

# Farewell to Joseph Milic-Emili

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*To steal from one author is plagiarism, but to steal from many is science  
J. Milic-Emili*

## Joseph Milic-Emili

Joseph Milic-Emili was born in 1931 in the village of Sezana, then part of Italy, but now in Slovenia. After obtaining his medical degree from the University of Milan in 1955, he was appointed Assistant Professor in the Department of Physiology in that institution, where he carried out research on exercise physiology with Rodolfo Margaria. He was enticed to move to the University of Liège in 1958 by the Belgian physiologist Jean-Marie Petit, with whom he developed methods to measure pleural pressure with the esophageal balloon catheter as well as the electrical activity of the diaphragm using esophageal electrodes, techniques still applied in patients to this day. In 1960 Milic-Emili moved to Boston to work at the Harvard School of Public Health. Then in 1963, at the invitation of David Bates, Milic-Emili moved to McGill University, where he spent the remainder of his career. Milic-Emili was Chairman of the Department of Physiology at McGill between 1973 and 1978, prior to becoming Director of the Meakins-Christie Labs in 1979. He was appointed Professor Emeritus in the Departments of Physiology and Medicine at McGill in 1998. Throughout his career he received many honors and distinctions. He was elected Fellow of the Royal Society of Canada in 1980 and was conferred the Order of Canada in 1990. He was granted the degree of Doctor Honoris Causa by the Université Catholique de Louvain (1987), the University of Kunming (1988), Université de Montpellier (1994), and the University of Ljubljana (1999).

## Scientific contributions

These involved six main areas of respiratory physiology and physiopathology: 1) respiratory mechanics; 2) regional distribution of ventilation and perfusion within the lungs; 3) effects of mechanical loading on breathing; 4) control of ventilation; 5) assessment of respiratory mechanics in patients with acute respiratory failure; 6) assessment of expiratory flow-limitation.

## Respiratory mechanics

This research (1955–1963) resulted in the introduction of the measurement of the electrical activity of the diaphragm via esophageal electrodes and in the refinement of the esophageal balloon technique for indirect measurement of pleural pressure. Both techniques are now widely used both as research tools and for clinical assessment of patients. In addition, Milic-Emili and his co workers provided a systematic description of the mechanical work of breathing and the mechanical efficiency of breathing in normal subjects and in athletes. A variety of other aspects of respiratory mechanics were also dealt with. In particular, the study on the effects of the external resistance breathing on the respiratory work output has proved influential for subsequent research in this field.

## Regional distribution of ventilation and perfusion within the lungs

Systematic research in this area of respiratory physiology was carried out mainly in 1964–1970. This work provided the first systematic description

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of regional distribution of gas within the lungs. From these research arose the concept of 'closing volume' whose method of measurement was first described in 1967. These studies were extended to elderly subjects, obesity, smoking, asthma, pulmonary oedema, and liver cirrhosis. In addition, several factors which can influence regional distribution of gas within the lungs were assessed. In 1972, a theoretical study was published which predicted that ventilation distribution is affected by the inspiratory flow rate. Thus, in a period of less than 10 years, the knowledge of the regional lung function was advanced from indirect and scattered information to a mature field. The new information is of both basic and clinical interest.

### Effects of mechanical loading on breathing

Interest in this area began in 1963, but a systematic investigation of this area of physiology was undertaken only in 1971, centering first on the immediate respiratory responses to added loads to breathing. This was followed by systematic investigations on the ventilatory effects of body temperature, vagotomy, expiratory pressure loading, baroreceptor stimulation and SO<sub>2</sub> inhalation. Three articles published in this field were of particular importance. The first provided useful new information concerning the Hering Breuer inflation reflex. The second stressed the importance of the intrinsic properties of the respiratory muscles (force length and force velocity properties) in relation to control of breathing. The third introduced the airway (mouth) occlusion pressure as an index of neuromuscular inspiratory drive. Most importantly, the studies on mechanical loading of breathing led to the conclusion that 'mechanical loading of breathing (in particular airway occlusion) can be used to evaluate basic aspects of control of breathing' rather than just a study of the response of the respiratory system to loading. In addition, these studies have stressed the importance of the analysis of the breathing pattern in clinical assessment of control of breathing.

### Control of ventilation

The airway occlusion pressure technique first applied to anesthetized cats was subsequently modified for use in conscious humans. Thus, the PO.1 technique for assessment of control of breathing was introduced and applied in newborn animals and babies to study the maturation of control of breathing, and in anesthetized adult men and animals to assess the effects of anesthesia on respiratory mechanics and control. Most important are the clinical applications of the assessment of control of breathing based on analysis of the breathing pattern and the measurement of PO.1 in patients with chronic obstructive lung disease (COLD). The mouth occlusion pressure technique and the analysis of the breathing pattern are at present widely used in both clinical and physiological studies of control of breathing. The subsequent research of Milic-Emili and his group centered on: a) clinical assessment of control of breathing in

pulmonary fibrosis, cystic fibrosis, etc.; b) the development of non invasive methods for studying respiratory mechanics; and c) analysis of the neural, muscular, and mechanical factors which determine the morphology of the spirogram and pneumotachogram.

### Assessment of respiratory mechanics in patients with acute ventilatory failure

In the 1980s, Milic-Emili and his group developed a battery of new tests for non invasive assessment of respiratory mechanics in mechanically ventilated patients with acute respiratory failure; of particular interest is a new method for studying frequency dependence of compliance and flow resistance.

### Assessment of expiratory flow-limitation

A new method, the "negative expiratory pressure technique", has been recently developed which allows to determine the presence of expiratory flow-limitation at rest and during muscular exercise. This method does not require any cooperation of the patient and can be applied in stable patients, as well as during mechanical ventilation and exercise.

### The Greek chapter of Milic-Emili

Milic-Emili had a profound effect on the development of Modern Greek Pulmonology. He was the mentor of many professors and chest physicians, e.g. C. Roussos, N. Siafakas, P. Bechrakis, A. Rassidakis, N. Koulouris, A. Koutsoukou, and E. Kosmas, introducing them into the unknown waters of Respiratory Physiology-Pathophysiology.

He loved Greece and often visited the Departments of his Fellows (Athens, Crete Universities), working with young pulmonologists, mentoring, and helping them to accomplish their thesis, write research papers and coaching them for International Meetings. As a result, more than 30 papers were published and therefor many Greek scientists are indebted to Milic-Emili. For all these contributions to Greek Science he was granted the degree of Doctor of Honoris Causa by the University of Athens, in 1999.

It is obvious, that Greek Pulmonology flourished due to his timeless mentorship, friendship, and enthusiastic teaching. The English word enthusiasm, which of course derives from the Greek, indicates that 'God is within' and signifies knowledge deeper than faith and has a meaning of truth. He educated Greek Chest physicians how to present data, being honest presenting always the scientific truth, and not being arrogant.

### Milic-Emili a true leader and a wonderful person

We were privileged to work under his supervision. He made an enormous impact not only on our scientific careers but on our attitude to life. With his enthusiastic teaching abilities and outstanding mentorship and tremendous encouragement he kept us continuously stimulated, introducing us to

scientific logical thinking. His unique attitude towards life, his broad cultural experience, his historical knowledge, his humor and jokes, made him not only a scientific giant but an outstanding and warmhearted person, that affected the life of thousands of Fellows all over the World. His wonderful accent, his gestures, his laughter, his sparkling eyes, and his brilliant mind reflected the exceptional personality of a great man.

He disseminated Respiratory Physiology to the world via his scientific work, his fellows, and by travelling all over the world. Thousands of scientists owe him a great deal and promise to keep his legacy alive.

Dear Professor Milic-Emili, your *grantate immortalita* has become a reference model for Mentorship, Teaching, and Friendship for future generations.

### **CONFLICTS OF INTEREST**

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The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

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### **DISCLAIMER**

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