

## Influenza vaccination for children with asthma

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### ABSTRACT

**QUESTION** Parents of children with asthma are encouraged by many health organizations to vaccinate their children against seasonal influenza viruses. Is the influenza vaccine efficient in preventing asthma exacerbation? Are current vaccinations safe to administer to children with asthma?

**ANSWER** Infection with influenza viruses can cause substantial respiratory morbidity in children with underlying chronic disease such as asthma. Although vaccination against influenza does not reduce or shorten asthma exacerbations, the intramuscular trivalent vaccine is safe and has a beneficial effect on the quality of life of children with asthma.

### RÉSUMÉ

**QUESTION** De nombreuses organisations du secteur de la santé encouragent les parents d'enfants souffrant d'asthme à les faire vacciner contre les virus de la grippe saisonnière. Le vaccin antigrippal est-il efficace pour prévenir l'exacerbation de l'asthme? L'administration des vaccins actuels est-elle sans danger pour les enfants asthmatiques?

**RÉPONSE** L'infection au virus de la grippe peut causer une morbidité respiratoire considérable chez les enfants ayant une maladie chronique sous-jacente comme l'asthme. Bien que la vaccination contre la grippe ne puisse réduire ou raccourcir les exacerbations de l'asthme, le vaccin trivalent intramusculaire est sûr et a des effets bénéfiques sur la qualité de vie des enfants asthmatiques.

Asthma is the most common chronic disease in childhood and is one of the leading causes of hospitalization in the pediatric population.<sup>1</sup> Viral infections of the respiratory tract, including influenza, are the main causes of asthma exacerbations,<sup>2</sup> and several organizations (such as the Canadian National Advisory Committee on Immunization) advocate annual influenza vaccination for children with asthma.<sup>3</sup> Despite these recommendations, many children with asthma do not receive influenza vaccines.<sup>4</sup> One of the barriers to compliance is the uncertainty of parents and physicians about the benefits of influenza vaccination in this population and the role of immunization in preventing asthma exacerbations.<sup>5</sup>

### Influenza vaccination

Two main types of vaccines are available for the prevention of influenza: intramuscular, trivalent, inactivated vaccine and intranasal trivalent, cold-adapted, live, attenuated vaccine. Both vaccines are highly immunogenic and induce adequate immune response with a high level of seroprotection; however, their clinical effectiveness varies among seasons (owing to antigenic drift) and among age groups.<sup>6</sup> The new intranasal vaccine was shown to be more efficacious even when epidemic influenza viruses did not match the recommended vaccine antigens.<sup>7</sup> Nevertheless, safety concerns restrict the use of this vaccine in children with asthma.

### Does influenza vaccine prevent asthma exacerbations?

Infection with influenza can lead to diverse respiratory complications and might result in a substantial burden on the health system. However, influenza accounted for only 0% to 7% of viral-induced asthma exacerbations,<sup>2,8</sup> and evidence for a specific additional risk in children with asthma is lacking.

Can influenza vaccination directly reduce the number of asthma exacerbations? Studies in recent years resulted in contradictory outcomes.<sup>9-11</sup> In a retrospective cohort study during 3 consecutive influenza seasons, Kramarz et al used computerized databases of 4 large health maintenance organizations in the United States to evaluate the effectiveness of influenza vaccinations in children with asthma aged 1 to 6 years old. Unadjusted rates of asthma exacerbations were higher in the vaccinated group, and after adjustment for asthma severity and other confounding factors, the vaccine was found to reduce the risk of asthma exacerbation by 22% to 41%.<sup>9</sup> In another retrospective study in children 0 to 12 years old with asthma, a beneficial clinical effect (reduction in number of lower respiratory tract infections and acute otitis media) was identified in vaccinated preschool children.<sup>10</sup> Ong et al reported a reduction in the use of oral steroids in vaccinated children with asthma.<sup>11</sup> While these results are of interest, some limitations such as lack of adjustment for asthma severity and recall bias should be considered.

One randomized, double-blind, placebo-controlled trial conducted in the Netherlands aimed to answer the question of whether influenza vaccination was more effective than placebo in preventing asthma exacerbations. Children 6 to 18 years of age with asthma received either inactivated influenza vaccine (349 children) or placebo (347 children). The children were followed throughout influenza season, and pharyngeal swabs for detection of influenza virus were obtained during asthma exacerbations. This study failed to demonstrate a difference between the intervention and the control groups; there was no effect of influenza vaccination on the number or severity of influenza-related asthma exacerbations.<sup>12</sup> Further analysis of questionnaires and patient diaries found influenza vaccination to improve health-related quality of life, but when compared with placebo, respiratory symptoms and spirometric parameters during all seasons were similar.<sup>13</sup> Moreover, only 1.8% of all asthma exacerbations were influenza related, indicating the relatively small effect of this virus on the overall exacerbation rate in children with asthma.

## Does influenza vaccine induce asthma exacerbation?

A few reports, most anecdotal or with a small patient population, raised the concern that influenza vaccination might induce asthma exacerbation.<sup>14,15</sup> In 1998, a double-blind, placebo-controlled, crossover trial of adults with asthma demonstrated a higher rate of asthma exacerbations in the 72 hours after injection of a trivalent split-virus preparation or surface-antigen preparation compared with placebo. However, when participants with upper respiratory tract infections were excluded, there was no significant difference in the number of exacerbations between vaccine and placebo groups.<sup>16</sup> A Cochrane report reviewed several studies that aimed to assess this possible harm of vaccination; the authors concluded that the pooled results neither demonstrated any significant increase in asthma exacerbations in the 2 weeks following influenza vaccination nor any significant fall in peak expiratory flow rate, increased use of bronchodilators, or increased use of oral corticosteroids during this period.<sup>17</sup>

The most reassuring evidence comes from a double-blind, placebo-controlled trial of 1240 adults and 712 children with asthma. This study reported a similar frequency of asthma exacerbations during the 2 weeks after influenza vaccination and after placebo injection. Subgroup analysis based on severity of asthma, age, and other demographic characteristics reached the same results.<sup>18</sup>

## Safety of intranasal vaccine

The safety of live, attenuated (intranasal) vaccine was estimated in 4 large studies.<sup>19-22</sup> In an open prospective study, Fleming et al compared intranasal, live, attenuated influenza vaccine to trivalent, inactivated vaccine.

More than 2000 children with asthma aged 6 to 17 years were monitored for adverse events in the 15 days after vaccination. There was no significant difference found between the 2 groups in reported bronchospasms.<sup>19</sup> Two further studies compared intranasal with intramuscular vaccines in children 6 to 72 months old, some with a history of mild to moderate asthma.<sup>20,21</sup> The results of one study raised concerns when there was an association found between intranasal vaccine and an increase in hospital admission of children 6 to 11 months old, as well as an increase of medically significant wheezing in the first 42 days following vaccinations.<sup>21</sup> In the fourth study, children between 1.5 and 18 years old with history of intermittent wheezing received a single annual intranasal vaccination during a 4-year trial. There was no increase in health care utilization for acute respiratory illnesses during the 14 and 42 days after vaccination.<sup>22</sup> Nevertheless, until more clinical trials suggest otherwise, intranasal vaccination cannot be considered safe for children younger than 2 years of age and should be avoided in children aged 2 to 4 years with history of recurrent wheezing or older children with a diagnosis of asthma.<sup>3</sup>

## Clinical implications

Currently, evidence does not suggest that influenza vaccination reduces the number or severity of asthma exacerbations. With the other benefits of vaccination against annual influenza, children with and without asthma might benefit from the safe trivalent, inactivated vaccine in reducing common influenza-related complications. Children with asthma might also see some improvement in their quality of life.

### Competing interests

None declared

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