TDAP

Adacel and BOOSTRIX

Tetanus, Diphtheria and Pertussis Vaccination

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TDAP

Tetanus, Diphtheria and Pertussis Vaccination

indication

https://www.fda.gov/media/124002/download

https://www.fda.gov/media/119862/download

- active booster immunization against tetanus, diphtheria and pertussis. Adacel is approved for use in persons 10 through 64 years of age.
- immunization during the third trimester of pregnancy to prevent pertussis in infants younger than 2 months of age.

ingredients Adacel

Each 0.5 mL dose contains 5 Lf tetanus toxoid (T), 2 Lf diphtheria toxoid (d), and acellular pertussis antigens [2.5 mcg detoxified pertussis toxin (PT), 5 mcg filamentous hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM)]. Other ingredients per 0.5 mL dose include 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, ≤5 mcg residual formaldehyde, <50 ng residual glutaraldehyde and 3.3 mg (0.6% v/v) 2-phenoxyethanol (not as a preservative). The antigens are the same as those in DAPTACEL; however, Adacel is formulated with reduced quantities of diphtheria and detoxified PT.

BOOSTRIX

Each antigen is individually adsorbed onto aluminum hydroxide. Each 0.5-mL dose is formulated to contain 5 Lf of tetanus toxoid, 2.5 Lf of diphtheria toxoid, 8 mcg of inactivated PT, 8 mcg of FHA, and 2.5 mcg of PRN (69 kiloDalton outer membrane protein).

Each 0.5-mL dose contains aluminum hydroxide as adjuvant (formulated to contain 0.3 mg aluminum) and 4.4 mg of sodium chloride. The aluminum content is measured by assay. Each dose also contains ≤100 mcg of residual formaldehyde and ≤100 mcg of polysorbate 80 (Tween 80).

Research on Aluminum Exposure During Pregnancy

https://www.ncbi.nlm.nih.gov/books/NBK597305/

Following intramuscular administration of aluminum hydroxide or aluminum phosphate vaccine adjuvants in rabbits, increased levels of ^{26}Al were found in the kidney, spleen, liver, heart, lymph nodes, and brain (in decreasing order of aluminum concentration) (Flarend et al. 1997).

There is also evidence from animal studies indicating that aluminum administered parenterally accumulates to a small extent in the milk of lactating mothers, and that aluminum crosses the placenta and accumulates in fetal tissue (Cranmer et al. 1986; Yokel and McNamara 1985; Yumoto et al. 2000). Intraperitoneal exposure of pregnant mice to aluminum chloride on gestation days 7–16 has been associated with significantly increased concentrations of aluminum in both placental and fetal tissues (Cranmer et al. 1986). Following a single subcutaneous injection of ^{26}Al on gestation day 15, 0.2 and 0.21% of the dose was detected in the placenta and fetus, respectively, 5 days after the injection (Yumoto et al. 2000). Within the fetus, the level of ^{26}Al in the brain was as high as 30% of that in the fetal liver; in contrast, the level of ^{26}Al in the brain of the dam was only 1% of the level in the liver. Intravenous, intraperitoneal, or subcutaneous exposure of lactating rats, rabbits, or mice to aluminum lactate or aluminum chloride has been associated with increased concentrations of aluminum in milk (Muller et al. 1992; Yokel and McNamara

Research on Aluminum and Autism

https://pmc.ncbi.nlm.nih.gov/articles/PMC4609793/

The increase of ASDs prevalence cannot be fully explained by advances in diagnostics or sudden genetic shifts. There is a growing consensus among scientists and clinicians that ASDs ensue from an interaction between biological vulnerability factors and environmental or iatrogenic insults [2].

This points to the importance of environmental factors and raises the possibility of an etiological role for toxic exposures: either prenatal, postnatal, or in some cumulative pattern that combines the effect of maternal, gestational, and infant exposures [3].

Genetically, children with autism may be less able to detoxify toxic environmental agents, and this inability may predispose them to suffer neural damage consistent with autistic behavioral traits [4].

Women with chronic metal exposure (who have accumulated high tissue levels of mercury and other metals) may pass potentially toxic metals to their fetuses or intoxicate infants through nursing [5].

As regards Aluminum (Al). In the current study, the mean aluminum level in the autistic patients (59.19 ± 37.98 mg/Kg) was significantly higher than that of the controls (16.78 ± 17.3198 mg/Kg) with $P = 0.0001$. This is in agreement with Tomljenovic and Shaw [34], who showed that Al, a highly neurotoxic metal and the most commonly used vaccine adjuvant, may be a significant contributing factor to the rising prevalence of ASD in the Western world.

https://pmc.ncbi.nlm.nih.gov/articles/PMC4609793/

In 2009, Blaylock and Strunecka [43] reported that aluminum causes oxidative stress within brain tissue, exacerbating the clinical presentation of autism by worsening of excitotoxicity and by microglial priming. They suggested that the heterogeneous symptoms of autism spectrum disorders have a connection with dysregulation of glutamatergic neurotransmission in the brain along with enhancement of excitatory receptor function by proinflammatory immune cytokines as the underlying pathophysiological process. In this regard, dietary excitotoxins including aluminum can exacerbate the clinical presentation by worsening of excitotoxicity and by microglial priming. This opens the discussion to the use of nutritional factors that reduce excitotoxicity and brain inflammation as a maneuver to alleviate neurotoxic effects of aluminum [44].

Biological damage from heavy metals as a neurotoxic substance beside genetic susceptibility in the form of reduced ability to excrete heavy metals and/or increased environmental exposure at key times in development may play a causal role in autism.

The above study researched multiple environmental factors including, maternal fish consumptions, living nearby gasoline stations, and the usage of aluminum pans. Levels of mercury, lead, and aluminum in the hair of autistic children were higher than controls. “Environmental exposure to these toxic heavy metals, at key times in development, may play a causal role in autism.”

Research on Prenatal TDAP Vaccination and Autism

The American Academy of Pediatrics published a study in 2018 that stated, “Prenatal Tdap vaccination was not associated with an increased ASD [Autism Spectrum Disorder] risk.” However, it must be noted the researchers disclosed potential financial conflicts of interest with GlaxoSmithKline, the manufacturer of BOOSTRIX (TDAP vaccine).

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Prenatal Tetanus, Diphtheria, Acellular Pertussis Vaccination and Autism Spectrum Disorder

https://publications.aap.org/pediatrics/article-abstract/142/3/e20180120/81652/Prenatal-Tetanus-Diphtheria-Acellular-Pertussis?

POTENTIAL CONFLICT OF INTEREST: Drs Becerra-Culqui and Tseng and Ms Sy received funding from GlaxoSmithKline for a separate study of a tetanus, diphtheria, acellular pertussis vaccine (Boostrix) during pregnancy; and Dr Getahun and Ms Chiu have indicated they have no potential conflicts of interest to disclose.

FINANCIAL DISCLOSURE: Drs Becerra-Culqui and Tseng and Ms Sy received funding from GlaxoSmithKline Biologicals for a separate study of a tetanus, diphtheria, acellular pertussis vaccine (Boostrix) during pregnancy; Dr Getahun has received research grant support from Bayer AG for unrelated studies; Drs Tseng and Getahun and Ms Sy received research funding from the Centers for Disease Control and Prevention for the Vaccine Safety Datalink project; and Ms Chiu has indicated she has no financial relationships relevant to this article to disclose.

warnings + precautions

5.2 Guillain-Barré Syndrome and Brachial Neuritis

If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the risk of Guillain-Barré syndrome may be increased following a subsequent dose of tetanus toxoid-containing vaccine, including BOOSTRIX. A review by the Institute of Medicine (IOM) found evidence for a causal relationship between receipt of tetanus toxoid and both Guillain-Barré syndrome and brachial neuritis.[1]

5.3 Progressive or Unstable Neurologic Disorders

Progressive or unstable neurologic conditions (e.g., cerebrovascular events, acute encephalopathic conditions) are reasons to defer vaccination with a pertussis-containing vaccine, including BOOSTRIX. It is not known whether administration of BOOSTRIX to persons with an unstable or progressive neurologic disorder might hasten manifestations of the disorder or affect the prognosis. Administration of BOOSTRIX to persons with an unstable or progressive neurologic disorder may result in diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination.

5.4 Arthus-Type Hypersensitivity

Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine usually have a high serum tetanus antitoxin level and should not receive BOOSTRIX or other tetanus toxoid-containing vaccines unless at least 10 years have elapsed since the last dose of tetanus toxoid-containing vaccine.

5.5 Altered Immunocompetence

As with any vaccine, if administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the expected immune response may not be obtained.

5.6 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, including BOOSTRIX. Procedures should be in place to avoid injury from fainting.

Contraindications include severe allergic reaction to any component of a diphtheria toxoid, tetanus toxoid and pertussis antigen-containing vaccine and encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous pertussis antigen-containing vaccine.

potential adverse reactions

Blood and Lymphatic System Disorders

Lymphadenitis, lymphadenopathy.

Immune System Disorders

Allergic reactions, including anaphylactic and anaphylactoid reactions.

Cardiac Disorders

Myocarditis.

General Disorders and Administration Site Conditions

Extensive swelling of the injected limb, injection site induration, injection site inflammation, injection site mass, injection site pruritus, injection site nodule, injection site warmth, injection site reaction.

Musculoskeletal and Connective Tissue Disorders

Arthralgia, back pain, myalgia.

Nervous System Disorders

Convulsions (with and without fever), encephalitis, facial palsy, loss of consciousness, paresthesia, syncope.

Skin and Subcutaneous Tissue Disorders

Angioedema, exanthem, Henoch-Schönlein purpura, rash, urticaria.

pregnancy

Available data suggest the rates of major birth defects and miscarriage in women who receive Adacel within 30 days prior to pregnancy or during pregnancy are consistent with estimated background rates. *(*See *Human Data)*

Human Data

A retrospective passive surveillance study (NCT00258882) included women who received Adacel during pregnancy (n=225) and controls (n=675) matched by age and date of first positive pregnancy test. Of the 225 Adacel recipients, 39 women received Adacel within two weeks prior to the date of their last menstrual period (LMP), 110 were vaccinated during the 1st trimester (< 12 weeks gestation), 33 during the 2nd trimester (12 to < 27 weeks gestation), 14 in 3rd trimester (11 from 27 to <36 weeks gestation and 3 from ≥36 weeks gestation), and 29 were unknown. There were 21 reports of spontaneous abortion (9.3%) and 15 congenital anomalies (6.7%) in the Adacel exposed group, and 102 spontaneous abortions (15%) and 57 congenital anomalies (8.4%) in the control group.

However, it is important to note, that the control group referenced above still received a vaccine. According to the details of the study, "Overall, 124,139 people received Tdap5 vaccine from September 2005 through mid-October 2006, and 203,154 in the comparison cohort received a tetanus and diphtheria toxoid adsorbed vaccine (and no live virus vaccine) during the year prior to initiation of this study."

https://clinicaltrials.gov/study/NCT00258882?term=NCT00258882&rank=1&tab=results

Arm/Group Title	Adacel Vaccine Group	Control Groups
Arm/Group Description	Participants who received Adacel vaccine during the study period were sub-grouped as 1) pregnant at the time of vaccination or who became pregnant within 28 days after vaccination and 2) non-pregnant recipients classified by age at vaccination.	For each pregnant individual receiving Adacel vaccine, 3 control individuals not given Adacel vaccine were matched on age and month of their first positive pregnancy test. For non-pregnant individuals, age-matched individuals were identified who received Td vaccine but no live virus vaccine during the year prior to initiation of the study during the same month as Adacel vaccine recipient, but 1 year earlier.

As an informed consumer, it's important to always understand the details of the control groups to properly assess the study's findings.

https://www.cdc.gov/pertussis/hcp/vaccine-recommendations/vaccinating-pregnant-patients.html?

Tdap can be safely administered at any point during pregnancy but CDC recommends early in the third trimester for optimal protection.

However, according to the manufacturer:

Safety data from prospective clinical studies on the use of BOOSTRIX during the first and second trimester of pregnancy are not available.

mechanism of action

Tetanus

Tetanus is a disease manifested primarily by neuromuscular dysfunction caused by a potent exotoxin released by *C tetani*.

Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assay is considered the minimum protective level. (5) (6)

Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (5) Levels of 1.0 IU/mL have been associated with long-term protection. (7)

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by *B pertussis*. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined.

Per the manufacturer, the pathogenesis (process by which a disease develops in the body) and immunity to pertussis is not clearly defined.