

Early concepts on the mechanism of peritonitis with special regard to the experimental work of Karol Klecki

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Abstract: The term *peritonitis* is relatively new in medical language, however some of its symptoms were observed and noted even in antiquity. The proper recognition of peritonitis as a distinct pathological entity was made possible when progress in the clinical and experimental sciences give birth to the methodology needed for the investigation of the etiology and mechanism of peritoneal inflammation. Research concerning this clinical topic began to yield significant results in the second half of 19th century. This paper aims to give some insight into this pioneering period of scientific investigation focused on the etiology and pathology of peritonitis. From the work of von Recklinghausen in the 1860s, through the later research of Wegner and Gravitz, the next major step in this field was made by the Polish experimental pathologist and pathophysiologist Karol Klecki.

Key words: peritonitis, bacterial infection, pathology, pathophysiology, history of medicine.

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Introduction

For most of medical history, peritonitis was not a distinctly defined pathological state in the realm of medical knowledge. The lack of systematic research based on human autopsies hampered progress in the anatomical and pathological examination of this condition. Although the first historical mention of “inflammation of the peritoneum” is described and named *peritonitis* by the French physician and nosologist François-Boissier de la Croix de Sauvages around 1750, it was not until 1815 when it was recognized as a separate disease entity for the first time.

Abdominal surgery was also deprived of any important achievements until the 18th century; nevertheless, some clinical observations were slowly coming to the attention of the medical community. The 19th century was the turning point in the modern development of abdominal surgery, when the first successful elective laparotomy was performed by Ephraim McDowell in 1809 with the removal of an ovarian cyst [1].

Abdominal surgery could then evolve due to the research done on experimental physiology by Francois Magendie and Claude Bernard, as well as cellular pathology, first pioneered by Rudolf Virchow, and on the bacteriological theory of infectious diseases which was elaborated in the works of Louis Pasteur and Robert Koch. The technical skills of surgeons necessary to perform successful operations were now enriched by the basic understanding of the biological mechanism of infections [2]. It also formed new attitudes towards experimental methods enabling deeper research in the realm of pathophysiological problems.

Methods

The results presented in the published works of researchers exploring the possible mechanism of infection leading to peritonitis were comparatively analyzed. Original papers in French, German and English written on the subject constitute the main primary sources. Karol Klecki's scientific report was partly translated to English by Jan Guzek in the late 1980s and his text was used as a secondary source. Some papers dealing with the history of the scientific investigation of peritonitis were also analyzed.

Historical analysis

The first important experimental research concentrated on the physiology and pathophysiology of the peritoneum was conducted by Friedrich Daniel von Recklinghausen, who in 1863 published results of his investigation on the flow of solutes and particles across the peritoneal membrane. He clearly established the connection between the peritoneum and the lymphatic vessel system, and discovered the peritoneal lymphatic stomata [1, 3].

The next classical work was authored by the German physician Georg Wegner, who pioneered modern peritoneal surgery. In 1876, Wegner observed an increase of effluent volume when infusing a solution of glycerin into the peritoneal cavity in an experimental model. The results of this investigation allowed him to formulate a proper description of diffusion across the peritoneal membrane. Wegner could also calculate the absorption rate of various solutions in the peritoneum, showing that the important factors in peritonitis were connected with the surface area of the peritoneum. As Wegner observed, the peritoneum could also absorb and excrete large

amounts of different fluids. When experimenting with artificially provoked peritonitis on rabbits, he injected bile, serum, and urine, even introducing at one point ordinary atmospheric air into the peritoneal cavity. As Wegner noted, in all cases, those factors were not responsible for developing peritonitis, being instead simply absorbed. The mechanism of the encapsulation of solid particles present in the fluids was also recognized [4, 5].

Wegner then proceeded to introduce air and putrescible fluids together. These were purposely given above the level of absorption. This in turn provoked the observable decomposition of the introduced products and finally septicemia. An exception to this observation was defibrinated blood, which did not decompose in the above model. Further scientific investigation proved that the peritoneum could tolerate large bacterial loads [1, 5].

Wegner came to the conclusion that intraperitoneal wounds and inflammatory septicemia are the greatest pathological risk factors, although in his experimental model peritonitis was hardly ever provoked [1, 4].

The absorption and reabsorption mechanism in the peritoneum was the subject of later investigations by French researchers L. Dubar and Ch. Remy, who were experimenting with a chicken protein solution injected into rabbit peritoneum [5], and by the extensive experimental program of the German pathologist Paul Grawitz [7, 8]. Grawitz, following the inroads of von Recklinghausen's and Wegner's work, observed that the majority of microorganisms do not cause suppurative peritonitis even when introduced into the peritoneal cavity, and further, that the specific forms that can cause suppuration became active and infectious only under certain conditions.

In some respects, Grawitz replicated Wegener's research program in the experimental model when introducing ordinary forms of microorganisms into the healthy peritoneal cavity of rabbits "together with putrescible albuminous substances, cholera-bacilli and even of fecal matter" [5]. No peritonitis was provoked if the quantity was not greater than the peritoneum could absorb or safely encapsulate in a limited time. As Grawitz estimated, when the absorptive power of the peritoneum has been impaired, the absorption process was obviously much weaker, although still no peritonitis occurred. Septicemia was produced if the microorganisms introduced into the peritoneum could activate the decomposition of albumen [5].

Grawitz also observed that even bacterial cultures, which are connected with suppuration, do not produce inflammation if entering in small amounts in a normal peritoneum [7]. It was estimated that peritonitis could be provoked only when the wall of the peritoneum is damaged or wounded and when fluids on which microorganism can feed and grow were freely accessible for them. As Grawitz observed, pathogenic organisms can enter the peritoneum directly or through the lymphatic and blood vessel systems.

In the late 1880s and early 1890s, the mechanism of peritonitis was the subject of intensive investigation by many researchers, among them the Polish physician Karol Klecki.

Discussion

When Karol Klecki became the Professor of General and Experimental Pathology at Jagiellonian University in 1897, he was already a recognized investigator in the field of modern medical sciences. He finished his medical studies at Dorpat University (now Tartu), and then moved to Cracow to join the Surgical Clinic, where he was fortunate to work under one of the most talented clinical researchers, Professor Ludwig Rydygier. At the same time, Klecki, who was interested in basic and experimental sciences, was able to learn experimental methods in the laboratories of the Department of Physiology, then directed by the famous scientist Professor Napoleon Nikodem Cybulski. In 1893, Klecki was appointed assistant to the Professor of General and Experimental pathology Władysław Gluziński, simultaneously working in Department of Internal Medicine under Professor Stanisław Pareński. In 1894, Klecki received his MD degree. He then undertook a scientific tour to the Laboratories de Recherche in Paris, where he attended lectures given by Elie Metchnikoff and Emil Roux. At the same time, he was able to work in laboratories performing experimental investigations on the subject of the pathogenesis of peritonitis [9]. Before returning to Cracow, Klecki published the results of his research in a separate paper, which was of the greatest importance [10].

Klecki's research assured him that most natural peritoneal infections are caused by bacteria; however, he had to admit that peritonitis was still one of the most complex problems to be examined in the field of pathology. The first subject of his investigation was *Escherichia coli* (named then *Bacterium coli commune*), whose presence in the infections of the gastric tract, and specifically of the peritoneum, was reported earlier by L. Laruelle [11]. Nevertheless, there was discussion among researchers concerning the exact role of this bacterial pathogen in the mechanism of peritonitis. Some, like A.D. Pawlowsky, were pointing to other possible microorganisms as the main infectious agent, while others, like O. Barbacci, excluded *Escherichia coli* as a specific factor in the development of peritonitis [12, 13]. Contrary to Barbacci, Ernest Malvoz came to conclusion that *Escherichia coli* should be regarded not only as the specific pathogenic factor seen in peritonitis after intestinal perforation, but it is in fact responsible for all known cases of peritonitis [14]. The same conclusion was reached in the works of Paul Ziegler [15]. However, Malvoz and Ziegler were not able to give conclusive experimental evidence to support this hypothesis. One of the main obstacles in research with *Escherichia coli* was its natural tendency to polymorphism. In the early 1890s, there were over 30 types and subtypes of *Escherichia coli* recognized.

Klecki opened his scientific investigation by trying to estimate the virulency of *Escherichia coli*. Experimenting on guinea pigs which were infected through transperitoneal injections, he was able to estimate that *Escherichia coli* bacteria detected in the ileum are the most virulent, while those from jejunum, although active, have lower virulency. The least potent were those present in the colon.

His research provided evidence that if the bowel wall is intact, especially with regard to the integrity of its epithelium, then the possibility for bacteria to penetrate out of the gut is very low. Experimenting on dogs, Klecki could provoke acute general peritonitis when using a rubber ring for the artificial compression of a loop of bowel. The ligation of mesenteric vessels was used in some cases. Under such conditions, experimental animals were dying in 24 to 48 hours. Close pathological examination revealed that the desquamation of the epithelium was evident, and the mesenteric vessels were prone to dilation. The whole wall of ringed loop of bowel was subject to intensive infiltration. This led to the conclusion that isolated parts of gut could provide a good environment for more virulent strains and their increased virulence which, as Klecki believed, was the product of close symbiosis with other microorganisms and albuminous material collected and the decomposition in the ligatured loop of bowel [10].

In analyzing tissue structures, Klecki concluded that necrotic parts of the intestinal walls are the most suitable for microbic settlement and that microorganisms are detected in the subserosa, in even greater numbers than within the vessels. As Klecki hypothesized, blood vessels were the proper way for bacteria to spread the infection.

Repeating experiments with *Escherichia coli* grown on broth medium which were then used to infect guinea pigs, Klecki could observe that the virulence of bacteria grew rapidly when they penetrated into the abdominal cavity, but thereafter virulence decreased. Virulence depended, as Klecki speculated, on the presence of other bacterial organisms and their influence on *Escherichia coli*. Finally, he was convinced that although it should be considered as an important pathogenic factor in the mechanism of peritonitis, *Escherichia coli* was not to be considered as the sole etiological factor, and it should always be regarded in connection with other bacterial organisms [10].

Klecki's achievements were noticed by other researchers. In 1898 Frederick Treves made a wider reference to Klecki's experimental results when he recommended that during intestinal surgery "the handling of the bowel during the operation should be the gentlest, and that the evacuation of an obstructed loop is very desirable" [16]. An early remark on Klecki's work was done by Max Neisser when discussing the problem of the propensity of the intestinal wall for bacteria infiltration [17]. When S. Weil was writing his chapter devoted to peritonitis in the *Ergebnisse der Chirurgie und Orthopädie*, the results reported by Klecki were discussed [18]. August Jerome Lartigau, in reviewing the role of *Escherichia coli* in the mechanism of infections in 1902, also discussed the results of Klecki's investigations [19]. In a monograph titled

The Bacteriology of Peritonitis, published in 1905 —the first comprehensive book on the subject —Leonard Dudgeon and Percy Sargent refer to Klecki's observations concerning the differential virulence of *Escherichia coli* [20]. In 1912, Arthur Hertzler's extensive monograph devoted to the peritoneum refers to the experimental work of Klecki [21]. It was further acknowledged by Frank Meleney and his colleagues when in the early 1930s they presented the results of comparative clinical studies of over one hundred cases of peritonitis [22]. Klecki's publication was among those referenced when Willy Haas analyzed the bacterial content of portal blood and the development of liver abscesses [23]. One of most prominent French clinicians, Georges Dieulafoy, in the first volume of his *Textbook on medicine* claims: "The remarkable experiments of Klecki on the pathogenesis of peritonitis of intestinal origin have led me to investigate the pathogenesis of the closed cavity in appendicitis" [24].

Conclusion

Klecki's experimental work was an important step towards understanding the mechanism of peritonitis. It emerged directly from the early research results of Wegner and Grawitz. Klecki was able to point to the differences in the virulence of the bacterial component in animal models and proposed his own, original hypothesis explaining the roots of infection in close connection with the vessel system enabling contagious transmission from the gut into the peritoneum. The pathological processes and changes in the intestinal lumen were the most important mechanism of the development of peritonitis. The results and conclusions from Klecki's research were acknowledged and discussed by scientists developing their own research programs in that field in the late 1890s and the early 20th century.

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