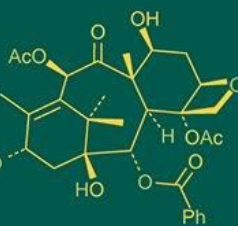
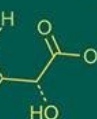


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2026): 5.29
IJABR 2026; 10(1): 891-896
www.biochemjournal.com
Received: 06-11-2025
Accepted: 09-12-2025

Shaimaa Jassim Dohie
Department of Chemistry,
College of Education for
Women, University of Al-
Shatrah, Iraq

Fatima Wisam Naji Wedaa
Department of Forensic
Science, College of Science,
University of Al Qadisiyah,
Iraq

Awid Alawi Awid Salman
Department of Chemistry
Sciences, College of Science,
University of Babylon, Iraq

**Zainab Bashir Abdulqader
Yehya**
Department of Medical
Microbiology, College of
Science, University of Mosul,
Iraq

**Shanaz Omer Ebrahim
Mahmod**
Department of Medical
Laboratory Sciences, College of
Health Sciences, Dohuk
University, Iraq

Corresponding Author:
Shaimaa Jassim Dohie
Department of Chemistry,
College of Education for
Women, University of Al-
Shatrah, Iraq

Diagnostic value of chemical and microbial indicators in differentiating acute and chronic infections

Shaimaa Jassim Dohie, Fatima Wisam Naji Wedaa, Awid Alawi Awid Salman, Zainab Bashir Abdulqader Yehya and Shanaz Omer Ebrahim Mahmod

DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i1k.7143>

Abstract

This difference between acute and chronic infections is a cornerstone of the discipline of medicine that greatly defines the clinical decision making in regard to the choice of treatment and the need to conduct further research. Acute infections are defined as quick healing; they heal within a short period, and at least in the early phases of inflammatory reaction it can be assumed that the symptoms and inflammation is bound to vanish as the body starts healing. Conversely, chronic infections are remarkable due to their capacity to last long and be active in the body over a long period, at times more than months and even years without elimination. A significant portion of medical literature emphasizes the significance of a range of chemical and microbial indicators, which can properly distinguish between the patients with acute and chronic infections. This distinction has extensive implications on clinical practice. Therefore, taking into account the inflammatory response and a range of other clinical manifestations, such pointers can potentially improve the temporal diagnosis of an infectious disease. They would help offer valuable insights into the duration of the infection, would give information that would otherwise be unattainable using standard descriptive words, and would inform the healthcare providers on the choice of the monitoring parameters that most effectively apply to the patients.

Keywords: Acute infection, chronic infection, inflammatory response, clinical biomarkers

1. Introduction

Humans can be infected by bacteria, viruses and fungi causing acute or chronic infections. The acute infections are usually cured in a few days or few weeks but chronic infections take months or years ^[1]. The clinicians need reliable mechanisms of distinguishing the two types of infections. Analytical evidence indicates that chemical and microbial contributors can be reliable to distinguish between acute and chronic infections. Introducing a rationalized overview of the premise underlining ideas, the framework outlines the role of pathogen survival protocols in mediating the host reaction and the disclosure in chemical and microbial markers. Later sections list recognized indicators, discuss dynamics and mechanisms, assess the methodology of analysis and decision levels, and discuss clinical evidence. The analysis will uphold the following fundamental hypotheses in regard to specificity, sensitivity and predictive value of chemical and microbial indicators.

Acute and chronic infections have different phenotypes that show the host pathogen interaction. The time scale of infection is one of the basic factors that are considered both analytically and therapeutically. Although years of research have been done, there are insufficient diagnostic techniques to differentiate between the two presentations ^[2]. The literature available provides the definition of acute and chronic infections as less than and more than 2 weeks, respectively. Discriminatory indicators therefore need to be analyzed over an appropriate period of time before the temporal signature of the infection may be lost ^[3]. However, chemical and microbial indicators are the good candidates.

2. Theoretical Framework

Clinical diagnosis of infection puts the onset of the disease, its progression and duration as the essential part of the management plan. The natural history and progression of acute and chronic infections differ and force the pertinent procedures and methods that distinguish

between the two conditions. Clinical assessments can be more reliable with the help of laboratory support that can be used to diagnose the condition early and make intervention. Conventional methods of diagnosis are geared towards detection of aetiological agents that decide whether the infection is acute or chronic [4].

Acute phase of infection is the stage of setting the pathogen and the formation of an adequate host reaction that jointly define the disease phenotype. At this stage, the agent plays an active role into the evolution of the condition and the appearance of signs of infection indicates the interactions between the host and the pathogen. The infection may be chronic in case of the host response inadequacy, or the pathogen may be able to avoid or neutralize this response. [5-7].

3. Indicators of Infection Chemical

The infection is one of the most widespread reasons to address medical care, too often it is not yet diagnosed adequately, or too late. Previous tests and patient history including C-reactive protein (CRP) testing can be valuable to the expert in deciding about the probable infection state acute and chronic. The time courses of host-pathogen interactions influence the expression of common chemical (inflammatory and metabolic) and microbial (indicators, symbiotic flora, and pathogen load) indicators, which may assist experts in distinguishing with more precision at least between more chronic and acute states due to laboratory findings [2].

Chemical indicators encompass inflammatory biomarkers, which vary during the initial phase of an infection, regulators of host energetic-metabolic response, and redox state and tissular damage of cellular markers. Some of the inflammatory compounds are transitory e.g. pro and anti-inflammatory cytokines or chemokines and permanent e.g. acute-phase proteins. Examples of energy-related compounds are lactate, pyruvate, tricarboxylic cycle intermediates, glucose, keto bodies, adenosine and other adenine nucleotides, examples of stress-related and damage indicators can be different indicating that include reactive-oxidative-species (ROS) intermediary elements and components of cells that are egressing or severely damaged (both indicators are still collected in the same medium, usually blood or plasma).

3.1 Inflammatory Biomarkers

The patterns of elevation of cytokines and acute-phase proteins are specific to the progression of the infection [2]. Diverse metabolites of energy and catabolic cues report endpoint flux along mechanistic pathways [8]. Oxidative stress and tissue damage markers can be used to differentiate infections that have led to the development of a chronic pathological condition.

The response to inflammation and its dysregulation have been at the center of pathogenesis of local infection and sepsis. Systemic inflammatory reactions involve the production of local and systemic effectors, which mediate the different but contingent inflammatory pathways [3]. These early host-pathogen interactions are characterized and the patterns of the associated markers offers a conceptual framework on which the continued differentiation between persistent and non-persistent infections is based.

3.2 Metabolic Signatures

There are characteristic metabolic patterns that indicate the host-pathogen interactions that produce acute and chronic infections. There exists a difference between uncomplicated and septic nephrolithiasis based on fourteen energy metabolites, where reduction of a61e04215-b588-49fb-b53a-5331f70163baosine triphosphate and an increase of a61e04215-b588-49fb-b53a-5331f70163baosine-5-diphosphate mark early acute infection [9]. An early metabolic response, such as elevated glucose, alanine, and kynurenine in community-acquired pneumonia, is an initial response to infection replaced by pathogen-specific changes later [10]. In addition to the microbial load, the duration of infection is associated with host metabolism and the extent of physiological dysfunction.

Acute infections lead to a rapid inflammatory response that allows the elimination of pathogens and the restoration of homeostasis, and chronic infections often imply more significant physiological alterations and long-term metabolic reactions. Major cellular metabolic pathways involved with cellular energy, macromolecule synthesis, redox homeostasis and antimicrobial defense are frequently impaired in further perturbation. Such when the urea cycle is depressed, e.g. supplying energy, metabolic precursors and protection against oxidative stress. There is a relationship between metabolic dysregulation and sepsis severity; metabolic informatics therefore provides information about the time of acute infections. Diverse inflammatory response is justified by cancer, autoimmune disease, and infection, but host metabolism is a unifying factor.

3.3 Markers of Oxidative Stress and Tissue Injury

Whenever infected, pathogen and host factors may cause oxidative stress in the host, which disrupts the antioxidant defense system leading to excessive generation of reactive oxygen species (ROS) and final products including lipid peroxidation, modified amino acids and protein oxidation [11, 12]. The biomarkers of levels of these oxidative stress and tissue damage can be connected to the period of infection because their increase and continued progression tend to be associated with chronic infection.

4. Microbial Indicators and Diagnostic Applications

The availability of classic signs and symptoms of infections (e.g. fever and sepsis) shows the vital role of time in the process of diagnosing current infections in comparison to recurrent ones. In fact, persistent infections, which are characterized by daily nutrient-time transformation of effect and biotrophic of nutrition mode require less time to recover, and appear reverse-reference angle in period repetition. Therefore, the same situation can be observed with the type of pathogen and its physical/biological morphologic parameters. This can be expressed into two fundamental hypotheses: First, as a difference in the differential infectious indicators will occur due to acute and chronic infections and subsequent and repeated infections may have identical physical form; Second, the mechanism of the physical parameters transformation of the pathogen and the difference in the indicators of infectious diseases are similar and this will result in a subsequent effect [2].

An acute infection is characterized by a rapidly increasing, persistent and exponentially increasing number of bacteria, but on the other hand, a chronic or detour infection is characterized by a non-continuous manner, and the manner

of a sickle curve of the number of infected bacteria is accordingly. In the chronic process, there is concurrent or subsequent acute reinforcement that takes place between daily regular intervening times. Between the acute and chronic infection pattern there is an intermediate zone which exists. When the ongoing and recurring end-around time respectively become equal to the elapsed time, the acute and chronic time can be measured ^[13].

4.1 Pathogen Type and Load Measures

Host-pathogen interaction is a dynamic balance wherein the host is characterized by an acute response to promptly rid the host of the invader and the pathogen is characterized by its attempt to establish a niche in which to effectively replicate itself. Continuous, uninhibited, and/or inefficient host pathogen replication disturbs the host pathogen situation into chronic infection ^[14]. This kind of persistence has clinical implications because pathogens can acquire microbial resistance in the course of treatment and/or biofilm that makes antibiotics ineffective. Consciousness of the period of infection is hence very important in the management process (Joosten and Netea, 2020).

4.2 Signatures of microbiomes in Infections

Markers obtained by microbiome have been linked to infection status and development in various environments. In acute bacterial sepsis, systemic immunity is shifted to neutrophil-activation and T-helper (Th) 17, which is replaced by Th2-dominant humoral immunity in culture-negative sepsis ^[15]. There is a stage difference in the neutrophil-to-lymphocyte ratio in murine influenza infection. A 7-gene signature demonstrates active infection in acute gastroenteritis, whereas a 10-gene panel differentiates patients with positive rotavirus, smectic virus, norovirus stool tests and healthy controls ^[16]. Reductions in a variety of gut taxa, mostly Firmicutes, are associated with the symptoms in infectious colitis and acute graft-versus-disease post-hematopoietic stem cell transplant and their recovery is associated with recovery ^[17].

Initial and consecutive alterations of the microbial structure of the gut onset portend *C. rodentium* or *Listeria monocytogenes* infection. In *C. rodentium* infection, it is Clostridiales that reduces when colitis appears and stays on an average level when it is resolved. Mucispirillum rises up to day 1 in the *L. monocytogenes* infection, Clostridaceae and Lactobacillus decrease during the acute phase, and either recovers or reestablishes at subsequent time points. In corroboration with this, a polymerase chain reaction-based test shows that infection of feces by *C. rodentium* is cleared by day 36. Local immune responses to bacterial peritonitis also take the form of microbiome-associated signals in patients under dialysis. These indications distinguish Gram-negative, Gram-positive cocci, and culture-negative episodes, which may hopefully be used to generate rapid pathogen-specific diagnostics.

4.3 The existence of antimicrobial resistance markers is one of the reasons for this phenomenon (2018). <[human]>The Presence of Markers of antimicrobial resistance is one of the causes of this phenomenon (2018)

The issue of antimicrobial resistance is also a global threat and can offer important information in distinguishing between the acute and chronic infection ^[18]. Biofilms and persister cells harbor microorganisms that are prone to attain

novel physiological conditions and become unresponsive to conventional antibacterial agents. Biofilm formation usually comes with a reduction in the level of antibiotic susceptibility which is shown by the decreased effective concentrations. The development of resistance to commonly used small-molecule inhibitors is a higher level of chronic infection. This results in reduced susceptibility and treatment failure due to the overproduction of β -lactamases including broad-spectrum variants.

5. Differences between Acute and Chronic Infections: Conceptual Essentials

There has been growing interest in the diagnostics field in the search of reliable biomarkers to differentiate between acute and chronic infections. It is agreeing that acute and chronic infections demonstrate different host reaction and pathogen traits that ought to lead to significant variation in the biomarker profiles.

The acute infection is usually characterized by the fact that the infectious process was formed quickly, and the host response is active, which contributes to the easy elimination of the causative agent. Depending on the chronic infections, variations of the same microorganism can cause acute disease, but at the acute stage, the dominant strain is stabilized. Majority of the infections begin as acute cases and develop to persistence. The load of pathogen usually increases dramatically when the infection is in its initial phases and later decreases due to the development of a meaningful response by the host. Chronic infections, in contrast are defined by the presence of a live pathogen and a persistent but frequently attenuated host response. There are also instances where at the acute stage, the process is not detected but the disease remains chronic. An example is the case of viral infections. Biomarkers possess characteristic time courses onset, peak, and resolution, and during the progression of an acute infection, they undergo both acute and chronic pathways and stages ^[19].

5.1 Biomarkers Dynamics over Time

The most significant danger to human life is caused by infection. The microbial diseases and infections are caused by the colonization and propagation of pathogen. The fate of the microbial and host species as well as the pattern of the chemical and microbial indicators generated depend on the host-pathogen interactions. The infection triggers an acute stage immediately after infection and forms the acute infection, in its turn, causes acute diseases but triggers instant protection mechanisms. In other instances, the reaction of the acute infection is not successful or the source of the infection cannot be eradicated; the host reacts to the continued existence of the pathogens as chronic infection; the indicators evolved are particular and differentiated ^[20]. The number of (even unlimited) cycles of infection is possible. In most cases, infection across various statistical regimes may have a range of biological characteristics simultaneously. Still, whether quantitative approach can be applied in diagnostic procedures with the aim of offering detail signatures and time courses respectively is also an unresolved question ^[21].

Upon infection, depending on an enormous number of factors, whether it is immunity instilled in the body by vaccination, resting state of the organism, previous contact with the disease, the pathogenic load in the number of organisms, or coated material or chemical agent and the

likes, comes into play the indicator may at any given moment indicate it immediately. The dynamics are produced by the multiplication of the pathogen, and nutrient turnover/addition and the decision to undergo the transitional process which occurs after the initial signal is by the oily state. During the preparation stage leading to the transition, there is the production and accumulation of a large amount of chemical and biological indicators, and has its flow transport that is signalling of the onset of infection or simply acute infection. The organized molecules of the first phase that is accrued during the progress gives a sufficient record of the organism property initiating infection of bacterial, viral or fungal origin ^[8].

5.2 Host Response Patterns

The shift between the acute and chronic infection is accompanied by pathophysiological, a change of the host response, and adaptation of the microbial agent to the new environment ^[22]. The host and the pathogen are constantly changing at this time and the two lead to the determination of the acute and chronic states. The inflammatory, metabolic, and oxidative stress pathways are likely to take different pathways, and they produce a typical trait of an acute or chronic infection ^[3]. Defining persistence is influenced by various factors including microbial load and virulence and this is applicable in cases where the agent is intrinsically resistant or exogenously resistant to treatment. Certain signs of current or past infection, which are quantified in clinical samples, are brought to diagnostic differentiation.

Considering the antimicrobial perspective, a responsive infection is a case where the treatment commences when a phase of multiplication of the microbes and then a descending pattern follows. On the other hand, there are recurrence agents with load stability during and rebound agents with late rise that are left. Adaptation of pathogens can cause the duration indicators that are harder to measure; in this case the emphasis is put on the identification of the new cases of acute and chronic within closed systems of treatment intervals.

5.3 Microbial Survival and Biofilm Formation

The benefits of biofilm formation include a number of solutions that enable microbial survival and enable the infection to become chronic ^[23]. It is a community of organisms with the exopolymeric matrix generated by the microbes that gives protection against the host defense mechanisms and antimicrobials, which eventually tend to promote treatment failure, relapse infection, and chronicity. It has been shown that frequent biofilm-positive profiles exist among patients who have relapsing or chronic infection, which implies their contribution to the persistence of infection over prolonged periods and even greater recovery durations than 100 days. The mechanisms linked to biofilm-related chronicity are decreased entry of antimicrobials to the deeply embedded cells, phenotypic resistance, metabolic inactivity, gene acquisition, and the detachment and spreading to new locations ^[24].

6. Methodological Considerations

The distinction between acute and chronic infections may be made based on the clinical process, response cycle of the host in comparison with the pathogen, and the signals of interest in biofluids. The discovery of chemical and

microbial markers exhibiting a different behavior in these two infections can enhance the accuracy of the diagnosis. The chemical indicators of a candidate divides into markers of inflammation, metabolic activity and oxidative stress, and microbial indicators such as identity, load, and community structure of a pathogen. Disagreements of the temporal dynamics of these signals allow the testable hypothesis that duration of time since the beginning of ongoing infection might be estimated, so that acute and chronic infections could be automatically or hand-classified as such.

Low false-positive rates may be maintained by indicator specificity whereas high sensitivity may allow estimating the length of continuing infection even in subjects who had already started with acute infection but had become chronic. The clear patterns of modulation of indicators and interaction make it possible to infer relations of the type and the stage of infection without complete information about the pathogen. Such analysis systems in combination with data assimilation, data analysis and decision making systems can be implemented on the premise of pathogen indication alone. ^[25-27].

6.1 Sample Collection and Pre-analytical Variables

The pre-analytical is a stage that involves voluminous variables that can have a significant impact on the performance of biomarkers in biological samples. Diagnostic systems based on the use of chemical or microbial indicators to detect the stage of infection are especially susceptible to collection and handling, as the type of specimen and its exposure to the environment may change indicator signatures. These indicators can be based on different biological compartments that include blood, exudates, tissues, etc., and each of them has their own collection and storage protocols and needs.

Basic issues regarding the sample collection and the treatment of the sample can be found in the following sections and are consistent with the standard operating procedures suggested in the laboratory analysis of chemical and microbial indicators ^[2]. The collection procedures are surveyed first on their potential impact on the measurement of the chemical and/or microbial indicators, material requirements are observed, and potential changes to the status of the indicators that may have occurred during sampling, stabilisation and processing are introduced. This is followed by the analysis of more specific pre-analytical conditions that alter the behaviour of indicators, in a different manner depending upon the type of chemical or microbiological indicator.

6.2 Analytical Systems and Checking

There are a lot of systems of analysis that can be used to measure biological indicators in human samples. At the same time, evaluation procedures allow determining the reliability, reproducibility, and reproducibility of the results. A number of distinct acute and chronic scenarios are where multiplex assays and mass-spectrometry-based systems are commonly applied. Specifically, the multi-analytic measurements of a given sample can be used to provide a detailed picture of the biological status of the participant. Bloodstream infections (BSI) diagnosis is based on the detection of the cost of infectious organisms in the blood. Traditionally, blood cultures are done, but these cultures are not sensitive and they require long to be processed. Therefore, another sure method is measuring the levels of

immune serum markers which are selectively discharged by host cells in case of an infection ^[2]. In gram-negative BSI, some of the cytokines increase more rapidly than conventional ones.

Absence detection in constituents after induction of target is a very effective methodology that can be used to measure BSI. In this regard, polymerase chain reaction (PCR) and MALDI-TOF mass spectrometry can be used to clarify the different microorganisms that cause the infection ^[28].

6.3 Data Integration and Interpretation

The data of the chemical and microbial indicators of acute and chronic infections must be integrated and interpreted in a specific way, which implies a specific focus on specific biomarkers, sampling procedures, analytical platforms, and contextual characteristics. The subsequent assessment of such indicators will allow a mechanistic hypothesis to be made and have a predictive value, descriptions of clinical outcomes in relation to the temporal dynamics of biomarker signatures, and the introduction of parameter thresholds that define acute vs. chronic infections.

These several surface-and non-surface-encoded virulence determinants shared by various pathogens, which are then matched with kinetic and outcome information on a biomarker pattern, further allow incorporation into a scheme to reproduce the overall classification pattern, and clarify clinical implications ^[29].

7. Conclusion

Acute and chronic infections are significant health threats because they have continued to affect the quality of life, raise the incidences of opportunistic infections, and pose the conditions of antimicrobial resistance. The problem of summarizing and classifying infections has existed over one hundred years, although some of the conceptual frameworks are still applicable. Focus on environmental persistence and pathogen latency does not incorporate other phenomenon like the genetic carrier states or latency and definitely does not reflect the host-pathogen interaction which is significant and common. The conceptual basis expressed makes use of time as one of its fundamental variables time since the infectious event or time since the onset of the infectious disease and is flexible enough to include a range of types and circumstances of infection that bind the core processes of infectious disease together. Diagnosis of infections and monitoring of the progression of the infection depends significantly on detecting infections and pathogens. The analysis took into account all the types of pathological entities, as well as the most common groups of pathogens, the major of which include those that are of high epidemiological significance.

8. References

1. Cheng H, Strouts F, Sweeney TE, Briese T, *et al.*, Integration of Next-Generation Sequencing, Viral Sequencing, and Host-Response Profiling for the Diagnosis of Acute Infections; 2017. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
2. Li X, Yuan X, Wang C. The clinical value of IL-3, IL-4, IL-12p70, IL17A, IFN- γ , MIP-1 β , NLR, P-selectin, and TNF- α in differentiating bloodstream infections caused by gram-negative, gram-positive bacteria and fungi in hospitalized patients: An Observational Study; 2019. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
3. Menéndez R, Miguel Sahuquillo-Arce J, Reyes S, Martínez R, *et al.*, Cytokine Activation Patterns and Biomarkers Are Influenced by Microorganisms in Community-Acquired Pneumonia; 2012. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
4. Galar A, Kulldorff M, Rudnick W, O'Brien TF, *et al.*, Biochemical Phenotypes to Discriminate Microbial Subpopulations and Improve Outbreak Detection; 2013. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
5. Macias-Paz IU, Pérez-Hernández S, Tavera-Tapia A, Luna-Arias JP, Guerra-Cárdenas JE, Reyna-Beltrán E. *Candida albicans* the main opportunistic pathogenic fungus in humans. *Revista Argentina de microbiología*. 2023 Apr 1;55(2):189-98. [sciencedirect.com](https://www.sciencedirect.com)
6. Mba IE, Sharndama HC. Vaccine development for bacterial pathogens: Advances, challenges and prospects, *Tropical Medicine & International Health*, Wiley Online Library; 2023. [wiley.com](https://www.wiley.com)
7. Graziosi G, Lupini C, Catelli E, Carnaccini S. Highly pathogenic avian influenza (HPAI) H5 clade 2.3. 4.4 b virus infection in birds and mammals," *Animals*; 2024. [mdpi.com](https://www.mdpi.com)
8. Christensen EE, Binde C, Leegaard M, Tonby K, *et al.*, Diagnostic accuracy and added value of infection biomarkers in patients with possible sepsis in the emergency department; 2022. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
9. Kauppi AM, Edin A, Ziegler I, Mölling P, *et al.*, Metabolites in Blood for Prediction of Bacteremic Sepsis in the Emergency Room; 2016. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
10. den Hartog I, Zwep LB, Vestjens SMT, Harms AC, *et al.*, Metabolomic profiling of microbial disease etiology in community-acquired pneumonia; 2021. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
11. Bwititi PT, Chinkwo K. Oxidative stress markers in infectious respiratory diseases: current clinical practice; 2017. [PDF]
12. Andresen M, Regueira T, Bruhn A, Perez D, *et al.*, Lipoperoxidation and Protein Oxidative Damage Exhibit Different Kinetics During Septic Shock; 2008. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
13. Rhoads DD, Wolcott RD, Sun Y, Dowd SE. Comparison of Culture and Molecular Identification of Bacteria in Chronic Wounds; 2012. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
14. Tam CC, Offeddu V, Anderson KB, Weg AL, *et al.*, Association between semi-quantitative microbial load and respiratory symptoms among Thai military recruits: a prospective cohort study; 2018. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
15. Zhang J, Friberg IM, Kift-Morgan A, Parekh G, *et al.*, Machine-learning algorithms define pathogen-specific local immune fingerprints in peritoneal dialysis patients with bacterial infections; 2017. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
16. Relman DA. Detection and identification of previously unrecognized microbial pathogens; 1998. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
17. Belzer C, Gerber GK, Roeselers G, Delaney M, *et al.*, Dynamics of the Microbiota in Response to Host Infection; 2014. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
18. Bhattacharya S. Early diagnosis of resistant pathogens: How can it improve antimicrobial treatment?; 2013. [ncbi.nlm.nih.gov](https://www.ncbi.nlm.nih.gov)
19. Zautner AE, Groß U, Emele MF, Hagen RM, *et al.*, More Pathogenicity or Just More Pathogens?—On the Interpretation Problem of Multiple Pathogen Detections

- with Diagnostic Multiplex Assays; 2017. ncbi.nlm.nih.gov
20. Seok H, Won Park D. Role of biomarkers in antimicrobial stewardship: physicians' perspectives; 2024. ncbi.nlm.nih.gov
21. de Lucio Delgado A, Antonio Villegas Rubio J, Rey Galan C, Prieto García B, *et al.*, Biomarkers and Fever in Children with Cancer: Kinetics and Levels According to Final Diagnosis; 2021. ncbi.nlm.nih.gov
22. Schutzer SE, Use of Host Factors in Microbial Forensics; 2011. ncbi.nlm.nih.gov
23. Sanchez CJ, Mende K, Beckius ML, Akers KS, *et al.*, "Biofilm formation by clinical isolates and the implications in chronic infections; 2013. ncbi.nlm.nih.gov
24. Di Domenico EG, Toma L, Provot C, Ascenzioni F, *et al.*, Development of an *in vitro* Assay, Based on the BioFilm Ring Test(®), for Rapid Profiling of Biofilm-Growing Bacteria; 2016. ncbi.nlm.nih.gov
25. Wang L, Zhang K, Xu L, Wang J. Understanding underlying physical mechanism reveals early warning indicators and key elements for adaptive infections disease networks, PNAS nexus; 2024. oup.com
26. Jeffrey M, Denny KJ, Lipman J, *et al.*, Differentiating infection, colonisation, and sterile inflammation in critical illness: the emerging role of host-response profiling, Intensive Care Medicine; 2023, Springer. cam.ac.uk
27. Tana C, Soloperto M, Giuliano G, Erroi G, Di Maggio A. Artificial intelligence for predicting lung immune responses to viral infections: from mechanistic insights to clinical applications, Viruses; 2025. mdpi.com
28. Jordana-Lluch E, Giménez M, Dolores Quesada M, Ausina V, *et al.*, Improving the Diagnosis of Bloodstream Infections: PCR Coupled with Mass Spectrometry; 2014. ncbi.nlm.nih.gov
29. Chick HM, Rees ME, Lewis ML, Williams LK, *et al.*, Using the Traditional Ex Vivo Whole Blood Model to Discriminate Bacteria by Their Inducible Host Responses; 2024. ncbi.nlm.nih.gov