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Beadle and Neurospora, Some Recollections

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Abstract
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In 1941 when I came to Stanford to do graduate study with Beadle, I had assumed that I would work with Drosophila, possibly on the eye-pigment system. As it turned out later to be the frequent case, Beadle was considerably ahead of me. Most of the Drosophila were in the form of larvae stored away in the freezer or in the form of extracts with which Tatum was doing biochemistry. The bulk of workers in the laboratory were manipulating bits of orange fuzz, which I learned to be Neurospora, an organism not yet recognized in the Agronomy Department at Nebraska, from where I had come. Auxotrophs, then called biochemical mutants, had already been found in some numbers, and queer-looking morphological mutants were turning up. No selection scheme for isolating mutants was then being utilized. Looking back I am astonished that a small technical crew provided enough mutant material to satisfy fairly well a substantial group of avid investigators. Beadle's eagerness to look at the results of each mutation run, and his obvious gratification when new mutants appeared, must have been bonus compensation that alleviated the monotony of spore picking and kept the technicians cheerful. Incidentally, the average of beauty among the technicians was much higher than found in random samples of the population. I do not know whether Beadle consciously was following a principle of laboratory management, but many of us felt that, other things being equal, a satisfying esthetic environment was good for morale.

1. Recollections can be treacherous, since it is often impossible to check their validity. For any distortions or errors, my personal memory is alone responsible.

Francis Ryan was a postdoctoral fellow at the laboratory in 1941-42. His major project was to work out the properties of Neurospora as they might be measured in growth tubes, known sometimes as "race tubes," for obvious reasons. I believe Beadle rather liked growth tubes for their own sake, but perhaps primarily because they seemed possibly utilizable with auxotrophs for purposes of bioassay. With mixed success, many of us, including Beadle, had a try at working out a bioassay as we got ahold of particular auxotrophs for analysis. The graduate students usually had a try also at making their own growth tubes, in competition with Beadle. Only when Herschel Mitchell arrived a couple of years later was Beadle's standard clearly surpassed. Mitchell was a skilled glass blower and quite honestly unable to understand how making growth tubes could present a challenge to anyone.

Beadle didn't confine his competitiveness to laboratory operations such as the making of better growth tubes. Late in the afternoon or at odd times on weekends, he was quite likely to be having a challenge match at tennis, ping pong, or at an even then outmoded field event called the standing broad jump. During certain seasons, poker flourished.

Beadle was a passionate gardener, of vegetables rather than flowers. At one point in time during the war, Beadle was growing vegetables at the Botany Garden as well as at home. My wife and I were occupying the caretaker's quarters at the Botany Garden. Like many graduate students today, we thought of Saturday night as a time for fun and Sunday morning a time to sleep in. The latter was not to be. On Sunday mornings, often well before seven, Beadle would come roaring into the Garden with his little Model A roadster. He was always cheerful, full of what he called spizzerinctum, and inclined to talk, not on these occasions about Neurospora but about tomatoes, squash, and, particularly, corn. Inevitably, a contest was arranged, with an unspecified prize to go to the one who grew the best sweet corn. The criteria were made clear, but as the corn matured no conceivable criterion would have let me claim to win. In subsequent years, competition centered around the biggest pumpkin grown by either of us.

Hard days and long nights at the lab were livened by an increasing number of distinguished visitors. The work of Beadle and Tatum with Neurospora had captured the imagination of geneticists, and of biochemists, and many of them wanted a first hand view. Beadle had an exciting story to tell, and to laboratory visitors he told it well and perceptively, without economizing on time. In the context of this Newsletter, I select for mention a visit by B. O. Dodge, who was clearly impressed and pleased at what he saw and heard but, if I remember correctly, highly sceptical that some of the more exotic morphologicals were indeed Neurospora. And, of course, there was an exciting visit by Barbara McClintock, who was to work out the basic meiotic cytology for Neurospora.

The central effort of Beadle's Neurospora laboratory at Stanford was on the genetic control of metabolism, work which crystallized ideologically as the one gene-one enzyme hypothesis. The typical laboratory situation was one in which particular investigators assumed responsibility for working out particular groups of mutants. Thus among the graduate students, Gus Doermann was working on lysine-requirers, Dave Regnery on leucine, Frank Hungate on serine, I on arginine, Taine Bell on something else, and later Howard Teas on threonine and Ester Zimmer on <u>paba</u>. Molly Hungate worked on the genetics of albino mutants, and Francis Haxo, a graduate student in another lab, worked on Neurospora carotenoids and their synthesis. In part the more senior investigators initially followed the same pattern. Thus the early work of Norm Horowitz was primarily with methionine synthesis, of Tatum and Dave Bonner with tryptophan, and so on. It was all new and exciting. The laboratory was not monofocal, however, and Beadle could become particularly enthusiastic about spurs off the main track. An example is the brilliant idea of Norm Horowitz appearing as "On the Evolution of Biochemical Synthesis," in PNAS in 1945. Another is the series of ideas on heterokaryosis, put together by Beadle and Verna Coonradt in a paper in Genetics, 1944. (I suspect that this paper is more seldom read today than is deserved.) And it has to be said also that Beadle persistently encouraged hard-core work on the genetics of the organism. At that time many of us were only minimally interested, but Mary Mitchell's patient, precise efforts provided a solid background.

Beadle, as a matter of conviction I am sure, was quite permissive with graduate students. That is, he did no day-to-day direction of our research, and seldom if ever suggested a particular experiment. But he was interested in results. He was responsive to questions and generous with equipment, materials, and other opportunities. One of the most rewarding of these opportunities was the chance to learn from Beadle's professional associates. Tatum, Horowitz, Bonner, Mitchell and others not only provided a lively and productive intellectual atmosphere, but were readily helpful in reference to particular problems. Their collective expertise in biochemistry not only reflected Beadle's sense of priorities in the genetics of the time but gave us a nearly unique learning situation under laboratory conditions. That Beadle, a strong personality and highly independently minded person himself, could choose and work effectively with a group having quite different but all strong personalities and great independence of mind is one of the best summarizing commentaries I can make on the early Neurospora days at Stanford.

The recollections I have written here have, of course, focused on Beadle. Inevitably, then, I have minimized the role of Ed Tatum, whose name, in the context of the earlier days of Neurospora, is indissociable from that of Beadle, and about whom some other but overlapping set of recollections should and could well crystallize. In any case, Tatum was held by us at a level of esteem similar to that we held for the man who many of the graduate students called the "boss." To call him "Dr. Beadle" on any but highly proper occasions seemed excessively formal in reference to someone who even at age forty was likely to challenge a standing broad jump contest on the piece of ground nearest the Neurospora laboratory. And "Beets," a nickname used by Beadle's associates, seemed excessively familiar. When I moved to Cal Tech at about the time Beadle did, someone, perhaps Sterling Emerson, pointed out to me that T. H. Morgan had been called the boss and that on the local scene Beadle might be uncomfortable with that epithet. I never asked Beadle's feelings on the matter, but did in fact begin calling him Beets. In the context of the Neurospora scene, however, "the boss" seems to me the appropriate title.