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Re-dictation of the talk that Dr. Joshua Lederberg gave at Caspary Auditorium, the Avery/McCarty celebration, February 3, 1994, taken from JL notes.

Once again, I'm the baby on this panel.

On February 1, 1944 I was a hospital corpsman at the USNaval Hospital St Albans -- in the far eastern reaches of Queens -- my main job was diagnosing blood smears for malaria, differentiating Plasmodium vivax and P. falciparum. Most of the Marine 3rd Division, returning from Guadalcanal was passing through our hospital, and many of them had malaria. I was not yet decked in the midshipman's uniform (that you saw) which I was to acquire that fall, when I entered Columbia medical school. I don't have any good photographs of myself as a gob; but the marine corporals and sergeants never let me forget that I was a lowly apprentice seaman.

I had not quite reached my 19th birthday. As soon as I reached 18, I had enrolled in the Navy and had qualified for the Navy V-12 medical officer training program. So I was "working my way through college" with alternate spells of active duty and completing my premedical course work at Columbia College.

Although I was off campus in February, I had already heard about the work at the Rockefeller Institute from a herald who frequently made the trip across town to Morningside Heights. This was Alfred Mirsky, who was collaborating with Arthur Pollister in cytochemical studies of chromatin; and it was a topic of lively discussion throughout 1944. Harriett Taylor, a graduate student who was completing her dissertation on the genetics of budding in yeast, had a particular interest and in fact was negotiating to be a postdoctoral fellow in Avery's laboratory the following year.

As an undergraduate, I was spending most of my time in Francis Ryan's laboratory, learning how to do biochemical genetics with Neurospora. I continued to do this after I began my medical studies in October: in fact shared an apartment with Kimball Atwood -- who died just recently -- near Morningside Heights to be close to the lab, which I valued far more than my classroom studies.

I did not actually read the article , Avery, MacLeod and McCarty 1944, SLIDE, SLIDE, until January 20th: Harriett Taylor lent me her copy, as the journal was not readily available on the Morningside Heights campus. And here is my immediate reaction:

SLIDE

But what to make of this? I was less preoccupied with the chemical identity of the Transforming Principle (TP) than with its biological meaning. The chemistry would, I was sure, be resolved by a clearly defined path of analytical testing. In retrospect, it is hard to recall how vague were our concepts of bacterial cells and bacterial genetics at the time. C.N. Hinshelwood, a world famous physical chemist and President of the Royal Society of London, would write a book replete with mathematical proofs that denied that bacteria could have genes at all. There were many other competing hypotheses as I would later enumerate in a review in 1956. SLIDE.

The simplest answer to these dilemmas of interpretation, I felt, would be to transform Neurospora" in the same paradigm as the pneumococcal studies. I did not for a moment dream of repeating the work reported from the Rockefeller Institute on the pneumococcal system itself. This just seemed too hard, too dangerous and too difficult to get routinely replicable results. So I spent the spring of 1944 trying to transform Neurospora. With Francis Ryan's very thoughtful encouragement and oversight, I prepared a number of very crude extracts of Neurospora and found that one could indeed find what apparent transformed clones, i.e., from leucine less to leucine independent by selection in minimal medium. But unfortunately this occurred with equal facility whether the extract was added or not. They were indeed spontaneous reversions. It is hard to believe that this was the first report of reverse mutation in microorganisms. So that was just not going to work. (Parenthetically, it would be about 35 years before anyone else learned all the tricks needed to transform Neurospora with DNA). I concluded that we should turn the problem on its head and instead look for a system of genetic crossing in bacteria, hitherto unknown, to provide a robust, theoretical framework for the transformation studies. The experimental design was one that would become quite routine in future years, SLIDE, SLIDE and amazingly enough it worked and rather promptly!

The future would bring me the chance to meet Mac McCarty; for Norton Zinder to be the first graduate student in my lab at the University of Wisconsin, and many other good things, for which I do owe Mac a great debt. We have much to celebrate.