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Review

Indications for Vaccinations in Preschool Children Subjected to Thymectomy: An Exhaustive Immunological and Clinical Analysis

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ABSTRACT

Neonatal thymectomy during pediatric cardiothoracic surgery causes profound immunological consequences, primarily iatrogenic premature immunosenescence and impaired central tolerance. This review analyzes the mechanisms of thymic deprivation, highlighting the loss of naive T-cells and the compensatory, oligoclonal expansion of memory T-cells. Given the heterogeneity of surgical cohorts, DiGeorge Syndrome (22q11.2DS) serves as a comparative clinical paradigm to establish evidence-based vaccination guidelines.

Inactivated vaccines are strongly recommended, although accelerated serological waning demands frequent monitoring and booster doses. Live attenuated vaccines (LAVs), including MMR and Varicella, can be safely administered if strict immunological thresholds (CD4+ ≥400 cells/mmc; CD8+ ≥200 cells/mmc) are surpassed. Conversely, live oral rotavirus and BCG vaccines are strictly contraindicated during severe lymphopenia or in the immediate post-operative window. Crucially, the live-attenuated Yellow Fever vaccine represents an absolute, lifelong contraindication due to the risk of fatal viscerotropic disease.

Rigorous flow cytometric and serological pre-vaccination evaluations, alongside permanent clinical documentation of thymic ablation, are essential to ensure safe immunization practices in this vulnerable pediatric cohort.

KEYWORDS: DiGeorge Syndrome, Thymectomy, Vaccinations

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INTRODUCTION

The profound immunological sequelae following neonatal thymectomy present an extraordinary challenge at the intersection of pediatric cardiothoracic surgery, clinical immunology, and vaccinology. For decades, surgical excision of the thymus was viewed merely as an anatomical necessity to facilitate median sternotomy, with surgeons operating under the flawed assumption that the organ's absence post-birth was clinically negligible [1]. However, the integration of high-resolution molecular biology, flow cytometry, and longitudinal immune tracking has fundamentally reversed this paradigm, establishing early thymectomy as a potent etiology of iatrogenic secondary immunodeficiency and premature immunosenescence [2,3]. This comprehensive analysis summarizes the complex pathophysiological mechanisms triggered by thymic deprivation and establishes a rigorous framework for navigating pediatric vaccination in this unique cohort.

MATERIALS AND METHODS

Literature Search Strategy

A targeted literature review was conducted utilizing the core keywords "DiGeorge Syndrome," "Thymectomy," and "Vaccinations". The search integrated global health guidelines from the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), pharmacovigilance data from Vaccine Adverse Event Reporting System (VAERS), Brighton Collaboration diagnostic criteria, and clinical consensus.

Study Selection and Data Extraction, Synthesis and Analysis

The review incorporated high-resolution molecular and clinical literature, including observational studies, cohort studies, single-cell RNA sequencing data, case reports, and pivotal clinical trials such as the MEDLEY trial. DiGeorge Syndrome (22q11.2DS) was utilized as the primary comparative genetic paradigm to safely extrapolate established vaccination thresholds to the surgically thymectomized cohort.

Data extraction systematically focused on three core parameters for risk stratification:

- Quantitative Cellular Profiling: Absolute counts and percentages of CD4+ and CD8+ T-cells.
- Molecular and Phenotypic Biomarkers: Quantification of TRECs and flow-cytometric ratios of naïve (CD45RA+) to memory (CD45RO+) T-cells.
- Qualitative Functional Validation: In vivo T-dependent serology (e.g., post-immunization Tetanus IgG titers), which replaces historically unreliable *in vitro* mitogen assays.

The extracted data was summarized to construct an integrated, multi-tiered clinical protocol and evidence-based table dictating strict immunological thresholds for authorizing or contraindicating vaccines and monoclonal therapies.

THE MOLECULAR ARCHITECTURE OF T-CELL ONTOGENY AND CENTRAL TOLERANCE

To understand the specific vulnerabilities of the thymectomized host, one must first examine the critical physiological role of the thymus in establishing the adaptive immune repertoire. The thymus acts as the master regulator of cellular immunity, providing the exclusive microenvironment for the maturation, somatic rearrangement, and rigorous clonal selection of naïve T-cells. Multipotent lymphoid progenitors migrate from bone marrow to the cortico-medullary junction of the thymus, where they begin a tightly orchestrated differentiation program [2,4].

The cornerstone of this process is the somatic rearrangement of the variable (V), diversity (D), and joining (J) gene segments that encode the T-cell receptor (TCR). During the enzymatic splicing of these genetic fragments, small circular portions of episomal DNA are permanently excised from the primary chromosomal genome. These molecular byproducts, designated as T-cell receptor Excision Circles (TRECs), are trapped within the cellular cytoplasm. Because TRECs lack the intrinsic ability to replicate during cellular mitosis, they are systematically diluted with each subsequent division. Consequently, the quantification of TRECs serves as a highly stable, incontrovertible molecular biomarker to measure the precise export rate of newly generated lymphocytes – Recent Thymic Emigrants (RTEs) – from the thymus into the peripheral blood [5].

Within the thymus, developing thymocytes must survive a dual selection process. Positive selection ensures that the TCR can adequately recognize self-MHC molecules, while negative selection strictly induces apoptosis in clones that exhibit high affinity for self-antigens, thereby establishing central tolerance. T-cells that successfully navigate this gauntlet exit into the periphery predominantly expressing the naïve CD45RA+ phenotype and the CD31+ surface marker. The surgical removal of the thymus abruptly halts this continuous systemic release of naïve, self-tolerant T-cells, permanently depriving the growing child of a vital source of immunological diversity [2,6,7].

PATHOPHYSIOLOGY OF IATROGENIC PREMATURE IMMUNOSENESCENCE

In the absolute absence of thymopoiesis, the human body instantly activates secondary rescue mechanisms to avoid fatal lymphopenia. Peripheral cellular homeostasis is rapidly assumed by the incessant expansion of already mature, circulating T-cells, driven predominantly by homeostatic tissue cytokines such as Interleukin-7 (IL-7). Immunological profiling of thymectomized children reveals a statistically significant negative correlation between absolute CD4+ T-cell counts and circulating plasma IL-7 levels, highlighting the physiological attempt to force cellular multiplication [8,9].

While this quantitative compensation successfully prevents total immune collapse, it results in profound qualitative deterioration of the adaptive immune compartment. The continuous forced division of a highly restricted number of pre-existing clones severely truncates the diversity of the TCR repertoire, leaving the individual with an inherently oligoclonal cellular network. Phenotypically, the physiological predominance of naïve T-cells (CD45RA+/CD31+) gives way to a massive, vicarious expansion of memory-phenotype T-cells expressing the CD45RO+ marker [7,8] (Tab. I).

This chronic state of forced proliferation induces rapid structural wear, clinically quantifiable through the premature shortening of lymphocyte telomeres and the acquisition of terminal senescence markers such as CD57 and PD-1. This condition, termed "iatrogenic premature immunosenescence," leaves preschool children with the functional immunological rigidity typically observed in the extreme elderly [10] (Tab. I).

The severity of this immunosenescence is drastically compounded by latent viral pathogens, most notably cytomegalovirus (CMV). CMV

TABLE I. Immunological Comparison Between Physiological and Post-Neonatal Thymectomy Profiles in Preschool Children.

Immunological Parameter	Physiological Profile (Preschool Age)	Iatrogenic Profile (Post-Neonatal Thymectomy)	Primary Pathophysiological Consequence
Generation of TRECs	Highly expressed and stable	Markedly reduced or virtually undetectable	Abolition of antigen-specific neogenesis and RTE export
CD45RA+ Subset (Naïve)	Dominant phenotype in periphery	Drastically contracted and progressively lost	Suboptimal primary response to novel pathogenic antigens
CD45RO+ Subset (Memory)	Minority, in physiological accumulation	Vicariously expanded via IL-7 homeostatic driving	Rigid dependence on a highly limited and wearing lymphocyte pool
TCR Repertoire	Heterogeneous, highly polyclonal	Restricted, oligoclonal (e.g., Vβ subset skewing)	Absolute absence of specific clones for rare vaccine epitopes
Cellular Senescence	CD28+ / CD57- (Immune Competence)	CD28- / CD57+ / PD-1+ (Terminal Senescence)	Defective co-stimulation and impaired immune synapse formation
Vγ9Vδ2 γδ T-cells	Baseline physiologic levels	Markedly increased, producing Granzyme	Reliance on innate-like, non-specific effector cellular subsets

This Table outlines the profound shift from a diverse, naive-dominant immune system to an oligoclonal, senescent profile following early thymectomy. Key alterations include the loss of T-cell receptor excision circles (TRECs) and the compensatory expansion of memory and innate-like T-cells, which collectively contribute to suboptimal primary responses to novel pathogenic antigens and premature immune aging.

imposes a continuous burden on the cellular immune system. In a thymectomized host, the unrenewable naïve T-cell pool is rapidly exhausted as the virus forces the continuous expansion of CMV-specific memory clones, effectively mirroring the "Immune Risk Phenotype" predictive of increased mortality in older adults [10].

Furthermore, high-dimensional single-cell RNA sequencing studies have uncovered complex third-order adaptations. Early-life thymectomy precipitates a marked, compensatory increase in innate-effector Vγ9Vδ2 γδ T-cells, which are characterized by high CD28 and CD161 expression and massive granzyme production. This profound shift demonstrates that the immune system is forced to rely on non-specific, innate-like cellular subsets to maintain immune surveillance due to the absolute failure of adaptive clonal generation [11] (Tab. I).

BREAKDOWN OF CENTRAL TOLERANCE AND THE PARADOX OF AUTOIMMUNITY

The failure of central tolerance represents a severe dual threat in the thymectomized host. Without the thymic medulla to rigorously delete auto-reactive T-cell clones, these aberrant lymphocytes escape into the periphery where they provide unregulated assistance to auto-reactive B-cells, triggering systemic autoimmunity [4].

In a landmark controlled cohort study, pathological autoantibodies were identified in 62% of children subjected to neonatal thymectomy, compared to 33% in age-matched healthy controls. The disruption of T-B cell cross-talk fundamentally skews the humoral profile, creating extreme vulnerabilities when combined with secondary immunosuppression. A critical case report details an adult patient who underwent thymectomy followed by targeted radiation therapy for a thymoma. This combined intervention triggered severe generalized urticaria, intractable lymphocytopenia, a critically low absolute CD4+ count, and an absolute failure to mount a serological response to pneumococcal vaccination. Over 8 years of longitudinal observation, the patient remained unable to regenerate the peripheral T-lymphocyte pool, unequivocally underscoring the lifelong necessity of the thymus for maintaining a balanced, non-autoreactive immune network [4,12].

DIGEORGE SYNDROME (22Q11.2DS) AS THE PREDICTIVE CLINICAL FRAMEWORK

Due to the heterogeneous nature of surgical cohorts, clinical immunology utilizes DiGeorge Syndrome (DGS) as the primary comparative genetic paradigm to safely guide the management of iatrogenic thymectomy. Driven by haploinsufficiency of the *TBX1* gene, DGS is characterized by severe mesenchymal defects that impair extracellular matrix assembly in the pharyngeal pouches, leading to varying degrees of thymic hypoplasia or complete glandular aplasia [13,14].

The immunological defect is identical: a severe depletion of naïve T-cells, a pathologically inverted naïve-to-memory cellular ratio, and a collapse in TREC levels signaling impaired thymopoiesis. Because robust, global safety and efficacy data regarding vaccine administration in 22q11.2DS populations already exist, clinicians apply these exact evidence-based thresholds to surgically thymectomized children. This comparative model allows for the precise flow-cytometric stratification required to authorize live vaccine administration[13,14] (Tab. II).

TABLE II. Clinical and Immunological Stratification of Thymic Hypoplasia in DiGeorge Syndrome (22q11.2DS)

DGS Hypoplasia Category	Clinical Prevalence in 22q11.2DS	Key Immunological Phenotype	Implications for TREC Diagnostics
Mild Thymic Hypoplasia	60-70%	Reduced CD3+ (<1,500 cells/mmc); expanded memory pool	Often unflagged as critically abnormal on standard newborn screens
Severe Thymic Hypoplasia	Variable minority	Low CD3+ (>50 and <400 cells/mmc); naïve T-cells <50%	Undetectable or severely depressed TRECs
Congenital Athymia	<1%	Very low CD3+ (<50 cells/mmc); naïve T-cells <5%	Undetectable TRECs, clinically mimicking SCID phenotypes

This table categorizes the severity of thymic defects in DiGeorge Syndrome, which serves as a comparative genetic paradigm for safely guiding the management of iatrogenic thymectomy. It highlights the correlation between the degree of hypoplasia, CD3+ T-cell depletion, the contraction of the naive T-cell pool, and the corresponding detectability of TRECs during diagnostic screenings.

PRINCIPLES OF VACCINOLOGY IN THE DEPRIVED HOST

The induction of robust, long-term humoral memory following the administration of protein subunit, inactivated, and conjugate vaccines is strictly dependent on the intervention of T-helper lymphocytes. Within the secondary lymph nodes, specialized T follicular helper (Tfh) lymphocytes localize to the germinal centers to establish an immunological synapse with antigen-specific B-cells. This interaction, heavily reliant on CD40-CD40L engagement and the secretion of interleukin-21, orchestrates B-cell isotype switching and somatic hypermutation, ensuring terminal differentiation into stable plasma cells [15].

In the prematurely aged and thymic-deprived immune system of a DGS or post-thymectomy patient, the severe deterioration of the T-helper compartment critically compromises this essential transition. Without a diverse repertoire of naive CD4+ T-cells to accurately recognize novel pathogenic or vaccine-derived epitopes, the downstream activation of B-cells is inherently flawed [15].

Recent high-resolution longitudinal studies provide striking clinical evidence of this mechanistic failure. Farpour et al. conducted a prospective observational study evaluating vaccine immunity in 41 patients with DGS. Despite the fact that the majority of these patients exhibited normal immunoglobulin levels and normal absolute lymphocyte counts at baseline during routine immunological work-ups, and despite having completed their primary childhood vaccination series, their long-term humoral memory was profoundly defective. The study revealed that while most patients maintained seroprotection against tetanus and diphtheria, and a substantial and alarming number of patients completely lacked seroprotection against varicella, measles, hepatitis B, and pneumococcus [15].

This specific deficiency highlights a critical pathophysiological consequence: the phenomenon of accelerated serological waning. Even when absolute lymphocyte counts appear sufficient to permit initial seroconversion, the underlying oligoclonality and accelerated senescence of the T-cell compartment prevents the sustainable maintenance of the plasma cell niche. Consequently, specific IgG titers decline rapidly, rendering patients highly susceptible to breakthrough infections. This vulnerability necessitates rigorous quantitative serological follow-up at 12 to 24 months post-vaccination, as repeated booster doses become strictly indispensable to maintain clinical immunity and prevent morbidity from encapsulated bacteria and viral threats [15].

RISK STRATIFICATION FOR LIVE ATTENUATED VACCINES

Existing literature supports the safety of live attenuated vaccines (LAVs) in DGS patients with partial thymic function. Cohorts evaluated by Perez [16], Moylett [17], Al-Sukaiti [18], and Lim [19] demonstrate that mild-to-moderate immunosuppression permits safe measles, mumps, rubella (MMR) and varicella vaccination, yielding primarily mild and transient adverse events. Notably, Lim et al. (2022) reported general tolerability even among patients with significant T-cell deficiency, defined as CD3+ < 500/mmc or CD8+ < 200/mmc. Furthermore, defaulting to complete vaccine avoidance poses a documented, high risk of contracting vaccine-preventable illnesses [19].

However, LAV safety is inextricably linked to specific cellular immune parameters. Hofstetter et al. demonstrated that proportional representations offer strong predictive value, showing that varicella vaccine recipients who developed adverse events had a significantly lower preceding CD4+ (24.8%) compared to those who tolerated it without incident (35.5%) [20]. Conversely, profound quantitative T-cell lymphopenia remains an absolute contraindication. This was illustrated by Waters et al., who reported the fatal dissemination of vaccine-strain varicella in an infant with profound cellular depletion, presenting with a CD3+ count of 396/mmc, a CD4+ count of 320/mmc and a CD8+ count of just 57/mmc. Crucially, this catastrophic outcome occurred despite a misleadingly "normal" *in vitro* phytohemagglutinin (PHA) proliferation assay prior to vaccination [21].

However, the live BGC and oral Rotavirus vaccines present a critical and unique danger. Scheduled during the immediate post-natal period, their administration frequently overlaps with palliative neonatal cardiac surgery. The physiological trauma of cardiopulmonary bypass, combined with radical thymic excision, induces a state of profound, transient T-cell lymphopenia that mimics severe combined

immunodeficiency (SCID). Consequently, these vaccines are absolutely contraindicated in this precise temporal window due to the catastrophic risk of vaccine strain reactivation [6,19,22].

THE YELLOW FEVER VACCINE PARADIGM: A FATAL CONTRAINDICATION

Prophylaxis against Yellow Fever (YF) represents the most absolute contraindication in the thymectomized cohort. Global health organizations uniformly prohibit the administration of the live-attenuated 17D YF viral strain to any patient with a history of surgical thymectomy or thymic dysfunction. In the immunocompromised host lacking diverse cellular surveillance, the 17D strain undergoes unchecked replication, triggering Yellow Fever Vaccine-Associated Viscerotropic Disease (YEL-AVD) [23,24].

YEL-AVD is a fulminant, catastrophic syndrome culminating in acute hepatic necrosis, severe coagulopathy, and multi-organ dysfunction syndrome. The Brighton Collaboration establishes rigorous criteria to identify this adverse event, encompassing severe hepatic, renal, musculoskeletal, respiratory, and platelet derangements. Pharmacovigilance tracking from the VAERS recorded a YEL-AVD incidence rate of 0.3 per 100,000 distributed doses between 2007 and 2013, noting that lethality increases exponentially with underlying immunodeficiency. A definitive CDC report documented the fatal case of an older woman in Oregon who rapidly succumbed to YEL-AVD following vaccination; post-mortem autopsies confirmed an undiagnosed underlying thymic pathology, reinforcing the direct mechanistic link between thymic absence and fatal viral escape [25,26].

MONOCLONAL INNOVATIONS: PASSIVE PROPHYLAXIS AGAINST RESPIRATORY SYNCYTIAL VIRUS

Due to their compromised cellular variance, infants subjected to secondary thymic ablation are highly susceptible to severe acute lower respiratory tract infections, particularly those caused by the Respiratory Syncytial Virus (RSV). RSV frequently triggers prolonged hospitalization and extreme cardiopulmonary distress in children with underlying CHD [27].

The prophylactic landscape for these vulnerable infants has been revolutionized by nirsevimab, an ultra-long-acting neutralizing monoclonal antibody. Nirsevimab incorporates highly specific "YTE" amino acid substitutions in its Fc region, dramatically enhancing its binding affinity to the neonatal Fc receptor (FcRn) within endosomes. This mechanism prevents lysosomal degradation, extending the antibody's serum half-life to confer prolonged passive immunity for an entire winter season following a single intramuscular injection. The pivotal MEDLEY trial conclusively demonstrated that nirsevimab achieves favorable safety profiles and optimal pharmacokinetic exposures in high-risk CHD infants, thus bridging the gap left by their defective adaptive immunity [28-30].

PRE-VACCINATION IMMUNOLOGICAL EVALUATION PROTOCOLS

Clinical guidelines for LAVs in patients with thymic defects, such as DGS, culminated in the 2023 Mustillo consensus, establishing a strict multi-tiered pre-vaccination protocol. First, quantitative cellular profiling via flow cytometry must confirm absolute counts of CD4+ $\geq$400 cells/mmc to coordinate the adaptive response, and CD8+ $\geq$200 cells/mmc to guarantee capacity for cytotoxic viral clearance. Second, phenotypic and molecular assessments must verify true thymic output; naive T-cells must outnumber memory cells (CD45RA+CD3+ >CD45RO+CD3+), and molecular TREC assays must definitively rule out congenital athymia. Third, qualitative functional validation represents a profound paradigm shift. Dangerously unreliable *in vitro* mitogen assays (like PHA) have been entirely replaced by in vivo T-dependent serology. Specifically, demonstrating a protective Tetanus IgG titer post-DTaP immunization provides incontrovertible proof of functional T-B cell cross-talk. Finally, longitudinal surveillance of specific IgG titers every 12 to 24 months is mandatory to counteract accelerated humoral waning and guide indispensable vaccine boosters[15,31] (Tab- III).

SURGICAL EVOLUTION AND LONGITUDINAL DOCUMENTATION

The profound immunological consequences of complete thymic ablation have successfully catalyzed a paradigm shift toward "tissue-sparing" approaches in pediatric cardiothoracic surgery. Longitudinal evaluations confirm that complete, but not partial, thymectomy drastically reduces T-cell-mediated immune responses for years post-surgery. If neonatal thymic tissue is carefully spared and its basal vascularization preserved, the intrinsic regenerative capacity of the remaining parenchyma — frequently verifiable via postoperative MRI — can facilitate the long-term restoration of the naïve T-cell compartment [2,32,33].

Ultimately, the safety of these patients relies on rigorous longitudinal documentation. The transition of care from specialized pediatrics to adult medicine must guarantee that the notation of "thymic ablation" or "thymectomy" is permanently engraved into all clinical databases. As demonstrated by the lethal administration of the yellow fever vaccine in adult cardiac patients, the omission of early childhood surgical history lays the uncorrectable foundation for fatal iatrogenic malpractice [24].

Ethical consideration

The nature of this study (a review) does not require ethical approval from an appropriate committee.

TABLE II. Evidence-Based Clinical Indications and Immunological Thresholds for Vaccination in Thymic Deprivation. This table summarizes the clinical, cellular, and molecular parameters required to safely authorize various vaccines in patients with compromised thymic function, such as those with 22q11.2DS or post-neonatal thymectomy. While inactivated vaccines are strongly recommended despite the need for frequent serological monitoring and boosters, live attenuated vaccines (like MMR and Varicella) strictly require surpassing specific CD4+ and CD8+ cell counts. Notably, the live-attenuated Yellow Fever vaccine remains an absolute contraindication regardless of any numerical thresholds due to the risk of Viscerotropic Disease.

Vaccine Type	CD4+ T-cell count/percentage thresholds	CD8+ T-cell counts	TREC (T-cell receptor excision circles) levels	PHA (Phytohemagglutinin) T-cell proliferation test responses	Clinical Recommendation / Contraindication
Inactivated Vaccines (e.g., DTaP, IPV, HepB, Hib, PCV, MenACWY, IIV)	Safe at any level; however, humoral response scales directly with CD4+ competence. T-helper deficit triggers accelerated waning.	Safe at any level.	Irrelevant for immediate safety; low TREC indicates risk of poor long-term memory formation.	Irrelevant for safety. The generation of Tetanus IgG confirms functional response in vivo.	Strongly recommended. Cornerstone of protection. Multiple booster doses and frequent serological monitoring (every 12-24 months) are strictly required due to accelerated antibody waning.
Live Attenuated Vaccines (LAVs): MMR & Varicella	Must be ≥400 cells/mmc. CD4% < 25% flags a high risk of adverse events.	Must be ≥200 cells/mmc. Absolute necessity to prevent fatal disseminated vaccine-strain infection.	Normal or Mild reduction (detectable RTEs). Undetectable TRECs strictly contraindicate LAVs.	Normal response traditionally required by older guidelines, but currently considered flawed. Tetanus IgG seroprotection is the superior surrogate for function.	Recommended if Thresholds Met. Well-tolerated in mild-to-moderate DGS/T-cell lymphopenia if all quantitative and qualitative thresholds are rigorously surpassed.
Live Oral Rotavirus	Assessment impossible pre-administration due to neonatal timing.	Assessment impossible pre-administration.	Undetectable TRECs (SCID/Congenital Athymia) strictly contraindicate.	Not applicable in the neonatal window.	Contraindicated in Severe Lymphopenia. Avoid if prenatal/neonatal indicators suggest severe DGS, complete athymia, or immediately post-cardiac surgery.
Live Attenuated BCG (Tuberculosis)	Contraindicated if significant T-cell lymphopenia is suspected.	Contraindicated if significant T-cell lymphopenia is suspected.	Undetectable or very low TRECs contraindicate.	Poor PHA response controindicates.	Contraindicated pending evaluation. Extreme risk of disseminated, fatal BCGitis. Must be withheld if 22q11.2DS/DTD is suspected until lymphopenia is fully excluded.
Live Attenuated Yellow Fever (17D Strain)	Absolute contraindication regardless of numerical threshold.	Absolute contraindication regardless of numerical threshold.	Irrelevant; the underlying thymic defect is an independent risk factor.	Irrelevant.	Absolute Contraindication. Any history of thymic dysfunction, 22q11.2DS, or surgical thymectomy independently triggers fatal Yellow Fever Vaccine-Associated Viscerotropic Disease (YEL-AVD).

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