

# Can Outstanding Research Be Done Under Less Than Ideal Conditions?

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## ABSTRACT

Great scientific discoveries rarely originate from small and poor countries. However, the lives and achievements of three Yugoslav scientists who were active in the biomedical sciences, Laza K. Lazarević (1851-1891), Ivan Djaja (1884-1957), and Pavao Stern (1913-1976), serve as an example of success in this environment. These scientists, as well as the majority of other successful investigators in small and poor countries, were trained in foreign and developed countries and, upon return, were given the freedom to start a self-dependent research program. They overcame many obstacles, including wars and civil unrests, to contribute significantly to certain medical fields. It is interesting that although a Jew, Stern was allowed to work during the World War II in Zagreb, which became capital of the so-called Independent State of Croatia, a puppet state under German control. Perhaps his good name among pharmacologists helped him to keep position during this tough period. Nowadays, new technologies needed for biomedical research are rather expensive, and poor countries cannot afford to finance many scientists. Thus, selection of the most productive researchers is the challenge for those who finance scientific work.

## INTRODUCTION

Great scientific discoveries rarely originate from small and poor countries. However, the lives and achievements of three Yugoslav scientists who were active in the biomedical sciences, Laza K. Lazarević (1851-1891), Ivan Djaja (1884-1957), and Pavao Stern (1913-1976), serve as an example of success in this environment. Two Nobel laureates of Yugoslav origin, Leopold Ružička (1887-1976) and Vladimir Prelog (1906-1998), are not included here because their scientific contributions were mainly performed in Switzerland.

### LAZA K. LAZAREVIĆ

Laza K. Lazarević was born in Šabac, Serbia. In 1879, he graduated from the Berlin Medical School and was soon appointed as head of the Department of Medicine at the General State Hospital in Belgrade. He suffered from pulmonary tuberculosis, and perhaps because he

sensed his early death, Lazarević, like Anton P. Chekhov and many other tubercular patients, was tremendously active. During a short period of professional activities, he published 80 papers and clinical observations. Lazarević also made exceptional literary contributions. His stories are masterpieces and placed his works among the classics of the nation. Lazarević participated in three Serbian-Turkish wars as a physician assistant or military doctor. Medical doctors and scientists share the fate of their societies; frustration arises when analytical and deductive minds try to interpret the logic of a society in war. Lazarević's frustration is echoed in the most powerful anti-war prose in Serbian literature.

Lazarević's most important study *Ischias Postica Cotunii*, published in the *Serbian Medical Journal* (Lazarević, 1880), a new sign for diagnosis of sciatica is presented. The test includes three steps that help to rule out affliction of the joints or muscles. In fact, he explained the origin of pain in sciatica; it comes from the stretch of the sciatic nerve and its roots and not due to the muscular compression of the nerve, as was the prevailing opinion (Kostić and Kanjuh, 2002). Lazarević's paper on sciatica was also published in German (Lazarević, 1884), and there is a good reason that the Lasegue sign is frequently called the Lasegue-Lazarević sign.

### IVAN DJAJA

Ivan Djaja (Jean Giaja) had a remarkable scientific career in Belgrade. In 1909, he got his doctoral degree in physiology from Sorbonne University, Paris. From 1910 to 1957, he lived in Belgrade where he was a chairman and founder of the Department of Physiology. Two short Balkan wars, World War I, and World War II interrupted his work. The worst period for him was the period of German occupation, 1941-1945. Djaja suffered like many Serbian intellectuals, and he was imprisoned for some time in the Banjica Concentration Camp. His co-worker, Stefan Djelineo, spent almost four years in the camp, along with Ivo Andrić, a Nobel laureate in literature who was placed under house arrest during this period.

Djaja published about 200 scientific papers, 3 philosophical books, and several stories. Djaja's main scientific contributions are in the field of thermoregulation (Figures 1 and 2). In 1938, he published two notable

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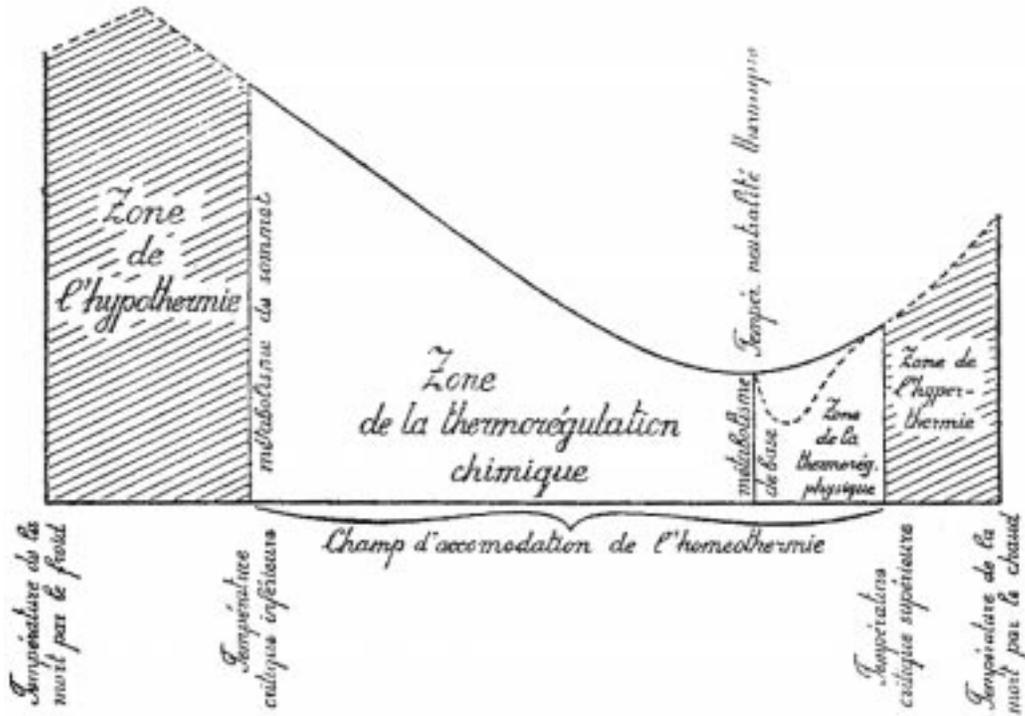


FIGURE 1 | The Diagram on Thermoregulation by Ivan Djaja (Giaja, 1938). This diagram is now called Giaja's Diagram.

books, *L'homéothermie and La thermorégulation* (Giaja, 1938), and his department soon became internationally known as the "Belgrade School of Physiology." Djaja's Ph.D. student, Radoslav Andjus (1926-2003), was the first to reanimate a rat that was in deep hypothermia, with a colonic temperature of 0 to 2°C (Andjus, 1953). Previous attempts to rewarm deeply cooled rats were regularly unsuccessful, and it was concluded by the German physiologists that below 15°C, non-hibernating animals could not be successfully reanimated. The closed vessel method of cooling animals, in which hypoxia and hypercapnia are combined, initiated an anecdote about this method introduced by Djaja; a narration made by Professor Kurt Weiss, a physiologist from Oklahoma City, was recently recorded (Igić, 2002a).

Enthusiasm for experimental work was a characteristic feature of all Claude Bernard pupils and their followers. Thus, Djaja proclaimed a motto "Nulla dies sine experimentum," and such enthusiasm resulted in his acceptance to the French Academy of Science, where he was elected as a replacement for Sir Alexander Fleming in 1956. Djaja died in Belgrade in 1957 during the International Symposium on Hibernation that was organized in his honor.

**PAVAO STERN**

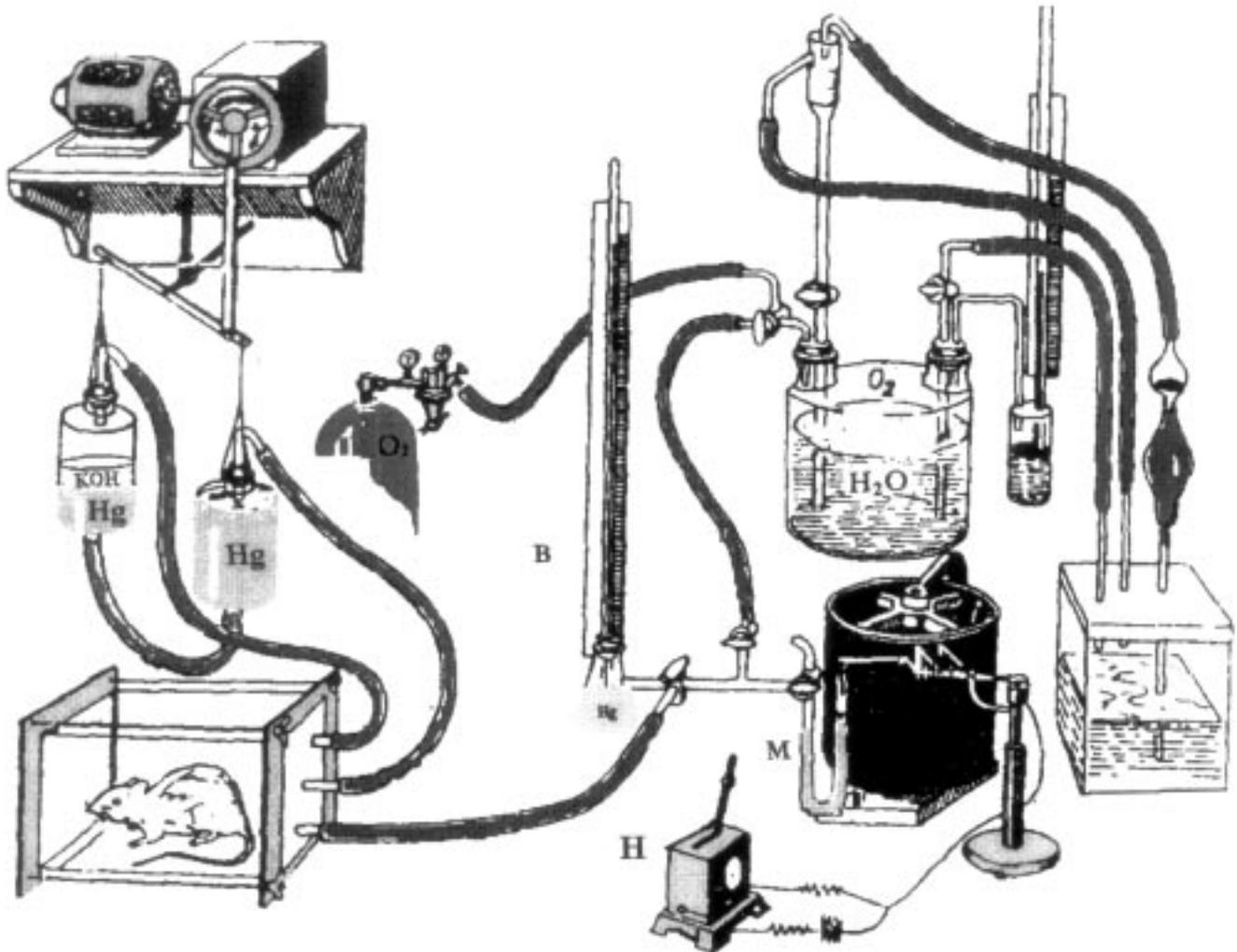
Right after the World War II, Dr. Pavao Stern was

assigned by the Yugoslav Government to come to Sarajevo from his hometown of Zagreb. The decision was made to open a medical school in the capital of Bosnia and Herzegovina, and Dr. Stern was appointed to organize the Department of Pharmacology.

After graduation from the medical school in Zagreb, Stern was trained in Austria and Germany, and he made a good name for himself among pharmacologists. Then, he worked in Zagreb at a pharmaceutical company, where he cooperated with Vladimir Prelog, who had a teaching position at the University of Zagreb. When the German Army occupied Yugoslavia, Prelog immigrated to Switzerland, but Stern stayed in Zagreb, which became the capital of a puppet state under German control. During the war, more than 500,000 Serbs, Jews, and Gypsies were brutally killed in this country. It is interesting that Stern, although a Jew, was allowed to work during the war. However, the police often threatened him. When I worked at his department in Sarajevo, he told me an interesting episode from his World War II years.

"One day a German officer entered the building where I was working and inquired about my location. My colleagues and assistants felt sorry for me because this time a highly ranked German Officer was looking for me. In all previous situations, ordinary policemen or Ustashe soldiers used to come and take me into a police station for questioning. When the officer came to my

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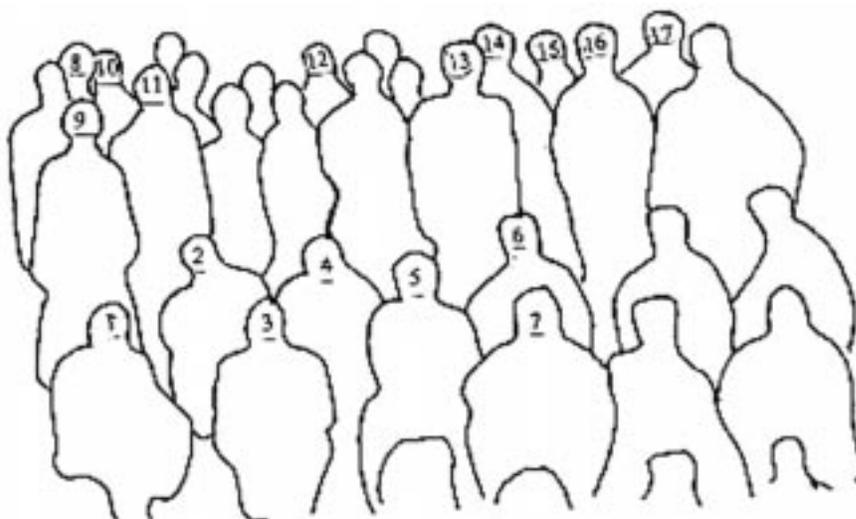


**FIGURE 2** | Djaja's Equipment for Measurement of Oxygen Utilization. In 1941, the Germans destroyed Belgrade by intensive bombing. Four years later, they were forced (by the Russians and Yugoslav Partisans) to retreat. Leaving Belgrade. The Germans burned many buildings and Djaja's laboratory disappeared. Only one piece of the equipment remained - equipment for measurement of oxygen utilization.

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**FIGURE 3** | Participants of the First International Symposium on Substance P, Sarajevo, June 9-10, 1961. The Symposium was presided by Professor P. Stern, Department of Pharmacology and Toxicology, University of Sarajevo. This meeting brought together some of the most influential physiologists of our time such as Von Euler, Pernow, and Gaddum. Professor J.H. Gaddum took this photograph of the participants. Another photograph, with Professor Gaddum among the participants, was taken by Professor Von Euler, and it was first published by him in the article "The History of Substance P" (*Trends Neuro. Sci.* 3:4-9.) (This photo is reproduced with permission).



1. E. Sturmer
2. F. Lembeck
3. B. Radmanović
4. D. Beleslin
5. V. Varagić
6. B. Pernow
7. G. Zettler
8. R. Košak
9. Olga Višnjevac
10. B. Bošković
11. Ivanka Gašparović
12. Martha Vogt
13. P. Stern
14. K. Lissak
15. S. Huković
16. U.S. von Euler
17. M. Milošević

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laboratory, he hugged and kissed me. It was my colleague and good friend, Dr. H. Konzett. We worked in the same laboratory when I was a postdoctoral fellow. My personnel got relief, and I was invited for a diner, and later on my safety was greater than before" (Stern, 1975).

Professor Stern founded the Department of Pharmacology in Sarajevo that now carries his name. For more than twenty years, this department was the most active in the former Yugoslavia. Stern and his associates significantly contributed to various areas of pharmacology and toxicology. He studied Substance P, Parkinson's and Wilson's Diseases, made original approach to the treatment of botulism by the black widow spider venom, and contributed to various aspects of neuropharmacology, immunology, and oncology. The history of medical sciences has already recorded his name among the discoverers of antihistamines (Kuschinsky et al., 1993), and he got praiseworthy credit as an organizer of the First International Symposium on Substance P (Von Euler, 1977). Professor Masanori Otsuka, Chairman of International Symposium on Substance P, Shizuoka, Japan, writes:

The First International Substance P Symposium was held in Sarajevo in Bosnia and Herzegovina under auspices of Prof. P. Stern in 1961. The number of participants listed in the Proceedings was 25. At the photo you can see Profs. Gaddum, Pernow and Lembeck, but Prof. Von Euler is missing. I once asked Prof. Von Euler why he was not in the picture, and he replied: "'I took it'" (Otsuka, 1993).

The author of this article was lucky to find another photo (Figure 3), with Von Euler and the participants taken by Gaddum, among the things that were to be discarded from the office of Professor Stern after his death, and it was later published in the book *Ulf Svante von Euler* (Igić, 1982). Unfortunately, the original photo was destroyed during the recent war in Bosnia when the Muslim forces searched my office at the medical school in Tuzla.

#### EPILOGUE

Three Yugoslav scientists successfully overcame the obstacles of wars and civil unrest and made significant contributions to biology and medicine. Yet, what do these researchers have in common? Lazarević, Djaja, Stern, as well as many other successful investigators in small and poor countries, were trained in foreign and developed countries. Upon return home, they received sufficient support and were given the freedom to initiate an independent research program. There is a consensus that the young scientists given such freedom, despite often losing a lot of time seeking adequate methods and discovering what they really want to study,

acquire an independent and critical way of thinking earlier than researchers who work in a research group with fixed research program and methods.

The Balkan region, so frequently engulfed in wars, is not considered a fertile ground for scientific research. Each generation in the former Yugoslavia is disturbed by at least one war. War and economic sanctions destroy, like a cancer, the normal functions of a society, and significantly damage scientific output (Igić, 2002b). Despite the odds, quite a few properly educated, curious, wise, and brave minds from this country have been able to make significant scientific contributions.

Science belongs to "one intellectual community," as Eugene Garfield used to say, and all scientists need to communicate freely and regularly with all members of scientific community. They must have free access to all foreign scientific innovations, including some new materials and equipment. Unfortunately, new technologies needed for biomedical research are rather expensive, and poor countries cannot afford to finance many scientists. Thus, selection of the most promising and productive scientists in such countries is the main challenge for those who make the decisions about how to run the financing of science.

#### NOTE

An abbreviated (approximately 750 words) form of this article, without figures, was submitted to *The Scientist*. Initially, *The Scientist* was not interested in the manuscript, but has agreed to publish the abstracted version in March of 2004.

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