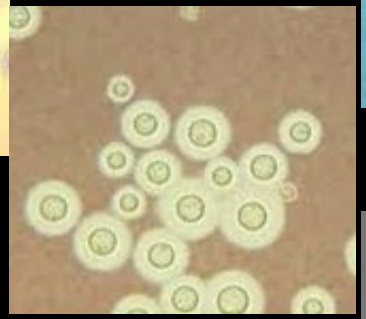


Pneumocystis spp.

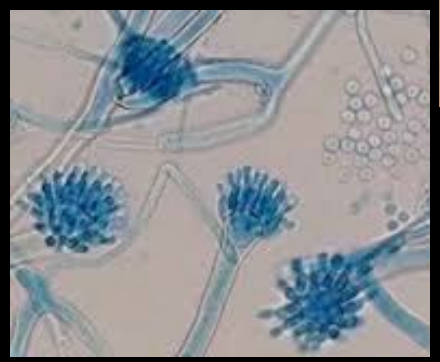
Environment



***Histoplasma* spp.**



***Cryptococcus* spp.**



Aspergillus spp.

***Coccidioides* spp.**

Blastomyces spp.

Requirements for Fungal Human Pathogenicity

Thermotolerance

- **Host associated such as Candida spp. already thermotolerant**
- **Only 6% of species in environment can tolerate > 37 ^{o}C (Robert & Casadevall JID 2009)**
- **Only a few 'major' pathogenic fungi *(Aspergillus, Cryptococcus, Histoplama, Sporothrix, Coccidioides spp.)***

Survival in host and replication

- **"Virulence factors"**
- **Survive, replicate and evade immune mechanisms**
- **Highly varied…**

Capsules

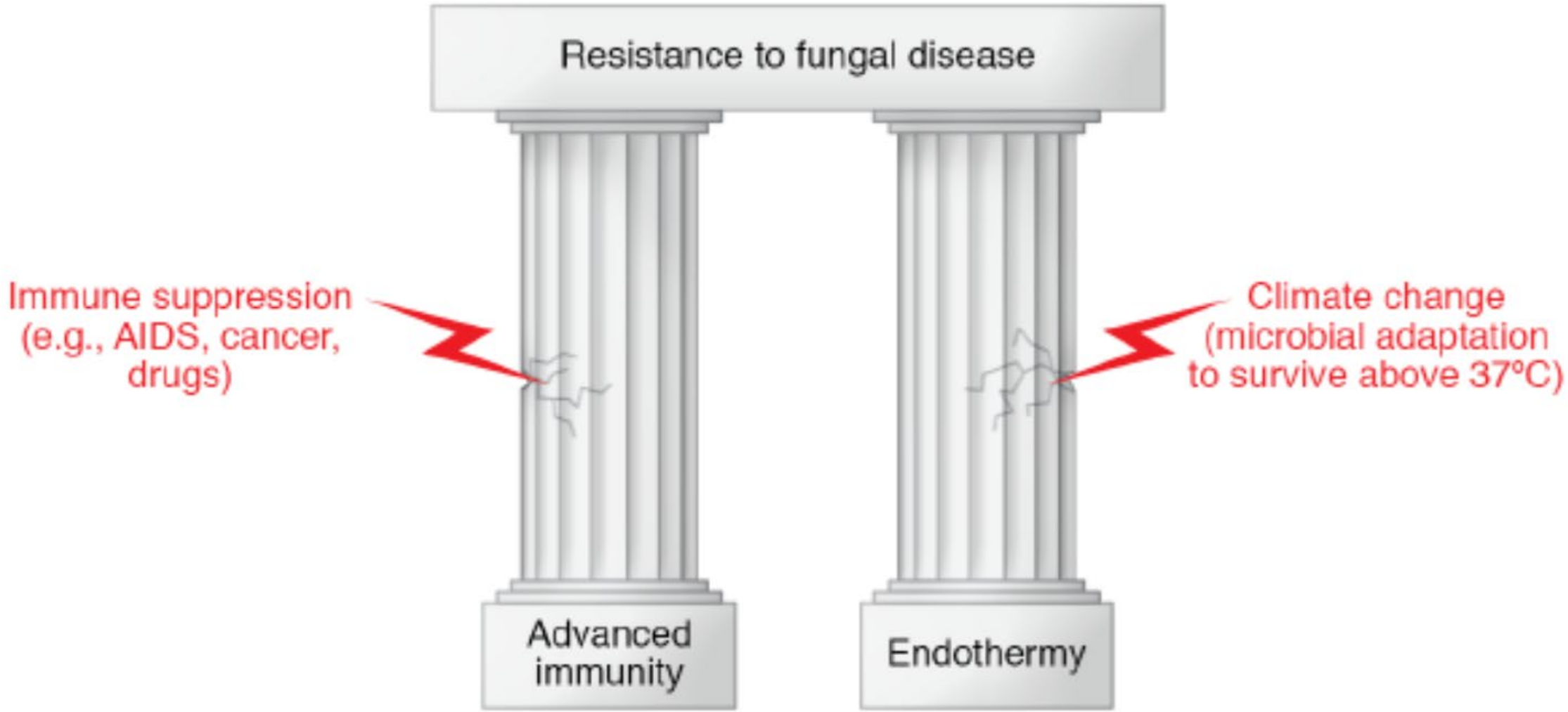
Toxins

Antioxidant systems

Intracellular replication

Stress resistance

etc., etc., etc.



Casadevall, JCI 2020

Fungal Diseases of Humans

- **Most not reportable so prevalence is an estimate with high uncertainty**
- **Often chronic and usually lethal if untreated**
- **Effective treatment often require prolonged therapy (months…years)**
- **Few antifungal drug classes**
- **Drug discovery hampered by the fact that animals and fungi are close relatives**
- **No licensed vaccines available**
- **New fungal diseases could emerge with global warming and some, like Candida auris, may arrive with high inherent drug resistance.**