A Dean Discusses Bioethics in his work

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I appreciate the invitation to participate in this seminar. The breadth and diversity of bioethical issues have grown steadily since I embarked on my medical career. Inevitably, bioethics has had a growing impact on the nature and scope of work of Deans, faculty, staff, and students. In public health, bioethical quandaries intrude with regularity. The resolutions are often tortuous and complex. However intriguing the challenges may be, decisions are requisite. And, whatever the resolutions, there inevitably will be a number who know that the Dean was wrong and are not hesitant in letting that be known.

A few personal reflections. These are a bit dusty or perhaps moldy with time. I must first caution that my experiences as a Dean terminated more than 25 years ago. I hasten to note that we did have electric lights by then— but for perspective I must point out that my service as dean preceded the tenure of one Sommer, two Bushes, one Clinton, a Klag, and an Obama. A great deal of water—or something-- has gone over the dam in that time.

For the first ramblings of 3 Deans, we were cautioned to take not more than 10 to 15 minutes to first review one's past personal experiences in public health and to offer gratuitous advice which might provoke response from the audience. Not an insignificant

challenge—given just 15 minutes. Whatever, the time constraint forces a serious effort at oratorical brevity – an attribute which is unfamiliar to Deans. Thus, as I learned, long ago, there was no way to keep me in check other than with a written script.

Bioethical issues are now more frequently and openly discussed today than once was the case. They span the public health agenda. Some of the most important and controversial relate to incidents that involve human subjects and the preferential assignment of treatments, care, vaccines or whatever. One of the largest and most intricate of vaccine studies commenced in 1954, only two years after Jonas Salk announced the discovery of polio vaccine. It involved more than 1.8 million children—an array of community studies of a magnitude never before attempted. At that time, I was in my first year at CDC in Atlanta, working with Dr. Alex Langmuir, formerly of Hopkins. He directed the CDC Epidemiology Branch and played a significant role in shaping the studies and many of my views.

A few words of polio history to begin. Poliomyelitis had been little known until early in the 19th century when outbreaks began to be reported in Europe and then the United States. The numbers of U,S. cases grew steadily and then rapidly reaching a peak of 58,000 cases in 1957. One-third of the cases were over 15 years of age. One victim was Franklin D. Roosevelt. There was panic and concern far exceeding that which we have observed in conjunction with the emergence of Ebola or ZIKA. When I

was a medical student in Rochester, a polio epidemic of significance occurred. As medical students, we were assigned to 8 hour shifts manning respirators. Aspiration of pharyngeal secretions was with a plain rubber tube, no filters.

A special foundation for the treatment of poliomyelitis cases was founded and generously supported by donations – the National Foundation for Infantile Paralysis. The Foundation was unique in that it supported the development of special research laboratories, one being at Hopkins. The objective was to create a vaccine. This was deemed by scientists and the public alike to be an emergency.

Albert Sabin, at Cincinnati, worked to attenuate each of three live polio strains. These would be given by mouth. By 1952, it was clear, however, that the live oral vaccine was not yet ready for safety testing. Meanwhile, Jonas Salk, working at Pittsburgh, focused on an inactivated vaccine – a highly virulent strain of each of 3 polio viruses was to be injected after they were inactivated. Tests in monkeys indicated that the inactivated vaccine was safe. But there was a serious problem. How to determine if it is both safe and effective in humans. The 1947 Nuremberg Code proscribed tests in humans unless there was informed consent. For a vaccine intended for children, this posed an impossible dilemma—how to test the oral vaccine strains. However, Hilary Koprowski, working quietly at Lederle Laboratories, announced in 1951 that he had developed one effective live polio vaccine strain which was protective and safe when

administered to some 20 institutionalized children. There was no permission of parental or other legal guardians.

The extent and intensity of debates that followed can only be imagined. The bioethical issues and options provided an unusually broad and intense national discussion and education of issues and options. Spurred by national concerns and anxious for early results, the Foundation decided to support needed trials for safety and efficacy at the earliest possible time and so began the planning for the largest vaccine control studies ever conducted.

A small, steadfast group of epidemiologists insisted on community-based supervised trials with a special emphasis on vaccine efficacy. Salk argued that no further trials were needed. Langmuir, then at CDC, was one of the most persistent that further trial were needed. And so my exposure to many discussions. Arguments for placebo-controlled trials emphasized the fact that polio did not occur randomly throughout the country; more cases were to be found among the poorest who might be the least likely to be vaccinated; diagnoses of milder cases were more difficult and, if in doubt, might be overlooked if, in fact, they had been vaccinated. Epidemiologists argued vehemently for blinded case-control studies in diverse towns across the country – half of the group to receive vaccine and half an identical-appearing placebo. Many wanted to vaccinate first and third graders and leave second graders as controls. Knowing that

polio occurred more frequently among children in poorer neighborhoods, a balance between neighborhoods had to be considered. It was a critical learning experience in bringing to the forefront of medicine and public health the essential needs for case-control trials. Many models were employed, in fact.

Participants, included nearly 900,000 children in 211 counties in 44 states. Among these, 148 developed polio. The vaccine was clearly effective; it was not perfect.

The Salk Trial gave impetus to the creation of Human Subjects Review Committees. The first was initiated in the early 1970s shortly before my arrival at Hopkins. Its policies and procedures became national models whose blueprints were substantially conceived by a group in this School with Marcia Pines and NIH staff. In 1978, the Belmont Report summarized ethical principles and guidelines for all research involving human subjects -- respect for persons, beneficence, and justice. Somewhat later, during my three year stint in the White House Science Office, we mandated adoption of bioethical codes and practices for NASA which thereby brought the astronauts under the code. Soon, thereafter the Department of Education was included. The "Common Rule" for Human Subjects Review finally included all parts of government.

But then, there have been exceptional circumstances in which deliberative bioethical approaches have been bypassed because of emergency circumstances. The months following the attack on the World Trade Towers was such a period. As you will remember, a surprise attack was made on the World Trade Towers on September 11, 2001. At the time, I was director of a new Hopkins Center for Civilian Biodefense Studies. On the Sunday afternoon immediately after the attack, I received a call from the Secretary of HHS. He requested my attendance at a 7 o'clock meeting in his office. He added: 7:00 o'clock tonight! A group of 8 of us met until midnight. The reason was that an intercept indicated that there would be a second attack on the U.S. and that smallpox was the likely weapon. Until that point, little had been done in emergency response planning should a biological weapons attack occur. My next 5 years were back in Washington.

Routine smallpox vaccination and production had stopped in the U.S. in 1972 and progressively in most other countries after eradication was declared in 1980. It was known that some 19 million doses of vaccine were in storage in CDC. A quick call to CDC revealed that there were actually only 90,000 doses available; most of the vaccine diluent had gone bad. They confirmed that there was no vaccine production capacity in the U.S.

We convened a small working group of some 10 experts and within a week reached several conclusions. The first was that a substantial quantity of vaccine should be produced urgently. We ascertained that there were fewer than 15 countries with vaccine sufficient to protect their own populations. Any sort of aerosol release would infect a great many individuals and spread rapidly to other parts of the world. At the same time, no country was able to produce as much as a few million doses in a year. U.S. manufacturers revealed that none could produce more than a few million doses in less than 6 years.

The decision was made to purify the existing vaccinia strain; convert production to a tissue culture system; test one of six clones only recently identified; contract for the one large scale tissue culture production center (in Austria); bypass restrictions on importation; undertake abbreviated human test trials; freeze and fill containers in the U.S. At the end of 18 months we had 200 million doses of freeze-dried vaccine ready for emergency use. Special Congressional authorization was needed for use of the vaccine and that was achieved.

The Message. There are occasions when speed is of the essence -- when actions are necessary that run counter to contemporary elaborate procedures, including traditional human subject reviews. The one thing I am not sure about is whether we can decide and act with sufficient speed when it is needed. As I have come to learn, a serious,

sometimes fatal epidemic of inter-agency committeeitis has emerged and spread and has threatened on more than one occasion to paralyse the Congress, even the Country! Due concern for bioethics practices and requirements are essential but the word "due" must be kept in mind.