

## John Atherton Young AO, FAA FRACP (1936-2004)

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For almost 40 years John Young was one of the leading figures in physiology in Australia. The importance of his contributions to scientific knowledge were recognized by election to Fellowship of the Australian Academy of Sciences, where he rose to be Vice-President and Secretary (Biological) and by the award of the prestigious Research Professorship of the Alexander von Humboldt Stiftung.

As long-term members of the Society will be aware, however, John Young was not only a leading researcher, he also played a major role in promoting physiology within Australia and internationally. He, together with a handful of others including Ian McCance, Chris Bell, Trefor Morgan, Dave Davey and Alan Boura, was one of the key personalities who kept the Australian Physiological and Pharmacological Society running efficiently and effectively from the 1970s through to the 1990s, serving as Councillor (1969-1973), Editor of the Proceedings (1973-1975), National Secretary (1983-1988) and President (1995-2000). He also served on the National Committee for Physiology of the Australian Academy of Sciences (1984-1990). Internationally, he was instrumental in the establishment of the Federation of Asian and Oceanian Physiological Societies (FAOPS) and was an inaugural member of its Council (1990-1994) before being elected Vice-President (1994-1998) and President (1998-2002). He also served as a member of the Council of the International Union of Physiological Sciences (1993-2001) where his presence ensured that the interests of Australian physiologists were adequately catered for in the Congresses organised by the Union. His impact in promoting linkages between Australian physiologists and between physiologists in Australia and those overseas was substantial. His impact on individuals was equally great. Many will have fond memories of impromptu sightseeing tours or visits to the opera organised by John to fill in lulls in the scientific program and have been amused and educated by his knowledgeable and witty conversation over meals in interesting restaurants in cities all over the world.

### Doctoral Training (1962-1964)

John Young undertook his doctoral studies at the Kanematsu Memorial Institute at Sydney Hospital under the supervision of Dr K.D.G. Edwards. His project was to investigate the renal handling of the anti-hypertensive methyldopa and in particular to establish whether therapy with methyldopa, an  $\alpha$ -amino acid, interfered with renal handling of other amino acids. To carry out this project, he successfully adapted the technique of stop-flow analysis<sup>1</sup> which had been just recently developed in the dog kidney<sup>2</sup> for studies in rats. To validate the technique, he first demonstrated that phenolsulphonphthalein secretion is localised to the proximal tubule<sup>3</sup> and then determined the

tubular segments responsible for transporting a wide variety of amino acids and other substances<sup>4</sup>. This work confirmed that previous findings in dogs (see for example<sup>5</sup>) were also applicable to rats. He then conducted an extensive pharmacological investigation of the absorption, metabolism and excretion of methyldopa and related catecholamines in order to characterise the extent of renal elimination of  $\alpha$ -methyldopa and its metabolites<sup>6</sup> and used the stop-flow technique to demonstrate that as predicted, the L-stereo-isomer of  $\alpha$ -methyl-dopa interferes with proximal tubular absorption of neutral amino acids such as histidine and serine<sup>6,7</sup>. Finally, he followed up the observation that the D-stereo-isomer of  $\alpha$ -methyldopa is not orally absorbed<sup>6</sup> by showing that in the rat jejunum, as in the proximal tubule,  $\alpha$ -methyldopa is absorbed by the same system that absorbs neutral amino acids<sup>8</sup>. These studies led to the award of the degree of MD from the University of Queensland in 1965. They also provided the basis of his first presentation to the Australian Physiological Society (as it then was) at its Sixth Meeting held at Monash from 20 to 22 May 1964.

### Post-doctoral Training (1965-1966)

John began working on the physiology of salivary glands in 1965 in the laboratory of Professor K.J. Ullrich at the Physiologisches Institut of the Free University in Berlin. At this time, Karl Ullrich was already well known for his studies on renal concentrating mechanisms, and John was expecting to continue working on renal physiology. Ullrich's group, however, was pioneering the application of micropuncture techniques to epithelial organs other than the kidney. In particular, J.R. Martinez had begun micropuncture studies on unstimulated rat mandibular glands<sup>9</sup> in order to test the applicability of the Thaysen 2-stage hypothesis to them. Ricardo had, however, returned to El Salvador, and the task of extending his work to rat mandibular glands during parasympathetic stimulation fell to John. John succeeded in confirming that, as predicted, the fluid in the intercalated ducts had a plasma-like composition which did not vary with secretion rate. The findings were of such importance, that the then doyen of salivary physiology, Sir Arnold Burgen FRS, when he heard John present his findings at a meeting of the Physiological Society at London Zoo, sought permission to include the data in a lecture he was giving at a conference in Birmingham, Alabama, as well as securing John an invitation to give a Plenary Lecture at the same conference.

While in Berlin, he collaborated with Eberhard Frömter who many Members will have met during his trips to Australia to visit John. Together they developed *in vivo* perfusion methods that permitted them to establish that the main excretory duct actively transported both Na<sup>+</sup> and K<sup>+</sup>

and that the apical membrane of this epithelium behaved like a Na<sup>+</sup>-selective electrode<sup>10</sup>. This work formed the basis of John's second presentation to the Australian Physiological Society, given at the tenth Meeting of the Society in Adelaide (24-26 May 1967) following his return to Australia.

### The Department of Physiology in Sydney (1966-2004)

In late 1966, John returned to Australia to a Senior Lectureship in Physiology at the University of Sydney. The choice between this position and one in Zoology at Macquarie University having been made on his behalf by the Heads of the two Departments in a chance meeting in a supermarket aisle. In order to more rigorously test the general applicability of the Thaysen 2-stage hypothesis, he extended his micropuncture studies to a wide variety of species and gland types, including the rat sublingual, the cat sublingual, the cat mandibular, the sheep parotid, and the rabbit mandibular glands as well as the parotid, mandibular and sublingual glands of a monotreme (the echidna, *Tachyglossus aculeatus*) (reviewed in<sup>11,12</sup>).

He also continued to study the mechanisms of ductal ion transport. His studies on ductal HCO<sub>3</sub><sup>-</sup> transport, in particular, led to the demonstration that ductal transport could be influenced by parasympathomimetic agonists<sup>13</sup>, an idea that he had first canvassed on the basis of his studies on the intact rat mandibular gland<sup>14</sup>. This finding, which was confirmed and extended to sympathomimetic agonists in subsequent studies<sup>15,16</sup>, disproved the then dogma that the rate of ductal electrolyte transport would be determined solely by the composition of the luminal fluid. The exploitation of its implications became the major focus of his work in the 1970s. Initially these studies were based on the mandibular duct perfused *in vivo*<sup>15</sup>, but during a sabbatical leave spent in the Max Planck Institut für Biophysik in Frankfurt am Main in 1971, he started to perfuse these ducts *in vitro*, using a technique that had just been developed by H. Knauf in Frankfurt. He exploited this technique to investigate the effects on ductal transport of a wide variety of hormones and neurotransmitters (see, for example<sup>17,18</sup>).

His interests were not, however, limited to salivary epithelia. He continued to carry out work on renal amino acid transport in collaboration with Akos Györy and Jennifer Lingard. In collaboration with Peter Harris he found that the concentration-response relation for angiotensin II on proximal tubular Na<sup>+</sup> transport is biphasic; low concentrations of angiotensin II being stimulatory and high concentrations being inhibitory<sup>19</sup>.

During this period, John became one of the stalwarts of the Society. He acted as the Local Secretary for the 13th meeting of the Society held in Sydney in August 1969. Importantly, the Society's meetings also provided the venue at which the succession of highly talented medical students who worked with John presented their micropuncture and duct perfusion data. In 1973, John presented the Society's Invited Lecture using the title "Electrolyte Transport by Salivary Epithelia". In it he made a point of making

particular mention of his students whose work had made the talk possible.

During the late 1970s and early 1980s, John started to investigate the mechanisms by which salivary endpiece cells secrete saliva. Research in this area had been impeded by the lack of a suitable *in vitro* preparation for studying salivary secretion. He had had some success in developing an *in vitro* perfused salivary gland preparation in the mid 1970s, but it was only when Maynard Case spent a sabbatical leave in his laboratory in 1977, that Arthur Conigrave and Ivana Novak succeeded in establishing a convincing *in vitro* preparation of the rabbit mandibular gland<sup>20</sup>. Subsequently, in collaboration with Ricardo Martinez in Columbia, Missouri, an isolated perfused preparation of the rat mandibular and sublingual glands was also developed<sup>21</sup>, which Masataka Murakami was later to make extensive use of in John's laboratories. These preparations permitted analysis of the mechanisms of salivary secretion at a level of detail that had never previously been possible. In rapid succession major studies were published on the role of HCO<sub>3</sub><sup>-</sup><sup>22</sup>, H<sup>+</sup><sup>23</sup> and Cl<sup>-</sup><sup>24</sup> in maintaining salivary secretion. This work culminated in the pharmacological identification of the transport proteins that underlie fluid and electrolyte secretion by the rat and the rabbit mandibular glands<sup>25,26</sup>.

Finally, during the 1980s and 1990s, John and I collaborated in studies that ranged from the mechanisms by which sheep salivary glands secrete, through to the mechanisms by which epithelial Na<sup>+</sup> channels are regulated by intracellular ions<sup>27</sup>.

John has also made substantial contributions to the study of the exocrine pancreas. These contributions include characterising the protein, fluid and electrolyte secretory responses of the rat pancreas<sup>28,29</sup> and the rabbit pancreas<sup>30</sup> to stimulation with secretin and cholecystokinin. They also include the development with Jennifer Lingard of an isolated and perfused rat pancreas preparation<sup>31</sup>. The driving force for the development of this preparation was the need for information on pancreatic secretory mechanisms that could be compared with the data emerging from studies on isolated and perfused salivary glands<sup>32</sup>. From these studies it became clear that rat pancreatic acinar cells secreted by a markedly different mechanism to that seen in salivary endpiece cells<sup>33,34</sup>.

John also exerted great influence on salivary and exocrine physiology through the reviews he wrote. These covered salivary morphology<sup>35</sup>, the composition of saliva<sup>36</sup>, salivary myoepithelial cells<sup>37</sup> and salivary electrolyte transport mechanisms<sup>11,12,38-40</sup> as well as more general overviews of the physiology of salivary glands<sup>41-44</sup> and salt glands<sup>45</sup>. Of particular note were those written together with Ernst Van Lennep (e.g.<sup>12,35,45</sup>).

### Administration (1976-2004)

John's success in research led to his rapid promotion. He was promoted to Associate Professor in 1972, and then appointed to one of the two chairs of Physiology in 1976. Once he became Professor, university

administration took up an ever greater proportion of his life. This was not simply due to the need to alternate with Liam Burke as Head of Department. It was also because John took on an amazingly wide range of tasks within the University. The first sign of this was his election, in 1976, to the Council of the Sydney Association of University Teachers, the academic staff union, of which he was President in 1977. He also served as Deputy Chair of the Academic Board (1978-1980), a position which required chairing of many key University Committees, including the Library Committee, the Admissions Committee, the Matriculation Committee, and the PhD Committee and he served on the University Senate (1978-81, 1984-85, 1988-89, 1990-93). Within the Faculty of Medicine, he became Sub-Dean of Academic Affairs in 1978 and remained in that post until his elevation to Dean of the Faculty in 1989. His activities while Dean of Medicine and later Pro-Vice-Chancellor in charge of the Faculties of Medicine, Dentistry, Health Sciences and Nursing (1994-2003) have been dealt extensively elsewhere; here it is sufficient to remind Members of John Young's role in the establishment of the Graduate Medical Curriculum at the University of Sydney and in the establishment of the Canberra Clinical School, which has subsequently developed to become the School of Medicine at the Australian National University.

### **John Young and the Australian Physiological Society**

As I have already mentioned, John played a leading role in the Society. While his students made major contributions to the scientific program of the meeting, he perhaps had his greatest impact during Annual General Meetings, where his tireless use of the Socratic method to get to the core of issues coupled with his enthusiastic support for the aims of the Society and a solid knowledge of Joske's *The Law and Procedure at Meetings in Australia and New Zealand* (5th edition) ensured a lively and engaging debate. On one memorable occasion, he successfully moved that the meeting would "no longer hear" a Member who had pressed his case in an unduly acrimonious and long-winded manner.

John also had a major impact on the Society's approach to conducting meetings. He believed that meetings should be enjoyable. He thus pushed Local Secretaries to ensure that the all social functions should be of a high quality. For example, the Conference Dinner of one meeting was held on a ferry on Sydney Harbour and facilitated interactions between participants with a keg of sherry. He was strongly of the view that the Society should emulate that famous dining society, the Physiological Society, and recommended to neophyte Local Secretaries that they arrange a meal in a top quality restaurant for the Council following its meeting on the day preceding the opening of the Meeting, and that they budget on one bottle of good wine per person in order to ensure that the "Society's serious interest in wine" was adequately catered for. His wish to emulate the best aspects of Physiological Society practice also included his oversight as Editor of a

system of printing draft books of abstracts before the meeting, which were corrected by meetings through comments and a vote at the completion of each presentation. John seemed pretty keen on the system, which although it needed a dedicated editor, involved audiences in a way we do not see today.

John's belief that the Society's meetings were as much a social event as a scientific event also led to his practice of driving or catching the train to meetings. This habit ensured that meetings became part of a very much larger experience, in which the students (often heavily subsidised by John) and colleagues who accompanied him were exposed to a wide range of culinary and tourist experiences in a wonderfully hospitable atmosphere. The previously mentioned Adelaide meeting, for example, included not only a tour of the Barossa and Clare Valley wine districts in which John acted as the expert guide. It also included one of John's more exuberant 'extra-curricular' contributions to the Society. This was a late-night induction for friends and colleagues to the game of 'slosh' on the precious billiard tables of one of Adelaide University's Residential Colleges. As many of the participants had become thoroughly sloshed during the course of the game it was not altogether surprising that, in the interests of preserving good order in respectable Adelaide, the entire group was unceremoniously asked to vacate the billiard room and not return. Members who were introduced to slosh by John will not be surprised to learn that a game some years later in the august Australian Club in Sydney resulted in one of his former students, Chris Martin, breaking a cue. John, who had recently been elected to the club, was left with a rather delicate and taxing exercise in diplomacy which led to his "donation" of the cue which bears his name in the club's billiard room.

John also contributed to the development of physiology, both in Australia and overseas through the many conferences that he organised. These included several major international symposia at Leura, and at a luxury hotel close to his beloved property at Bowral, as well the Satellite Symposium of the 1983 IUPS meeting held in the spartan conditions of the University of Sydney's Veterinary School at Camden.

Finally, he exerted an influence which, despite being difficult to document, had a major positive impact on Physiology in Australia. Through his service in the Society and on innumerable appointment committees and review boards, he came in contact with every professional physiologist in the country as well as many students. Many of the letters which I, and others, have received since his death have mentioned the profound impact that contact with John had in assisting these people to become more productive and happier scientists. He succeeded in fostering a collegial striving for excellence among Australian physiologists which contributed greatly to the success of the discipline.

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