

Ernest Gutmann Heritage, 30-year after

Aula Magna of the Palazzo Bo, University of Padova (Italy), April 12, 2007.

This Special Issue of BAM contains a collection of papers from the 2007Spring PaduaMuscleDays: The Long Lasting Denervated Muscle, a conference held in Padua&Terme Euganee (Italy) to honor 30 years after his premature death Ernest Gutmann, a seminal figure of muscle research.

Born July 16, 1910 in Czechoslovakia, Ernest Gutmann died August 6, 1977 during a visit in England. After his 1936 M.D. at the Charles University in Prague, he went to England in 1939 to work with J.Z. Young in Oxford, where he obtained his PhD publishing some fundamental papers on nerve regeneration. In 1945 he returned to Czechoslovakia, where he worked first as a physician looking after people returning from concentration camps, later he continued his research on nerve regeneration in the Institute for Brain Research of the Charles University in Prague. In 1954 Ernest Gutmann became head of one of the divisions of the Institute of Physiology of the Czechoslovak Academy of Sciences. The main research topic was the study of nerve-muscle interactions, and that of course included the study of denervated muscle. Gutmann was in favor of a multidisciplinary approach that was very fruitful, and leads to the publication in 1962 of the book: The denervated muscle.

In spite of the relative isolation from the rest of the scientific community due to the cold war, Ernest Gutmann and his colleagues managed to establish many international contacts. After 1968, when the Russians invaded Czechoslovakia, Gutmann signed a proclamation condemning his invasion (so called “two thousand words”) and was persecuted by the official communist establishment. He nearly lost his job, but miraculously still continued to produce high quality experimental work with many international colleagues, some of which contributed papers for this Special Issue. Unfortunately he did not live long enough to see the liberation of Czechoslovakia.

The commentaries of Gerta Vrbova, Dirk Pette, Bruce Carlson and of Gutmann’s daughter Anna Koffer-Gutmann describe the personality of Ernest Gutmann and underline his continuing impact on Myology. On the issue of nerve influence on muscle, Gutmann favored the hypothesis of neurochemical regulation. In spite of the difficulties to identify and chemically purified the molecular factors, and the evidences that “muscle activity” (induced by quantal liberation of acetylcholine at the neuron-muscle synapsis) has a major effect on muscle size and fiber-type regulation, some biological features of the nerve-muscle relations continue to suggest their existence. Anyhow Ernest Gutmann was an open-mind researcher: the book “The Denervated Muscle” offers a still valid description of the nerve-mimicking effects of electrical stimulation on denervated muscle and of its potential clinical applications.

I was a young student of the Padua School of Medicine in the Prof. Aloisi laboratory, when Ernest Gutmann went to Padova on his way to England. Muscle fiber types and their control by the motor neurons were hot topics (the cross-reinnervation model was in his infancy). The denervated muscle (usually a few-day denervated muscle to study effects of peripheral nerve stump length) was a popular study-model also in the Aloisi’s Lab. During a tee break (American coffee breaks were not yet common) some one mentioned the paradoxical effects of muscle denervation during early few-day denervation of the rat hemi diaphragm and of the chicken pectoralis muscle (see Gerta Vrbova Commentary in this Issue). Just to continue conversation, I asked Aloisi what was known about “long-term denervation” of muscle fibers. His reply cut down the discussion: the myofibers can’t survive denervation, though some muscles may show a paradoxical hypertrophy early after denervation. That query remained in my back-ground thoughts, so when a few years later I discovered that a group of “lost” rats had six-month denervation of the hemi diaphragm, I collected the muscles, extracted as usual myosin and did its SDS PAGE analysis. The results showed that the denervated hemi diaphragm still contained myosin, but its isomyosins were shifted from a mixed to a fast myosin composition [1, 2]. To study this model I then added to our analytical tools SDS PAGE of myosin light chains, 2D SDS PAGE of myosin light chains, embryonic type included [3], and finally I defined the electrophoretic condition to separate fast and slow Myosin Heavy

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Chains (SDS PAGE of MHC) [4]. Such molecular markers were used and continue to be used to study adaptations of muscle to denervation and muscle plasticity/regeneration (see Dirk Pette Commentary and Bruce Carlson Article in this Issue, and Carraro U and others [5-10]).

I introduced the concept that long term denervation is accompanied by myofiber death and (thus) regeneration [5, 6]. Recently, in collaboration with Helmut Kern of the Vienna Wilhelminenspital we showed that this is valid also for human muscles [8-10]. Indeed this also occurs during a Functional Electrical Stimulation (FES) training [8], that recovers in many subjects size and function of long term peripherally denervated thigh muscle after Spinal Cord Injury [9, 10]. "The Denervated Muscle" anticipated many of these results, and indeed has been and continue to be our "Myology Bible".

The denervated muscle (in particular at very late phases) continues to surprise myologists. The last new is that long term denervation-induced muscle degeneration (i.e., substitution of muscle fibers with adipose and fibrous tissue), that occurs four to six months after denervation in the rat (see Carlson article in this BAM issue), appears in large mammals, humans included, much later (two to four years after denervation) [5, 6].

The fruits of the legacy of Ernest Gutmann is well documented by the papers published in this issue of Basic and Applied Myology, and by those that will be printed in "Special Sections on Myology" of the journal Neurological Research.

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