

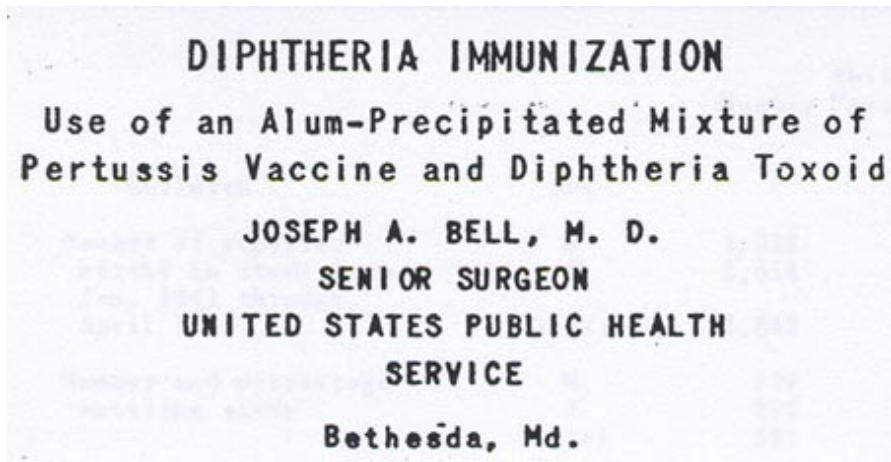
Records

[Key Passage\(s\)](#) [JLL Article\(s\)](#) [Portrait\(s\)](#) [Context](#)

[Download key passages/title pages as a PDF](#)

Bell JA (1948b). Use of an alum-precipitated mixture of pertussis vaccine and diphtheria toxoid. JAMA 137:1009-1016.

Key passages



FUNDAMENTAL CRITERIA FOR STUDY

To answer the foregoing questions on diphtheria immunity, it was predetermined that the following fundamental criteria would be essential for an adequate and fully controlled clinical trial of the mixed product. The criteria are listed as outlined in 1941 and all have been meticulously adhered to throughout the study.

(a) An alum-precipitated mixed or test product and an alum-precipitated unmixed or control product must be prepared so that each dose of each product contains the same quantity of alum-precipitated diphtheria toxoid from the same lot of crude toxoid. The test and control products must be prepared so that each will be identical in all respects except that each dose of the alum-precipitated diphtheria toxoid in the mixed product will contain 10,000,000,000 killed *Hemophilus pertussis* organisms.

(b) A study group of children must be preselected so as to be an adequate and representative sample of young children in a sizable United States community who are routinely available for voluntary immunizations. This is essential so that the results of the study may safely be projected to reflect the results expected from general use of the study products.

(c) A predetermined strictly random sampling procedure, based on a simple attribute entirely unrelated to immunologic phenomena, must be used to divide the study children into a test and a control group. This is essential to insure that all known and unknown

attributes which might influence the occurrence of diphtheria or pertussis immunity (aside from the study products given) would be distributed between the two groups as equally as possible within the range of chance sampling variation.

(d) No person other than the visiting nurse observers and the physicians conducting the study should know that a study of pertussis vaccine is involved, and neither the nurses nor the physicians should know which child belonged to the test or control group, or which child received which study product, or whether any one child received the same product as any other child. This is essential to neutralize any possible human bias on the part of observers or informants in the recognition of immunologic phenomena. This is also essential to maintenance of the test and control groups as strictly

random samples of the combined groups throughout the period of observation. When no one knows that pertussis vaccine has been given to any of the study children, no disproportionate treatment can be given to either of the random groups and all known and unknown attributes will have a nearly equal influence on each group; e.g., a nearly equal proportion of each group will receive pertussis vaccine by private physicians, and a nearly equal proportion of each group will depend on immunization rather than shielding their child from exposures to pertussis and other diseases.

(c) An intensive effort must be made to see that two doses of the test or control product are given to each study child as selected by the predetermined sampling process, that the products be given with a four-week interval between doses to children in the age band 2 to 23 months and that the products be given without inquiry or regard to a prior history of pertussis or pertussis vaccination. All children who receive at least one dose of the study product must be placed under uniform and routine monthly observation as long as they remain in the study area by one of the two specially trained public health nurses.

(f) A controlled Schick test is to be used as an index of diphtheria immunity, and a single lot of Schick toxin is to be used throughout the study, providing tests on animals indicate its potency is maintained. An intensive effort must be made to give Schick tests to all children remaining under observation one year after receiving the study products and simultaneously to give Schick tests to the mothers of such children. All disease diagnoses must be made, and all Schick reactions read and classified by me or by Dr. J. P. Leake.