

«Common sense, proper training and sound reasoning» – Koch's postulates and 20th century medicine

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The paper analyses the origins of the so-called Koch's postulates and the influence they exerted in 20th century medicine. Koch himself never devised such rules for establishment of infectious causation. Instead it was his colleague Friedrich Löffler who in 1884 wrote down the well-know three steps of isolation, cultivation and inoculation as conditions for establishing a microbial pathogen. They are frequently invoked in textbooks of medical history, but seem to have had little relevance in medical research. The assumed inventor Koch made numerous variations in his own methodology. However, underlying his work there was a sort of trivial ontology of diseases which rendered an experimental reconstruction of human pathologies meaningful. Ways to pursue this end there were many. Given that, it is not surprising that references to Koch's postulates in the 20th century usually refer to the spirit rather than the literal meaning of the postulates. E.g. proponents of virology or molecular medicine would devise variations of Koch's postulates that serve to relate their work to Koch's bacteriology. The later is envisioned as being the outset of modern experimental medicine. The nature of such references is more anecdotal than historical: referring to a historical object that did not exist as such, the references produce credentials ex traditio for experimental medicine.

I

It is one of the peculiarities of historical conscience of modern man that one's own place in history is seen as being subjected to change. Our perception, it seems, focuses more on change than on permanence. Furthermore, it is through the work of Reinhard Koselleck that we have learned that men and women for about 200 years have seen this change as a type of process that is open towards the future.¹

¹ Koselleck 1979.

The history of modern medicine provides an example to the case. In common textbooks it will usually be presented as a process characterised by rapid change and continuous innovation. The driving force behind this seems to be the so-called progress of science, which – for better or for worse – sets limits for what counts as relevant. Quite independently if is employed for critical or more affirmative statements, Bernard Naunyn’s statement of 1905 “Medicine will be a science or it will not be”, can arguably be taken as headline for the history of modern medicine.²

By framing the history of modern medicine as turmoil of successive inventions other, more stable elements of that same history disappear from our radar. What is relevant for historical processes without being subjected to change to a high degree is easily overseen. A way to identify such basic trends is to analyse common historical references and to see if and how they change over time. References to the Hippocratic Oath provide an example³ and for the history of experimental medicine, which is my focus, Koch’s postulates can serve that purpose. The common view in this case is that these postulates are a set of rules serving to determine infectious causation and that they were devised by the German physician Robert Koch (1843-1910) in the 1880s.⁴ Classically they consist of the three steps of isolation (of a suspected pathogen in infected tissues), cultivation (in the so-called pure culture) and inoculation (in animal experiments with the intention to reproduce the original pathology). The customary wisdom is that they provide an „unchanging standard for determining causation in medicine”⁵ and references to them in scientific and popular literature are numerous.

This historical phenomenon has two surprising characteristics. For once, there is no original reference, meaning that despite the existence of a Wikipedia entry on these postulates, Koch himself phrased no such postulates. Secondly and unsurprisingly in relation to what I just stated, views on the number of such postulates and their content differ widely. In the following I will try to explore somewhat deeper both of these characteristics, but will chiefly focus on the later one – that is on the variations of Koch’s postulates that have been phrased during the 20th century.⁶ My purpose is to explore those basic trends of medical thinking that I have mentioned above.

² Quoted in: Pfohl 1987.

³ Cantor 2002.

⁴ As introductions to Koch’s work: Brock 1988; Gradmann 2005. On the postulates: Carter 1985; Evans 1993; Gradmann 2008.

⁵ Fredericks and Relman 1996: 18.

⁶ For a more detailed analysis I point to my paper Gradmann 2008.

II

In relation to the first point the historical evidence looks like this. Koch, whose fame rested and still rests on etiological work on diseases such as anthrax, cholera and tuberculosis, preferred rather factual statements when it came to methodology and generally avoided considerations that went beyond technical matters and into theories of diseases in general. If we judge his own work on the classical three steps, it is usually not in line with them. He could leave out the establishment of animal models or work without pure culture and would still be convinced to have elucidated the aetiologies of infectious disease on such occasions. The idea of Koch as the author of his postulates is in a sense a misunderstanding. It can be traced back to the instance that one of his collaborators, Friederich Loeffler (1852–1915) in 1884 laid down the methodology they had used in their work on tuberculosis in the years previously in a more authoritative form to serve as a role model to be followed and provided it with the name ‘postulates’.⁷

Still, it would be inaccurate to say that there are no constant elements in Koch’s work. However, these are not to be found in his methodology to establish aetiology, but in a kind of trivial ontology of infectious diseases that is implicit in many of his writings. Naturally, it is not easy to spell out something that is implicit but I would propose the following four statements.

1. A description of causes is suited to develop an essential understanding of diseases.
2. Such causes should be framed as necessary ones. Yet it is assumed that they also provide sufficient explanations for pathogenesis.
3. An experimental reconstruction of human pathologies for example in animal models is possible and meaningful.
4. The identification of the pathogen provides a possibility of control – „Find the cause, then find the cure“⁸ that’s how one could phrase the mission of modern biomedicine in a nutshell.

III

It is in this sense not surprising that the 20th century is full of invocations of Koch’s postulates, which may differ substantially in relation to their content and the occasion upon which they are produced. Of course most of these are simple cases of so-called eponymy where the name-phrase is

⁷ Loeffler 1884: 424.

⁸ Epstein 1996: 31.

repeated at random for merely illustrative purposes.⁹ Still, some are more original and of these I have chosen two to discuss in more depth, since they relate to my quest for underlying trends.

The first group of such text is one that focuses on updating the postulates in relation to new objects and methods. In this case two major impulses can be identified: The formulation of the virus concept around mid-century and a few decades later the arrival of molecular biology and gene technology in particular in medical microbiology.

As far as viruses are concerned the concept of them being a class of microbes of their own slowly evolved over the first three decades of the 20th century. What initially simply appeared as a kind of ultra-bacterium, capable of passing through bacteria tight filters gradually became more different from what was known about bacterial life.¹⁰ In 1937 the president of the American Society of Bacteriologist, Thomas Rivers (1887-1963), produced an inventory of the young field of virology. While doing so he developed a remarkable critique of Koch's postulates.¹¹ At the time when they were laid down they had indicated a breakthrough to an understanding of infectious diseases that was based on scientific methods. Problems arising thereafter had in fact been resulting from the magnificent successes of medical bacteriology in the later decades of the 19th century. An overemphasis on aetiology in relation to understanding diseases developed, while the role of the host organism and of its immune system was not duly recognised.

The popularity of Koch's postulates had overshadowed the fact that other phenomenons such as immunological reactions in serological tests were no less suitable to identify infectious diseases than the pursuit of Koch's methodology.¹² All in all, the concept of a microbe had been narrowed down to bacteria and people had lost sight of the fact that entirely different pathogens existed. „Blind faith“¹³ had produced a series of misjudgements. An example is that streptococci for a period were considered to be the pathogen of poliomyelitis. They could be identified with regularity, cultivated and it was even possible to produce some kind of paralysis when employing them in animal experimentation. Questioning, however, whether paralysis in this animal model stood in relation to human poliomyelitis did not come to people minds. The real pathogen, a virus, had not been considered for it was too difficult to cultivate and identify in

⁹ Merton 1985.

¹⁰ Helvoort 1992, Helvoort 1993, Helvoort 1994.

¹¹ Rivers 1937.

¹² Rivers 1937: 3.

¹³ Rivers 1937: 4.

tissues. As a consequence of his criticism, Rivers demanded postulates that were modified in relation to the needs of virology.¹⁴ He then continued in a way that reminds me of Koch's down-to-earth handling of principal issues, namely by sufficing himself to discussing proper technique. He would for example explain on a given example why an obligatory proof of the presence of a pathogen in tissues was not feasible for virology. Koch's postulates, Rivers concluded, were outdated in their content, but up-to-date in their spirit:

„it can be said that the causes of viral diseases is known and that Koch's postulates as proposed by him do not have to be fulfilled in order to prove that a virus is the cause of a disease. However, the spirit of his rules of proof still hold in that a worker must demonstrate that a virus is not only associated with a disease but that it is actually the cause. [...] To obtain best results [...] ingenuity must be tempered by priceless attributes of common sense, proper training and sound reasoning.”¹⁵

Rivers' critique of Koch's postulates stands at the outset of a long series of modifications of these that we can find all the way through the later half of the 20th century. In one way or another they usually focus on the establishment of infectious causation in relation to the given technology of their days. While in the first decades after World War II the focus was mostly on viruses the horizon began to widen from the 1960s.¹⁶ Austin Bradford Hill (1897-1991) tried to adapt the postulates to epidemiology¹⁷ and more recently such criteria have been developed for the arguably most uncommon pathogens of our times, the prions.¹⁸

Remarkable changes got under way in the 1980s when molecular biology and gene technology made their entry into microbiology.¹⁹ While traditional technologies of staining and cultivation of microbes were replaced by sequencing, views on the taxonomy of the microbial world underwent changes that were no less radical. In particular, the number of microbial inhabitants of the human body rocketed and few of these newly discovered microbes appeared as classical pathogens. Stanley Falkow has repeatedly attempted to adapt Koch's postulates to this situation. For example knock-

¹⁴ Rivers was also referring to criticism that had been put forward between the wars by bacteriologists and epidemiologists. See Mendelsohn 1998, vgl. Engelhardt 1985.

¹⁵ Rivers 1937: 11.

¹⁶ Evans 1976; Huebner 1957.

¹⁷ Hill 1965.

¹⁸ Walker, et al. 2006.

¹⁹ Einführend Chadarevian and Kamminga 1998.

out models of bacteria, where so called virulence genes can be activated or inactivated were be employed to establish infectious causation and subsequently to draft up-to-date versions of Koch's postulates.²⁰

Others would try more fundamental critiques. Arturo Casadevall and Liise Pirowski insisted that Koch's model, which was based on a clear distinction of host and pathogen, had become untenable in the age of molecular medicine. It provides too little space for interactions of hosts and pathogens and does not enable one to see their encounter as an individual event that may evolve in several directions. As an explanatory strategy, classical bacteriology favours pathogenesis, which – in face of the multitude of non-pathogenic inhabitants of human bodies – should better be considered an exception rather than the rule.²¹

IV

What is remarkable, is that such debates have become more frequent in the last two decades of the 20th century. At the same time the focus of the contributions has been expanded. They are now less regularly on infectious diseases or their suspected pathogens and instead address a wide range of subjects in relation to disease causation, such when environmental toxins, autoimmune diseases or neurotransmitters are discussed. To understand this, it certainly helps to have a glance at the larger historical context of these decades. The so called short 20th century, which is currently the dominant model of interpretation in general history²², has found an interesting echo in the history of infectious disease. While common infectious diseases were pushed aside in public health around World War One by cancers and coronary heart diseases the threat that is posed by them has returned from the 1980s on.²³ Triggered by the AIDS-epidemic and fuelled by the rise of antibiotic resistance, SARS (severe acute respiratory syndrome), avian flu other events infectious diseases have reclaimed a prominent place in the public debates of developed countries. This is also visible in the remarkable instance that in parallel to this resurgence of infections several chronic diseases have been re-interpreted as being infectious rather than being caused by environmental or inherited factors. The standard example in this case is the gastric ulcer or respectively the *Helicobacter pylori*, which was identified

²⁰ Falkow 2004, Falkow 1988.

²¹ Casadevall and Pirofski 2003.

²² Hobsbawm 1994

²³ King 2004.

as the cause of that condition.²⁴ What this indicates most and for all is that the resurgence of the infectious principle took place in an atmosphere where genetic and infectious diseases became harder and harder to distinguish. For Robert Koch this had been a clear cut distinction. It was gradually undermined by virology in the following decades. Towards the end of the 20th century, in the context of research on so called emerging infections from about 1990, a combination of evolutionary biology and infection research was attempted that was specifically inspired by the combination of these two concepts to understand disease.

The evolutionary biologist Paul Ewald has put forward an example of this fundamental critique of Koch's postulates.²⁵ What he succeeds in sounds contradictory in the first place: while completely denying the obligatory character of any possible postulates he simultaneously expands the importance of the infectious principle as such. If we follow his argument, the employment of Koch's postulates as a „gold standard of evidence of infectious causation“²⁶ has had two contradictory effects. While the aetiology of important infectious diseases was elucidated the concept of infection as such was narrowed. By focusing on pure culture and animal models the accent was laid on infections that developed swiftly, appeared in a regular fashion as far as clinical symptoms are concerned and finally mostly occurred in epidemic form. The result was an implicit division of infectious vs. inherited disease. In chronic illnesses, where a hereditary factor could be identified, the role of microorganisms was usually not considered.

Ewald's line of argument is obviously more inspired by evolutionary biology than by microbiology. His basic hypothesis is that any disease that is dominant in heredity and has serious health consequences for those affected should normally disappear from the affected species over a few generations, in accordance with laws of inheritance. Given that only two types of diseases can be expected to have prevalence above the mutation rate of their affected species: Those who have a microbiological co-factor like slow virus infections in carcinogenesis or those where their bearers do actually profit from it in relation to an infection. An example of the later would be sickle cell anaemia, a hereditary blood disease, which however has the side-effect of rendering its bearers immune to malaria.

²⁴ Thagard 1999. Notably, the identification of the *Helicobacter pylori* as a pathogen of the common ulcer earned Robin Warren and Barry Marshall the 2005 den Nobel Price for physiology or medicine. It was, in fact, the first such price awarded for a pathogenic bacterium for a very long time.

²⁵ Ewald 1994; Cochran, et al. 2000.

²⁶ Cochran, et al. 2000: 441.

What all this adds up to is that beyond the usual common infections there is what Ewald calls a crypticity of infections which can hardly be undervalued. In this sense it is not sufficient to go on and modify Koch's postulates on ever new technologies and objects of study. Instead the fundamental model of host and pathogen as a model of infection needs to be put in question:

„The reliance for Koch's postulates has diminished out of necessity. [...] Although limitations of Koch's postulates have been addressed in medical science, the emphasis has been on ways in which causative organisms can be identified even without Koch's postulates. [...] Our focus is different. Considering the increasing difficulty of identifying etiologic agent as causes of chronic diseases, we emphasise the need to focus on discovery of infectious causation as a goal that may sometimes be distinct from the identification of etiologic agents.“²⁷

The type of causality that is spelled out in Koch's postulates, suddenly appears to be only one of several options. Infectious diseases are a phenomenon of the co-evolution of micro and macro-organisms as such. It can even be understood without knowing every single pathogenic microbe. In this sense it is not surprising that Ewald forcefully argued in favour of simply assuming the infectious character of any disease that occurred with a certain frequency and for instance to try anti-infective therapies on that basis. Ewald was, of course, a supporter of the idea of the infectious character of gastric ulcers. He did, however, also not stop at proposing pretty much the same in relation to homosexuality.

V

So what is it that the popularity of Koch's postulates can tell us about 20th century medicine? In their numerous variations they represent a trivial ontology of disease. The customary practice of doing this is usually a discussion of proper methods done in more or less stringent relation to Koch's or in fact rather more Loeffler's views. What is trivial here is, of course, the way of making references to history rather anything else that is discussed in such texts. As a rhetoric tool the invocation of Koch's works functions like anecdotes do: These present a plausible story about an important object in a way that reduces complexity. Quite independently of factual contents anecdotes are supposed to contain truth. In our given case the result is that the authors state with some regularity that these postulates are out-dated in their content, yet still up-to-date in their spirit. Historians from Plutarch (46-120 AD) to Jacob Burckhardt (1818-1997) have emphasised that the

²⁷ Cochran, et al. 2000: 439.

value of anecdotes is related to typical rather than factual representations of histories. If we follow that argument, discussing Koch's postulates usually includes an anecdote about the origins of experimental medicine.²⁸

Talking about Koch's postulates is in this sense an invocation of a tradition of experimental pathology. No matter how many or which postulates are mentioned on a given occasion, the argument usually serves to reiterate and confirm certain basic assumptions that render the experimental reconstruction of diseases plausible. In this sense the countless variations of Koch's postulates do not represent change but stability! Discussing the postulates and proposing modifications is usually about updating them, not about their replacement. When in 1990 the technology of sequencing had radically transformed microbiology, two researchers set out to compare their machinery with what had been employed in the days when Koch had supposedly laid down his postulates. Unsurprisingly they stated that the postulates were outdated in their literal form, yet they reminded their readers that "the principles behind Koch's postulates still hold".²⁹ Adding to this they explicitly cautioned their readers against a too simple understanding:

„Unfortunately, Koch's postulates have frequently been applied to issues of causation with a mathematical zeal that is not warranted in the biological world. [...] The power of Koch's postulates comes not from their rigid application, but from the spirit of scientific rigor that they foster."³⁰

That leaves one final question open. If talking about Koch's postulates invokes a tradition of experimental medicine, why point to Koch and not to Claude Bernard (1813-1878), Paul Ehrlich (1854-1915), Louis Pasteur (1822-1895) or some other heroes of experimental medicine? My answer to that question would be that the continuous rephrasing of this topic in particular is bound up to the historical relevance of medical bacteriology. The idea that infectious diseases can be explained by employing microbial aetiologies was certainly put forward not just by Koch and it did not acquire popularity overnight. Still, the result was not just that miasmas became a case for medical historians, but that laboratories and pathogenic bacteria that can be studied inside of these acquired the status of a foundation of modern medicine. Koch's postulates do not stand for any particular methodology. Instead they depict a worldview that can be represented in numerous methodologies.

²⁸ Gossmann 2003.

²⁹ Fredericks and Relman 1996: 31.

³⁰ Fredericks and Relman 1996: 20.

In this sense it is not contradictory that Koch's postulates are modified continuously while at the same time their invocation stages a rhetorical obligation of the speaker to 19th century medical bacteriology.³¹ This ominous bacteriological revolution that critical medical historians have tried to bury repeatedly remains alive and kicking in the memory of medical researchers, yet as an object that is easy to see, but hard to explain.³² Robert Koch's ill-defined postulates are the congenial representation of a certain historical consciousness that seems to be shared by many medical researchers in the 20th century. Like it or not, in a certain sense "we are all bacteriologists".³³

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³¹ Barnes 2003.

³² Tomes and Warner 1997.

³³ Cunningham 1992: 239.

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Christoph Gradmann
christoph.gradmann@medisin.uio.no
Professor of medical history
University of Oslo
Institute for General Practice and Community Medicine
P.O. Box 1130 Blindern
0318 Oslo
Norway