SCIENCE & DIPLOMACY

A quarterly publication from the AAAS Center for Science Diplomacy

Marguerite Jiménez, "Epidemics and Opportunities for U.S.-Cuba Collaboration," *Science & Diplomacy*, Vol. 3, No. 2 (June 2014*). http://www.sciencediplomacy.org/article/2014/epidemics-and-opportunities-for-us-cuba-collaboration.

*The complete issue will be posted in June 2014.

Epidemics and Opportunities for U.S.-Cuba Collaboration

Marguerite Jiménez

ALBERT Sabin, most famous for his research on polio, was a pioneer in scientific diplomacy, tirelessly advocating for international scientific cooperation unimpeded by ideological differences. His work on polio led him to successful collaborations with Soviet scientists from which he drew important lessons about how to build personal and institutional relationships despite Cold War animosities. In the 1960s, he turned his attention to Cuba, and although his 1967 attempt to forge an agreement between the Academy of Sciences of Cuba and the U.S. National Academy of Sciences failed, his efforts laid the foundation for the collaborative work now underway between U.S. and Cuban scientists and offer contemporary lessons for promoting collaboration and exchange across the Florida Strait.

Sabin and the Soviet Union: A Precedent for Vaccine Diplomacy

At the end of 1955, Sabin received a telephone call from a representative of the U.S. Public Health Service (USPHS). The Department of State had invited a group of Soviet medical scientists to visit polio laboratories in the United States and requested Sabin's participation in the important visit.[1] Sabin agreed, and after a highly successful tour, Henry van Zile Hyde, chief of international affairs at the USPHS, wrote to Sabin to thank him for his hospitality and expressed a desire for continued "reciprocal medical missions between the United States and the Soviet

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Union," in the hopes that they might also improve relationships in the medical field.

In May 1956, Sabin received an invitation to visit the Soviet Union and spent several weeks touring Soviet virus laboratories and vaccine production facilities. That trip, Sabin said, was the start of a significant increase in person-to-person exchanges between his and other U.S. laboratories and virus laboratories in the Soviet Union.[2]

Over the course of the next year, Sabin expanded collaboration with his Soviet colleagues, especially Mikhail Chumakov, on a range of virological studies, including live poliovirus vaccine studies. They exchanged the results of ongoing laboratory tests and circulated drafts of scientific articles for advice and editing. Sabin secured invitations for Soviet scientists to attend North American professional association meetings and scientific conferences, and he helped introduce Soviet researchers to scientific and medical communities in the United States.

These person-to-person exchanges served as a confidence building exercise and helped pave the way for more formal institutional collaborations between U.S. and Soviet academies of science. Proponents of vaccine diplomacy, such as American vaccine and tropical disease expert Peter Hotez, argue that these more formal institution-to-institution collaborations are an essential component of effective and sustainable international biomedical cooperation and science-driven diplomacy.[3] Sabin understood the importance of translating personal relationships into institutional ones. While he continued his individual collaborative endeavors, he also worked to facilitate greater cooperation between scientific institutions in the two countries, serving as an interlocutor between national academies of science in the United States and Soviet Union between 1956 and 1958. Indeed, after Detlev Bronk—the president of the U.S. National Academy of Sciences who had been in close contact with Sabin about a proposed institutional partnership—visited Moscow in 1958, the first in a series of agreements was signed between the United States and the Soviet Union outlining different possibilities for bilateral scientific exchanges. Also that year, cooperative agreements focused on combating a handful of diseases including polio, cancer, heart disease, and influenza were signed by senior public health officials from the two governments. The agreements outlined different priority health areas for each country where scientists would be chosen to participate in study tours and conferences to facilitate regular and ongoing collaborative work and information exchange.

As part of the series of agreements, Sabin's laboratory in Cincinnati as well as the Division of Biological Standards at the National Institutes of Health (NIH), were established as the institutions responsible for the exchanges of virologists. The Soviet counterpart to Sabin's laboratory was that of Chumakov, Sabin's primary collaborator in polio research.

These exchanges and collaborative studies facilitated the further development and field testing of the live oral polio vaccine (OPV) in the late 1950s. Ultimately, Sabin and Chumakov worked together on the largest OPV field trials ever

conducted, which eventually helped to pave the way for the licensing, production, and use of OPV in the United States in the early 1960s. As a result of this Cold War collaboration, OPV became one of the most widely used and affordable vaccines in the world, helping to dramatically reduce polio incidence globally during the decades that followed.

Sabin's vaccine diplomacy with the Soviet Union at the height of the Cold War offers several lessons relevant for contemporary vaccine diplomacy efforts. First, individual, person-to-person collaboration was an essential way to build confidence and served as a stepping stone to more formal government-to-government and institutional collaboration. In reflecting on his engagement with the Soviet Union thirty years after the fact, Sabin wrote, "The most important lesson to me is the respect, confidence, and mutual trust that develop during cooperative efforts in a struggle against a common enemy."[4]

Second, the success of U.S.-Soviet collaboration depended upon allowing scientists from both countries to travel back and forth, participate in scientific forums, conduct direct and unrestricted communication with one another, and have access to an unobstructed flow of new ideas and information.

Third, both countries had resources and expertise to offer, giving both an incentive to collaborate and make their combined efforts more effective than either could have realized alone—in this case, expanding access to OPV, a life-saving intervention. Soviet and U.S. scientists viewed one another as colleagues and the flow of new information, technology, and expertise was in both directions with scientists in both countries benefiting from the exchanges.

Fourth, initial cooperation on a high-profile problem of great mutual concern ultimately helped to create opportunities to expand the scope of cooperation to include a wider range of issues.

The lessons from the U.S.-Soviet vaccine diplomacy initiative in the 1950s and early 1960s are highly relevant for a contemporary vaccine diplomacy effort between the United States and Cuba, a project in which Sabin was also a pioneer.

A Scientific Envoy to Cuba

Several years after his collaborative breakthrough with the Soviet Union, Sabin set his sights on a much smaller Communist collaborator, one that was much closer to home. Sabin had traveled to Cuba multiples times prior to the Cuban revolution in 1959, however he had been unable to return since the early 1950s. Despite receiving multiple invitations from public health officials on the island during the early 1960s, the escalation of hostilities between the United States and Cuba made such a high-profile visit by a famous U.S. scientist all but impossible.

Sabin's enthusiastic pursuit of collaborative opportunities with the Soviet Union during the 1950s foreshadowed his efforts in Cuba to overcome political obstacles and diplomatic melodrama. Accordingly, at the end of 1965 when the

Department of State announced an easing of restrictions on travel to Communist nations by certain categories of professionals, Sabin quickly seized the opportunity. The Department of State reported that the relaxation had been in response to the "urging of the medical community," and had been done for reasons of "humanity" to promote greater international cooperation in combating diseases.[5] While medical research justified the humanitarian nature of the move, the *New York Times* reported, "The hope in official circles was that the medical scientists could open the door to closer cooperation in other scientific areas."[6] Sabin immediately sent copies of the announcement to colleagues in Cuba and within twenty-four hours he received an invitation through Cuba's Permanent Mission to the United Nations.

Finally, after almost two years of planning, Sabin arrived in Havana on December 4, 1967. While in Cuba, he had the opportunity to visit and meet with people in a wide range of scientific and medical institutions, as well as hospitals, polyclinics, and research facilities. While other elements of his trip became public thanks to a handful of newspaper articles on the subject published in both the United States and Cuba, what is not commonly known is that during his trip, Sabin met with Antonio Nuñez Jimenez, a prominent young leader within Fidel Castro's regime and the president of the Academy of Sciences of Cuba. Sabin described Jimenez as a "pistol packing" and "very pleasant" person.[7]

In the course of their meeting the two men discussed the possibility of establishing a collaborative relationship between the United States and Cuba through their respective national academies of sciences, in spite of the fact that the two countries did not have formal diplomatic ties. Much as he did with the Soviet Union, Sabin was enthusiastic to serve as an interlocutor between senior officials in both countries. Accordingly, Jimenez sent Sabin home with a proposal outlining the suggested exchange intended for review by senior leaders within the U.S. National Academy of Sciences in the United States.[8]

Sabin returned from his fact-finding trip to Cuba in 1967 by way of Washington, DC, in order to attend a meeting at the National Institutes of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland. When he arrived at the airport, he was met by Central Intelligence Agency officials who questioned him and dropped him off at his destination in Bethesda (incidentally the home of Robert Chanock, future head of the NIAID and often referred to by Sabin as his "scientific son").[9]

In a highly complimentary and comprehensive follow-up report[10] written at the request of his new CIA contacts, Sabin provided extensive information on the status of Cuban public health initiatives as well as his assessment of Cuba's scientific and medical research institutions. In addition to outlining his discussions with the Academy of Sciences of Cuba pertaining to a possible collaborative agreement, Sabin spoke at length about the Cuban government's investment in biomedical research. In particular, he noted that the Cuban government was allocating a large

amount of scarce resources to science and research related to arboviruses and vector-borne diseases, with assistance from several scientists, including Sabin's colleagues, from the Soviet Union. Among the Cuban scientists listed in the report, several had received advanced virology training in the Soviet Union under Sabin's Soviet collaborator, Chumakov.

Epidemics and Incentives: The Case of Vector-Borne Diseases

Cuba's heavy investment in vector-borne and infectious disease research during the 1960s—the island's first years of genuine autonomy from the United States since the late 1800s—is hardly surprising when understood within a broader historical context. During Cuba's war of independence (part of what would become known as the Spanish-American War), mosquitoes transmitting yellow fever were responsible for more casualties within the Spanish army than combat. Indeed, poor health and the potential for the spread of epidemics were among the many justifications for U.S. involvement in Cuba's war with Spain in 1898. Epidemic yellow fever was not only bad for the war; it was bad for business and for the future of commercial transactions between the United States and Cuba. So concerned were U.S. officials after Cuba's war with Spain had been won, that a safeguard to protect against epidemics on the island was included in the Platt Amendment of 1901. If Cuba wished to maintain even its nominal independence and avoid future U.S. military intervention, certain conditions would have to be met. Accordingly, Article five of the Platt Amendment stated

> The Government of Cuba will execute, and, as far as necessary, extend the plans already devised, or other plans to be mutually agreed upon, for the sanitation of the cities of the island, to the end that a recurrence of epidemic and infectious diseases may be prevented, thereby assuring protection to the people and commerce of Cuba, as well as to the commerce of the Southern ports of the United States and the people residing therein.[11]

Once the Platt Amendment had been established granting the United States the right to military intervention in Cuban affairs if sanitary conditions on the island deteriorated, health in Cuba became an issue of national security, vital to the very sovereignty of the Cuban nation.

Public health, including but not limited to the control of infectious diseases, became a top priority in Cuba after Castro and his revolutionaries took power. Less than a month after marching into Havana in January of 1959, the new revolutionary government signed a collaborative agreement with the Pan American Health Organization (PAHO) to launch a nationwide anti-malaria and vector-borne disease control campaign. As a result, thanks to the aggressive eradication program

throughout the island and heavy investment in disease surveillance and reporting initiatives, 1967—the year of Sabin's visit—was also the last year epidemic malaria was reported in Cuba.

Cuba's early investment in vector-borne disease research and surveillance came in very handy in 1981 when Cuban officials were confronted with an outbreak of dengue hemorrhagic fever. In addition to Cuba's own preexisting domestic resources and expertise, another critical element shaping Cuba's response to the outbreak was an informal biomedical exchange that involved Cuban and U.S. scientists at the end of 1980. In addition to its impact on the dengue outbreak, the exchange also helped launch Cuba's biotechnology sector and served as a jumping off point for subsequent scientific collaboration between scientists in the two countries.

The initial exchange began in November of 1980 when Randolph Lee Clark, a world-renowned oncologist and the founding president of Houston's MD Anderson Cancer Center, joined a delegation traveling to Cuba. (Clark earlier served as a sort of biomedical science and research advisor to President Richard Nixon.) While in Cuba, Clark had the opportunity to discuss with Castro Clark's own groundbreaking research on interferons, a family of proteins involved in the immune system. The two men were similarly enthusiastic about interferons' potential in the field of cancer research and beyond, which served as the starting point for a small-scale biomedical diplomacy initiative between scientists in Houston, Havana, and, later, Helsinki.

As a result of his discussions with President Castro, Clark agreed to host two Cuban scientists at his Houston-based interferon laboratory several months later. Additionally, after returning to the states, Clark provided his new Cuban colleagues with scientific articles not readily available on the island and information from his own research. Clark also helped to connect the Cuban scientists to Kari Cantell, a pioneer in interferon research whom Clark had visited in his Helsinki-based laboratory shortly before traveling to Cuba. Following Clark's suggestion and Cantell's subsequent invitation, in March of 1981 a small group of Cuban scientists led by Manuel Limonta spent several weeks in residence studying with Cantell who shared his expertise concerning the large-scale reproduction of interferon. At the time interferon was not yet used in clinical settings, although many researchers, the Cubans included, were eager to test its more applied potential.

Over the course of the next several months, and in frequent contact with Clark and Cantell, Cuban researchers developed the domestic capacity to produce large quantities of interferon. Accordingly, when a dengue outbreak occurred on the island in mid-1981, the first outbreak of its kind in the Americas in over a century, Cuban scientists and public health officials applied their newly acquired expertise, effectively using interferon as a prophylactic intervention.[12]

After their interferon-related breakthrough (at the time, Cuba was the only country outside of the advanced industrialized world capable of producing

interferon and the first to put it to this sort of clinical use) and the subsequent explosion of research and scientific innovation on the island, Cuba emerged as an applied biotechnology hub in the hemisphere and indeed among lower- and middle-income countries worldwide. Cuba began hosting regular interferon and broader biotechnology symposia that quickly gained the attention and interest of scientists from all over the world, including Sabin. Indeed, in 1983 Sabin returned to Cuba (along with other notables such as Clark) to attend Cuba's First International Seminar on Interferon, with the keynote address given by Cantell.

Several years later, in April of 1987, Sabin returned to Havana to receive Cuba's highest biomedical science award, the Carlos J. Finlay Prize, which President Castro presented in recognition of Sabin's contributions to medical research and his efforts to promote international collaboration for the benefit of humankind. (The award is aptly named for Carlos J. Finlay, the Cuban scientist who first identified the *Aedes aegypti* mosquito as the carrier of the yellow fever virus in the late 1800s and who went on to collaborate with U.S. scientists, including Walter Reed, on the Yellow Fever Commission in 1900.) Sabin's 1987 visit included a series of meetings with key actors such as Ismael Clark, then vice-president of the Academy of Sciences of Cuba; Gustavo Kouri, Director of the Pedro Kouri Institute of Tropical Medicine; Julio Teja, Cuba's minister of health; and Limonta, one of the founding fathers of biotechnology on the island and original interferon pioneers.

Within days of returning from his trip, on April 24, 1987, Sabin wrote to Health Minister Teja proposing a joint U.S.-Cuba collaborative initiative focused on dengue. Sabin's interest in dengue and involvement in international dengue research dated back to the 1940s when he served as a commissioned officer in the Army Medical Corps during World War II and his decades of involvement with the Armed Forces Epidemiological Board's dengue-related work. In fact, years before his breakthrough with the oral polio vaccine in the late 1950s, Sabin had focused on developing a vaccine to combat a specific strain of dengue affecting troops stationed in the South Pacific during the 1940s. As a result of his long-time interest in the issue, Sabin was particularly intrigued by Cuba's emerging expertise and the potential for collaborative research.

In his letter to Teja, Sabin explained that he had requested permission to receive strains of the dengue virus from Cuba's 1981 epidemic for further study at the NIH. Kouri was quickly authorized to send the requested virus strains to Chanock, who was a rising star at the National Institutes for Allergy and Infectious Diseases at NIH. Because of bureaucratic barriers involving U.S. customs enforcement, the PAHO agreed to serve as an intermediary, transporting the dengue virus samples to Chanock's laboratory in Bethesda. Several months later Cuba hosted the first international course on dengue in collaboration with PAHO and the World Health Organization (WHO), launching a new era in international cooperation on dengue-related research, education, and innovation.

Today, Cuban scientists and medical practitioners have more than thirty years of innovative and applied dengue-related research to draw on as they share the fruits of their labors and experience with the world. In addition to Cuba's own national research institutions, Cuba is also home to the WHO/PAHO Collaborating Center for the Study of Dengue and its Vector, which is located within the Pedro Kouri Institute of Tropical Medicine in Havana. The course, originally launched in 1987, has evolved into a comprehensive two-week multidisciplinary biannual seminar that includes hundreds of scientists, public health officials, and other experts from all over the world. It has become a focal point for global dengue education and research.

An Opportune Time for U.S.-Cuba Cooperation

Cuba's expertise and resources such as the dengue course and PAHO collaborating center have become increasingly important in the Americas and beyond in recent years. While rare prior to the mid-1970s, dengue has reemerged with a vengeance during the past several decades and the Americas currently have the highest annual incidence of any region in the world. The *Aedes aegypti* mosquito, which can transmit dengue, chikungunya, and yellow fever viruses, can be found in every country in the Western Hemisphere with the exception of Canada and mainland Chile.

The reemergence and spread of dengue provides a promising opportunity for bilateral cooperation between the United States and Cuba for a number of reasons. First and foremost is proximity. In the late 1800s and early 1900s, yellow fever epidemics traveled freely and frequently across the Florida Strait. Scientists and public health officials in both the United States and Cuba came to view cooperation and collaborative research as necessities. The rationale that led to the establishment of cooperative yellow fever research and the establishment of the Reed Commission in 1900 remains valid more than a century later, particularly as it relates to dengue and other vector-borne diseases.

Second, dengue is on the rise throughout the hemisphere and the United States is no longer an exception. Hawaii experienced a dengue outbreak in 2001 and 2002, as did southern Texas in 2005 and Florida in 2009 and 2010. The increase of both imported and locally acquired cases prompted officials within the Centers for Disease Control and Prevention (CDC) to add dengue to the CDC's list of Nationally Notifiable Infectious Conditions in 2010, thereby placing greater importance on surveillance, reporting, and early detection. Cuba's expertise and experience on these issues could be highly beneficial for public health officials in the United States at both local and national levels. Additionally, both countries would benefit from increased bilateral cooperation on vector-borne disease monitoring, surveillance, and reporting. This is especially true for emerging disease threats such as chikungunya, another mosquito-borne virus that has only been recently

found in the Western Hemisphere. First reported in St. Martin in December of 2013, chikungunya also appeared in the Dominican Republic in April of 2014 and in Haiti during the first week of May 2014. With a handful of cases reported in Florida during the third week of May 2014, public health officials in the United States rightfully fear the continued spread of the virus along the Eastern Seaboard and U.S. mainland. Proactive cooperation is vital and entirely feasible.

Third—thanks to effective interventions, widespread use of aggressive vector-control programs (including the use of pesticides), and large-scale improvements in sanitation—dengue (and other vector-borne diseases) virtually disappeared in the United States by the end of the 1940s. A consequence of this early success is that now, several dengue-free decades later, medical professionals and public health officials in the United States are far less familiar with dengue and other vector-borne diseases and they are often slow to recognize their symptoms. The dearth of first-hand experience has been noted by CDC researchers in relation to dengue-related deaths in the United States in recent years. This lack of applied knowledge and hands-on experience is dangerous but also solvable. Here again, increased cooperation and information exchange could play an important role.

The biannual dengue course offered in Havana could be an enormous resource for scientists and public health officials in the United States. However, current U.S. travel restrictions and bureaucratic obstacles make it complicated and often impossible for U.S. citizens, let alone public health officials, to participate in conferences or educational courses sponsored by Cuban institutions. Making it easier for (and even encouraging) U.S. scientists and public health officials to travel to Cuba to participate in the dengue course, as well as other Cuban scientific symposia, would have far reaching benefits for the United States.

Small political openings and shifts in U.S. foreign policy toward the Soviet Union helped to create a window of opportunity for expanding biomedical cooperation in the late 1950s. There was no dramatic or singular event that significantly changed the broader political atmosphere surrounding the Cold War, but a slight thawing of relations made an unprecedented level of scientific exchange possible, with long-lasting benefits for both countries. Perhaps such a thaw is currently underway (or at least on the horizon) between the United States and Cuba.

Sabin demonstrated that if governments will simply get out of the way, scientists will eagerly cooperate with one another against disease—what Sabin identified as humanity's "common enemy." 2013 marked the twentieth anniversary of Sabin's death, but his example of how to foster international scientific cooperation is still timely, and Cuba is an opportune place to put it into practice. **SD**

Endnotes

1. Correspondence between Henry Van Zile Hyde and Albert Sabin, file "USSR Visitors, 1955-1956," Hauck Center for the Albert B. Sabin Archives, University of Cincinnati.
2. Albert Sabin, interview by Saul Benison, June 3, 1976 (side 2, pg. 10), Hauck Center for the Albert B. Sabin Archives, University of Cincinnati.
3. Peter Hotez (president and director of the Sabin Vaccine Institute), in a discussion with the author, June 6, 2013.
4. Albert Sabin, "USA-USSR Relations in Science: My Role with the Soviet Union," *Perspectives in Biology and Medicine* (Autumn 1987): 62.
5. John Finney, "U.S. Removes Ban on Doctors' Trips to 5 Red Nations," *New York Times*, December 30, 1965.
6. Ibid.
7. Albert Sabin, report to the CIA, 1968, OPV series under the sub-series correspondence, in box 2, folder 2, in a file titled Cuba 1962-1968, Hauck Center for the Albert B. Sabin Archives, University of Cincinnati.
8. Ibid.
9. Albert Sabin to Sheldon M. Wolff, May 19, 1977, Hauck Center for the Albert B. Sabin Archives, University of Cincinnati.
10. Sabin, report to the CIA.
11. The Platt Amendment, Article V, 1903, http://www.mtholyoke.edu/acad/intrel/platt.htm.
12. For more on this episode and Cuba's biotechnology industry more broadly, see
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