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View Point

Digital Twins for *Entamoeba histolytica*: Towards Predictive and Personalized Management of Amoebiasis

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Abstract

Amoebiasis, caused by *Entamoeba histolytica*, continues to pose a significant global burden, especially in developing countries with overcrowding, poor sanitation, and limited access to timely diagnostics. While most infections remain asymptomatic, a subset progresses to colitis, dysentery, or life-threatening liver abscess. This heterogeneity in infection, immune response, and treatment remains difficult to anticipate using conventional tools. Digital twins are adaptive computational representations that continuously reflect an individual's biological, behavioral, and clinical picture, offering a novel opportunity to improve prediction, diagnosis, and personalized management of amoebiasis. By capturing parasite biology and behavior, host immune dynamics, liver involvement, therapeutic exposure, and clinical outcome, a digital twin for *E. histolytica* could move clinical care from reactive management to prospective decision-making. Here, we propose a conceptual framework for constructing digital twin for amoebiasis, examine potential applications across clinical and public-health settings, and discuss key challenges.

Introduction

Entamoeba histolytica remains one of the most important parasitic pathogens worldwide, responsible for intestinal amoebiasis and life-threatening extraintestinal disease such as liver abscess (1,2). Although many infections remain asymptomatic, a significant number progress unpredictably, with substantial variation in severity, tissue invasion,

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and response to therapy (3). This variability arises from a complex interplay of parasite virulence, host immunity, nutritional and microbiome factors, patterns of exposure, environmental conditions, and the timing and efficacy of treatment. Existing clinical tools provide only a snapshot of infection status, making it difficult to anticipate who will deteriorate, which patients will develop invasive disease, or when relapse or recurrence will occur (4,5).

Digital-twin technology

Digital twin technology is an adaptive computational model that continuously track and simulate a patient's changing biological state, offering a new opportunity to transform how we understand, monitor, and manage amoebic disease. The promise of digital twins in infectious disease has expanded rapidly in recent years, with notable advances in virology and immunology demonstrating that personalized simulation models can link mechanistic biological knowledge with real-world data to forecast outcomes and optimize treatment (6-9). For example, a digital-twin approach has been suggested to study host–virus interactions and simulate infection dynamics in real time (8).

The distinguishing feature of a digital twin is the creation of a continuously updating virtual representation of a biological system that receives data from the real world, recalibrates its internal structure, and produces forecasts that can influence future decisions. The exchange is bidirectional: clinical or physiological signals update the virtual model and the model's projections guide intervention. This feedback loop allows the twin to evolve in parallel with the patient. By simulating disease trajectories and treatment responses before they manifest, digital twins can support earlier recognition of deterioration, personalized therapy choices, and scenario testing in ways that conventional analytics cannot achieve.

Recently, an infectious-disease digital twin was applied at population scale. CitySEIRCast integrates an agent-based transmission engine with a city-wide digital-twin environment to forecast COVID-19 dynamics, identify high-risk spatial clusters, and guide county-level intervention planning on a recurring basis. The platform has been used operationally to support situational awareness and public-health decision-making (10).

Constructing a digital twin for E. histolytica

These principles can be extended to protozoan parasitic infections, where disease dynamics involve intricate interactions across multiple biological scales. A digital twin for *E. histolytica* would capture, in a continuously updating way, the shifting relationships among exposure, parasite load, trophozoite to cyst transformations, host inflammatory responses, tissue invasion, and pharmacologic treatment effects. Construction of such a system would require the definition of core components including data acquisition modules that ingest clinical observations, stool antigens, blood biomarkers, inflammatory mediators, imaging snapshots, and drug exposure metrics; mechanistic submodels that encode parasite replication rates, epithelial disruption, hepatic invasion, and pharmacokinetic and pharmacodynamic relationships for metronidazole or second-line drugs; machine learning layers that recognize nonlinear effects of immune activation, metabolic state, microbiome dysbiosis, adherence behavior, and comorbidities; and a clinical interface through which new observations are assimilated and used to recalibrate predictions. Collectively these aspects shall convert fragmented information into an executable representation of amoebic disease that updates as the patient changes. A practical implementation would likely involve three interacting computational layers.

The first is a mechanistic layer that encodes causal biological relationships, including trophozoite replication, cyst formation, epithelial invasion, inflammatory activation, and hepatic dissemination. The second is a data-driven layer that applies statistical learning to

identify nonlinear associations between laboratory parameters, symptoms, comorbidities, microbiome state, and drug exposure. The third is a personalization layer that will analyze individual-level observations, as well as longitudinally, and adjust model coefficients that should forecast and reflect a specific patient rather than a population average. This multilayer structure will maintain biological interpretability while still allowing adaptive learning, which will be critical for clinical relevance and application. Because amoebiasis is concentrated in low- and middle-income countries where diagnostic infrastructure may be limited, models that accommodate sparse laboratory inputs, intermittent data streams, and mobile-based symptom reporting will be essential for equitable deployment. Such a system could move amoebiasis care away from reactive clinical management toward predictive decision-making, enabling early recognition of high-risk states and personalized therapeutic strategies (11,12).

Digital twin for *E. histolytica* would not simply track exposure events, which are notoriously unpredictable. Instead, it would focus on what unfolds after infection is established. The central component of such a model would represent the interaction between the parasite and host tissues, capturing epithelial disruption, invasion, inflammatory signaling, and the onset of systemic responses such as fever, fluid shifts, or hepatic involvement. Twin would reflect measurable biological signals such as stool antigen concentration, circulating inflammatory markers, hepatic enzymes, drug levels, and physiological parameters such as abdominal perfusion, heart rate variability, hydration status, and metabolic stress. These signals could represent the patient's likelihood of progressing to severe colitis, developing an abscess, responding to therapy, or experiencing delayed recovery (13,14).

Such a twin would integrate mechanistic elements such as parasite replication rates, tissue destruction dynamics, and pharmacokinetic-pharmacodynamic relationships of metronidazole or newer drugs with machine-learning components that capture nonlinear interactions between immune activation, drug adherence, comorbidities, microbial dysbiosis, and healing trajectories (12,15). These computational layers would be continuously updated through data generated during routine care including blood tests, symptom scores entered via mobile applications, stool antigens, and early imaging findings. Rather than relying on fixed thresholds to guide decisions, the model would provide probabilistic forecasts in real time, identifying patients on a path toward complications (11). Operationalizing such a system may follow staged implementation beginning with retrospective digitization of case records, laboratory values, and imaging archives to define early parameter boundaries and generate baseline mechanistic assumptions. Prospective patients can then be used for validation in which discrepancies between predicted and observed response can be used to recalibrate the computational layers, if needed. Once reliability improves, electronic records, stool antigen platforms, and point of care biomarkers can be linked for near real time updates, enabling clinicians to visualize trajectories and test alternative treatment scenarios before acting. This sequential path reflects how digital twins have progressed from conceptual engineering tools to clinically deployed decision support assets in cardiology and oncology (6,9).

Forecasting disease progression and personalizing therapy

One of the most immediate applications would be the prediction of treatment response. At present, the duration of therapy is largely standardized, even though patients show marked variability in how quickly they improve. A digital twin capable of estimating the individual's clearance could allow clinicians to tailor duration, escalate therapy earlier, or shift to alternative regimens in patients unlikely to

respond to first-line treatment. This is especially important because delays can lead to unnecessary hospitalization, increased risk of perforation, progression to extraintestinal disease, or prolonged treatment. A personalized forecast could support decisions such as when to repeat imaging, whether liver abscess drainage is likely to be beneficial, or when symptoms should trigger evaluation for complications. Severe amoebic colitis can escalate rapidly, and identifying early signals of hemodynamic compromise, mucosal necrosis, or systemic inflammation is challenging. Continuous assimilation of physiological data including heart rate variability, oxygen saturation, early changes in liver enzymes, patterns of abdominal pain would allow the digital twin to detect shifts that precede overt deterioration. Instead of waiting for classical warning signs, clinicians could be alerted when the twin's internal state crosses a risk threshold for severe disease. This predictive signal could prompt early intensification of monitoring, addition of supportive therapy, or timely referral to a higher level of care. For liver abscesses, the twin could help anticipate whether the lesion is likely to resolve with medical therapy alone or whether drainage will be required, based on dynamics of fever response, inflammatory markers, liver function, and the model's inferred rate of tissue liquefaction (9).

Recovery trajectories, adherence, and comorbidity signals

Although amoebiasis is often considered an acute infection, recovery varies considerably. Some patients improve rapidly, while others have prolonged inflammation, persistent pain, or slow resolution of abscess cavities. A dynamic model could provide personalized recovery trajectories, estimating how long symptoms or imaging abnormalities should take to resolve, and highlighting divergence from expected paths.

One of the advantages of a digital-twin approach is its ability to incorporate behavioral and treatment-adherence factors. Adherence patterns, captured through pharmacy data or self-reported intake, can substantially influence treatment success. Instead of assuming full adherence, the twin could simulate alternative therapeutic outcomes depending on real-time adherence patterns, identifying when suboptimal dosing is the likely explanation for delayed improvement (14). Similarly, comorbidities such as diabetes, malnutrition, immunosuppression, or chronic liver disease could be encoded into the model, allowing it to recalibrate expectations based on the individual's biological capacity to control inflammation and regenerate tissue (16,17).

Future implementation

For future therapeutic development, digital twins could also provide virtual trial environments, where candidate regimens are tested on simulated patients built from real biological data. This would be particularly valuable given the difficulty of enrolling large cohorts for amoebiasis drug trials. Virtual simulation environments could explore dosing strategies, treatment combinations, or supportive-care protocols before they reach clinical testing (6,8,18). The implementation of a digital twin for *E. histolytica* requires data quality, interpretability, and patient trust. Unlike chronic viral infections, data collection for amoebiasis tends to be sparse. However, even minimal data streams including lab tests, symptom diaries, vital-sign monitoring, and imaging snapshots can be sufficient when combined with mechanistic models that encode fundamental biological processes (19). Interoperable clinical platforms would allow seamless updating of the twin and integration into clinician workflows. Nonetheless, regulatory acceptance will ultimately require transparent model validation, documentation of uncertainty, and demonstration that simulated outputs consistently improve clinical decisions rather than introduce risk.

Ethical considerations should ensure that predictive outputs enhance clinical care rather than stigmatize patients or create unwarranted

anxiety (20). The goal is to identify risk early, supports timely decision-making, and guide recovery. By shifting the focus from unpredictable environmental exposure to the predictable dynamics of treatment and healing, a digital-twin framework offers an opportunity to make amoebiasis management more personalized, proactive, and precise. Adaptive forecasting of treatment response, early warnings of deterioration, and individualized recovery trajectories could significantly improve outcomes in a disease where timely decisions make a substantial difference. As computational technologies advance, these models hold promise for transforming amoebiasis from a condition managed through episodic decisions into one guided by continuous, patient-centered insight.

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Conflict of interest

The authors declare that there is no conflict of interests.

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