

The Macrobiome: *It's not just the Microbiome that Matters!*

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Microbiome

The ecological community of commensal, symbiotic and pathogenic microorganisms that literally share our body space

Joshua Lederberg

Review of the Microbiome

We now know of the strong link between a stable biodiverse microbiome on our skin and in our gastrointestinal tract, and our health:

- Digestive Health
- Mental and emotional health linking enteric to central Nervous System primarily through Vagus nerve: serotonin, dopamine, GABA levels
- Immune System Health
- Metabolic Syndrome and obesity
- Possible link to autism

The Macrobiome

A new term (you heard it here first!) defined as:

The broader ecological community (ecosystem) of micro- and macro-organisms that we belong to, the vigor and vitality of which has direct influence on our health as members of that community.

Distinguishing the Macrobiome from classic Environmental Health

Environmental Health traditionally focuses on exposure to toxins and its negative impact on health including the supremely important issues of toxic load, occupational health, environmental racism, and Environmental Justice*.

Examples: particulates, heavy metals, pesticides and other agricultural and industrial chemicals, placement of pollutant sources, etc.

*There is in fact a close link between E.J. and the Macrobiome – *hold that thought*.

In contrast, the Macrobiome focuses on ecological health

Just as health is more than the mere absence of illness, the health of an ecosystem is more than the mere absence of pollution.

This is often quantifiable through the lens of biodiversity (species richness)

Biodiversity has now been linked to:

- Infectious disease transmission
- Allergy / atopic conditions
- Chronic, inflammatory conditions ranging from autoimmune disease to various cancers
- Depression and other mental illness

Keesing et al., 2010

von Hertzen et al., 2011

A Case Study: *Mycobacterium vaccae*

- Found in soil, mud, first isolated from cow dung
- Down regulation of inflammatory states through T regulatory cell induction (psoriatic arthritis, allergic/atopic disorders, some cancers)
- Seratnergic effects on the CNS (anti-depressant, anxiolytic); possible impact on norepinephrine

Rook, Lowry, The hygiene hypothesis and psychiatric disorders, TRENDS IN IMMUNOLOGY · MAY 2008
Impact Factor: 12.03 · DOI: 10.1016/j.it.2008.01.002 ·

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Biodiversity and Pathogenic Disease

Table 1 | Biodiversity loss can increase transmission

Disease	Mechanism	Reference
Amphibian limb malformation	B	12
Bacteriophage of <i>Pseudomonas syringae</i>	B	52
Coral diseases	A	53
Fungal disease of <i>Daphnia</i>	B	54
Hantavirus disease	A, B	23,55–57
Helminthic parasite of fish	A*	58
Lyme disease	A, B	18,22,59
Malaria	A	60
<i>Puccinia</i> rust infection of ryegrass	A*	10
Schistosomiasis	B	12
Trematode diseases of snails and birds	B	61–63
West Nile fever	A*, B*	7–9,64

Disease examples are since 2005. A more complete table, including several counterexamples, is available from the corresponding author. Mechanisms for effects were reported by authors or demonstrated in the text (A = host/vector abundance; B = host/vector/parasite behaviour; see Box 1 for details). Asterisks indicate a suggested mechanism. Other studies have been reviewed elsewhere^{21,65}.

Keesing et al., Impacts of biodiversity on the emergence and transmission of infectious diseases, *Nature* 468, 647–652 02 December 2010
doi:10.1038/nature09575

Also: Yellow fever, Dengue, Leishmaniasis, Chikungunya fever, Avian flu, Ebola, HIV

Vultures and Lyssavirus (Rabies): Case Study India

By 2006 India's population of vultures had declined by 97 percent.

"Over the same period, there was a drastic rise in cases of rabies in India...*Roughly 36 percent of the world's rabies deaths — the majority of them children — occur in India, according to the World Health Organization.*"

Santora, *Vulture Populations Wane, Poisoned by Man*, NY Times, 8/26/15



Vultures and Lyssavirus (Rabies): Case Study India

Causation was proven to be a pharmaceutical painkiller fed to livestock, the tissue of which was then consumed by vultures and which had a lethal toxic effect on the birds.

Feral dogs took advantage of the now open niche for scavengers, and acted as a vector for Lyssavirus.

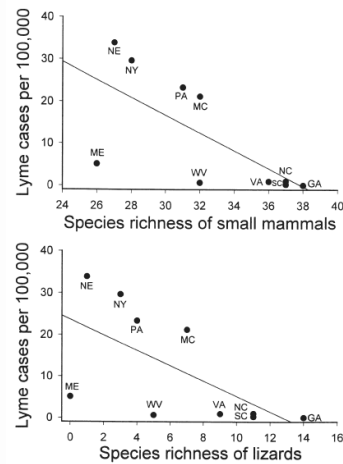
"Dr. Virani described what he called apocalyptic scenes, with hordes of wild dogs numbering in the thousands, scavenging the remains of livestock. Estimates vary, but some put the feral dog population in India now as high as 25 million."



Lyme and Biodiversity

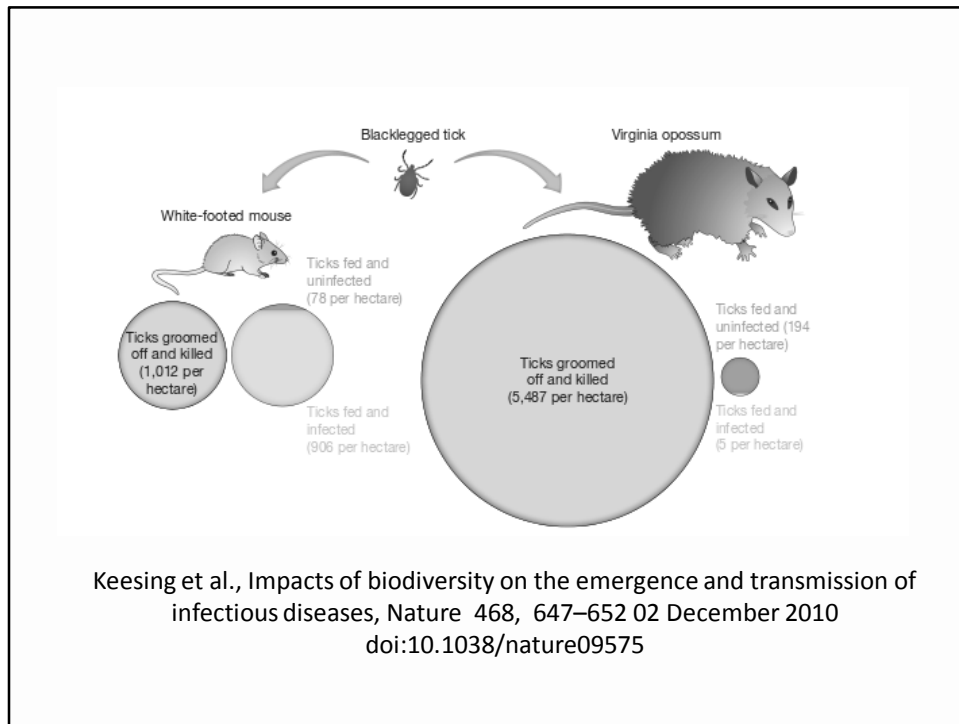
Reduced biodiversity has strong correlation to a larger population of *Borellia*-infected ticks and populations of white-footed mice, the primary vector

Ostfeld and Keesing, Biodiversity and Disease Risk: the Case of Lyme Disease 2009
Conservation Biology, 722-728 Vol 14, No. 3, June 2000

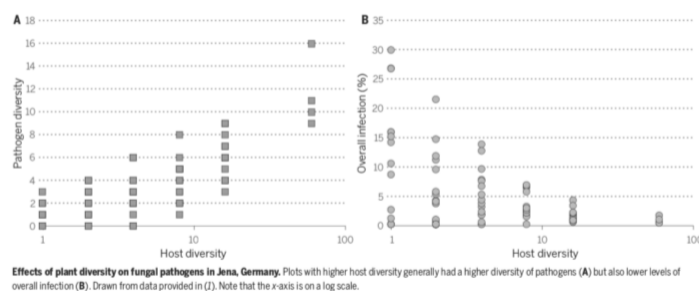


Foxes and Opossums: Inverse Relationship of Populations with Incidence of Lyme





Higher Biodiversity in General= Higher Biodiversity of Potential Pathogens, but Lower Incidence of Infection



Rottstock et al., Higher plant diversity promotes higher diversity of fungal pathogens, while it decreases pathogen infection per plant *Ecology* 95:1907–1917

Biodiversity inhibits parasites: Broad evidence for the dilution effect

Meta-analysis of over 200 studies, both laboratory/controlled and observational, in >60 host-parasite relationships (plant, animal including human).

We find overwhelming evidence of dilution, which is independent of host density, study design, and type and specialization of parasites.

A second analysis identified similar effects of diversity in plant–herbivore systems. Thus, biodiversity generally decreases parasitism and herbivory. Consequently, human-induced declines in biodiversity could increase human and wildlife diseases and decrease crop and forest production.

Civitello, PNAS, vol. 112 no. 288667–8671, 10.1073/1506279112

We are Living/Causing the Sixth Mega-Extinction (*the Holocene Extinction*)

17,291 species out of 47,677 assessed species are threatened with extinction:

- 21 percent of all known mammals
- 30 percent of all known amphibians
- 12 percent of all known birds
- 28 percent of reptiles
- 37 percent of freshwater fishes
- 70 percent of plants
- 35 percent of invertebrates

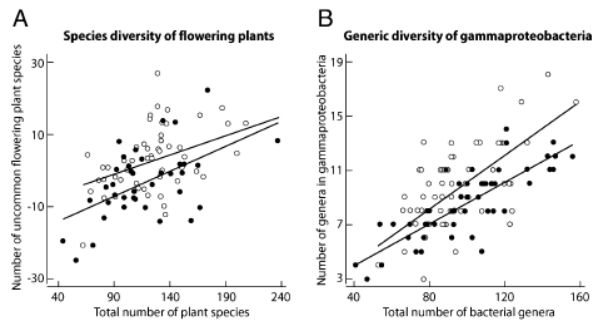
-IUCN Red List of Threatened Species

Est. 15 billion trees (of 3 trillion total) are cut down each year, with a total forest loss of 46% since onset of “civilization”

Crowther, T. W. et al. Mapping tree density at a global scale, Nature <http://dx.doi.org/10.1038/nature14967> (2015)

“The current rate of species extinction [of plants] is about 100 times the natural rate”

-Stuart L. Pimm,
Doris Duke Professor of Conservation Ecology,
University of Tennessee, Knoxville



There is a demonstrated inverse relationship between the biodiversity of native angiosperms around one's home and atopic sensitization (i.e. allergic disposition), mediated (at least in part) through the genetic diversity of the gammaproteobacterial genus *Acenitobacter* on the skin

A Biodiverse Macrobiome is An Important Element of Equity and Justice

Plant Diversity (by genus) was found to be double in neighborhoods with median income above \$50,750/yr.

The positive relationship between plant diversity and wealth is particularly interesting, because it seems to mirror the well established link between quality of the social environment and socioeconomic status.

Hope, D., *Socioeconomics drive urban plant diversity*, PNAS, vol. 100 no. 15 8788–8792, doi: 10.1073/pnas.1537557100

Mean family income, census tract area, and ethnicity were some of the dominant variables that correlated with most of the variation in the bird community.

Melles, Human Social Diversity and Economic Inequality in Vancouver, British Columbia, URBAN HABITATS, VOLUME 3, NUMBER 1 • ISSN 1541-7115

Shinrin-yoku or forest bathing

- Physiological impact of various senses have been investigated: sight, sound, touch, smell
- Reestablishes yin-yang balance of the Parasympathetic and Sympathetic states through “relaxing stimulation”

Tsunetsugu et al., Environ Health Prev Med
(2010) 15:18–26

Shinrin-yoku or forest bathing

- Blood glucose: significantly decreased from 179 to 108 mg/dL independent of the distance walked. (Ohtsuka et al.)
- Immune Health:
 - Significant increase in natural killer (NK) cell activity and immunoglobulin A, G, and M levels after 8 hours in the forest (Ohira et al.)
 - 3 day/ 2 night stay in a forest significantly increased NK cell production, which persisted for up to seven days after immersion in the forest. (Li et al.)
- Decreased levels of cortisol and other stress hormones, decreased blood pressure, and overall regulation of the hypothalamus-pituitary-adrenal cortex (HPA) axis and the hypothalamus-sympathetic nervous system-adrenal medulla (SAM) axis (Tsunetsugu et al., 2009)

Cryptomeria japonica, Japanese cedar A Case Study in Volatile Oils / Phytoncides (mainly monoterpenes)

- D-limonene emitted from *C. japonica* forests exhibited antianxiety and antinociceptive effects
- Isopulegol appears to decrease depression and anxiety.
- Citral, myrcene, and limonene reduce locomotor activity and increase muscle relaxation.



-Wei-Wen Cheng et al., J Wood Sci (2009) 55:27–31

Old Growth vs. New Growth

The distinctive spatial structure of the old-growth forests gave subjects greater impressions of comfort, beauty, gentleness and coolness than did the control (50-year-old) forest, and may have helped to relieve the emotional tensions, anxieties, feelings of suppression, melancholy, and fatigue of forest walkers and increase their vitality.

Takayama, *The therapeutic effect of taking in the atmosphere of a forest*

Is this information of practical use to the herbalist?



Case Study

- 58 y.o female
- Diagnosed with Rheumatoid arthritis, Hashimoto's thyroiditis, bronchiectasis, suspicion of Lyme

"When I go to the Botanic Garden, my arthritis disappears."

Protocol (abbreviated)

- *Immunomodulation with Ganoderma, daily mushroom broth (Grifola, Lentinula) with seaweeds*
- *Down regulation of inflammation: Scutellaria baicalensis, Curcuma, Boswellia, Zingiber*
- *Digestive bitters, pre- and probiotics, pungent / spicy foods in moderation*
- *Forest bathing*

First the Word, Then the Plant,
Lastly the Knife

Asclepius of Thessaly
via Rudolf Weiss, Herbal Medicine

First the Word Encompassing Mind
and Approach to Life, Then the
Plant.

*And the Knife I leave to Someone
Else!*

me

Conclusions

- Health is not merely the absence of disease; one's family, community, and Society are an extension of one's Self. And one's ecosystem?
- When we think about and discuss the increase in infectious disease, autism, autoimmune disease, we rightly focus on pollutants, modern diet and food, but we have ignored ecological biodiversity as a factor *possibly equal to these*.

Conclusions

- It is time to integrate the traditional, indigenous value of Human health being as much an ecological issue as an individual issue, not merely in an abstract “environmentalist” way but in directly quantifiable and measurable ways relating to one’s local ecosystem.
- The *macrobiome* can be part of our practice and work with clients, as much as diet, physical activity, sleep quality, emotional wellbeing, etc.

Thank you

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