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A Rare Case of Pneumonia Caused by Tropheryma Whipplei

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Abstract

Objective: To report a rare case of pneumonia caused by Tropheryma whipplei (TW) and to explore its clinical characteristics, diagnostic approach, and therapeutic strategy, aiming to provide a reference for the recognition of atypical pulmonary infections. **Methods:** The clinical data, imaging findings, and laboratory results of the patient were retrospectively analyzed. Relevant literature from recent years was reviewed to summarize the diagnostic and therapeutic experience of pulmonary infection caused by T. whipplei. **Results:** The patient presented with fever, cough, and fatigue. Chest CT revealed multiple patchy opacities and bilateral pleural effusions. Metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF) identified T. whipplei (9747 specific reads), confirming the diagnosis of Whipple's disease-related pneumonia. The patient was treated with meropenem combined with doxycycline, and no recurrence was observed during a 3-month follow-up. **Conclusion:** Tropheryma whipplei can cause isolated pulmonary infection with nonspecific clinical manifestations. mNGS plays a pivotal role in establishing the diagnosis. Early recognition and adequate antimicrobial therapy can significantly improve prognosis.

Keywords

Whipple's Disease, Pneumonia, Metagenomic Next-Generation Sequencing, Rare Pathogen

1. Introduction

Whipple's disease (WD) is a systemic chronic infectious disease first described by George Whipple in 1907. Initially, the observed intestinal lipid malabsorption was mistakenly attributed to a lipid metabolic disorder rather than infection. The bacterial etiology was suspected in 1952, when antibiotic therapy appeared effective. However, the causative organism was not identified until 1992 by molecular meth-

ods and was initially named Tropheryma whippelii, later corrected to Tropheryma whipplei in 2001 [1] [2]. Typical clinical features include malabsorption, weight loss, arthralgia, and fever, while pulmonary involvement is extremely rare.

T. whipplei primarily infects the monocyte-macrophage system, leading to chronic inflammatory responses. In recent years, with the advancement of metagenomic next-generation sequencing (mNGS), the detection rate of T. whipplei infection in atypical sites—such as the central nervous system, cardiac valves, and lung tissue—has increased [3]. However, isolated pulmonary infections remain exceedingly rare and are often misdiagnosed as interstitial or atypical bacterial pneumonia.

This study reports a case of Tropheryma whipplei pneumonia confirmed by metagenomic next-generation sequencing (mNGS) and discusses its clinical characteristics, diagnostic approach, and key therapeutic considerations.

2. Case Presentation

1) General Information

A 53-year-old male farmer was admitted with a one-month history of cough, sputum production, and dyspnea, aggravated for two days. The patient had received empirical treatment at a local hospital with no improvement. He denied a history of tuberculosis, diabetes, or immunosuppression, and had no history of long-term medication or hereditary disease.

2) Clinical Manifestations

On admission, the patient's temperature was 36.7˚C, respiratory rate 20/min, and heart rate 138 bpm. He was intubated and placed on assisted ventilation. Physical examination revealed a barrel-shaped chest, coarse breath sounds bilaterally, and diffuse moist rales. No rash, joint swelling, or abdominal distension was noted.

3) Laboratory Findings

Laboratory evaluation revealed an elevated white blood cell count, neutrophil percentage, C-reactive protein, and interleukin-6 levels, with decreased serum albumin. Fecal occult blood was positive. Tumor markers and adenosine deaminase were within normal limits, and the serum GM test was negative.

Chest CT demonstrated increased pulmonary markings, multiple patchy opacities in both lungs, and bilateral pleural effusions. (**Figure 1**, **Figure 2**)

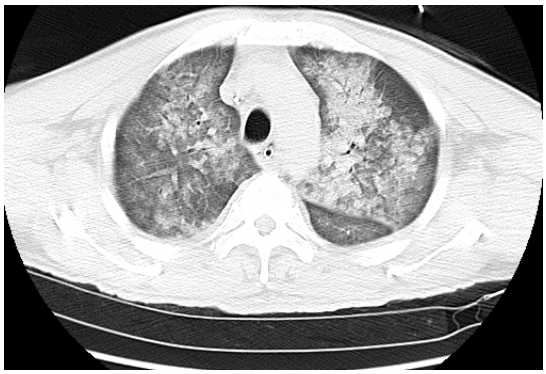

Figure 1. Pulmonary CT at admission microbiological findings.

Bronchoalveolar lavage fluid was analyzed using mNGS, which detected T. whipplei with 9,747 reads and high coverage depth, confirming true infection rather than contamination. Prior conventional diagnostic tests, including routine bacterial and fungal cultures of sputum and BALF, as well as specific PCRs for common respiratory pathogens, were all negative, highlighting the diagnostic utility of mNGS in this atypical pneumonia case.

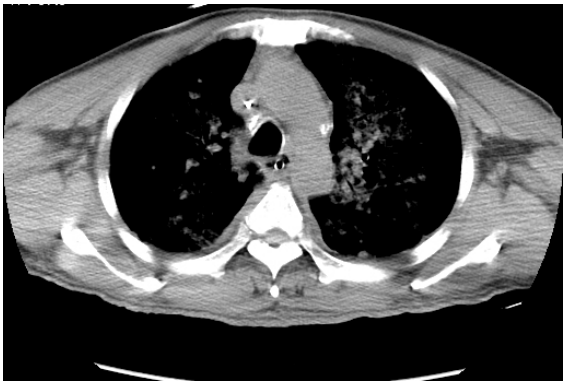

Figure 2. Pulmonary CT at admission.

4) Treatment

Based on clinical presentation, imaging findings, and mNGS results, a diagnosis of T. whipplei pneumonia was made. The patient received intravenous meropenem combined with doxycycline, chosen for broad-spectrum coverage, effective tissue and pulmonary penetration, and demonstrated activity against T. whipplei in previous reports. After one week of treatment, he was successfully extubated and transitioned to high-flow oxygen therapy. Cough and dyspnea improved significantly. Follow-up CT showed marked resolution of the left upper-lobe infiltrates and decreased pleural effusion (**Figure 3**, **Figure 4**).

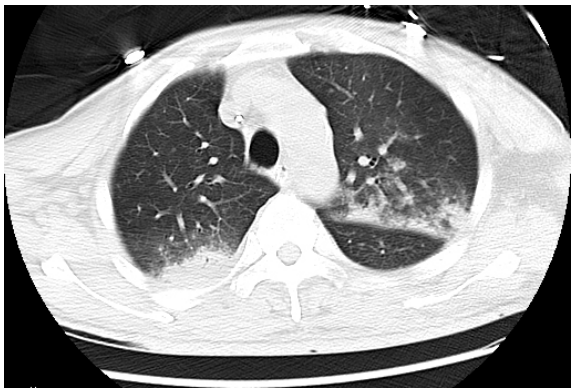

Figure 3. Treatment of lung CT for one week.

At one-month follow-up, the chest CT (**Figure 5**, **Figure 6**) revealed almost complete absorption of pulmonary lesions, with no recurrence during the subsequent three months.

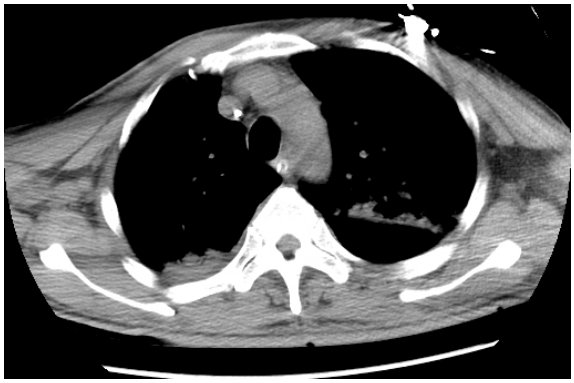

Figure 4. Treatment of lung CT for one week Outcome.

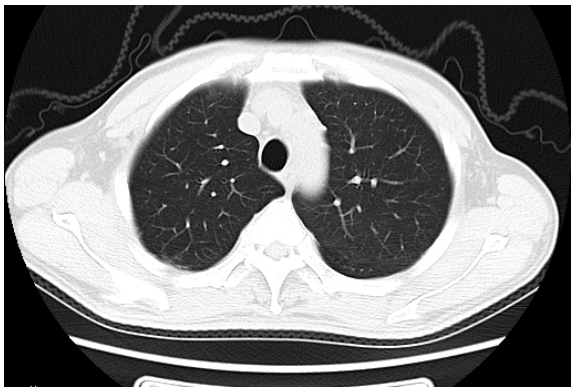

Figure 5. Review of lung CT.

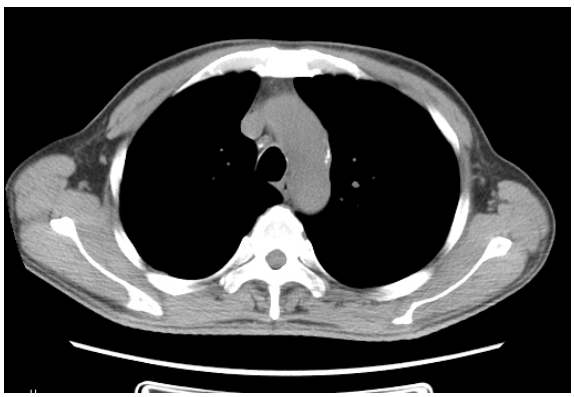

Figure 6. Review of lung CT.

3. Discussion

1) Biological and Clinical Features of Tropheryma whipplei

T. whipplei is a Gram-positive, PAS-positive, non-acid-fast bacillus. Its core is enclosed within a plasma membrane surrounded by a trilaminar cell wall rich in polysaccharides, which accounts for its PAS positivity [4]. Clinically, it mainly causes chronic gastrointestinal symptoms and seronegative arthritis [5]-[7]. However, it can also lead to systemic infection involving the endocardium, nervous system, uveal tract, lymph nodes, and skin [8] [9].

2) Epidemiology

Whipple's disease is rare, with an estimated incidence of 1 - 3 cases per million in North America and Europe, typically affecting middle-aged men (male-to-female ratio 8 - 14: The disease has been associated with the HLA-B27 haplotype [10] [11]. Notably, the patient's occupation as a farmer may represent a potential epidemiological risk factor, as T. whipplei has been identified in soil, and occupational exposure could contribute to bacterial transmission.

3) Pulmonary Involvement and Pathogenesis

The mechanism of pulmonary involvement remains unclear. T. whipplei can impair macrophage degradation capacity, reduce cytokine secretion, and induce host cell apoptosis [12]. The pathogenesis primarily involves macrophage dysfunction and impaired type 1 T-cell responses, leading to intestinal injury, bacterial dissemination, and systemic involvement [4] [5].

In the present case, chest CT scans revealed pulmonary nodules, alveolar and interstitial infiltrates, and bilateral pleural effusions. According to previous studies, nodular lesions are the most common radiological manifestation of TW pneumonia, followed by interstitial changes and patchy infiltrates, which may be accompanied by mediastinal lymphadenopathy, pleural thickening or adhesion, and pleural effusion. In rare cases, cavitary lesions have been reported [13]. The radiological diversity of TW pneumonia may be related to its tropism for macrophages, which are the principal target cells of TW. Alveolar macrophages are abundant in pulmonary interstitial tissue—particularly around sub-bronchiolar lumens and within alveolar septa—providing a favorable environment for bacterial survival [14]. Some of these macrophages migrate into the alveolar space to become alveolar macrophages. The highly variable chest CT findings are believed to reflect the distribution and inflammatory response of these infected macrophages within the lung parenchyma, explaining the wide range of radiologic presentations in TW pneumonia. Therefore, the chest CT findings of TW pneumonia are highly variable, including nodules, interstitial changes, patchy infiltrates, and cavities, lacking specific radiologic characteristics.

4) Diagnostic Strategies

Routine culture of T. whipplei is technically challenging. PAS-positive foamy macrophages in biopsy samples are characteristic but not specific [15]. PCR testing of fecal or saliva samples has been used for screening, though false positives may occur with nonspecific primers [16].

Early and precise pathogen identification is crucial for appropriate antimicrobial selection and prognosis [17]. In the early stages of infection, when pathogen concentrations are low, diagnostic tests may be nonspecific and inefficient; without accurate targeted therapy or with inappropriate antibiotic use, adverse outcomes may occur [18] [19]. mNGS, introduced into clinical practice in 2014, enables unbiased detection of rare pathogens, providing high sensitivity and specificity for atypical infections [20] [21]. Additionally, it can identify resistance and virulence genes, aiding antibiotic stewardship.

Clinicians should maintain a high index of suspicion for T. whipplei pneumonia in patients with prolonged fever, cough, and radiological findings inconsistent with common bacterial or viral pneumonia, especially when conventional cultures are negative and empirical therapy fails.

5) Treatment and Prognosis

Acute T. whipplei pneumonia carries a high risk of respiratory failure and requires prompt intervention. Commonly used antibiotics include ceftriaxone, penicillin, meropenem, streptomycin, tetracycline, trimethoprim-sulfamethoxazole (TMP-SMX), and hydroxychloroquine.

Recommended first-line therapy consists of intravenous ceftriaxone (2 g/day) or meropenem (3 g/day) for 14 days, followed by oral TMP-SMX for 12 months [22]. However, T. whipplei lacks the dihydrofolate reductase gene targeted by trimethoprim and harbors multiple mutations in the folP gene encoding dihydropteroate synthase, leading to potential TMP-SMX resistance [23] [24].

Alternative regimens combining doxycycline (200 mg/day) with hydroxychloroquine (600 mg/day) for at least 12 months have shown efficacy, though lifelong doxycycline may be required in some cases [25]. However, long-term doxycycline administration can lead to resistance, and both doxycycline and hydroxychloroquine are associated with adverse effects [26]-[28]. The primary toxicities of hydroxychloroquine include retinal toxicity, followed by cardiotoxicity and neuromuscular toxicity [25], whereas doxycycline commonly causes gastrointestinal and dermatologic side effects [28].

Antibiotic therapy remains the cornerstone of treatment for T. whipplei infection. Given the high relapse and mortality rates of Whipple's disease, prolonged treatment is required. A regimen of ceftriaxone or meropenem for 14 days followed by TMP-SMX for 12 months is one established approach [29] [30]. While other reports suggest that a combination of hydroxychloroquine and doxycycline may be a more rational alternative [31].

For acute TW pneumonia, however, the optimal duration of therapy and the risk of reinfection remain undefined and warrant further investigation. In the present case, the patient achieved full recovery following standardized therapy, highlighting the importance of early recognition and long-term antibiotic management.

Nevertheless, this report represents a single case, and the findings may not be generalizable. However, it contributes valuable clinical insight into the rare presentation of isolated TW pneumonia.

4. Conclusions

Tropheryma whipplei pneumonia is an extremely rare entity with nonspecific clinical and radiologic features. mNGS is indispensable for the accurate identification of such uncommon pathogens, particularly when routine cultures are negative. Early recognition and prolonged, appropriate antibiotic therapy are crucial to preventing relapse and achieving complete recovery.

Approval

The patient has provided informed consent for this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Durand, D.V., Lecomte, C., Cathébras, P., Rousset, H. and Godeau, P. (1997) Whipple Disease: Clinical Review of 52 Cases. *Medicine*, **76**, 170-184. https://doi.org/10.1097/00005792-199705000-00003

[2] Dutly, F. and Altwegg, M. (2001) Whipple's Disease and "*Tropheryma whippelii*". *Clinical Microbiology Reviews*, **14**, 561-583. https://doi.org/10.1128/cmr.14.3.561-583.2001

[3] Huo, Y., Wu, C. and Ma, D. (2025) Application of Metagenomic Next-Generation Sequencing in the Diagnosis and Treatment of Acute Pneumonia Caused by *Tropheryma whipplei*. *BMC Pulmonary Medicine*, **25**, Article No. 207. https://doi.org/10.1186/s12890-025-03657-2

[4] Marth, T. (2015) *Tropheryma whipplei*, Immunosuppression and Whipple's Disease: From a Low-Pathogenic, Environmental Infectious Organism to a Rare, Multifaceted Inflammatory Complex. *Digestive Diseases*, **33**, 190-199. https://doi.org/10.1159/000369538

[5] Marth, T., Moos, V., Müller, C., Biagi, F. and Schneider, T. (2016) *Tropheryma whipplei* Infection and Whipple's Disease. *The Lancet Infectious Diseases*, **16**, e13-e22. https://doi.org/10.1016/s1473-3099(15)00537-x

[6] Puéchal, X. (2001) Whipple Disease and Arthritis. *Current Opinion in Rheumatology*, **13**, 74-79. https://doi.org/10.1097/00002281-200101000-00012

[7] Lagier, J., Lepidi, H., Raoult, D. and Fenollar, F. (2010) Systemic *Tropheryma whipplei*: Clinical Presentation of 142 Patients with Infections Diagnosed or Confirmed in a Reference Center. *Medicine*, **89**, 337-345. https://doi.org/10.1097/md.0b013e3181f204a8

[8] Lagier, J., Fenollar, F. and Raoult, D. (2017) Acute Infections Caused by *Tropheryma whipplei*. *Future Microbiology*, **12**, 247-254. https://doi.org/10.2217/fmb-2017-0178

[9] Fenollar, F., Birg, M., Gauduchon, V. and Raoult, D. (2003) Culture of *Tropheryma whipplei* from Human Samples: A 3-Year Experience (1999 to 2002). *Journal of Clinical Microbiology*, **41**, 3816-3822. https://doi.org/10.1128/jcm.41.8.3816-3822.2003

[10] Biagi, F., Balduzzi, D., Delvino, P., Schiepatti, A., Klersy, C. and Corazza, G.R. (2015) Prevalence of Whipple's Disease in North-Western Italy. *European Journal of Clinical Microbiology & Infectious Diseases*, **34**, 1347-1348. https://doi.org/10.1007/s10096-015-2357-2

[11] Hujoel, I.A., Johnson, D.H., Lebwohl, B., Leffler, D., Kupfer, S., Wu, T., *et al.* (2018) *Tropheryma whipplei* Infection (Whipple Disease) in the Usa. *Digestive Diseases and Sciences*, **64**, 213-223. https://doi.org/10.1007/s10620-018-5033-4

[12] Boumaza, A., Ben Azzouz, E., Arrindell, J., Lepidi, H., Mezouar, S. and Desnues, B. (2022) Whipple's Disease and *Tropheryma whipplei* Infections: From Bench to Bedside. *The Lancet Infectious Diseases*, **22**, e280-e291. https://doi.org/10.1016/s1473-3099(22)00128-1

[13] Zhang, W.M. and Xu, L. (2021) Pulmonary Parenchymal Involvement Caused by

Tropheryma whipplei. *Open Medicine*, **16**, 843-846. https://doi.org/10.1515/med-2021-0297

[14] Dolmans, R.A.V., Boel, C.H.E., Lacle, M.M. and Kusters, J.G. (2017) Clinical Manifestations, Treatment, and Diagnosis of *Tropheryma whipplei* Infections. *Clinical Microbiology Reviews*, **30**, 529-555. https://doi.org/10.1128/cmr.00033-16

[15] La Scola, B., Fenollar, F., Fournier, P.E., Altwegg, M., Mallet, M.N. and Raoult, D. (2001) Description of *Tropheryma whipplei* Gen. Nov., Sp. Nov., the Whipple's Disease Bacillus. *International Journal of Systematic and Evolutionary Microbiology*, **51**, 1471-1479. https://doi.org/10.1099/00207713-51-4-1471

[16] Duss, F., Jaton, K., Vollenweider, P., Troillet, N. and Greub, G. (2021) Whipple Disease: A 15-Year Retrospective Study on 36 Patients with Positive Polymerase Chain Reaction for *Tropheryma whipplei*. *Clinical Microbiology and Infection*, **27**, 910.e9-910.e13. https://doi.org/10.1016/j.cmi.2020.08.036

[17] Xie, Y., Du, J., Jin, W., Teng, X., Cheng, R., Huang, P., *et al.* (2019) Next Generation Sequencing for Diagnosis of Severe Pneumonia: China, 2010-2018. *Journal of Infection*, **78**, 158-169. https://doi.org/10.1016/j.jinf.2018.09.004

[18] Zhang, F., Chen, J., Huang, H., Deng, X., Zhang, W., Zeng, M., *et al.* (2021) Application of Metagenomic Next-Generation Sequencing in the Diagnosis and Treatment Guidance of *Pneumocystis jirovecii* Pneumonia in Renal Transplant Recipients. *European Journal of Clinical Microbiology & Infectious Diseases*, **40**, 1933-1942. https://doi.org/10.1007/s10096-021-04254-x

[19] Shen, J., Zhou, X., Shan, Y., Yue, H., Huang, R., Hu, J., *et al.* (2020) Sensitive Detection of a Bacterial Pathogen Using Allosteric Probe-Initiated Catalysis and CRISPR-Cas13a Amplification Reaction. *Nature Communications*, **11**, Article No. 267. https://doi.org/10.1038/s41467-019-14135-9

[20] Wilson, M.R., Naccache, S.N., Samayoa, E., Biagtan, M., Bashir, H., Yu, G., *et al.* (2014) Actionable Diagnosis of Neuroleptospirosis by Next-Generation Sequencing. *New England Journal of Medicine*, **370**, 2408-2417. https://doi.org/10.1056/nejmoa1401268

[21] Forbes, J.D., Knox, N.C., Ronholm, J., Pagotto, F. and Reimer, A. (2017) Metagenomics: The Next Culture-Independent Game Changer. *Frontiers in Microbiology*, **8**, Article 1069. https://doi.org/10.3389/fmicb.2017.01069

[22] Feurle, G.E., Junga, N.S. and Marth, T. (2010) Efficacy of Ceftriaxone or Meropenem as Initial Therapies in Whipple's Disease. *Gastroenterology*, **138**, 478-486. https://doi.org/10.1053/j.gastro.2009.10.041

[23] Bakkali, N., Fenollar, F., Biswas, S., Rolain, J. and Raoult, D. (2008) Acquired Resistance to Trimethoprim-Sulfamethoxazole during Whipple Disease and Expression of the Causative Target Gene. *The Journal of Infectious Diseases*, **198**, 101-108. https://doi.org/10.1086/588706

[24] Fenollar, F., Rolain, J., Alric, L., Papo, T., Chauveheid, M., van de Beek, D., *et al.* (2009) Resistance to Trimethoprim/Sulfamethoxazole and *Tropheryma whipplei*. *International Journal of Antimicrobial Agents*, **34**, 255-259. https://doi.org/10.1016/j.ijantimicag.2009.02.014

[25] Lagier, J., Fenollar, F., Lepidi, H., Giorgi, R., Million, M. and Raoult, D. (2013) Treatment of Classic Whipple's Disease: From *in Vitro* Results to Clinical Outcome. *Journal of Antimicrobial Chemotherapy*, **69**, 219-227. https://doi.org/10.1093/jac/dkt310

[26] Keinath, R.D., Merrell, D.E., Vlietstra, R. and Dobbins, W.O. (1985) Antibiotic Treatment and Relapse in Whipple's Disease. Long-Term Follow-Up of 88 Patients. *Gastroenterology*, **88**, 1867-1873. https://doi.org/10.1016/0016-5085(85)90012-5

[27] Joyce, E., Fabre, A. and Mahon, N. (2012) Hydroxychloroquine Cardiotoxicity Presenting as a Rapidly Evolving Biventricular Cardiomyopathy: Key Diagnostic Features and Literature Review. *European Heart Journal*: *Acute Cardiovascular Care*, **2**, 77-83. https://doi.org/10.1177/2048872612471215

[28] Smith, K. and Leyden, J.J. (2005) Safety of Doxycycline and Minocycline: A Systematic Review. *Clinical Therapeutics*, **27**, 1329-1342. https://doi.org/10.1016/j.clinthera.2005.09.005

[29] Li, W., Zhang, Q., Xu, Y., Zhang, X., Huang, Q. and Su, Z. (2021) Severe Pneumonia in Adults Caused by *Tropheryma whipplei* and *Candida* sp. Infection: A 2019 Case Series. *BMC Pulmonary Medicine*, **21**, Article No. 29. https://doi.org/10.1186/s12890-020-01384-4

[30] Shen, Y., Cui, S., Teng, X. and Han, M. (2024) Acute Pneumonia Due to *Tropheryma whipplei* Diagnosed by Metagenomic Next-Generation Sequencing and Pathology: A Case Report. *Heliyon*, **10**, e26747. https://doi.org/10.1016/j.heliyon.2024.e26747

[31] Fenollar, F., Puéchal, X. and Raoult, D. (2007) Whipple's Disease. *New England Journal of Medicine*, **356**, 55-66. https://doi.org/10.1056/nejmra062477