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In memory of Professor Geoffrey Burnstock

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On June 2, 2020, one of the most outstanding representatives on contemporary neurophysiology and neuropharmacology, Professor Geoffrey Burnstock, passed away.

Burnstock was born in London on May 10, 1929. From his childhood, he was interested in medicine, but his repeated attempts to enter any medical school were unsuccessful. He himself related this with quite strong class distinctions in pre-war Great Britain, and since he descended from a family of poor Jewish shopkeepers, at all interviews, he was given to understand (sometimes in a rather rude form) that he had no chance for a prestigious profession of a doctor.

However, this did not break the young Geoffrey, as he was always proud to be a fighter in life. He entered the King's College, University of London, and then graduate school at University College London (UCL), where he studied the contractile activity of the intestines of different fish in a comparative aspect. After earning a PhD degree, Burnstock worked for 2 years at the Department of Pharmacology at Oxford University where he was involved in the implementation of the sucrose gap method for recording electrophysiological signals from smooth muscle tissues. In 1959, Burnstock was invited to hold the position of professor at the Department of Zoology at the University of Melbourne in Australia, where he later became the department head and worked until 1975. It was in Australia that Burnstock put forward two of his ingenious hypotheses, which subsequently were fully confirmed.

The first hypothesis of cotransmission concerns the refutation of the classic principle of the eminent neurophysiologist Henry Dale "one neuron, one transmitter." Well established in those days, this principle states that acetylcholine is the only transmitter of cholinergic nerves, and norepinephrine is the only transmitter of adrenergic nerves. Burnstock suggested, and now it is known to all students of biological and medical departments, that stimulation of any nerves releases a whole "cocktail" of biologically active substances, transmitters, and modulators, which, to varying degrees and under different circumstances, can significantly affect the effect of the main transmitter. The idea of cotransmission was not accepted by the scientific community for a long time, since the scientific prestige of the Nobel Prize laureate Henry Dale was incomparably higher than that of Professor Burnstock who was of little distinction at that time.

His second hypothesis was even more revolutionary. According to it, there are also some "noncholinergic, nonadrenergic" nerves in the autonomic nervous system aside from cholinergic and adrenergic nerves, and the effects of which are not mediated by classical mediators, acetylcholine, and noradrenaline. After conducting many of his own experiments and analyzing the literature available that time, Burnstock suggested that purine compounds (adenosine and adenosine-5′-triphosphoric acid [ATP]) serve as mediators in these nerves, and therefore, he called the nerves, from which they emerge, purinergic nerves [1].

At that time, everyone was already well aware of the role of the adenosine nucleoside in the construction of nucleic acids and ATP nucleotide as a source of intracellular energy. Both of these purines are widespread in the body and are present in absolutely all cells that it was difficult, say the least of it, to imagine their role as specific signaling molecules in the nervous system. For this reason, Burnstock received a barrage of criticism. He was told that ATP could not be a mediator because of its widespread occurrence, molecule instability, and high molecular electric charge. One critic of the theory, using a play on English words, wrote that the *puri*nergic nerves are Burnstock's *pure* fiction.

However, the purinergic hypothesis soon became one of the most hotly debated topics in neurophysiology and neuropharmacology, and in 1975, Professor Burnstock was invited to London to his *alma mater*—UCL—where he was the head of one of the largest departments of anatomy and developmental biology in the universities of England for 22 years (until 1997).

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During the flight of the Burnstock family from Australia to London, they made two stops—one with friends in Japan and the other in Leningrad with a report at the congress of physiologists. Irina Andreevna Studentsova, who subsequently became a professor of the Department of Pharmacology of Kazan Medical University, my scientific adviser, was also a participant in this congress. Irina Andreevna said that Burnstock and his family left a lasting impression on the entire community of the congress.

First of all, Burnstock's three daughters, Tammy, Dina, and Aviva, were a sensation, as they were dressed in an equally nonstandard manner. They were wearing a canvas bag with three holes for the head and hands and behaved very naturally. Geoffrey Burnstock also behaved unconventionally, and during his speech, he first took off his jacket and threw it on the back of a chair, rolled up his shirt sleeves, and started to report on purinergic nerves very emotionally, with jokes and anecdotes. It was very unusual, and Irina Andreevna admitted that she immediately fell in love with Professor Burnstock and subsequently inspired me with her love for this unusual person.

I was extremely fortunate to have worked for almost 4 years (1992–1995) in the laboratory of Professor Burnstock in London at UCL (Fig. 1). These were the years of the peak of the purinergic theory popularity; the receptors for adenosine and ATP were finally identified, their structure was established, the receptors were cloned, and the search for specific agonists and antagonists was successfully conducted.

Professor Burnstock's scientific group, which included up to 20–25 members of its best years, consisted of the British by one-third and of international specialists by two-thirds. Besides me, there were representatives from China, Japan, Iran, Nigeria, France, Germany, and many other countries. The professor was an internationalist, and he made no distinctions by nationality, skin color, and religion. The only thing he looked for in young people who came to him from all over the world for training was a sincere passion for science, knowledge, life in all its aspects, art, and culture. This created a powerful favorable atmosphere in the laboratory, where everyone tried to find something new, unknown, and interesting, but at the same time, there was a single team with feeling of fellowship.

The professor organized the work of the group so that every month he talked with each member of the scientific group for an hour and a half. He carefully asked about activities the person had been involved in during the last month and about his achievements or problems. At the same time, he wrote everything down, and during the next meeting, he reread his notes and asked about the progress. Each of us was looking forward to such a meeting with impatience but was also very worried because sometimes the professor expressed frankly his dissatisfaction with the quality or number of the results obtained or the publications prepared. Furthermore, each of us left the professor inspired by his interest, cheered with his enthusiasm and energy, and ready to move heaven and earth, and we have achieved a lot. At the end of the 20th century, Professor Geoffrey Burnstock was one of the world's most cited authors in the field of pharmacology and toxicology.

Fig. 1. Professor G. Burnstock with the Ziganshin family. London, 1993.

Every year in December, at Christmas, the professor and his wife went to Australia for what he called "summer vacation," as in Australia this time is high summer. He mainly devoted this vacation to his other passion—artistic creativity. Since childhood, he painted well but achieved perfection in woodcarving. In Australia, he used a special kind of hardwood and created masterpieces from it. He was an amazing wood sculptor and embodied in his works various human emotions—love, passion, pain, and fear. His works could beautify the halls of the most famous art museums.

After my return to Kazan, we, together with Professor Burnstock, received an international grant that enabled me to equip a scientific laboratory at Kazan State Medical University. This gave me the opportunity to create my own research group, conduct scientific research at the highest level, receive new grants, and publish articles in the top journals.

In 1997, Professor Burnstock left the department and became the director of the Autonomic Neuroscience Institute. During this time, the expansion and elaboration of the purinergic theory continued. One of the most important advances in pharmacology of this time was the introduction into clinical practice of a new group of antiplatelet

Fig. 2. Professor Geoffrey Burnstock with the staff of the Department of Pharmacology, September 2000.

Fig. 3. Professor G. Burnstock with the Kazan purinergic group, 2000.

agents that are blockers of platelet purinergic $P2Y_{12}$ receptors. The drugs of this group, clopidogrel and ticlopidine, are currently widely used for preventing thrombotic complications in angina pectoris, post-infarction, and post-stroke patients. Professor Burnstock actively promoted the purinergic theory, traveled a lot around the world, and gave plenary lectures at international congresses of pharmacologists and physiologists.

The members of our Kazan purinergic group will forever remember the two visits of Professor Burnstock to Kazan. The first time was in September 2000 at a conference organized by Professor E.E. Nikolsky (Figs. 2 and 3). We accommodated him in the recently built Safar hotel in a room with a view of Kazanka and the Kremlin. I remember that the Professor was constantly admiring the beauty of our city, and looking from his room at the Kazan Kremlin, illuminated in the evening in the reflections of the river, he said "It looks like Disneyland!"

I remember one episode from this trip. Professor Burnstock made an excellent report at the conference, and in the evening, a picnic was organized on the Volga embankment. To make the moment ceremonial and to emphasize the importance of the eminent guest, the motorcade with the conference participants was accompanied to the picnic by traffic police cars with beacon lights and siren horns. We were traveling in the first car right behind the traffic police car, and seeing this, Professor Burnstock was somehow nervous and asked me cautiously what was happening. I explained that this was an escort, dignities, and respect to our guests, but he said that in England, only criminals are transported in this way.

The second visit of Professor Burnstock was in 2011 (Figs. 4 and 5), during which two other remarkable episodes occurred.

Burnstock always preferred airplanes for his trips, but this time, his colleague, who was accompanying him to our conference, persuaded him to travel together from Moscow to Kazan by train. "It is just one night and the train is very comfortable," he told Burnstock. Certainly, we bought the best seats in the Tatarstan train, a two-berth sleeper compartment, for the professor and his colleague. But the first thing that the professor told me after that night on the train, when we met at the Kazan railway station, that he would not go anywhere by train anymore and asked to buy a return plane ticket. I was surprised by this, but later, it turned out that rather than the train itself or its comfort, the professor did not like the company of his colleague, who tried to have alcoholically heart-to-heart talks with him all night.

Fig. 4. Professor G. Burnstock in the presidium of the conference. Kazan, 2011.

After being accommodated at the hotel, Professor Burnstock asked not to present chak-chak to him since he tried it the last time and he did not like it. We took this request peacefully; we have many other things to treat. The denouement of the story took place on the last day when our entire scientific group of 10–12 people came to see off and say goodbye to the professor at the hotel. One of my graduate students decided to present a farewell gift and handed him a chocolate chak-chak, which in those days was rare and the most delicious treat.

Fig. 5. Professor G. Burnstock with the Kazan purinergic group and Kazan colleagues, 2011. In his hands, the Professor is holding the classification of purinoreceptors presented to him, engraved on a wooden panel.

Obviously, she was the only one in the group who was not aware of the professor's preferences since the whole group cheerfully laughed at the words of Burnstock: "Oh, the famous chak-chak!"

Professor Burnstock was a Fellow of the British Royal Society of Science, Fellow of the Australian Academy of Sciences, Honorary Fellow of the British Royal Society of Physicians, Honorary Fellow of the British Royal Society of Surgeons, President of the International Society for Autonomic Neuroscience, Honorary President of the British Medical Association, Editor-in-Chief of two journals (*Purinergic Signaling* and *Autonomic Neuroscience: Basic and Clinical*), and a member of the editorial board of more than 20 leading scientific journals in the field of neurobiology. He is the author of more than 1,400 original articles, over 100 reviews, about 150 chapters in monographs, and over 20 books.

Professor Burnstock was awarded the Gold Medal of the British Queen Elizabeth II for outstanding scientific achievements. He was nominated twice for the Nobel Prize.

It should be noted that Professor Geoffrey Burnstock has always provided support to Kazan State Medical University. He was a member of its international scientific council and a member of the editorial colleague of the Kazan Medical Journal.

The death of Professor Geoffrey Burnstock is an irreplaceable loss for world neurophysiology and neuropharmacology. For me, this is the loss of a teacher, a very congenial soul, a colleague, an associate, and a family friend.

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REFERENCES

1. Burnstock G. Purinergic nerves. *Pharmacol. Rev.* 1972; 24: 509–581.