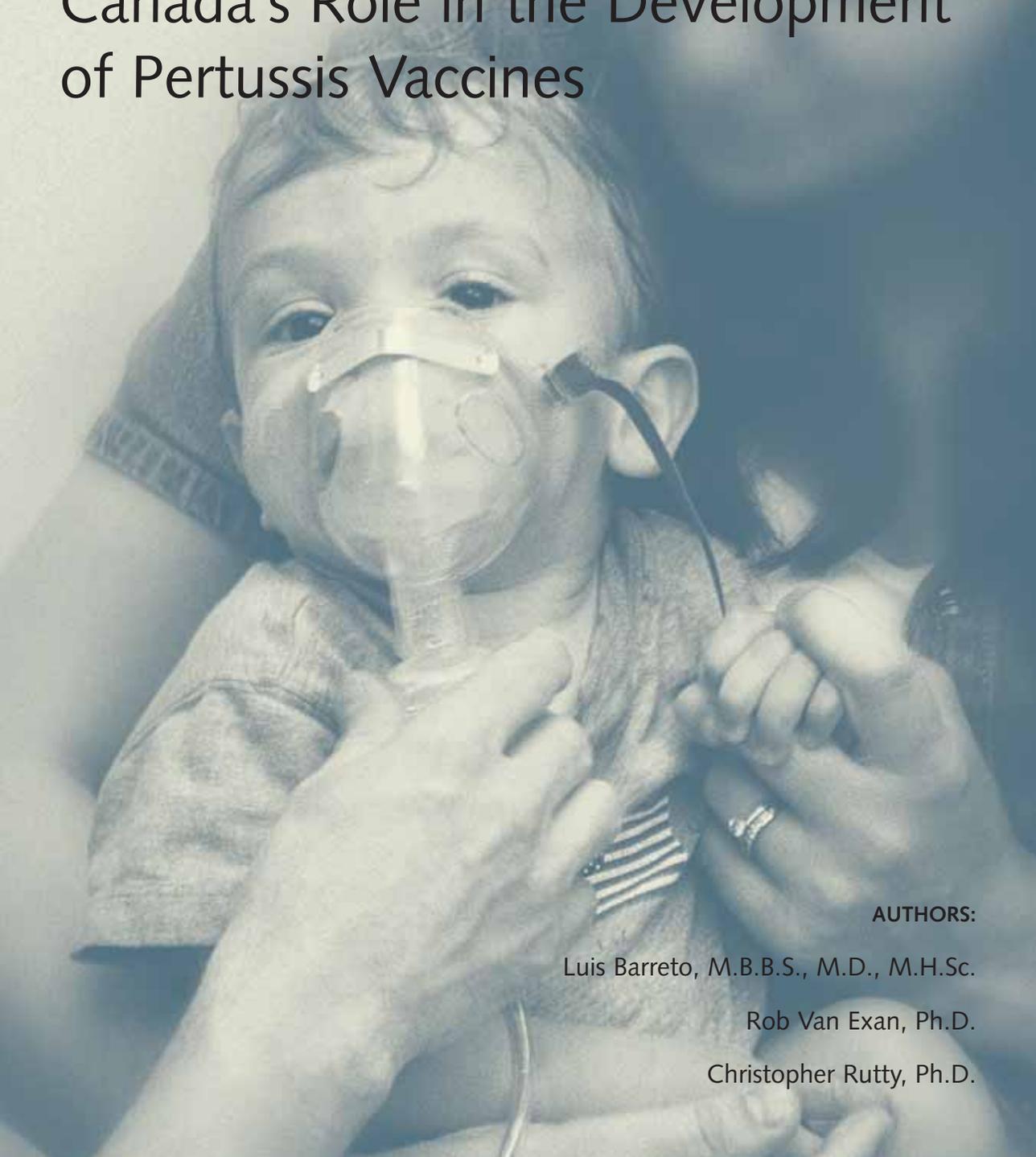


The Challenge of Whooping Cough:

Canada's Role in the Development
of Pertussis Vaccines



AUTHORS:

Luis Barreto, M.B.B.S., M.D., M.H.Sc.

Rob Van Exan, Ph.D.

Christopher Rutty, Ph.D.

Early Battles Against Pertussis

Pertussis, commonly known as “whooping cough,” is a stubborn respiratory infection. It is often debilitating and can be deadly in infants and young children. By the early 20th century, pertussis was a major public health concern, challenging scientists and public health leaders in Canada to develop an effective vaccine.

1900s - 1920s



1906

PERTUSSIS BACTERIUM DISCOVERED

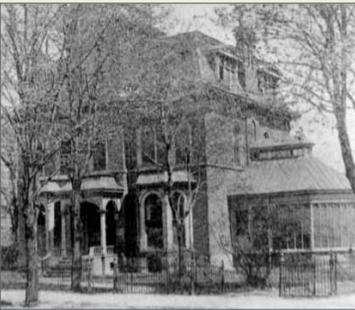
Bordetella pertussis – the bacterium that causes whooping cough – was first isolated by Belgian bacteriologists **Jules Bordet** and Octave Gengou.



1910s

EARLY PRODUCTION

The first pertussis vaccines were prepared from standard strains of *B. pertussis*, grown on a solid medium in petri dishes, collected and then inactivated.



1918

FIRST CANADIAN PERTUSSIS VACCINE

Canada's first domestic supply of pertussis vaccine was prepared and distributed by the Ontario Board of Health Laboratory.



CONNAUGHT ANTITOXIN LABORATORIES
UNIVERSITY OF TORONTO
Established for research investigation in Preventive Medicine and for the production and distribution of all Public Health Biological Products at Minimum Prices.

SERVICE TO THE EMPIRE

<p>VACCINES For Prevention</p> <p>SMALLPOX TYPHOID FEVER WHOOING COUGH HYDROPHOBIA</p>		<p>SERUMS For Prevention or Cure of</p> <p>DIPHThERIA LOCK JAW (TETANUS) PNEUMONIA (CERTAIN CASES) EPIDEMIC MENINGITIS</p>
---	--	---

This map shows the success of the effort to prepare and distribute these life-saving products at minimum prices.
BY THE UNIVERSITY OF TORONTO.

1926

MADE IN CANADA

The University of Toronto's Connaught Laboratories began to supply Canadian public health departments with a standard strain pertussis vaccine, under the direction of **Dr. Donald T. Fraser**. Connaught also exported this pertussis vaccine.

1920s

PERSISTENT PERTUSSIS PROBLEM

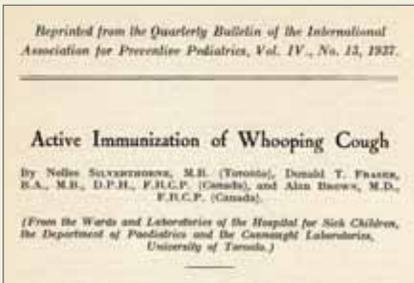
Pertussis caused more illness and deaths among young children than diphtheria, measles or scarlet fever. A better vaccine was needed.

A "Fresh" Generation of Pertussis Vaccine

During the 1930s, Canadian researchers at Connaught Laboratories (known today as sanofi pasteur) developed a more effective "fresh" strain pertussis vaccine.

Connaught scientists maintained this global lead in pertussis vaccine development, constantly improving and refining production technologies.

1930s - 1940s



1930s

CANADIAN PERTUSSIS VACCINE PIONEER

At his clinical practice at the Hospital for Sick Children in Toronto, **Dr. Nelles Silverthorne** began collecting fresh samples of the pertussis bacterium on cough plates from his young patients with whooping cough. Working as a Senior Research Fellow at Connaught Laboratories, Silverthorne and colleagues then developed a whole-cell pertussis vaccine based on the fresh strains of *B. pertussis* he collected.



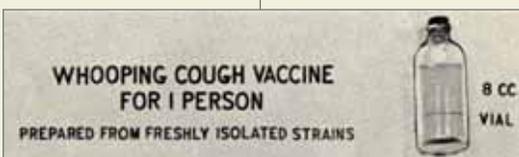
HOSPITAL FOR SICK CHILDREN



1936 - 1937

CONNAUGHT LAUNCHES NEW PERTUSSIS VACCINE

Connaught's fresh strain pertussis vaccine was a major step forward in the fight against whooping cough. National distribution of the vaccine began through provincial public health departments across Canada.



IMPROVED LARGE-SCALE PRODUCTION

In a quest to develop a more efficient method for pertussis vaccine production, Connaught's Dr. Robert J. Wilson began experiments based on a fluid culture medium, known as Hornibrook's. **Dr. Leone Farrell** and Dr. Edith Taylor next focused on developing a larger scale production method, using the liquid Hornibrook medium in a rocking bottle apparatus. In the early 1950s, Dr. Farrell would further adapt this method to make Salk polio vaccine production possible.



Combination Vaccines: Canada Leads the Way

Starting in the 1940s, Connaught Laboratories and Canadian public health officials led the way in combination vaccines, minimizing childhood injections and streamlining immunization programs. Combination vaccines led to high vaccination rates and a dramatic decline in disease incidence.

1940s - 1990s

1941 - 1959

CANADIAN LEADERSHIP IN COMBINED VACCINES

The introduction of pertussis vaccine created a new challenge – an extra course of childhood needles. Under the leadership of **Dr. Robert J. Wilson**, Connaught combined pertussis vaccine with the well-established diphtheria toxoid (DP) to protect children against both diseases at the same time. By the mid-1940s, simultaneous protection against tetanus was also possible with DPT. After the introduction of Salk polio vaccine, Connaught developed a new generation of combined vaccines, known as DPT-Polio, DT-Polio and T-Polio.



1950s - 1980s

PRODUCTION PROGRESS

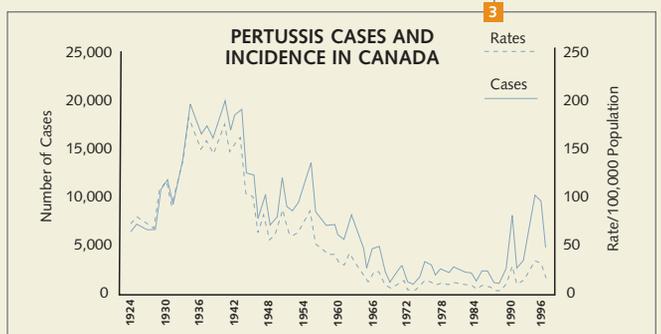
Under the leadership of Drs R.J. Wilson, **J.M. Corkill** and **Dennis Stainer**, Connaught researchers further improved pertussis vaccine production quantity and quality. Shifting to more efficient fermentors was a critical advance, as was the development of a purely synthetic nutrient medium for cultivating the pertussis bacterium; Connaught's "Stainer-Scholte" medium quickly became the global standard for pertussis vaccine production by the early 1970s.



1992 - 1994

NEW COMBINATIONS WITH HIB VACCINE

A new conjugate vaccine for *Haemophilus influenzae* type b (Hib - the leading cause of meningitis in infants and children) was introduced in the early 1990s. Connaught integrated this new vaccine with its line of paediatric pertussis combinations DPT-Hib and PENTA (DPT-Polio-Hib). These combination vaccines led to high immunization rates and a dramatic decline in disease, particularly Hib.

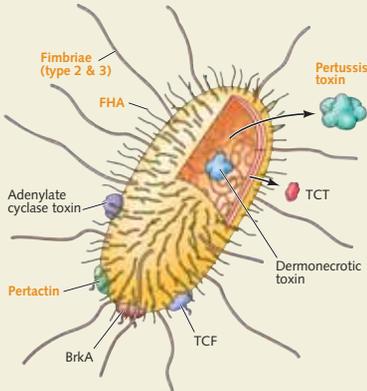


Component Pertussis Vaccine: "The Gold Standard"

Researchers at Connaught developed the world's first five-component acellular pertussis vaccine. Since its licensing in 1996, this Canadian vaccine has become the international gold standard for pertussis prevention, and is the foundation of sanofi pasteur's paediatric combination vaccines PENTACEL[®], PEDIACEL[®], QUADRACEL[®] and DAPTACEL[®].

1980s - 1990s

PERTUSSIS AND ITS KEY COMPONENTS



1980s - 1990s

ACELLULAR ADVANCES

By the early 1980s, international researchers focused on developing an acellular pertussis vaccine that only included specific components of the pertussis bacterium – instead of the whole cell – necessary to safely stimulate immunity to the disease. A team of researchers at Connaught identified and isolated **five key components of the bacterium** that played a role in stimulating protection against the disease. They then developed the complex purification, isolation and chemical inactivation processes needed to mass produce this highly purified vaccine.

1996

GOLD STANDARD

After extensive clinical trials in several countries, Connaught's five-component acellular pertussis vaccine was licensed and soon became the gold standard. Considered the most efficacious pertussis vaccine by key opinion leaders globally, it also causes significantly fewer reactions than its whole-cell predecessors, and is free of interactions between all of its antigenic components.

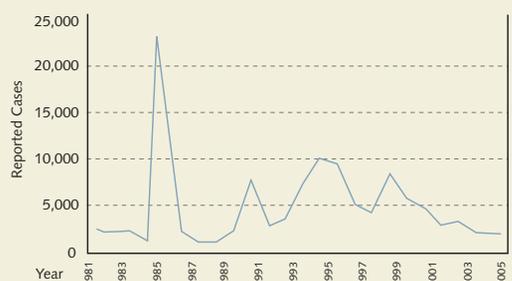


1997

PENTACEL[®] LAUNCHED

Today, with Connaught's five-component acellular pertussis vaccine as its base, PENTACEL[®] is the universal paediatric vaccine in Canada, protecting children against five diseases in one shot. PENTACEL[®] has been especially important in reducing pertussis among children and breaking what had been a regular five-year cycle of higher incidence in Canada. Further research has led to the development of a fully liquid version of PENTACEL[®] called PEDIACEL[®].

PENTACEL HAS CONTROLLED PERTUSSIS OUTBREAKS

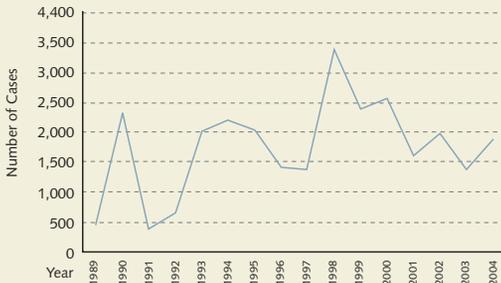


Pertussis: Current and Future Challenges

The marked increase in adolescent and adult pertussis in the last decade has presented new challenges and has stimulated the development of special five-component pertussis combinations like ADACEL® and ADACEL-POLIO to attack the problem.

Now & in the Future

WHOOPIING COUGH IN ADOLESCENTS AND ADULTS (CANADA 1989-2004)



1999

ADACEL® LAUNCHED

Pertussis immunity from childhood vaccinations fades over time, thus leaving older people vulnerable to pertussis infections. In the last decade, pertussis incidence in adolescents has increased sharply. Connaught pioneered the combined ADACEL® vaccine – containing an adult dose of five-component acellular pertussis vaccine along with the adult formulation of diphtheria and tetanus toxoids. This vaccine was specifically developed to reduce the persistent pertussis risk in adolescents and adults.



IMMUNIZATION STRATEGIES

Whooping cough remains a serious and deadly problem for infants who have not completed their entire primary series of vaccines (under 6 months of age). ADACEL® can now be used in a “cocoon” strategy to protect infants by immunizing parents, older family members and other close contacts to reduce the infant’s exposure to the pertussis organism.

COMPONENT PERTUSSIS COMBINATION VACCINES FOR THE WORLD

All of sanofi pasteur’s five-component pertussis combination vaccines are manufactured in Canada, where the vaccine was originally researched and developed. From the Connaught Campus in Toronto, sanofi pasteur distributes these vital combination vaccines around the world.

30 MILLION DOSES DISTRIBUTED WORLDWIDE SINCE 1999 - 2006

