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## Review

# Creativity needs some serendipity: Reflections on a career in ingestive behavior



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## HIGHLIGHTS

- Careers in ingestive behavior are often multidisciplinary
- Early studies on thirst sensations and mechanisms are described
- The path from studies of models of obesity to human eating behavior is detailed
- The importance of translation of basic science to practical strategies is emphasized

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## ABSTRACT

I describe my 50 year career in ingestive behavior in the hope of inspiring young scientists to join in the excitement of discovering why animals, especially the human animal, eat and drink. My interest in ingestive behavior started by chance in a freshman biology class at the University of Pennsylvania taught by Alan Epstein. Once I was exposed to the thrill of doing research my plans for medical school were abandoned and I traveled to the University of Cambridge in England where with James Fitzsimons I completed a Ph.D. in physiology on studies of thirst in rats. After I moved on to the University of Oxford, the early training in biologic mechanisms provided a good basis for studies in humans. We characterized the sensations associated with thirst and the mechanisms involved in its initiation and termination. We also continued to work with animal models in a series of studies of dietary obesity. The effect of dietary variety on rat's intake led to studies of sensory-specific satiety in humans. In recent years the primary interest of my lab has been how food properties affect intake, satiety, and body weight. At the Johns Hopkins School of Medicine and now at The Pennsylvania State University, we have conducted systematic studies of the effects of the macronutrients, variety, portion size, and energy density in both adults and children. Currently our research aims to understand how to leverage the robust effects of variety, portion size, and energy density to encourage healthy eating and drinking. Throughout my career I have been lucky to have been in supportive environments surrounded by creative, insightful, and diligent colleagues.

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**1. Introduction**

The recipients of the Bart Hoebel Prize for Creativity awarded by the Society for the Study of Ingestive Behavior (SSIB) are encouraged to share their reflections on the discoveries that led to being honored. With gratitude to SSIB for selecting me for the Hoebel Prize, I share some highlights and insights from my career with a particular emphasis on the early years.

While all scientists strive for creativity, even the most creative need some serendipity. We cannot plan the twists and turns our research paths will take. Over the 50 years that I have been studying drinking and eating behavior there have been many unforeseen developments and opportunities that have driven discovery. How could any of us have imagined where the advances in technology would take us? Nor could we have completely controlled the mentors and colleagues who would impact our ideas and provide opportunities to test them. Let's start at the beginning and journey over my serendipitous 50 years in ingestive behavior.

While growing up I was exposed to extremes of eating behavior. My dad was a six foot tall bean pole who ate mountains of food just to maintain his weight while my mom, who seemed to eat little, at least around us, was obese. With this family background and some struggles with my own "freshman" weight gain, I found myself in an introductory biology class taught by Alan Epstein at the University of Pennsylvania. Harry Kissileff was the lab instructor. Somehow among all the undergrads I caught their attention. Harry claims it was because I took my fetal pig back to my dorm room to continue the dissection. With Alan, I sought him out. I worked on diverse projects in his lab, from the genetics of

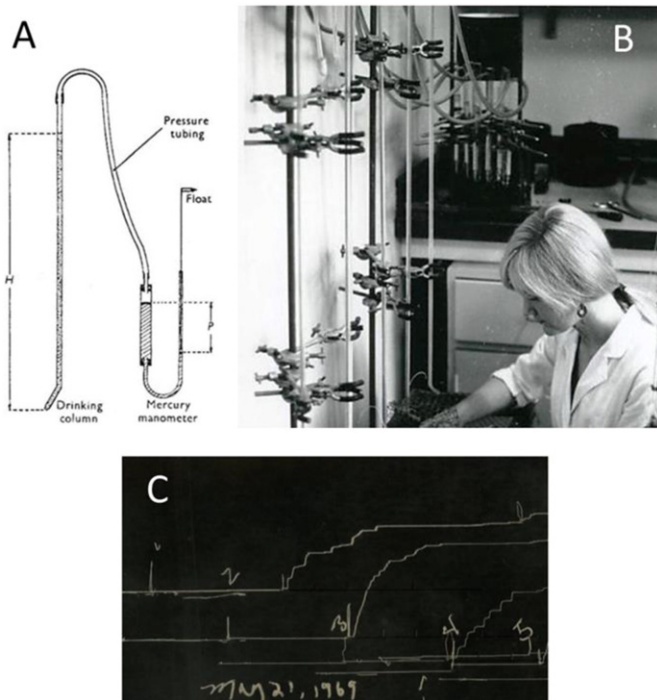
fruit flies to stereotaxic brain surgery in rats. As an undergraduate I was welcomed into the inner circle of ingestive behavior at Penn that has spawned so many of us in this field: the famous "Feeding Seminar" with luminaries such as Phil Teitelbaum, Paul Rozin, Eliot Stellar, and Alan Epstein. I do not recall if I ever dared speak up in the intense debates about such topics as the role of the hypothalamus or the definition of a motivated behavior.

Even with this early exposure to the excitement of our science, I planned to go to medical school. While in high school I had been a participant in an immersive summer experience at Georgetown Medical School to encourage kids to become doctors, so the idea of medical school had been implanted early on. I applied to only two medical schools, Penn and Cornell, and was accepted by both—quite a feat as at the time only 4% of the students were women. In the interviews I was consistently asked how I would manage when I had a family and children. I must have given an appropriate response—it is good such questions are now taboo. Even then I knew that I wanted to do research, not be a clinician. Shortly after I accepted my place at Penn Med, a fellow premed student came to class bragging that Alan Epstein was recommending him for a fellowship to study in England. I stormed off to Alan and demanded to know why I was not the one being sent to England. The reason was that women were not eligible! Let's just say we got that changed and many women have since participated in the program. Off I went with a Thouron Scholarship to promote "Anglo-American affairs" and to study in the Department of Physiology at the University of Cambridge (where there were no female graduate students) with James Fitzsimons as my mentor. It was meant to be just for a year after which I would come back to Penn Med. I stayed 18 years in England starting in 1966.

**2. University of Cambridge: studies of thirst**

Although I did not know it, Alan had a hidden agenda. He had met James at a meeting in Japan and they were eager to collaborate. I was the facilitator—a very lucky go-between. I arrived in the Fitzsimons lab (it consisted of just him, he had never had a graduate student or post-doc) when he was in the midst of seminal studies showing that the kidney is a homeostatic organ that plays a critical role not just in excretion, but also in the control of fluid intake [1]. In a series of meticulous experiments he had shown that restriction of blood flow to the kidney caused rats in normal fluid balance to increase their water intake, and he suggested there was a thirst stimulus in the kidney, probably renin. James went on to show that intravenous renin was indeed a potent stimulus to drinking. I had joined the lab by this time, and in the next study we infused angiotensin intravenously since the effects of renin are usually mediated by angiotensin. Like renin, intravenous angiotensin caused drinking in rats which were in fluid balance [2]. This series of studies supported the view that the renin-angiotensin system plays a role in thirst caused by depletion of blood volume, that is, the extracellular fluid compartment.

When I think back on this exciting introduction to experimental science, I cannot help but recall the simplicity of the equipment at our disposal. James had developed a device to record a rat's water intake [3] which consisted of a long glass tube a glassblower had formed into a spout at the rat end (Fig. 1a). The tube was connected by air-filled pressure tubing to the upper end of a mercury manometer (an instrument for measuring the pressure acting on a column of fluid). A float in the open end of the manometer moved a stylus up as the water level went down. This stylus rested on and etched lines in the thick black



**Fig. 1.** A: The original drawing of the drinking meter developed by Fitzsimons (reproduced with permission from ref. [3]). B: The kymograph drum connected to the drinking tubes can be seen in the background at the top of the photo. C: An original drinking record from 1969 showing intakes by five rats tested simultaneously.

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