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How do young babies respond to a 6-in-1 vaccine when their mothers received dTpa vaccine during pregnancy?

GSK would like to thank all the babies who took part in this clinical study and their parents. We think it is important that you know the study results. We hope it helps you understand and feel proud about your important role in medical research.

Overview

Why was this study conducted?

The 6-in-1 vaccine is commonly used to immunise babies against diphtheria, tetanus, whooping cough, hepatitis B, Hib and polio. This was a study to see if responses to this vaccination were similar in babies born to:

1. mothers vaccinated against diphtheria, tetanus, whooping cough (dTpa) during their pregnancy
2. mothers not vaccinated against dTpa during their pregnancy

What was studied?

- Antibodies formed against diphtheria, tetanus, whooping cough, polio, hepatitis B and Hib.
- Vaccine safety.

Who was in this study?

- Healthy babies (285 girls and 316 boys) from Australia, Canada, Czechia, Finland, Italy, and Spain.
- Babies were 6 to 14 weeks old when they were first vaccinated in this study.

What kind of study was it?

This was a controlled study. We compared two groups of babies vaccinated with the 6-in-1 vaccine:

1) Babies of mothers vaccinated against dTpa during pregnancy (dTpa group).

2) Babies of mothers not vaccinated against dTpa during pregnancy (Control group).

Main results

After 6-in-1 vaccination:

- All babies were protected against diphtheria and tetanus.
- In both groups more than 94% of babies were protected against hepatitis B, Hib and polio.
- Antibody levels against whooping cough were lower in the dTpa group than in the Control group.
- The vaccine safety was similar in both groups (dTpa and Control) and side effects were not serious and of short duration.

NCT number: NCT02422264
EudraCT number: 2014-001117-41

General information about the research study

When was the study done?

The study started on 22-January-2016 and ended on 7-March-2018.

Why was this study done?

The study was done to find out if babies' responses to the 6-in-1 vaccine were influenced by whether their mothers received dTpa vaccination during pregnancy.

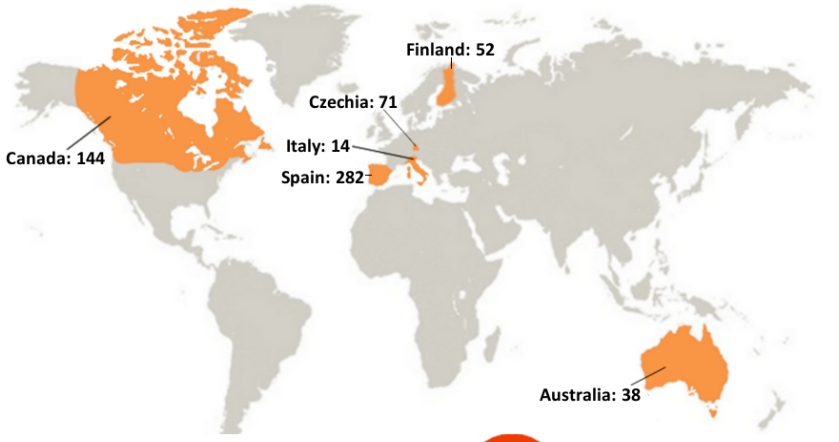
In an earlier study, researchers learnt that mothers who got the dTpa vaccine during pregnancy passed their antibodies on to their babies. But, we did not know if those antibodies would make it harder for the babies to make their own antibodies.

In this study, babies got a 6-in-1 vaccine against diseases that can lead to permanent damage or even death. The vaccine was against diphtheria, tetanus, whooping cough, hepatitis B, polio and diseases (like meningitis and pneumonia) caused by *Haemophilus influenzae* type B (Hib). This vaccine has been routinely used in babies for many years throughout the world

The babies also got a pneumonia vaccine. Antibodies against pneumonia were measured. These results are not presented here because it was not a main goal of the study. They may be found in the clinical trials summary.

Who took part in this study?

601 healthy babies
from 6 countries



6 to 14 weeks old when they got the first vaccination

285 girls (47%)
316 boys (53%)

Babies could take part in the study if they

- Were born to mothers who received dTpa vaccine during pregnancy or after delivery in a previous GSK study
- Were born within the pregnancy period of 27 to 36 weeks

Babies could not take part in the study if they

- Were not in good health
- Got previous vaccination against diphtheria, tetanus, whooping cough, polio, hepatitis B, Hib and pneumococcus

Which vaccines were studied?

In a previous study mothers of all babies received the dTpa vaccine either during pregnancy or after giving birth. All babies in this study got 2 vaccines.

- **6-in-1 vaccine**: A combination vaccine to protect against 6 infectious diseases: diphtheria, tetanus, whooping cough, hepatitis B, Hib and polio.
- **Pneumococcal vaccine**: A vaccine to protect against pneumonia.

How was the study done?

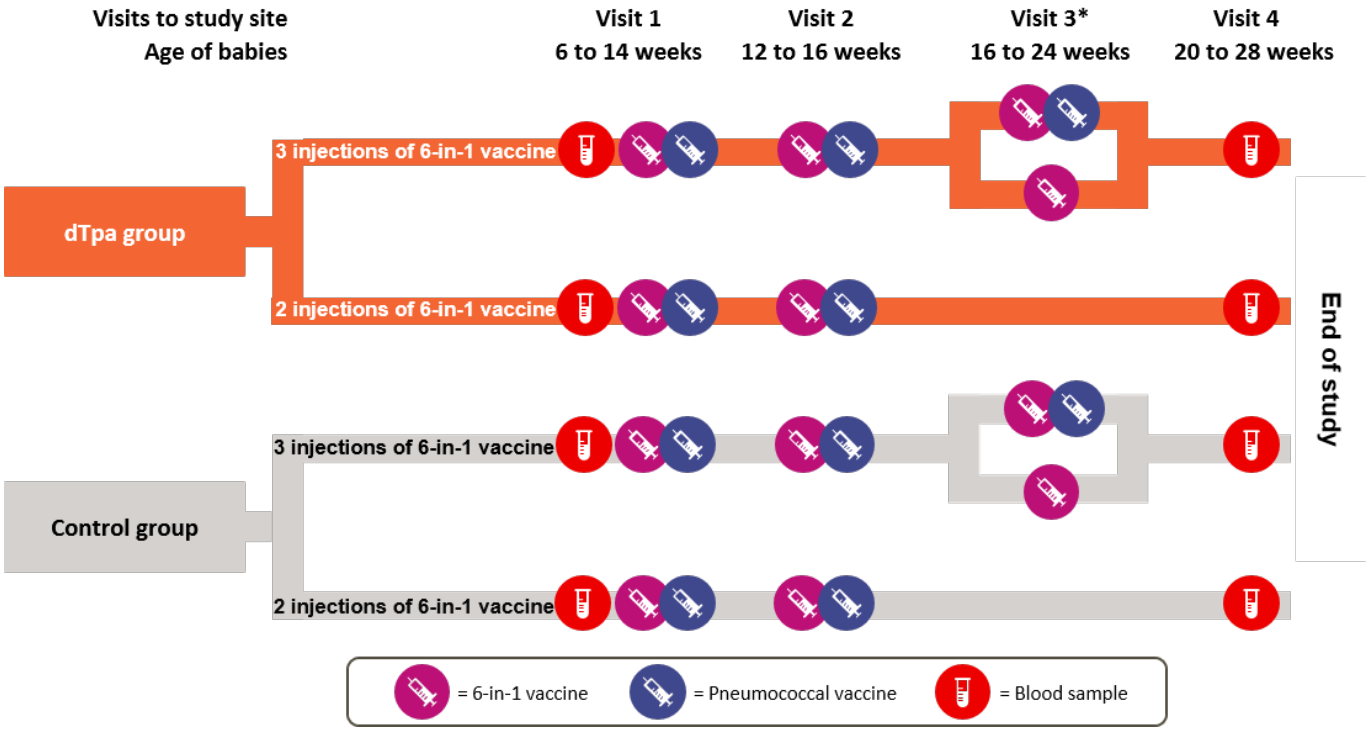
The babies were assigned to one of two study groups:

- **dTpa group:** Babies of mothers vaccinated against diphtheria, tetanus, and whooping cough **during pregnancy**.
- **Control group:** Babies of mothers vaccinated against diphtheria, tetanus, and whooping cough **after birth**.
- Babies in both groups got either 2 or 3 shots of the 6-in-1 vaccine and pneumococcal vaccine, depending on the approach in their country (**Figure 1**).

Blood samples were taken before the first and after the last vaccination. The blood samples were used to measure the amounts of antibodies.

It took about 3 to 5 months for each baby to complete the study.

Figure 1: Study design



**Babies who got 3 injections of the 6-in-1 vaccine got either 2 or 3 injections of the pneumococcal vaccine, depending on which country they were from.*

What were the main results of the study?

This summary focuses on the results of the main study goals. All results may be found in the clinical trials summary.

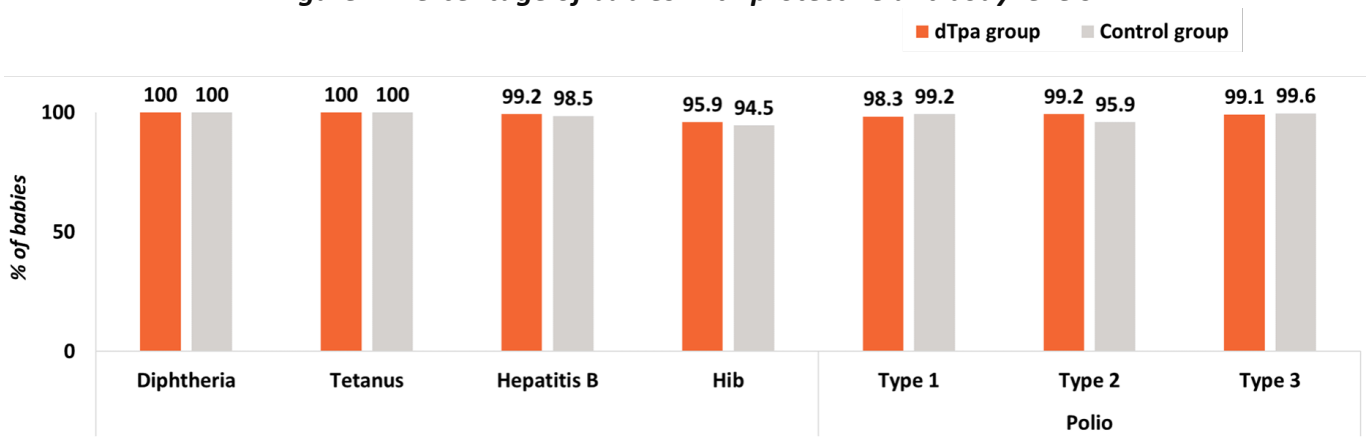
Did babies make antibodies against diphtheria, tetanus, hepatitis B, Hib, and polio?

Most people are protected against these diseases if the amounts of antibodies in their blood is above certain levels. These are called the **protective antibody levels**.

Babies' response to the 6-in-1 vaccine were studied by measuring the protective antibody levels. After the 6-in-1 vaccination (**Figure 2**):

- All babies in both groups had protective antibody levels against diphtheria and tetanus
- Almost all babies (>94%) in both groups had protective antibody levels against hepatitis B, Hib, and polio (Type 1, 2 and 3)

Figure 2: Percentage of babies with protective antibody levels



Whooping Cough

Whooping cough is different from the other diseases (above) as we do not know the protective levels of antibodies. So, we measured the amount of antibodies to assess the babies' response to vaccination.

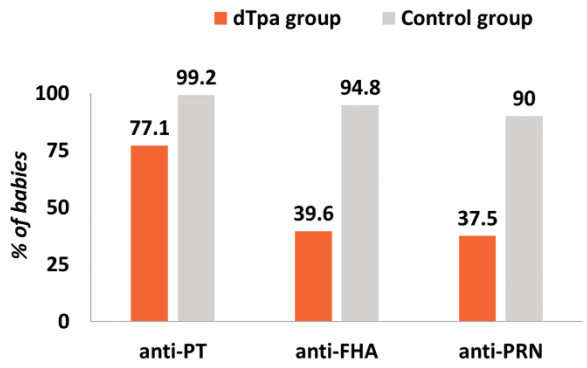
In this study, we measured 3 kinds of antibodies ('anti-PT', 'anti-FHA' and 'anti-PRN') to learn how babies respond to the vaccine against whooping cough.

What we found:

- Babies in the dTpa group had higher levels of whooping cough antibody before the vaccine than the Control group (**Figure 4**). These were the maternal antibodies that had passed from the mother to the baby.
- After they got the vaccine, babies in the dTpa group made less antibody against whooping cough than those in the Control group (**Figure 3).**
- Antibodies passed from mother to baby may reduce the babies' ability to make whooping cough antibody after the 6-in 1-vaccination (**Figure 4**).

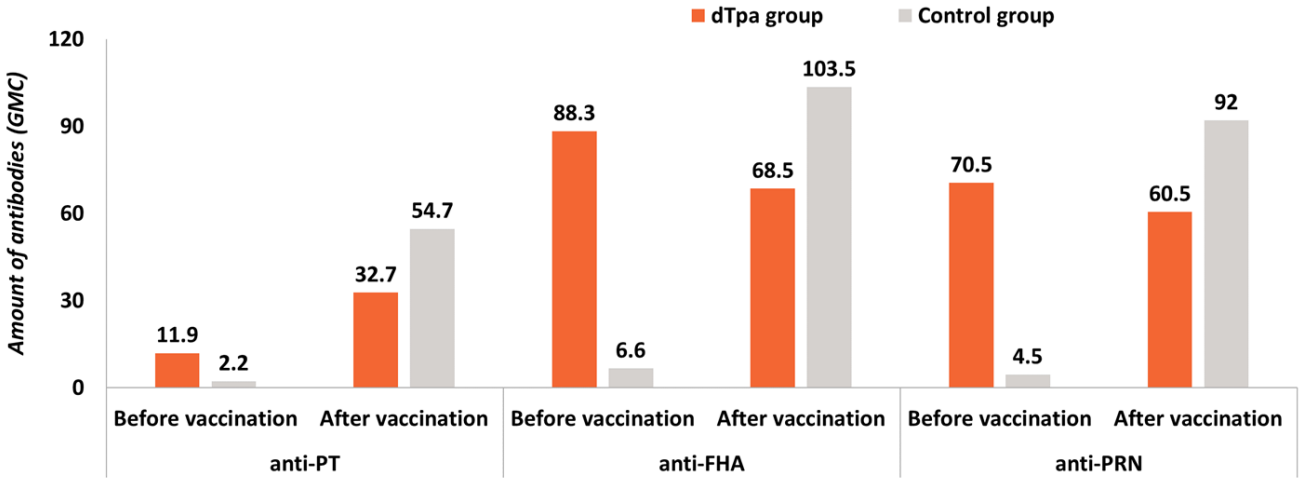
**The use of the term side effects in this summary may be different to that in the Informed Consent or other documents related to the vaccine*

Figure 3: Babies' ability to make antibodies against whooping cough



anti-PT= anti-pertussis toxoid; anti-FHA=anti-filamentous haemagglutinin; anti-PRN=anti-pertactin

Figure 4: Amounts of antibodies against whooping cough



GMC=geometric mean concentration was used for calculating the amount of antibodies
anti-PT= anti-pertussis toxoid; anti-FHA=anti-filamentous haemagglutinin; anti-PRN=anti-pertactin

What were the vaccine side effects?

Unwanted medical events (adverse events) can happen to babies when they receive a vaccine. The study doctors record all these events. A summary of all events reported in this study may be found in the clinical trials summary.

If the study doctor thinks that the event was caused by the vaccine, they record this as a possible side effect (adverse reaction). In this summary, "side effects*" refer to those events that the study doctors thought may have been caused by the study vaccine.

Figure 5 shows the side effects at the place where the vaccines were given. The 6-in-1 vaccine was given in the right thigh. The pneumococcal vaccine was given in the left thigh. Study doctors could tell the difference between vaccine side effects only at the injection sites.

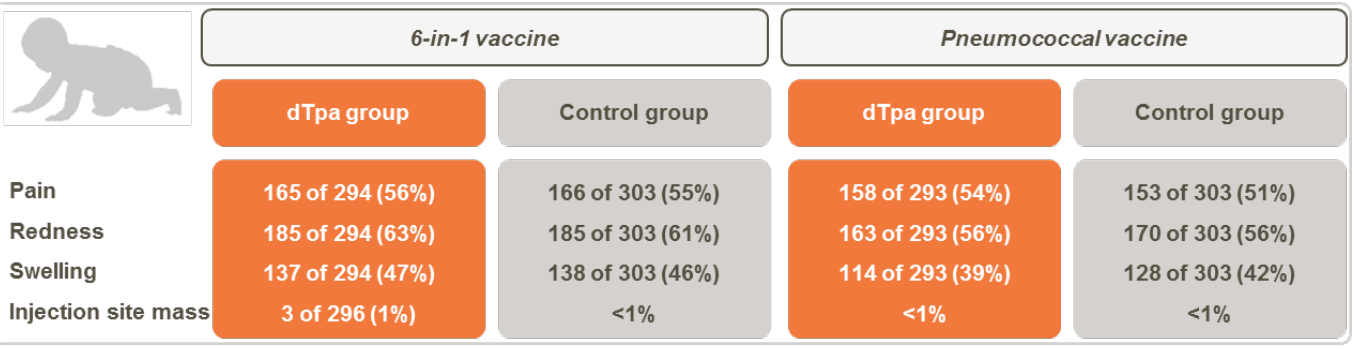
Figure 6 shows the other vaccine side effects.

**The use of the term side effects in this summary may be different to that in the Informed Consent or other documents related to the vaccine*

What we found:

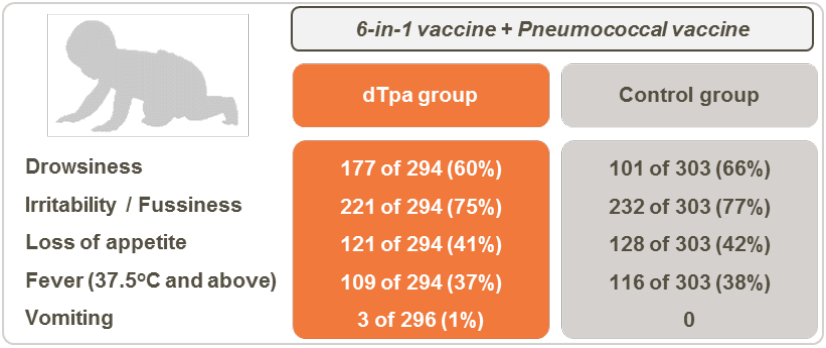
- Side effects were similar in both groups, not serious and lasted only a short time.
- The most common side effect at the injection site was redness for both vaccines (**Figure 5**).
- The most common other side effect was fussiness and irritability for both vaccines (**Figure 6**).

Figure 5: Side effects at the injection site in at least 1% of babies



	6-in-1 vaccine		*Pneumococcal vaccine*	
	dTpa group	Control group	dTpa group	Control group
Pain	165 of 294 (56%)	166 of 303 (55%)	158 of 293 (54%)	153 of 303 (51%)
Redness	185 of 294 (63%)	185 of 303 (61%)	163 of 293 (56%)	170 of 303 (56%)
Swelling	137 of 294 (47%)	138 of 303 (46%)	114 of 293 (39%)	128 of 303 (42%)
Injection site mass	3 of 296 (1%)	<1%	<1%	<1%

Figure 6: Other side effects in at least 1% of babies



	6-in-1 vaccine + Pneumococcal vaccine	
	dTpa group	Control group
Drowsiness	177 of 294 (60%)	101 of 303 (66%)
Irritability / Fussiness	221 of 294 (75%)	232 of 303 (77%)
Loss of appetite	121 of 294 (41%)	128 of 303 (42%)
Fever (37.5°C and above)	109 of 294 (37%)	116 of 303 (38%)
Vomiting	3 of 296 (1%)	0

How has this study helped patients and researchers?

This study helped researchers, doctors and parents understand that:

- Vaccinating pregnant mothers against diphtheria, tetanus and whooping cough did not affect the ability of the 6-in-1 vaccine to protect against diphtheria, tetanus, hepatitis B, Hib or polio.
- The whooping cough antibodies transferred from mothers to babies during pregnancy:
  - may protect their newborns from the moment of birth but also,
  - may reduce the babies' ability to make their own antibodies against whooping cough.
- The safety of the 6-in-1 vaccine in babies of vaccinated and non-vaccinated mothers:
  - was similar,
  - was consistent with known safety information on this vaccine.

Are there plans for further studies?

The parents of babies who took part in this study were asked if their child could participate in another follow-up study. If parents give their permission, the babies will be given another shot of the same 6-in-1 vaccine.

Where can I find more information about this study?

The detailed title for this research study is:

A phase IV, open-label, non-randomized, multicenter study to assess the immunogenicity and safety of *Infanrix hexa* administered as primary vaccination in healthy infants born to mothers given *Boostrix* during pregnancy or post-delivery in 116945 [DTPA (BOOSTRIX)-047].

Clinical studies have unique study numbers. Below are the unique study numbers associated with this study.

Organization	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2014-001117-41
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02422264

Your doctor can help you understand more about this study and the results. You should not make changes to your care based on the results of this or any single study.

This document provides a short summary of this study for a general audience. You can find more information in scientific summaries of the study. Links to those summaries are provided at the end of this document.

This document was developed and approved by GSK on 22-May-2019. The information in this summary does not include additional information available after this date.

For readers of this document in text form, the websites associated with the hyperlinks above are:

EudraCT summary:
https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-001117-41

US NIH/clinicaltrials.gov:
https://clinicaltrials.gov/ct2/show/NCT02422264

For the previous study, the website associated with the hyperlink above is:

US NIH/clinicaltrials.gov:
https://clinicaltrials.gov/ct2/show/NCT02377349