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Time to say goodbye to the Krebs Cycle

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For decades, millions of students have memorized the Krebs Cycle for tests and forgotten it immediately afterwards. Here I propose a new approach, based on understanding rather than memorizing, and on teaching about the spectacular accomplishment of the men and women who solved the riddle; about the human solidarity that allowed Krebs to flee the Nazis; and about how newer study of the cycle helps us understand and treat cancer, sleeping sickness and other ailments.

The life of Hans Krebs was in danger when, in April 1933, the Nazis canceled his contract because it had been found that he had Jewish ancestry. Yet, he was a lucky man; he had already been saved from danger before when, as a young man, the First World War ended shortly after he got enlisted in the army. Now, Frederick Hopkins, another scientist, who admired Kreb's work, got him a job at the University of Cambridge. No one thought, at the time, that millions of students would later suffer trying to memorize the cycle that we know as The Krebs Cycle. Lucky as he was, he probably never had to do that. Krebs lived happily with his wife and three children, and died in Oxford, after a brief illness, in 1981[1].

The Krebs cycle explains the extremely complex series of chemical reactions used by cells to extract energy from matter and to produce chemicals needed. So, a few things need to be said now; one is that Krebs was only one contributor to understanding the parts of this complex cycle. Another is that work on the cycle not only happened in Krebs' time, but it also continues today. For example, its role in the immunological system that allows the body to defend

itself; in the growth of cancer tumors; and in diseases such as the sleeping sickness transmitted, among others, by the infamous tse-tse flies.

Hans Krebs (1933-1981). Source: Wikipedia.

But the subject of this article is how we, as educators, have completely misunderstood the cycle and how we should teach it. I had to memorize it many times in high school and at the university. And, just like many other millions, I forgot everything about it every time, except for the name. This other cycle, a cycle of young minds forced to memorize a meaningless process just to pass exams, has possible led many away from science. And of course, it serves no purpose at all; as I said, I even doubt that Krebs himself could just sit and draw it from memory, he had better things to do.

There are even tricks online, in text and video, to help with its memorization (Kreb's Cycle Mnemonic, and How to Remember the Krebs Cycle).

Of course, I have little, if any, hope that teachers will read this and think, “Hey, maybe Julián is right and we can improve how we teach this, let’s try”. But just in case there are some receptive minds out there, I will explain. Except for the few people who work directly with it, learning the cycle makes no sense because we do not need to remember it. What we should teach is that the way by which cells extract energy, in a chain that starts with the food we eat, is extremely complex. We should teach that Krebs did not work alone, he was only part of a group of men and women who solved the riddle; it is this group that should be admired for the spectacular accomplishment of unraveling what happens inside the cell even if we cannot see it at all. That is impressive!

We should also teach about the life of Hans Krebs; about the human solidarity that allowed him to flee the Nazis, establish a home in a democracy, and continue his work that now helps us understand and treat cancer, sleeping sickness, and other ailments. And never, ever, should we ask students to memorize it. During exams, the cycle should be posted on the wall, or the screens, or whatever you have in your class, and, at most, if we need to, we should ask them to tell us their overall logic while looking at the image.

To those interested, we can tell, as I am telling you, that new research on the cycle continues to appear in the scientific literature. For example, it was discovered that *Trypanosoma brucei*, the unicellular parasite that produces the pain, confusion, and alterations of the sleep cycle (“sleeping sickness”), uses a modified version of the Kreb’s cycle to improve efficiency while passing through different organs of hosts [2].

Genetic and epigenetic alterations of Krebs cycle enzymes favor the shift of cancer cells from oxidative phosphorylation to anaerobic glycolysis, and understanding this may improve cancer treatment [3,4]. But the cycle is also basic for our defense, as the central immunometabolic hub of the macrophage [5].

There is now evidence that parts of the cycle originated in the primitive Earth, even before life itself [6]. The traditional Krebs cycle

that liberates CO_2 and yields ATP, is the same in all organisms, except *Chlorobium limicola*, a mysterious photosynthetic bacterium in which the cycle operates in reverse [7]. Wahy all of this? There is, still, much fascinating mystery in the Krebs Cycle.

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