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Immunisation deferral practices surrounding congenital heart surgery

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Original Article

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Abstract

Background: Perioperative immunisation administration surrounding congenital heart surgery is controversial. Delayed immunisation administration results in children being at risk of vaccine-preventable illnesses and is associated with failure to complete immunisation schedules. Among children with CHD, many of whom are medically fragile, vaccine-preventable illnesses can be devastating. Limited research shows perioperative immunisation may be safe and effective. *Methods:* We surveyed Pediatric Acute Care Cardiology Collaborative member centres and explored perioperative immunisation practices. We analysed responses using descriptive statistics. *Results:* Complete responses were submitted by 35/46 (76%) centres. Immunisations were deferred for any period prior to surgery by 23 (66%) centres and after surgery by 31 (89%) centres. Among those who deferred post-operative immunisation, 20 (65%) required deferral only for patients whose operations required cardiopulmonary bypass. Duration of deferral in the pre- and post-operative periods was variable. Many centres included exceptions to their policy for specific vaccine-preventable illnesses. Almost all (34, 97%) centres administer routine childhood immunisation to patients who remain admitted for prolonged periods. *Conclusions:* Most centres defer routine childhood immunisation for some period before and after congenital heart surgery. Centre specific practices vary. Immunisation deferral confers risk to patients and may not be warranted in this population. Further research would be necessary to understand the immunologic impact of these practices.

Perioperative immunisation administration surrounding surgery for CHD is controversial. Children with CHD are at risk for under-vaccination. Predictors of under-vaccination in this population include prolonged hospitalisation(s) during the first year of life, primary care in a state other than where they receive their cardiac care, multiple comorbidities, and cardiac surgery requiring cardiopulmonary bypass.[1] Multiple studies have found gaps in immunisation rates for infants with CHD: only 60% of infants in one study were considered fully immunised at 1 year of age, infants with heterotaxy and CHD were shown to unsatisfactory pneumococcal vaccination rates, and in a study of the high-risk single-ventricle population 17% had received no immunisations prior to the Glenn surgery and only 6% had received three DTaP immunisations.[1–3]

There are three primary arguments for not administering immunisations in the perioperative period.[4] First is the desire to avoid iatrogenic fever as a reaction to an immunisation which may delay surgery while assessing for infection or lead to more aggressive investigation or antimicrobial therapy due to concern for post-operative bacterial infection. Second, there is concern that exposure to blood products can modify immunisation efficacy due to existing immunoglobulins in donor blood.[5] This concern is not specific to the CHD surgical population. Lastly, there is concern related to whether cardiopulmonary bypass impairs the efficacy of immunisations by changing the recipient's immune response or by removing antibodies. While the idea of giving ineffective immunisations is clearly undesirable, it is not actually known whether bypass impairs immunisation efficacy nor for what duration these effects deleterious to immunisation efficacy might last. Limited data show that cardiopulmonary bypass may not significantly impact infant titres of typical childhood immunisations,[6,7] but that it may impact specific titres such as SARS-COV-2.[8–10] Regardless of the rationale, delayed immunisation administration is associated with failure to complete immunisation schedules which puts children at risk for vaccine-preventable illnesses.[11] Though there are numerous reasons children may be under-immunised,[12,13] recommendations for pre- and/or post-operative deferral by cardiologists and heart centres likely contribute to the overall burden of low immunisation rates in this vulnerable population.[1] Given the absence of clear data or available guidelines/best practices, we undertook this study on behalf of the Pediatric Acute Care Cardiology

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Table 1. Survey questions

Question number	Question stem	Response options
1.	Does your centre recommend deferral of childhood immunisations for any period of time prior to heart surgery?	Yes/No
1a—only shown if "yes" to 1	Please provide any additional information regarding which vaccines are deferred prior to surgery and for what time period	Write in
2.	Does your centre recommend deferral of childhood immunisations for any period of time after heart surgery?	Yes/No
2a—only shown if "yes" to 2	Are immunisations deferred for all surgical patients or only those who had cardiopulmonary bypass?	All surgical patients/Those who had cardiopulmonary bypass only
2b—only shown if "yes" to 2	For how long are immunisations deferred following surgery?	Write in
2c—only shown if "yes" to 2	Are there any exceptions for vaccine deferral practices (i.e., influenza immunisation during influenza season or COVID-19 immunisation)?	Yes/No
2d—only shown if "yes" to 2c	What are the exceptions to the immunisation deferral policy?	Write in
3.	Are there any patient populations with specific recommendations related to immunisation (e.g., interstage patients)?	Yes/No
3a—only shown if "yes" to 3	What patient populations have specific recommendations or policies surrounding immunisation administration?	Write in
4.	Does your centre administer routine childhood immunisations to patients who are inpatient pre- or post-operatively for prolonged periods overlapping with when they would be due for immunisations? (e.g., a patient has a prolonged admission following Norwood operation and passes 2 or 4 months of age—would the 2 or 4 month vaccines be administered?)	Yes/No
5.	Is there any other aspect of immunisation administration practices you would like to share with us?	Write in

Collaborative (PAC^3) to understand current practice at North American paediatric heart institutes.

Material and methods

We created a de novo survey built in REDCap[14] hosted at Children's Hospital of Los Angeles (UL1TR001855) exploring pre- and post-operative immunisation deferral for children undergoing congenital heart surgery. The survey had five questions with branching logic allowing for additional questions depending on responses to stem questions (Table 1). A de novo survey was used because no pre-existing or validated tool existed to explore this topic. The survey questions were developed by the research team and evaluated for clarity and content by the PAC^3 Quality Improvement committee. The survey was pilot-tested with two PAC^3 members to assess clarity of questions. An invitation to participate was then sent via email to the primary clinical representative from each of the 46 PAC^3 member sites across the United States and Canada. Two follow-up emails were sent 4 and 6 weeks from the initial invitation. Responses were analysed with descriptive statistics. Denominators used for percentages were changed for relevance (i.e., in the setting of branching logic, denominator was changed to reflect only the group of respondents for whom the branched question was presented). This study was deemed exempt by the institutional review board (protocol CHLA-22-00363).

Results

Complete responses were submitted by 35/46 (76%) centres. Immunisations are deferred for any period prior to surgery by 23 (66%) centres. Duration of pre-operative deferral ranged from 1 to 6 weeks with three centres having immunisation-specific deferral durations. Post-operative deferral for any period is required by 31 (89%) centres. Among those who defer post-operative immunisations, 20 (65%) require deferral only for patients whose operations required cardiopulmonary bypass. Post-operative deferral ranged from 2 to 12 weeks with seven centres reporting immunisation-specific deferral durations. Among these immunisation-specific durations, the deferral period for live virus immunisations was considerably longer at 5–7 months at five centres. Many centres have exceptions to their deferral policy for specific vaccine-preventable illnesses such as influenza and COVID-19 (Table 2). Among these exceptions, some centres reported administering these immunisations on the day of discharge, while others reported administering them the night prior to discharge to allow for the opportunity to observe the patient after administration. Almost all (34, 97%) centres administer routine childhood immunisations to patients who remain admitted for prolonged periods. Only four (11%) centres have no policy of immunisation deferral pre- or post-operatively. Lastly, we inquired regarding policies for special populations (Table 1, question 3) but did not receive any answers that demonstrated deviation from routine Centers for Disease Control recommendations.

Discussion

Despite the absence of clear data or guidelines to support practice, most North American paediatric heart institutes surveyed in this study require periods of both pre- and post-operative immunisation deferral. The variable duration of deferral underlies the lack of clarity on whether this practice is needed and for what rationale.

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Table 2. Details of pre- and post-operative immunisation deferral

Pre-operative immunisation deferral duration	n (%)
1 week	2 (9%)
2 weeks	15 (65%)
4 weeks	2 (9%)
6 weeks	1 (4%)
Variable based on type of vaccine	3* (13%)
Post-operative immunisation deferral duration	**n (%)**
2 weeks	4 (13%)
3–4 weeks	12 (39%)
6 weeks	7 (23%)
12 weeks	1 (3%)
Variable based on type of vaccine	7** (23%)
Exceptions to post-operative deferral policy	**14 (45%)**
COVID-19 and influenza immunisations given prior to discharge	13 (42%)
Rotavirus and influenza immunisations given prior to discharge	1 (3%)

*All three reported shorter deferral for inactivated virus vaccines and longer deferral for live virus vaccines.
**5/7 reported 5–7 month deferral for live virus vaccines.

The question of whether cardiopulmonary bypass alters titres remains incompletely answered. Existing data are from single-centre studies with relatively small sample sizes and suggest cardiopulmonary bypass impacts titres differentially based on the specific immunisation.[6–10] Additionally, this limited data reflects a mix of adult and paediatric research further diminishing generalisability of the findings as adult and infantile/pediatric immune systems differ.[15] Systematic research is needed to clarify whether cardiopulmonary bypass exposure warrants vaccine deferral. However, in balancing the risks of under-vaccination and vaccine-preventable illness in the vulnerable CHD population compared to the theoretical risk of an ineffective immunisation, perhaps providers should default to immunisation administration with potential titre checks rather than withholding a potentially life-saving intervention until clearer data exist.

The Centers for Disease Control recommend deferral of the measles, mumps, and rubella, rotavirus, and varicella vaccines after exposure to blood products because of the possibility that antibodies in the transfused blood products may blunt response to the live vaccine.[5] Importantly though, the recommendation for deferral is 3–11 months. This contrasts with responses in our study which indicate that centres with specific deferral policies for live vaccines choose 5–7 months and the length of this range, 3–11 months, belies the muddiness of the data on which this recommendation is based. Further, recent research has shown that younger blood donors have lower measles, mumps, and rubella antibodies compared to earlier generations, reducing the risk of blunted vaccine–immune response in children receiving transfusions from individuals born after 1976.[16] Research has also shown favourable response to measles, mumps, and rubella vaccination in transfusion-dependent or chronically transfused populations which introduces the possibility that children with blood product exposure due to CHD surgery may also achieve an effective immune response without a delay in administration schedule.[17]

Regarding iatrogenic, vaccine-associated fever as a reason to defer immunisations, it is worth considering the pre- and post-operative periods separately. Pre-operatively, justification for immunisation deferral due to vaccine-associated fever hinges on utilisation optimisation and reduction of patient/family inconvenience due to cancelled or delayed cases. Vaccine-associated fevers tend to last no more than 1 day, and specific immunisations are more pyrogenic than others.[18] Despite this, most centres requiring pre-operative deferral in this cohort impose a deferral of 2 weeks or longer. Avoidance of immunisation in the days immediately preceding surgery or avoidance of specific, pyrogenic immunisations may be reasonable, but given that vaccine-associated fevers should be isolated and self-limited, this may be a clear area where prolonged deferral of immunisations confers greater risk than benefit. Post-operatively, fever can raise concern for surgical site infections, endocarditis, blood stream infections, and other serious bacterial infections. Despite this, the self-limited nature of vaccine-associated fever and absence of other systemic symptoms should, in theory, make it easy to distinguish from serious aetiologies of fever. Further, laboratory testing and examination can often be sensitive to a fever secondary to viral or bacterial infection. In this light, post-operative deferral of immunisation for the sole reason of fever avoidance may also confer more harm than benefit.

Among the three primary reasons for immunisation deferral, concern related to the impact of cardiopulmonary bypass on the efficacy of immunisations and concern related to live virus immunisations after blood product transfusion has the most validity in the face of conflicting evidence. Despite some evidence supporting deferral for SARS-COV-2[8-10] and live virus imunisations,[5] the current duration of pre- and post-operative deferral at most centres is likely far longer than is needed for most immunisations. Lastly, the problem of under-immunisation is not limited to children with CHD and examining barriers to immunisation in other populations can shed light on challenges CHD patients may experience. In the general population, poverty, urbanicity, and transportation challenges have been associated with under-immunisation.[12,13] There has also been a "backslide" in immunisation rates with the COVID-19 pandemic prompting public health initiatives.[19] While each of these under-vaccination predictors has not been specifically demonstrated in the CHD population, they likely play a role. Cardiologists should consider whether their patients have these additional risks to under-vaccination, aside from CHD surgery deferral recommendations. Limitations to this study include the need to use a novel survey with analysis limited to submitted data. Additionally, this survey was only administered to PAC^3 sites, so the generalisability to non-PAC^3 organisations may be limited. However, PAC^3 represents most congenital heart centres across North America, including all centres with the largest surgical volumes. Thus, the practices described here impact a large volume of children undergoing CHD surgery in North America. Lastly, we were unable to assess for variation within centres that may not have been captured here.

Research is needed to clarify the need and duration of immunisation deferral surrounding CHD surgery. Through history, physical examination, laboratory testing, and knowledge of patterns of vaccine-associated fever,[18] fever avoidance can probably be removed as a reason to significantly defer pre- and post-operative immunisation. While immunisation is impacted by family beliefs, interaction with and access to primary care

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providers, and societal and political discussion, deferral recommendations from heart institutes contribute to lower immunisation rates among children with CHD.[1] Deferral of immunisations leaves these children vulnerable to vaccine-preventable illness and increases the likelihood they will never complete their immunisation series. Until there is more clarity, both paediatric cardiologists and paediatricians will need to be mindful of immunisation catch-up for these children.

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