Environmental Effects on Infectious Disease and a Schistosomiasis Example

Song Liang, Ph.D.
College of Public Health
The Ohio State University

Dhaka, Bangladesh
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Outline

• Environmental Determinants & Infectious Disease
  – EnvID Framework
    • Environmental Change
    • Disease Transmission Dynamics
    • Disease Burden

• A Schistosomiasis Example
  – Background
  – Environment & the Disease
  – A Systems Approach
  – Implications for Public Health
Environmental Effects on Infectious Disease

• Why infectious disease?
  – … still leading causes of deaths and disability worldwide
  – New threat from emerging & re-emerging diseases

• Why environmental effects?
  – Environmental change is occurring worldwide at varying scales
  – Discoveries that emerging and re-emerging pathogens have their origin in environmental change
What are ‘environmental determinants’ of infectious disease?

Environmental factors in which their changes have causal links to introduction, reemergence, intensification, and propagation (e.g., spatial) of infectious diseases.
Environmental Determinants

Current research – environmental sciences

Distal Environmental Changes

Proximal Environmental Characteristics

Changes in Disease Status

Causal link
Environmental Determinants

Current research – public health

- Distal Environmental Changes
- Proximal Environmental Changes
- Changes in Transmission Cycle
- Changes in Disease Status

Causal link
A research priority in understanding environmental contribution to infectious disease

- Distal Environmental Changes
- Proximal Environmental Characteristics
- Changes in Transmission Cycle
- Changes in Disease Status

?
The Environmental Effects & Infectious Disease (EnvID) Framework

Environmental changes and characteristics → Transmission cycle → Disease burden

Distal
- Climate change
- Road projects
- Deforestation
- Urbanization
- Agricultural practice
- Dam projects

Proximal
- Migration patterns
- Soil cover
- Population density
- Water salinity
- Water flow rate
- Wind speed
- Fecal contamination

Population levels (human, hosts, vectors)
Behavior (contact rate)
Organism properties (probability of infection)

Changes in infectious disease patterns and human health
The impact of proximal environmental characteristics on disease burden is mediated through transmission cycles.

<table>
<thead>
<tr>
<th>Transmission group</th>
<th>Transmission pathway</th>
<th>Modes of transmission</th>
<th>Environmental factors</th>
<th>Transmission cycle</th>
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</thead>
<tbody>
<tr>
<td>I. Directly transmitted diseases</td>
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<tr>
<td>AIDS, gonorrhea, syphilis, chlamydia</td>
<td>Human-human</td>
<td>Fluid exchange (intercourse, transfusion)</td>
<td>Pathogens cannot survive long in the environment. Factors governing transmission: close personal contact</td>
<td>Humans</td>
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<tr>
<td>Measles, rubella, smallpox, pertussis, diphtheria</td>
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<td>Physical touch</td>
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<td>Humans</td>
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<td>Influenza, severe acute respiratory syndrome (SARS)</td>
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<td>Droplet spray</td>
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<td>Humans</td>
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<tr>
<td>Tuberculosis</td>
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<tr>
<td>II. Vectorborne diseases</td>
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<tr>
<td>Malaria</td>
<td>Human–vector</td>
<td>Vector biting a host (human or nonhuman)</td>
<td>Pathogens survive outside host in arthropod vectors; humans are the only host. Factors governing transmission: biting rate, vector survivorship, host-seeking behavior</td>
<td>Humans</td>
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<tr>
<td>Dengue fever</td>
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<td>Onchocerciasis</td>
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<td>Trypanosomiasis, filariasis</td>
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<tr>
<td>IIIa. Environmentally mediated diseases—no nonhuman host</td>
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<tr>
<td>Cholera</td>
<td>Human–environment</td>
<td>Water ingestion</td>
<td>Pathogens survive long periods of time in the environment. Cholera has free-living stage</td>
<td>Humans</td>
</tr>
<tr>
<td>Diseases caused by hepatitis A, hepatitis E, rotavirus, enteroviruses, noroviruses, typhoid fever, shigellosis, amebiasis, ascans, trichuris, hookworm, strongyloides</td>
<td></td>
<td>Food ingestion</td>
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<td>Humans</td>
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<tr>
<td>IIIb. Environmentally mediated diseases—nonhuman host</td>
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<tr>
<td>Same as IIIa, except for some bacteria infection that occurs through consumption of infected meat</td>
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<td>Dermal contact</td>
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<td>Humans</td>
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<tr>
<td>Diseases caused by tapeworms, <em>Echinococcus</em></td>
<td></td>
<td>Inhalation</td>
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<td>Humans</td>
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<tr>
<td>IIIa. Environmentally mediated diseases—no nonhuman host</td>
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<tr>
<td>Same as IIIa, except nonhuman hosts can be infected and transmit pathogens or infect humans through consumption of meat</td>
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<tr>
<td>IVa. Zoonotic diseases</td>
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<tr>
<td>Lyme disease</td>
<td>Human–environment</td>
<td>Zoonotic transmission; vectorborne with nonhuman hosts; humans are dead-end hosts</td>
<td>Pathogens survive outside host in arthropod vectors; humans are the only host. Factors governing transmission: biting rate, vector survivorship, host-seeking behavior</td>
<td>Host</td>
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<tr>
<td>Yellow fever, West Nile virus, Japanese encephalitis</td>
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<td>Vectorborne biting nonhuman hosts</td>
<td></td>
<td>Human</td>
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<td>Bubonic plague</td>
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<td>Vector</td>
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<td>IVb. Zoonotic diseases</td>
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<tr>
<td>Rabies</td>
<td></td>
<td>Zoonotic transmission (involves nonhuman hosts); humans are dead-end hosts</td>
<td>Same as those in groups I, II, and III. Factors governing transmission: nonhuman host ecology</td>
<td>Host</td>
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<tr>
<td>Hantavirus, toxoplasmosis</td>
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<tr>
<td>Trichinellosis</td>
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<td>Anthrax</td>
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<td>Botulism, tetanus</td>
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</tbody>
</table>
Matrix for mapping the relationship between proximal environmental characteristics and transmission

<table>
<thead>
<tr>
<th>Proximal Environmental Characteristics</th>
<th>Population Size</th>
<th>Organism Properties</th>
<th>Human-Human Contact</th>
<th>Human-Vector Contact</th>
<th>Human Environment Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pathogen</td>
<td>Vector</td>
<td>Host</td>
<td>Human</td>
<td>Pathogen Virulence</td>
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<tr>
<td></td>
<td>Host</td>
<td>Immune Status</td>
<td>Sexual Contact</td>
<td>Close Contact</td>
<td>Biting Rate</td>
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<td>Host Seeking</td>
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<td>Dermal Contact</td>
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<td>Inhalation</td>
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<td>Food Ingestion</td>
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<td></td>
<td></td>
<td>Ingestion</td>
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<tr>
<td>Water</td>
<td>Presence/Absence</td>
<td>Flow Rate</td>
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<td></td>
<td>Nutrient Content</td>
<td>Chemical Composition (Inorganic Pollution)</td>
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<td></td>
<td>Fecal Matter Content (Organic Pollution)</td>
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<td></td>
<td>Salinity</td>
<td>Turbidity</td>
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<td>Climate</td>
<td>Temperature</td>
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<td>Precipitation</td>
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<td>Humidity</td>
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<td>Cloud Cover/Sunlight Exposure</td>
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<td>Wind Speed</td>
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<td>Air</td>
<td>Particulates</td>
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<td></td>
<td>Chemical Composition</td>
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<tr>
<td>Animals</td>
<td>Diversity (Non-Domesticated)</td>
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<td>Magnitude (Non-Domesticated)</td>
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<td>Density (Non-Domesticated)</td>
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<td>Pets</td>
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<td>Livestock</td>
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<td>Plants</td>
<td>Diversity (Non-Domesticated)</td>
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<td>Density (Non-Domesticated)</td>
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<td>Crop Cover</td>
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<td>Genetic</td>
<td>Prevalence of antibiotic resistance genes</td>
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<td>Prevalence of GMO genes</td>
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<td>Prevalence of virulence factors</td>
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<td>Human Practice</td>
<td>Migration</td>
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<td>Travel</td>
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<td>Human Contact with Environment</td>
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<td>Human Environment Practice</td>
<td>Physical Barriers to Exposure</td>
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<td>Living Structures</td>
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<td>Sanitation Infrastructure</td>
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<td>Density</td>
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<td>Other Structures</td>
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Outline

• Environmental Determinants & Infectious Disease
  – EnvID Framework
    • Environmental Change (in the context of public health)
    • Disease Transmission Dynamics
    • Disease Burden

• A Schistosomiasis Example
  – Background
  – Environment & the Disease
  – A Systems Approach
  – Implications for Public Health
What is schistosomiasis?

- Schistosomiasis is a water-related, tropical parasitic disease, caused by the digenetic trematode *Schistosoma*

- Five species affect humans, among them three have major public health impacts – *Schistosoma haematobium*, *S. mansoni*, and *S. japonicum*

- It is endemic in 76 countries, 80 million people are infected annually, 200 ~ 300 million people are at risk of infection
Global distribution of Schistosomiasis

**Senegal**
An epidemic of schistosomiasis along the Senegal river basin caused by water-resource development schemes continues unabated.

**Egypt**
Praziquantel chemotherapy coupled to a vigorous media campaign has resulted in a significant decrease in the morbidity and prevalence of schistosomiasis infection.

**Iran, Morocco, and Saudi Arabia**
Schistosomiasis control has been successful in those areas with elimination of the infection contemplated.

**China**
Schistosoma continues to be a major public health problem in the lake and marshy regions despite successful control in other endemic areas.

**Lao People's Democratic Republic**
Schistosoma mekongi control has been successful around Khong Island with prevalence reduced from 42% to < 2%.

**Djibouti and Somalia**
Displacement of people by war and instability has introduced intestinal schistosomiasis to these countries.

**North-east Brazil**
Urban schistosomiasis now present in and around many major cities.

**Ghana**
Intestinal schistosomiasis has increased due to the construction of the Akosombo Dam and other much smaller dams.

**sub-Saharan Africa**
More than 85% of the estimated 200 million people globally with schistosomiasis and the majority of patients with severe disease live on this continent.

**Indonesia**
Schistosomiasis has been controlled in the Lindu region of Sulawesi such that the prevalence of infection is lower than 2%.

Source: WHO
• Seven provinces still endemic;

• An estimated 800,000 people are infected annually and ~ 60 - 90 million people are at risk of infection.
Why this study...

• Global climate change

• The Three Gorges Dam
  • A number of studies underway ...
  • Hotez et al. speculated that the formation of the lake behind the dam will generally increased both snail habitat and human disease transmission (1997);
  • Lessons learned form Africa – the Aswan Dam, dams in Senegal etc.

• Eliminating schistosomiasis through medical interventions
Mountainous Region
Schistosomiasis transmission in mountainous regions of Sichuan, China
Questions

• What are the risk factors determining transmission intensity of schistosomiasis in this environment?

• If identified, can they be used to make predictions and to design intervention strategies? And How?

• What is the environmental contribution to persistence or control of transmission?
20 villages (out of 260), inhabited by over 3,900 residents, were chosen for the study in the winter of 2000.
Monthly rainfall (bars) superimposed with weekly mean temperature (solid line) in the Xichang Study Area in 2000.
• Human prevalence of infection (red bar) ranges between 3% ~ 73%;
• Human infection intensity (measured as e.p.g., blue bar) ranges between 0.1 and 110.
Epidemiological findings

• Residence and occupation (farmer, student, other) are key risk factors, while age and sex are statistically insignificant;

• Animals play a marginal role in the disease transmission;

• Land-use determines risk at the village level;

• Environmental risk (e.g. cercarial bioassay) is a strong predictor of human infections;
An application of EnvID framework

- Water contact survey
- Human infection survey
- Snail survey
- Land-use pattern
- Microclimatic measurements
- Cercarial bioassay

Dynamic model
Transmission Model Development

Input 1: Praziquantel control

Spatial interaction between cercariae and exposure

Output 1: Egg count ($EPG_i$)

Risk Group $i$

Mean Worms $w(i)$

Mortality $\mu_w + \mu'_w$

Egg excretion

Output 4: Worms in sentinel mice

Spatial interaction between miracidia and snails $\gamma_{ik}$

Input 2: Snails surveyed

Input 3: Snail control

Output 2: Snail abundance

Output 3: Infected snails

Environment $k$

Infected snails $\tau_k$

Mortality $\mu_z + \mu'_z$

Snails $x_k$

Mortality $\mu_z + \mu'_z$

$E_i$

$E_k$

$M_k$

$C_k$

$s_I(T)$

$\gamma_{ik}$

$\mu_{w}$

$\mu'_{w}$

$\mu_{z}$

$\mu'_{z}$

$\rho I_m(T)$

$\gamma$
Findings

- The transmission model analyses reflect a bimodal transmission in both humans and snails; the time-varying environmental factors drives the disease transmission pattern;

- Location and timing of water contact, microclimatic conditions, snail abundance, and land use are important factors influencing the disease transmission;
Control options

• Chemotherapy
• **Snail control**
  – Mollusciciding
• **Environmental intervention**
  – Concretizing irrigation ditches
  – Converting wetland to dry land
  – Changing agricultural structure
• **Egg control (via waste management)**
• Health education
• Provision of sanitary water
Evaluation of Public Health Intervention – Three Scenarios

• Scenario 1 – interventions that actually occurred in the field (i.e. two chemo in 2002 and 2003, coupled with sustained environmental interventions);

• Scenario 2 – The 2002-03 chemo (as in Scenario 1 but no environmental interventions), followed by annual chemo at 50% coverage until 2008;

• A combination of Scenarios 1 and 2.
Evaluation analysis

A comparison of mean infection intensity for the largest risk group, farmers, in the three scenarios;

35% of snail habitat controlled; 25% of households installed bio-gas digesters.
Disease Transmission Potential

• The disease transmission potential is determined by both site-specific and biological (site-invariant) parameters;
• A crude Ro is approximated:

\[ R_0 \approx \frac{P_b P_s}{\mu_z \mu_w} \]
• Where,

\[ P_b = \frac{\alpha \sigma \rho h e^{-\mu_w \tau_w} e^{-\mu_z \tau_z}}{2} \]

\[ P_s = \frac{A_n S \gamma X \xi g_0 n}{\mu_z A_s^2} \]

- Habitat
- Fertilization pattern
- Number of Humans
- Exposure
- Susceptible snails
- Humans
\[ P_s = \frac{A_h S \gamma X \xi g_0 n}{\mu_z A_s^2} \]
• Chemotherapy alone doesn’t change transmission potential, which is determined by local environmental factors;

• Sustained transmission interruption has to rely on chemotherapy, coupled with sustained environmental control or modifications.
Policy implications

- Although the work focused on a small geographical area, it has important implications for the ongoing disease control programs in China, and possibly in Africa in the near future;
- Some new evidence reconfirms results reported above;
- Transmission control matters;
- A need to re-consider comprehensive control.
Control, elimination, eradication and re-emergence of infectious diseases: getting the message right

David L Heymann

During the 25 years since the certification of smallpox eradication there has been considerable debate among public health practitioners about how existing health technologies can best be used to decrease infectious disease incidence and prevalence. Interruption of transmission has often been envisaged as the ultimate goal, and standard public health concepts of disease reduction have been defined or re-defined. In 1998, Dowdle proposed a definition of control as a reduction in the incidence, prevalence, morbidity or mortality of an infectious disease to a locally acceptable level; elimination as reduction to zero of the incidence of disease or infection in a defined geographical area; and eradication as permanent reduction to zero of the worldwide incidence of infection.1

Whereas the proposed definition of eradication emphasizes that routine intervention measures are no longer needed once interruption of transmission has been certified worldwide, inherent in the definitions of control and elimination is the need for continued intervention measures to prevent re-emergence and re-establishment of transmission. It is this need for continued intervention after reaching control or elimination targets that has been the source of confusion among public health workers, health policy-makers and the politicians who, including mollusc control, chemotherapy, health education and provision of clean water. Surveillance to determine where disease was present in humans, snails and cattle underpinned control activities and continued in some form in most counties after attainment of control targets. Most other interventions to control infection in the snail vector and human host were, however, discontinued.2

The authors underscore the role of mobility of humans and cattle in the re-introduction of schistosomiasis from adjacent counties where control targets had not yet been met, and the role that cessation of control activities played in the subsequent re-emergence of indigenous transmission. They cite decreased funding, lack of awareness, and apathy as causes for the cessation of control activities, and describe the weakness in surveillance that resulted in late detection of smallpox.3

In today’s world of rapid travel and transport, re-introduction of infectious diseases occurs not only locally: humans, insects, livestock and food products carry infectious agents from country to country and from continent to continent. Infectious agents carried by humans are often asymptomatic or in the incubation period, while those carried by vectors, livestock and food often remain silent.4

The spread of poliomyelitis from and international resources. When wild poliovirus was re-introduced there was therefore no protective barrier to transmission, and polio re-emerged in 18 polio-free countries. As in the Sichuan Province, surveillance that had been maintained after attainment of polio-free status detected re-emergence and has guided the vaccination response.5

In 1980, after the certification of smallpox eradication, routine smallpox vaccination was discontinued in all countries. Noting that the smallpox virus was (and still is) maintained in two laboratories, the Smallpox Eradication Advisory Group concluded that the risk of accidental release from these laboratories could not be reduced to zero. It therefore recommended that smallpox surveillance be continued and that an international stockpile of smallpox vaccine be maintained.6 Reports of possible smallpox cases are still received by WHO 25 years later, and each report is epidemiologically investigated in the field and followed by confirmatory diagnosis in a WHO reference laboratory.7

Lessons learned from smallpox eradication and experiences such as those of the Sichuan Province of China and the global polio eradication initiative are clear. Microbes are dynamic and resilient: they spread locally, nationally and internationally with ease in our
Acknowledgments

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