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PANDAS in the post-COVID era: links to group A Streptococcus and implications for pediatric neuropsychiatry – a narrative review

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Summary

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) are defined by the abrupt onset of tics and/or obsessive–compulsive symptoms temporally linked to group A Streptococcus (GAS). Post-pandemic reports note a rebound of pediatric invasive GAS (iGAS), providing an epidemiologic backdrop for more frequent neuropsychiatric presentations. This narrative review (2020–2025; PubMed/MEDLINE, ScienceDirect, Wiley Online Library, MDPI, plus snowballing) synthesizes evidence on the PANDAS/PANS–GAS relationship, clinical spectrum, differential diagnosis with Sydenham chorea (SC), immunopathogenesis, and treatment. Beyond classic OCD and motor tics, the phenotype includes speech disfluency, ocular tics, and acute eating restriction with functional and nutritional risk. Immunologic data support molecular mimicry, Th17/IL-17–driven neuroinflammation, blood–brain barrier dysfunction, and antineuronal or folate receptor-α antibodies; however, no single validated biomarker exists, and antistreptolysin O (ASO), anti-DNase B document exposure only. Management is individualized and multimodal: antibiotic eradication (with prophylaxis in selected, frequently relapsing cases), immunomodulation (steroids, intravenous immunoglobulin (IVIG), therapeutic plasma exchange) for severe/refractory courses, and Cognitive Behavioral Therapy/Selective Serotonin Reuptake Inhibitors (CBT/SSRIs) for core psychiatric symptoms. Contemporary data strengthen a post-streptococcal, immune-mediated framework while underscoring heterogeneous case definitions and the paucity of high-quality trials; prospective biomarker and treatment validation remain priorities.

Key words: tics, obsessive-compulsive disorder, Sydenham chorea.

Introduction and aim

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) are rare but clinically significant neuropsychiatric conditions in children, characterized by the abrupt onset of symptoms such as obsessive–compulsive disorder (OCD), motor tics, and mood changes in the context of a preceding group A Streptococcus (GAS) infection [1, 2]. In recent years, a worrisome increase in the frequency and severity of GAS infections has been observed, particularly in the post–coronavirus disease 2019 (COVID-19) period. Data from Poland, Spain, and other European countries indicate a significant increase in invasive GAS (iGAS) among children following the lifting of pandemic restrictions. iGAS refers to a severe form of infection caused by *Streptococcus pyogenes* in which the bacterium is isolated from a normally sterile site (such as blood, cerebrospinal fluid, pleural fluid, or deep tissues). iGAS includes clinical syndromes such as bacteremia, pneumonia, necrotizing fasciitis, and streptococcal toxic shock syndrome (STSS). In Poland, a retrospective study of hospitalized children showed that 69% of GAS infections were iGAS, and 13% presented with sepsis with STSS [3]. Children with iGAS more often experience neurological and neuropsychiatric complications, including mood changes, emotional lability, sleep disturbances, tics, and OCD symptoms. This study aimed to analyze current evidence on the association between GAS infections and PANDAS, with particular emphasis on post-COVID-19 changes in GAS/iGAS epidemiology and their potential clinical implications (given the limited number of direct comparisons of the PANDAS course before versus after the pandemic). Because PANDAS and Sydenham chorea (SC) share an association with GAS and a basal-ganglia autoimmunity hypothesis, SC is referenced herein as a mechanistic background and a framework for differential diagnosis (pathophysiology, differentiation), without a separate systematic synthesis of its literature.

Method

We conducted a non-systematic narrative review. Sources: PubMed/MEDLINE, Elsevier/ScienceDirect, Wiley Online Library, and MDPI; timeframe 1 January 2020–31 August 2025; reference snowballing added records missed by database searches. The strategy combined free-text and MeSH for "PANDAS," "Pediatric Acute-Onset Neuropsychiatric Syndrome/PANS," "Streptococcus infections," "Group A Streptococcus," "GAS," and "COVID-19." "Sydenham chorea/SC" was deliberately not a search term; SC papers were cited only contextually as a mechanistic background. No language limits at search; screening focused on English/Polish full texts. Eligibility: original studies (cohort, cross-sectional, retrospective, interventional), case reports/series, and reviews addressing PANDAS/PANS linked to streptococcal infection in children/adolescents (≤18 years). Exclusions: pre-2020 records, items without a GAS/iGAS link, and low-evidence formats (comments, letters). Exceptions: three epidemiologic papers on pre/post-COVID streptococcal burden (background), a 10-year Italian cohort (2013–2023; published ≥2020) bridging pre/during/post-pandemic

periods, Thienemann et al. (2017) – a clinical guidance document on psychiatric and behavioral management in PANS/PANDAS, cited exclusively in the section outlining treatment principles, and Swedo et al., (1998, historic diagnostic context); none entered synthesis. Two reviewers screened titles/abstracts and full texts; extraction covered design, diagnostic criteria, GAS ascertainment, and key outcomes. Due to heterogeneity, the results were synthesized narratively; therefore, ethics approval was not required.

Results

1. Impact of the COVID-19 pandemic on the epidemiology of GAS infections and PANDAS

1.1. PANDAS epidemiology before the pandemic

Before 2020, PANDAS was described as an uncommon but clinically recognizable syndrome. It most often affected early school-aged children, with a peak onset around 6–7 years of age [4, 5]. A male predominance was consistently reported, whereas the true frequency was difficult to estimate due to the lack of definitive laboratory criteria and substantial symptom overlap with OCD and Tourette syndrome. In the Italian cohort, a male predominance and a median age of approximately 7 years were confirmed, and the phenotype was characterized primarily by motor tics with variable severity of OCD symptoms [5]. In the pre-COVID-19 period, no abrupt changes were observed in the frequency of PANDAS diagnoses or in signals suggesting increased clinical severity of the syndrome. The disease course was described as relatively stable, with relapses typically correlating with individual exposure to GAS infections rather than with broader epidemiological shifts [1, 2, 6].

1.2. Dynamics of streptococcal infections in the post-COVID-19 period

The COVID-19 pandemic profoundly altered the transmission of infectious diseases. Non-pharmaceutical interventions led to a decline in GAS infections in 2020–2021. After restrictions were lifted, many European countries observed a rebound effect, with marked increases in both GAS and iGAS incidence. Reports from Poland, Spain, and other countries indicate not only higher incidence but also more severe clinical courses: greater proportions of pediatric intensive care unit (ICU) admissions, more frequent neurological complications, and longer treatment compared with the pre-pandemic period [3, 7, 8]. Polish analyses highlighted that concurrent or antecedent viral infections and higher C-reactive protein (CRP) values significantly increased the risk of iGAS in children, which may partly explain the more severe post-pandemic courses. In Spain, 2022–2023 saw an abrupt rise in pediatric iGAS with more ICU admissions [7]. Elsewhere in Europe, investigators drew attention to growing neuropsychiatric sequelae after GAS infections that resembled PANDAS/PANS phenotypes [1, 9]. In contrast to the pre-pandemic period, following the lifting of restrictions there has been not only an increase in the incidence of GAS infections but also a clear shift in

their clinical profile, with a predominance of iGAS. This change in the epidemiological landscape may provide an important background for more frequent presentations of acute neuropsychiatric syndromes in children, including PANDAS, particularly in the context of heightened inflammatory responses after iGAS infections [3, 7, 8].

2. Clinical presentation and symptom spectrum

2.1. The classic PANDAS phenotype

PANDAS classically presents with abrupt-onset OCD and motor tics after streptococcal infection, often with an episodic course of flares and remissions [1, 2, 9], unlike the more insidious trajectory of typical pediatric OCD. Emotional lability, irritability, and rapid mood shifts are common and functionally impairing. In cohort studies, the clinical phenotype may be dominated by motor tics, whereas the occurrence of OCD symptoms appears to be variable; magnetic resonance imaging (MRI) and electroencephalography (EEG) were usually unremarkable. These findings support a broad phenotypic view beyond OCD alone [5, 27].

2.2. Atypical phenotypes

Beyond the classic picture, numerous atypical variants complicate diagnosis. Case reports describe co-occurrence of PANDAS with cerebellitis as well as gastrointestinal symptoms such as abdominal pain or intestinal obstruction [6, 10]. Complex phenotypes with alternating flares have been reported, including episodes of self-injury, sleep disturbances, and even transient visual–auditory hallucinations [11]. Given this heterogeneity, PANDAS can be mistaken for neurological or neuropsychiatric disorders and requires careful differential diagnosis.

2.3. Eating disturbances and anxiety symptoms

Eating disturbances are a particularly important problem in pediatric patients and may emerge abruptly in PANDAS/PANS. Clinical reports describe an abrupt refusal to eat or acute dietary restriction, which carries a medical risk of malnutrition and may necessitate hospitalization as part of an acute PANDAS/PANS phenotype [4, 6]. In some cases, improvement has been observed with concurrent treatment of the infection and initiation of psychiatric care; however, the available evidence is derived primarily from case reports and does not allow standardized management recommendations [4].

2.4. Speech symptoms and ocular tics

In a Swedish survey, 54.5% of caregivers reported speech-fluency problems – rapid rate, excessive fillers, verbal blocks – often overlapping with stuttering and co-occurring with facial tics [12]. Ocular tics are frequent and have been associated with elevated anti-DNase B and inflammatory markers, suggesting immunological

underpinnings [13]. These features broaden the PANDAS spectrum beyond classic OCD/tics to include speech and motor-system disturbances [13, 14].

2.5. Differential diagnosis: PANDAS versus Sydenham chorea

SC, a classic manifestation of acute rheumatic fever (ARF) after GAS infection, must be considered [14]. PANDAS presents with an abrupt onset of OCD/tics occurring in close temporal proximity to pharyngitis and a relapsing–remitting course, whereas SC features generalized or hemichorea with hypotonia and characteristic signs ("milkmaid's grip," "darting tongue"), with OCD less prominent [15,16]. Timing differs: PANDAS flares follow shortly after GAS infection, while SC may begin weeks to months later and can appear as isolated chorea [14]. Suspected SC warrants electrocardiography (ECG) (PR interval) and echocardiography, with diagnosis guided by revised Jones criteria [14]. Anti-streptolysine O (ASO) and anti-DNase B may be elevated in both, but lack specificity, underscoring the absence of a single validated biomarker for PANDAS [6, 17]. Accordingly, PANDAS remains a clinical diagnosis – abrupt OCD/tics temporally linked to GAS after excluding other causes, including autoimmune encephalitis (AE) [18] – whereas SC requires an ARF-oriented workup. Both likely reflect post-streptococcal basal-ganglia autoimmunity, with motor features predominating in SC and neuropsychiatric features in PANDAS [2, 14, 16].

3. Implications for diagnostic management

3.1. Pathophysiology and biomarkers

The contemporary conceptualization of PANDAS/PANS assumes that these conditions represent syndromes with a probable autoimmune background, in which exposure to GAS may trigger cross-reactive immune responses directed against structures of the central nervous system (CNS), particularly the basal ganglia [1, 2]. A practical diagnostic implication of this model is that the diagnosis remains primarily clinical, while laboratory and neuroimaging studies serve a supportive role, simultaneously documenting prior exposure or infection and excluding alternative etiologies, especially in cases where immunomodulatory treatment is being considered. According to current literature, infectious, inflammatory, and metabolic diseases of the brain should be excluded prior to initiating immunomodulatory therapy, which determines both the sequence and scope of the diagnostic workup in patients with suspected PANDAS/PANS [19].

3.2. Assumptions regarding pathomechanisms and interpretative framework for diagnosis

Molecular mimicry is considered the central pathophysiological mechanism, analogous to SC, in which antibodies induced by GAS may bind neuronal antigens within the basal ganglia and trigger neuroimmunological processes [1, 2, 16]. From

a diagnostic perspective, this implies that biomarkers should be interpreted as supportive evidence for a post-infectious autoimmune model rather than as definitive diagnostic tests. At the same time, in the post-COVID era, the increasing burden of GAS/iGAS infections may enhance immunological exposure in the pediatric population and facilitate the emergence of post-infectious phenotypes in susceptible children. This provides a rationale for the systematic documentation of GAS exposure in the course of acute neuropsychiatric syndromes, without postulating a distinct or novel pathogenesis of the disorder [1, 3, 7, 8].

3.3. Documentation of the association with GAS and identification of the infectious focus

In diagnostic practice, a critical step is confirmation of GAS infection or credible exposure, as this element differentiates PANDAS from the broader category of PANS and from other causes of acute-onset neuropsychiatric syndromes. According to current literature, clinical assessment of upper respiratory tract infection alone is insufficient, as the majority of infections in the pediatric population are viral in origin; therefore, a throat swab (rapid antigen or PCR detection test or culture) is recommended to assess active GAS infection [19]. It has also been emphasized that throat swabs should be obtained at the initial presentation and during each exacerbation in order to reliably evaluate the temporal relationship between infection and symptom relapse. A positive result in the absence of symptoms may reflect colonization, whereas infections may present with minimal or no symptoms, necessitating an active search for alternative sites of infection. This aspect should be explicitly incorporated into the diagnostic algorithm as a mandatory step involving the "search for a source or focus of infection" [19].

3.4. Streptococcal serology as supportive evidence for diagnosis

Current literature indicates that the classical serological markers of exposure to GAS include ASO titers and anti-DNase B antibodies; however, their utility in the diagnosis of PANDAS/PANS is supportive rather than definitive, due to variability in the kinetics of the humoral immune response and the lack of standardized interpretative thresholds specific to these syndromes [6, 17]. Serological testing may be particularly helpful in cases of suspected paucisymptomatic or asymptomatic infection, as well as when microbiological investigations fail to confirm active infection despite a high level of clinical suspicion. Within this framework, serial measurements assessing changes in antibody titers over time are of greater diagnostic value, whereas a single positive result should not be regarded as conclusive evidence of a causal association with GAS [19]. Taking into account epidemiological observations from the post-COVID-19 period, including an increased incidence and severity of GAS/iGAS infections, it has been emphasized that in clinical practice, a streptococcal etiology is more frequently considered in children presenting with an acute onset of neuropsychiatric symptoms, even in the presence of equivocal serological results. This context further supports the interpretation of serology as a supportive diagnostic element that should be evaluated

in conjunction with clinical and microbiological findings and in temporal relation to symptom relapses and exacerbations [3, 7, 8].

3.5. Immunological biomarkers and autoantibodies: significance and limitations of validation

The literature consistently distinguishes routine investigations (ASO, anti-DNase B) from more advanced immunological assessments, which may provide data supporting the hypothesis of autoimmunization but do not constitute definitive biomarkers for PANDAS/PANS [1, 2, 6]. In this context, the Cunningham Panel has been discussed; it includes assessment of calcium/calmodulin-dependent protein kinase II (CaMKII) activity and autoantibodies directed, among others, against dopaminergic receptors and tubulin [20]. It has been reported that changes in antineuronal autoantibody titers may parallel fluctuations in symptom severity, and that reductions in CaMKII activity may coincide with clinical improvement [20]. At the same time, available data do not establish these measures as diagnostic tests with clearly defined sensitivity and specificity, and the heterogeneity of clinical definitions of PANDAS/PANS, together with the lack of validation in large cohorts, limits their use to supportive and research-oriented applications [1, 2, 6, 20].

A separate and emerging line of research concerns antibodies to folate receptor alpha (FRAA). Positive FRAA have been identified in a substantial proportion of patients with PANS/PANDAS (63.8%), with a predominance of blocking antibodies [17]. These findings suggest the possibility of identifying a subgroup of patients with a potential disturbance of folate-related pathways, in whom supplementation with leucovorin (folinic acid) may be considered as an adjunctive intervention [21]. However, it is emphasized that these observations require prospective confirmation, and that FRAA cannot be regarded as a definitive diagnostic biomarker; therapeutic decisions should be based on the overall clinical profile in conjunction with positive FRAA results, without extrapolation to the entire patient population [21].

3.6. Inflammatory markers and the Th17/IL-17 axis: mechanistic indicators rather than decision-making tools

Growing evidence indicates the involvement of inflammatory processes in the pathogenesis of PANDAS/PANS, with particular emphasis on the T helper 17 (Th17) cell axis and interleukin-17 (IL-17) [6, 17]. Elevated concentrations of IL-17 have been reported in serum and cerebrospinal fluid (CSF) of children with acute neuropsychiatric syndromes, including PANDAS/PANS [17]. From a mechanistic perspective, IL-17 is postulated to increase blood–brain barrier (BBB) permeability and to promote the migration of inflammatory cells into the CNS, potentially amplifying neuroinflammation within circuits associated with the basal ganglia [2, 6, 17]. At the same time, significant methodological limitations have been highlighted, including heterogeneity of CSF control groups, lack of validation of the assays used for CSF analysis, and the absence of a consistent and predictable pattern of IL-17 dynamics following im-

munomodulatory treatment in retrospective analyses [6, 17]. Consequently, IL-17 should be regarded as a mechanistic marker of inflammatory axis activity during the acute phase, with no current basis for its use as a marker of treatment response or as a decision-making parameter in clinical practice [6, 17].

3.7. Extended diagnostic evaluation: CSF, neuroimaging, and links with SC

As PANDAS/PANS remain diagnoses of exclusion, it is emphasized that in atypical, severe, or treatment-refractory cases, an extension of the diagnostic workup is warranted to exclude other infectious, inflammatory, and metabolic disorders of the CNS, particularly before qualification for immunomodulatory therapy [22, 23]. Within this framework, CSF analysis and neuroimaging studies serve primarily a differential diagnostic purpose, including the exclusion of AE, rather than constituting investigations that definitively establish the diagnosis of PANDAS/PANS [22, 23]. From a pathophysiological perspective, BBB permeability has been highlighted as a mechanism that may facilitate the entry of inflammatory cells and autoantibodies into the central nervous system, thereby activating neuroinflammatory processes within the basal ganglia [2, 6]. Reports from neuroimaging studies, including MRI and positron emission tomography (PET) – particularly PET using ligands targeting the 18 kDa translocator protein (TSPO) – have been interpreted as potentially indicating increased microglial activation, thus supporting a neuroinflammatory model. However, these findings are subject to limited specificity when applied to the diagnostic evaluation of individual patients [2, 22]. Consequently, neuroimaging, serological testing, and immunological assays (e.g., the Cunningham Panel/CaMKII) should be interpreted as supportive rather than definitive evidence [20, 22, 23, 27].

SC remains a key reference model of post-infectious autoimmune involvement of the CNS system following GAS infection [2, 15, 16]. In SC, the presence of antibodies against dopaminergic receptors (D1R/D2R) and CaMKII activation correlating with the severity of motor and behavioral symptoms has been described; the potential contribution of the Th17/IL-17 axis and increased BBB permeability in facilitating autoantibody access to the CNS has also been suggested [15, 18]. This comparison allows PANDAS to be situated within a coherent immunological framework while simultaneously underscoring the clinical differences between these entities [15]. In the post-COVID-19 setting, with an increased incidence of GAS infections, the number of clinical scenarios requiring differentiation of acute neuropsychiatric syndromes with a possible post-infectious background has increased. This supports the continued use of SC as a pathophysiological reference framework, without excessive diagnostic extrapolation [1, 3, 7, 8, 15].

4. Treatment

Management remains a subject of ongoing debate, as no unified international guidelines are currently available [5]. In the post-COVID era, particular emphasis has been placed on the infectious component of treatment, reflecting the observed increase

in both the incidence and severity of GAS/iGAS infections, which may potentially exacerbate the relapsing course of neuropsychiatric symptoms [1, 7, 8]. Clinical care is multimodal in nature, encompassing eradication of GAS, modulation of the autoimmune response, and treatment of core psychiatric symptoms, with variable clinical outcomes reported [2, 22].

4.1. Anti-infective management

Case reports and observational studies describe clinical improvement following treatment with amoxicillin, cephalosporins, or macrolides; some children achieve remission after short courses of therapy, whereas others experience relapses [2]. It should be emphasized that *S. pyogenes* remains universally susceptible to penicillin (PNC), which supports its use as a first-line agent for eradication therapy [24]. In clinical practice, a trial of antibiotic therapy for approximately three weeks is often recommended while awaiting improvement of neuropsychiatric symptoms. Clinical improvement may occur rapidly (within 24–48 hours), but more commonly emerges after 1–2 weeks. In the absence of a therapeutic response after approximately 14 days, a change in antibiotic class and extension of treatment for an additional 10–14 days is suggested, whereas in cases of significant clinical improvement, continuation of therapeutic doses for a further 2–4 weeks may be considered [2, 22]. Some authors suggest a follow-up throat swab approximately one week after completion of therapy with retreatment advised if the result remains positive [8, 22]. These observations support an individualized, response-guided approach to treatment duration rather than rigid, predefined antibiotic regimens.

4.2. Prophylaxis in selected patients

In patients with frequent exacerbations temporally associated with GAS infection, antibiotic prophylaxis may be considered. A retrospective cohort study from Italy, covering a 10-year observation period, supports the use of intramuscular benzathine PNC administered every 21–28 days (600,000 IU in children weighing <27 kg and 1,200,000 IU in those weighing >27 kg). The median duration of prophylaxis was 14 months, and a high rate of complete remission was observed in the group receiving benzathine PNC [5].

4.3. Immunomodulation

Immunomodulatory approaches include glucocorticoids, intravenous immunoglobulin (IVIG), and therapeutic plasma exchange (TPE). Data from clinical studies and case series indicate that IVIG and TPE may result in clinically meaningful reductions in OCD and tic severity in a subset of patients, particularly in severe or treatment-refractory cases [22]. In routine practice, decisions regarding immunomodulatory therapy are made on an individual basis, taking into account symptom severity, disease dynamics, and response to prior interventions. TPE has also been described in

older adolescents and adults with persistent PANDAS/PANS symptoms, with reported improvement in some patients [4, 25].

4.4. Psychiatric treatment

Psychiatric and behavioral care should be implemented concurrently with infection – and immune-targeted treatment, as rapid symptom control reduces patient distress, improves family functioning, and facilitates the implementation of other therapeutic components [2, 9, 26]. Management generally follows established standards for pediatric OCD and tic disorders; however, in PANDAS/PANS it often requires greater individualization due to the abrupt onset of symptoms, marked symptom fluctuations, and the frequent coexistence of somatic and neurological manifestations [9, 12, 26]. Psychotherapeutic interventions form the foundation of care, particularly cognitive behavioral therapy (CBT) with exposure and response prevention (ERP) supplemented by family-based interventions (psychoeducation, reduction of family accommodation, and behavioral management techniques), especially when the child is not yet ready to engage actively in CBT [26]. Educational accommodations are frequently required in clinical practice, including flexible attendance, modified assessment methods, and support for cognitive and graphomotor functioning, tailored to symptom fluctuations during exacerbations [26]. Pharmacotherapy is primarily symptomatic. Selective serotonin reuptake inhibitors (SSRIs) are preferred for the treatment of OCD; however, in patients with PANDAS/PANS, very low starting doses and slower titration are recommended, with dose adjustments no more frequent than approximately every two weeks and careful monitoring for adverse effects (e.g., behavioral activation, irritability, increased anxiety, or tic exacerbation) [2, 11, 26]. In severe, debilitating presentations of OCD with agitation or aggression, short-term adjunctive treatment (e.g., antipsychotic medication) may be considered under close monitoring and in accordance with safety principles [26]. Regardless of the treatment modality, systematic risk assessment is essential, particularly with respect to refusal of food or fluids, dehydration, self-injurious behavior, or suicidality; when such risks are identified, urgent escalation of care, including hospitalization, may be required [26]. Parallel implementation of psychiatric and infection–immune interventions promotes symptom stabilization and reduces the risk of symptom persistence.

4.5. Adjunctive treatment

Among adjunctive therapies, leucovorin (folinic acid) has attracted attention in patients with positive antibodies to the FRAA, where it has been associated with reported improvements in neuropsychiatric functioning and good tolerability [21].

Limitations

This narrative review focuses on 2020–2025 with targeted earlier inclusions, improving relevance to post-COVID epidemiology but limiting comparability with

pre-2020 literature. Studies varied in PANDAS/PANS definitions and outcomes; retrospective designs and case reports predominate, increasing selection and publication bias and precluding pooled estimates. SC is referenced for mechanism and differential diagnosis rather than systematically synthesized. Laboratory signals are constrained by assay limitations (e.g., non-validated CSF IL-17, heterogeneous CSF controls) and variable ASO/anti-DNase B kinetics across age and geography [6, 7, 11]. Language was limited to English and Polish.

Conclusions

Available evidence supports the conceptualization of PANDAS/PANS as syndromes with a probable post-infectious immune-mediated background, in which exposure to GAS may facilitate acute, fluctuating neuropsychiatric phenotypes. In the post-COVID-19 era, a rebound increase in the incidence both GAS and iGAS infections in children has been observed, providing an important epidemiological context for more frequent suspicion of PANDAS/PANS and underscoring the need for heightened clinical vigilance in cases of acute-onset neuropsychiatric syndromes. In clinical practice, the diagnosis of PANDAS remains primarily clinical, as no definitive, validated biomarkers or standardized serological thresholds are currently available; laboratory and neuroimaging studies therefore serve a supportive role. Diagnostic evaluation should focus on the assessment of abrupt onset, a relapsing–remitting course, and a temporal association with GAS infection or exposure, alongside careful differentiation from conditions that may mimic an acute neuropsychiatric phenotype, including SC/ARF and AE. Confirmation of a streptococcal component should preferentially rely on microbiological diagnostics, whereas serological markers (ASO/anti–DNase B) should be interpreted cautiously, ideally using serial measurements and in correlation with the clinical course. Management should be multimodal, integrating psychiatric symptom treatment with diagnostic evaluation and management of infection, and – in selected severe or refractory cases – consideration of immunomodulatory therapy after exclusion of alternative infectious, inflammatory, and metabolic disorders of the CNS. Given the need for concurrent psychiatric and anti-infective treatment, close interdisciplinary collaboration between a psychiatrist and an infectious disease specialist experienced in neuropsychiatric disorders is essential. Priority should be given to the standardization of clinical criteria and to prospective, multicenter validation of biomarkers and therapeutic strategies, which would improve comparability of findings and the quality of clinical recommendations.

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