

Medical History

Robert Koch and the cholera vibrio: a centenary

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On 2 February 1884 Robert Koch reported from Calcutta to the German Secretary of State for the Interior his reasoned conviction that the vibrio found in the intestines and stools of cholera victims was the causal agent of the disease.¹ This was the sixth of seven dispatches sent over a period of 24 weeks, all but the third of which were published in the German official gazette and thus made available to the German press as they were received. It would be difficult to find a parallel for this published step by step description of research in progress, as opposed to the conventional retrospective account, arranged as a tidy sequence of events with the benefit of hindsight.

Koch had originally started in Alexandria, where he arrived on 24 August 1883 as the leader of a German mission that included two other medical members, Georg Gaffky and Bernhard Fischer, and a technician, and his first dispatch was dated 17 September.² By this time the mission had made bacteriological investigations on 12 patients with cholera and carried out necropsies on 10 who had died of the disease. In the stools a multitude of different organisms had been found, none of which was preponderant. Conversely, necropsies showed the constant presence of a specific bacillus in the intestinal mucosa of subjects dying from cholera but not from other diarrhoeal diseases. Koch concluded that there could be no doubt that this bacillus stood in some relation to the cholera process, but whether the relation was causal or consequential remained to be determined. This question could be resolved, he stipulated, only by isolating the bacillus, growing it in pure culture, and reproducing a similar disease in animals. He had not yet obtained a pure culture, but attempts to infect monkeys, dogs, mice, and hens with choleraic material had proved fruitless.

On 10 November Koch sent a second report, explaining why he had telegraphed to request authorisation for the mission to proceed to Calcutta.³ The cholera epidemic in Egypt had subsided, and he had been advised by British officials that Calcutta would be the most promising place for further investigations.

The French mission

By the time that Koch had arrived in Alexandria a French medical mission (Isidore Straus, Emile Roux, Edmond Nocard, and Louis Thuillier), financed by its government on the initiative of Pasteur, had already been there for nine days. It had carried out essentially the same investigations as the German mission, finding the bacillus that Koch was also to describe, and failing to infect guinea pigs, rabbits, mice, hens, pigeons, quails, pigs,

a jay, a turkey, and a monkey. The French expedition was marred by tragedy, for on 17 September Thuillier fell ill, and he died of cholera two days later at the age of 27.

On 7 October the three remaining members of the mission left Egypt. After their return to Paris they presented a brief account of their findings to the Société de Biologie,⁴ publishing a definitive report in the following year.⁵ In this they concluded that they could not attribute a specific action to "the microbe that we have encountered in the greatest abundance in the greatest number of cases." On the other hand, they had seen in the blood small bodies that might have some causal relation to cholera. Koch was later to express the view that these were in fact blood platelets.

Thus the researches in Egypt of the French mission for almost two months and the German for almost three had been unsuccessful in their attempts to unravel the secret of cholera.

Koch sails for Calcutta

The fact that Koch's third dispatch was not published is mentioned in an editorial footnote to the fourth dispatch,⁶ but the reason for this is unclear; it may be that it referred only to administrative arrangements. In the fourth he reported on 16 December that the mission had arrived in Calcutta on 11 December, having left Egypt on 13 November, and proceeded to outline an exhaustive plan of further research.⁶ This included the performance of necropsies and the comparison of the microscopical findings with those seen in Egypt; attempts to grow the characteristic bacillus in pure cultures with a view to using them to produce experimental infections in animals; and investigations of the soil, water, and air, and of any special characteristics of the population and its environment in epidemic districts.

In his fifth dispatch on 7 January 1884 Koch announced that he had successfully isolated the bacillus in pure culture.⁷ The necropsy findings had been the same as those in Egypt, and should it be possible, he argued, to confirm that the bacillus was to be found exclusively in patients with cholera, it would hardly be possible to doubt its causal relation to the disease—even though it might not be possible to reproduce a similar disease in animals. Here, Koch was renouncing one of the elements of proof that he had himself stipulated almost four months before in his first dispatch.

It was in his sixth dispatch, dated 2 February, that Koch stated that the bacillus was not straight, like other bacilli, but "a little bent, like a comma" (*ein wenig gekrümmt, einem Komma ähnlich*).¹ Other properties of the bacillus were its ability to proliferate in moist soiled linen or damp earth and its pronounced susceptibility to drying and to weakly acid solutions. Koch then pointed out that the specific organisms were always found in patients with cholera but never in those with diarrhoea from other causes. In the early stages of cholera they were relatively rare in the evacuations, but as these progressed to become "rice water stools" the bacilli were present in almost pure

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culture; in those patients who recovered, the bacilli gradually disappeared from the stools. Though, he added, it would have been desirable to reproduce the disease in animals, this had proved impossible. All the evidence suggested that, as with typhoid and leprosy, animals were not susceptible to the disease, and naturally infected animals were not to be found even in areas where cholera was endemic throughout the year.

On 4 March Koch sent his seventh and last dispatch.⁸ Since its arrival in Egypt, the mission had made investigations on a total of 40 patients with cholera and performed necropsies on 52 who had died of the disease. The weather had become "intolerably hot," and there was "no choice but to interrupt the work" and return to Berlin.

The reception of Koch's thesis

At the time when the French and German missions started their work, the nature of cholera had been the subject of national and international polemics for more than half a century. Opinions were sharply divided as to whether the disease was transmissible, directly or indirectly, from person to person or whether it was "purely epidemic," in the sense that it struck large numbers of people simultaneously in the presence of a conjunction of atmospheric, climatic, and telluric conditions and of insalubrious wastes. At four international sanitary conferences convened expressly to formulate uniform maritime quarantine regulations, no agreement had been possible, though in 1874 the 21 governments represented at the fourth of these conferences voted unanimously that "the ambient air is the principal vehicle of the generative agent of cholera."^{9 11}

Against this background of longstanding and sharply divided differences of opinion, and an almost mystical conception of cholera in many quarters, it was unlikely that any simple explanation of its aetiology would gain universal acceptance. Nevertheless, on their return to Berlin on 2 May members of the commission were treated as national heroes, Koch receiving from the Crown Prince the Order of the Throne (Second Class) with Star, and from the *Reichsgesundheitsamt* a life size bust of the Kaiser.¹⁰

On 26 July 1884 a "Conference for the discussion of the cholera question" opened in Berlin and was attended by a brilliant gathering of German medical scientists.¹¹ A notable absentee was Max von Pettenkofer, who for 30 years had been promoting his bizarre "ground water" theory of cholera involving three factors that he denominated x, y, and z. He had been chairman of the former Imperial Cholera Commission, and for his many admirers throughout the world was the greatest of all experts on the disease. For him, Koch must have represented a threat to the complex theoretical edifice that he had constructed over much of a lifetime. Pettenkofer's absence was all the more conspicuous in that Koch and his colleagues had broken their journey back to Berlin to pay a courtesy call on him at Munich.

At the conference Koch was the principal speaker, and he outlined the work of the German mission, of which he was to publish, with Gaffky, the definitive account three years later.¹² In the discussion Rudolf Virchow sounded a note of caution by pointing out that absolute proof of Koch's thesis was still lacking. As to the dynamics of the disease, Koch erroneously concluded that the cholera toxin not only acted on the intestinal epithelium but also exerted a paralytic action on the cardiovascular system.

In Germany the response to Koch's thesis was mixed, some supporting it while others—especially Pettenkofer and his followers—regarded it as little short of heresy. In France reactions—doubtless influenced by the conclusions of the French mission to Egypt—were almost entirely negative, a leading article in one medical journal declaring: "The great microbe hunter has followed a completely false trail. (Will he give back his decorations?)"¹³ But the most emphatic rejection came from Britain. On 6 August 1884 a British mission consisting of Emanuel Klein, Heneage Gibbes, and a technician sailed for Calcutta to check Koch's findings.¹⁴ In their report they referred to

Pettenkofer as "justly to be considered the greatest living authority on cholera" and not only flatly repudiated Koch's thesis but also dismissed the role of drinking water. To consider the report the Secretary of State for India appointed a committee of 13 distinguished physicians, eight of whom submitted memorandums endorsing the conclusions of Klein and Gibbes.¹⁵ One member, Sir William Gull, declared his conviction that "cholera as cholera does not produce cholera." Another, Sir John Burdon-Sanderson (as he later became), stated in a public lecture that Koch's investigations had been "an unfortunate fiasco."¹⁶

At the sixth international sanitary conference, which opened in Rome in May 1885, and at which 28 governments were represented, the British delegation successfully blocked any "theoretical discussion on the aetiology of cholera," though Koch himself was one of the German delegates.¹⁷

Epilogue

While to Koch must go the credit of having ultimately convinced the world, in the teeth of almost fanatical opposition, of the true aetiology of cholera, he had in fact been anticipated 30 years before by Filippo Pacini of Florence. In 1854 Pacini published a paper on "Microscopical observations and pathological deductions on cholera,"¹⁸ in which he described the "miriadi di vibrioni" seen in cholera and came to the same conclusions as Koch for the same reasons. In a series of publications in 1865, 1866, 1871, 1876, and 1880 he further developed his thesis, correctly describing the disease of cholera, which Koch later misunderstood, as a massive loss of fluid and electrolytes due to a purely local action of the vibrio on the intestinal mucosa, and recommending in extreme cases the intravenous injection of 10 g sodium chloride in a litre of water.

Pacini died in 1883—the year in which Koch's mission sailed for Egypt—his pathbreaking work on cholera, as painstaking as it was conclusive, having been totally ignored. Koch appears to have been entirely unaware of this work.

Posthumous recognition came to Pacini 82 years after his death when the judicial commission of the international committee on bacteriological nomenclature adopted "*Vibrio cholerae* Pacini 1854" as the correct name of the cholera vibrio.¹⁹

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USSR Letter

Mother care for children in hospital

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Few measures of "throughput" in the Soviet health service can be obtained easily, and such published data as exist do not refer to the work of paediatric hospitals and departments. The only available measure of their activity is implied in a set of planning norms for major specialties that were to be implemented during the years 1980-5. For this period the Soviet Health Ministry envisaged a hospital admission rate of 24.2% of the total population each year and, from the fact that the actual rate for 1981 stood at 24.0%, it can be inferred that the norms are being observed.

So far as young patients are concerned the minimum level of hospital activity is suggested by figures for two categories specified in the Health Ministry's document of guidance.¹ Thus there were to be 26.9 admissions per 1000 total population to "children's somatic" departments and 7.5 per 1000 to children's infectious disease beds. (Both targets represent an increase on the admissions recorded for 1970.) Unfortunately, the maximum planned level cannot be established without knowing what additional provision for the age group in question is concealed within the norms for certain other specialties—for example, psychiatry and tuberculosis.

Although these are incomplete and surrogate data, they at least point to a strategy that accords heavy (and increasing) emphasis to the treatment of children in hospital. Such a background lends added importance to a recent article conveying the varying responses of Soviet doctors to the question: Are mothers needed on the ward? The article comprises a review of correspondence received by *Meditsinskaya Gazeta* after its account of how the Penza regional children's hospital established a system whereby mothers could participate in the care of their own—and other people's—children.²

For and against

Most letters endorsed the initiative shown at the hospital in Penza, though, as will be shown later, concern for a child's psychological well being was not the sole consideration. Only one letter contained a statement of unequivocal opposition and that may be said fairly to bristle with prejudice. From three doctors at a children's department in Novorossisk came the

condemnation: "This idea is not only illogical: it is harmful," and even: "what has been thought up in Penza is criminal." According to their perception, mothers in hospital are unauthorised persons who merely distract the staff with idle questions.

As for the trauma of separation from parents, these doctors show a totally dismissive attitude by asserting that: "A child gets accustomed to his new surroundings and becomes attached to the medical staff." In the same vein they comment: "without mothers, children are good as gold" (an obscurantist view also familiar to British pioneers in this subject). Whether justifiably or not they claim that mothers insist on taking children home before they are fit for discharge, and they make the recommendation (bizarre but consistent with their viewpoint) that "it is better to set up closed circuit television so that mothers can observe their children at fixed times."

One of the signatories of this letter was the head of department, who had worked as a paediatrician for 32 years. The next letter to be cited came from a doctor with a record of 50 years' service and is interesting for the light it casts on the progressive practice of an older generation—or more precisely of two revered clinicians, A A Kisel and N I Krasnogorski. Kisel was an advocate of the doctrine that "children are calmer when their parents are present, misbehave less, eat better and get to sleep more quickly in a bed made by mother's hands." Krasnogorski (born in 1882) had apparently pioneered the concept of "duty parents" and recognised the need to provide facilities within his clinic where parents could drink tea, rest, and relax.

Another correspondent identified a pragmatic consideration which, though logically unrelated to the emotional needs of young patients, points to the same conclusion. After paying tribute to the inventiveness and sensitivity of the Penza doctors he refers to misgivings expressed by several colleagues that the scheme could entail additional expenditure. Highlighting the broader implications, however, he notes that financial advantages would accrue if mothers perform the tasks of orderlies and if the children recuperate more rapidly in their presence. For the sake of clarity it should be added that an acute shortage of orderlies (*sanitarki*) is a management problem that most Soviet hospitals have had to cope with over many years.

Some readers raised questions that reflected concern about economic costs external to the health service. The point here is that mothers with jobs—the overwhelming majority of all Russian mothers—would generally require a sickness certificate to validate their absence from work. Possession of a sickness certificate, obviously enough, entitles the mother to social security payments, and they represent a financial burden on the state.