Prof. Andrzej Szczeklik
Immunologist, writer and Vice-Rector of the Jagiellonian University for Medical Affairs, Poland

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, Wrocław (1999); Warsaw (2001); Katowice (2002) and Łódz (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., Niżankowski, R., Skawinski, S., Szczeklik, J., Głuszko, P., Gryglewski, R.J., Successful therapy of advanced arteriosclerosis obliterans with prostacyclin, *Lancet*, 26, pp. 1111-4 (1979); Szczeklik, A., Sładek, 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., Musiał, 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., Sładek, K., Soja J., Adamek, Ł., Niźankowska, 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., Musiał, 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., Musiał, J., Undas, A., Reasons for resistance to aspirin in cardiovascular disease, *Circulation*, 106, e181-182 (2002); Undas, A., Sydor, W.J., Brummel, K., Musiał, 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., Niźankowska, 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., Niźankowska-Mogilnicka, E., Kiełbasa, 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.