

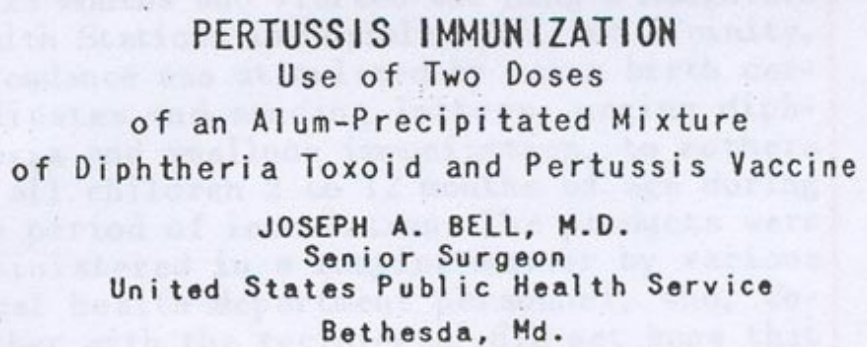
## Records

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**Bell JA (1948c).** Use of two doses of an alum-precipitated mixture of diphtheria toxoid and pertussis vaccine. JAMA 137:1276-1281.

### Key passages



PERTUSSIS IMMUNIZATION  
Use of Two Doses  
of an Alum-Precipitated Mixture  
of Diphtheria Toxoid and Pertussis Vaccine  
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## MATERIALS

The mixed product used in this study was prepared by mixing 2 parts of crude diphtheria toxoid with 1 part of a pertussis vaccine suspension. The mixture was then precipitated with alum, washed twice and resuspended in isotonic sodium chloride solution. The unmixed product was prepared at the same time, using the same lot of toxoid. It was prepared in an identical manner except that 1 part of isotonic sodium chloride solution was added to the toxoid prior to precipitation instead of adding the pertussis vaccine. Thus, the mixed and unmixed products were identical in every respect except that each dose of the mixed product contained 10,000,000,000 killed *H. pertussis* organisms and the unmixed product contained no pertussis vaccine. The two products were packaged in twenty-dose vials, and each vial was labeled "A-P diphtheria toxoid." The vials were identical in appearance except that each had a different code number, consisting of three digits. In 1941 Dr. J. P. Leake selected the code numbers from Tippett's "Random Sampling Numbers"<sup>7</sup> and placed them on the vials, so that the sum of the first two digits was odd when the vial contained the mixed product and the sum was even when the vial contained the unmixed product. The contents of the vials could be determined only by the code numbers, and during the observation period this code was unknown to the author and the visiting nurses.

## PROCEDURES

The use of two, the mixed and unmixed, products permitted a study arrangement which approaches an epidemiologist's ideal. All of the children received one or the other product, and no one concerned knew which product was given. The products were given from January 1942 to June 1943 to children aged 2 to 23 months who visited the King's Daughters Health Stations in Norfolk; Va., and vicinity. Attendance was stimulated by using birth certificates and sending letters, urging diphtheria and smallpox immunization, to mothers of all children 2 to 12 months of age during the period of inoculation. The products were administered in a routine manner by various local health department personnel, who, together with the recipients, did not know that pertussis vaccine was involved in the study. The personnel gave to each child the product from a vial designated by certain lay persons who had no other connection with the study and who also did not know that pertussis vaccine was involved. The recipients were told that a study of communicable diseases, including diphtheria, was being made and that the children would receive a Schick test one year after immunization to assure their protection against diphtheria. By use of the code numbers on the vials, all children who were born in an odd month (as January, March, May) were to receive the mixed product and children born in an even month (as February, April, June) were to receive the unmixed product. All children who received one or more doses of the study products were under observation from the date of the injection to March 1, 1947, unless they left the study area or otherwise could not be located. Most of the children were under observation since birth. Two full time public health nurses, specially trained in communicable diseases, made routine monthly home visits and made weekly or more frequent visits during the occurrence of communicable

disease in the household. They made records of the clinical symptoms and signs of such diseases and of all known and suspected attributes which might influence the occurrence of such diseases. The nurses worked under my close supervision, and I made household visits as necessary to check the records and to establish diagnoses. Dr. Leake made these visits and conducted the study from July 1943 to July 1945, when I was on overseas duty. To prevent Dr. Leake from knowing which product a child had received, he was given the age rather than the birth date of the children visited and the vial number indicating the product given was concealed with gummed paper. As a minimum, Dr. Leake or I made at least one household visit whenever a study child or any member of his family household had definite or suspicious symptoms of clinical pertussis. The criteria for diagnosis<sup>8</sup> of a definite case of pertussis were the same as that used in another study.<sup>9</sup> Neither the author nor the nurse observers knew that the month of birth determined what product a child was to receive. Throughout the observation period none of the observers knew which child received which product, which child belonged to which group or whether any one child received the same product as any other child. This assured uniform observation and treatment of all children in both groups. This further assured that the two groups, which were comparable at the time the injection was given, would remain comparable throughout the period of observation. There was no way in which the household informants or the investigators could possibly bias the observations in favor of either group and no possible way for them to destroy the comparability of the test and control groups.