The Review Of
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Multidisciplinary Collaboration In Diagnosing And Managing Complex Chronic Infections

Dr. Faisal Fwuaran Alharbi[1] , Dr. Mohammed Abdulhafez Mahboob, Md[2] , Dr-Sameer Hatim Salih Atwah[3] , Dr-Mohammad Fouad Khatib Sambas[4] , Dr -Dhyy Abdullah Alqurashi[5] , Dr- Mashail Taha Sakhakhni[6] , Dr-Nada Hassan Fatani[7] , Dr Hamed S. Qutbuddeen[8] , Dr Wafaa Moghram Alshehri[9] , Dr-Amal Abdullah Banjer[10]

[1]Infectious Disease Consultant King Abdulaziz Hospital Makkah
[2]Consultant, Internal Medicine And Infectious Diseases King Abdulaziz Hospital, Makkah, Saudi Arabia
[3]Nephrology Consultant King Abdul Aziz Hospital
[4]Infectious Disease Consultant King Abdulaziz Hospital
[5]General Physician Alnoor Hospital
[6]Internal Medicine Consultant King Abdulaziz Hospital
[7]Internal Medicine And Infectious Disease Consultant King Abdulaziz Hospital Makkah
[8]Orthopedic Spine Surgeon King Abdulaziz Hospital
[9]Medical Resident King Faisal Hospital
[10]Neurology Consultant King Abdulaziz Hospital

1. Introduction

Infections have been linked to acute and chronic kidney diseases. This review considers the etiology, epidemiology, and molecular mechanisms underlying chronic infection-induced renal injury and the range of clinical presentations that occurs, including glomerulonephritis, interstitial nephritis, pyelonephritis, and amyloidosis. The role of infection in development of renal disease is often difficult to prove, particularly in chronic cases, where relationships can be indirect and prolonged. A multidisciplinary approach is essential in establishing the cause and managing chronic renal infections. Chronic infections can result from a range of microbial etiologies, produce mild and non-specific clinical symptoms, and damaging immune-mediated mechanisms. Consequently, microbial infection is sometimes invoked as a potential initiating or perpetuating pathology in cases in which disease processes are not yet fully understood. While a definitive pathological role for causal microbial agents remains to be established in many chronic conditions, neuroradiological imaging and pathological evidence have highlighted associations, emphasizing the need for multidisciplinary engagement in diagnosis and treatment. The potentially damaging effect of such infections on the nervous system and other vital physiological processes, including renal function, requires urgent consideration (L. Romanò et al., 2022). Interdisciplinary teams are essential in the diagnosis, management, and prevention of complex infections including those with neurological and renal consequences. Specialist teams are commonplace in prosthetic joint infections because of the complexity that arises from multifaceted diagnostic and treatment protocols. Such teams typically involve collaboration between Orthopaedic, Infectious Disease, Microbiology, allied health, and nursing departments to improve patient care (Sires et al., 2022). Management of complex neurological infections requires collaborative consideration among surgical specialties related to the site and type of infection, the likelihood of progression, and potential neurological sequelae. Non-surgical teams involved in diagnosis and treatment may include Diagnostic and Interventional Radiology, Infectious Diseases, Microbiology, Neurology, and Nephrology (Therese R. Madelar & Ito, 2023). Multidisciplinary teams also consider macroscopic and microscopic

characteristics of the host, which may dictate an operative, device retention, suppressive, or palliative medical management strategy to provide the best patient outcome.

2. Understanding Chronic Infections

A chronic infection is a situation in which an infectious pathogen remains for a prolonged period of time after the initial clinical presentation. By this definition, chronic infections include airways infections such as tuberculosis and cystic fibrosis, long-standing wounds that may have polymicrobial biofilms, infections related to implanted medical devices and deep,

2.1. Definition and Classification

Collaborative support from nephrologists and neurologists is crucial for accurate diagnosis and timely treatment when chronic infections lead to renal and/or neurological damage. The information presented here is consistent with the Infectious Diseases Classification of Public Health (Seclas-Serna et al., 2022).

Chronic infections are characterized by an extensive or local pathological inflammatory process caused by an infectious agent that has evaded host immune surveillance. This evasion allows the pathogen to persist and replicate at the site of injury or in other locations where the agent or its products are deposited. Chronic infections are generally classified as follows:

• Infections where damage results from the acute infection phase, such as in poststreptococcal glomerulonephritis. • Infections where the damage is due to the chronic infectious process itself, as observed in tuberculosis, leprosy, neurocysticercosis, or HIV infection. • Infections that cause toxic damage to the kidney or central nervous system through products released by the infectious agent, exemplified by diphtheria and anthrax.

Epidemiological evidence indicates that most of these infections primarily generate organ damage in developing countries, with emerging infectious agents also causing similar lesions in developed nations.

2.2. Epidemiology

A multidisciplinary approach is essential for the diagnosis and management of intricate chronic pathologies. Chronic infections represent a large group of diseases caused by distinct microorganisms, capable of producing systemic manifestations and affecting multiple organs and tissues. Renal and neurological functions are especially vulnerable to the adverse effects of active infection; however, the pathophysiological mechanisms underlying this impairment are not yet fully understood. Laboratory testing and image studies support preliminary diagnostic and prognostic orientations; nevertheless, collaboration among nephrologists, neurologists, and other medical specialties enhances clinical conclusions for patients with deteriorating renal function and neurological diagnoses during the course of an infectious disease.

These diverse clinical manifestations originate from pathophysiological factors such as the presence of cytokines and endotoxins or the direct infiltration of the central nervous system. Both uremia and chronic neurological symptoms significantly impact patient homeostasis. A multidisciplinary team-based methodology engendering collaborative communication among specialists is fundamental in the comprehensive clinical evaluation of such complex cases. The collective assessment of laboratory and image studies thus improves the accuracy of diagnoses that involve complex associations of acute and chronic processes with active infections.

2.3. Pathophysiology

Chronic infections represent an important cause of secondary organ damage, potentially leading to impairment of one or more functions or organs. The kidney is among the targets of secondary

damage occurring during various diseases. Pathological changes in renal parenchyma during infectious diseases may be due to the circulation of infectious agents in the bloodstream with direct nephrotoxic effect, indirect products of infectious agents, or immune complexes. Once the pathological changes in the kidneys have occurred, they rarely resolve completely. Sometimes they evolve rapidly towards renal failure, incurable in the absence of early diagnosis and treatment. Furthermore, the long-term evolution of chronic infections is also characterized by neurological impairment.

The chronic nature of infections such as brucellosis favors endothelial dysfunction, followed by the release of pro-inflammatory cytokines and vasoactive substances, and the formation of atheromatous plaques. These lesions extend to arteries of the brain, with possible ischemic lesions. The alteration of cerebral vessels, the associated protein alterations, and the synthesis of immunoglobulins induce damage at the brain parenchyma level. Cerebral injury explains the occurrence of neurological manifestations during long evolution of chronic infectious diseases. The manifestation of chronic kidney disease also supports the expression of neurological impairment during the course of one or more of the complex infectious chronic diseases.

Table 1: Etiological Classification of Pathogenic Agents in Chronic Infections and Their Association with Organ Pathologies

Etiological Class	Representative Pathogenic Agents	Pathophysiological Mechanisms of Renal Injury	Pathophysiological Mechanisms of Neurological Injury	
Etiological Class		Bartonella henselae, Borrelia burgdorferi, Chlamydia pneumoniae, Escherichia coli, Helicobacter pylori, Mycobacterium tuberculosis	- Direct injury to the renal parenchyma by the pathogen or its toxic products . - Deposition of circulating immune complexes.	- Endothelial dysfunction of the vasculature . - Induction of pro-inflammatory cytokine release . - Development of cerebral ischemic lesions resulting from atheromatous plaques.
Etiological Class	Epstein–Barr, hepatitis, herpes simplex, rubella, measles, cytomegalovirus. Herpes simplex virus 1.	- Immune-mediated mechanisms, including the formation of infection-associated immune complexes.	- Induction of chronic or uncontrolled neuroinflammation . - Breakdown of the blood-brain barrier . - Release of neurotoxic factors leading to neuronal cell death.	
Fungal		Aspergillus, Candida spp., Malassezia	- Systemic infections can lead	- Fungal agents may reach the CNS through various pathways, inducing

		spp., Saccharomyces spp.	to abscess formation or pyelonephritis.	neuroinflammation . - Fungal proteins have been documented to co-localize with amyloid plaques in Alzheimer's disease patients.
Protozoan		Toxoplasma gondii, Trichomonas	- Systemic infections may trigger immune-mediated renal pathologies such as interstitial nephritis.	- Direct invasion of CNS tissues, as in neurocysticercosis . - Systemic immune responses affecting neurological function.

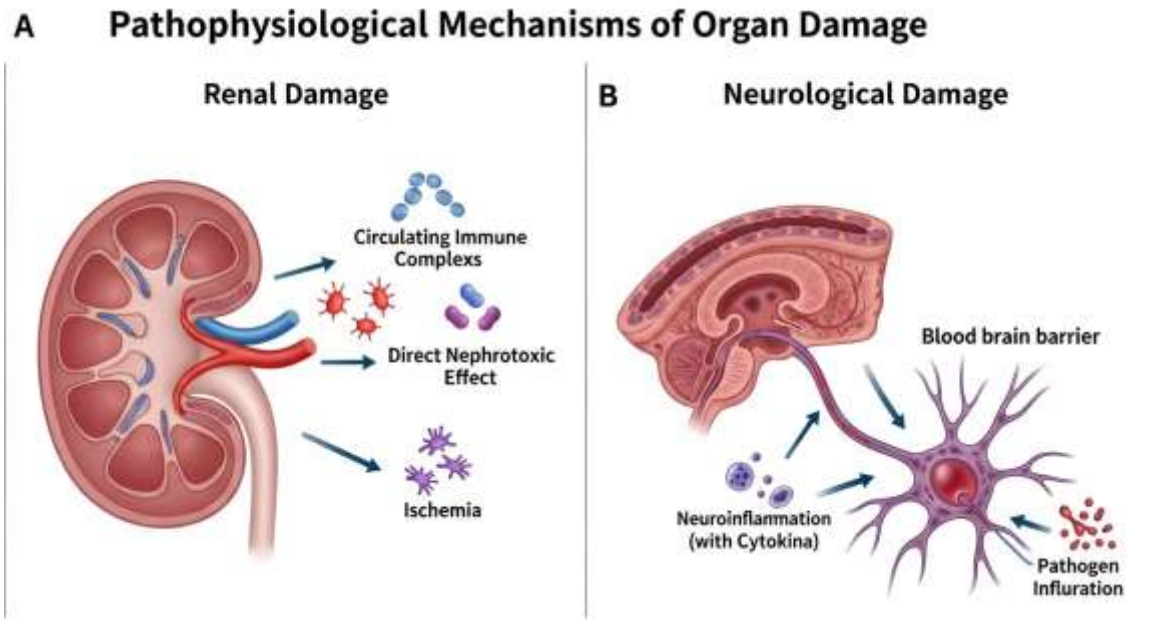
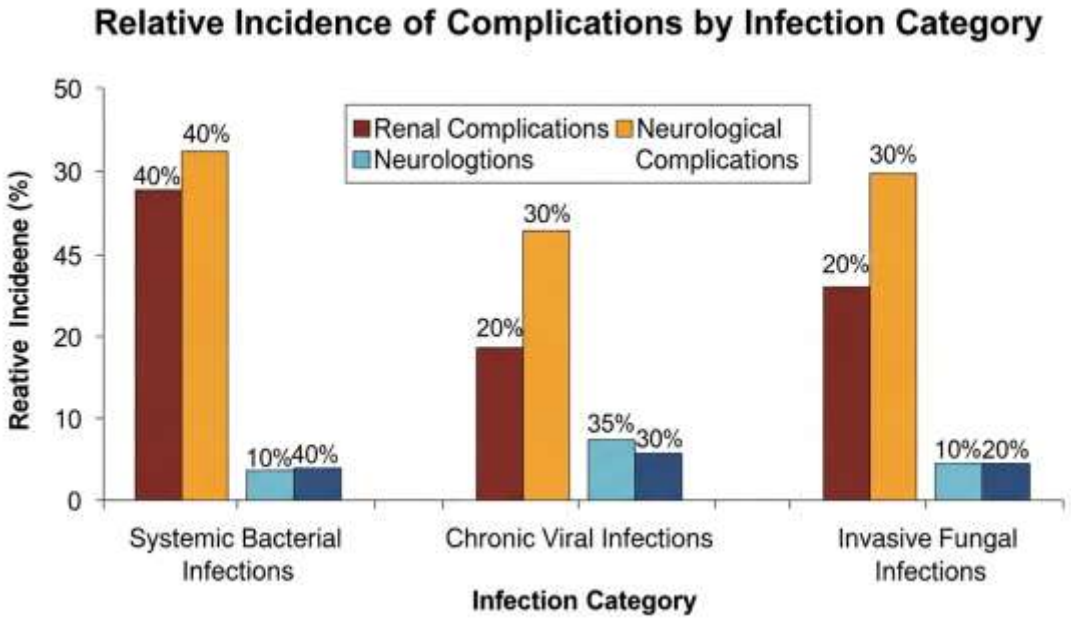


Figure 1: Comparative Pathophysiological Mechanisms of Renal and Neurological Damage in Chronic Infections.

3. Impact of Chronic Infections on Renal Function

Chronic infections are defined as infectious diseases in which the causative agent persists in the body for prolonged periods, often months or years, despite the presence of an adequate immune response to clear it. These infections are classified into: latent infections, in which the microorganisms remain dormant without producing symptoms but have the potential to reactivate; chronic focal infections, where the pathogen causes damage at the site of infection with or without systemic manifestations; and chronic systemic infections, characterized by continuous or recurrent symptoms with the continuous or intermittent presence of the pathogenic agent.

The epidemiology of chronic infections varies significantly with the sterility of the anatomical site involved; as such, focal infections of the oral cavity are most frequent, followed by chronic infections in the respiratory tract and other mucous membranes. Pathogens responsible for chronic infections are diverse and include specific, nonspecific, bacterial, and fungal agents capable of producing injury to different organs and systems. Although any system or organ may be affected, the mechanisms by which these pathogens trigger renal and neurological damage, the main clinical manifestations observed, their diagnosis, and treatment should be analyzed independently.



Graph 1: Illustrative Relative Incidence of Renal and Neurological Complications by Infection Category.

3.1. Mechanisms of Renal Damage

Chronic infections can lead to renal damage through several mechanisms. Patients with chronic kidney disease (CKD) frequently suffer from substantial residual renal damage that impairs renal function. Residual renal damage increases the risk of the glomerular filtration rate falling below one and is linked to higher mortality. Hemodialysis patients have a 26-fold greater risk of death from infection than the general population. CKD is associated with the highest infectious mortality rate of any comorbidity, and patients with moderate renal impairment exhibit a sevenfold increased risk of infection-related hospitalization compared to those with normal renal function (Lamarche et al., 2019). Etiology of CKD includes diabetes, autoimmune diseases, systemic infections, drugs, neoplasia, tubulointerstitial diseases, vascular diseases, cystic and congenital diseases, and structural issues. Vascular diseases such as atherosclerosis and hypertension cause low blood flow, resulting in poor wound healing. Urinary tract infection in patients with cystic disease or structural damage is another common etiology. Infection with ascending contamination often leads to complications such as abscess, bacteremia, and death. Renal infection due to pyelonephritis or cyst infection is less frequent but constitutes a serious complication. In CKD G3-5 patients, treatment failure arises from renal hypoperfusion that reduces drug concentrations in the kidney and cysts remaining larger, precluding antibiotics from reaching effective concentrations. Shorter treatment durations may fail to prevent recurrence, especially in patients with postrenal obstruction.

3.2. Clinical Manifestations

Multiple mechanisms trigger neurological damage from chronic infections that, due to their systemic effects, may produce ischemia, hypoxemia, disruption of metabolism, and cytokine-mediated immune responses, all of which affect biodistribution and nerve function (L. Romanò et al., 2022). Neurological manifestations of chronic infections appear in conditions such as vascular injury, meningitis, meningoencephalitis, pyridoxine deficiency, abscesses, cerebrovascular disorders, and radiculopathies (Therese R. Madelar & Ito, 2023). Organic brain syndrome, a frequent diagnosis seen in a multidisciplinary outpatient setting, encompasses symptoms such as acute confusional states, hallucinations, disorientation, and acute cognitive dysfunction, and mirrors the clinical pattern of infection severity. The Multidisciplinary Diagnostics and Therapeutics (MDT) team takes a leading role in investigating and managing chronic CNS infections, presenting specific challenges when dealing with persistent bacterial, viral, or parasitic pathogens that harm cerebral vessels and the meninges.

3.3. Diagnostic Approaches

Diagnostic approaches for complex chronic infectious diseases involve laboratory, imaging, and clinical evaluations (Coulongeat et al., 2022). Laboratory tests on blood, urine, or cerebrospinal fluid include cultures, polymerase chain reaction (PCR) assays, and serology to identify causative agents and detect infection-associated alterations that affect renal and neurological functions. Imaging techniques such as ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI) are employed to visualize structural or functional abnormalities linked to immuno-inflammatory processes or infections. Detailed clinical assessments rely on patient history, physical examination, and specific questionnaires to characterize symptoms and differentiate relevant clinical phenotypes in which the pathogenesis drives the fate of infection, influenced by bacterial variant, immune activation, and environmental cofactors.

3.4. Management Strategies

Effective management of complex chronic infections necessitates a multidisciplinary approach, particularly in the presence of renal and/or neurological impairment (Therese R. Madelar & Ito, 2023). These infections impose significant social and economic burdens across both developed and developing nations. Persistent or recurring infection can create systemic infectious foci that challenge clinical resolution. Diagnostic uncertainty leads to delays in treatment initiation.

Multidisciplinary collaboration has become the norm in managing prosthetic joint infections and other musculoskeletal infections, aiming to enhance treatment timeliness and efficiency. Such teams typically encompass orthopaedic surgeons, infectious disease specialists, internists, radiologists, microbiologists, and nursing staff, integrating diverse expertise to improve patient responsiveness and outcomes (Sires et al., 2022).

4. Impact of Chronic Infections on Neurological Function

Several specific neurological syndromes induced by chronic infections frequently emerge in clinical practice. The neuropathology of Alzheimer’s disease, Parkinson’s disease, and multiple sclerosis currently constitutes one of the most debated and intriguing fields. A long-standing hypothesis at the nexus of Neuroinflammation and neurodegeneration focuses on the pathophysiological processes behind such neurodegenerative disorders. Recent studies analyzing brain samples, cerebrospinal fluid, or peripheral blood of affected patients have supported the role of several infectious agents in the onset and/or chronification of neurodegeneration (Thi Ai Tran et al., 2022).

Microbiome-derived factors ’activate microglia and induce astrocyte reactivity through Toll-like receptor 4 signalling, driving a transcriptional phenotype that further sustains pro-inflammatory and neurodegenerative processes’. Herpes simplex virus 1 represents the infectious agent found in

both Alzheimer's disease and Parkinson's disease patients. Fungal infections upheld by Candida spp., Malassezia spp., and Saccharomyces spp. also emerge in brain parenchyma of Alzheimer's disease patients, while 'fungal and bacterial proteins co-localize with amyloid plaques'. The brain itself does not host a resident microbiota similar to the skin and gut. Such microbes may reach the central nervous system following multi-organ interactions, including the nose-brain and lung-brain axes or indirectly through a Circulating Immune Complex (CIC)-mediated immune-mediated injury.

Inflammation constitutes a physiologically relevant defensive response of the central nervous system against trauma, ischemic and neurodegenerative pathologies, and infectious challenges. Neuroinflammation mainly involves microglia within the parenchyma, astrocytes and oligodendrocytes, endothelial cells of the blood-brain barrier and periphery-derived immune cells infiltrating the central nervous system. Such response astutely shapes a niche to contain (or eradicate) tissue damage and ultimately foster brain regeneration. Neuroinflammation turns detrimental when chronic or uncontrolled activation of neuroimmune cells leads to the release and sustained production of neurotoxic factors.

Chronic infections can alter the equilibrium and local tissue microenvironment by evoking remarkable changes in central nervous system homeostasis. Brain resident cells from subjects, who develop or exhibit predisposing factors for neurodegenerative diseases, are particularly vulnerable to such stimulus, resulting in accelerated progression of the disease or sustained onset of symptoms. Reactive oxygen intermediates, pro-inflammatory and neurotoxic factors released by exaggerated inflammatory responses give rise to synaptic damage and loss, impaired neurogenesis, blood-brain barrier breakdown, neuronal injury and irreversible cell death. Altogether, those events concur to the onset and acceleration of neurodegeneration.

4.1. Mechanisms of Neurological Damage

The central nervous system (CNS) supports sensory, motor, and cortical functions and is normally exposed to the external environment only through the protective periphery: the nasal mucosa, lung alveoli, and gastrointestinal tract. This arrangement, combined with the blood brain barrier, restricts direct access to the CNS, as well as the resident microbiome (Thi Ai Tran et al., 2022). Microbial neuroinflammation (infection or post-infectious immune activation) is well described as a cause of CNS injury in acute bacterial, viral, or fungal infections, but methods of sustained access to the CNS are less well established. Measurements of blood/CSF microbial nucleic acid or protein, and indirect molecular approaches, continue to identify persistent microbial signatures within the CNS, but it is also evident that microbes and their products are typically eliminated rapidly, such that the composition seen in chronic infections, such as in Alzheimer's disease (AD) or Parkinson's disease (PD), is distinct from normal microbiota. Sustained microbial recruitment of the CNS in chronic infections is highlighted by advances in neuropathological imaging and molecular investigations. Multiple routes promote microbial recruitment of the CNS and may support chronic infections (Malik & Shroff, 2022).

4.2. Clinical Manifestations

Chronic infections exert clinical effects on various systems, including potential involvement of the respiratory, cardiovascular, hepatic, renal, and neurological systems. Objective evaluations may reveal renal or neurological damage, necessitating a multidisciplinary approach for accurate diagnosis and effective management (L. Romanò et al., 2022). Chronic infections such as chronic afebrile pulmonary tuberculosis, tuberculous pleurisy, Brucellosis, viral hepatitis, infectious endocarditis, osteomyelitis, septicaemia, and purulent appendicitis can cause varying degrees of renal impairment. The commonest late manifestation of chronic infections is neurological involvement, which may occasionally present solely as central nervous system symptoms.

4.3. Diagnostic Approaches

Diagnostic ApproachesIn complex presentations, a combination of diagnostic laboratory testing, clinical studies, and image analysis often facilitates the confirmation of chronic infections in conjunction with renal or neurological impairment. The diagnostic workup usually consists of three components: common and advanced microbiological investigations (some of which require close coordination with the clinical microbiology laboratory), clinical assessments, and imaging studies. Urine testing—particularly microscopy, culture, and sensitivity (MC&S)—is the preferred initial diagnostic tool for urinary tract infections. Further sampling methods may depend on the clinical scenario and local microbiological preferences. Mycobacterial investigations are determined by the history, clinical findings, and the results of the initial urine testing.

The use of multidisciplinary diagnostic and management teams is growing and can improve the care of patients with complex chronic infections and associated systemic involvement. Long-term outpatient antimicrobial therapy frequently necessitates teamwork among infectious diseases specialists, clinical microbiology laboratories, and clinical teams (Nori et al., 2023).

4.4. Management Strategies

Management of complex chronic infections such as chronic osteomyelitis, inflammatory bowel disease, and systemic lupus erythematosus relies increasingly on multidisciplinary collaboration, which incorporates clinical, laboratory, and medical imaging data. Integrating nephrology and neurology expertise is especially important, since these infections often impact both renal and neurological function. A multidisciplinary approach combines various pharmacological and non-pharmacological interventions with innovative new therapies. To support this integrated management, multiple diagnostic procedures are utilized in a single procedure that combines information from laboratory tests, imaging studies, and clinical evaluation.

5. Multidisciplinary Collaboration

Multidisciplinary collaboration among specialists is essential for determining the etiology of complex chronic infections and devising treatment for patients with renal and neurological impairment (L. Romanò et al., 2022). Complex infections often necessitate laboratory confirmation and imaging; in challenging cases, pathology from infected tissues procured during debridement or surgery may be indispensable, guiding disease involvement and disease activity through features of chronic inflammation (Therese R. Madelar & Ito, 2023). For instance, in pyogenic spondylodiscitis, multidisciplinary management by a specialized team including orthopedic surgeons, infectious disease specialists, internists, radiologists, and microbiologists enables comprehensive cooperation to improve the efficiency of treatment strategies. As with other infectious diseases presenting with renal or neurological complications, teamwork is paramount to clarify the diagnosis and establish treatment for chronic infections resulting from other pathogens.

5.1. Importance of Teamwork

The identification of patients with complex, treatment-refractory infections is fundamental in the quest to resolve polymicrobial infections and to provide improved patient care. Even when a single agent is identified, clinicians often face diagnostic challenges when infection disseminates to multiple organs.

The management of infectious diseases has evolved, with many institutions establishing dedicated teams that may include infectious disease specialists, microbiologists, pharmacists, and other health care workers (L. Romanò et al., 2022). These teams commonly apply a range of guidelines to mediate and support the attending physician. The World Association against Infection in Orthopedics and Trauma and the Société Internationale de Chirurgie Orthopédique et de Traumatologie emphasize the establishment of multidisciplinary teams with infectious disease specialist involvement to enhance patient care. Similarly, multidisciplinary teams enhance

treatment efficiency and quality of care by facilitating cooperation among specialized professionals (Therese R. Madelar & Ito, 2023). For instance, in the treatment of complex infections such as pyogenic spondylodiscitis, a multidisciplinary approach involving orthopedic surgeons, infectious disease experts, radiologists, and microbiologists is essential.

The multidisciplinary team (MDT) leader ensures balanced participation among members, while a coordinator manages communication and record keeping, fostering effective collaboration. The primary physician initiates management, with subspecialists engaged according to patient needs; the team jointly discusses and formulates a treatment plan that emphasizes care objectives, proceeding by consensus to implementation. In complex scenarios, multidisciplinary communication strategies aim to standardize broadly accepted views, reduce unnecessary discussion time, and ensure appropriate specialist involvement. Because patients with complex infections typically consult multiple specialists prior to referral to an infectious disease expert, many physicians find their diagnostic and therapeutic ability limits reached, resulting in delayed diagnosis and exacerbated infection—outcomes that might have been mitigated through collaborative multidisciplinary teams.

Figure 2: The Patient-Centered Multidisciplinary Team (MDT) Collaborative Model

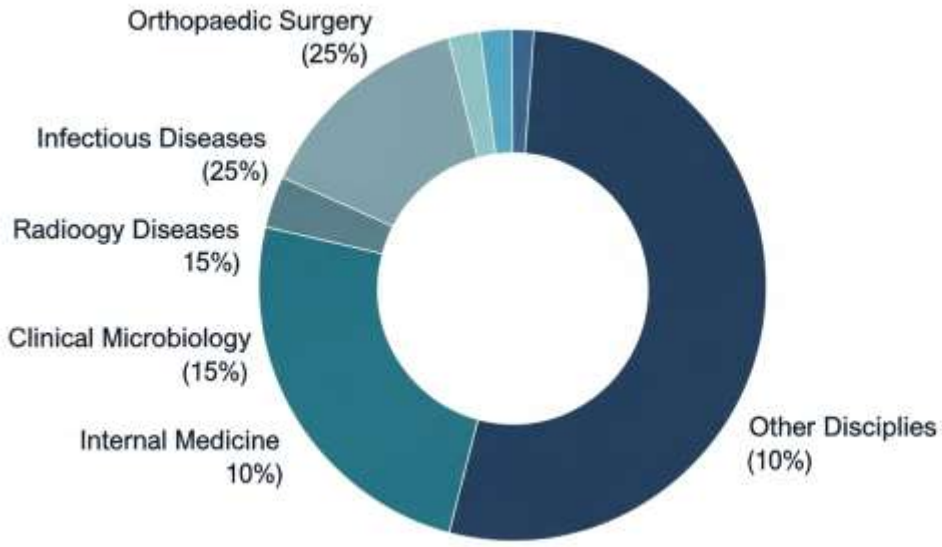
5.2. Roles of Different Disciplines

The management of complex chronic infections necessitates multidisciplinary collaboration to effectively diagnose and treat conditions with renal and neurological involvement. Infectious disease specialists, orthopaedic surgeons, internists, microbiologists, and radiologists form multidisciplinary teams (MDTs) that work synergistically, coordinating patient referrals and sharing expertise to address multifaceted cases (L. Romanò et al., 2022). MDTs improve outcomes in infection management by facilitating comprehensive assessments and fostering consensus on treatment plans. The complexity and increased incidence of infections prompting bone destruction further underscore the value of multidisciplinary approaches in achieving prompt, accurate diagnosis and optimal therapy of renal and neurological complications.

Table 2: Characterization of Roles and Responsibilities within the Multidisciplinary Team (MDT) for Managing Complex Chronic Infections

Clinical Discipline	Core Diagnostic Responsibilities	Core Therapeutic Responsibilities

Infectious Disease Specialist	- Leading the etiological investigation and interpreting microbiological findings . - Close collaboration with the clinical microbiology laboratory.	- Formulating and modifying antimicrobial therapeutic protocols . - Overseeing long-term outpatient antimicrobial therapy (OPAT).
Nephrologist	- Assessing the degree of renal injury and classifying pathological patterns (e.g., glomerulonephritis).	- Managing acute and chronic renal dysfunction . - Adjusting drug dosages according to the glomerular filtration rate.
Neurologist	- Evaluating neurological manifestations and defining clinical syndromes (e.g., meningitis, encephalopathy).	- Managing the neurological complications of systemic infections . - Participating in the treatment plan for CNS infections.
Radiologist	- Performing and interpreting medical imaging studies (CT, MRI, PET/CT) to localize infection and assess structural damage.	- Providing radiological guidance for interventional procedures, such as guided biopsies and abscess drainage.
Clinical Microbiologist	- Isolating and characterizing pathogenic agents from biological samples using culture, molecular assays (PCR), and mass spectrometry (MALDI-TOF).	- Performing antimicrobial susceptibility testing to guide optimal therapy.
Surgeon (e.g., Orthopaedic)	- Procuring tissue samples during surgical procedures for histopathological and microbiological diagnosis.	- Performing surgical debridement to remove infected and necrotic tissue . - Collaborating in the management of complex infections like pyogenic spondylodiscitis.
Internist	- Conducting a comprehensive clinical assessment of the patient, considering comorbidities . - Facilitating cooperation and coordination among different disciplines.	- Managing the patient's general medical status, including vital organ function support.



Graph 2: Composition of a Model Multidisciplinary Team for Prosthetic Joint Infection.

5.3. Communication Strategies

Effective communication within multidisciplinary teams (MDTs) is an essential component of healthcare for patients with complex and chronic infections that affect renal and neurological function. Various specialists—including nephrologists, neurologists, internists, rheumatologists, general practitioners, infectious disease physicians, rehabilitation specialists, as well as nurses and other healthcare professionals—coordinate treatment to improve outcomes and reduce latency for patients experiencing varied symptoms that are difficult to distinguish (Therese R. Madelar & Ito, 2023). A diverse knowledge base allows groups to pool knowledge and identify appropriate diagnostics and treatments, yet teams often experience significant communication challenges. Understanding the factors that influence communication and referral patterns within a health care team is crucial to improve the delivery of collaborative care.

Group and individual communication patterns for an integrative medicine team were explored in the context of chronic low back pain, which benefits from multimodal and multidisciplinary management (B. O'connor et al., 2015). Cross-referrals and in-depth practitioner interviews were among the qualitative methods employed to reveal distinctive communication structures; the nature of referrals depended on the role, relationship, and professional boundaries between practitioners.

A clearly defined leadership structure, multiple communication channels, avenues for information sharing, and mechanisms for promoting involvement are essential for the effective functioning of any MDT. Comprehensive team engagement is vital as various specialists may maintain their own network of related contacts to address cases that extend beyond their expertise.

5.4. Case Studies of Successful Collaboration

The complexity of chronic infections demands collaboration among healthcare professionals, researchers, and policymakers. Numerous specialists, including neurologists and nephrologists, frequently participate in case discussions (O Attwood et al., 2022) ; (Sires et al., 2022) ; (Tan et al., 2018). The exchange of clinical information is standardized through various communication

methods to ensure all specialists possess the prerequisite knowledge to influence clinical decisions effectively.

Multidisciplinary case conferences have been implemented for patients with infective endocarditis, with sustained participation over 24 months. Although no significant changes in morbidity and mortality were observed, the study's design and small size limited the detection of clinical outcome differences. Despite these limitations, the approach has been instrumental in developing local team-based protocols, underscoring the potential benefits of multidisciplinary collaboration in managing complex infections.

6. Diagnostic Approaches in Multidisciplinary Settings

In a multidisciplinary setting, the use of laboratory testing and imaging techniques is essential in identifying the presence of an active or latent infectious agent, which should be addressed by a team of healthcare professionals to prevent further damage (Cottin et al., 2022). Therefore, laboratory tests and imaging methods serve as complementary tools that must be further supported by clinical evaluation when more serious conditions develop and represent the mainstay of diagnostic approaches in complex cases. Large-bore random biopsy of the superficial femoral vein under local anesthesia in association with the employment of the Kistner sheath is an effective procedure for removing chronic deep venous obstructions . Modern diagnostic methods such as magnetic resonance imaging, invasive venography, and intravascular ultrasonography have renewed interest in venous obstruction as a potential cause of chronic venous insufficiency and ulceration . With the advancement of diagnostic techniques that can be performed either in the hospital as an outpatient or in the office, the employment of multidisciplinary teams has become of great value to achieve a diagnosis and provide a management plan when chronic infections induce both altered renal and neurological function. Moreover, diagnostic procedures are essential to frame the extent of damage and follow up the response to treatments.

Table 3: A Comparative Assessment of Diagnostic Modalities Employed in the Context of Complex Chronic Infections

Diagnostic Modality	Specific Techniques and Applications	Diagnostic Advantages	Limitations and Constraints
Laboratory Tests	- Culture of biological samples (blood, urine, cerebrospinal fluid). - Molecular assays (e.g., PCR). - Serology. - Microscopy.	- Precise etiological characterization of the pathogen . - Provides antimicrobial susceptibility data to guide therapy . - High accuracy and speed in some molecular techniques.	- Culture results may be affected by prior antimicrobial therapy. - Specialized assays can be associated with increased costs . - Some cultures may be slow to yield results.
Imaging Techniques	- Ultrasonography, Computed Tomography (CT), Magnetic Resonance Imaging (MRI). - 18F-FDG Positron Emission Tomography/CT (PET/CT). - Single-Photon Emission	- Visualization of structural and functional abnormalities . - Precise localization of inflammatory or infectious foci . - Assessment of disease extent .	- Modality selection is subject to considerations of availability, cost, and local expertise . - Findings may be non-specific for infection and can overlap with other inflammatory processes .

	Computed Tomography/CT (SPECT/CT).	- High sensitivity for inflammatory processes (PET/CT).	- Conventional X-ray has limited utility in certain differential diagnoses.
Clinical Assessments	- Patient history and physical examination. - Tissue biopsies. - Electromyography (EMG).	- Characterization of clinical phenotypes and identification of pathological syndromes . - Biopsies can provide definitive histopathological and microbiological confirmation . - Allows for a holistic patient evaluation within the context of immune and environmental factors.	- Initial clinical manifestations may be non-specific, limiting their independent diagnostic value . - Invasive procedures such as biopsies carry inherent risks.

6.1. Laboratory Tests

Laboratory tests continuously feed medical, surgical, epidemiological, pharmacological, and many other clinical considerations. Long-term outpatient antimicrobial therapy (OPAT) patients pose a frequent diagnostic challenge (Nori et al., 2023).

The microbiologic diagnosis strongly impacts optimal care. Decisions made without the laboratory's input do not benefit from the >160 years of laboratory-derived diagnostic expertise, from microscopy, agglutination and culture to PCR and mass spectrometry. The clinical microbiology laboratory routinely offers tools that conclusively establish a rare or unexpected diagnosis, identify a highly resistant organism, or differentiate among species with divergent treatment options. An investigation that rules out certain diagnostic considerations is as valuable as one that makes a positive identification.

Close collaboration between infectious diseases specialists and the clinical microbiology laboratory for routine or specialized molecular testing (MALDI-TOF MS, target-specific PCR assays) enables much more accurate diagnoses, streamlined antimicrobial regimens, and substantially improved patient outcomes. Specialized testing with expensive reagents or complex instrumentation increases costs, but the benefits of even a marginally improved diagnosis and a better-managed patient typically balance this and are therefore justified. Assistance, reassurance and education accompany this specialized service.

Examples from institutional experience highlight the importance of microbiological collaboration, even in "routine" infections where treatment success remains elusive, but especial care is warranted during the diagnostic work-up of patients presenting with fever and other non-specific symptoms.

6.2. Imaging Techniques

Imaging techniques serve as integral components of multidisciplinary diagnostic and monitoring strategies for complex chronic infections, including those affecting cardiovascular systems (Anna Erba et al., 2022). Effective management requires timely recognition of clinical manifestations. Two principal imaging strategies prevail: one focuses on the microorganism responsible for infection, the other targets inflammatory response elements exhibiting host reaction; an understanding of the relative strengths and limitations of each approach underpins selection of the

most appropriate tool. Expanding on earlier discussions of selection criteria, the choice of modalities remains dictated by availability, cost, and local expertise (Luca Romanò et al., 2020). Available technologies encompass planar techniques, hybrid study protocols, and tomographic analyses. An illustrative overview of alternative nuclear imaging options includes selected PET tracers, single-photon emitters (either in kinetic or static modes), and combine approaches. 18F-FDG-PET/CT constitutes a first-line diagnostic instrument for patients presenting with inflammatory diseases and/or fever of unknown origin. Increased uptake by 18F-FDG is caused by high glycolytic metabolism of activated inflammatory cells, as exemplified by detection of prosthetic joint infection in a patient undergoing non-invasive diagnostic workup after Fig. 2. Tracer Uptake in Esophago-Jugular Fistula Discovery of a vascular infection, such as an esphageo-jugular fistula. Hybrid techniques enhance combination of functional and anatomical data, improving localisation of lesions and assessment of disease extent. For precise localisation of bone uptake, SPECT/CT often accompanies WBC scintigraphy. PET/MRI, offering superior soft-tissue evaluation and absence of radiation burden, may represent a more favourable future technique, though its role in prosthetic joint infection remains under assessment. Conventional X-ray lacks usefulness in differential diagnosis of prosthetic joint infection.

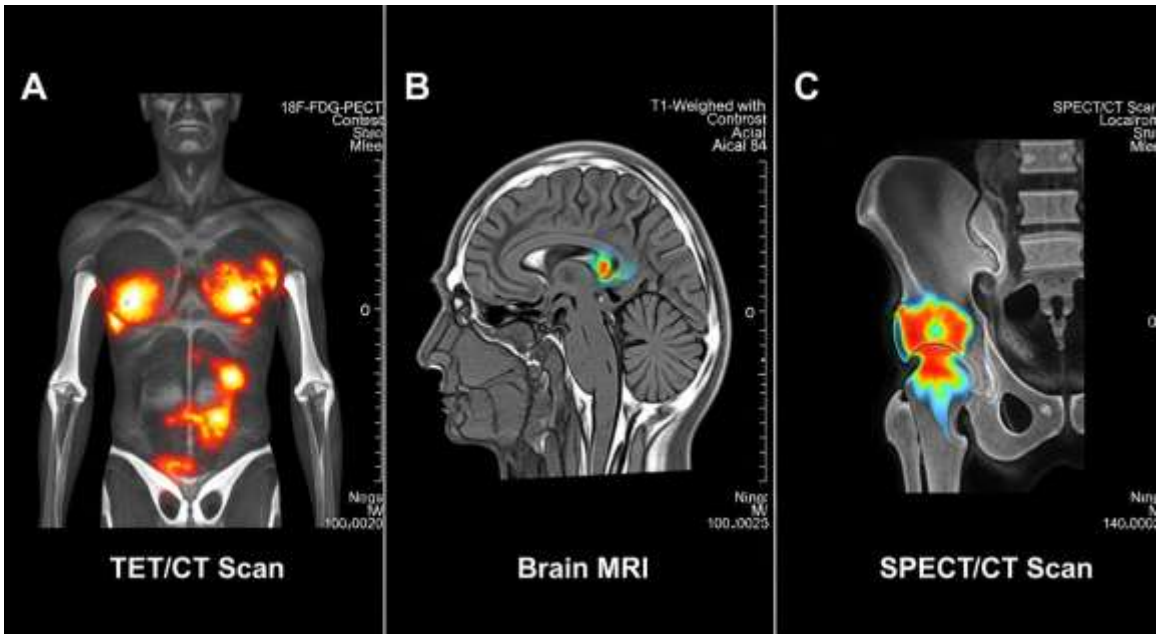


Figure 3: Examples of Advanced Imaging Modalities in the Diagnosis of Complex Chronic Infections

6.3. Clinical Assessments

Laboratory evaluations facilitate the investigation of various parameters, including autoimmune markers, human leukocyte antigen (HLA) status, immunoglobulin levels, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and specific biomarkers such as transforming growth factor beta-1 (TGF-β1), complement components C3a and C4a, and vascular endothelial growth factor (VEGF). Assessment of toxic substances encompasses screening for heavy metals, mold toxins, and pesticides. Allergy evaluations incorporate immunoglobulin E (IgE) quantification as well as identification of food and environmental allergens. Nutritional status is appraised through the measurement of amino acids, fatty acids, and mineral concentrations. Mitochondrial dysfunction is explored by analyzing clinical response to supportive interventions and examining mitochondrial DNA (mtDNA) mutations for inherited defects. Psychological health assessments target conditions such as depression, anxiety, obsessive-compulsive disorder (OCD),

and post-traumatic stress disorder (PTSD). A comprehensive neurological work-up includes clinical examinations, electromyography (EMG), tissue biopsies, and imaging studies. Endocrine function is evaluated by determining hormone levels and precursors like dehydroepiandrosterone sulfate (DHEA-S) and pregnenolone. Sleep disorders undergo clinical evaluation and hormone testing. Autonomic nervous system dysfunction is investigated through tilt-table testing and continuous monitoring of blood pressure and heart rate. Gastrointestinal pathology is examined via endoscopy, colonoscopy, and stool analyses for bacterial, parasitic, and fungal elements. Hepatic involvement is monitored by measuring liver enzymes—alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase—and bilirubin levels. Pain syndromes receive clinical examination, EMG, and laboratory assessment for autoimmune markers. Deconditioning necessitates evaluation to determine the need for physical therapy (I. Horowitz & R. Freeman, 2018).

7. Treatment Modalities

Together with multidisciplinary teams, specialists and other healthcare professionals must be able to combine diagnostic, therapeutic, epidemiological and public health skills to achieve sustainable and high-quality care. Treatment for complex chronic infections usually consist of a combination of pharmacological and non-pharmacological interventions that target both the underlying cause of the infection and its renal or neurological complications. Various pharmacological options may be used, such as antibiotics or antifungal agents to eradicate the offending micro-organisms, anti-inflammatory or immunomodulatory drugs to reduce inflammation and immune response, and symptomatic relief agents to alleviate pain, fever, edema or other clinical manifestations (Therese R. Madelar & Ito, 2023). New and innovative therapies are also increasingly explored, including phage therapy, gene therapy, nanotechnology, stem cell therapy and immunotherapy, among others, that offer additional tools to overcome microbial resistance, host susceptibility and tissue damage associated with chronic infections.

7.1. Pharmacological Interventions

Pharmacological interventions combining antibiotics, antifungal agents, and immunomodulators remain the cornerstone of treatment. Regimens must be carefully tailored to patient history, coinfections, and anticipated toxicities (K. Sikka et al., 2021). Drugs with significant central nervous system penetration may treat brain infections effectively and potentially counter neuroinflammation caused by chronic systemic infection. Developing detailed protocols, including decision trees, pharmacophores, and hierarchies, could assist clinicians in making optimal choices aligned with personalized immunopharmacological treatments (M. Matt, 2021).

7.2. Non-Pharmacological Interventions

A great variety of non-pharmacological treatment options are available to help patients afflicted with musculoskeletal conditions effectively manage their symptoms and maintain functional independence. Among these approaches, multidisciplinary clinics have garnered notable attention and popularity in recent years and possess a wide range of benefits for those with chronic musculoskeletal disorders. An effective treatment modality in its own right, at its core, multidisciplinary clinics allow for patients seen within the same setting to benefit from the collective expertise of a broad team of professionals to receive a finely tailored care plan that addresses the broad and dynamic range of challenges and impairments faced by these patients.

Working synergistically with their clinical colleagues, physiatrists provide essential medical insights into the coordination of multidisciplinary care and play a pivotal role in the development and execution of individualized plans in both outpatient and inpatient settings. Skilled in the evaluation and examination of multiple organ systems, including musculoskeletal, neurologic, cardiorespiratory, psychiatric, and other domains, these specialists conduct comprehensive assessments of patients to delineate pertinent treatment priorities. They collaborate closely with

clinical and surgical providers to establish safety guidelines facilitating appropriate therapeutic interventions, including physical and occupational therapy, which when employed judiciously, confer substantial benefits. Depending on the unique circumstances and objectives of each patient, physiatry services encompass a diverse array of interventions aimed at optimizing functional outcomes and enhancing quality of life.

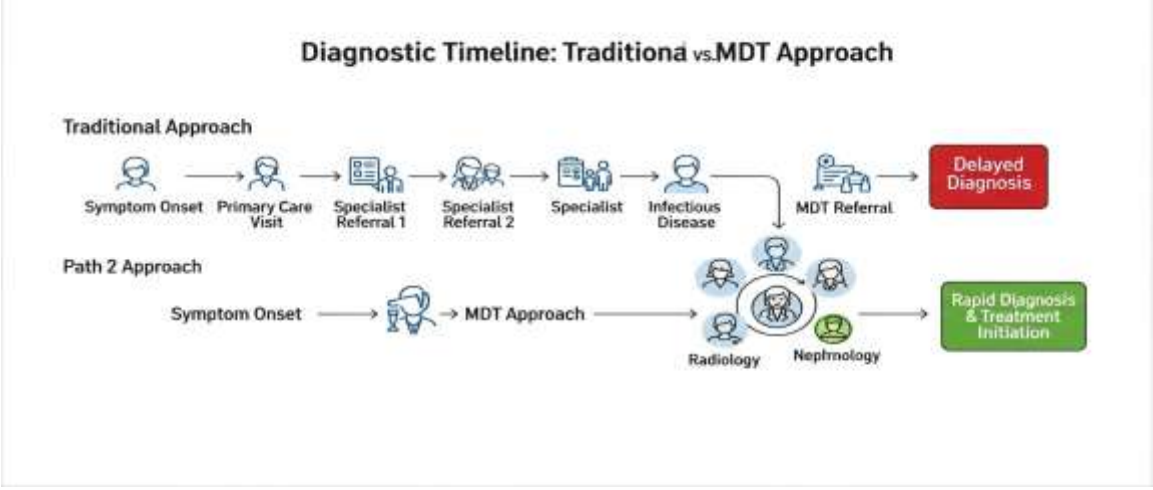
Emerging as an indispensable component within a vast array of clinical specialties, both physiatrists and multidisciplinary clinics constitute a crucial and well-established treatment option capable of helping patients of diverse ages, backgrounds, and sociodemographic statuses navigate the multifarious challenges encountered throughout the continuum of musculoskeletal care (L. Romanò et al., 2022) (Therese R. Madelar & Ito, 2023).

7.3. Innovative Therapies

Apart from conventional treatments with repurposed drugs, natural products and remedies could constitute a major source of alternative medicaments for tackling, both the bacterial antibiotics resistance crisis, and the slow-pace drug discovery procedures (L. Romanò et al., 2022). They have demonstrated remarkable success for the obliteration of several bacterial pathogens, including intracellular infections (Aston et al., 2018) , and possess a significant variety of mechanisms of actions, mechanisms of resistance and target molecules. In this framework, the repurposing of these compounds, as novel therapeutics for invasive infections in people who inject drugs (PWID) (O Attwood et al., 2022) , can be envisioned as a key element for combating the US epidemic of infectious complications associated with injection drug use. The pharmacokinetics of the natural drugs and/or products of interest should be carefully investigated in the body, by using common techniques such as conjunction with labelled-DNA.

8. Challenges in Managing Complex Chronic Infections

Managing complex infections remains a challenge despite major scientific advances. Healthcare systems worldwide face increasing demands from population ageing coupled with rising multimorbidity and complex disease presentations. Uncoordinated care and insufficient interdisciplinary collaboration among healthcare professionals often compromise patient outcomes, affecting quality of life and increasing healthcare costs (S AlMaghrabi et al., 2023). Large numbers of multidisciplinary team (MDT) meetings are therefore held to plan personalised care pathways and blends of interventions. Clinicians commonly recognise that the organisational quality of meeting discussions has a significant impact on aspects such as surgical decisions, patient choice, treatment timing and delivery, patient outcomes and engagement of patients in treatment management discussions. Video conferencing meetings and other electronic collaborative approaches play an important role in facilitating and supporting MDTs, but adequate infrastructure and good quality leadership remain essential to secure productive discussions and successful outcomes (L. Romanò et al., 2022).



Graph 3: Comparative Diagnostic Timelines: Traditional Approach vs. the Multidisciplinary Team (MDT) Approach.

8.1. Barriers to Effective Treatment

Complex and chronic infections are associated with significant lost productivity in hemodialysis patients due to missed workdays and incapacitation during hospital stays. Despite their economic importance, information on the epidemiology, causative agents, resistance patterns, and outcomes of such infectious diseases remains scarce. Delayed and inaccurate diagnosis contributes to disease transmission, unnecessary treatments, organ and tissue damage, and increased mortality. Mounting evidence demonstrates that many complex and chronic infections adversely affect renal and neurological function; therefore, earlier laboratory and/or imaging investigation is warranted. Multidisciplinary teams enhance diagnostic accuracy and enable specialists from diverse fields to provide a more comprehensive therapeutic approach, limiting the impact on renal and neurological function. However, healthcare providers encounter considerable challenges when treating such infections and implementing multidisciplinary care. (Pedro Ramos et al., 2023)

8.2. Patient Compliance Issues

Patients may not always comply with instructions related to infection control and therapy in the context of complex chronic infections, despite specialist advice. Lack of engagement in the decision-making process contributes to misinformation, frustration and anxiety, which in turn lead to non-adherence to prescribed antimicrobial regimes and loss to follow-up. Poor communication by healthcare professionals and the provision of inadequate information are the main factors involved, frequently driving patients to seek advice from less reliable sources, such as the internet. Education for healthcare providers on patient engagement is crucial. This can be supplemented by effective interventions to enhance communication and information provision. Adopting mechanisms to inform healthcare professionals and thereby provide patients with proactive, accurate information about their infection and its management has the potential to improve a variety of outcomes (M Rawson et al., 2016).

8.3. Resource Allocation

Advanced and well-equipped medical interface institutions must investigate methods of special coordination for patients who cannot access the source institution for diagnosis and treatment despite readmission after evaluation by a multidisciplinary team of specialists from infection and other departments. Positivity for chronic infections can appear at the re-evaluation stage in a post-discharge area that includes urological practice, which cannot be sufficiently handled by the primary medical institution alone, indicating the need for a broader scope of intervention through primary, secondary, and tertiary cooperation.

9. Future Directions in Research

As chronic infectious diseases evolve, so too does the obligation of healthcare professionals to adapt their strategies and collaboration methods. A multidisciplinary approach remains essential when addressing the complexities of diagnosis and treatment, yet the emergence of new pathogens signifies an ongoing need to adjust the strategies of involved specialists. Future research must focus on accelerating the identification of causative agents and expanding therapeutic options to effectively safeguard renal and neurological function (Little et al., 2021). Although a consensus has been reached regarding the three primary categories of chronic infection, defining an all-encompassing universal classification remains elusive. An in-depth examination of existing categorized conditions is recommended to identify those that warrant reassignment or removal. Enhanced classification could stimulate the generation of further data and indices that aid in the definitive characterization of this condition.

Novel pathogens capable of inducing chronic infections continue to emerge, including isolated cases of Cryptococcus neoformans, Cryptococcus gattii and Nocardia asiatica infection. The emergence of such pathogens often requires specialists to undertake extensive research. Proposals aimed at expediting this process include the creation of specialized groups dedicated to the analysis and characterization of new agents. Such endeavours would facilitate the timely adoption of appropriate therapeutic measures by multidisciplinary teams. Concurrently, in-depth reference studies are needed to integrate comprehensive data offerings within these sectors. Preliminary epidemiological evaluations have already been undertaken in this context and merit continuation. Ongoing efforts will also improve awareness of rare or unreported complications, addressing a notable gap in the current literature.

9.1. Emerging Pathogens

The pursuit of novel understandings in infection continues to awaken appreciation for the breadth of infections affecting humans. Working together, provides an approach for assessing the impact of chronic infections on renal and neurological function. Some pathogens have only recently been identified as human pathogens through technologic advances. An emerging pathogen may be a reemerging pathogen whose epidemiologic niche has recently changed, for example, through expansion into previously unrecognized geographic areas, or one whose clinical importance is newly recognized, such as a commensal organism associated with severe disease. Even including organisms described less than 20 years ago, the spectrum of emerging renal and neurological pathogens remains incomplete.

Adding a new etiologic agent to an already complex body of knowledge requires integrating numerous observations and can span decades of investigations. Initially, a rapidly fatality associated with an organism may capture attention; subsequently, other clinical manifestations may be recognized. Differences in host-pathogen interactions therefore modulate the location within the host and the extent of disease. Kidney and brain involvement in infections also depend on the pathogen, the host, and their interaction during ongoing inflammation.

9.2. Advancements in Diagnostic Technologies

Multidisciplinary teams make clinical decisions based on laboratory tests, imaging studies, and clinical evaluations, including examinations by nephrology and neurology specialists (M. Caliendo et al., 2013). Diagnostic accuracy in these challenging cases is vital. Chronic infections, acknowledged increasingly for their renal and neurological complications, illustrate such scenarios (Cheng et al., 2017).

9.3. Novel Therapeutic Approaches

A multidisciplinary team approach offers the highest standard of care in managing chronic infections because it aims to expedite at-risk patients to proper treatment and reduce the incidence of complications. Multidisciplinary collaboration between infectious disease specialists, clinical microbiologists, and orthopedic surgeons is critical in this respect (L. Romanò et al., 2022). Cancer research indicates that the quality of care and clinical outcomes continue to improve by incorporating a multidimensional framework into a multidisciplinary team (Therese R. Madelar & Ito, 2023). Novel approaches should be developed to improve multidisciplinary collaborations, and the synergy provided by teams of competent nephrologists, infectious disease specialists, and neurologists is essential for optimal patient outcomes.

10. Ethical Considerations

In the initial phase, dimensioning informs ethical service design at the multidisciplinary interface, a critical factor in complex cases. Communication at the healthcare interface raises ethical issues concerning the transition from comprehensive interdisciplinary care with central patient involvement to dedicated monodisciplinary approaches. Historically, ethics in multidisciplinary

teams have centered on legal and moral obligations as a matrix for decision-making at the interface. The inherent tension between the committee approach—where the interplay of individual statements from multidisciplinary members can alter the relevance of exponentially combined positions—and the inherent risk of losing the patient view in purely mathematical approaches highlights that quantification is not an exclusive property of statistical interaction and probability theory; dimensions cannot be reduced to numbers without acknowledging interface-generated values. Multidisciplinarity provides novel means for quality assurance and is a pivotal tool in case review sessions (Therese R. Madelar & Ito, 2023). Additionally, ethical considerations in multidisciplinary teams encompass informed consent, patient privacy, and equitable access to care; understanding these dimensions enables care providers to appreciate the broader context of core ethical issues and their interactions with other problems at the interface (Wiles et al., 2016).

10.1. Informed Consent

Informed consent processes are well-established within diagnostics and therapeutics. These lengthy procedures expedite standardized consent for subsequent operations during laboratory requests and clinical interventions by nephrologists and neurologists. With patient privacy always maintained, clinicians encourage open discussion of potential risks, outcomes, and long-term sequencing to obtain verbal patient agreement before progressing further. This approach also facilitates patient queries regarding specific mistrust or uncertainty before procedures commence.

Providing informed consent constitutes a legal obligation for clinicians, forming an integral communication link between practitioner and patient. Whenever treatments remain ongoing, the process similarly obtains necessary and contextual approvals. Yet questions endure about whether relinquishing the patient's freedom of choice becomes unavoidable when treatments compel instant decision-making. Reports nevertheless affirm that consent—preferably founded upon understanding—should clarify objectives, describe treatment stages continually, and secure explicit patient affirmation throughout a session. When symptomatic changes emerge or the prevailing risk-to-benefit ratio shifts, investigators require heightened engagement before proceeding. While example forms offering blanket authorizations indeed prove practical, inevitably thereby risking certain moral compromises due to their simultaneous disclosure of multiple therapies. Consequently, providers learn to identify critical points at which authorization proves appropriate during phase transitions. Moral validity therefore derives ultimately from a sustained, educative, and relational dialogue ensuring sufficient information accumulation to permit autonomous, personal choice. This moment-by-moment framework thereby closely aligns with the dynamic interplay characteristic of multidisciplinary approaches despite its current limited adoption within the field (Antony J. Porcino et al., 2014).

10.2. Patient Privacy

The central aim of patient privacy legislation and guidelines is to ensure that identifying information is not wrongly shared. Trust is a fundamental principle underpinning the doctor-patient relationship, and the disclosure of patient information without consent could undermine that trust. Preserving privacy helps patients to talk openly with their doctors.

The requirement to protect patient privacy goes beyond the actions of the healthcare professional. Third parties such as hospital business and IT staff, interpreters, and office personnel should also be informed of their privacy obligations.

10.3. Equity in Healthcare Access

Chronic infections impose a growing burden worldwide, posing an important public health challenge (Coulongeat et al., 2022). Healthcare access disparities affect chronic disease management and emergency department utilization (Goodridge et al., 2019). Multidisciplinary approaches form the cornerstone of managing chronic infections, ensuring such patients receive the

expert care they require. Equity in healthcare access must be promoted to reduce health inequities and improve care for underserved populations.

Multidisciplinary Management Case studies exemplify how multidisciplinary frameworks contribute positively to achieving substantial improvements and resolving the most troublesome problems for patients.

11. Conclusion

Multidisciplinary collaboration plays a critical role in diagnosing and managing complex chronic infections with renal and neurological impact. These infections can reduce renal and neurological function and require input from multiple specialties. Infections can become chronic when the immune response fails to eliminate a pathogen (L. Romanò et al., 2022). Chronic infections can be caused by bacteria such as Bartonella henseii, Borrelia burgdorferi, Campylobacter jejuni, Chlamydia pneumoniae, Escherichia coli, Helicobacter pylori, Legionella pneumophila, Mycobacterium tuberculosis, Mycoplasma pneumoniae, Rickettsiaprowazekii, Treponema pallidum, Vibrio cholerae, and Yersinia pestis; viruses such as Epstein–Barr, hepatitis, herpes simplex, rubella, measles, and cytomegalovirus; protozoans such as Toxoplasma gondii and Trichomonas; or fungi such as Aspergillus and Candida (O Attwood et al., 2022). Even previously unknown viruses, associated recently with chronic conditions such as UK flu, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, fibromyalgia, and long COVID-19, may cause persistent immune dysregulation (Tan et al., 2018).

To address this public health problem, a multidisciplinary team consisting of nephrologists, neurologists, specialists in infectious diseases and public health, radiologists, biochemists, clinical microbiologists, hygienists, and other infectious disease specialists should analyze diagnostic and therapeutic strategies. These specialists must be supported by general practitioners and surgeons. Precise definitions are necessary for terms such as acute, chronic, persistent, focal, systemic, localized, disseminated, bacterial, viral, parasitic, protozoan, and fungal. Interdisciplinary collaboration and work division allow each specialist to contribute their knowledge and experience, leading to more accurate and faster diagnoses and more effective treatments.

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