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CASE REPORT

A Case of Pulmonary Infection Caused by *Rhodococcus equi* in an AIDS Patient and Literature Review

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Abstract: *Rhodococcus equi* is a rare opportunistic Gram-positive bacterium that primarily affects immunocompromised individuals, particularly those with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). The infection often presents as a multisystem, disseminated disease with rapid progression and high mortality if not promptly diagnosed and treated. We report the case of a 34-year-old male AIDS patient who developed pulmonary infection due to *Rhodococcus equi*. Cultures from bronchoalveolar lavage fluid, metagenomic next-generation sequencing (mNGS), and bronchoscopic brushing all indicated infection with *Rhodococcus equi*. Following combined anti-infective treatment, the pulmonary infection was controlled, and his condition improved. Clinicians should be alert to the possibility of *Rhodococcus equi* infection in AIDS patients, emphasizing early diagnosis and targeted therapy to improve patient outcomes.

Keywords: AIDS, *Rhodococcus equi*, rare opportunistic infection, mNGS

Introduction

Rhodococcus equi (*R. equi*), an opportunistic pathogen, predominantly affects immunocompromised individuals, particularly those infected with HIV/AIDS. In recent years, with the escalating incidence of HIV/AIDS and advancements in medical technology, *R. equi* infections have become increasingly prevalent. HIV/AIDS patients are particularly vulnerable due to their immunosuppressed state, which facilitates rapid disease progression and elevates mortality rates if prompt diagnosis and effective treatment are not administered. The diagnosis of *R. equi* infection in HIV/AIDS patients poses significant challenges due to the morphological resemblance of *R. equi* to normal respiratory flora, stringent culturing requirements, slow growth characteristics, and lengthy traditional diagnostic procedures. Although molecular diagnostic techniques offer the potential for rapid and accurate diagnosis, their utilization remains suboptimal. Currently, the treatment of *R. equi* infections lacks standardization, relying heavily on case reports and expert consensus. Multi-antimicrobial therapy is frequently employed; however, antibiotic resistance and drug interactions pose significant complications, particularly in HIV/AIDS patients who are often prescribed multiple medications. Research in this area is imperative to elucidate the epidemiology, microbiology, antibiotic sensitivity profiles, and optimal treatment strategies for *R. equi* infections. This understanding is crucial for providing targeted diagnostic and therapeutic recommendations to clinicians. Additionally, the exploration of novel diagnostic and treatment modalities is essential to enhance the management of *R. equi* infections.[1,2]

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We retrospectively review a case of pulmonary infection caused by *R. equi* in an AIDS patient managed at our institution, and conducts a comprehensive review of relevant literature to summarize and analyze the clinical characteristics, bacterial identification methods, and treatment modalities of this condition.

Case Presentation

The patient was a 34-year-old male worker with a history of male homosexual behavior for 8 years. He was admitted to our hospital on April 6, 2024, presenting symptoms of cough, expectoration, and fever lasting over three months, worsening in the last half month. More than three months prior, the patient experienced recurrent coughing with white phlegm, accompanied by fever-reaching a maximum temperature of 39°C-without hemoptysis, blood in sputum, chest distress, or pain. His cough and expectoration intensified two weeks before admission, presenting with low afternoon fevers (37.5°C–37.7°C), night sweats, fatigue, but no dizziness or headaches. The patient sought treatment at a local hospital, where laboratory results indicated a white blood cell count of 6×10^9/L (normal range 4×10^9-10×10^9/L), neutrophilia at 82% (normal range 50–70%), and C-reactive protein (CRP) was elevated at 48 mg/L (normal range 0–8 mg/L). A positive T-SPOT test noted, alongside chest CT revealing a right middle lobe shadow. Treatment included azlocillin, ceftriaxone, and moxifloxacin, with no marked improvement. During this process, the patient's appetite remained good with normal sleep patterns, though he experienced a weight loss of approximately 5 kg. On April 6, the patient was admitted to our hospital for further diagnosis and treatment. The patient was diagnosed with Human Immunodeficiency Virus (HIV) infection by HIV antibody supplementary test on April 1, 2024, with a viral load of 5.54×10^5 IU/mL and no antiviral treatment.

Physical examination upon admission showed a body temperature of 36.8°C, pulse rate of 105/min, respiration at 20/min, and blood pressure of 127/95 mmHg. The patient was conscious, in fair spirits, with no palpable superficial lymphadenopathy. Auscultation revealed coarse breath sounds and scattered moist rales in the right lung. Additional diagnostic tests showed a white blood cell count of 4.58×10^9/L, with neutrophils at 72.3%, CRP at 54.5 mg/L, and a $CD4^+$ T lymphocyte count of 26/μL (normal range 550–1440 μL). EBV DNA levels were at 1.31×10^4 copies/mL (normal range 0–500 copies/mL), and CMV DNA was at 1.09×10^4 IU/mL (normal range 0–200 IU/mL). Other assessments including liver and renal function tests, autoimmune screens, and fungal cultures revealed no significant abnormalities. Bronchoscopy revealed unobstructed bronchial passage with no visible tumors. The bronchoalveolar lavage fluid (BALF) was inoculated onto Columbia blood agar plates and incubated at 35°C under 5% CO_2 for 24–48 hours. The colonies were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. The culture results revealed the concentration of *R. equi* exceeding 10^5 CFU/mL (Figure 1). The mNGS assay was performed in our clinical laboratory, as previously described in our publications.[3] Briefly, BALF was processed to release microbial nucleic acids or genomes after cell lysis.

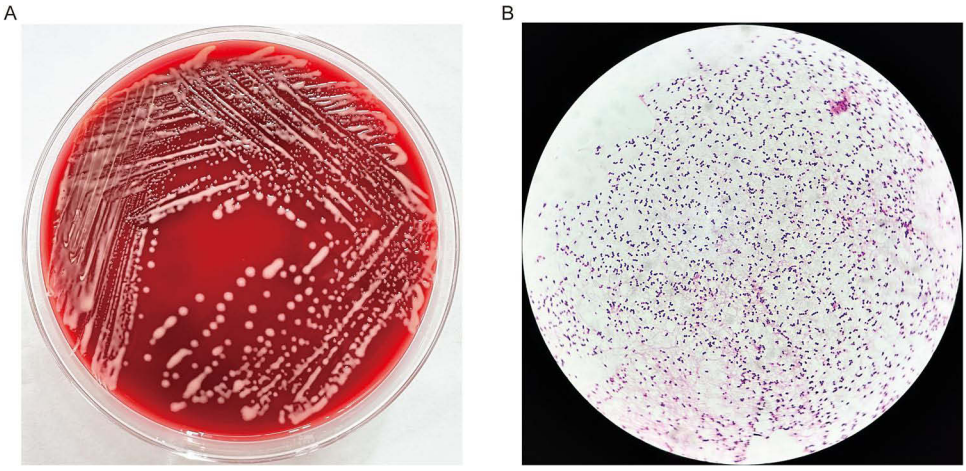

Figure 1 Microbiological findings of *R. equi*. (**A**) After 48 hours of incubation, Orange-red mucoid colonies appeared on blood agar plate. (**B**) Gram stain for 48 hours showed Gram-positive coccobacilli.

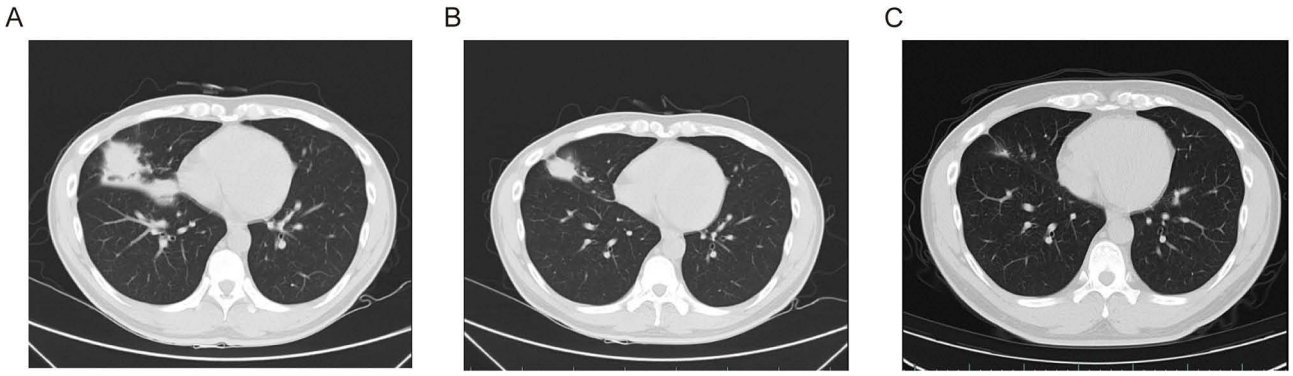

Figure 2 Lung imaging changes during anti-infective therapy in AIDS patients with pulmonary infection by *R. equi*. (**A**) Before treatment (April 6, 2024): mass shadow in the middle lobe of the right lung, with scattered blurred shadows in both lungs; (**B**) After 4 weeks of combined anti-infective treatment (May 2, 2024): the lesion in the middle lobe of the right lung was absorbed and reduced; (**C**) Last follow-up (October 31, 2024): the lesion in the right lung was significantly reduced compared with before.

Nucleic acids were extracted using the QIAamp® kit, and libraries were constructed with the NextEra XT DNA Library Prep Kit (Illumina). Sequencing was conducted on the Illumina NextSeq CN500, producing approximately 20 million reads per sample through 75-bp or 50-cycle single-end sequencing (SE-75 or SE-50). Low-quality reads were removed, human sequences filtered, and remaining reads aligned to a microbial database for species identification. The results showed that *R. equi*, cytomegalovirus, and Epstein-Barr virus were detected (with sequence numbers 8758, 11, and 2, respectively). A plain and enhanced CT scan of the lungs indicated a mass shadow in the right lung's middle lobe, with scattered blurred shadows bilaterally (Figure 2A). The treatment plan initiated included nasal cannula oxygen inhalation (98%–100%, oxygen under 3 L/min), vancomycin (500 mg three times daily), moxifloxacin (400 mg once daily), and methylprednisolone (40 mg once daily). For cytomegalovirus, ganciclovir (150 mg three times daily) and foscarnet sodium (3 g twice daily) were administered, along with trimethoprim/sulfamethoxazole to prevent opportunistic infections. Post-treatment, the patient exhibited normalized temperature and improved cough and expectoration. By April 30, white blood cell counts had decreased to 2.44×10^9/L, neutrophils to 67.2%, and CRP to 1.50 mg/L, with CMV DNA at 4.98×10^2 IU/mL. Chest CT showed a reduced lesion in the right lung's middle lobe (Figure 2B). The patient was discharged on May 4. Post-discharge, he was prescribed azithromycin (500 mg once daily) and linezolid (600 mg twice daily) for continued treatment against *R. equi*. By the last follow-up on October 31, the $CD4^+$ T lymphocyte count was 108 cells/μL, and HIV RNA was 30 copies/mL. Symptoms of cough, expectoration and fatigue were significantly improved, and the lesion in the right lung is significantly resorpted than before. (Figure 2C).

Literature Review

We conducted a search on PUBMED for all cases of human *R. equi* infection reported up to the end of 2024, totaling 346 cases. An analysis was conducted on the underlying diseases, affected sites post-infection, and prognosis of these cases. Among these cases, 178 (52.05%) were associated with HIV/AIDS patients, followed by immunocompetent patients with 64 cases (18.71%), and patients post-organ transplantation with 42 cases (12.28%) (Figure 3A). The sites affected after infection were predominantly the lungs (72.22%), followed by bloodstream (11.99%), brain (9.36%), pericardium and endocardium (3.80%), skin and soft tissues (3.51%), etc. (Figure 3B). Of the cases where the prognosis was explicitly mentioned (231 cases), 169 cases (73.16%) improved or were cured, while 57 cases (24.68%) resulted in death (Figure 3C). Additionally, we compared the mortality rates among different groups: the mortality rate for HIV/AIDS patients was 35.24%, whereas it was 10.87% for immunocompetent patients, showing a statistically significant difference (OR 0.31; 95% CI 0.13–0.83; P = 0.0172) (Figure 3D).

Discussion and Conclusions

R. equi is an aerobic, Gram-positive bacillus characterized by pleomorphism and negative motility. As an intracellular pathogen capable of zoonotic transmission, it is commonly found in soil and animal manure. The first human case of

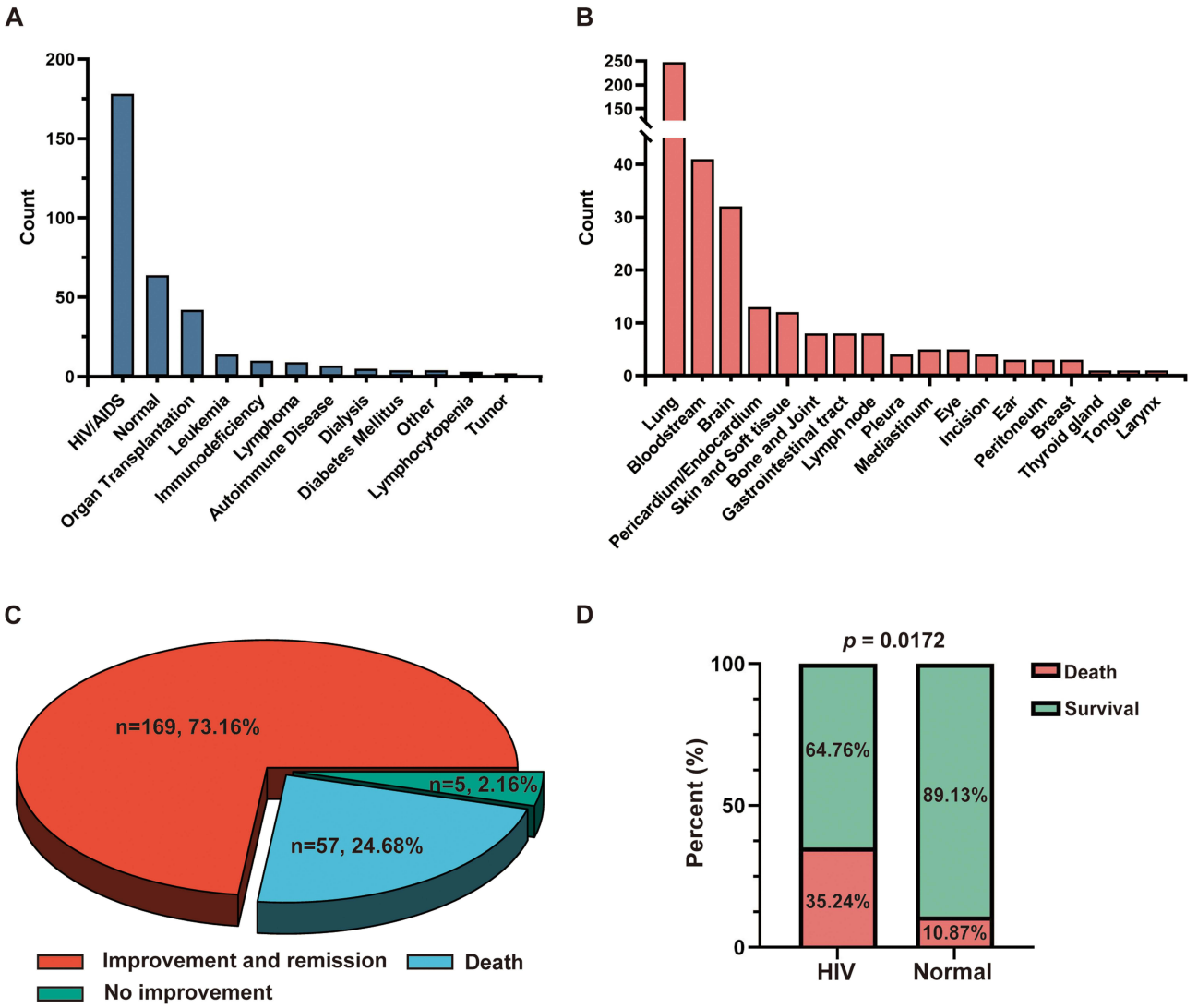

Figure 3 Underlying diseases, affected sites post-Infection, and prognosis in cases of *R. equi* Infections in Humans. (**A**). Among these cases, 178 (52.05%) were associated with HIV/AIDS, 64 (18.71%) involved immunocompetent patients, and 42 (12.28%) occurred post-organ transplant. The remaining cases included patients with concurrent conditions such as leukemia, immunodeficiency disorders, lymphoma, autoimmune diseases, dialysis, diabetes mellitus, lymphocytopenia, tumor, etc. (**B**) The primary affected sites following infection were the lungs (72.22%), bloodstream (11.99%), brain (9.36%), pericardium and endocardium (3.80%), and skin/soft tissue (3.51%). Infections can also involve other areas such as bones, joints, gastrointestinal tract, lymph nodes, pleura, mediastinum, eyes, incisions, ears, peritoneum, breast, etc. (**C**) In these literatures, prognosis was explicitly mentioned for 231 cases, among which 169 cases (73.16%) improved or were cured, 57 cases (24.68%) resulted in death, and 5 cases (2.16%) did not improve. (**D**) The mortality rate among HIV/AIDS patients infected with *R. equi* was 35.24%, compared to 10.87% for immunocompetent patients, a difference that is statistically significant (OR 0.31; 95% CI 0.13–0.83; P=0.0172).

R. equi infection was reported in 1967, involving a patient with autoimmune hepatitis.[4] Subsequently, cases of *R. equi* infection have been reported globally in immunocompromised individuals, including HIV-infected patients, leukemia patients, cancer patients, and organ transplant recipients, as well as in those with normal immune function.[1,5] The primary route of infection for *R. equi* involves inhalation of contaminated aerosols and dust, secondary intestinal infections can occur through the aspiration of tracheal secretions or direct contact via wounds and mucosal membranes.[6] Some previous reports of infections included cases with a clear history of animal contact,[2,7,8] but not all cases can trace their origins to such interactions.[9,10] In this case, the patient had no history of animal husbandry or agricultural activities, leaving the source of infection ambiguous.

Clinical manifestations of *R. equi* pulmonary infection are often non-specific. Approximately 80% of cases present symptoms such as cough, chest pain, fever, and dyspnea.[6] Physical exams may reveal decreased breath sounds and moist rales. Radiological presentations can vary widely, displaying infiltrative lesions, nodules, cavitations, pleural effusions,

and enlarged mediastinal lymph nodes. Immunocompromised individuals may experience disseminated infections, including bacteremia, brain abscesses, and osteomyelitis.[11–13] Given that *R. equi* can yield positive results in modified acid-fast staining, its clinical symptoms may overlap with those of *Mycobacterium tuberculosis* and Nocardia species, contributing to potential misdiagnosis. Bacterial culture remains the gold standard for diagnosing *R. equi* infections. Suitable specimens include blood, cerebrospinal fluid, pleural and ascitic fluid, sputum, pus, bronchoalveolar lavage fluid, lymph nodes, and tissue samples.[14–16] Histopathological examination typically reveals necrosis-like changes, dense histiocytic infiltration, microabscesses rich in neutrophils, and the presence of Michaelis-Gutmann bodies.[6] The implementation of mNGS has substantially expedited the diagnosis of rare opportunistic pathogens, including *R. equi*.[17,18] The patient presented with a clinical profile suggestive of tuberculosis, however, multiple cultures and mNGS results excluded common pathogens and ultimately identified *R. equi* as the causative agent. The significant improvement in clinical symptoms and absorption of lung lesions after targeted therapy further confirmed the diagnosis.

Although no standardized treatment plan exists for *R. equi* infections, it is generally recommended to use antibiotics with strong tissue penetration and varied mechanisms over prolonged periods. Most isolates are sensitive to agents such as rifampicin, vancomycin, linezolid, imipenem, macrolides, and fluoroquinolones. Current US ABX guidelines and the updated Sanford Guidelines on Antimicrobial Therapy recommend using drug combinations to enhance effectiveness.[19,20] The use of penicillins, cephalosporins, combination sulfonamides, clindamycin, and tetracyclines should be avoided.[21] Some strains may also exhibit resistance to macrolides and rifampin,[22,23] so it is necessary to refer to in vitro drug sensitivity tests to select sensitive antimicrobial agents or guide adjustments to the treatment regimen. Patients with immunodeficiency typically require 2–6 months of anti-infective therapy, depending on the severity of the infection.[24] In cases involving extensive lesions or large abscesses, surgical intervention may be warranted.[21,25] Recurrence rates can approach 50% post-treatment,[26] potentially linked to inadequate treatment duration, poor adherence to antiretroviral therapy, and low $CD4^+$ T lymphocyte counts.[13] Successful immune reconstitution following antiretroviral therapy has been shown to significantly reduce relapse rates in AIDS patients.[24] In this case, following the diagnosis of *R. equi* pulmonary infection, the patient was treated with a combination of vancomycin and moxifloxacin. Afterward, the regimen was adjusted to azithromycin and linezolid, alongside optimized antiretroviral therapy, achieving good control of HIV-RNA levels and recovery of $CD4^+$ T lymphocyte counts, improved symptoms, and absorption of lung lesions compared to before.

There are some limitations in this article. Firstly, the lack of animal contact history in the patient makes tracing the source of *R. equi* infection challenging, given its zoonotic nature and potential exposure through contaminated environments. Secondly, despite symptomatic improvement following treatment, complete resolution of pulmonary lesions was not observed, emphasizing the need for long-term follow-up to monitor for potential recurrence, particularly in immunocompromised patients. Thirdly, while this case report offers valuable insights into the clinical aspects of *R. equi* pulmonary infection in an AIDS patient, the conclusions drawn are constrained by the single-case nature of the study and require validation through larger, multi-center research to elucidate the broader epidemiology and optimal treatment strategies for *R. equi* infections.

In conclusion, in cases of pulmonary infections in patients with compromised immune systems, such as AIDS, it is crucial not to overlook the possibility of rare opportunistic pathogens like *R. equi*, in addition to recognizing common pathogens such as *Pneumocystis jiroveci, Mycobacterium tuberculosis*, and Cytomegalovirus. Successful management of these complex cases hinges upon the prompt and comprehensive application of various diagnostic techniques to achieve rapid and accurate diagnosis, thereby guiding tailored treatment strategies. For the treatment of *Rhodococcus equi* infections, combination therapy stands as a critical approach, utilizing multiple antimicrobial agents in conjunction to counter the intracellular survival traits of the pathogen and mitigate the emergence of drug resistance. Antibiotic susceptibility testing plays a pivotal role in guiding therapeutic decisions, with vancomycin being a commonly employed option, albeit with varying susceptibility profiles observed among other drugs, necessitating vigilance against resistance development. The duration of treatment must be individualized, considering the patient's clinical condition and immune status. In patients with HIV/AIDS, particular attention should be paid to potential drug interactions, with timely dose adjustments made as needed.

Future directions encompass the development of rapid diagnostic techniques, the formulation of personalized treatment plans, and the research and development of novel antimicrobial agents to address drug resistance. Additionally, the establishment of an effective monitoring system to adjust treatment regimens based on ongoing assessments is crucial. Interdisciplinary collaboration and multi-center studies will drive the application of these innovative strategies.

Ethics Approval and Consent to Participate

This study has been reviewed and approved by the ethical research committee of the First Affiliated Hospital, Zhejiang University School of Medicine. The ethics committee approved the waiver of the patient's informed consent, with the justification that this was a retrospective study whose information was obtained from medical records and that the data were deidentified and anonymously analyzed.

Consent to Publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Disclosure

The authors report no conflicts of interest in this work.

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