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2 - Development of Epidemiology
2.1 - Historical Background (K. Krickeberg)

The word “epidemic”, i.e. something that falls upon people (□□- upon; □□□s - people), which was in use in ancient Greece, already reflected one of the basic ideas of modern epidemiology, namely to look at diseases on the level of *populations*, or *herds* as they also have been called, especially in the epidemiology of infectious diseases. The link with the search for *causes* of illness was present in early writings of the Egyptians, Jews, Greeks, and Romans (Bulloch 1938). Both Hippocrates (ca. 460–ca. 375 BC) and Galen (129 or 230–200 or 201) advanced etiological theories. The first stressed atmospheric conditions and“miasmata”but considerednutrition and lifestyle as well (Hippocrates 400 BC). The second distinguished three causes of an “epidemic constitution” in a population: an atmospheric one, susceptibility, and lifestyle. The basic book by Coxe (1846) contains a classification of Galen’s writings by subject including the subject “etiology”. For a survey on the various editions of Galen’s work and a biography see the essay by Siegel (1968). Regarding more specific observations, the influence of dust in quarries on chronic lung diseases wasmentioned in aRomantext of the first century. Paracelsus in 1534 published the first treatise on *occupational diseases*, entitled “Von der Bergsucht” (On miners’ diseases); see his biography in English by Pagel (1982).

Ramazzini (1713) conjectured that the relatively high incidence of breast cancer among nuns was due to celibacy. Sixty-two years later, Percival Pott (1775) was among the first ones to phrase a comparative observation in quantitative terms. He reported that scrotal cancer was very frequent among London chimney sweeps, and that their death rate due to this disease was more than 200 times higher than that of other workers. The most celebrated early observational epidemiological study is that of John Snow on cholera in London in 1853. He was able to record the mortality by this disease in various places of residence under different conditions of water supply. And by comparison he concluded that deficient quality of water was indeed the cause of cholera (Snow 1855).

Parallel to this emergence of observational epidemiology, three more currents of epidemiological thinking have been growing during the centuries and interacted among them and with the former, namely the debate on *contagion* and *living causal agents*, *descriptive* epidemiology in the classical sense of health statistics, and *clinical trials*. A contagion can be suspected from recording cases and their location in time, space, families, and the like. The possibility of its involvement in epidemics has therefore no doubt been considered since time immemorial; itwas alluded to in the early writings mentioned at the beginning. Nevertheless, Hippocrates and Galen did not admit it. It played an important role in the thinking about *variolation*, and later on *vaccination* as introduced by Jenner in 1796 (Jenner 1798). The essay by Daniel Bernoulli on the impact of variolation (Bernoulli 1766) was the beginning of the theory of *mathematical modeling* of the spread of diseases. By contrast to a contagion itself, the existence of *living* pathogens cannot be deduced from purely epidemiological observations, but the discussion around it has often been intermingled with that about contagion, and has contributedmuch to epidemiological thinking. Fracastoro (1521)wrote about a *contagium animatum*. In the sequel the idea came up again and again in various forms, e.g. in thewritings of Snow. It culminated in the identification of specific parasites, fungi, bacteria, and viruses as agents in the period from, roughly, 1840 when Henle, after Arabian predecessors dating back to the ninth century, definitely showed that mites cause scabies, until 1984 when the HIV was identified. As far as we know, the term “epidemiology” first appeared in Madrid in 1802. From the late 19th century to about the middle of the 20th, it was restricted to *epidemical infectious* diseases until it took its present meaning (see Sect. 2.2 and Greenwood 1932).

Descriptive epidemiology had various precursors, mainly in the form of church and military records on one hand (Marshall and Tulloch 1838), life tables on the other (Graunt 1662; Halley 1693). In the late 18th century, local medical statistics started to appear in many European cities and regions. They took a more systematic turn with the work of William Farr (1975). This lasted from 1837 when he was appointed to the General Register Office in London until his retirement in 1879. In particular, he developed classifications of diseases that led to the first International List of Causes of Death, to be adopted in 1893 by the International Statistical Institute. Farr took also part in the activities of the London Epidemiological Society, founded in 1850 with him and Snow as founding members, and apparently the oldest learned society featuring the word "epidemiological" in its name. Geographic epidemiology, i.e. the presentation of health statistics in the form of maps, also started in the 19th century (Rupke 2000).

If we mean by a clinical trial a *planned*, *comparative*, and *quantitative* experiment on humans in order to learn something about the efficacy of a curative or preventive treatment in a clinical setting, James Lind is considered having done the first one. In 1747 he tried out six different supplements to the basic diet of 12 sailors suffering fromscurvy, and found that citrus fruits, and only these, cured the patients (Lind 1753). Later he also compared quinine to treat malaria with less well-defined control therapies (Lind 1771). The first more or less rigorous trial of a preventive measure was performed by Jenner with 23 vaccinated people, but he still used what is now being called "historical controls," i.e. he compared these vaccinated people with unvaccinated ones of the past who had not been specially selected beforehand for the purpose of the trial (Jenner 1798). In the 19th century some physicians began to think about the general principles of clinical trials and already emphasized probabilistic and statistical methods (Louis 1835; Bernard 1865). Some trials were done, for example on the efficacy of bloodletting to treat pneumonia, but rigorous methods in the modern sense were established only after World War II (see Sect. 2.2), beginning in 1948 with the pioneer trial on the treatment of pulmonary tuberculosis by streptomycin as described in Hill (1962).

Let us conclude this all too short historical sketch with a few remarks on the history of applications of epidemiology. *Clinical trials* have always been tied, by their very nature, to immediate applications as in the above mentioned examples; hence we will not dwell on this anymore. *Observational* epidemiology, including classical descriptive epidemiology, has led to hygienic measures. In fact, coming back to a concept of Galen (1951), one might define *hygiene* in a modern and general sense as applied observational epidemiology, its task being to diminish or to eliminate causal factors of any kind. For example, the results of Snow's study on cholera found rapid applications in London but not in places like Hamburg where 8600 people died in the cholera epidemic of 1892. Hygienewasamatter ofmuchdebate andactivityduringthe entire 19thcentury, although, before the identification of living pathogens, most measures taken were necessarily not directed against a known specific agent, with the exception of *meat inspection* for trichinae. This wasmade compulsory in Prussia in 1875 as proposed by Rudolf Virchow, one of the pioneers of modern hygiene and also an active politician (Ackerknecht 1953).

Hygienic activities generally had their epidemiological roots in the descriptive health statistics mentioned above. These statistics usually involved only factors like time, place of residence, sex, and age, but Virchow, for example, analyzed during the years 1854–1871 the mortality statistics for the city of Berlin and tried to link those factors with social factors like poverty, crowded dwellings, and dangerous professions, thus becoming a forerunner of *social epidemiology*. As a result of suchreflections aswell asof politicalpressure, large*sewage systems* were built in Europe and North America, the *refuse disposal* was reorganized and the *water supply* improved. Other hygienic measures concerned the structure and functioning of *hospitals*, from reducing the number of patients per room and dispersing wards in the formof pavilions to antiseptic rules. The latter had mainly been inspired by more or less precise epidemiological observations on infections after the treatment of wounds and amputations (Tenon 1788; Simpson 1868–1869, 1869–1870; Ackerknecht 1967), and on puerperal fever (Gordon 1795;Holmes 1842– 1843; Semmelweis 1861).