Ecology and Geography of Human Monkeypox Case Occurrences Across Africa

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-
- Monkeypox
  - Ecological Niche Modeling
  - My Project

Introduction to Monkeypox

Monkeypox – Virus

- *Orthopoxvirus, Poxviridae, Chordopoxvirinae*
  - cowpox, vaccinia, variola
- Central genome tightly conserved
  - Key functions:
    - transcription, virus assembly
- Genes at termini are more variable
  - Associated with virus-host interactions

Monkeypox – Virus

- 2 geographically distinct clades
  - Congo Basin clade
  - West African clade
- 99% identical
  - Diversity is located in the terminal regions
- West African clade
  - Less virulent
  - Less transmissible

Monkeypox – Human Disease

- “Emerged” in 1970-1971
  - After successful eradication of smallpox
    - West and Central Africa
      - rural, tropical rainforest areas

Monkeypox – Human Disease

2003: United States 72 cases: 37 confirmed

Monkeypox – Human Disease

Source of virus

Source of human infection

www.nps.gov
photos.igougo.com
www.pets-classifieds.co.uk
www.everwonder.com/david/bullwinkle

Monkeypox – Clinical Presentation

- 10-14 day incubation
- 1-3 day prodrome
  - Fever, malaise, lymphadenopathy, URT illness
- 2-4 weeks: febrile rash illness:
  - Begins on the trunk, spreads centrifugally
  - Macular, papular, vesicular, pustular stages
- Complications
  - DIC, ocular lesions, CNS disease, multi-organ failure
  - Death
    - Case fatality 10% (range: 1.7 – 17%)
      - Children < 10 years

Monkeypox - Epidemiology

- Endemic to West and Central Africa
  - Tropical rainforest regions
- Epidemiologic range not definitively identified
- Human cases occur sporadically in clusters
  - 80% in the DRC (Congo Basin)

Monkeypox - Epidemiology

- Transmission:
  - Direct contact
    - infected animals
  - Human-to-Human (~ 9%)
    - direct contact
    - respiratory aerosol
    - body fluids

Monkeypox - Epidemiology

- Zoonotic Reservoir Host(s) – unknown
- WHO and CDC ecological surveys
  - 13 rodents
  - 10 primates
  - 3 other mammals
  - 2 birds
- Virus isolated twice
  - 1985
  - 2003

Monkeypox – Why Is It Important?

- WHO: “the most significant orthopoxvirus infection of man with regards to surveillance and research”
- Possible bioterrorism agent
- Clinically similar to smallpox
- Preventable but not eradicable

Monkeypox – Why Is It Important?

- Broad host range:
  - Large number of potential hosts
  - Endemic and novel landscapes
- Increasing incidence?
  - Encroachment
  - Ecosystem degradation
  - Susceptible individuals
  - Concomitant disease
  - Socioeconomic factors
  - Better surveillance?

Introduction to Niche Modeling

Ecological Niche Modeling

- Ecological niche
  - Set of environmental conditions capable of maintaining a population without immigration
- Ecological niche model
  - A set of environmental conditions classified as suitable (*versus* unsuitable) for the species, based on
    - localities of known occurrence
    - environmental variables
  - Integrated into a GIS system

Ecological Niche Modeling - Uses

- Biogeographic research
- Conservation biology
- Ecology
- Paleoecology
- Wildlife conservation
- Spatial epidemiology

Ecological Niche Modeling

Spatial Epidemiology

- The geographic distribution of disease is an epidemiological event

occurring at the convergence of each participating population's ecological niche

Ecological Niche Modeling

Spatial Epidemiology

ENMs can:

Clarify environmental variables associated with disease transmission

Identify unknown components of transmission cycle

Anticipate unknown foci of disease occurrence

Ecological Niche Modeling

Spatial Epidemiology

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Ecological Niche Modeling

Spatial Epidemiology

ENMs can:

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Identify unknown components of transmission cycle

Anticipate unknown foci of disease occurrence

ENM Example:

Invasion of the USA by *Aedes albopictus*

Mark Q. Benedict et al
Vector-Borne and Zoonotic Diseases. March 1, 2007, 7(1): 76-85.
doi:10.1089/vbz.2006.0562.

- Invader
  - Fastest spreading mosquito in the world
- Aggressive
  - Daytime biter
- Transmits
  - Dengue, WNV
  - Encephalitis viruses
    - (LCE, SLE, EEE)
  - Ross River fever
  - Rift Valley fever

Aedes albopictus: Native Range

Present predicted distribution, native range in Asia

Aedes albopictus: USA invasion

Projected Asian niche into USA to create an invasion risk-map.

Aedes albopictus: USA invasion

My Project

Ecology and Geography of Human Monkeypox Case Occurrences Across Africa

- Goal:
  - 1) Identify ecological factors relevant to the geographic distribution of monkeypox in Africa
  - 2) Use this knowledge to understand better the geography of monkeypox across Africa
  - 3) Perform a comparative assessment of ENM methodology

Occurrence Data

- Occurrence Data:
  - CDC and WHO
    - outbreak investigation and surveillance data
- Case Definition:
  - Laboratory confirmed
    - Published reported case
    - Non-redundant unpublished case

Occurrence Data

- Georeferencing Case Occurrence
  - Country
  - Region
  - District / Zone
  - Municipality
  - Specific locality

Democratic Republic of the Congo

Occurrence Data

■ Georeferencing Case Occurrence

- Country
- Region
- District / Zone
- Municipality
- Specific locality

Democratic Republic of the Congo -- Equateur

Occurrence Data

Democratic Republic of the Congo – Equateur – Bumba

■ Georeferencing Case Occurrence

- Country
- Region
- District / Zone
- Municipality
- Specific locality

Occurrence Data

Democratic Republic of the Congo – Equateur – Bumba – Gemena

■ Georeferencing Case Occurrence

- Country
- Region
- District / Zone
- Municipality
- Specific locality

Occurrence Data

Democratic Republic of the Congo – Equateur – Bumba – Gemena – Ebata

■ Georeferencing Case Occurrence

- ☐ Country
- ☐ Region
- ☐ District / Zone
- ☐ Municipality
- ☐ Specific locality

Occurrence Data

- Started with: 404 cases
- Georeferenced: 216 localities
- But, you can't just georeference the occurrence and call it good...
- Must account for .....

Occurrence Data

- Error....
- Spatial uncertainty
  - Extent of named places
  - Imprecise locality descriptions
  - Incomplete locality descriptions
  - Datum error
    - 10 cm – 1000 meters

Sheep dip

Prairie dog town #2

Highway marker #82

North side of Rio Grande

Near sand dunes

A few miles east
of Maxwell

Next to Land Rover

Bridge east of lodge

North side of Elko

3 miles from Greeley

www.manisnet.org

“georeferencing” or “geocoding,” can be rather complicated.”

- Georeferencing Manual
  - Contains information about assigning
    - Geographic coordinates to locality descriptions
    - Extent to those coordinates
- Georeferencing Calculator
  - Corrected GPS coordinates
  - Assigns an error extent
  - Result: greater spatial precision

Occurrence Data

Point-radius method:

A locality is a geographic point surrounded by an error extent
Summarizes effects of error-related factors

All MPX occurrences were
assigned an error radius

Restricted analysis to sites
with a precision = 10 km²

139 occurrences for
final analysis

Environmental Data (raster GIS data layers)

www.mnforstustain.org/americas_northern_plains

■ Climate

- Weather station data
- Long temporal applicability

■ WorldClim

- www.worldclim.com

■ Soil characteristics

■ Vegetation data

■ UNEP GeoData Portal

- www.geodata.grid.unep.ch/data

Environmental Data (raster GIS data layers)

- Topography
- USGS Hydro-1K DEM
  - www.edc.usgs.gov

- Normalized Difference Vegetation Index (NDVI)
- University of Maryland
  - AVHRR satellite
  - www.glc.f.umiacs.umd.edu

Environmental Data

- Environmental Data – 30 total layers
  - Climate - 19 variables
  - Topography - 4 variables
  - Soil & Vegetation - 5 variables
  - Surface reflectance (monthly NDVI composites) - 12 variables
- Must determine
  - How much data is enough....
  - Which variables are best suited for model construction....

Ecological Niche Modeling: Maxent

[www.es.princeton.edu~schapire/maxent](http://www.es.princeton.edu/~schapire/maxent)

- General purpose maximum entropy-based machine learning method
- Origins:
  - Statistical mechanics
  - Bayesian statistics
- Entropy:
  - A measure of the disorder or randomness in a closed system
  - The tendency for all matter and energy to evolve toward a state of disorder

Ecological Niche Modeling: Maxent

[www.es.princeton.edu~schapire/maxent](http://www.es.princeton.edu/~schapire/maxent)

- Estimates the EN as a probability distribution
  - Closest to maximum entropy

subject to the constraint that higher probabilities
will occur under conditions associated with observed presence

- Performs statistical analysis
  - Environmental variable suitability
- Niche model construction:
  - Presence-only occurrence data
  - 10,000 random background points representing non-occurrence
  - Environmental data

Analysis of Ecological Factors

- Jackknife Analysis
  - N layers (N = 30 total # layers used)
  - N-1 layers
    - omitted each variable sequentially
    - assess importance of variables by examining effects of their omission
- 2 analyses
  - Suites of environmental variables
  - Individual variables

Environmental Data

Analysis 1: Grouped Variables

Environmental Data

Analysis 2: Individual variables

Monkeypox Ecology and Geography

Monkeypox Ecology and Geography

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Monkeypox Ecology and Geography

Monkeypox Ecological Niche

Monkeypox Ecological Niche

Ecological Niche Variable Ranges

	Areas of Known Occurrence	Areas of Predicted Favorable Environment
Mean annual precipitation	1500 – 2100 mm	500 – 3500 mm
Precipitation of wettest month	2000 – 2500	600 – 4500 mm
Mean annual temperature	21 – 26 °C	15 – 30 °C
Maximum temperature warmest month	30 – 34 °C	25 – 42 °C
Potential evapotranspiration	80 - 120 mm	60 – 160 mm
Net primary productivity	800 – 1100 Kcal/ m ² / year	100 – 1200 Kcal/ m ² / year
Soil pH	5 – 6	5 – 7.5
Soil carbon	4 – 10 %	1 – 11 %

Characterizing Distributional Limits

mean annual precipitation (mm)
vs.
mean annual temperature (°C)

Characterizing Distributional Limits

November NDVI
vs.
soil moisture (mm)

Monkeypox Ecology and Geography

Comparison with Previous Study

OPEN ACCESS Freely available online

Ecological Niche and Geographic Distribution of Human Monkeypox in Africa

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Monkeypox virus, a zoonotic member of the genus *Orthopoxviridae*, can cause a severe, smallpox-like illness in humans. Monkeypox virus is thought to be endemic to forested areas of western and Central Africa. Considerably more is known about human monkeypox disease occurrence than about natural sylvatic cycles of this virus in non-human animal hosts. We use human monkeypox case data from Africa for 1970–2003 in an ecological niche modeling framework to construct predictive models of the ecological requirements and geographic distribution of monkeypox virus across West and Central Africa. Tests of internal predictive ability using different subsets of input data show the model to be highly robust and suggest that the distinct phylogenetic lineages of monkeypox in West Africa and Central Africa occupy similar ecological niches. High mean annual precipitation and low elevations were shown to be highly correlated with human monkeypox disease occurrence. The synthetic picture of the potential geographic distribution of human monkeypox in Africa resulting from this study should support ongoing epidemiologic and ecological studies, as well as help to guide public health intervention strategies to areas at highest risk for human monkeypox.

Citation: Levine RS, Peterson AT, Yorita KL, Carroll D, Damon IK, et al (2007) Ecological Niche and Geographic Distribution of Human Monkeypox in Africa. PLoS ONE 2(1): e176. doi:10.1371/journal.pone.0000176

This study

Serologic Evidence for Novel Poxvirus in Endangered Red Colobus Monkeys, Western Uganda

Goldberg TL et al

Emerging Infectious Diseases, May 2008, 14(5): 801-803

Levine et al.

Comparison with Previous Study

- Levine et al.
  - Climate, topography, landcover
  - 156 occurrences, no error “filter”
  - Assessment of variable importance
    - Student’s t-test
    - Kappa statistic
- This study
  - Climate, soil, vegetation, NDVI
  - 139 occurrences, used an error “filter”
  - Assessment of variable importance
    - Jackknife

Summary

- Niche models are useful in identifying ecological parameters associated with disease occurrence

	Areas of Known Occurrence	Areas of Predicted Favorable Environment
Mean annual precipitation	1500 – 2100 mm	500 – 3500 mm
Precipitation of wettest month	2000 – 2500	600 – 4500 mm
Mean annual temperature	21 – 26 °C	15 – 30 °C
Maximum temperature warmest month	30 – 34 °C	25 – 42 °C
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Summary

- Niche model quality is affected by
  - Georeferencing methodology
    - Use of spatial precision filters
      - MaNIS point radius method
  - Quality and types of environmental data
    - Data sources
    - Statistical analysis

Summary

- Niche models have applicable and versatile uses in spatial epidemiology
  - Identify environmental characteristics associated with disease occurrence
  - Identifying Identify components of transmission cycle
  - Identify foci of disease occurrence

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Questions?