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TALES OF IRON

Iron is mostly perceived as a metal of economic significance which played such an important role in the history of human civilization that the era when it became the main material for tools has been named the Iron Age. It has always been within the reach of human hand. It could be obtained and melted from easily available bog iron. The fact that iron is the fourth most common element, and the second most common metal in the Earth's crust indicates just how widely available it is. The presence of iron in everyday life resulted in its presence in everyday language. We commonly use proverbs and phraseological structures centered around the word 'iron'. Most such expressions refer to physical features of the metal — to its plasticity (strike while the iron is hot), hardness (iron will) and strength (a cast-iron promise or iron man). Interestingly, few of us notice that such reference is partly false, because iron corrodes and therefore such phrases as "all oak and iron bound" or "cast-iron stomach" meaning resistible to illness and showing solid physical strength are questionable, to say the least. This trap of iron symbolism was noticed by the French theologian and philosopher Pierre Theillard de Chardin. His collection of iron artifacts – plough fragments, shrapnel shells, old horseshoes "expressed the longing for the permanent and changeless among the passing forms of matter". In the thick texture of iron he hoped to find permanence and indestructibility. However he soon noticed that "... a piece of metal which was shining not long ago is covered with rust in time". Such duality of iron also has its biological dimension and is the leading motif of the best part of articles under the keyword iron.

The aim of our Tales of Iron series is to draw the Readers' attention to iron's peculiarity as a biometal. One of the theories concerning the beginnings of life on Earth, the iron-sulfur world theory proposed by Gunter Wachtershauser, implies iron's unique place in biology. According to the theory, the first organic compounds on Earth formed from carbon oxide with the catalytic participation of pyrite (iron sulfide, FeS_2) on the surface of suboceanic craters or in the outlets of hydrothermal vents. In this context, pyrite formed through geochemical reaction appears to be the archetype of iron-sulfur centers, enzymatic co-factors so widely participating in bioorganic catalysis. The fact that the only known up-to-date living organisms showing iron abstinence are bacteria of genus *Lactobacillus* (lactic acid bacteria) proves the uniqueness of iron in biology. In living organisms, iron ions, thanks to their redox properties determine the activity of several dozen enzymes, which participate in key metabolic processes. And yet, even among biologists and physicians iron is too often associated only with hemoglobin, erythropoiesis and anemia. Moreover, views on iron physiology are dominated by concepts dating back to the nineteen-sixties. Meanwhile, in the last 15 years, a veritable revolution has taken place in the study of molecular bases of cellular and systemic iron homeostasis and the revolutionary effervescence is still at large.

The agent which has formed iron metabolism in presently living organisms is oxygen (O_2). The appearance of oxygen in Earth's atmosphere around one billion years ago was directly linked to the process of photosynthesis in blue-green algae. Since then, for subse-

quent 300 million years, oxygen reached a high level of concentration in environments inhabited by living organisms and became a substrate for obtaining energy, which was released in the process of oxidative phosphorylation, subsequently used for ATP synthase. On the other hand, the appearance of oxygen was the greatest ecological disaster in the history of our planet. Although the O_2 molecule itself is relatively poorly reactive with organic compounds, the so called reactive oxygen species display powerful oxidant properties. The appearance of oxygen in the Earth's atmosphere became a major threat for biological functions of iron. Inasmuch as ferrous ion — Fe(II) is soluble in saline solutions, ferric ion — Fe(III) — the dominant form of ionic iron in oxygen environment, practically does not form in aqueous solutions. One of the evolutionary strategies limiting the negative interaction of oxygen and iron was a complex system of proteins which specifically bind iron ions. On the one hand, the proteins ensure solubility of Fe(III) ions, facilitating iron transportation in biological liquids, its crossing through biological membranes, its delivery in adequate quantities to the places of its destination in the cell and in the organism, i.e. to the iron-dependant proteins, which perform various metabolic roles. On the other hand, this strictly regulated circulation of iron in the cell and in the organism reduces toxicity of iron to the minimum. Thus, iron, like the Roman god Janus, is a two-faced element. Its other face looks toward the dark side — pathology. The biological basis of iron's toxicity is Fenton's reagent, catalyzed by ferrous ions — Fe(II), whose product is a hydroxyl radical, a highly reactive biotoxin. The interaction of oxygen and iron does not end here. Hypoxia, i.e. the state of low oxygen concentration in tissues, results in dramatic changes in the expression of many genes which code proteins of iron metabolism (this occurs largely through transcription factors induced by hypoxia), which are meant to raise accessibility of iron in the process of erythropoiesis, stimulated by decreased $O^{\bullet}$.

The construction of our Tales of Iron series is based on the contrast between the first article, which presents an outline of iron physiology, and the rest, which show the extent to which disorders of iron metabolism cause pathology. Thus, GRZEGORZ BARTOSZ'S article is about the basic mechanism of iron toxicity — Fenton reaction. The authors of subsequent articles argue how iron homeostasis disorder leading to iron excessive accumulation in individual organs destroys the functioning of the liver (KATARZYNA SIKORSKA), the brain (JOLANTA GAŁĄZKA-FRIEDMAN and ANDRZEJ FRIEDMANN) and the cardio-vascular system (PIOTR and DOROTA FORMANOWICZ). JOLANTA ARTYM and MICHAŁ ZIMECKI write about the issue of competition over iron between a host organism and pathogenic bacteria in the course of infectious diseases. JOLANTA MAŁYSZKO recounts how kidney inflammation influences the reduction of iron accessibility for erythropoiesis, which in turn entails the development of anemia. The two following articles also are about anemia, but of different etiology. In the first one, PAWEŁ LIPIŃSKI looks at the problem of anemia caused by iron deficiency, which is the most common nutritional deficiency in humans. Then, EWA ŻEKANOWSKA describes the molecular mechanisms through which obesity, a lifestyle disease, causes iron deficiency leading to anemia. In the next article EWA JANKOWSKA raises a relatively poorly known issue of the relationship between iron deficiency and heart insufficiency. Finally, MAŁGORZATA LENARTOWICZ characterizes molecular bases of copper metabolism as well as copper deficiency induced pathologies appearing in humans. It is not by accident that the last article has found a place in the series. The connection between copper and iron in biology is very strong. It is often presented symbolically as the image of the intimate relationship of Mars (Fe) and Venus (Cu) in Roman mythology.

I hereby would like to dedicate our Tales of Iron series to Romek Raczek. I didn't know him when the idea for this notebook of Kosmos was emerging almost a year ago. Now, when I'm writing these words he is no longer among us. The time when the idea grew and developed was also spent on my numerous visits to the mountain range of Beskid Niski, where Romek lived and painted. During these visits, we sat facing each other — the one who is leaving and the one who is staying a while longer, as Andrzej Stasiuk writes in his commemoration of Romek. Tales of Iron, for a moment, have joined the two perspectives. Thanks to them, we both sat vis a vis — the one who tells and the one who listens.