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BCG VACCINATION

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NOTE

*Authors alone are responsible for views
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COLLABORATORS

The investigations were undertaken under the joint auspices of the International Tuberculosis Campaign, the Danish Statens Seruminstitut, and the WHO Tuberculosis Research Office. The Tuberculosis Research Office was responsible for the planning and execution of the field programme, and the Statens Seruminstitut prepared and supplied the vaccine and tuberculin used and carried out the supplementary laboratory work. The salaries of the field personnel and their expenses were paid by the International Tuberculosis Campaign and later by the United Nations International Children's Emergency Fund.

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INTRODUCTION

This report describes an adventure in international research, planned to meet an international need and carried through with the help of health authorities, doctors, and laymen in many lands.

Tuberculosis constantly threatens the health and lives of peoples throughout the world, especially in areas with scanty medical resources. Because immediate full control of this disease is out of the question, hopes of prevention on a large scale have become centered on vaccination with BCG ; and during the past few years millions of people have been tuberculin-tested and vaccinated in vast international campaigns sponsored and directed by international health agencies—at first the International Tuberculosis Campaign (ITC) * and later the World Health Organization and the United Nations International Children's Emergency Fund.

Yet much remains to be learned about BCG vaccination. Despite laboratory evidence that it protects animals against virulent infection, and limited studies suggesting that it may also protect man, when the mass campaigns were started in the fall of 1947 there was little precise information about the vaccine itself, its variability, its keeping qualities, how it should be applied, and particularly its immediate and long-term effects. Nor was it known whether the methods used in Scandinavia and adopted for the campaigns could be applied indiscriminately to peoples in other parts of the world. It was therefore no surprise when serious problems were brought forward at the Conference on European BCG Programmes, September 1949—a meeting of national and international leaders of the mass-vaccination campaigns directed by the International Tuberculosis Campaign. One of the most serious problems was the unexplained failure, in some areas, of vaccination to induce what was deemed to be sufficient tuberculin allergy. The conference discussed possible causes—over-aged vaccine, inadequate refrigeration of stored vaccine, poor vaccination technique, and so on—but it soon became clear that the answer to this question (and to more fundamental questions concerning the production and evaluation of BCG-induced allergy) would not be found by discussion. The urgent need for scientifically controlled investigations on BCG vaccine and vaccination could no longer be denied.

Facilities for such research were at hand in Denmark ; and WHO, through its Tuberculosis Research Office (TRO), in collaboration with the

* The International Tuberculosis Campaign, or "Joint Enterprise" as it was known in the official agreements, was created by the United Nations International Children's Emergency Fund, the Danish Red Cross, the Norwegian Relief for Europe, and the Swedish Red Cross, for the purpose of assisting national governments in conducting mass BCG-vaccination.

Danish Statens Seruminstitut and the International Tuberculosis Campaign, agreed to conduct an intensive investigation of basic problems of tuberculosis immunization, with special reference to BCG. The Statens Serum-institut, through its BCG section, offered to prepare the vaccine and carry out laboratory work. The ITC headquarters office in Copenhagen provided the necessary link between the every-day field problems in the international mass campaigns on the one hand, and the research programme on the other. The field work was readily integrated with the large-scale tuberculin testing and vaccination of Danish schoolchildren which was already in progress. Finally, the medical-statistical staff of TRO undertook to plan, co-ordinate, and direct the field research.

The programme has included short-term investigations of immediate practical problems arising in the field, together with more basic studies of the response of man to BCG vaccine. It is generally assumed that satisfactory vaccine properly injected will give rise to a good "take" at the site of vaccination and fairly long-continued tuberculin allergy. This implies not necessarily that allergy and immunity are closely related, but that an allergic person, compared with a non-allergic person, will react more promptly and strongly to contact with the infecting bacterium or its products, and so localize the infection more quickly and effectively—a response that may be important in the development of immunity. In the absence of a clear understanding—or even a yardstick—of immunity to tuberculosis, tuberculin allergy has been taken as the guide, however imperfect, to the effectiveness of BCG vaccination. The present world-wide programme of BCG vaccination underlines the need to learn more about tuberculin allergy and to improve the method of its measurement; and therefore in our work much emphasis has been placed on the study of post-vaccination tuberculin allergy. The local reaction at the vaccination site has also been carefully studied; the usefulness of these observations in children is not yet known, but it should be remembered that the potency of the vaccine is assessed by the local reaction in guinea-pigs.

Since this investigation has been done in schoolchildren, it has certain limitations. First, the groups studied were composed largely of children aged 7-14 years. From one point of view this is a distinct advantage, because it is with children of this age that most mass-vaccination campaigns are chiefly concerned. On the other hand, we have no experience with pre-school children; and there is reason to believe that the response to vaccination, particularly at the site of injection, may be different in the younger age-groups. Secondly, most of the studies were carried out in Danish children vaccinated with Danish vaccine; and work in other countries and with other vaccines indicates that the research programme must be extended racially and geographically to elucidate the different patterns of response among different peoples. A third, and possibly the most

important, limitation is the absence of an unvaccinated control-group. Such a group could not be formed within the framework of the school arrangements ; and we have thereby lost an important control for several of the questions investigated.

This monograph sets out the work done during the first three years of the research programme, from November 1949 to September 1952. More than 40,000 schoolchildren in four different countries have been tuberculin-tested before vaccination, and over half of them have been vaccinated in 27 separate studies dealing with different vaccines and techniques. Tuberculin tests have been done, and the reactions at the site of vaccination examined, 6-12 weeks after vaccination in all studies, one year after vaccination in 20 studies, and two years after vaccination in 8 studies. Complete quantitative data for all of the tests and examinations, constituting a "source book" for ourselves and others working in this field, are given in tabular form as appendices. From these basic tables, we have selected material, grouped according to the subject under investigation, and prepared chapters illustrating and summarizing the findings that we regard as the most interesting and significant. (Not all of the material is reviewed in these chapters, which, however, include references to the appropriate "source" tables.) Some of the findings must be viewed as preliminary and the conclusions as tentative, pending further investigation. But many of the results are, we believe, based on solid foundations : some studies have been repeated so frequently and with such consistent findings as to warrant valid conclusions, even though often they are not in accord with prevalent views about BCG.

* * *

Since the end of the late world war there has been a quickening awareness among the family of nations that technical aid to underdeveloped countries, by promoting their well-being and thereby contributing to world peace, is not only a proper but a vital concern of the United Nations and its specialized agencies. Already, however, experience has shown that what is practicable in one country or region may not suit others with different environmental, economic, or social conditions. To apply the lessons learned in one area to a different people in a far land may require research extending beyond national or even continental boundaries, and for this the ordinary research institutions were not constituted and are not equipped. The investigation reported in this monograph illustrates a way in which a worldwide medical problem may be approached by co-ordinated international research.
