

INGESTION / THE X FACTOR

D. GRAHAM BURNETT

The second half of the nineteenth century saw the heroic rise of modern bacteriology, a new science that promised to save humanity from the age-old curse of epidemic disease. Generations of debate about the causes of fatal plagues (were they the product of divine spite? infelicitous astrological conjunctions? fetid emanations from the center of the earth?) fell by the wayside as the original “microbe hunters,” Louis Pasteur and Robert Koch, leveled their microscopes at the true culprits: tiny one-celled organisms called *germs*. Successful in tying specific micro-organisms to specific maladies, Pasteur and Koch laid the groundwork for the biomedical study of infectious disease and thereby took up places of honor in the pantheon of scientist-gods.

In the winter of 1901, one of the last hold-outs against this world-view, the aged and leonine Bavarian chemist-apothecary Max Josef von Pettenkofer, pressed a small revolver to his temple and ended a distinguished career. Born in 1818 in the Danubian marshes as the fifth of eight children to a modest customs officer and his wife of peasant stock, Pettenkofer acceded by his native brilliance and fanatical hard work to the highest ranks of the European scientific professoriate, publishing widely on organic and inorganic chemistry, *materia medica*, and public health. Mercurial and romantic, he drifted in and out of favor at the court of Ludwig I, avidly pursued his lovely cousin Helen, dabbled in art restoration, penned a volume of peculiar sonnets, and found time to moonlight in the demimonde of the Augsburg theater under an assumed name.

It was this last activity that stood him in good stead in later life, as he made a memorably melodramatic last stand against the triumphant microbial theories of Pasteur and Koch. Pettenkofer bridled at what he took to be their overly simplistic notion that germs alone caused sickness. What about when they did not? While he is mostly now remembered as a quixotic defender of miasmaticism (the idea that diseases arise from swampy emanations, from “bad air”—the original meaning of *mal-aria*), Pettenkofer in fact adopted a more sophisticated and interesting position on the problem, particularly as evidence mounted that micro-organisms of some sort did appear to be involved in many disease processes. As the text below explains, Pettenkofer ultimately settled on a multi-factor analysis: disease happened when an x factor (the germ) intersected with a y factor (some miasmatic condition of the region) and a z factor (some

susceptibility on the part of the individual). Looked at charitably, this can be understood as a strikingly forward-looking insistence on environmental, hygienic, nutritional, and immunological conditions. Looked at uncharitably, he wound up on the wrong side of history.

Not that he didn’t try to alter the course of that history. In 1892, to confound his adversaries, he notoriously drank, under elaborate experimental conditions, enough pure cholera bacteria (known as the “comma bacillus” or “comma vibrio” at the time, for its shape) to kill a village. And he lived. His point? Germs alone do not cause disease. The whole episode represents an unlikely intersection of the modern laboratory and the medieval trial by ordeal.

The text below is a report of Pettenkofer’s self-experiment as published in the *British Medical Journal* of 19 November 1892.

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We are indebted to the courtesy of Dr. B. Spatz, editor of the *Münchener medicinische Wochenschrift*, for advance proofs of an address on Cholera with Reference to the Last Epidemic at Hamburg, delivered by the veteran hygienist and epidemiologist Professor Max von Pettenkofer, on November 12th, before the Munich Medical Society.

THE CHOLERA EQUATION

He said that the only question now appeared to be how the comma bacillus was to be destroyed, or at any rate prevented from multiplying. He recalled that many years ago he said that the etiology of cholera was an equation with three unknown quantities, namely, x , a specific germ, disseminated by human intercourse; y , a factor dependent on place and time, which he called “local disposition”; and z , the individual predisposition.

The simplicity of Koch’s theory commended it to those who only looked at the individual patient, and not at the course of a long series of epidemics. Places as well as persons often enjoyed immunity, and places which

opposite: *Portrait eines Cholera Präservativ Mannes*, artist unknown, first half of the nineteenth century. This satiric prototype of a cholera-preventing outfit includes a face-mask, a bag of warm sand worn on the chest, camphor-soaked cotton balls stuffed in the ears, a nose-mounted smelling-bottle of *vinaigre des quatre voleurs* (vinegar compounded with garlic, rosemary, sage, mint, rue, and other herbs), a calamus root sprig held in the mouth, a shirt and vest infused with chlorinated lime, stockings marinated in vinegar, water pots strapped to the calves, ipecac root and thistle root and chamomile oil stored in the pockets, and a hat topped with a tureen of boiling barley soup. The supplies in the cart include a small bathtub, a steam-bath apparatus, several rolls of flannel, bricks, and a “comfortable” stool. “Thus accoutred is a man protected against cholera,” reads the caption. Indeed. Courtesy the National Library of Medicine.



suffered at one time remained free at another, even when two of the factors x and z were present. The determination of y was not so easy as that of the others, and the speaker could only say that the nature and degree of moisture of the soil had an important influence. The constant occurrence of the comma bacillus in the excreta of cholera patients indicated that the microbe had something to do with the process, but it was still open to question whether it alone was the cause of the disease.

PERSONAL EXPERIMENTS WITH THE COMMA VIBRIO

Professor von Pettenkofer had made some experiments on himself with bacilli obtained from Hamburg. Several of his pupils offered themselves as subjects in his place, but acting on the principle *Fiat experimentum in corpore vili*, he thought he himself—74 years old, glycosuric, without a tooth in his head, and with other infirmities of age—was the fittest person to run whatever risk there might be in the experiment. From pure agar cultures of the comma bacillus made by Professor Gaffky, a bouillon culture was prepared in the ordinary way by Drs. Pfeiffer and Eisenlohr. Gruber having shown that fresh cultures are more active than those which had been kept for some days, Professor von Pettenkofer chose one which had not been quite twenty-four hours in the incubator. A plate culture of this showed that one cubic centimetre even of a thousandth dilution contained numberless comma bacilli, far more than could possibly be conveyed by a man's hand to his mouth. As Koch has shown that the gastric juice was capable of killing even a large number of comma bacilli, Professor von Pettenkofer was careful to take his dose of microbes two hours and a quarter after a light breakfast, when, according to a calculation made by von Voit, there could not have been so much as 100 cubic centimetres of gastric juice with 0.3 per cent of hydrochloric acid in his stomach. In order to neutralise even this small amount of acid, however, he took 1 gramme of bicarbonate of soda dissolved in 100 cubic centimetres of Munich conduit water. He then measured out one cubic centimetre of the fresh culture, swallowed it at a draught, and washed out the glass with 50 cubic centimetres of water, which he also swallowed, so as to ensure the ingestion of as many bacilli as possible. This was on October 7th. His temperature was then 36.7° C.; his pulse 86. On October 9th severe colicky pains and moderate diarrhoea came on, and did not entirely cease till October 15th. During that time the urine was normal in amount, and contained no albumen. He took no medicine whatever during the attack, but took his customary food with good appetite, and pursued his usual avocations without any interruption, feeling perfectly well except for the

symptoms mentioned. While the diarrhoea lasted the stools were examined bacteriologically by Drs. Pfeiffer and Eisenlohr, who found them swarming with comma bacilli. Professor von Pettenkofer asks rhetorically how many *milliards* of these microbes there must have been in his intestines during these eight days, and yet he had no symptoms of Asiatic cholera. He thinks, however, that his experiment might have had a fatal result if it had been carried out in Hamburg, where not only x but y was present in full force. An exactly similar experiment was made on himself by Professor Emmerich on October 17th, with much the same result, except that the colic and diarrhoea were much more severe; otherwise he felt perfectly well.

CONCLUSIONS

According to Professor von Pettenkofer, these experiments show conclusively that the comma bacillus during its sojourn in the intestine does not produce the specific poison which causes Asiatic cholera, and they agree with the results obtained by Bouchard, who was able to induce the symptoms of cholera in rabbits by giving them the excreta (alvine or urinary) of human cholera patients, but not by giving them pure cultures of comma bacilli or their metabolic products. Anticipating the possible objection that both he and Emmerich had suffered from an attack of genuine cholera, though very slight, he brings witnesses to the contrary in the persons of the well-known physicians Professor Bauer and Dr. von Ziemssen, both of whom have had considerable experience of cholera. Professor von Pettenkofer, while not denying that the comma bacillus has some etiological importance, says he cannot believe it is the x which, without the assistance of y , can cause epidemics of cholera. He reiterated his well-known views on the influence of the soil, especially in connection with the rainfall. His practical teaching may be summarised in the formula that it is the y , that is, the local physical and sanitary conditions, that must be attended to; each place must, in short, be made cholera-proof by sanitation.