For a quarter of a century the APHA has had a group of committees looking into the problems of producing, judging, evaluating the safety and determining the optimum regimen for the use of products employed to create immunity against diseases such as diphtheria, whooping cough, and others. The record of this group is presented here, and it makes clear the important contributions to which it has given rise.

HISTORY OF THE ANTIGEN COMMITTEES OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

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IN 1936, over a quarter of a century ago, the Subcommittee on Evaluation of Administrative Practices of the American Public Health Association under the Committee on Administrative Practices established a group of subcommittees, each of which had responsibility for a communicable disease. Among these committees were three which were primarily concerned with problems in active immunization. We have arbitrarily called these the antigen committees. One was the Diphtheria Committee, largely established through the efforts of Henry Vaughan at the instigation of V. K. Volk. The others were a Whooping Cough Committee and a Scarlet Fever Committee. All committees had the benefit of the encouragement and guidance of Haven Emerson, who had a clear vision of their potential value.

The committees were established because public health administrators had unanswered problems related to immunization, and because diphtheria, pertussis, and scarlet fever were causing great concern to the public health worker. Table 1 contrasts the prevalence of these diseases in 1936-1938 versus 1961-1962 and explains the degree of interest in them in the decade 1930-1940. The data also emphasize the subsequent progress made in the prevention of diphtheria and pertussis.

In diphtheria, the major question was: Among the available antigens—toxin-antitoxin, fluid toxoid, and alum-precipitated toxoid—which was the best from the public health standpoint? The preferred antigen having been selected, the next problem was the determination of optimal dosage and the preferred interval between injections; and, finally, was a booster injection desirable and, if so, what should it be and when should it be given?

In pertussis, there was the need for sound, well-controlled data on the value of pertussis immunization. This was a particularly difficult field because there was no adequate test for the individual's immunity. Also, there was much work to be done to answer the questions: What is a satisfactory pertussis antigen?

Table 1

Number of Reported Cases, USA	1938[1]	1961[2]
Diphtheria	30,508	617
Pertussis	227,319	11,648
Scarlet fever including streptococcal sore throat	198,037	338,410
Number of Deaths, USA	**1936[3]**	**1962[4]**
Diphtheria	3,065	41
Pertussis	2,666	83
Scarlet fever including streptococcal sore throat	2,493 (scarlet fever only)	102

How can it be tested to know that it is satisfactory? What strains should be used, and how does one maintain the strains to make sure they will give a good antigen?

In scarlet fever, the important question hinged on the public health value of the five-injection procedure in current use for protection against scarlet fever.

The committees went to work, obtained answers, and established procedures which became public health routine for years.

The Diphtheria Committee

There was great interest in problems of diphtheria immunization in 1936. Sessions on diphtheria immunization were held at APHA meetings for the the five years preceding 1936 and were very well-attended. There were so many unanswered questions on choice of antigens, optimum dosage, intervals between dosages, use of a booster injection, and the affect of age of the individual on each of the above, that the Diphtheria Committee was established largely through the efforts of Volk, Vaughan, and Emerson. D. T. Fraser was chairman; other members were W. T. Harrison, G. F. McGinnes, W. H. Park, M. V. Veldee, and V. K. Volk. In 1937, W. E. Bunney was added; in 1938, J. A. Doull, M. V. Frobisher, W. Frost, D. G. Gill, and K. Maxcy; in 1939, J. T. Tripp; in 1941, A. G. Gilliam, W. Grossman, E. L. Stebbins; in 1942, F. A. Calderone; and in 1944, Erich Seligman. The Diphtheria Committee began a series of studies which was carried on without interruption until 1952, when it was absorbed by the Multiple Antigen Committee. All studies were designed to discern the optimum regimen for the use of diphtheria antigens in the prevention of diphtheria from the public health standpoint, as well as from that of the individual being immunized.

Saginaw County, Mich., was selected for studies designed to answer questions on the choice of diphtheria antigens and their optimum use. These studies were recommended to the Subcommittee on Evaluation of Administrative Practices by the Diphtheria Immunization Committee, and they were approved. Financing was undertaken by the American Public Health Association, the W. K. Kellogg Foundation, the U. S. Public Health Service, the Michigan Department of Health, and the Saginaw County Department of Health. Meetings of the Diphtheria Committee, besides those held at APHA conventions in 1936 and subsequent years, were held in 1936 in Battle Creek and Saginaw, Mich. From 1936 to 1943 four papers were presented before the American Public Health conventions, and were subsequently published in the American Journal of Public Health.[5-8]

As a result of these studies, the Diphtheria Committee was asked to recommend to the APHA practices for diphtheria immunization. This was done, the recommendations were approved by the Governing Council, and subsequently published.[9] The recommendations were for the use of two injections of alum-

precipitated diphtheria toxoid or three doses of fluid diphtheria toxoid, at four-week or one-month intervals in children nine months to ten years of age, with a half-dose booster injection for previously immunized children on entering school. The use of one dose of alum-precipitated toxoid was suggested only in communities where two doses were impracticable. After ten years of age, fluid toxoid or toxin-antitoxin was recommended. The discontinuance of two doses of fluid toxoid was advised.

The Whooping Cough Committee

The Subcommittee on Pertussis informally started at the time of the field studies on active immunization against pertussis, carried on in Grand Rapids, Mich., by Kendrick, et al. With the publication in 1936 of a Progress Report,[10] the Pertussis Study Group of the Michigan Department of Health Laboratories, Grand Rapids Division, consisting of Kendrick, Eldering, et al., were invited to discuss their current results with the Subcommittee on the Evaluation of Administrative Practices, and were later named as a Pertussis Study Group of the subcommittee. In naming the Whooping Cough Committee, the subcommittee stated that J. A. Doull, Pearl Kendrick, and G. McL. Lawson were already working on problems of immunization against whooping cough. They suggested that N. H. Becker, F. L. Kelly, and J. J. Miller consider problems particularly related to diagnosis. Subsequently, Grace Eldering and D. T. Fraser served on the committee.

At that time, there was particular interest in trying to explain the discrepancies in results of several different field trials of pertussis vaccine. At the request of the Subcommittee on the Evaluation of Administrative Practices, Wade Frost agreed to review the data upon which the progress report had been based. After going to Grand Rapids for this purpose, he recommended a statistical analysis. To make this possible, the Subcommittee on Evaluation of Administrative Practices obtained funds for a statistician and a clerk. The resulting final report of the first field trial in Grand Rapids was made in 1939,[11] and the evidence presented for protection due to vaccination supported the results of the progress report. Subsequent reports[12,13] gave additional evidence.

In 1942, the Pertussis Study Group of the Subcommittee on Evaluation of Administrative Practices recognized that pertussis vaccine prepared and administered under conditions defined for particular field studies had been shown to confer substantial protection against whooping cough. However, wide use of pertussis vaccine could be advocated by the subcommittee only when it became possible to define a satisfactory product according to recognized standards rather than merely in terms of a manufacturing procedure. In planning for further research, therefore, the study group emphasized the immediate need for investigation of suitable methods for testing potency of particular lots of pertussis vaccine, and outlined a study to be carried out in the Michigan Department of Health Laboratory in Grand Rapids. First, a comparison was to be made among interested laboratories of the densities of bacterial suspensions as a basis for subsequent work. This was to be followed by a study of antigenicity of different lots of vaccine in terms of animal protection, with the hope of laying a foundation for a practical potency test.

Financial assistance was requested and in March, 1943, a fund of over $2,000 was available in the office of the American Public Health Association through contributions of seven member firms of the Biologic Section of the American Drug Manufacturing Association, following a plan developed by Bun-

ney. Sponsored by the subcommittee, and with this financial assistance, the proposed study was started in Grand Rapids.

A year later, a report on comparative tests of the density of bacterial suspensions submitted by the cooperating laboratories (including direct counts and photometric readings) was made to the subcommittee. Also, preliminary results with active and passive protection tests were reported; they concerned the choice of animals, route of injection, dosage, and the like, in relation to a possible potency test.

In the fall of 1944, a report of a second series of comparative density determinations was made to the committee. There was much closer agreement among laboratories than in the first series, and most of the preparations stimulated good agglutination titers in rabbits. Preliminary results were given with mouse protection tests in which the intracerebral route was used for challenge infection.

After discussion of these results with the subcommittee and with the members of the Biologic Section of the American Drug Manufacturers Association during the American Public Health Association meeting in New York in the fall of 1944, it was decided to determine as soon as possible whether or not results of the mouse protection tests were reproducible in different laboratories. Funds were continued and, with the cooperation of the manufacturing laboratories and with the participation of the National Institutes of Health, a comparative series of tests was organized and carried to completion during 1945. Surprisingly comparable results by the various laboratories were summarized in a report to the Subcommittee on Evaluation of Administrative Practices and to the Biologic Section of the American Drug Manufacturing Association at their spring meeting in 1946, together with the results of protection tests in which different cultures of H. pertussis had been used as antigens.[14,15]

During this same year, 1946, the National Institutes of Health sent out to manufacturing laboratories a tentative outline of procedure for a potency test on essentially the same lines, and further comparative tests were not undertaken by the study group.

With continued financial aid, the Pertussis Study Group, during 1947, turned to the question of choosing antigenic cultures for vaccines; they studied the virulence and agglutinative properties of cultures in relation to antigenicity; and also the protective properties of certain antisera. During the next year, 1948, an investigation was started on cross protection among pertussis, parapertussis, and bronchiseptica cultures.[16] In the experimental work of the next few years, there was emphasis on testing the effect of certain technical procedures and conditions on the antigenicity and stability of pertussis vaccine.[17] Previous experiments with vaccines prepared from growth on Bordet-Gengou medium were extended to include fluid medium vaccines.

An interesting development was the collaborative work with the Whooping Cough Immunization Committee of the Medical Research Council of Great Britain. At their request, Kendrick of the study group was sent to England by the World Health Organization to review with them their procedures in current field trials in comparison with those of the Grand Rapids studies. Arrangements were made to use a reference vaccine to be prepared by the Michigan Department of Health Laboratories for comparison with their own preparations in further trials. Also it was decided to run mouse protection tests on all lots of vaccine used in their trials—in England, in the National Institutes of Health, and in the Michigan Department of Health Laboratories. The volume of comparative data they obtained

on the correlation of the protective value of many different lots of vaccine—in children by field trial, and in mice by laboratory tests—gave the required basis for establishing the validity of the mouse potency test for pertussis vaccine.

Also, under WHO, Kendrick assisted in plans for immunization programs in Colombia, Chile, and Brazil, and subsequently with financial support provided by the Pan American Sanitary Bureau, arrangements were made for lots of vaccine prepared in South America for use in WHO programs to be tested in the Michigan Department of Health Laboratories.

A natural outgrowth of the investigative work has been the accumulation of a large stock of smooth strains of Bordetella (Haemophilus) pertussis, from which laboratories have been supplied on request.

The Scarlet Fever Committee

The Scarlet Fever Committee, established in 1936 by the Committee on Evaluation of Administrative Procedures, consisted of G. W. Anderson, secretary; J. P. Koehler; G. H. Ramsay; and M. V. Veldee, referee. D. T. Fraser and Francis Blake were added in 1938.

The committee was organized to determine what if any materials and methods prepared for the active or passive artificial immunization against scarlet fever could be recommended as safe and effective means for controlling scarlet fever. The committee was given $3,500 from a Kellogg Foundation grant.

In December, 1937, the Scarlet Fever Committee reported[18] that the five-injection procedures then in use had no possibility of causing scarlet fever in active form, but that the combined reactions following the injection not infrequently approach and in some instances may exceed those accompanying an average attack of scarlet fever. They also reported that the five injections rendered 90 per cent of the individuals Dick negative and that the negative phase endured. They reported that epidemiological evidence indicated that the method affords satisfactory protection against the disease for at least three years. Their final conclusion was that the number of injections were too many and the cost of administration excessive over that desirable in a satisfactory immunizing procedure. In 1939, the committee recommended[19] that further studies be postponed until the state of antigenic substances for immunization against scarlet fever reached a more practicable stage.

In 1946, Franklin Top reported[20] that the Scarlet Fever Committee was resuming on a broadened scope covering hemolytic streptococcus infections and not just scarlet fever. A conference was held on this subject on November 6 and 7, 1950, at the Harvard School of Public Health, and the conclusions of the group were included in the 7th edition of "Control of Communicable Diseases in Man."[21]

The Multiple Antigen Committee

In 1942, combined diphtheria and pertussis antigens were used by Kendrick, Eldering, and others, and found to be at least as effective and perhaps superior to the antigens given separately.[22] The immunization workers and the biologic industry became interested in the potentialities of multiple antigen immunizations and W. E. Bunney, vice-president of E. R. Squibb & Sons, requested V. K. Volk, of Saginaw, to undertake a five-year study of multiple antigen immunization containing the following antigens: diphtheria, tetanus, pertussis, typhoid fever, and scarlet fever.

When the need for such a study was established, the Saginaw Multiple Antigen Study Advisory Committee was se-

lected, and this committee met on numerous occasions and guided the study from its inception in 1943 to its completion in the year 1950. The members of the committee were:

Franklin H. Top, M.D., chairman
W. L. Bradford, M.D.
T. M. Kopps, M.D.
Philip M. Stimson, M.D.
F. S. Leeder, M.D.
J. A. Toomey, M.D.
Milton V. Veldee, M.D.
V. K. Volk, M.D., Secretary
W. E. Bunney, Ph.D., special adviser

Meanwhile, in 1943, the American Public Health Association, again through the Committee on Administrative Practices, established a Multiple Antigen Committee composed of the following:

W. E. Bunney, Ph.D.
V. K. Volk, M.D.
Franklin H. Top, M.D.
Donald T. Fraser, M.D.
Milton V. Veldee, M.D.
Pearl Kendrick, Sc.D.
Haven Emerson, M.D., consultant

The purpose of the Multiple Antigen Committee was to explore the feasibility of multiple antigens. Was a multiple antigen practical? Would it immunize as well, better, or worse than the individual antigens given separately? Was it safe? What was the proper dosage and the proper interval between the doses? Would a booster injection be effective and what should the booster injection be and when should it be given? Answers were obtained that established another procedure which has become routine in public health in the United States. The work of this committee is still continuing, although the name of the committee was changed in 1962 to "The Technical Committee on Immunization," as being more descriptive of its scope of responsibility.

The Multiple Antigen Committee of the American Public Health Association had annual meetings during the APHA conventions, reviewed progress reports, and approved for publication several studies dealing with multiple antigens. These studies resulted in the presentation of several reports before the APHA Annual Meeting.[23-27]

It was established that multiple antigen preparations were safe, and finally that a booster injection of a multiple antigen preparation is a very effective reimmunizing agent.

Since most of the questions on diphtheria immunization were answered, except on the effectiveness of diphtheria antigen as one component in a multiple antigen preparation, the Diphtheria Committee, at its own suggestion, was abolished in 1952 as an entity and was combined with that of the Multiple Antigen Committee. Prior to that time, the Diphtheria Committee had been active over a period of 16 years.

Reorganized Committee on Multiple Antigens

The Pertussis Committee had been transferred from the Subcommittee on Administrative Practices to Research and Standards in 1949. In 1954, the activities of the Multiple Antigen Committee were combined with those of Pertussis and the reorganized committee expanded to cover the progressively widening interests of the group. To the original members of the Multiple Antigen Group of Bunney, Top, and Volk, and the Pertussis Study Group—Eldering, Fraser, and Kendrick—were added Johannes Ipsen and Gordon Brown, and by 1956 also William Bradford, Geoffrey Edsall, and Roderick Murray. By 1959, additional members included H. D. Anderson, R. Gottshall, R. Wilson, and A. Langmuir. In addition, the current membership includes C. D. Barrett, Jr., R. Serfling, D. A. Henderson, G. A. Hottle, and Charles Cockburn of WHO, Geneva. The chairmen of this committee have been Pearl Kendrick (1954-1958); Johannes Ipsen (1959);

W. E. Bunney (1960), continuing. The committee now works under the name Technical Committee on Immunization and has had its home in the Epidemiology Section of the Association since 1959.

An unusual degree of continuity of effort has been achieved by the committee because some of the members have worked and planned together from the time the special projects committees were established as working groups in 1936. As an example, in 1955 the committee became concerned with the question whether or not children given multiple antigens before starting school or soon after starting school would have an immune status that adequately would respond to a booster injection of a multiple antigen 7 to 12 years later when the children reached college or draft age. The committee agreed that the answer could perhaps be found in a follow-up study of several thousand children inoculated in Saginaw between 1943 and 1950. The selection of Saginaw as a place for a study was especially desirable because the original study titration records were still intact, were very complete, and because, in addition to the free-living individuals, part of the original group was still available as a captive group in state institutions.

This study was started in 1955, has been reported in four papers to date,[28-31] and is still in the process of investigation. The studies resulted in additional knowledge on the duration of immunity and resulted in some important information on the need for, and the timing of, booster injections.

While these studies were in progress, members of the Multiple Antigen Committee became interested in some other aspects of immunization, particularly in polio immunization.[32,33] In 1958, a study on multiple antigen-containing polio vaccine was undertaken by members of the committee and it has been reviewed by the committee annually. The report of the study on Polio Immunization in Early Infancy[34] is of particular significance because the committee is also interested in determining whether or not immunization is being initiated too early and if there is too much interference with the antigenic processes through the presence of maternal antibodies.[35] The committee also has been studying immunization reports of other workers in the field and had several meetings with C. D. Barrett, author of the Quadrigen Study, in Detroit. Barrett also presented the first paper on the subject of Quadrigen Immunization before the APHA Committee.

In October-November, 1962, five members of the committee, Bunney, Volk, Kendrick, Brown, and Hottle, served as an Exchange Delegation on Immunology to the USSR.

Conclusion

We think there are two comments worth making. The first is to point out that it is possible for a group of persons with diverse backgrounds but common interests to work productively together over a 25-year span. The second and more important comment is that the productivity of these committees points up the fact that perhaps here is a unique tool in public health, one which may not be possible anywhere else except in an organization such as the American Public Health Association. A committee like the Technical Committee on Immunization, made up of a health officer, epidemiologists, immunologists, those skilled in the manufacture of the products used, those expert in the titration of antigenic response, laboratory and clinical research scientists, a biostatistician, and an administrator of the governmental control of products used in immunization, has proved to be a productive committee over a long period.

We think it worth while to point out that bringing these varied talents, abilities, interests, skills, and resources to bear on planning studies, evaluating them in progress, interpretation of the results, and in effecting collaboration between local and international groups, are unique and valuable tools in forwarding the progress of public health. It is for this reason that we emphasize the accomplishments of these committees. Their work is available in dozens of papers in the scientific literature, but an over-all perspective may not be readily apparent to present and future leaders of the American Public Health Association, and we believe that fact justifies this report. Finally, we would like again to give recognition to the foresight and guidance of such men as Drs. Henry Vaughan and Haven Emerson.

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Postgraduate Course in Preventive Dentistry

A short course in "Preventive Dentistry" will be offered October 25-29 by the U. S. Army Institute of Dental Research, Walter Reed Army Medical Center. The course director will be Lt. Colonel James Cassidy, chief of the institute's Division of Preventive Dentistry.

The purpose and scope of the course will be to stimulate dentists to develop and implement preventive dental health programs in order to reduce the incidence of dental disease and prevent the loss of teeth. A comprehensive review will be presented of dental health problems of the Army, preventive dentistry aspects of clinical dental practice, and technics of personal and oral hygiene.

In addition, the course will stress the importance of preventive dental practices by the clinician, the importance of oral hygiene discipline for commanders and for the individual soldier. Seminars on the preventive aspects of peridontics, prosthodontics, oral surgery, restorative dentistry, endodontics, and dental research will be conducted.

Enrollment is open to Dental Corps officers of the Federal Services on active duty, Reserve and National Guard officers not on active duty, and to qualified civilians. Officers on active duty must have six months remaining to serve in order to qualify for "inservice" training. There is no tuition fee.

For further details write to: Director, U. S. Army Institute of Dental Research, Walter Reed Army Medical Center, Washington, D. C. 20012.