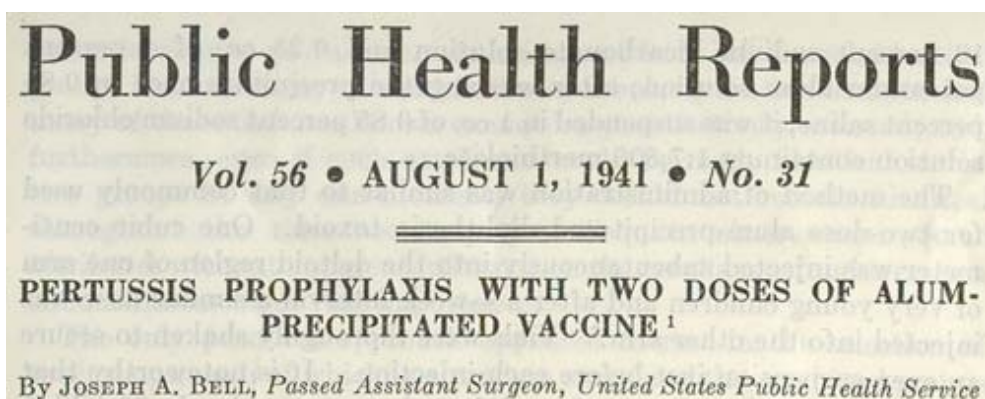


Bell JA (1941). Pertussis prophylaxis with two doses of alum-precipitated vaccine. Public Health Reports 56:1535-1546.

Key passages



The single question to be answered by this report is whether the vaccine confers any real protection against the disease. Since the public health aspect of the disease is of chief concern, it was necessary that the observed children be representative of the general population. To answer the question it was necessary to have a clinical-epidemiological arrangement whereby a large group of children injected with the vaccine could be uniformly observed together with a group of children not injected with the vaccine but otherwise identical in all attributes which might influence the results. Three major problems were immediately evident: (1) The obtaining of an injected group identical in such attributes with a noninjected group; (2) the uniform observation of injected and noninjected groups over a period of time long enough to give an adequate experience of pertussis; and (3) the definition of pertussis as a clinical entity which, within the limits of observation available, could be uniformly and readily recognized in the injected and noninjected groups.

The first problem was that of locating for observation a group of children to be vaccinated, identical, in all attributes which might influence the occurrence and recognition of pertussis, with another

group to receive no vaccine. It is impossible to select such identical groups because many of the attributes involved are not known, and many of those that are known cannot be quantitatively assessed; and, furthermore, even if such attributes could be made identical in the two groups at any one moment, they would not remain identical throughout the time necessary for adequate observation. Some attributes without apparent influence on the results may under certain circumstances be of real importance.

The only practical approach appeared to rest in the selection of two groups, each of which is a random sample of the combined groups in the exact sense of the term. Thus only can the prediction be made that should the vaccine have no real influence on the occurrence of pertussis, the occurrence in each group will approximate that of the combined group, deviating therefrom strictly within the range of chance sampling variation. On the other hand, if the vaccine confers real protection against the disease, or otherwise really influences its occurrence, the occurrence in each group will differ from that of the combined group outside the range of chance sampling variation. Obviously it is not practically possible to preselect two large strictly random groups of children who are representative of the general population and to insure that every child in one group receives the vaccine while every child in the other group receives no vaccine during the observation period. Children in the general population have the prerogative to refuse vaccine offered and the liberty to obtain other vaccine when desired. In these premises there is no known way of changing the two groups so that one would include only children actually vaccinated, and the other include only children not vaccinated, without destroying the randomness of the selection and to that extent possibly invalidating the answer to the question asked. After it has been established that the vaccine confers protection, then questions concerning the amount and duration of such protection might in part demand direct comparison of the experience of the children actually vaccinated with those not vaccinated, providing adequate data are at hand to equalize the two groups with respect to attributes which apparently influence the occurrence of the disease.

For this report, the approach to the primary problem involved the preselection of two large strictly random groups of children and the subsequent injection of a large proportion of only one group with the vaccine. All analyses herein presented are a comparison of the experience of such preselected groups regardless of their actual status with respect to receiving the vaccine. The difficulties encountered in this approach are chronologically described in detail so that the reader may evaluate any possible errors involved.

During March, April, and May, 1938, a public health nurse transcribed the names of children born between May 1, 1935, and March

31, 1938, who were on the various rolls of the King's Daughters Visiting Nurse Association. All of the names were not transcribed. Children whose records indicated that they had had prior whooping cough, children who were known to have left the city permanently, and a few of the children of well-to-do parents who, the nurse thought, were subject to pertussis vaccination apart from that given in the course of this study, were not transcribed.

The city of Norfolk, adjacent suburbs, and South Norfolk were divided into 14 geographic sections. The definition of boundaries of each section was the result of an endeavor to group people somewhat according to their usual association in schools, churches, theaters, and shopping districts. The children in each section are either white or colored, no one section having both.

A total of 1,954 names was transcribed, together with information as to sex, birth date, and address of residence, as recorded on the rolls from which they were copied. The names were transcribed in 14 groups according to geographic section of residence. In each group the names were listed in alphabetical order for each year of birth and the years of birth were ordered chronologically. A numbering machine was used to stamp a serial number after each name in the above order. Using the "Random Sampling Numbers" as assembled and published by L. H. C. Tippett (2), the allotted numbers in each section were divided at random into two equal groups hereinafter designated as the "V" and "N" groups.

The nurses did not know which of the children were in the "V" or "N" group and made every reasonable effort to avoid knowing which of the children had received pertussis vaccine. Of course, informants not infrequently would invite the nurses' attention to children supposed to have received the vaccine, but little credence was given to such information because some parents were obviously confused between pertussis and diphtheria injections.

A consulting pediatrician was employed to examine many of the cases and suspected cases of pertussis and to make a written report especially noting other diseases which might influence severity or obscure diagnosis. He did not know what criteria the author used for the diagnosis of clinical pertussis, and his report was not submitted until the end of the observation period here reviewed; he did not have access to the nurses' records and his opinions were not made known to them during the course of the study.⁴ The author also made at least one visit with the nurse to every case of suspected pertussis, evaluated symptoms elicited, and arrived at a conclusion with respect to diagnosis. This was done entirely independently of the consulting pediatrician, and, like him, without knowledge of whether the child had had pertussis vaccine or had been selected in the "V" or "N" group.