

## Reminiscences From Montreal (1954-1956)

Much has been written already about the “early days” of Biochemistry in Canada and therefore I will limit my recollections to two short but memorable years at McGill University between 1954 and 1956. This was before the Canadian Biochemical Society had emerged from its parent Physiological body. Those were halcyon years when the relatively small number of biochemists working in that vibrant city knew each other well and would meet regularly at various Montreal restaurants to present their latest findings. Many of those from this club went on to become leaders in their field.

I arrived into this stimulating environment from England in October 1954 after a stormy, week-long Atlantic crossing on the SS Atlantic. I was still fresh with Ph.D., my wife (Mary) and fortified by the youthful enthusiasm that goes with such accomplishments! I had spent the previous years working on the metabolism of synthetic estrogens related to diethylstilbestrol under the nominal direction of Professor Sir Charles Dodds who was Director of the Courtauld Institute of Biochemistry at the Middlesex Hospital Medical School. He was a supportive but extremely busy man so that my de facto Ph.D. supervisor became Wilfred Lawson, an exceptionally talented organic chemist who had been Sir

Robert Robinson's (President of the Royal Society) personal research assistant. He had already synthesized more than a hundred stilbene derivatives to test for estrogenic potency in an extensive structure-activity study. This was just prior to the establishment of the estrogen receptor concept. Lawson was a strict disciplinarian and used to give me a hard time whenever I wanted to take Saturday morning off to play in an “away” rugby football match! Another person who had an impact on me was Sylvia Simpson who with her subsequent husband Jim Tait, were involved in the isolation of the mineralocorticoid, aldosterone, before its novel structure had been elucidated. I remember that we

had a “pool” to predict its structure but none of us were anywhere near to envisaging the unusual aldehyde side-chain in this steroid.

The question of where to go for my “postdoctoral” was pre-ordained by the emerging use of radiolabelled compounds to study metabolism. The chemical synthesis of  $^{14}\text{C}$ -containing steroids had been accomplished recently and presented me with the opportunity of building on my expertise with estrogens. Here was an exciting new field of research in which the biogenesis of the naturally-occurring estrogens could be studied in vivo under near-physiological conditions! R.D.H. (Don) Heard at McGill University and his group, which included Sam Solomon, Vince O'Donnell, Jim Webb, Graham Bligh, Malcolm Cann and Judith Saffran, to mention a few, had already laid some of the groundwork in this area. A postdoctoral position had become available and my previous experience with estrogens – albeit synthetic ones – helped me in being selected. In those days funding for research was no problem, particularly in well-established Universities such as McGill.

The problem assigned to me was the biosynthesis of estrone, which is excreted in horse urine in very large amounts. Enough could be isolated in a day from a pregnant mare that it could be crystallized. It was already known from non-isotopic evidence that androgens were the probable estrogen precursors, but this could now be firmly established by administering a very small dose of  $[4\text{-}^{14}\text{C}]$  testosterone and measuring the specific  $^{14}\text{C}$ -radioactivity of estrone in the urine. I had become used to working with rats and rabbits to identify metabolites, but I was not quite prepared for the logistics of isolating steroids from almost 13 litres of urine. The radiolabelled androgen, dissolved in a small volume of ethanol, was injected into the jugular vein of a mare in the 6th month of gestation. She was one of many kept on a farm in Alexandria, Ontario, which provided a source of “Premarin” – a mixture of equine estrogens – for Ayerst laboratories based in Montreal at the time. Five decades later, it is still the most commonly prescribed estrogen preparation for replacement therapy in estrogen-deficient women. Gallons of urine were collected by the company, initially employing speedy young men with buckets, which they used

Harry Jellinck  
Department of  
Biochemistry  
Queen's University  
February 2001



whenever a tail went up, and later by a more elegant method – truck tires, split in half, harnessed under the horses.

Our mare's reaction to the alcohol passing directly to its brain was predictable, but after an initial head droop, it recovered and went on as if nothing had happened. The next procedures, which involved acid hydrolysis to release steroids from their conjugates and extraction with liters of toluene was not only a challenge, but a health hazard and a source of great unpopularity in the Department of Biochemistry. The whole building was permeated by the pungent aroma of the refluxing urine, which also impregnated hair and clothing. The air flow in the fume hoods was checked repeatedly after that, but it took many months to be forgiven! However, the experiment was a success and I managed to isolate over 150 mg of pure estrone, containing significant amounts of  $^{14}\text{C}$ -radioactivity. It took me another month of repeated crystallizations, conversion to the benzoate followed by regeneration of the estrone with no decrease in specific radioactivity before I managed to convince Don Heard that the conversion of testosterone to estrone had really occurred. I remember going into the Laboratory on Dec. 25 – we lived nearby, at the corner of University and Pine – to count the last batch of estrone crystals, which by now had dwindled to 5 mg, and the joy of finding that they had still retained their radioactivity. It was probably the best Christmas gift that I ever received! This experiment was part of the studies by Don Heard's group on elucidating the pathway of biosynthesis of the ring B unsaturated estrogens, equilin and equilenin, which bypass cholesterol involved in the formation of all the other classical steroid hormones. The problem of this alternate pathway of steroidogenesis was taken up more recently, by Bhagu Bahvnani while still at McMaster University.

Naturally, not all experiments are a success and one of my more memorable failures in Montreal was missing the boat to show that human placental microsomes provided an exceptionally active aromatizing system. Not only was my anatomical knowledge inadequate to dissect out the appropriate areas from the large mass of blood-engorged tissue but I was disheartened by the procedure needed to obtain the placentas. I would be informed by phone from the delivery room at the Royal Victoria Hospital that a birth was imminent and would then rush up the hill from McGill during the humid mid-summer days with a large, ice-

filled bucket. On one occasion, while waiting with the nervous father, I heard one of the nurses shout: "It is O.K., you can forget about the baby, it is only the placenta that he wants"! I need hardly add that this was said as a joke.

I have not mentioned many other memorable events or some of the well-known scientists such as J.H. Quastel and Hans Selye who were active in Montreal at the time. Others, such as Tim Parsons who recently won the prestigious Japan prize and Andrew Schally (who took over our Pine St. apartment) were at the beginning of their careers. The latter shared the 1977 Nobel Prize in Physiology and Medicine with Roger Guillemin and Rosalyn Yallow. Those indeed were the "good old days"!

### **Biography**

*Harry Jellinck was born in 1928 in Paris, France and is married with 3 daughters. He obtained his undergraduate Degree in Natural Sciences at Trinity College, Cambridge in 1948 and an M.Sc. and Ph.D. from the University of London (1952 and 1954). After 2 years as a Postdoctoral Fellow (National Research Council) at McGill University and 3 years as a Lecturer at two Medical Schools in London, he returned to Canada to join Dr. R.L. Noble at the newly established Cancer Research Centre, University of British Columbia. He was promoted to Full Professor before moving in 1967 to Queen's University as Head of the Department of Biochemistry. He stepped down from this position in 1978 and became Emeritus in 1993. He has also been a Visiting Professor at Rockefeller University, since his first sabbatical in New York in 1978. He has published 3 textbooks, over 100 scientific papers and is still active in research, albeit at a reduced pace.*