Ludwik Fleck where are you now that we need you? Covid-19 and the genesis of epidemiological facts

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By

Tests for Covid-19 and the politics of big numbers

We are incessantly flooded with data on the evolution of the Covid-19 pandemic. WHO and the Johns Hopkins coronavirus resource provide information on the daily number of Covid-19 cases and deaths worldwide, while national media supply details on the dynamics of the pandemic in each state, region and city. These data are used to shape public policies. In early spring, during the first frightening phase of the pandemic, there was a relative consensus in Europe and North America about the necessity of stringent containment measures. A few months later, sanitary policies were increasingly criticized and contested. However, such criticism was usually focused on the perceived failings of the proposed interventions – too much, too little, mistaken targets, the wrong priorities. It seldom extended to questioning the data used to legitimate specific interventions. This is puzzling, since it is far from being obvious what should count as a 'case of Covid-19', and how such cases should be made visible.

When the WHO's director, Tedros Adhanom Ghebreyesus, in his 'simple message to all the nations' on 16 March 2020, exhorted countries everywhere to 'test, test, test' for Covid-19, he omitted to mention that such testing is far from being an unproblematic production of 'scientific facts' (Ghebreyesus, 2020). A 'Covid-19 case' is an individual who has received a positive result from a diagnostic test for the presence of the SARS-CoV2 virus in the body. The test seen as the 'gold standard' of SARS-CoV2 detection, RT-PCR (reverse transriptase polymerase chain reaction), reveals the presence of viral RNA in the body's secretions. Another test, which looks for the presence of proteins from the virus's envelope, is much more rapid than the PCR test, yielding results in 15-30 minutes rather than hours, but it is considered somewhat less accurate. Tests that display antibodies against coronavirus are also seen as somewhat less accurate than the 'classic' PCR test. They are positive only in later stages of the infection, and usually stay positive when the virus is no longer present in the organism. They may thus be less adequate for clinical use but, as some specialists have argued, more adequate for following the progress of infection in populations (Mina et al, 2020). The accuracy of testing for SARS-Cov2 depends on the sensitivity and specificity of the test used, the reliability of the preparation of the samples studied (this is especially important for nasopharyngal swabs), the quality of the reagents and instruments, and the skill of the technicians who perform the tests. It also depends on the prevalence of SARS-CoV2 in the tested population: if this prevalence is low, the chances of false positive and false negative results are higher.

In addition, PCR tests for SARS-CoV2 may yield ‘true false postive results,’ that is, results that are technically correct but are devoid of clinical and epidemiological significance. Some people are infected by the pathogen while the viral load in their body is probably too low to make them sick or dangerous to others. Whether they will be classified as ‘Covid-19 cases’ depends on the calibration of the PCR test. The apparently technical decision – how many cycles of amplification of RNA are necessary to detect SARS-CoV2 in a sample – strongly affects the number of positive results. The majority of PCR tests in the US perform 37 to 40 amplification cycles, and in France 40-45 cycles. Some experts have proposed decreasing this number to 30 cycles or even less, in order to detect only clinically/epidemiologically relevant cases (Sénécat, 2020). As of now (October, 2020), diagnostic tests for Covid-19 are far from being homogenized worldwide, or even within a single country. Accordingly, ‘facts’ about the prevalence of Covid-19 are hererogenous as well.

Another, and more crucial source of difficulty in studies of the prevalence of Covid-19, are divergent choices of the scope of testing. A significant percentage of people infected by SARS-CoV2 are entirely symptom-free or have only mild symptoms, easily confused with the common cold. It is not entirely clear what proportion of people infected with SARS-CoV2 are asymptomatic, and therefore difficult to reach through standard testing strategies. Evaluations vary from 20 to 80%, with a majority of estimations in the 20-40% range (Oran and Topol, 2020). It is assumed that asymptomatic carriers of coronavirus, or at least asymptomatic adults and adolescents, can infect others (Schuman and Simmank, 2020). In the early stages of the pandemic some countries elected to test only people with severe clinical symptoms, a decision often prompted by the shortage of tests, while other countries tested all symptomatic individuals and their contacts. Today public health authorities in the majority of countries declare that they have adopted the second approach, and favor large-scale diffusion of tests. The implementation of testing in many countries is, however (in early fall 2020), heterogenous, confused and patchy; the same may be true for the centralization of test results (Hanagen 2020;Coq-Chodorge, 2020a). Moreover, some specialists argue that testing limited to symptomatic individuals and their contacts may provide an inaccurate image of circulation of the virus. Only systematic testing of random samples from tested populations can display the hidden circulation of SARS-CoV2 (Wallard, 2020).

When a country or region modifies its testing strategy, it becomes difficult to compare epidemiological data collected in different stages of the pandemic. The French Health Ministry recorded, on 24 September 2020, 18,096 new cases of Covid-19, while at the peak of the spring outbreak, on the 1April 2020, it recorded 6,300 new cases. Data on new hospitalizations for Covid-19 are very different: 613 hospitalizations on 24 September 2020 as compared to 4,146 hospitalizations on 1 April 2020 (Baruch et al, 2020). Or, to put it differently, more than half of the people diagnosed in France at the peak of the epidemic were hospitalized, while in mid-September less than 5% of the 'positive cases' ended up in a hospital. The important increase in the volume of testing led to detection of numerous mild or asymptomatic cases of Covid-19. Mild cases are more frequent among younger people. The rise in the proportion of young people among those found to be infected with SARS-CoV2 reflects the combination, in unknown proportions, of changes in the scope of testing and the effects of shielding older people (Coq-Chodorge, 2020b). Important disparities in the volume and quality of testing are also a major obstacle for international comparisons.It is difficult to juxtapose data on the prevalence of Covid-19 from countries that have widespread and reliable testing with those where it is much patchier and more heterogeneous (Roucaute, 2020). Nevertheless, the number of cases of Covid-19 – a shorthand for the number of people who test positive for the presence of SARS-CoV2 – continues to be presented by the media and in public discourse as a simple 'scientific fact'.

Ludwik Fleck and the tangle of diagnosis

To untangle the confusion around the meaning(s) of diagnostic tests for Covid-19and examine the ways 'diagnostic facts' shape perceptions and policies, we may turn to Ludwik Fleck's 1935 study, *Genesis and Development of a Scientific Fact*. The 'scientific fact' studied by Fleck is the Wassermann test for the diagnosis of syphilis. Syphilis, a disease perceived in the early 20thcentury to be a major threat to individual and collective health, is defined as a pathology produced by infection with the bacillus *Treponama pallidum.* Syphilisis a very complex disease, with variable expressions, multiple manifestations, and latent (invisible) stages ; it is therefore difficult to diagnose accurately. The elaboration of a blood test for syphilis was retrospectively presented as an important scientific discovery made by August Wassermann and his collaborators in 1906. Fleck studied the long and complex trajectory that led from the original 1906 article that described a blood test for syphilis, to the transformation of this test into an efficient diagnostic tool (Fleck, 1935).

Ludwik Fleck (1896-1961) is seen today as a pioneer of the constructivist philosophy of science, the investigation of epistemological principles, scientific practices, laboratory studies, and visual cultures of science. His innovative approaches to the study of the sociology of scientific knowledge (or, to use the term coined in 1925 by the Polish sociologist Florian Znaniecki, the science of science – 'naukoznawstwo') was grounded in his professional experience as a microbiologist and public health expert.All the positions occupied by Fleck in prewar and postwar Poland involved the containment of transmissible diseases. Fleck's strong links with public health escaped, however, the attention of the majority of the scholars who rediscovered his thought (for a notable exception, see Rosenkranz, 1981). Fleck's strong links with public health might have been overlooked because he presented himself as a basic researcher rather than a practitioner, but also perhaps because in the late 1970s and early 1980s the control of infectious diseases was not seen as an important topic. Many people believed then that with the progress of modern medicine the dangers of transmissible pathologies belonged to a bygone past. The situation has changed dramatically since then. Indeed, as a public health expert who studied diagnosis as a collective endeavour and a political issue, Fleck is an important guide to today's pandemic times.

The starting point of Fleck's reflections on the collective production of a 'diagnostic fact' was the idea that diseases are not natural entities but artificial classificatory units produced by medical experts in a given place and time. Classifications of human pathologies in European medicine are not the same as those of Chinese medicine, and diseases of the Renaissance are different from those of the 20thcentury. The rise of bacteriogy produced an additional complication. With the concept of 'inapparent' (today, asymptomatic) infection, the presence of a specific 'disease' was dissociated from the display of characteristic symptoms (Fleck, 1927). A definition of 'disease' is valid within a given social group ('thought collective') which shares knowledge, concepts and practices ('thought style'). It is often transformed through its circulation among other 'thought collectives'. During a routine diagnosis of diphtheria in a child, Fleck explained, a microbiologist provides a careful description of a microscopic preparation: "presence of some microorganisms with the characteristics of diphteria baccilli." This description is translated by the child's physician as "the laboratory found diphtheria germs in the throat swab", and is transmitted to the child's mother as a simplified statement: "your child has diphtheria." (Fleck, 1935: 110-114).

During their professional training microbiologists learn how to recognize typical pathogens under the microscope. They also learn that an accurate diagnosis is possible only if they rigorously follow a standarized protocol which defines the exact condition of the culture, staining and observation of microrganisms. When experts who produce a diagnosis belong to the same 'thought collective' and thus receive similar training and adhere to the same basic principles, they can agree on the 'right' diagnostic criteria and produce reliable and reproducible 'diagnostic facts.' (Fleck, 1935: 92-93). It may happen however, that more than one 'thought collective' is involved in the production of 'diagnostic facts.' If that is the case, each collective may produce its own 'facts.' Fleck illustrates this point through a controvery over the diagnosis of scarlet fever. Scarlet fever is a disease produced by infection with the baccillus *Streptococcus haemoliticus*. This baccilus is identified by its capacity to secrete a substance that destroys red blood cells (hemolysis). Bacteria from the patient's throat are grown on a culture medium that contains red blood cells. If among them one can observe colonies of streptococcus surrounded by a well-defined transparent halo – a sign of destruction of red blood cells – the conclusion is that the patient has scarlet fever. If there are no such colonies, the patient does not have it.

But what happens when one finds only 'borderline' colonies surrounded with a small halo, a situation not unlike finding SARS-Cov2 RNA after 45, but not after 30 cycles of amplification of nucleic acid? Will the patient be defined as a scarlet fever case? It depends, Fleck explains, on who is making the decision. If it is a basic researcher who is investigating the pathophysiology of scarlet fever, s/he will declare that a patient who is not infected with a 'typical' *Streptococcus haemoliticus* should not be classified as a confirmed case of scarlet fever. If it is an epidemiologist, s/he will follow a precautionary principle and classify a patient infected with a 'borderline' baccilus as a scarlet fever case. Both the basic scientist and the epidemiologist provide a 'correct' answer, but their answers are not the same, and may lead to very different estimations of the prevalence of scarlet fever in a given location : "one arrives at divergent and non exchangeable truths depending on the purpose of the investigation."(Fleck, 1929: 51). Moreover, the basic scientist's and the epidemiologist's approaches to the diagnosis of diphtheria are equally valid, but they are not symetrical. The epidemiologist's definition of diphtheria is not 'more true' than that of the basic scientist's, but an epidemiologist has an immediate responsibility to a potentially endangered community. As an epidemiologist quoted by Fleck explained, "it seems more correct in doubtful cases rather to diagnose the presence of haemolytic streptococci than the absence. For if we disregard them, any error is liable to have serious consequences." (Fleck, 1929: 52).

Ludwik Fleck and the politics of diagnosis

Syphilis was perceived to be an extremely dangerous disease. It not only put individuals at risk but also threatened the well-being of future generations. Accordingly, the development of a diagnostic test for this pathology was shaped by societal considerations. The initial elaboration of a serological test for syphilis was stimulated by international competition, mainly between Germany and France.From the very beginning the rise of the Wassermann reaction was not based upon purely scientific facts alone. A rivalry between nations in a field that every layman considered very important, and a kind of vox populi personified by a ministry official, constituted a social motif for the work. The effort expended on this scientific project was correspondingly great (Fleck 1935: 68-69). It involved the cooperation of hundreds of experts and the publication of thousands of scientific articles (Fleck, 1935, 78-79). Moreover, it included not only a local homogenisation of practices, but also international collaboration. A series of workshops sponsored by the League of Nations between 1923 and 1930 compared the specificity of several versions of the Wassermann reaction (Mazumdar 2003). Other interventions, such as consensus conferences, diffusion of information in the press and educational campaigns, consolidated the standarization of the Wasserman test and its transformation into a reliable diagnositic tool (Fleck, 1935: 80-81).

The 'collective experimentation' that led to the genesis and development of the diagnosis of syphilis started with political considerations. It ended with political decisions. The 'scientific fact' studied by Fleck was not only an intriguing piece of new scientific knowledge but also a development that directly affected people's lives. 'Wasserman-positive' individuals were told that they were carrying dangerous germs that put at great risk their own physical and mental health, and the health of their sexual partners and children. This information, coupled with the persistence of a stigma attached to syphilis (at least until the advent of penicillin) often changed the ways they saw themselves and were perceived by others. It was also enshrined in law. In the late 1930s and 40s many countries introduced mandatory prenuptial testing for syphilis, and obligatory testing of other social groups, such as soldiers or pregnant women (Brandt, 1985). In the late 1930s the Wasserman test was transformed into a juridical and political fact. The story of the transformation of this test into an efficient diagnostic tool, told by Fleck in 1935, had however a twist. In the late 1940s and early 1950s experts found that many positive results of the Wassermann tests were 'true false positives.' The positive result did not display an infection with the etiological agent of syphilis but was produced by the presence of another pathology/anomaly, such as an auto-immune disease or liver pathology (Zalc, 1985).The proportion of such 'true false positives' was low in settings with a high prevalence of syphilis such as venereal diseases clinics, but much higher when screening the general population. The definition of syphilis as a disease induced by infection with *Treponema pallidum* did not change from the early 20th century on, but numerous certified 'syphilis cases' in 1935 would not have been classified as such in 1955.

The strength of science, Fleck insisted, stems from its collective nature.

This may also be a source of its weakness. Fleck, who lived through the dark times of the rise of fascism in the 1930s and was a prisoner in a concentration camp, was acutely aware of the dangers of non critical acceptance of some forms of collective thinking. In 1960 he warned against the excessive power of selected groups of experts. A thought collective, he explained, is at the same time creative, refractory and dangerous like an elemental power. This danger can be reduced through the democratization of science (Fleck, 1960). To prevent an excessive accumulation of power in the hands of a small group of experts, it is important to make scientists accountable and their actions transparent, and to support public control over techno-scientific power.Fleck wished to stimulate the development of the 'sociology of scientific styles' – a discipline that promotes the understanding of how science works, not as an abstract ideal but as a concrete, situated social practice.

The bioethicist Leon Eisenberg ends his text "Rudolf Ludwig Karl Virchow, where are you now that we need you?" with a telling anecdote. Virchow, who worked in the 1850s as an assistant to the pathology professor Johann Schonlein, contradicted his boss's opinion that the patient died from a brain hemorrhage by demonstrating an obstructing embolus in an artery. Schonlein, who unlike his assistant held conservative ideas, then remarked to Virchow, "you see barricades everywhere" (Eisenberg, 1984, 531). Fleck, one may propose, 'saw collectives everywhere', and believed that a widespread understanding of how'scientific facts' are produced and stabilized would promote the democratization of science and society. The Covid-19 pandemic has led to multiple instances of lack of confidence in 'science' – not infrequently linked to contraditory and confused statements presented, especially by politicians, as 'scientific facts.' In 1935 Fleck studied the origins and uses of a diagnostic test for syphilis to explain how scientists, but also, to follow Mary Douglas, institutions, think and act (Douglas, 1987). His insightful analysis of that 'diagnostic fact' can still teach us how to investigate what science can, and what it cannot do.

Ilana Löwy *is a senior researcher emerita at INSERM, Paris. Trained as a biologist, she then retrained as a historian of science. Her main research interest are relationships between laboratory sciences, clinical medicine and public health, material culture of science and medicine, and intersections between gender studies and biomedicine.*

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