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Pediatric anaphylactic adverse events following immunization in Victoria, Australia from 2007 to 2013

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ABSTRACT

Background: Anaphylaxis is a rare life-threatening adverse event following immunization (AEFI). Variability in presentation can make differentiation between anaphylaxis and other AEFI difficult. This study summarizes pediatric anaphylaxis AEFI reported to an Australian state-based passive surveillance system.
Methods: All suspected and reported pediatric (<18 years) anaphylaxis AEFI notified to SAEFVIC (Surveillance of Adverse Events Following Vaccination In the Community) Melbourne, Australia, between May 2007 to May 2013 were analyzed. Clinical descriptions of the AEFI, using the internationally recognized Brighton Collaboration case definition (BCCD) and final outcome were documented.
Results: 93% (25/27) of AEFI classified as anaphylaxis met BCCD criteria, with 36% (9/25), assessed as the highest level of diagnostic certainty (Level 1). Median age was 4.7 years (range 0.3–16.2); 48% of cases were male. The vaccine antigens administered included: diphtheria, tetanus, acellular pertussis (DTaP) alone or in combination vaccines containing other antigens in 11 of 25 cases (44%); and live attenuated measles mumps rubella (MMR) vaccine for six (five also had other vaccines concomitantly administered). The estimated incidence rate of anaphylaxis for DTaP vaccines was 0.36 cases per 100,000 doses, and 1.25 per 100,000 doses for MMR vaccines. The majority of cases had rapid onset, but in 24% (6/25) of cases, first symptoms of anaphylaxis developed ≥30 min after immunization. In 60% (15/25) of cases, symptoms resolved ≤60 min of presentation. Intramuscular adrenaline was administered in 90% (18/25) of cases. All cases made a full recovery with no sequelae identified.
Conclusion: This comprehensive case series of pediatric anaphylaxis as an AEFI identified that diagnostic criteria are useful when applied to a passive vaccine surveillance system when adequate clinical information is available. Anaphylaxis as an AEFI is rare and usually begins within 30 min of vaccination. However, healthcare professionals and vaccinees/parents should be aware that onset of anaphylaxis can be delayed beyond 30 min following immunization and that medical attention should be sought promptly if anaphylaxis is suspected.

1. Introduction

Australia has a standardized childhood National Immunisation Program (NIP) schedule approved and reviewed on a regular basis by the Australian Technical Advisory Group on Immunisation (ATAGI) and authorized by the National Health and Medical Research Council (NHMRC) [1]. It includes infant and early childhood immunization, as well as a secondary school (age 12–16 years) program for catch-up vaccines (Hepatitis B, Varicella) and new vaccines (e.g. Human papillomavirus (HPV) vaccine introduced for females in 2007; males in 2012) [2]. There are also specific special risk groups with additional vaccine requirements (e.g. Aboriginal and Torres St Islanders).

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Table 1
Case vaccination demographics.

Gender	Age at vaccine (years)	Vaccine NAME	Dose No.	BCCD level	Adrenaline administered
Male	8.7	Fluvax	1	Level 2	Y
Female	16.5	Gardasil	2	Level 2	N
Male	4.7	Infanrix-IPV, Priorix	4, 3	Level 2	Y
Female	16.0	Gardasil	3	Level 1	N
Male	4.1	Infanrix-IPV, Priorix	4, 2	Level 2	Y
Male	1.3	Varilrix	1	Level 2	Y
Female	1.0	Priorix	1	Level 2	N
Female	0.4	Infanrix Hexa, Prevenar, RotaTeq	2, 2, 2	Level 1	Y
Female	4.0	Infanrix-IPV, Priorix	4, 2	Level 1	Y
Male	13.4	H-B-Vax II Adult formulation	2	Level 2	Y
Female	12.8	H-B-Vax II Adult formulation, Gardasil	2, 3	Level 2	Y
Male	4.9	Infanrix-IPV, Priorix	4, 2	Level 2	Y
Male	8.4	Twinrix Junior (360/10), Typherix	1, 1	Level 2	Y
Female	7.7	Panvax H1N1	2	Level 2	Y
Female	10.6	Fluvax	1	Level 2	N
Male	13.1	H-B-Vax II Adult formulation	1	Level 2	Y
Female	9.4	Influvac	1	Level 2	Y
Female	1.3	Prevenar 13	4	Level 1	Y
Female	16.2	Boostrix	1	Level 2	Y
Male	0.6	Infanrix Hexa, Prevenar 13	2, 2	Level 1	N
Male	0.6	Infanrix Hexa	3	Level 1	Y
Female	15.3	Boostrix	1	Level 3	Y
Male	0.9	Vaxigrip Jr	1	Level 1	N
Female	0.3	Infanrix Hexa, Rotateq, Prevenar 13	2,2, 2	Level 1	N
Male	4.3	Infanrix-IPV, Priorix	4, 2	Level 1	Y

Table 2
BCCD symptom presentations of anaphylaxis[a].

Category	Major	Minor
Dermatological/Mucosal	Generalized urticaria/erythema Angioedema (localized/generalized) Generalized pruritus with skin rash	Generalized pruritus without skin rash Generalized prickle sensation Localized injection site urticaria Red/itchy eyes
Cardiovascular	Measured hypotension Shock (clinical diagnosis with ≥3 of tachycardia, cap refill >3 s, reduced central pulse volume, decreased level of consciousness)	Reduced peripheral circulation (≥2 tachycardia, capillary refill >3 s without hypotension, decreased level of consciousness)
Respiratory	Bilateral wheeze Stridor Upper airway swelling Respiratory distress (>2 tachypnea, accessory muscle use, recession, cyanosis, grunting)	Persistent dry cough Hoarse voice Difficulty breathing without wheeze/stridor Sensation of throat closure Sneezing/rhinorrhea
Gastrointestinal		Diarrheal Abdominal Pain Nausea Vomiting
Laboratory		Raised mast cell tryptase

[a] Adapted from Gold et al. [9].

As part of the NIP, any adverse event following immunization (AEFI) can be reported via appropriate state or territory procedures. All reports are forwarded to the centralized national body, the Therapeutic Goods Administration (TGA). Likewise, reports directly to the TGA are redirected back to SAEFVIC for local clinic follow-up and evaluation [3]. Anaphylaxis is a rare but potentially life-threatening AEFI [4], with an estimated incidence of approximately one case per million vaccine doses [5,6]. It can manifest in a wide constellation of non-specific symptoms. This variability in presentation can make it difficult to differentiate between anaphylaxis and other isolated allergic AEFI such as urticaria or angioedema [7]. Anaphylaxis is usually an immediate IgE-mediated phenomenon, requiring allergy workup including skin prick and intradermal testing and if indicated supervised vaccine challenge(s) [8] (Table 1).

The Brighton Collaboration is an internationally recognized body who developed a case definition for anaphylaxis as an AEFI (Table 1), outlining levels of diagnostic certainty (Table 2) [9]. By providing a standardized objective definition to apply to AEFI reports, it is hoped that the accuracy of reports can be verified and that standardized management across the pediatric population would prove easier to disseminate and implement.

Surveillance of Adverse Events Following Vaccination In the Community (SAFEVIC) is a passive surveillance system monitoring all AEFI across the state of Victoria, Australia. Established in May 2007, it provides specialized outpatient services for both children and adults [10]. SAEFVIC maintains a database of all reported adverse events and the follow-up details of each case. The population of Victoria, Australia, in 2013 included over 1.05 million children under 18 years of age [11].

The primary aim of this study was to accurately detail the occurrence, diagnosis and management of anaphylaxis post-immunization by applying the Brighton case definition to all reported pediatric anaphylaxis cases in the SAFEVIC database. A secondary aim was to review which vaccines were temporally associated with anaphylaxis, vaccine specific incidence rates, management strategies (e.g. use of adrenaline) and outcome.