The importance of concord between nations for scientific progress in cardiopulmonary resuscitation. A literature review

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Abstract

Conflict between nations harms not only its direct victims, but often the next generations. History teaches us that concord and international cooperation favors the progress of science, especially medicine, while wars and violence provoked by different religious, ideological, political, and sociocultural contexts hinder scientific research to the detriment of humanity. The objective of this article is to recall some notable figures in the history of cardiopulmonary resuscitation (CPR), focusing on the negative consequences of ideological persecution for the science of CPR.

Introduction

The history of medicine boasts a plethora of remarkable individuals who have changed the course of science through their personal dedication and suffering. Different sociocultural contexts – including wars, dictatorships, ideologies, and religious fanaticism – have put these scientists to the test on many occasions, but the quest for knowledge has prevailed over difficult and even tragic circumstances.

The convulsive history of Cardiopulmonary Resuscitation (CPR) is rooted in fundamental concepts of human anatomy and physiology that, while first described more than 500 years ago, only came to light centuries later due to the complex ideological situation of the epoch. While CPR in its current form is a relatively modern discipline, dating from the 1950s, we can postulate that the lack of international cooperation and the prevalence of totalitarian ideologies which characterized the 20th century constituted an obstacle for the free development and divulgation of this life-saving technique.

This paper aims to describe and analyze some of the most representative figures from the history of CPR whose contributions to science had to overcome different political, ideological, and sociocultural barriers, standing today as a monument to mankind's tenacity in the search for knowledge.

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Hard beginnings

Erasistratus of Ceos (304-250 a.C.) and Herophilus of Chalcedon (335-280 a.C.), the two founders of the medical school of Alexandria, Greece, carried out the first described dissection of a human cadaver more than 2000 years ago. However, their experiment would have to wait around 1700 years to be reproduced in a European university. Later, Greek scholars abandoned the practice of dissection, considering it of little use. During the Middle Ages in Europe, the dissection of human cadavers was considered blasphemous and, as such, prohibited by religious authorities. Finally, in 1315, a professor of surgery at the University of Bologna - Mondino de' Liuzzi - carried out the first public systematic dissection of the human body, abandoned and officially banned since the time of Erasistratus and Herophilus.[1,2]

Can we use rain that fell a thousand years ago?

Born in Einseideln, near Zurich, in 1493, Paracelsus (Phillipus Aureolus Theophrasus Bombastus von Hohenheim, 1493-1541) is one of the most controversial figures of the Renaissance. He is recognized as an important reformer of medicine and known as the founder of several disciplines including biochemistry, pharmacology, toxicology, and therapeutics. He was also famed for his capability to upset his colleagues and overturn traditional teachings of the epoch. At the young age of 23, he graduated from medical school, and began to travel throughout Europe acquiring a profounder knowledge of traditional and popular medicine. Paracelsus sustained a conflictive relationship with traditional doctrines. He used his treatise on epilepsy to voice the prevalent anticlericalism of his time, denouncing the religious and monastic orders for their extravagance and for abandoning the poor.[3] After being appointed *Stadtartzt* (doctor of the city) and professor of physics and surgery of Basel in 1527, he made the dramatic gesture of burning the works of Galen and Avicenna in front of his students. The teach-

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ings of Galen had been upheld as the standard of medical science for 15 centuries, while Avicenna's *Cannon of Medicine* had become a reference for European medicine five centuries ago.[3,4] However, Paracelsus condemned all teaching not based on experimentation. He stated, "medicine can only be learnt from what the eyes can see and the fingers touch… practice should not be based on speculative theory, but instead, theory should be derived from practice." He held traditional teaching in contempt. "Can we use the rain that fell a thousand years ago?", he asked rhetorically, "only that which falls today is useful".[3,5] William Osler writes that he "made men think. Paracelsus stirred the pool as had not been done for fifteen centuries".[6] At the time of his death, only a few of Paracelsus' works had been published. Posthumously, his disciples published many manuscripts that he had left throughout different European cities. Paracelsus perfected older techniques of mouth-to-mouth resuscitation, described since antiquity, by inserting a bellows into the nasal fossa of apneic patients, trying to inflate their lungs to reanimate them. In 1530, he inserted a bellows to blow heated air into the nasal fossae of an apneic patient, providing ventilatory support. During almost 300 years, Paracelsus' 'bellows method' was used throughout Europe, earning him the title of 'father of mechanical ventilation' according to some authors.[3,7,8]

Faith and science

Miguel Servet (Miguel Serveto y Conesa/Michael Servetus) (1511-1553) was a Spanish doctor and religious reformer. In his treatise on theology, Christianismi Restitutio (the Restitution of Christianity), published in 1546, Servet described his discovery of the pulmonary circulation. His work, along with his person, was burnt in 1553 due to the religious fanatism of the moment in Europe.[9,10] Later, Realdo Colombo and Valverde de Amusco propagated his discovery throughout Europe.[11] Servet was a zealous defender of freedom of thought, as his writings suggest; "no authority, whether ecclesiastic or civil, has the right to impose their beliefs or limit the freedom of thought of every individual".[9,10] Alcalá wrote that, "Servet is the first Christian thinker to proclaim the fundamental principle of the right to liberty of conscience".[12]

Seeing, hearing and feeling science

The Belgian anatomist Andreas van Wesel (Andreas Vesalius, Versalio or Vesalio, 1514 to 1564) is considered one of the most important physicians and surgeons of all time. The judge of the penal tribune of Padua took an interest in Vesalius' work and, in 1539, gave the young scientist access to the corpses of executed criminals in order to perform human dissections. In 1543, Vesalius wrote his magnum opus *De Humani Corporis Fabrica* (The Structure of the Human Body), an outstanding treatise on human anatomy. With the publication of *De Humani Corporis Fabrica*, Vesalius began to overturn the old Galenic superstitions about human anatomy that had been believed firmly for over 1300 years, due to his work with human cadavers. He stated - heretically for his time - that "human anatomy can only be learnt from the dissection and direct observation of the body." Until then, anatomy had only been learnt from textbooks, principally those of Galen.[13,14]

Some authors consider Vesalius as the father of modern anatomy and CPR. Vesalius described the first known attempt of cardiac resuscitation on the hearts of dogs and pigs, using tracheotomies, intubations, and bellows to expand their lungs intermittently, trying to simulate natural breathing.[15] The medical historian Arthur Barrington Baker (1939) remarks that such an important experiment was underestimated to the point of camouflage and speculates that Vesalius was afraid of reprisals from ecclesiastical authorities, thus avoiding undue attention. Vesalius' life ended tragically while returning from a forced pilgrimage maybe in order to escape the Inquisition.[10,14-16]

A life dedicated to science

Born in Libau (Latvia) to a Jewish family, Lina Solomonovna Stern (Schtern) (1878-1968) was educated in an atmosphere of Western internationalism and religious freethinking. At the University of Geneva, she studied under Prevost and Battelli, going on to become her alma mater's first female professor from 1918 to 1925. Other positions she would go on to hold included Director of the Institute of Physiology of the USSR Academy of Sciences and the first woman elected as an ordinary member of the Academy in 1938.[17]

In 1925, Stern decided to abandon the academic stability and peace of Geneva to direct a department of physiology at the second Medical University of Moscow. Her friends and colleagues in Geneva tried to dissuade her, reminding her of the complicated political situation in the Soviet Union. Nonetheless, Stern, who had been offered the positions of chair of physiology and head of the medical school's laboratory, left Geneva.[17,18]

During May 1948, Lina was fully occupied leading research on the effects of electric shocks on the induction of arrhythmias and defibrillation, with the young doctoral student Naum Gurvich as principal investigator, when she was informed that the Academy of Sciences had decided to move her laboratory to Leningrad and appoint Konstantin Bykov as director. Her entire staff was fired, including Gurvich.[17] On January 24, 1949, during the Stalinist dictatorship, Lina Stern was imprisoned. The death of the dictator in 1953 put an end to Stalinism and its arbitrariness, and Lina was allowed to return to Moscow, where she was officially rehabilitated in 1958. Her ties to Switzerland and Geneva, whose university awarded her an honorary Doctor of Science in 1960, were never severed.[17,18]

An Oscar for the best supporting actor!

Naum Lazarevich Gurvich (1905-1981) was born in Timkovich (Belarus) and is considered one of the most important contributors to the development of defibrillation therapy, yet his figure is almost unknown in the West. He lived and worked under one of the worst dictatorships in history, cut off from the international cardiology and scientific community. However, his devotion to medicine and physiology despite adversity is worthy of admiration. Gurvich deserves to take his rightful place in medical history for the discovery, development, and clinical implementation of the biphasic transthoracic defibrillator, as well as for his contributions to the theory of fibrillation and cardiovascular physiology.[18,19]

Gurvich first reported using the rounded biphasic waveform for defibrillation as early on as 1939. His physiological findings and theories were presented in two complete monographs in Russian, published in 1957 and 1975, but he was unable to travel outside the Soviet borders and present his studies to the international scientific community until much later.[20,21] In the early 1950s, Gurvich designed the first commercially available direct-current

transthoracic defibrillator. In 1970, he introduced the first biphasic transthoracic defibrillator, which swiftly became the gold standard in Soviet medical practice, preceding its Western analogues by more than a decade.[22,23]

The scientific father of humanity

Peter J. Safar (1924-2003) was born in Vienna in 1924. In 1938, the Nazis occupied Austria. Peter's father refused to join the Nazi party and his mother was considered 'non-Arian' due to her Jewish grandmother; in consequence, both were forbidden to practice their medical profession. Peter was sent to a labor camp in Bavaria where he was abused both physically and psychologically. In 1942 he was called to join the army but was able to trick the Nazi authorities by provoking eczemas with tuberculin, finally being declared unfit for service in 1944.

Two years after graduating from the Faculty of Medicine of Vienna in 1948, he left for the United States of America with his wife, four suitcases and scarcely five dollars in his pocket. In 1952, he achieved certification as an anesthesiologist. Due to problems with his visa, he was forced to leave the USA for a year, travelling to Peru and founding an anesthesiology unit at the National Institute of Cancer in Peru. Despite the impoverished surroundings, he was able to demonstrate that good practice is possible, even when resources are lacking.[24,25] After returning to the USA, in 1961 he founded an intensive care unit at Pittsburgh University, integrating medical and surgical professionals from different disciplines and starting an educational program. This unit would soon become a leading reference in CPR worldwide.[26]

In the 1950s, together with the head of the ambulance service in Baltimore, Safar implemented a new design for ambulances, incorporating a seat for an assistant. Highly conscious of the fact that many acute patients reached hospitals too late for medical care, in 1967 he created an emergency ambulance service with the aid of the Falk Foundation. The pilot project, named Freedom House Enterprise Ambulance Service, initially served the most disadvantaged areas of Pittsburgh, hiring Afro-American citizens (who suffered higher unemployment rates) as paramedics. Safar realized that it was vital to train his paramedics in order to provide optimal prehospital care, including CPR, to maximize patients' chances of survival. Safar's idea was imitated in many different cities around the USA.[24]

After the tragic loss of his 11-year-old daughter in 1966 due to respiratory failure, Safar fought to convince the scientific community of the importance of maintaining cerebral perfusion, as, while the heart may recover after 20 minutes of cardioplegia, brain cells start to die just a few seconds after being deprived of oxygen and glucose.[27]

Safar was a convinced pacifist and a respected member of associations such as Physicians for Social Responsibility and International Physicians for the Prevention of Nuclear War. He founded the International Resuscitation Research Center at the University of Pittsburgh, renamed the Safar Resuscitation Research Center in 1994 by its then director, Patrick Kochanek. The center has been considered a pioneer in the field of CPR research since 1956.[26] Safar collaborated with scientists from all over the world, regardless of ideological, religious, political, and cultural differences, despite the severe limitations of the Cold War. In 1962, amidst the tensions of the "Iron Curtain" and the Cold War, he established scientific collaboration between Pittsburg and Moscow with Vladimir Negovsky, traveling to his Moscow laboratory. Safar would always remember his trip as 'well-accompanied' by Russian officials.[28] The collaboration between Safar and Negovsky lasted until the death of both scientists in 2003. Many members of both American and Russian research centers still uphold the research philosophy of the two pioneering scientists today.

The scientific end of the Cold War

Born in the Chernigov region of present-day Ukraine, Vladimir Alexandrovich Negovsky (1909-2003), launched the world's first laboratory for experimental resuscitation research in 1936 at the age of 27. In 1986, his laboratory was renamed the USSR Academy of Medical Sciences' Institute of Resuscitation.[29] Negovsky introduced the terms 'terminal state', 'agonic state', 'clinical death' (the period without blood flow that is potentially fully reversible), 'biological death' (irreversible brain-dead cardiac arrest), and the 'post-resuscitation disease' of multiple systems and/or organs, particularly the most vulnerable, the brain.[30-33]

Negovsky published a pioneering work on post-resuscitation syndrome, with detailed descriptions of the effects of cardiac arrest on all vital organs. Peter Safar commented, "I had the privilege of recommending and accompanying this book for publication in the West. The post-insult disorders described therein allude to what was later labelled as 'reoxygenation injury'". Negovsky's post-resuscitation syndrome, however, describes more than free-radical reactions, which could not be scientifically proven until the 1980s.[33]

During World War II, in the spring of 1943, Negovsky formed first-line resuscitation teams and successfully resuscitated more than 40 wounded men, some of whom were clinically dead from exsanguination. He used the resuscitation method he had developed, infusing warm, oxygenated blood and epinephrine, and applying centripetal arterial pressure towards the heart, accompanied by artificial ventilation using bellows.[33-35]

Negovsky's publications transcended less than they deserved due to language issues and the complicated international politics of the time.[34] In 1951, Negovsky had already published his observations on the changes suffered by the brain during death and resuscitation, in Russian.[33] In 1959, he created the first Moscow Center for the treatment of shock and terminal states, and later, in 1962, the first resuscitation unit. In 1959, a group from the Negovsky laboratory started to organize mobile resuscitation teams in Moscow to provide specialized aid for prehospital medical care.[34] The USSR's first hospital intensive care unit (ICU) was established at the Botkin Hospital in 1962 by Negovsky's collaborator Vladimir Kassil (1934-2017) and others. The hospital ICUs developed in the 1950s in Scandinavia and Baltimore (USA) may have stimulated the development of similar units in the former USSR.[33]

In 1962, Negovsky was able to meet with Safar and other resuscitation specialists in the city of Pittsburgh during an international symposium, despite the political restrictions imposed by the Cold War. On this occasion, the first system of cardiopulmonary and cerebral resuscitation was defined, incorporating techniques for cerebral protection during cardiac arrest.[36] In Safar's words, "one can only speculate as to whether research in resuscitation would have flourished faster, had Negovsky's findings and spirit been made accessible to the outside world between 1936 and 1962, without World War II and the Iron Curtain isolating our colleagues in communist countries".[33] Curiously, it was an American politician who initiated the task of bridging the scientific gap between East and West, especially in the field of cardiology and CPR. In

1958, Minnesotan Senator and future US Vice-President Hubert H. Humphrey visited Moscow to meet with Soviet Communist Party leader and prime minister, Nikita Kruschev (Kruschov/Khrushchev/Kruschey). During a single 8-hour meeting, they discussed numerous issues, including nuclear non-proliferation, economic cooperation, and CPR. Humphrey visited the Moscow Institute of Resuscitation, where he met with its director, Vladimir A. Negovsky, and lead defibrillation researcher, Naum L. Gurvich. The senator represented his state well; Minnesota would go on to become the implantable biomedical device industry's world capital. Humphrey immediately recognized the importance of defibrillation, with several leading American cardiologists following his example and visiting Gurvich's laboratory.[18] In 1962, before the US Senate, Humphrey called for the creation of a medical program, alleging, "I affirm that it is one of the most important of all areas of medical research, because it deals with the most universal of the interests of the man, the prolongation of human life, the postponement of death and, perhaps, the reversibility of death... I urge the United States to compete with the USSR in boldly investigating the conquest of death... that our scientists cooperate with Russian scientists on this topic…".[18,37] Although the call for international cooperation had more than merely scientific objectives, it signified important progress for the science of CPR.

Conclusions

The 1700 year gap between Erasistratus and Herophilus's dissection of a human cadaver and that of Mondino de' Liuzzi signified a long delay in the progress of science due to the dogmas, superstitions, and fears which controlled the scientists of the epoch. Centuries later, Paracelsus's hectic life was made even more so by his non-conformist character, to the detriment of his scientific contribution to society. At a time of less ideological radicalism, and in an environment which permitted more freedom of thought, his contributions to the scientific community would plausibly have been much greater.

Likewise, at another time in history, Miguel Servet could have contributed much more to science through his determination to search for the origins of natural and supernatural phenomena.

Finally, Vesalio's forced journey to the Holy Land maybe to escape the persecution of the Inquisition changed the course of his life and that of science.

Lina Stern dedicated her life to science. The Stalinist dictatorship halted both her personal life and her research, paralyzing progress in the field of electrical treatment of ventricular fibrillation. In the same context, the achievements of her colleague Gurvich were initially published only in Russian and inaccessible to the rest of the international scientific community. In another situation, with greater freedom for international relationships, Gurvich would have probably contributed even more to the development of the science of CPR. As a result of joint US-Russian research, the science of CPR progressed over four decades more than ever in modern history. Peter Safar, the most renowned author on CPR in the international sphere, together with Vladimir Negovsky, made this collaboration possible during one of the most difficult moments in the history of the 20th century. The fruits of this transatlantic collaboration have saved countless lives through CPR techniques.

Looking back at history, today we can affirm that international cooperation and peace between nations are necessary for science to progress.

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