

George W. Comstock, MD, DrPH



Recipient of the 2003 Maxwell Finland Award
for Scientific Achievement



There must be few living individuals who have made a greater impact on tuberculosis—one of the oldest known and one of the most prevalent infections of human beings—than has George W. Comstock, M.D., Dr.P.H., this year's recipient of the Maxwell Finland Award for Scientific Achievement.

For almost 60 years Dr. Comstock has devoted himself to the control of tuberculosis. "His thoughtful, carefully organized and meticulously conducted research has formed the basis for the modern epidemiologic control of tuberculosis. His work has left a major mark on one of the most important infections in the history of mankind," says Dr. Richard Chaisson, director of the Center for Tuberculosis Research at Johns Hopkins University School of Medicine.

Dr. Comstock's studies in Muscogee County, Georgia provided new data on the incidence of tuberculosis and the risk of reactivation of the disease as well as a critical evaluation of the use of vaccination with the bacillus of Calmette and Guérin (BCG), information that remains useful today half a century later. In pioneering studies among the Alaskan native population he

demonstrated the proper use of isoniazid preventive therapy in containing epidemic tuberculosis.

His careful and thorough studies led to a revision of the national guidelines on the use of isoniazid in tuberculosis prevention and have influenced approaches regarding the use of BCG vaccination world-wide.

After graduating from Harvard Medical School in 1941, Dr. Comstock joined the Public Health Service. While serving an internship at the PHS Hospital in Baltimore there was a call for doctors to care for those working on the Alaska highway. "I'd always wanted to go to Alaska so I volunteered," said Dr. Comstock. "Instead they sent me to Miami." He was assigned to the US Coast Guard Infirmary there.

Dr. Comstock recalls that Miami during wartime wasn't a very pleasant place. So, acting on a tip that those who went to the course on tropical medicine at Walter Reed got sent to the South Pacific, "I said to myself, I'll volunteer for the course and they won't know where I'm asking to go. Instead, I was sent to sea duty in the Atlantic. I've never volunteered for anything since."

After the war Dr. Comstock was assigned to the then newly created division of tuberculosis control. While a medical student he had worked for two summers at a tuberculosis sanatorium, but whether this was a factor in his assignment to the tuberculosis control division or whether it was pure chance he says he has no idea. "But it got me into tuberculosis and as it turned out it was probably the luckiest day of my life. At that time the division of tuberculosis control was an exceptionally vital organization and it was new so there were lots of opportunities," he notes.

After assignments in Cleveland, Ohio and in Richmond, Virginia where he served as acting director of

the Tuberculosis Outpatient Services in the Virginia State Health Department, in 1946 Dr. Comstock became director of the Muscogee County Tuberculosis Study in Columbus, Georgia. The major purpose of the study was to evaluate the role of mass chest x-ray surveys in controlling tuberculosis. The data from these trials provided information on the incidence of tuberculosis among tuberculosis reactors and the risks of reactivation among persons with inactive tuberculosis.

In addition to the x-ray survey, from 1947 to 1950 Dr. Comstock and his associates conducted controlled trials of BCG vaccination in two locations. One was in Muscogee County, Georgia and the other in Russell County, Alabama. There were about 64,000 volunteers over the age of five years who had satisfactory skin tests with purified protein derivative of tuberculin and whose chest films showed no pulmonary abnormalities. Approximately half of the non-reactors were vaccinated with a strain of BCG.

Subsequently, in the journal *Public Health Reports*, Dr. Comstock and his associates reported that there were 36 cases of tuberculosis among the controls and 32 among the vaccinated group. The fact that so little tuberculosis developed among those eligible for vaccination, along with the finding that the vaccine causes false positive tuberculin reactions and that the vaccine gave little protection were major considerations against BCG vaccination in the United States, said Dr. Comstock.

According to Dr. Chaisson, this was a pivotal study which showed that BCG vaccination had low efficacy in the United States and contributed virtually nothing to tuberculosis control. Furthermore, the use of BCG results in a positive tuberculin skin test, making epidemiologic

investigation of the disease ineffective. Nevertheless, BCG is included in the World Health Organisation's Expanded Programme of Immunization. Only two countries, the Netherlands and the US, do not recommend vaccination of children with BCG. Dr. Comstock has a typically modest comment: "I guess I've had some influence in keeping us from using it on everybody."

"Of course we were never sure that BCG had any potency anyway," Dr. Comstock adds. "There's been a lot of misunderstandings there. In the first place there is no such thing as BCG, there are many BCG vaccines. That's one thing that has to be understood. Some have been very effective, some have been ineffective, and some might even have been harmful. So there's a wide range.

"Secondly, I'm not against BCG vaccination per se. I am just against using it where it's not indicated, where its use would be counter productive, which has been the case in this country for 50 years. I think we've been far better off for that. This is not to say that there isn't a place where I would be advising its use. It all depends on the infection rate in the population."

In 1956 Dr. Comstock finally realized his ambition to go to Alaska. He had gone to Johns Hopkins to, as he says, "write up the research we had done in Georgia." At the time the Public Health Service was starting an ambulatory chemotherapy program in Alaska because there were so many TB cases.

"I soon found that the tuberculosis problem in Alaska was absolutely unbelievable. In fact they didn't believe me when I came back and told them about it," Dr. Comstock recalls. In the 1920's and 1930's about one in every three native Alaskans died of tuberculosis, and the tuberculosis rate was 12 times that of

Alaskan whites. In 1950 nearly 90% of 10-year-olds were infected with tuberculosis. In 1952, when the tuberculosis rate in Alaska was first tallied, it was nearly 400 cases per 100,000 persons. Among Alaskan natives it was 1854 cases per 100,000, according to the Centers for Diseases Control and Prevention.

By the time Dr. Comstock went to Alaska the Public Health Service had already started several major trials with isoniazid. So, he says, "this seemed like an opportunity to try this agent on a community-wide basis and in a community where tuberculosis was just unbelievably rampant."

On the basis of a placebo-controlled trial of isoniazid in 22 Alaskan communities that resulted in a 70% reduction in the risk of developing tuberculosis, Dr. Comstock introduced isoniazid treatment to the entire Alaskan native population in the original 22 study villages. Over the next seven years, tuberculosis infection rates in children fell by more than 90%, and the incidence of the disease in the population dropped significantly.

His work showed that, to be optimally effective, the duration of isoniazid therapy should be given for nine months, resolving a major controversy about the duration of isoniazid preventive therapy. "It has turned out to be one of the major programs to have had an effect on public health policy about dealing with tuberculosis," said Dr Comstock.

"To be sure", he says, "preventive therapy helps, but you have to give a lot of credit to treatment. In fact at one time one out of every 30 native Alaskans was in a tuberculosis hospital. That involves an almost unheard of expenditure. You have to credit the Alaska health department for getting the treatment program

going, not to mention the cooperation of the population and to the Public Health Service for providing the resources. It was one of the greatest triumphs the Federal government has ever accomplished in combating disease," says Dr. Comstock.

After retiring from the PHS in 1962, Dr. Comstock became director of the Training Center for Public Health Research in the Johns Hopkins Bloomberg School of Public Health in Hagerstown, Maryland. Dr Comstock says that, along with tuberculosis, "I've dabbled in a bit of everything else." From 1979 to 1988 he was editor of the American Journal of Epidemiology. He has applied his expertise to population-based studies of cardiovascular disease and cancer. "Here in Washington County it's mostly looking for biomarkers and risk factors for cancer," he says. "The epidemiology of disease often gives clues as to how it might be tackled effectively. When you know where and how much, this gives you a tip on where to put the most effective effort. Epidemiology is still the fundamental discipline of public health."

