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The first demonstration of lactic acid in human blood in shock by Johann Joseph Scherer (1814–1869) in January 1843

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Abstract Lactic acid was first found and described in sour milk by Karl Wilhelm Scheele (1742–1786) in 1780. The German physician–chemist Johann Joseph Scherer (1841–1869) demonstrated the occurrence of lactic acid in human blood under pathological conditions in 1843 and 1851. In this article we honour the forgotten observations by Scherer and describe the influence of Scherer’s finding on further research on lactic acid at the end of the 19th century. We conclude that Scherer’s 1843

case reports should be cited as the first description of lactic acid in human blood after death and also as the first demonstration of lactic acid as a pathological finding in septic and haemorrhagic shock. Carl Folwarczny was, in 1858, the first to demonstrate lactic acid in blood in a living patient.

Keywords Lactic acid · Lactate · Shock · Leukaemia · Johann Joseph Scherer · Historical article

Introduction

Lactic acid was first found and described in sour milk by the Swedish chemist Karl Wilhelm Scheele (1742–1786) in 1780 [1]. The Swedish chemist Jöns Jakob Berzelius (1779–1848) found lactic acid in fluid extracted from meat in 1808 [2, 3], and the German chemist Justus von Liebig (1803–1873), who established the world’s first school of chemistry at Giessen, proved that lactic acid was always present in muscular tissue of dead organisms [4]. In 1859, Emil Heinrich du Bois-Reymond (1818–1896) published several articles on the influence of lactic acid on muscle contraction [5–9]. Araki and Zillessen found that if they interrupted oxygen supply to muscles in mammals and birds, lactic acid was formed and increased [10–14]. This was the first demonstration of the relationship between tissue hypoxia and the formation of lactate. The occurrence of increased lactic acid in blood (hyperlactataemia) nowadays reflects severe illness, in which the increased blood lactate levels may result from both anaerobic and aerobic production or from a decreased clearance.

It was the German physician–chemist Johann Joseph Scherer who first demonstrated the occurrence of lactic

acid in human blood under pathological conditions after death in 1843 and 1851 [15, 17], and Carl Folwarczny in 1858 who first demonstrated lactic acid in blood of a living patient. In this article we wish to honour Scherer’s forgotten observations and describe the influence of his finding on further research on lactic acid at the end of the 19th century.

Biography of Johann Joseph Scherer

Born on 18 March 1814 in Aschaffenburg, Germany, Scherer studied medicine, chemistry, geology and mineralogy at the university of Würzburg between 1833 and 1836. He obtained his PhD in medicine and surgery in 1838 with a thesis entitled “*Versuche über die Wirkung einiger Gifte auf verschiedene Thierclassen*” (Experiments on the action of some poisons on several classes of animals). He practised medicine in Wipfeld, but inspired by the chemist Ernst von Bibra (1806–1878) he completed his studies in chemistry at the University of Munich between 1838–1840 [18]. In 1840 he was employed at the laboratory of Justus Liebig at Giessen, and became professor at

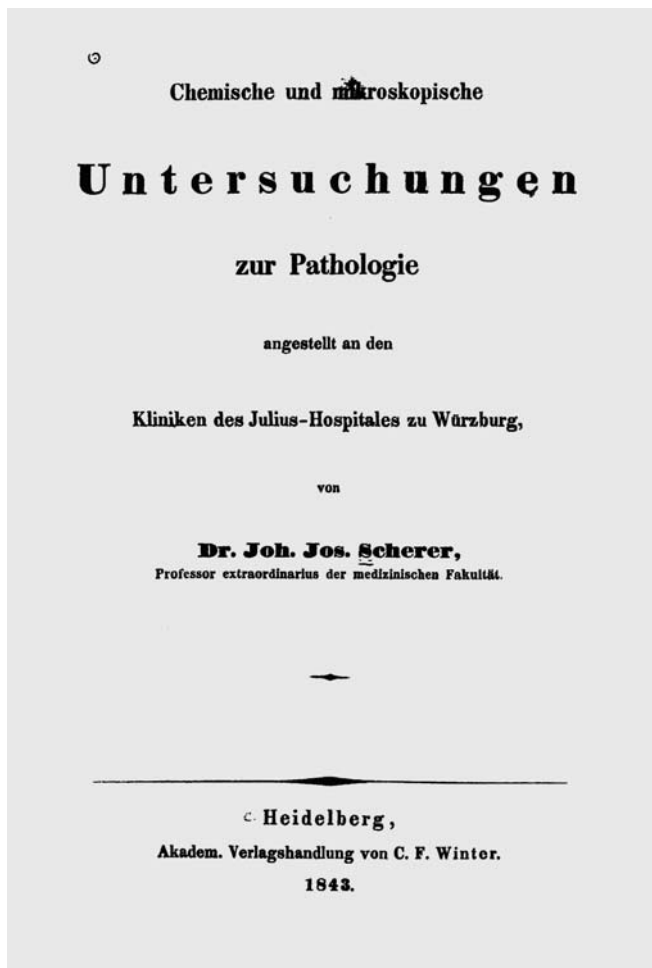


Fig. 1 Title page of Scherer's 1843 book

the medical faculty in 1842, professor of organic chemistry in 1847, and later professor of general, anorganic and pharmaceutical chemistry. His work especially concerned quantitative research on blood and urine in pathological conditions. In 1843 he published his book '*Chemische und Mikroskopische Untersuchungen zur Pathologie angestellt an den Kliniken des Julius-Hospitales zu Würzburg*' (Chemical and microscopic investigations of pathology carried out at the Julius Clinic at Würzburg) [15] (Fig. 1), in which he described 72 case reports, giving details on clinical course, diagnosis, and results obtained during autopsy and analysis of body fluids. Scherer died on 17 February 1869 [18].

The 1843 cases

In one chapter in his 1843 book entitled '*Untersuchungen von krankhaften Stoffen bei der im Winter 1842–1843 in Würzburg und der Umgegend herrschenden Puerperal-Fieber-Epidemie*' (Investigations of pathological sub-

stances obtained during the epidemic of puerperal fever which occurred in the winter of 1842–1843 in and around Würzburg) Scherer described the cases of seven young women who all died peripartum.

One of the women, the 23-year-old primipara Eva Rumpel, gave birth to a healthy child on 9 January 1843. The same night she developed a painfully swollen abdomen and became ill, feverish, and sweaty, with rapid pulse and severe thirst. The initiated treatment was bloodletting and clystering. The next evening she deteriorated, became delirious, with anxious breathing, a tense abdomen, cold extremities and rapid pulse, finally losing consciousness. Again, bloodletting followed. At 4:30 a.m., 36 h after the onset of the first symptoms, she died. During autopsy, severe purulent endometritis, vaginal pus, pulmonary oedema, and shock liver and shock spleen were found. The blood that was obtained directly from the heart was chemically analysed, in which lactic acid was found. Most likely this unfortunate woman had died from a fulminant septic shock caused by group A haemolytic streptococci (*Streptococcus pyogenes*). Scherer diagnosed this case as perimetritis with secondary peritonitis.

Another patient, the 28-year-old, 7 months pregnant (second pregnancy) Margaretha Glück, was, after being icteric, nauseous, vomiting and complaining about epigastric pain for 8 days, admitted to the lying-in birth clinic on 6 February 1843. Four days later she was transferred to the hospital with severe nosebleeds and generalised exanthema or purpura. In the evening she suffered from severe gastric bleeding and epistaxis, showing rapid pulse, cold extremities and dizziness. The next morning, she was transferred back to the birth clinic, where she gave birth to a premature child (30 weeks) and suffered from a severe post-partum fluxus. She was again transferred to the hospital with the following symptoms: cold clammy skin, tachycardia, severe lochia and persistent exanthema or purpura, but without signs of an acute abdomen. During the night of February 11, she became aphasic and restless, followed by chills and profound sweating. On the morning of February 13, she further deteriorated and bilirubinuria was detected. The next day she was comatose, finally developed rattling breathing and convulsions. Death occurred during the following night. Autopsy revealed a small intracerebral haematoma, normal lungs without pulmonary oedema, ascites and an anaemic, foul smelling uterus filled with purulent and decayed tissue and pus. Blood was also obtained directly from the heart during autopsy and lactic acid was found.

In this case we could think of a haemorrhagic shock and cerebral haemorrhage due to clotting disorders possibly resulting from either acute fatty liver of pregnancy/HELLP syndrome, idiopathic thrombocytopenic purpura, thrombotic microangiopathy (TTP/HUS) or DIC. The case was most likely complicated by a sepsis (endometritis). Scherer himself diagnosed this case as septic endometritis.

In the conclusions of his 1843 book, Scherer attached high importance to the fact that he found lactic acid in cases of puerperal fever, which he had not found before in healthy persons. He held the opinion that lactic acid was formed in blood during bodily deterioration in severe diseases like puerperal fever. Lactic acid was thus described for the first time in human blood and was demonstrated for the first time as a symptom of septic and haemorrhagic shock.

In the same period a junior obstetrician in Vienna, Ignaz Philipp Semmelweis (1818–1865), discovered in 1847 that physicians carried infectious particles on their hands from the mortuary to the obstetrical clinic, causing puerperal fever and puerperal sepsis, and he introduced a successful method for its prevention. Louis Pasteur (1822–1894) found in 1879 that infection with streptococci was the most important cause of puerperal fever [16].

The 1851 article

Scherer worked closely with the famous pathologist Rudolf Virchow (1821–1902) on several projects (Fig. 2). In 1851 Virchow performed an autopsy on a patient who had died from leukaemia and offered Scherer blood from this patient for analysis. The results of this analysis were published the same year in the *‘Verhandlungen der Physikalisch-Medicinischen Gesellschaft in Würzburg’* [17]. Virchow and Scherer had previously studied the spleens of patients who died from leukaemia, and were curious if they could find the same results in the blood. Scherer reached the conclusion that: the blood of this patient contains: *“Ameisensäure, Essigsäure und Milchsäure, die gleichfalls von mir schon früher als in der Milzflüssigkeit vorkommend bezeichnet wurden”* (Formic acid, acetic acid, and lactic acid, as also found by me previously in fluids from the spleen).

Further research

Scherer’s observations inspired others to conduct further research, primarily in patients with leukaemia [19–22], but also in patients with other conditions and diseases and in animal experiments with dogs and rabbits [23]. While Scherer found lactic acid in blood obtained after death during autopsy, Mosler and Körner [19] mention an observation made by Carl Folwarczny, published in the *Allgemeinen Wiener Medicinischen Zeitung* in 1858, where blood was withdrawn from a leukaemia patient during life, analysed according to Scherer’s method, and found positive for lactic acid. In addition, Carl Folwarczny described in 1863 in his *‘Handbuch der Physiologischen Chemie’* [24] that lactic acid can be found in the blood of patients with leukaemia, septicaemia (pyaemia) and in



Fig. 2 Johann Joseph Scherer (left) and Rudolf Virchow (right) in 1849

conditions leading to septicaemia like puerperal fever, the latter probably after Scherer’s observations.

In an extensive article, the Berliner physician Georg Salomon [25], who had serious doubts that the occurrence of lactic acid in blood was mostly related to leukaemia, proved in 1878 that lactic acid was also present in the blood of patients who were suffering and died from other diseases. He studied blood obtained during autopsy from cadavers, but also blood from patients obtained by bloodletting or cupping, and in some cases he compared the blood before and after death. He was able to demonstrate lactic acid in the blood of patients suffering from leukaemia, (pernicious) anaemia, congestive heart failure, chronic obstructive pulmonary disease, pleuritis, pericarditis, pneumonia and several solid malignant tumours.

Gaglio [26] is often erroneously mentioned as the first author to find lactic acid in blood [27–29]. He was able to demonstrate lactic acid in fresh arterial blood withdrawn from dogs and rabbits after bloodletting. Berlinerblau [30] confirmed these observations in mammalian and venous human blood. Both Gaglio and Berlinerblau, however, neglected previous research, as indignantly described by Salomon in 1888 [*Ich erlaube mir, den Inhalt meiner Arbeiten, die von Gaglio nur ganz flüchtig, von Berlinerblau gar nicht berührt sind, in Kürze zu reproduciren*] (I take the liberty of summarizing the contents of my work, which was mentioned only briefly by Gaglio and not at all by Berlinerblau) [31].

The Japanese chemist Trasaburo Araki showed that the amount of lactic acid in exhausted muscle results from muscle activation [11]. Irisawa [32], inspired by the results obtained by Salomon and Gaglio, obtained fresh blood of 11 dying patients with serious conditions. In six cases he found hyperlactataemia, in four cases normal values. He speculated on the aetiology of hyperlactataemia, the most plausible cause being the severe hypoxia during the dying process. In an experiment in which he made a dog anaemic for several days, he found a rise in lactic acid levels during the time leading up to death.

In Cambridge (UK), Walter Morley Fletcher (1873–1933) and Frederick Gowland Hopkins (1861–1947) worked together on the metabolic changes occurring in muscular contractions and rigor mortis under anaerobic conditions, and found that lactate was the product of carbohydrate metabolism [33]. Their classic 1907 paper demonstrated rigorously that muscle contraction is accompanied by the anaerobic formation of lactic acid, which is removed aerobically, at a rate depending on the level of exposure to oxygen [34].

Poul Astrup and John Severingshaus mentioned Scherer's 1851 article as first demonstration of lactic acid in blood, but overlooked the 1843 cases and Folwarczny's work [35]. In conclusion, Scherer's 1843 case reports [15] should be cited as the first description of lactic acid in human blood and also as the first demonstration of lactic acid as a pathological finding in septic and haemorrhagic shock. Folwarczny, in 1858, was the first to demonstrate lactic acid in blood in a living patient.

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