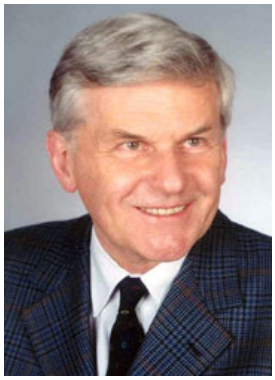
Andrzej Szczeklik



Krakow, Poland, 29 July 1938 - 3 Feb. 2012

Nomination 16 Oct. 1994

Field Medicine

Title Professor

Commemoration – I am honored and grateful to speak in memory of our beloved colleague Andrezej Szczeklik. I met him for the first time at our Academy in 1994 and I will always remember his self-presentation, modest and to the point. He gave a moving testimony of his admiration and love for Pope John Paul II. A few years later he gave me as a gift his inspiring book *Catharsis: On the Art of Medicine* with a foreword by the great Polish humanist and poet Czes#aw Mi#osz. A continuation of this book is called *Kore#: On Sickness, the Sick, and the Search for the Soul of Medicine*, a suggestive title that reveals the spirit and mission of a man totally dedicated to his patients and to science.

Andrezej Szczeklik was born in 1938 in Cracow, where he studied medicine. He did post-doctoral training and research at the Karolinska Institut, Uppsala University and North Carolina-Chapel Hill. He became professor and chairman of the Jagiellonian University School of Medicine, Cracow, and president of the Copernicus Academy of Medicine. He was a member of the Polish Academy of Arts and Sciences, the Royal College of Physicians, the American College of Physicians and the Pontifical Academy of Sciences. He became an active participant in all our Plenary Sessions. He received honorary doctorates from the Schools of Medicine of Wroc#aw, Warsaw, Katowice and #o#dz. He was awarded the Gloria Medicinae Medal by the Polish Society of Medicine. He received the first prize of *The Lancet* for his paper on genetic polymorphism of leukotriene C4 synthase. In 2001 he was awarded the Gold Medal and The Robert A. Cook Memorial Lectureship by the American Academy of Allergy, Asthma and Immunology.

His whole life was dedicated to the study and treatment of cardio-pulmonary diseases. He was one of the first to discover the mechanisms of non-steroidal anti-inflammatory drugs that precipitate asthma attacks in sensitive patients by inhibiting cyclooxygenase (COX-1), a key enzyme in the metabolism of eicosanoids (substances produced by arachidonic acid). He was a leader of the European Network on Aspirin-Induced Asthma centered in Cracow. He discovered the genetic polymorphism and over-expression of leukotriene C4 synthase in patients with aspirin-induced asthma and the alteration of the metabolism of arachidonic acid common to asthma and urticaria.

He studied the history of salicylates, the forbears of aspirin, the drug that was produced by the pharmaceutical firm Bayer in 1899 and became the most popular drug in the world. His paper The history of aspirin: the discoveries that changed contemporary medicine presented at our Plenary Session 2004 and published in Paths of Discovery was a remarkable contribution to our understanding of clinical investigations.

He also worked in the mechanisms related to blood clotting after the discovery by his colleague Ryszard Gryglewski in 1976 of prostacyclin in humans, a local substance produced by the lining of blood vessels that produces vasodilation and inhibits blood clotting. In his book *Catharsis* he vividly described the first test of the drug in themselves at the Hospital of Cracow using a sample of the molecule synthesized by Joseph Fried, and how he was affected with high fever after the intravenous infusion (the prostacyclin was contaminated by bacteria) and how Gryglewski lost consciousness (because of the massive vasodilation and the lowering of blood pressure). After further experiments on himself without any complications they started to treat patients with serious diseases of peripheral vessels. I quote “How many days and nights we spent at their bedsides, listening out for the piercing pain in their feet to quieten down, and not believing our own eyes where the deep ulcers on their skin shrank and dwindled as the blood was mixed with a daily dose of prostacyclin”. Today stable

analogues of prostacyclin are used in the treatment of pulmonary hypertension and also in the treatment of arteriosclerosis. It was further discovered that aspirin inhibits blood clotting and that those statins that reduce blood cholesterol also inhibit blood clotting.

Szczeklik, the remarkable internist and scientist, the mentor of generations of Polish physicians who published more than six hundred papers, was also a humanist, writer, musician, lover of the arts and a man of deep faith that practiced medicine as a sublime humanitarian art. He said “An internist is like a symphony orchestra conductor; specialists are like individual instrumentalists. They do the playing, but only the conductor knows all the instruments and what to expect from them”. In his book *Catharsis* he wrote that “Medicine concerns perhaps the strongest of human desires – our longing for love, which is usually unfulfilled”. We will miss him.

Antonio Battro

Most important awards, prizes and academies

Awards: Sniadecki Award of the Polish Academy of Sciences (1974); G. Sadoul Award of the European Respiratory Society (1990); Gloria Medicinae Award of the Polish Medical Society (1995); First Prize of The Lancet for the paper on genetic polymorphism of leukotriene C4 synthase (1997); First Award of the Polish Science Foundation (1998); a medallion and stand for the Robert Cook Memorial Lectureship, American Academy of Allergy and Immunology (1980). *Academies*: Polish Academy of Arts and Sciences (1990); Pontificia Academia Scientiarum (1994); Polish Academy of Sciences (1995); Royal College of Physicians, London (1998); American College of Physicians (2007). *Honorary Degrees*: University Schools of Medicine, Wroc#aw (1999); Warsaw (2001); Katowice (2002) and #ódz (2003).

Summary of scientific research

Szczeklik's main contributions are in the field of cardio-pulmonary diseases. His early work led to the formation of the hypothesis explaining the mechanism of aspirin-induced asthma, a relatively common clinical syndrome affecting 10% of adult asthmatics. The hypothesis, proved true in the following years, states that aspirin and several other nonsteroidal anti-inflammatory drugs precipitate attacks of asthma in sensitive patients by inhibiting cyclooxygenase (COX-1), the key enzyme in the metabolism of eicosanoids, substances produced from arachidonic acid by most of the cells of our bodies. He then demonstrated a profound overexpression of leukotriene C4 synthase in bronchi of patients with aspirin-induced asthma, and discovered genetic polymorphism of this enzyme, associated with severe type of the disease. This work, awarded first prize by *The Lancet*, stimulated research on the involvement of eicosanoids in pulmonary diseases, and led to the establishment of the European Network on Aspirin-Induced Asthma, which combines 25 university departments from 14 countries, with Cracow serving as a coordinating center. Interestingly, his recent research unveiled alterations in arachidonic acid metabolism which are common to asthma and urticaria. In 1977 A. Szczeklik injected prostacyclin into himself and his colleagues, a newly discovered local hormone produced by the lining of our blood vessels. He described the powerful actions of prostacyclin in man (vasodilatation, inhibition of blood clotting) and introduced it into the therapy of vascular disorders. Today, analogs of prostacyclin and its close congeners are routinely used for the treatment of peripheral vascular disease, inflammatory diseases of arteries and primary pulmonary hypertension. His most recent research resulted in the discovery of a novel action of aspirin: it inhibits the generation of thrombin in clotting blood. The dampening of the powerful blood clotting mechanism by aspirin may explain, partially at least, its beneficial prophylactic and therapeutic effects in ischemic heart disease and stroke. Interestingly, this action of aspirin is blunted in hypercholesterolemia and also in a common genetic polymorphism of blood platelet glycoproteins. Thus, subjects with high blood cholesterol or the genetic variant of platelets might profit less than others from the antithrombotic effect of the drug. These studies led to a development of a new sensitive model for studying thrombin generation in vivo, demonstration that statins, powerful blood cholesterol lowering drugs, depress the specific reactions of the blood clotting mechanism.

Main publications

Szczeklik, A., Gryglewski, R.J., Czerniawska-Mysik, G., Relationship of inhibition of prostaglandin biosynthesis by analgesics to asthma attacks in aspirin-sensitive patients, *Br. Med. J.*, 11, 1, pp. 67-9 (1975); Szczeklik, A., Gryglewski, R.J., Czerniawska-Mysik, G., Clinical patterns of hypersensitivity to nonsteroidal anti-inflammatory drugs and their pathogenesis, *J. Allergy Clin. Immunol.*, 60, pp. 276-84 (1977); Szczeklik, A., Ni#ankowski, R., Skawinski, S., Szczeklik, J., G#uszko, P., Gryglewski, R.J., Successful therapy of advanced arteriosclerosis obliterans with prostacyclin, *Lancet*, 26, pp. 1111-4 (1979); Szczeklik, A., S#adek, K., Szczerba, A., Dropinski, J., Serum immunoglobulin E response to myocardial infarction, *Circulation*, 77, pp. 1245-9 (1988); Szczeklik, A., Krzanowski, M., Góra, P., Radwan, J., Antiplatelet drugs and generation of thrombin in clotting blood, *Blood*, 80, pp. 2006-11 (1992); Szczeklik, A., Musia#, J., Undas, A., Swadzba, J., Góra, P., Piwowarska,

W., Duplaga, M., Inhibition of thrombin generation by aspirin is blunted in hypercholesterolemia, *Arterioscl. Thromb. Vasc. Biol.*, 16, pp. 948-54 (1996); Sanak, M., Simon, H.U., Szczeklik, A., Leukotriene C4 synthase promoter polymorphism and risk of aspirin-induced asthma, *Lancet*, 350, pp. 1599-1600 (1997); Szczeklik, A., Gryglewski, R.J., Vane, J.R., (eds), *Eicosanoids, aspirin and asthma*, Marcel Dekker, Inc., New York-Basel-Hong Kong (1988); Cowburn, A.S., S#adek, K., Soja J., Adamek, #., Ni#ankowska, E., Szczeklik, A., Lam, B.K., Penrose, J.F., Austen, F., Holgate, S.T., Sampson, A.P., Over-expression of leukotriene C4 synthase in bronchial biopsies from patients with aspirin-intolerant asthma, *J. Clin. Invest*., 101, pp. 834-46 (1998); Undas, A., Brummel, K., Musia#, J., Mann, K.G., Szczeklik, A., Pl(A2) polymorphism of beta(3) integrins is associated with enhanced thrombin generation and impaired antithrombotic action of aspirin at the site of microvascular injury, *Circulation*, 27, 104, pp. 2666-72 (2001); Szczeklik, A., Musia#, J., Undas, A., Reasons for resistance to aspirin in cardiovascular disease, *Circulation*, 106, e181-182 (2002); Undas, A., Sydor, W.J., Brummel, K., Musia#, J., Mann, K.G., Szczeklik, A., Aspirin alters the cardioprotective effects of the factor XIII Val34Leu polymorphism, *Circulation*, 107, pp. 17-20 (2003); Bochenek, G., Nagraba, K., Ni#ankowska, E., Szczeklik, A., A controlled study of 9alpha,11beta-PGF2 (a prostaglandin D2 metabolite) in plasma and urine of patients with bronchial asthma and healthy controls after aspirin challenge, *J. Allergy Clin. Immunol*., 111, pp. 743-9 (2003); Szczeklik, A., Stevenson, D.D., Aspirin-induced asthma: advances in pathogenesis, diagnosis, and management, *J. Allergy Clin. Immunol*., 111, pp. 913-21 (2003); Szczeklik, A., Sanak, M., Ni#ankowska-Mogilnicka, E., Kie#basa, B., Aspirin intolerance and the cyclooxygenase-leukotriene pathways, *Curr. Opin. Pulm. Med*., 10, pp. 51-6 (2004); *Catharsis, On the Art of Medicine*, by A. Szczeklik, A. Lloyd-Jones (translator), University of Chicago Press, December 2005, pp. 172.