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Medical Conan Doyle-Leucocytes, Bacteria and Phagocytosis Before Metchnikoff

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ABSTRACT

Conan Doyle and Leucocyte Phagocytosis

In March 1883, Arthur Conan Doyle published an article entitled "*Life and death in the blood*", in which he provided a scientific description of the last advances in bacteriology and in leucocytes biology that implied activity of phagocytosis of bacteria in the blood. This discussion immediately suggests Metchnikoff's theory of phagocytosis. However, Conan Doyle could not have known about this theory, since Metchnikoff's first article about it was only published in November 1883. Furthermore, Conan Doyle could not have learned of Metchnikoff's crucial experiment, performed in Messina in late December 1882, by participating in scientific assemblies, since at that time he was permanently practicing in Southsea, where he also received the proofs of his article in January 1883. On the other hand, leucocyte phagocytosis had been previously studied and Conan Doyle undoubtedly knew about these studies, given his specific interest in the subject deriving from his previous work on leukemia. In the manuscript, he specifically mentioned experiments carried out with the hot stage, likely referring to Max Schultze's functional study performed in 1865. Additional studies, such as those of Joseph Leidy, Alexander Ogston, Karl Roser and George Sternberg among others, may also have influenced Doyle's article. As in other circumstances, he subsequently used a scientific topic as a creative starting point for literary production.

Key words: Arthur Conan Doyle - Leucocyte phagocytosis - Elie Metchnikoff - Max Schultze

Background

Arthur Conan Doyle (1859-1930), the creator of Sherlock Holmes, was an experienced physician. A graduate of the Medical Faculty in Edinburgh (Bachelor of Medicine and Master of Surgery in 1881; MD in 1885), he practiced the profession in Southsea from 1882 until 1890. Conan Doyle made his last medical experience in 1900, serving as a volunteer doctor in South Africa during the "Anglo-Boer War" (1899-1902). He himself said: "There are few phases of medical life of which I have not had a personal experience"[1].

Literary success ended Conan Doyle's many years of family indigence and hard work, while he was striving to establish himself as a physician. On the one hand, scientific articles, such as those published in *The Lancet*[2] and in the *British Medical Journal*[3], were intended to help him build a reputation as a medical doctor. In a letter addressed to his mother, he wrote: "There is no mistake I must get a house surgeonship, and if possibly in a large town... my game is clear – observe cases minutely, improve in my profession, write to the Lancet"[4]. On the other hand, his abundant and parallel non-scientific literary production was aimed at supplementing the meager income he made as a doctor. In 1879, after the story "The American's Tale" was published in the magazine *London Society*, Conan Doyle wrote that he had "learned that shillings might be earned in other ways than by filling phials"[5].

One such article written for financial needs was "Life and death in the blood". Published in the March 1883 issue of the monthly British popular periodical *Good Words*[6], in Conan Doyle's own words this article brought in "money in time to help the rent"[7]. Originally entitled "The fishes of the blood"[8], this article impresses with its imaginative introduction, in which Conan Doyle invited readers to imagine a man reduced in size to less than one thousandth of an inch and traveling through the bloodstream amid blood components. As previously noted[9], this was a definite anticipation of the 1966 science fiction movie, *Fantastic Voyage*. However, Conan Doyle's article was not a science fiction novel, but rather a very up-to-date and informative essay on current advances in bacteriology and on the successes gained by vaccination. He himself defined the article "scientific"[10]. Andrew Lycett wrote that in this article Conan Doyle "presented himself as a scrupulous advocate of modern science"[11]. Shrinking readers to a microscopic dimension, Conan Doyle gave them the chance "to glance at some of the work done of late in this direction" directly from the perspective of the blood streaming through a functioning vessel, that is, at the level at which those "living creatures so minute as to be hardly detected by our highest lenses" were studied. Bacteria represented the "deadly side" to which he alluded in the final title of the *Good Words* article, for many of them were "endowed with such fearful properties that the savage tiger or venomous cobra have not inflicted one fiftieth part of the damage upon the human race"[12]. Conan Doyle would use the vivid comparison between the damaging power of the tiger, well known to nineteenth century British imperialists familiar with the jungles of India, and that of bacteria, twice again: once in

The Narrative of John Smith, a story dated to 1884[13], and the other in a review article he would write in 1890 about Koch's putative cure for tuberculosis[14].

But what was, then, the "life side" mentioned in the title? That of the "leucocytes, or white blood-corpuscles, the only creature possessing the attributes commonly associated with life, found in healthy human blood"[15]. The *Good Words* article was not Conan Doyle's first one dealing with leucocytes. In 1882, he had published in *The Lancet* a note describing a patient affected by leukemia[16]. Even though the note was signed "Cowan Doyle", I have recently demonstrated that Conan Doyle was the real author[17]. In the note, Conan Doyle proved to be extremely up-to-date with scientific literature by consistently using the term "leucocythaemia," a word introduced in 1852 by the Edinburgh physician John Hughes Bennett (1812-1875)[18] as an alternative to that of "leukämie" previously employed by Rudolf Virchow (1821-1902)[19]. In 1879, the British neurologist William Richard Gowers (1821-1902) had endorsed Bennett's terminology, confirming that "the name leucocythaemia, proposed by Bennett, is preferred to that of Virchow (leukaemia)"[20].

Even though Conan Doyle mentioned leukemia, saying that "in certain diseased conditions white corpuscles multiply enormously until they outnumber the straw-coloured discs", that is, red blood cells, the *Good Words* article dealt with the biology of leucocytes. Conan Doyle's previous knowledge of the literature on leukemia turned out to be instrumental to this purpose, since in the pre-Ehrlich era much of the knowledge about leucocytes came from studies on leukemia and inflammation[21]. He delivered a rather precise description of leucocytes morphology, depicting them as "bodies gelatinous in consistence, and irregular in shape, slow and ungainly in their motions. No differentiated organs are to be seen in it, save a dark mass of pigment in its centre", that is, the nucleus. The lack of a mention of the cytoplasmic granules is not surprising, since up to 1883 their existence in white blood cells was still a mere suggestion based on the studies of Gottlieb Gluge (1812-1898)[22], Thomas Wharton Jones (1808-1891)[23] and Julius Vogel (1814-1880)[24]. To have a clear-cut demonstration of cytoplasmic granulations, we had to wait for Paul Erlich's (1854-1915) studies with aniline dyes staining of blood specimens[25].

Did Conan Doyle know Metchnikoff's experimental work on phagocytosis?

More remarkable, however, was Conan Doyle's account of the leucocytes' ability to ingest foreign bodies. Conan Doyle represented them as polyps "of gigantic proportions and formidable aspect, capable of pushing out long prehensile tentacles, with which to envelope its food and draw it into its interior. Digestion is its strong point, for it has the power of seizing upon any oily particle which may drift in its direction, and of introducing by the simple method of surrounding it without any preliminary ceremony of swallowing." This is both a vivid and accurate portrayal of leucocytes acting as phagocytic cells.

What makes Conan Doyle's article so interesting is that this image of phagocytosing leucocytes is followed by the statement that "in human blood in diseased conditions appear little organisms whose relation to disease has been duly appreciated in the last few years". It seems inevitable to link the phagocytic activity of circulating leucocytes to the presence in the blood of pathogenic bacteria, that is, to imply that leucocytes removed bacteria from the blood. This conclusion is strengthened by a later speech that Conan Doyle delivered to the students of St. Mary Hospitals for the opening of the medical school in 1910. In his words, "it was a familiar thought, even in my student days, that the leucocyte or white corpuscle was the guardian of the body, and that he devoured and digested every microbe which penetrated the blood-stream. He floated in the clear fluid or blood plasma always ready to destroy the intruder"[26].

At the end of 1882, the presence of bacteria in the blood of sick people had been already established in many acute diseases[27]. As a case in point, Conan Doyle described the blood of people affected by relapsing fever as containing "countless creatures, thin and long, with snake-like body and spiral motion", that is, the spirochæta discovered in 1868 by Otto Obermeier (1843-1873). In this pathological condition, he wrote, "the spirilla of relapsing fever were writhing their way among white blood-corpuscle" (Fig. 1a). Since Conan Doyle had depicted leucocytes as "omnivorous pieces of jelly", "floating stomachs" characterized by their ability to ingest any foreign bodies drifting in their direction, it seems logical to conclude that leucocytes might engulf spirilla and dispose of them. This was exactly what Metchnikoff reported in 1887, showing that the spirilla of relapsing fever were eaten up by the wandering leucocytes, and thus rendered harmless[28].

Therefore, it is no surprise that, regarding the *Good Words*, article Lorenzo Servitje wrote: "although Doyle doesn't mention Metchnikoff's immunity explicitly, he does prefigure it in his discussion of leukocytes"[29]. The name of Elie Metchnikoff (1845-1916) and his theory of leucocyte phagocytosis had been already evoked in 1984 by Jack Key, when reviewing Conan Doyle's article[30]. Key, together with Alvin Rodin, further argued that Conan Doyle's "knowledge of recent concepts of medicine is indicated by the fact that Metchnikoff's first presentation on phagocytosis was in 1883"[31]. Servitje interpreted this assertion as a suggestion that Conan Doyle knew about Metchnikoff' work[32]. However, this seems impossible, since Metchnikoff published his first article on the theory of phagocytosis in the 15 November 1883 issue of *Biologisches Centralblatt*[33], that is, almost eight months after the publication of Conan Doyle's article. Therefore, Conan Doyle cannot have learned of Metchnikoff's experimental work from published articles.

However, the possibility exists that, given his specific interest in the subject of leucocytes, Conan Doyle might have attended scientific meetings where Metchnikoff's new theories on immunity might have been discussed. Even this hypothesis, however, appears to be unsupported. It is well known that Metchnikoff's crucial experiment was performed in Messina in late December, 1882[34]. The precise day is uncertain, even though

a plaque located in "the Ringo" suburb of Messina, where Metchnikoff's family settled from the autumn of 1882[35], reported that the discovery was made during Christmas time, 1882. According to Fred S. Rosen the discovery was made on a Saturday afternoon[36]. Therefore, Saturday, December 23 1882, might be a plausible date. At that time, Conan Doyle was practicing in Southsea, where he spent the Christmas holidays with his mother and his brother Innes. From a letter addressed from Southsea to his mother Mary, we learn that he had received the proofs of "The fishes of the blood" by the end of January 1883[37]. Again, his correspondence proves that he never moved from Southsea before that date[38]. Furthermore, the time required to write the article, mail it to the journal, get it accepted, and get the proofs printed and sent back to the author must also be taken into consideration. The month that passed between the Messina Metchnikoff's discovery and receipt by Conan Doyle of the proofs at Southsea seems far too short a time-frame to also include participation in some conferences abroad.

Additionally, neither Metchnikoff's name nor the word "phagocytosis" appears in Conan Doyle's two autobiographical sources, his *Memoirs*[39] and his *Letters*[40]. Similarly, a search conducted in the *Arthur Conan Doyle Encyclopedia*[41], a database that contains all his printed works, demonstrated that term was ever used by him in written texts. Finally, investigation of some of the major biographies of Arthur Conan Doyle failed to pinpoint Metchnikoff's name or the words "phagocytosis/amœba"[42,43,44,45].

On the other hand, there is no evidence that Metchnikoff left Messina before the summer of 1883, when he "moved to Riva del Garda in northern Italy, where he wrote an article on his new idea"[46]. Then, on his way back to Odessa, Metchnikoff stopped in Wien, where he met his friend Carl Friedrich Wilhelm Claus (1835-1899), who proposed the word "phagocyte" and invited Metchnikoff to publish his findings in *Biologisches Centralblatt*[47]. To the best of my knowledge, the first presentation by Metchnikoff of the new phagocytic theory was made at the 7th Congress of Russian Natural Scientists and Physician, held in Odessa in August 1883[48].

Taken altogether, these separate pieces of evidence demonstrate that, at the end of January 1883, Conan Doyle could not have learned of Metchnikoff's experiments on phagocytosis.

What were the relevant scientific sources for Conan Doyle's article?

Metchnikoff was not the first one to observe the phenomenon of cellular phagocytosis, but he was the first to elaborate a theory of acquired cellular immunity to infectious diseases based on it. At the time Conan Doyle wrote his article, the literature on phagocytosis was already abundant[49,50]. Clearly, Conan Doyle's views on it relied on these previous works.

In the *Good Words* article, Conan Doyle informed readers about the identity of the microscopic unicellular organism to which white blood corpuscles were to be compared, in relation to their ability to move and to engulf foreign particles, "the prototype from

which they are hardly recognizable, viz: the tiny amœba which may be washed from damp moss and detected under the microscope." The name "amœba" derives from the Greek word for "change" and refers to the changes in shape that characterize the moving animalcule. In a popular treatise, the Scottish zoologist Andrew Wilson (1852-1912) wrote: "perpetually changing its shape, the *Amœba* well merits its name, *Amœba,* 'change'"[51]. Thomas Wharton Jones had been the first one to describe "changes of shape" of granular white blood-cells[52]. Even though Jones never used the term "amœba", his description of "the spontaneous changes in shape and other movements of the colourless corpuscles in the blood" is considered the first description of the so-called "amœboid movements" of white blood-cells[53]. By 1882, "amœba" was the universally accepted paradigm for describing movements of white cells. In the words of Wilson, "when placed under the object glass of the microscope, the *Amœba* is seen to comport itself in an exactly similar fashion to the white blood-corpuscle...The likeness of the animalcule to blood-corpuscle of our veins is so marked that it cannot escape to most casual observer. We name the blood-corpuscles movements *amœboid,* or "amœba-like", *because* they are *de facto* those of the animalcule... The identity of the amœba's movements with those of the blood corpuscles is complete, unmistakable, and remarkable"[54]. Therefore, when matching up white blood corpuscles to amœba, Conan Doyle was just sticking to a view universally held at that time.

Whence came this power of movement? Wilson argued that the ability to move was a universal feature of all living beings, be plants or animals, even if it was often only detectable at the microscopic level. This, in turn, was because both types of cells contained "the universal basis of life known to everyone under the name of *protoplasm* or living matter... Life is nowhere known to exist save in connection with this jelly-like matter"[55]. The concept of protoplasm as the physical basis of life, common to both plants and animals, had been put forward by the German microscopic anatomist Max Johann Sigismund Schultze (1825-1874). In 1861 Schultze published a paper[56], that "more than any other single event marked the birth of the protoplasmic theory of life"[57]. From this article dates the assignment of the term "protoplasm" to the contents of cells. Based on functional observations, "and with special emphasis on contractility and irritability, Schultze demonstrated that a single substance, called protoplasm, was the substratum of vital activity in the tissue of all living organisms"[58].

Already in 1855 the Austrian botanist Franz Unger (1800-1870) had described "protoplasm as a half-fluid contractile substance"[59], having the intrinsic property of being constantly in motion, a phenomenon described long since[60] and called "cyclosis" or "protoplasmic streaming". Accordingly, the movement of amœba and white blood-corpuscles depended on the contractile properties of protoplasm[61]. Wilson wrote Wherever this *protoplasm* exists, motion is its universal characteristic". He explained amœba's and white blood corpuscles movements as "a primary property and heritage of the protoplasm of which the animalcule is composed, and the same we must assume of the white blood

corpuscle", since "the blood-corpuscle of our veins and the ameba of the pool are simple specks of protoplasm, alike in chemical composition and physical properties"[62]. Conan Doyle's statement that white corpuscles were "the only creature found in healthy blood possessing the attributes commonly associated with life", was based on the fact that they were made of protoplasm and were able to move, differently from red blood cells.

The ability of amœba of thrusting out protoplasmic processes explained its capacity to engulf solid bodies into the protoplasm. Of particular interest in this respect was a communication made in 1875 by the American physician Joseph Mellick Leidy (1823-1891)[63]. He reported that amœba swallowed its food by including it between two finger-like pseudopods, whose endings "gradually approached, came into contact, and then actually became fused". Conan Doyle' description of phagocytosis by leucocytes is quite similar. They were "capable of pushing out long prehensile tentacles with which to envelop and to draw into its interior any particle by the simple method of surrounding."

The name of Leidy might already have been known to Conan Doyle, since he was likely the first to use a microscope in forensic medicine for solving a murder mystery. As early as 1847, acting as a Coroner's Physician in Philadelphia, Leidy "was called upon to determine whether certain blood stains in a murder case were human or those of a chicken. As a results of his studies, he testified that they were not due to chicken blood"[64], as the suspect had claimed. The suspect later confessed to the murder. It is worth mentioning that Dr. Watson's first meeting with Sherlock Holmes takes place in the chemistry laboratory of the St. Bartholomew hospital, where Holmes is trying to develop a test that can unequivocally demonstrate the hematological origin of bloodstains on clothes[65]. In fact, Holmes thinks that microscopic examination can only be conducted on fresh bloodstains, as was precisely the case in which Leidy was involved. As can be deduced from Sherlock Holmes' stories, Conan Doyle had a strong interest in forensic medicine, deriving from his acquaintance of the toxicologist and physician Sir Robert Christison (1797-1882), who taught Materia Medica and held the Chair of medical jurisprudence and medical police at the University of Edinburgh during Conan Doyle's medical studies.

The description of phagocytosis by Invertebrates and Vertebrates cells followed the observations on amœba. In 1862, the German zoologist Ernst Hackel (1834-1919) first found that, after injecting a mollusk with indigo, dye granules were to be found inside the white blood corpuscles[66]. The same result was obtained when vermilion was injected into the blood of frogs (Figure 1c)[67]. In 1871-1872, the Italian researcher Giulio Bizzozero (1846-1901)[68] described cellular phagocytosis of pus corpuscles in studies that were cited by Metchnikoff[69]. In 1876, the renown Canadian physician Sir William Osler (1849-1919) provided the first description of what are now known as "dust cells" (Figure 1c), that is, lung macrophages filled with carbon particles, occasionally grouped around a piece of carbon to form what is now called a foreign-body giant cell[70].

Regarding the functional role of phagocytosis, in the case of amoeba it was universally accepted that it served for nutrition. Vice-versa, in the case of white blood cells

the matter was still uncertain. In 1882, Wilson remarked that "some physiologists believed that the wandering blood corpuscles through the tissues of our bodies, escaping through the walls of blood vessels, may serve to afford nourishment to the tissues at large"[71], an old-fashioned concept that had been put forward by the German zoologist Ernst Hackel (1834-1919), who "comparing the leucocytes of the newt with those of the lower amoeboid organisms indicated that this process [that is, ingestion of foreign bodies] was the remaining evidence of a normal nutrition process common to amœboid cells in whatever position they may exist"[72]. The greatness of Metchnikoff has been to frame the functional role of leucocytes phagocytosis within the body's defense mechanisms against infectious diseases.

Referring to leucocytes, in the *Good Words* article Conan Doyle wrote: "When removed and placed upon a surface kept at the same temperature as that to which they have been accustomed [that is, the body temperature], white corpuscles are capable of carrying on an independent existence for some time"[73]. With these words Conan Doyle plainly referred to the experiments carried out in 1865 by Max Schultze[74] "on the movements of white blood-corpuscles, in which he was aided by his admirable invention of the hot stage"[75], that is, a microscope whose brass plate might be warmed up in the range of 35°-45° C in a controlled way by spirit lamps, thereby monitoring the temperature of the object on the plate (Fig. 2). The development of this microscopic apparatus opened the possibility to perform functional studies on white blood corpuscles at the physiological body temperature. The blood taken from mammals had to be carefully heated to the temperature of 30-35° C. In the study "with his warm stage microscope, Schultze established that finely granular and coarse granular human blood cells moved and phagocytosed small particles"[76]. "*Prof. Max Schultze's* was the first fairly successful hot stage"[77]. Conan Doyle's reference to Schultze's experiment is further warranted by his statement that leucocytes had "the power of seizing up any oily particle", that is, milk globules that Schultze widely used as an alternative to granular dyes.

Schultze did not follow up on these seminal observations made on phagocytosis, as the study of phagocytosis by leucocytes *per se* was not his primary interest. As pointed out by Douglas Brewer, "he was interested in the concept of protoplasm as the basis of living matter"[78]. Therefore, his study on leucocyte movement and phagocytosis was aimed at further and better investigate the nature and properties of the protoplasm. For example, he observed that "in the resting rounded white cells little can be determined of the fine structure of the protoplasm. The flattened, spread, moving cells provide a much better insight"[79]. Therefore, this important paper remained his single study on leucocytes phagocytosis. Consequently, "these findings had little influence on current thought regarding the function of phagocytes"[80].

The presence of microbes within white blood corpuscles of patients affected by infectious diseases had been already demonstrated before Metchnikoff. In 1872 the German pathologist Felix Victor Birch-Hirschfeld (1842-1899) reported that, when

moderate amounts of fluids containing micrococci were injected into animal blood, the white blood corpuscles took them up in large numbers[81]. In 1881 the British surgeon Alexander Ogston (1844-1929) published drawings of white-blood cells containing cocci (Fig. 1d). This last article was published in the *British Medical Journal*, a journal Conan Doyle knew very well and that had his sympathies. As already mentioned, while still a student and contrary to his expectations[82], in 1879 he succeeded in publishing a note in it. According to a letter written to his mother and dated November 16, 1880, he was going to write another case for this medical journal, but we do not know if such an article was ever written[83]. Finally, the *British Medical Journal* is the one mentioned in the Sherlock Holmes' story "The Adventure of the Stockbroker's Clerk", published in 1893. In this novel, Sherlock Holmes visits his recently married friend Dr. Watson and finds him absorbed in reading the *British Medical Journal* after breakfast. Finally, in 1882, while studying diphtheria, Horatio C. Wood (1841-1920) and Henry F. Formad (1847-1892) reported the presence of micrococci inside white blood corpuscles.

The usual explanation for these observations was that the germs had attacked the leucocytes. However, the alternative explanation that bacteria were actively ingested by white blood cells already circulated. As early as 1874 Peter Ludvig Panum (1820-1885) had vaguely suggested that cell ingestion of bacteria might represent a method for the destruction of microbes[84].

In 1881 the young German surgeon Karl Roser (1856-1905) published a study[85] in which he held that phagocytosis was an essential factor in the resistance of certain lower animals to bacteria and pathogenic fungi[86]. Apparently, this report did not make a great impression on the scientific community. To the best of my knowledge, Roser's article was reviewed only once, and the anonymous reviewer completely failed to grasp the importance of Roser's observation on the phagocytic power of leucocytes[87]. Metchnikoff later remarked that "the author himself did not claim any great value for them"[88].

Finally, in the same year 1881 George Miller Sternberg (1838-1915), Surgeon of the United States Army and a bacteriologist famous for the discovery of pneumococcus, read a paper at the thirtieth meeting of the American Association for the Advancement of Science held in Cincinnaty, Ohio, in which he suggested the "possibility that it is the office of the white blood corpuscles to pick up and destroy bacterial organisms which find their way into the blood"[89]. As Roser did, Sternberg did not pursue his observation that white blood corpuscles devoured bacteria, because his main interest was the pathogenesis of yellow fever. After the publication of Metchnikoff's works, "in The Sanitarian for October 1885, Dr. Sternberg claimed for himself priority in attributing the acquired immunity from infectious diseases to a "*vital resistance*" of the cells"[90]. Sternberg reiterated his claim at length[91], but he was not the only one[92].

It is impossible to know whether Conan Doyle knew about these works. He might have read Roser's essay in the German language, since he had "a fair knowledge of conversational German"[93]. What is certain is that Conan Doyle was up to date with the

latest experimental findings. In the *Good Words* article Conan Doyle quoted the most recent work by Robert Koch (1843-1910) on the microbial etiology of tuberculosis, which was published in April 1882: "Koch has demonstrated the existence of a little rod-like creature in tubercle or consumption, which swarms in the diseased lungs, and which, if transferred to another body, will establish itself and breed, thereby proving the malady to be really an infectious one"[94]. He might have read either the original paper or the extensive English reviews published by the *British Medical Journal*[95]and the *Medical Times and Gazette*[96]. Furthermore, in the *Good Words* article Conan Doyle wrote that "Arloing, Cornevin and Thomas, of Lyons, have attenuated the organism of another deadly cattle disease, named the "Maladie de Chabert", after its discoverer, and have by inoculation demonstrated the possibility of stamping it out". Conan Doyle was referring to vaccination experiments against symptomatic bovine antrax carried out by French veterinarians Saturnin Arloing (1846-1911), Charles Etienne Cornevin (1846-1897) and Thomas Onésine (Louis Nicolas Onésime). Initially, they vaccinated animals by intravenous injection with non-attenuated bacteria but, starting from June 1882, they devised a method of inoculation with a heat-attenuated bacterium. The results of these last experiments were communicated for the first time at the meeting of the Paris Academy of Sciences on July 24 1882[97]. This communication was indexed in the September 1882 issue of the *Index Medicus*[98]. Results on both types of vaccination were finally summarized in a monograph published in 1883[99]. However, Conan Doyle must have known of these results before the publication of the monograph, since in it the authors mentioned vaccination experiments performed in May 1883, that is, a couple of months after the publication of Conan Doyle's *Good Words* article.

The relationship between Conan Doyle and leukocyte phagocytosis did not end with the *Good Words* article. In 1913, Conan Doyle wrote a true story of terror, "The horror of the heights", which unfolds around the attempt by the bravest air-pilot of England to establish the height record, flying with its plane to dizzying heights[100]. But he soon discovered that the higher layers of the atmosphere were patrolled by large bodies made of some transparent, jelly-like substance with great projections from the outer surface, whose "method of progression was to throw out a long, glutinous streamer in front of it, which in turn seemed to draw forward the rest of the writhing body. So elastic and gelatinous was it that never for two successive minutes was it the same shape." Eventually, long tentacles shot out from the mass of floating blubber and reached the plane of the pilot, literally devouring them both. As the phagocytic cells, which often did throw out the useless remnants of digested foreign bodies, the remains of the plane and of a notebook stained with the pilot's blood were found on the ground. It is not difficult to recognize in those gigantic jelly-like bodies, moving in the higher space with amoeboid movements and finally engulfing and devouring the aviator, the equivalents of leucocytes and bacteria described in the *Good Words* article, in which Conan Doyle had already foreseen the unhappy end of the novel, when he wrote: "small hope for

our poor little mite of humanity [the microscopic human being] should one of these floating stomachs succeed in seizing him in its embrace." As for many other articles and stories, the creative cue came from Conan Doyle's medical knowledge, testifying to how valuable his medical training remained during his literary career, even if he did not remain long in the medical profession.

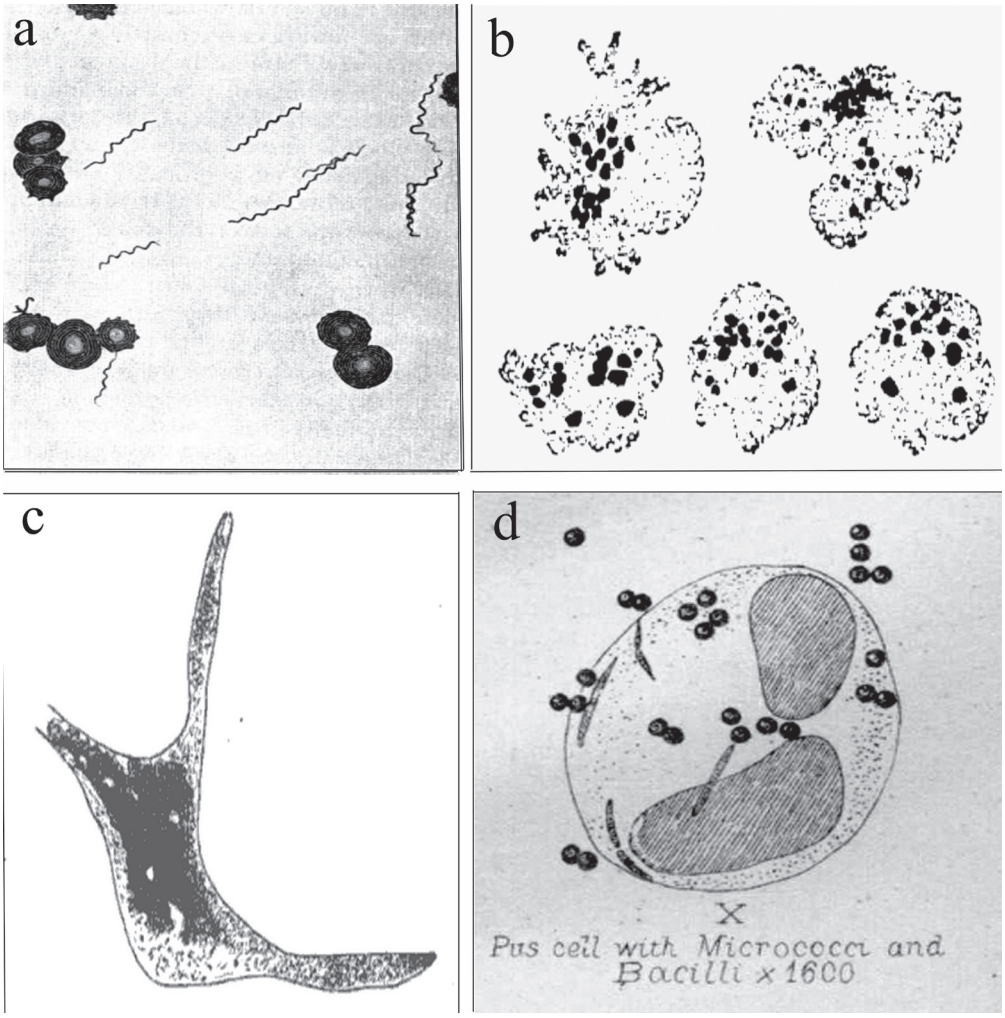

Fig. 1. a) "Blood of relapsing fever (human). Blood corpuscles and spirilla Obermeyeri (After Koch)". Originally figure 184 from Klein E, Micro-organisms and Disease. London: MacMillan and Co.; 1896. b) "White blood-corpuscles of the frog, containing granules of vermilion and showing amœboid movements". Originally figure VI, Plate I from Klein E, Noble Smith E. Atlas of Histology. London: Smith, Elder & Co.; 1880. c) A fibrous septa of the lung, with a dense accumulation of cells filled with carbon particles. Originally figure 4 from Osler W. On the Pathology of Miner's Lung. Canada Med. Surg. J. 1876; 4:145-168. d) Small groups of cocci in or on a leucocyte. Originally figure 10 from Ogston A, Report upon micro-organisms in surgical diseases. Brit. Med. J 1881;1(1054):367-375.

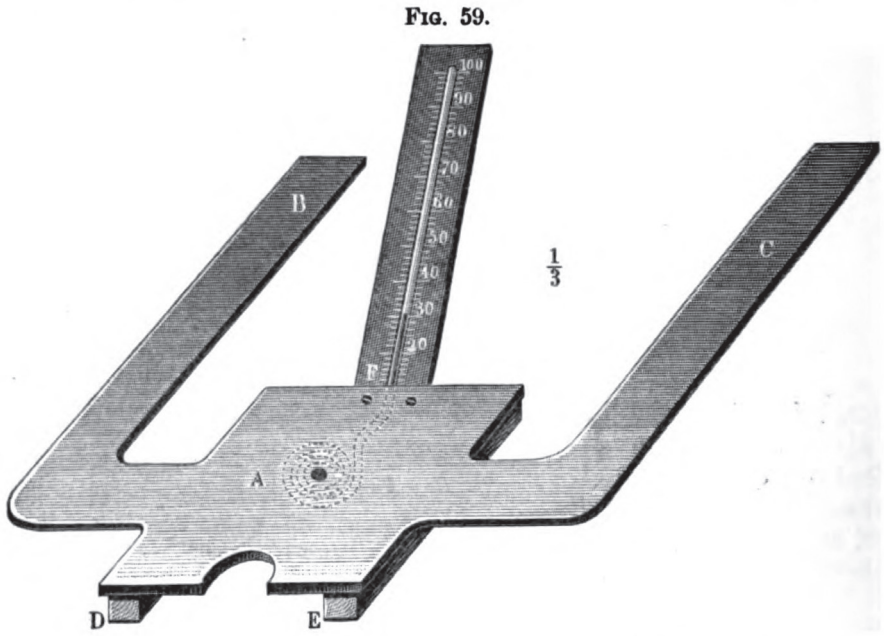

Fig. 2. Max Schultze's hot stage. It consisted of a brass plate (A) with two arms (B, C). Spirit lamps were placed under the arms. In this way the object on the plate could be readily heated to a temperature of 35°-45° C. The temperature of the object was recorded by a thermometer (F) (Taken from the *Journal of the Royal Microscopical Society*, April, 1887, p.304, fig. 59).

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