

Hospital epidemiology: from Semmelweis to the post-antibiotic era

Epidemiologia Hospitalaria: De Semmelweis a la Era Post Antibiótico

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In mid-1948, at the Allgemeines Krankenhaus general hospital in Vienna, Ignaz Philipp Semmelweis proposed the use of chlorine solutions for washing doctors' hands. He suggested that this measure should be performed before and after attending and examining women who were in labor. This was the most effective measure to reduce the high mortality rates from puerperal fever. At that time, Semmelweis sowed the seed that would germinate one of the most important branches of public health, Hospital Epidemiology (1). This Hungarian obstetrician had to extend the frontiers of knowledge beyond the cold walls of the paradigms of the time. With few, but novel, statistical and epidemiological tools, he managed to combine all the steps of clinical and hospital research, from a shrewd and critical observation on the mortality of women in labor and newborns.

Semmelweis framed his research question through the causality of the event. The challenge was how he would find and demonstrate such causality, which is unknown or at least "confused" by the traditional variables that were, by traditional doctors, customarily invoked to explain this event. Semmelweis conducted a review and analysis of the historical records of births, deaths, and mortality rates from the opening of the hospital in 1784 to 1848. Analyzing two exposure groups, one exposed to the attention of medical students and the other group exposed to the attention of midwives, he was able to configure his analytical design. This allowed him to formulate his hypothesis: the cause of puerperal fever was the cadaverous particles present in the hands of the students that were rotating through the morgue.

In a last step, this epidemiologist by nature and health care practitioner by intuition developed his experimental study to evaluate the effectiveness of hand washing in preventing puerperal fever, reducing mortality rates from 12.1% (in 1842) to 1.3% (in 1848). Once again the visionary Semmelweis, assuming as a shield of protection the overwhelming evidence of his findings, before his fellow detractors, laid the foundations of the most cost-effective hospital epidemiology action known to mankind today: hand washing (2). To this growing discipline, as yet unnamed, Florence Nightingale, a British nurse and statistician, the first woman to be admitted to the Royal Statistical Society and recognized as the mother of nursing, made an important contribution to the duty that, "The only thing a hospital should not do is make you sick". Nightingale demonstrated the benefits of comprehensive hospital care following five components (biological, psychological, social, spiritual and beliefs), together with the improvement of sanitary methods, 24-hour care, humanization of the service, lighting and ventilation of the wards, the provision of clean water to drink and

heal wounds, clean bedding, asepsis and the disposal of healing utensils, which reduced hospital mortality from 40% to 2% (3).

Other important advances of the so-called "Century of the awakening of science", would have repercussions in the nascent hospital epidemiology. The bacteriologist and chemist Louis Pasteur and the German physician Robert Koch developed the foundations of the germ theory of diseases, which allowed the conceptual leap from the era of miasmas to modern microbiology. These concepts continued to nurture the already adolescent hospital epidemiology.

In the 20th century, humanity made important advances in all areas of knowledge. Antibiotics appeared in 1928, thanks to the accidental findings of Alexander Fleming, however, it was not until 1941 that the first clinical trial of penicillin with humans was carried out. Its use was widespread until the Second World War, due to the need to cure the wounds of the soldiers. "We Have Defeated Infectious Diseases" was the first shout of victory that resounded on those battlefields. Humanity, however, could not have been more wrong, as that was only the beginning of the arms race between microorganisms and the pharmaceutical industry. The hospitable environment was now the new battlefield: each time a new antibiotic molecule is developed, bacteria present novel resistance mechanisms (4).

Microorganisms such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium* and *Staphylococcus aureus* are the main human pathogens, responsible for a wide range of infections of hospital and community origin (5,6). Their structural and biochemical characteristics, as well as their varied and extensive arsenal of virulence factors, allow them to adhere, colonize and invade any tissue, under a diverse range of clinical manifestations (7,8). Their great capacity to share virulence factors and resistance mechanisms through mobile genetic elements such as plasmids, transposons and insertion sequences, even with microorganisms from other species have given bacteria a great capacity to adapt and survive in hostile environments. The treatment of these infections has become a real challenge (9,10).

Parallel to the development of antibiotics, humanity has made other important advances in all areas of knowledge. In the field of biomedical sciences, for example, technological and pharmaceutical development allows us to have increasingly better diagnostic methods and better surgical and therapeutic techniques that have made important triumphs possible in the control and treatment of those diseases that historically represented a threat to human life. These advances, together with public health and environmental sanitation

policies, resulted in a significant increase in the life expectancy of human beings (11). Due to this increase in life expectancy, and the increasing availability of health services, however, human beings are increasingly exposed to the risks of the hospital environment, either as patients, workers or occasional visitors (12).

Today hospitals are considered the gateway to and from life. Infections Associated with Health Care (IAH) are considered the main threat to patient safety, representing the first cause of complications in hospitalized patients. The Center for Disease Control and Prevention (CDC) defines IAAS as any localized or systemic infection that results in an adverse reaction to the presence of an infectious agent or its toxins, which is acquired during or because of the provision of a health service, and that was not present or in the incubation period at the time of admission of the patient (13,14).

Worldwide, the calculated risk of developing an IAH has been estimated to range between 5% and 10% in all hospitalized patients (15); Due to the increase in morbidity, mortality, and excess costs, IAHs have become the most important adverse event related to institutionalized medical care (16). About 2 million IAHs are reported each year in the United States and at least 100,000 patients lose their lives from related complications (17). 25% of IAHs are reported in patients admitted to Intensive Care Units (ICU) and these are the fifth leading cause of death in this environment (18). IAH cause an excess in hospital stay between 4.2 and 15.6 days, in addition they double the cost of nursing care, tripling the cost of drugs and raising the cost of laboratory tests up to six times; in ICUs they represent more than 20% of the total cost derived from health care; the total excess hospital cost can reach US \$ 5.7 billion per year (19). In high-income countries, device-associated IAHs are the most frequent, and represent the highest burden and highest mortality of all IAHs reported in ICUs (20). The most frequent are: urinary tract infection associated with urinary catheter (UTI-UC); ventilator associated pneumonia (VAP); venous catheter-associated bloodstream infection (STI-CVC); and surgical site infections (ISO). Apparently, the impact of IAHs and bacterial resistance in developing countries like Colombia is even greater.

Due to their clinical and economic impact, both IAHs and bacterial resistance are considered by the WHO to be a serious global public health problem, with serious clinical and social consequences. They have become an indicator of the quality of the provision of health services and the management of patient safety. Based on the evidence reported in all hospitals in the world, the WHO has warned about the progressive bacterial resistance to antibiotics, as well as the sustained increase in IAH produced by resistant germs, which led to a declaration during the 1998 World Health Assembly, that these nosocomial events are a real threat to humanity.

Based on this alert, the World Health Organization (WHO) and other scientific societies of the world, support member countries in the creation and strengthening of epidemiological surveillance systems in nosocomial events (IAAS and BR), to implement prevention strategies and control these events, to promote the rational use of antibiotics, to reduce the use of antimicrobials in food production and to regulate the manufacture, distribution and sale of antibiotics. In this way, a series of strategies have been

developed to reduce the impact of IAHs and bacterial resistance. In 2004, the World Alliance for Patient Safety was created, from which programs such as "Clean care is safer care" (2005 and 2006), "Safe surgery saves lives" (2007 and 2008). The importance of responsible antibiotic prophylaxis as a marker of good care was included in these programs, and in others such as "The fight against antimicrobial resistance" (2008 and 2009) (21). These strategies strengthened hospital epidemiology, making it the standard in the hospital fight against infectious diseases.

In Colombia, concrete actions from hospital epidemiology began around the year 2000, when some research groups such as GREBO in Bogotá, GERMEN in Medellín and CIDEIM and RENOVA in Cali independently published the first reports on the resistance profiles of isolated microorganisms in some hospitals. The interest and actions of these groups developed vertiginously as they understood that this was a public health problem that transcends the walls of health institutions, and puts the entire system at risk. In this manner, the experiences of these research groups provided the scientific and methodological support upon which the Epidemiological Surveillance System in Colombia for IAH and bacterial resistance was built.

Undoubtedly, to achieve a true impact on the prevention and control of bacterial resistance and IAH, collaboration is required from all actors within the Colombian Health system at the institutional, regional and national levels, in terms of improving their capacities and competencies in epidemiological surveillance, studying outbreaks and ensuring the rational and responsible use of antibiotics. This is only possible, however, with the participation of academics, since in Colombia there is no formal education program focusing on hospital epidemiology and Infection control. This is an invitation to the leading scientific and academic experts in the country to build University-level training programs that allow all health professionals to contribute to containing the threat of the century.

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